

The Effects of Ultraviolet Filters and Sunscreen on Corals and Aquatic Ecosystems

Bibliography

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Background & Scope

The NOAA Coral Reef Conservation Program (CRCP) is in the process of evaluating research pertaining to coral reef health, especially as concerned with ultraviolet (UV) filters in sunscreen. To that end, the NOAA Central Library reviewed and reorganized an existing EndNote library on the topic that was compiled by Cheryl Woodley of the CRCP. The NOAA Central Library also conducted a literature search to identify any material that might be missing from the EndNote library. This bibliography is the result of the Library's reorganization and literature search from the original EndNote library.

Section I – Corals and UV Filters

This section includes literature that directly studies the impacts of UV filters on corals.

Section II – Endocrine Disruption/Toxicology of Coral Reef Associated Organisms

This section includes literature that directly studies the endocrine disruption and toxicology effects of UV filters on coral reef associated aquatic organisms found within the marine environment. Laboratory studies on endocrine disruption and toxicology of UV filters are included in Section V.

Section III – Environmental Fate and Life Cycle of UV Filters in Marine Environments

This section includes literature on the environmental fate of UV filters in the marine environment, specifically the chemical life cycle of the filters through degradation. This section includes laboratory studies as well as studies within the environment.

Section IV – Concentrations of UV Filters in Marine Environments

This section includes literature on the measured environmental concentrations of UV filters in marine environments, including but not limited to coral reef ecosystems.

Section V – Laboratory Studies on the Toxicity and Endocrine Disruption Effects of UV Filters

This section includes literature on the toxicity and endocrine disruption effects of UV filters, specifically laboratory studies. The literature here includes studies done on non-aquatic organisms and cell lines, including those done on humans and human cell lines.

Sources Reviewed

The Library consulted the following sources for literature: ScienceDirect, Clarivate Analytics' Web of Science, Google Scholar, EBSCO Academic Search Complete and Environment Complete, Proquest's Aquatic Sciences and Fisheries Abstracts, JSTOR, and BioOne Complete.

Section I: Corals and UV Filters

Corinaldesi, C., Marcellini, F., Nepote, E., Damiani, E., & Danovaro, R. (2018). Impact of Inorganic UV Filters Contained in Sunscreen Products on Tropical Stony Corals (*Acropora* Spp.). *Science of The Total Environment*, 637-638, 1279-1285 <https://doi.org/10.1016/j.scitotenv.2018.05.108>

Most coral reefs worldwide are threatened by natural and anthropogenic impacts. Among them, the release in seawater of sunscreen products commonly used by tourists to protect their skin against the harmful effects of UV radiations, can affect tropical corals causing extensive and rapid bleaching. The use of inorganic (mineral) filters, such as zinc and titanium dioxide (ZnO and TiO₂) is increasing due to their broad UV protection spectrum and their limited penetration into the skin. In the present study, we evaluated through laboratory experiments, the impact on the corals *Acropora* spp. of uncoated ZnO nanoparticles and two modified forms of TiO₂ (Eusolex(R)T2000 and Optisol), largely utilized in commercial sunscreens together with organic filters. Our results demonstrate that uncoated ZnO induces a severe and fast coral bleaching due to the alteration of the symbiosis between coral and zooxanthellae. ZnO also directly affects symbiotic dinoflagellates and stimulates microbial enrichment in the seawater surrounding the corals. Conversely, Eusolex(R) T2000 and Optisol caused minimal alterations in the symbiotic interactions and did not cause bleaching, resulting more eco-compatible than ZnO. Due to the vulnerability of coral reefs to anthropogenic impacts and global change, our findings underline the need to accurately evaluate the effect of commercial filters on stony corals to minimize or avoid this additional source of impact to the life and resilience ability of coral reefs.

Danovaro, R., Bongiorno, L., Corinaldesi, C., Giovannelli, D., Damiani, E., Astolfi, P., . . . Pusceddu, A. (2008). Sunscreens Cause Coral Bleaching by Promoting Viral Infections. *Environmental Health Perspectives*, 116(4), 441-447 <https://doi.org/10.1289/ehp.10966>

BACKGROUND: Coral bleaching (i.e., the release of coral symbiotic zooxanthellae) has negative impacts on biodiversity and functioning of reef ecosystems and their production of goods and services. This increasing world-wide phenomenon is associated with temperature anomalies, high irradiance, pollution, and bacterial diseases. Recently, it has been demonstrated that personal care products, including sunscreens, have an impact on aquatic organisms similar to that of other contaminants. **OBJECTIVES:** Our goal was to evaluate the potential impact of sunscreen ingredients on hard corals and their symbiotic algae. **METHODS:** In situ and laboratory experiments were conducted in several tropical regions (the Atlantic, Indian, and Pacific Oceans, and the Red Sea) by supplementing coral branches with aliquots of sunscreens and common ultraviolet filters contained in sunscreen formula. Zooxanthellae were checked for viral infection by epifluorescence and transmission electron microscopy analyses. **RESULTS:** Sunscreens cause the rapid and complete bleaching of hard corals, even at extremely low concentrations. The effect of sunscreens is due to organic ultraviolet filters, which are able to induce the lytic viral cycle in symbiotic zooxanthellae with latent infections. **CONCLUSIONS:** We conclude that sunscreens, by promoting viral infection, potentially play an important role in coral bleaching in areas prone to high levels of recreational use by humans.

Downs, C. A., Kramarsky-Winter, E., Fauth, J., Segal, R., Bronstein, O., Jeger, R., . . . Loya, Y. (2014). Toxicological Effects of the Sunscreen UV Filter, Benzophenone-2, on Planulae and *in Vitro* Cells of the Coral, *Stylophora Pistillata*. *Ecotoxicology*, 23(2), 175-191 <https://doi.org/10.1007/s10646-013-1161-y>

Benzophenone-2 (BP-2) is an additive to personal-care products and commercial solutions that protects against the damaging effects of ultraviolet light. BP-2 is an “emerging contaminant of concern” that is often released as a pollutant through municipal and boat/ship wastewater discharges and landfill leachates, as well as through residential septic fields and unmanaged cesspits. Although BP-2 may be a contaminant on coral reefs, its environmental toxicity to reefs is unknown. This poses a potential management issue, since BP-2 is a known endocrine disruptor as well as a weak genotoxicant. We examined the effects of BP-2 on the larval form (planula) of the coral, *Stylophora pistillata*, as well as its toxicity to in vitro coral cells. BP-2 is a photo-toxicant; adverse effects are exacerbated in the light versus in darkness. Whether in darkness or light, BP-2 induced coral planulae to transform from a motile planktonic state to a deformed, sessile condition. Planulae exhibited an increasing rate of coral bleaching in response to increasing concentrations of BP-2. BP-2 is a genotoxicant to corals, exhibiting a strong positive relationship between DNA-AP lesions and increasing BP-2 concentrations. BP-2 exposure in the light induced extensive necrosis in both the epidermis and gastrodermis. In contrast, BP-2 exposure in darkness induced autophagy and autophagic cell death. The LC50 of BP-2 in the light for an 8 and 24 h exposure was 120 and 165 parts per billion (ppb), respectively. The LC50s for BP-2 in darkness for the same time points were 144 and 548 ppb. Deformity EC20 levels (24 h) were 246 parts per trillion in the light and 9.6 ppb in darkness.

Downs, C. A., Kramarsky-Winter, E., Segal, R., Fauth, J., Knutson, S., Bronstein, O., . . . Loya, Y. (2016). Toxicopathological Effects of the Sunscreen UV Filter, Oxybenzone (Benzophenone-3), on Coral Planulae and Cultured Primary Cells and Its Environmental Contamination in Hawaii and the U.S. Virgin Islands. *Archives of Environmental Contamination & Toxicology*, 70(2), 265-288
<https://doi.org/10.1007/s00244-015-0227-7>

Benzophenone-3 (BP-3; oxybenzone) is an ingredient in sunscreen lotions and personal-care products that protects against the damaging effects of ultraviolet light. Oxybenzone is an emerging contaminant of concern in marine environments-produced by swimmers and municipal, residential, and boat/ship wastewater discharges. We examined the effects of oxybenzone on the larval form (planula) of the coral *Stylophora pistillata*, as well as its toxicity in vitro to coral cells from this and six other coral species. Oxybenzone is a photo-toxicant; adverse effects are exacerbated in the light. Whether in darkness or light, oxybenzone transformed planulae from a motile state to a deformed, sessile condition. Planulae exhibited an increasing rate of coral bleaching in response to increasing concentrations of oxybenzone. Oxybenzone is a genotoxicant to corals, exhibiting a positive relationship between DNA-AP lesions and increasing oxybenzone concentrations. Oxybenzone is a skeletal endocrine disruptor; it induced ossification of the planula, encasing the entire planula in its own skeleton. The LC50 of planulae exposed to oxybenzone in the light for an 8- and 24-h exposure was 3.1 mg/L and 139 microg/L, respectively. The LC50s for oxybenzone in darkness for the same time points were 16.8 mg/L and 779 microg/L. Deformity EC20 levels (24 h) of planulae exposed to oxybenzone were 6.5 microg/L in the light and 10 microg/L in darkness. Coral cell LC50s (4 h, in the light) for 7 different coral species ranges from 8 to 340 microg/L, whereas LC20s (4 h, in the light) for the same species ranges from 0.062 to 8 microg/L. Coral reef contamination of oxybenzone in the U.S. Virgin Islands ranged from 75 microg/L to 1.4 mg/L, whereas Hawaiian sites were contaminated between 0.8 and 19.2 microg/L. Oxybenzone poses a hazard to coral reef conservation and threatens the resiliency of coral reefs to climate change.

Fel, J.-P., Lacherez, C., Bensetra, A., Mezzache, S., Béraud, E., Léonard, M., . . . Ferrier-Pagès, C. (2018). Photochemical Response of the Scleractinian Coral *Stylophora Pistillata* to Some Sunscreen Ingredients. *Coral Reefs*, 38(1), 109-122 <https://doi.org/10.1007/s00338-018-01759-4>

Ultraviolet (UV) filters and preservatives, which are common constituents of sunscreens and other cosmetics, are reported as a threat for coastal coral reef ecosystems; however, few studies have assessed the effects of these compounds on coral health. This study presents the chronic effects (of measured, long-term and low concentrations) of some preservatives (ethylparaben, butylparaben), mineral UV filter (zinc oxide, ZnO) and organic UV filters (terephthalylidene dicamphor sulfonic acid, drometrizole trisiloxane, ethylhexyltriazone, butylmethoxydibenzoylmethane and 2-ethylhexyl 2-cyano-3,3-diphenylacrylate) on the maximal photosynthetic efficiency (Fv/Fm) of the symbionts associated with the scleractinian coral *Stylophora pistillata*. It first shows that for many organic filters, measured concentrations were significantly lower than nominal concentrations, due to the lipophilic nature of the compounds. In addition, the Fv/Fm was more sensitive to ZnO than all other sunscreen ingredients, with exposure to 90 µg L⁻¹ ZnO for 35 d, reducing Fv/Fm by 38% compared with controls. The other UV filters tested showed no adverse effect on coral symbionts or animal tissue up to the concentration corresponding to their water solubility limit (and even above). Similarly, no adverse effect was observed in our conditions with the preservative ethylparaben, but the preservative butylparaben decreased the Fv/Fm by 25% at the highest concentration of 100 µg L⁻¹. None of the sunscreen ingredients were as toxic to corals as the reference pollutants tributyltin, diuron and monuron, which significantly inhibited Fv/Fm at 10, 1 and 0.1 µg L⁻¹, respectively. Overall, this study highlights the need to improve our knowledge on the in situ concentrations of UV filters and preservatives as well as their individual and combined effects on corals.

He, T., Tsui, M. M. P., Tan, C. J., Ma, C. Y., Yiu, S. K. F., Wang, L. H., . . . Murphy, M. B. (2019). Toxicological Effects of Two Organic Ultraviolet Filters and a Related Commercial Sunscreen Product in Adult Corals. *Environmental Pollution*, 245, 462-471
<https://doi.org/10.1016/j.envpol.2018.11.029>

Corals are exposed to organic ultraviolet (UV) filters and other personal care product (PCP) ingredients in the environment, but the toxicities of organic UV filters and their related PCP to corals are not well understood. In this study, 7-day exposures were conducted to evaluate the toxicities and bioaccumulation of two organic UV filters, ethylhexylmethoxy-cinnamate (EHMC; octinoxate) and octocrylene (OC) (single- and combined-chemical tests), and diluted sunscreen wash-off water containing both active ingredients to the adult life stage of two hard coral species, *Seriatopora caliendrum* and *Pocillopora damicornis*. In the single-chemical tests, death (33.3%) and bleaching (83.3%) were only observed in the 1000µg/L EHMC treatment of *S. caliendrum*. In the sunscreen product exposures, 5% sunscreen water (containing 422.34±37.34µg/L of EHMC and 33.50±7.60µg/L of OC at Day 0) caused high mortality in *S. caliendrum* (66.7-83.3%) and *P. damicornis* (33.3-50%), and tissue concentrations were up to 10 times greater than in the single-chemical exposures; co-exposure to EHMC and OC at similar levels to those in the sunscreen product resulted in bioaccumulation similar to the single-chemical tests. These results confirm the bioaccumulation potential of EHMC and OC and show that other ingredients in sunscreen products may increase the bioavailability of active ingredients to corals and exacerbate the toxicity of sunscreen products. Future studies on the toxicities of PCPs to aquatic organisms should not only focus on the toxicities of active ingredients.

He, T., Tsui, M. M. P., Tan, C. J., Ng, K. Y., Guo, F. W., Wang, L. H., . . . Murphy, M. B. (2019). Comparative Toxicities of Four Benzophenone Ultraviolet Filters to Two Life Stages of Two Coral Species. *Science of The Total Environment*, 651(Pt 2), 2391-2399
<https://doi.org/10.1016/j.scitotenv.2018.10.148>

The benzophenone (BP) organic ultraviolet (UV) filters have been measured in seawater at ng/L to mug/L levels, but more data on their effects in non-target marine organisms are needed. Corals can be exposed to BPs due to wastewater discharges and coastal recreational activities. In this study, toxicities and bioaccumulation of BP-1 (2,4-dihydroxybenzophenone), BP-3 (oxybenzone), BP-4 (sulisobenzene) and BP-8 (dioxibenzone) to larvae and adults of two coral species, *Pocillopora damicornis* and *Seriatopora caliendrum*, were assessed at concentrations ranging from 0.1-1000mug/L. BP-1 and BP-8 exposure caused significant settlement failure, bleaching and mortality of *S. caliendrum* larvae [lowest observed effect concentration (LOEC): ≥ 10 mug/L] compared to the other BPs, while none of the tested compounds and concentrations affected *P. damicornis* larvae. Nubbins were more sensitive to BP-3, BP-1 and BP-8 than larvae. Overall, BP-1 and BP-8 were more toxic to the two tested species than BP-3 and BP-4, which matches the relative bioaccumulation potential of the four BPs (BP-8>BP-1 approximately BP-3>BP-4). A conservative risk assessment using the effect concentrations derived from this study showed that BP-3, BP-1 and BP-8 pose high or medium risk to the health of corals in popular recreational areas of Taiwan and Hong Kong. Our study suggests that future ecotoxicological studies of corals should take their sensitivities, life stages and metabolic capacities into consideration.

Jovanovic, B., & Guzman, H. M. (2014). Effects of Titanium Dioxide (TiO₂) Nanoparticles on Caribbean Reef-Building Coral (*Montastraea Faveolata*). *Environmental Toxicology and Chemistry*, 33(6), 1346-1353 <https://doi.org/10.1002/etc.2560>

Increased use of manufactured titanium dioxide nanoparticles (nano-TiO₂) is causing a rise in their concentration in the aquatic environment, including coral reef ecosystems. Caribbean mountainous star coral (*Montastraea faveolata*) has frequently been used as a model species to study gene expression during stress and bleaching events. Specimens of *M. faveolata* were collected in Panama and exposed for 17 d to nano-TiO₂ suspensions (0.1 mg L⁻¹) and 10 mg L⁻¹). Exposure to nano-TiO₂ caused significant zooxanthellae expulsion in all the colonies, without mortality. Induction of the gene for heat-shock protein 70 (HSP70) was observed during an early stage of exposure (day 2), indicating acute stress. However, there was no statistical difference in HSP70 expression on day 7 or 17, indicating possible coral acclimation and recovery from stress. No other genes were significantly upregulated. Inductively coupled plasma mass spectrometry analysis revealed that nano-TiO₂ was predominantly trapped and stored within the posterior layer of the coral fragment (burrowing sponges, bacterial and fungal mats). The bioconcentration factor in the posterior layer was close to 600 after exposure to 10 mg L⁻¹ of nano-TiO₂ for 17 d. The transient increase in HSP70, expulsion of zooxanthellae, and bioaccumulation of nano-TiO₂ in the microflora of the coral colony indicate the potential of such exposure to induce stress and possibly contribute to an overall decrease in coral populations.

Kung, T. A., Lee, S. H., Yang, T. C., & Wang, W. H. (2018). Survey of Selected Personal Care Products in Surface Water of Coral Reefs in Kenting National Park, Taiwan. *Science of The Total Environment*, 635, 1302-1307 <https://doi.org/10.1016/j.scitotenv.2018.04.115>

Kenting National Park (KNP) located in the Hengchun Peninsula in southern Taiwan is a popular tourist spot, annually attracting millions of visitors, who engage in water sport and amusement activities. In this region, sewage is directly discharged into the marine environment. In this study, the concentrations of five organic UV filters [benzophenone (BP), 2,4-dihydroxy benzophenone (BP-1), 2-hydroxy-4-methoxy benzophenone (BP-3), 2,2'-dihydroxy-4-methoxy benzophenone (BP-8), and 4-methylbenzylidene camphor], five preservatives [methylparaben (MeP), ethylparaben, propylparaben (PrP), butylparaben, and benzylparaben], one disinfectant [triclosan (TCS)], and twenty-four detergent derivatives

[nonylphenol (NP), nonylphenol ethoxylates (NP2EO-NP12EO), octylphenol (OP) and octylphenol ethoxylates OP2EO-OP12EO] were detected in seawater and river water samples collected from eight beaches in KNP and two major river estuaries in the Hengchun Peninsula. BP-3 was detected at all sampling sites and was higher in concentration than the other organic UV filters. The highest concentration of BP-3 was 1233ng/L collected from Wanlitong Beach. MeP and PrP were the main preservative components in seawater. The highest total content of preservative agents was 164ng/L collected from Houwan Beach. Moreover, NP was detected at all sampling sites, with the highest concentration found at Sail Rock Beach (26.5ng/L). The highest concentration of OP was 113ng/L in the Boli River estuary. The widespread use of personal care products (PCPs) has resulted in the release of their major ingredients into natural ecosystems. Therefore, the potential long-term effects of multi-PCPs at low concentration exposure to on the coral reef ecosystem in KNP must be considered and monitored.

Raffa, R. B., Pergolizzi, J. V., Jr., Taylor, R., Jr., Kitzen, J. M., & Group, N. R. (2019). Sunscreen Bans: Coral Reefs and Skin Cancer. *Journal of Clinical Pharmacy and Therapeutics*, 44(1), 134-139
<https://doi.org/10.1111/jcpt.12778>

WHAT IS KNOWN AND OBJECTIVE: Hawaii will ban two major ingredients of sunscreens. This article reviews the reasons and future directions. Hawaii recently enacted legislation that will ban the use of two major ingredients of the majority of commonly used sunscreens. The reason for the ban is the ingredients' putative deleterious impact on marine ecosystems, particularly coral reefs. But sunscreens also save lives by decreasing the risk of UV-induced skin cancers. We review both sides of the issue and potential implications for the healthcare system. COMMENT: Coral reefs consist of organisms in delicate equilibria that are susceptible to small changes in their surroundings. Recent natural and man-made disruptions, direct or indirect, such as changes in ocean temperature and chemistry, ingress of invasive species, pathogens, pollution and deleterious fishing practices, have been blamed for the poor health, or even the outright destruction, of some coral reefs. The most popular sunscreen products contain two ingredients-oxybenzone and octinoxate-that have also been implicated in coral toxicity and will be banned. This creates a healthcare dilemma: Will the protection of coral reefs result in an increase in human skin cancers? WHAT IS NEW AND CONCLUSION: Concentration estimates and mechanism studies support an association-direct or indirect (via promotion of viral infection)-of sunscreens with bleaching of coral reefs. A ban on the two most common sunscreen ingredients goes into effect in Hawaii on January 1, 2021. Proponents suggest that this is a trend, just the first of many such bans worldwide; opponents warn of a dire increase in human skin cancers. As a result, alternative sunscreen compounds are being sought.

Stien, D., Clergeaud, F., Rodrigues, A. M. S., Lebaron, K., Pillot, R., Romans, P., . . . Lebaron, P. (2018). Metabolomics Reveal That Octocrylene Accumulates in Pocillopora Damicornis Tissues as Fatty Acid Conjugates and Triggers Coral Cell Mitochondrial Dysfunction. *Analytical Chemistry*
<https://doi.org/10.1021/acs.analchem.8b04187>

Octocrylene (OC) is an ingredient used in many sunscreens and cosmetics worldwide. Our group evaluated the toxicity of OC in corals. Adult Pocillopora damicornis coral was treated with OC at concentrations of 5, 50, 300 and 1000 microg/L. Most polyps were closed at concentrations of 300 microg/L and higher. Further, metabolomic profiling provided crucial information regarding OC accumulation in coral tissues and OC toxicity. First, we demonstrated that OC was transformed into fatty acid conjugates via oxidation of the ethylhexyl chain, yielding very lipophilic OC analogs that accumulate

in coral tissues. Second, the differential analysis of coral profiles revealed higher levels of 15 acylcarnitines, suggesting abnormal fatty-acid metabolism related to mitochondrial dysfunction. The formation of OC analogs suggests that OC concentrations measured in the environment and organisms may have been largely underestimated. Overall, these results call for an in-depth evaluation of OC toxicity and the reevaluation of the actual OC accumulation rate in the ocean's food chain, including OC-fatty acid conjugates.

Tang, C. H., Lin, C. Y., Lee, S. H., & Wang, W. H. (2017). Membrane Lipid Profiles of Coral Responded to Zinc Oxide Nanoparticle-Induced Perturbations on the Cellular Membrane. *Aquatic Toxicology*, 187, 72-81 <https://doi.org/10.1016/j.aquatox.2017.03.021>

Zinc oxide nanoparticles (nZnOs) released from popular sunscreens used during marine recreation apparently endanger corals; however, the known biological effects are very limited. Membrane lipids constitute the basic structural element to create cell a dynamic structure according to the circumstance. Nano-specific effects have been shown to mechanically perturb the physical state of the lipid membrane, and the cells accommodating the actions of nZnOs can be involved in the alteration of the membrane lipid composition. To gain insight into the effects of nanoparticles on coral, glycerophosphocholine (GPC) profiling of the coral *Seriatopora caliendrum* exposed to nZnOs was performed in this study. Increasing lyso-GPCs, docosapentaenoic acid-possessing GPCs and docosahexaenoic acid-possessing GPCs and decreasing arachidonic acid-possessing GPCs were the predominant changes responded to nZnO exposure in the coral. A backfilling of polyunsaturated plasmalyncholines was observed in the coral exposed to nZnO levels over a threshold. These changes can be logically interpreted as an accommodation to nZnOs-induced mechanical disturbances in the cellular membrane based on the biophysical properties of the lipids. Moreover, the coral demonstrated a difference in the changes in lipid profiles between intra-colonial functionally differentiated polyps, indicating an initial membrane composition-dependent response. Based on the physicochemical properties and physiological functions of these changed lipids, some chronic biological effects can be incubated once the coral receives long-term exposure to nZnOs.

Tashiro, Y., & Kameda, Y. (2013). Concentration of Organic Sun-Blocking Agents in Seawater of Beaches and Coral Reefs of Okinawa Island, Japan. *Marine Pollution Bulletin*, 77(1–2), 333-340 <https://doi.org/10.1016/j.marpolbul.2013.09.013>

The concentration of UV filters (UVFs) and UV light stabilizers (UVLSs) were measured in seawater and river water collected from sites at four beaches, two reefs, and one river on Okinawa Island, Japan. UVFs and/or UVLSs of 8–10 types were detected in beaches samples and 6–9 types were detected in reef samples. The total UVF concentrations at the beach sites were highest either in July or August with a maximum of 1.4 $\mu\text{g L}^{-1}$. The concentrations at the reef sites did not show peaks in summer and the maximum values were close to 10 ng L^{-1} . The detected UVF profiles reflected the ingredients of sunscreens used in each region. The highest UVLS concentrations at the reefs were observed not only in summer but also in June and September. The UVLS concentrations at the reefs were similar to or even higher than that at the beaches or in the river.

Tsui, M. M. P., Lam, J. C. W., Ng, T. Y., Ang, P. O., Murphy, M. B., & Lam, P. K. S. (2017). Occurrence, Distribution, and Fate of Organic UV Filters in Coral Communities. *Environmental Science and Technology*, 51(8), 4182-4190 <https://doi.org/10.1021/acs.est.6b05211>

Organic ultraviolet (UV) filters are widely used in personal care products and occur ubiquitously in the aquatic environment. In this study, concentrations of seven commonly used organic UV filters were determined in seawater, sediment and five coral species collected from the eastern Pearl River Estuary of South China Sea. Five compounds, benzophenone-1, -3, and -8 (BP-1, -3, and -8), octocrylene (OC) and octyl dimethyl-p-aminobenzoic acid (ODPABA), were detected in the coral tissues with the highest detection frequencies (>65%) and concentrations (31.8 +/- 8.6 and 24.7 +/- 10.6 ng/g ww, respectively) found for BP-3 and BP-8. Significantly higher concentrations of BP-3 were observed in coral tissues in the wet season, indicating that higher inputs of sunscreen agents could be attributed to the increased coastal recreational activities. Accumulation of UV filters was only observed in soft coral tissues with bioaccumulation factors (log₁₀-values) ranging from 2.21 to 3.01. The results of a preliminary risk assessment indicated that over 20% of coral samples from the study sites contained BP-3 concentrations exceeding the threshold values for causing larval deformities and mortality in the worst-case scenario. Higher probabilities of negative impacts of BP-3 on coral communities are predicted to occur in wet season.

Wood, E. (2018). *Impacts of Sunscreens on Corals*. International Coral Reef Initiative (ICRI) April 30, 2019. Retrieved from <https://www.icriforum.org/icri-documents/icri-publications-reports-and-posters/impacts-sunscreens-coral-reefs>

There is intense concern about the future health and ecological integrity of coral reefs in the face of global climate change. This is considered to be one of the greatest threats to reefs worldwide and is causing coral bleaching and ecosystem change at unprecedented levels. Coral reefs are also under considerable stress from overfishing, destructive fishing, coastal development and pollution. There is universal agreement that coral reefs face an unpredictable future and that action needs to be taken at all levels if their integrity and values are to be maintained. In recent years, a number of studies have shown that sunscreens and other cosmetic products contain chemical substances that are adding to the pollution burden faced by coral reefs. Exposure to ultraviolet (UV) solar radiation poses a threat to public health, including the risk of sunburn, photo-aging and skin cancer (Pathak, 1987), and growing concern about these harmful effects has led to an increase in use of sunscreens. The world's coastal population and coastal tourism are expected to grow during this century and it is anticipated that the use of sunscreens and cosmetics containing UV-filters will rise further. Given the status of reefs, it is essential that the impact of sunscreens on corals is assessed and addressed.

Section II: Endocrine Disruption/Toxicology of Coral Reef Associated Organisms

Abd El-Atti, M., Desouky, M. M. A., Mohamadien, A., & Said, R. M. (2019). Effects of Titanium Dioxide Nanoparticles on Red Swamp Crayfish, *Procambarus Clarkii*: Bioaccumulation, Oxidative Stress and Histopathological Biomarkers. *The Egyptian Journal of Aquatic Research*, 45(1), 11-18
<https://doi.org/10.1016/j.ejar.2019.01.001>

The widespread use of titanium dioxide nanoparticles (TiO₂ NPs) in many applications has led to its significant release to aquatic systems. Hence, the present study was performed to evaluate effects of TiO₂ NPs on crayfish *Procambarus clarkii*, which is often used as a bioindicator of water pollution. Adult male specimens were treated with 25, 125, and 250 mg/l of TiO₂ NPs for 28 days. Mortalities were 0, 3.3, and 10% for animals treated with 25, 125, and 250 mg/l of TiO₂ NPs, respectively. The level of titanium bioaccumulation in different tissues was as follows, gills > hepatopancreas > green

glands > muscles. TiO₂ NPs-exposed crayfish showed significant increase in the levels of catalase, glutathione-S-transferase, glutathione peroxidase, gamma-glutamyl transferase, glutathione, and metallothioneins in the hepatopancreas. Exposure of the crayfish to 250 mg/l TiO₂ NPs caused severe histopathological alterations. In the hepatopancreas, the most prominent pathological changes were tubular disruption and inflammatory infiltration. Under transmission electron microscope (TEM), ruptured microvilli, deformed mitochondria and fragmentation of rough endoplasmic reticulum (RER) were observed. In the gills, swelling of gill lamellae, disorganization and degeneration of epithelial cells were noted under the light microscope (LM). Under electron microscope (EM), gills of crayfish treated with 250 mg/l TiO₂ NPs showed vacuolation, dense granules, and diminution in the number of apical plasma membrane infoldings. In conclusion, TiO₂ NPs caused alteration in antioxidant activities and severe histopathological changes.

Alonso, M. B., Feo, M. L., Corcellas, C., Gago-Ferrero, P., Bertozzi, C. P., Marigo, J., . . . Barcelo, D. (2015). Toxic Heritage: Maternal Transfer of Pyrethroid Insecticides and Sunscreen Agents in Dolphins from Brazil. *Environmental Pollution*, 207, 391-402
<https://doi.org/10.1016/j.envpol.2015.09.039>

Pyrethroids (PYR) and UV filters (UVF) were investigated in tissues of paired mother-fetus dolphins from Brazilian coast in order to investigate the possibility of maternal transfer of these emerging contaminants. Comparison of PYR and UVF concentrations in maternal and fetal blubber revealed Franciscana transferred efficiently both contaminants to fetuses (F/M > 1) and Guiana dolphin transferred efficiently PYR to fetuses (F/M > 1) different than UVF (F/M < 1). PYR and UVF concentrations in fetuses were the highest-ever reported in biota (up to 6640 and 11,530 ng/g lw, respectively). Muscle was the organ with the highest PYR and UVF concentrations (p < 0.001), suggesting that these two classes of emerging contaminants may have more affinity for proteins than for lipids. The high PYR and UVF concentrations found in fetuses demonstrate these compounds are efficiently transferred through placenta. This study is the first to report maternal transfer of pyrethroids and UV filters in marine mammals.

Araujo, M. J., Rocha, R. J. M., Soares, A., Benede, J. L., Chisvert, A., & Monteiro, M. S. (2018). Effects of UV Filter 4-Methylbenzylidene Camphor During Early Development of Solea Senegalensis Kaup, 1858. *Science of The Total Environment*, 628-629, 1395-1404
<https://doi.org/10.1016/j.scitotenv.2018.02.112>

The inclusion of organic UV filters in personal care products (PCPs) has increased in recent years. 4-Methylbenzylidene camphor (4MBC) is one of the most used UV filters, and thus it is commonly found in aquatic ecosystems, with proved negative effects on aquatic organisms. Effects on early life stages of marine vertebrates are largely unknown. Therefore, the main goal of this work was to evaluate 4MBC effects on Senegalese sole (*Solea Senegalensis* Kaup, 1858) larvae at different levels of biological organization. *S. senegalensis* were exposed to increasing concentrations of 4MBC from egg stage until 96h. Mortality, growth, malformations, behaviour and biochemical responses, including enzymatic biomarkers were studied. The exposure to 4MBC until 96h post-fertilization (hpf) induced mortality and malformations in a dose-response manner. Besides, reduced growth with increasing concentrations was observed. The exposure to 4MBC also caused alterations on behaviour, including overall lower swimming time during light and dark periods. Biomarker alterations caused by 4MBC included imbalance of neurotransmission related endpoints (increased acetylcholinesterase activity) and decreased activity of enzymes related to anaerobic metabolism (lower cellular lactate dehydrogenase activity) at the lower

concentrations tested. Furthermore, our results suggest that 4MBC do not induce oxidative stress in *S. senegalensis* larvae, since catalase and lipid peroxidation levels were not significantly altered by 4MBC. *S. senegalensis* revealed to be a good model species for vertebrate animal testing in the marine environment. Sub-lethal concentrations of 4MBC induced toxic effects at all organizational levels. Swimming behaviour was a sensitive endpoint and showed that exposure to 4MBC causes impairment on response to light stimulus which is possibly linked with the observed imbalances on cholinesterase activity in larvae. Conservation concerns along distribution range of *S. senegalensis* should consider that increasing levels of UV filters in marine environment might have impact on the ecology of the species.

Atobiolye, S. O. (2019). *Determination of Contaminants of Emerging Concern: Oxybenzone, Flofibrate, and Sulfamethoxazole in Water, Sediment, and Fish from the Galveston/Clear Creek Areas*. (Master of Science), Texas Southern University, Retrieved from [no URL available]

Environmental Chemical contaminants have been of major concern. These contaminants can cause serious health effects in single or multiple forms. As a result, several of the chemicals have been banned, but are still present in trace amounts in the environment. They are resistant to degradation and are persistent in the environment for years. The contaminants are variously derived from different activities and include pesticides, additives, surfactants, personal care products, pharmaceuticals, and byproducts of various industrial processes. They are also known as contaminants of emerging concern (CEC) as they are being detected in the environment at very low concentrations. They are of growing concern because of the possibilities of their interacting with biological systems in multiple forms and multiple pathways at molecular levels to cause toxicity. They are continuously being used and released intentionally or accidentally into the environmental media, thereby finding their ways into waterbodies and food sources. Galveston Bay and Clear Creek receive waters from residential areas, shopping complexes, industrial complexes, and parks. Based on the facts that these waters are a collection of runoffs from several sources, it is envisaged that CEC are present in significant amount and with a high possibility for human exposure to these contaminants. In addition, various pharmaceuticals and personal care products from the wastewater treatment plants, runoffs, and beach users' bodies will be present in these waters. There is, therefore, a high possibility and potential for adverse effect at the concentrations (though low) and following interactions with other chemicals present. The effects of these contaminants on humans, human environment, and the ecosystem can range from acute chronic and are of significant importance. This research determined the presence of selected chemicals of concern: oxybenzone, sulfamethoxazole, and clofibrate in the water, sediment, and fish samples from the Galveston Bay and Clear Creek areas. The study also evaluated the accumulation of these contaminants in fish relative to the concentrations in sediment and water. The samples were subjected to liquid-liquid and solid-liquid extraction methods following standard protocols. Apart from the water and sediment samples, tissues from different organs of the fish were subjected to the extraction process. The samples were analyzed using HPLC/UV-Vis with amended EPA conditions. The results of this study show that oxybenzone and clofibrate are present at different concentrations in samples from different locations analyzed. Results indicated a possible build-up of these chemicals in large bodies of water that receive water from different sources. The average concentration of oxybenzone in water and sediment samples are 1.85 ± 0.82 and 1.30 ± 1.55 ppm respectively. Oxybenzone was detected at an average of 38.49 ± 14.64 ppm in the fish tissues/organs, this concentration is approximately 2,081% and 2,961% of its concentration in the water and sediment samples respectively. Mean concentration of Clofibrate of 0.45 ± 0.31 and 2.28 ± 3.76 ppm were detected in the water and sediment samples respectively. The mean concentration of clofibrate of 7.76 ± 2.46 ppm found in the fish tissues/organs, on the other hand, is approximately 17 and 3 times greater than the levels in water and sediment respectively. Sulfamethoxazole was below detection limits, as such, it was not found in the samples. In conclusion, the results revealed that

oxybenzone and clofibrate are present in the environment and they accumulate more in fish tissues/organs. Therefore, high consumption of certain types of fish and/or other seafood sources could lead to the accumulation of these chemicals in the body. This may possibly lead to some deleterious processes or toxicity. The data from this research is an impetus for the continuous monitoring of the levels of CEC/PPCPs in the Galveston/Clear Creek areas bodies of water and the aquatic environment.

Balmer, M. E., Buser, H.-R., Müller, M. D., & Poiger, T. (2005). Occurrence of Some Organic UV Filters in Wastewater, in Surface Waters, and in Fish from Swiss Lakes. *Environmental Science & Technology*, 39(4), 953-962 <https://doi.org/10.1021/es040055r>

Organic UV filters are used in personal care products such as sunscreen products, and in cosmetics, beauty creams, skin lotions, lipsticks, hair sprays, hair dyes, shampoos, and so forth. The compounds enter the aquatic environment from showering, wash-off, washing (laundering), and so forth via wastewater treatment plants (WWTPs) ("indirect inputs") and from recreational activities such as swimming and bathing in lakes and rivers ("direct inputs"). In this study, we investigated the occurrence of four important organic UV filter compounds (benzophenone-3, BP-3; 4-methylbenzylidene camphor, 4-MBC; ethylhexyl methoxy cinnamate, EHMC; octocrylene, OC) in wastewater, and in water and fish from various Swiss lakes, using gas chromatographic/mass spectrometric analyses. All four UV filters were present in untreated wastewater (WWTP influent) with a maximum concentration of 19 µg L⁻¹ for EHMC. The data indicate a seasonal variation with influent loads higher in the warmer season (June 2002) than in the colder one (April 2002). The influent loads were in the order EHMC > 4-MBC ~ BP-3 > OC. The concentrations in treated wastewater (WWTP effluent) were considerably lower, indicating substantial elimination in the plants. 4-MBC was usually the most prevalent compound (maximum concentration, 2.7 µg L⁻¹), followed by BP-3, EHMC, and OC. UV filters were also detected in Swiss midland lakes and a river (Limmat) receiving inputs from WWTPs and recreational activities. However, all concentrations were low (<2–35 ng L⁻¹); no UV filters (<2 ng L⁻¹) were detected in a remote mountain lake. Data from passive sampling using semipermeable membrane devices (SPMDs) supported the presence of these UV filters in the lakes and the river and suggested some potential for accumulation of these compounds in biota. SPMD-derived water concentrations increased in the order Greifensee < Zürichsee < Hüttnersee. This order is reversed from that observed for methyl triclosan, used as a chemical marker for WWTP-derived lipophilic contaminants in the lakes. This indicated inputs of UV filters from sources other than WWTPs to the lakes during summer, for example, inputs from recreational activities. Fish (white fish, *Coregonus* sp.; roach, *Rutilus rutilus*; perch, *Perca fluviatilis*) from these lakes contained low but detectable concentrations of UV filters, in particular, 4-MBC (up to 166 ng g⁻¹ on a lipid basis). 4-MBC concentrations relative to methyl triclosan were lower in fish than in SPMDs exposed in the same lakes, suggesting that 4-MBC is less bioaccumulated than expected or metabolized in fish. The lipid-based bioconcentration factor (BCFL) estimated from the fish (roach) data and SPMD-derived water concentrations was about 1–2.3 × 10⁴ and thus approximately 1 order of magnitude lower than expected from its Kow value.

Barmo, C., Ciacci, C., Canonico, B., Fabbri, R., Cortese, K., Balbi, T., . . . Canesi, L. (2013). In Vivo Effects of N-TiO₂ on Digestive Gland and Immune Function of the Marine Bivalve *Mytilus Galloprovincialis*. *Aquatic Toxicology*, 132-133, 9-18 <https://doi.org/10.1016/j.aquatox.2013.01.014>

Due to the increasing production of nanoparticles (NPs) and their potential release in the aquatic environment, evaluation of their biological impact on aquatic organisms represents a major concern. Suspension feeding invertebrates, in particular bivalve mollusks, may play a role in NP biotransformation

and transfer through food webs and may represent a significant target for NP toxicity. In this work, the in vivo effects of titanium dioxide (n-TiO₂), one of the most widespread NPs in use, were investigated in the bivalve *Mytilus galloprovincialis*, largely utilised as a sentinel for marine contamination. Mussels were exposed for 96h to different concentrations of n-TiO₂ suspensions (1, 10 and 100µgL⁻¹) and multiple responses were evaluated in the digestive gland and immune cells, the haemocytes. In the digestive gland, n-TiO₂ affected lysosomal and oxidative stress biomarkers and decreased transcription of antioxidant and immune-related genes. In the haemocytes, n-TiO₂ decreased lysosomal membrane stability-LMS and phagocytosis, increased oxyradical production and transcription of antimicrobial peptides; moreover, pre-apoptotic processes were observed. The effects of n-TiO₂ on digestive gland and haemocytes were distinct, also depending on the endpoint and on nominal NP concentrations, with many significant responses elicited by the lowest concentrations tested. The results show that n-TiO₂, at concentrations close to predicted environmental levels, significantly affected different functional and molecular parameters of mussel digestive gland and immune cells. In particular, the observed changes in immune parameters that represent significant biomarkers of exposure at the organism level suggest that exposure to n-TiO₂ may pose a serious risk to mussel health.

Barone, A. N., Hayes, C. E., Kerr, J. J., Lee, R. C., & Flaherty, D. B. (2019). Acute Toxicity Testing of TiO₂-Based Vs. Oxybenzone-Based Sunscreens on Clownfish (*Amphiprion Ocellaris*). *Environmental Science and Pollution Research* <https://doi.org/10.1007/s11356-019-04769-z>

Given the prevalence of skin cancer, sunscreens are recommended by dermatologists including the American Academy of Dermatology to protect skin from harmful ultraviolet rays. Unfortunately, this leads to an estimated 14,000 tons of sunscreen entering waterways each year. Many of the chemicals in sunscreens, such as oxybenzone and benzophenone-2, are indicated to have adverse effects on corals and other aquatic life. As an eco-conscious alternative, physical barrier sunscreens, such as non-nano-titanium dioxide (TiO₂), have been suggested as a replacement. This study examines the impact of a non-nano-TiO₂-based sunscreen over a nationally sold brand of sunscreen containing oxybenzone, on clownfish (*Amphiprion ocellaris*). Animals were evaluated for mortality, swimming behavior, and feeding behavior. Our data indicate that at an exposure level of 100 mg/L oxybenzone-containing sunscreen had a negative impact on mortality, leading to 25% death by the end of the 97-h testing period. Negative impacts on behavior were even more dramatic for the 100 mg/L oxybenzone-containing sunscreen, with 100% of the animals failing to feed over the first 49 h of testing and 100% of animals demonstrating abnormal swimming behavior over the entire testing period. By comparison, the non-nano-(TiO₂) sunscreen at 100 mg/L had little (6.7%) negative impact on mortality and feeding. While swimming behavior was disrupted during the first 25 h of testing (26.7% abnormal movement), animals recovered well over the remainder of the testing period (out to 97 h).

Bell, L. J., Ucharm, G., Patris, S., Diaz-Cruz, M. S., Roig, M. P. S., & Dawson, M. N. (2017). *Sunscreen Pollution Analysis in Jellyfish Lake Coral Reef Research Foundation Palau*. Coral Reef Research Foundation. Retrieved from <https://coralreefpalau.org/wp-content/uploads/2017/10/CRRF-UNESCO-Sunscreen-in-Jellyfish-Lake-no.2732.pdf>

Jellyfish Lake in Palau is part of the Koror State Rock Island Southern Lagoon (RISL), a UNESCO World Heritage site and is famous for its Golden Jellyfish population. Palau has seen a dramatic increase in its visitors, now over 100,000 per year, and most of those visit Jellyfish Lake, causing concern for the continued health of the lake. Our preliminary sampling for sunscreen chemicals in 2014 indicated the presence of oxybenzone (BP-3), a compound that is extremely common in personal care products,

including sunscreens. The present study builds on those results, using more rigorous sampling and analytical methods to look for sunscreen products in water, sediment and jellyfish samples in Jellyfish Lake (tourism site) and three other sites (non-tourism) for comparison. Our results showed that sunscreen compounds or their transformation products (such as metabolites) are wide spread in Jellyfish Lake. They were also present in the sites presumed to be 'pristine' with little human use. In general, water samples had low levels of sunscreen compounds, while jellyfish tissues and sediment had relatively higher levels of these compounds and metabolites. This is an indication of bioaccumulation of these chemicals. Comparing different lakes and ocean/lagoon sites, Jellyfish Lake had the highest levels of sunscreen compound concentrations. The levels of sunscreen compounds and their metabolites in Jellyfish Lake indicates that: 1) personal care product pollution is entering the environment through tourist use, i.e. sunscreen washing off, and 2) jellyfish are absorbing and metabolizing BP3. Compounds were also detected in Ngermeuangel Lake, i.e. what should have been a control and uncontaminated lake. These may be from effluent/sewer leaking from the nearby population center into the adjacent watersheds, indicating that there are more widespread issues with marine pollution from different sources. The Golden Jellyfish medusa stage is relatively short lived, with a life span of about 6 months. The presence of sunscreen chemicals in the medusae and their presence in the sediment in Jellyfish Lake and other marine lakes is cause for concern. The medusae stage may not live long enough to be directly affected, but their benthic polyp stage, critical to their life cycle, could be. We feel in the short term the known presence of UV filters should be addressed in a practical manner to try to stabilize their levels in Jellyfish Lake and minimize additions of them to the system.

Chen, T. H., Chou, S. M., Tang, C. H., Chen, C. Y., Meng, P. J., Ko, F. C., & Cheng, J. O. (2016). Endocrine Disrupting Effects of Domestic Wastewater on Reproduction, Sexual Behavior, and Gene Expression in the Brackish Medaka *Oryzias Melastigma*. *Chemosphere*, 150, 566-575
<https://doi.org/10.1016/j.chemosphere.2016.02.057>

The objective of this study was to investigate the endocrine disrupting effects of domestic wastewater on fish using the brackish medaka *Oryzias melastigma* as the animal model. Estuarine water samples were collected from Sihchong Creek and Baoli Creek estuaries, Taiwan, in March of 2012 to assess the whole effluent toxicity (WET) of domestic wastewater produced by the local residents and tourists. Chemical analysis detected various pharmaceuticals and personal care products (PPCPs) in the field water samples. Some of these PPCPs are endocrine disrupting chemicals. In the laboratory-based bioassay, breeding pairs were exposed to the water samples (Sihchong, Baoli, and control) for 21 days. Cumulative number of eggs spawned was significantly higher in the Sihchong group. While fish swimming activity was not affected, sexual behavior of the male fish was significantly induced in both Sihchong and Baoli groups. Male and female gonad histology was not affected. Expression level of biomarker genes CYP1A1, HSP70, and VTG was significantly induced in the Sihchong group. This study indicates that the mixture of contaminants contained in the estuarine water may cause endocrine disrupting effects in fish.

Dang, Z., & Kienzler, A. (2019). Changes in Fish Sex Ratio as a Basis for Regulating Endocrine Disruptors. *Environment International*, 130, 104928 <https://doi.org/10.1016/j.envint.2019.104928>

Fish sex ratio (SR) is an endpoint potentially indicating both endocrine activity and adversity, essential elements for identifying Endocrine Disrupting Chemicals (EDCs) as required by the EU regulations. Due to different protocols and methods in the literature studies, SR data vary greatly. This study analyses

literature SR data and discusses important considerations for using SR data in the regulatory context for the hazard identification, classification, PBT (persistent, bioaccumulative and toxic) assessment, testing, and risk assessment. A total number of 106 studies were compiled for SR of zebrafish, medaka and fathead minnow exposed to 84 chemicals or mixtures. About 53% of literature studies determined SR by methods different from the standard histology method, leading to uncertainty of quantifying SR and differential sensitivity. SR was determined after depuration in 40 papers, which may lead to chemical-induced SR changes reversible to the control. SR was responsive to chemicals with EAS (estrogen, androgen, steroidogenesis) activity and also to those with thyroid and progesterone activity. Besides, SR was influenced by non-chemical factors, e.g., inbreeding and temperature, leading to difficulty in data interpretation. The ECHA/EFSA/JRC Guidance suggests that SR and gonad histology data can be used for identifying EDCs. Due to reversibility, influence of confounding factors, and responsiveness to chemicals with endocrine activity other than EAS, this study suggests that SR/gonad histology should be combined with certain mode of action evidence for identifying EDCs. Important considerations for using SR data in the identification, classification, PBT assessment, testing, and risk assessment are discussed.

Díaz-Cruz, M. S., & Barceló, D. (2009). Chemical Analysis and Ecotoxicological Effects of Organic UV-Absorbing Compounds in Aquatic Ecosystems. *TrAC Trends in Analytical Chemistry*, 28(6), 708-717 <https://doi.org/10.1016/j.trac.2009.03.010>

A large number of ultraviolet (UV)-absorbing compounds, usually present in personal-care products, textiles exposed to UV radiation and plastics materials, elicit hormonal activity in vitro and in vivo. Induction of vitellogenin, alterations in gonads, decrease in fertility and reproduction, and feminization in sex characteristics of male fish have been associated with frequently-used UV filters, including benzophenones and camphor-related substances. The lowest effect concentrations determined (3 µg/L for 3-benzylidene camphor) are generally higher than those measured so far in the environment (ng/L to lower µg/L in water). However, the propensity for rapid accumulation and the potential for mixture effects warrant further research to evaluate the fate and the disposition of UV filters in the aquatic ecosystem. Moreover, the amounts of UV filters added to products are increasing, to date usually 10% (w/w), as a consequence of the higher protection factors demanded, and that requires formulations with higher percentages of UV filters or multi-component mixtures with more UV-absorbing substances. In addition, long-term exposure to UV-absorbing compounds may have negative effects at concentrations much lower than those considered at present. This article provides an overview of the most outstanding findings reported on toxic effects of UV filters in the aquatic environment. We also include environmental levels detected and analytical methodologies applied.

Du, Y., Wang, W. Q., Pei, Z. T., Ahmad, F., Xu, R. R., Zhang, Y. M., & Sun, L. W. (2017). Acute Toxicity and Ecological Risk Assessment of Benzophenone-3 (Bp-3) and Benzophenone-4 (Bp-4) in Ultraviolet (UV)-Filters. *International Journal of Environmental Research and Public Health*, 14(11) <https://doi.org/10.3390/ijerph14111414>

Ultraviolet (UV)-absorbing chemicals (UV filters) are used in personal care products for the protection of human skin and hair from damage by UV radiation. Although these substances are released into the environment in the production and consumption processes, little is known about their ecotoxicology effects. The acute toxicity and potential ecological risk of UV filters benzophenone-3 (BP-3) and benzophenone-4 (BP-4) on *Chlorella vulgaris*, *Daphnia magna*, and *Brachydanio rerio* were analyzed in the present study. The EC50 values (96 h) of BP-3 and BP-4 on *C. vulgaris* were 2.98 and 201.00 mg/L, respectively. The 48 h-LC50 of BP-3 and BP-4 on *D. magna* were 1.09 and 47.47 mg/L, respectively. The

96 h-LC50 of BP-3 and BP-4 on *B. rerio* were 3.89 and 633.00 mg/L, respectively. The toxicity of a mixture of BP-3 and BP-4 on *C. vulgaris*, *D. magna*, and *B. rerio* all showed antagonistic effects. The induced predicted no-effect concentrations of BP-3 and BP-4 by the assessment factor method were 1.80×10^{-3} and 0.47 mg/L, respectively, by assessment factor (AF) method, which were both lower than the concentrations detected in the environment at present, verifying that BP-3 and BP-4 remain low-risk chemicals to the aquatic ecosystem.

Fastelli, P., & Renzi, M. (2019). Exposure of Key Marine Species to Sunscreens: Changing Ecotoxicity as a Possible Indirect Effect of Global Warming. *Marine Pollution Bulletin*, 149, 110517
<https://doi.org/10.1016/j.marpolbul.2019.110517>

Sunscreens can induce ecotoxicological effects and may cause significant impacts in the aquatic ecosystem. In spite of that, ecotoxicological responses of key marine species to sunscreens are scarcely studied in Mediterranean ecosystems, and literature data are lacking. Furthermore, changes in water salinity induced by global warming could significantly affect the ecotoxicological responses of marine species exposed to sunscreens. This research focuses on the evaluation of ecotoxicological responses of *Phaeodactylum tricornutum* (algae), *Corophium orientalis* (macroinvertebrate), and *Paracentrotus lividus* (echinoderms) exposed to sunscreens, which include both chemical- and physical-based. This study, also, analyzes the changes in ecotoxicological responses of the tested species linked to increase in salinity. Results showed that salinity stress significantly increases the toxicity of sunscreens on the tested marine species. Physical-based sunscreens resulted in more toxicity at higher salinity than chemical-based ones toward *C. orientalis* and *P. tricornutum*. This study evidenced that risk classifications of sunscreens recorded under standard salinity conditions could be significantly different from that recorded in the natural environment under salinity stress. The collection of a complete dataset on the ecotoxicological effects of sunscreens on marine species tested under salinity stress could be useful to correctly weigh risks for the marine environment under possible future ecological changing scenarios following the global changing driver.

Gadelha, J. R., Rocha, A. C., Camacho, C., Eljarrat, E., Peris, A., Aminot, Y., . . . Almeida, C. M. R. (2019). Persistent and Emerging Pollutants Assessment on Aquaculture Oysters (*Crassostrea Gigas*) from Nw Portuguese Coast (Ria De Aveiro). *Science of The Total Environment*, 666, 731-742
<https://doi.org/10.1016/j.scitotenv.2019.02.280>

The study aim was to determine a range of relevant persistent and emerging pollutants in oysters produced in an aquaculture facility located in an important production area, to assure their safety for human consumption. Pollutants, including 16 PAHs, 3 butyltins (BTs), 29 flame retardants (FRs, including organophosphate and halogenated FRs), 35 pesticides (including 9 pyrethroid insecticides) and 13 personal care products (PCPs, including musks and UV filters), were determined in oysters' tissues collected during one year in four seasonal sampling surveys. The seasonal environmental pollution on the production site was evaluated by water and sediment analysis. Furthermore, oysters' nutritional quality was also assessed and related with the consumption of healthy seafood, showing that oysters are a rich source of protein with low fat content and with a high quality index all year around. Results showed that most analysed pollutants were not detected either in oyster tissues or in environmental matrixes (water and sediments). The few pollutants detected in oyster tissues, including both regulated and non-legislated pollutants, such as a few PAHs (fluorene, phenanthrene, anthracene, fluoranthene, pyrene and indenopyrene), FRs (TPPO, TDCPP, DCP, BDE-47, BDE-209 and Dec 602) and PCPs (galaxolide,

galaxolidone, homosalate and octocrylene), were present at low levels (in the ng/g dw range) and did not represent a significant health risk to humans. The observed seasonal variations related to human activities (e.g. tourism in summer) highlights the need for environmental protection and sustainable resource exploration for safe seafood production.

Gago-Ferrero, P., Alonso, M. B., Bertozzi, C. P., Marigo, J., Barbosa, L., Cremer, M., . . . Barcelo, D. (2013). First Determination of UV Filters in Marine Mammals. Octocrylene Levels in Franciscana Dolphins. *Environmental Science and Technology*, 47(11), 5619-5625
<https://doi.org/10.1021/es400675y>

Most current bioexposure assessments for UV filters focus on contaminants concentrations in fish from river and lake. To date there is not information available on the occurrence of UV filters in marine mammals. This is the first study to investigate the presence of sunscreen agents in tissue liver of Franciscana dolphin (*Pontoporia blainvillei*), a species under special measures for conservation. Fifty six liver tissue samples were taken from dead individuals accidentally caught or found stranded along the Brazilian coastal area (six states). The extensively used octocrylene (2-ethylhexyl-2-cyano-3,3-diphenyl-2-propenoate, OCT) was frequently found in the samples investigated (21 out of 56) at concentrations in the range 89-782 ng.g(-1) lipid weight. Sao Paulo was found to be the most polluted area (70% frequency of detection). Nevertheless, the highest concentration was observed in the dolphins from Rio Grande do Sul (42% frequency of detection within that area). These findings constitute the first data reported on the occurrence of UV filters in marine mammals worldwide.

Gago-Ferrero, P., Diaz-Cruz, M. S., & Barcelo, D. (2012). An Overview of UV-Absorbing Compounds (Organic UV Filters) in Aquatic Biota. *Analytical and Bioanalytical Chemistry*, 404(9), 2597-2610
<https://doi.org/10.1007/s00216-012-6067-7>

The purpose of this article is to summarize biological monitoring information on UV-absorbing compounds, commonly referred as organic UV filters or sunscreen agents, in aquatic ecosystems. To date a limited range of species (macroinvertebrates, fish, and birds), habitats (lakes, rivers, and sea), and compounds (benzophenones and camphors) have been investigated. As a consequence there is not enough data enabling reliable understanding of the global distribution and effect of UV filters on ecosystems. Both liquid chromatography and gas chromatography coupled with mass spectrometry-based methods have been developed and applied to the trace analysis of these pollutants in biota, enabling the required selectivity and sensitivity. As expected, the most lipophilic compounds occur most frequently with concentrations up to 7112 ng g(-1) lipids in mussels and 3100 ng g(-1) lipids (homosalate) in fish. High concentrations have also been reported for 4-methylbenzilidenecamphor (up to 1800 ng g(-1) lipids) and octocrylene (2400 ng g(-1) lipids). Many fewer studies have evaluated the potential bioaccumulation and biomagnification of these compounds in both fresh and marine water and terrestrial food webs. Estimated biomagnification factors suggest biomagnification in predator-prey pairs, for example bird-fish and fish-invertebrates. Ecotoxicological data and preliminary environmental assessment of the risk of UV filters are also included and discussed.

Gago-Ferrero, P., Diaz-Cruz, M. S., & Barcelo, D. (2015). UV Filters Bioaccumulation in Fish from Iberian River Basins. *Science of The Total Environment*, 518-519, 518-525
<https://doi.org/10.1016/j.scitotenv.2015.03.026>

The occurrence of eight organic UV filters (UV-Fs) was assessed in fish from four Iberian river basins. This group of compounds is extensively used in cosmetic products and other industrial goods to avoid the damaging effects of UV radiation, and has been found to be ubiquitous contaminants in the aquatic ecosystem. In particular, fish are considered by the scientific community to be the most feasible organism for contamination monitoring in aquatic ecosystems. Despite that, studies on the bioaccumulation of UV-F are scarce. In this study fish samples from four Iberian river basins under high anthropogenic pressure were analysed by liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Benzophenone-3 (BP3), ethylhexyl methoxycinnamate (EHMC), 4-methylbenzylidene camphor (4MBC) and octocrylene (OC) were the predominant pollutants in the fish samples, with concentrations in the range of ng/g dry weight (d.w.). The results indicated that most polluted area corresponded to Guadalquivir River basin, where maximum concentrations were found for EHMC (241.7 ng/gd.w.). Sediments from this river basin were also analysed. Lower values were observed in relation to fish for OC and EHMC, ranging from below the limits of detection to 23 ng/gd.w. Accumulation levels of UV-F in the fish were used to calculate biota-sediment accumulation factors (BSAFs). These values were always below 1, in the range of 0.04-0.3, indicating that the target UV-Fs are excreted by fish only to some extent. The fact that the highest concentrations were determined in predators suggests that biomagnification of UV-F may take place along the freshwater food web.

Grabicova, K., Fedorova, G., Burkina, V., Steinbach, C., Schmidt-Posthaus, H., Zlabek, V., . . . Randak, T. (2013). Presence of UV Filters in Surface Water and the Effects of Phenylbenzimidazole Sulfonic Acid on Rainbow Trout (*Oncorhynchus Mykiss*) Following a Chronic Toxicity Test. *Ecotoxicology and Environmental Safety*, 96, 41-47 <https://doi.org/10.1016/j.ecoenv.2013.06.022>

UV filters belong to a group of compounds that are used by humans and are present in municipal wastewaters, effluents from sewage treatment plants and surface waters. Current information regarding UV filters and their effects on fish is limited. In this study, the occurrence of three commonly used UV filters - 2-phenylbenzimidazole-5-sulfonic acid (PBSA), 2-hydroxy-4-methoxybenzophenone (benzophenone-3, BP-3) and 5-benzoyl-4-hydroxy-2-methoxy-benzenesulfonic acid (benzophenone-4, BP-4) - in South Bohemia (Czech Republic) surface waters is presented. PBSA concentrations (up to 13µg/L) were significantly greater than BP-3 or BP-4 concentrations (up to 620 and 390ng/L, respectively). On the basis of these results, PBSA was selected for use in a toxicity test utilizing the common model organism rainbow trout (*Oncorhynchus mykiss*). Fish were exposed to three concentrations of PBSA (1, 10 and 1000µg/L) for 21 and 42 days. The PBSA concentrations in the fish plasma, liver and kidneys were elevated after 21 and 42 days of exposure. PBSA increased activity of certain P450 cytochromes. Exposure to PBSA also changed various biochemical parameters and enzyme activities in the fish plasma. However, no pathological changes were obvious in the liver or gonads.

Guan, X., Shi, W., Zha, S., Rong, J., Su, W., & Liu, G. (2018). Neurotoxic Impact of Acute TiO₂ Nanoparticle Exposure on a Benthic Marine Bivalve Mollusk, *Tegillarca Granosa*. *Aquatic Toxicology*, 200, 241-246 <https://doi.org/10.1016/j.aquatox.2018.05.011>

The release of nanoparticles (NPs) into the ocean inevitably poses a threat to marine organisms. However, to date, the neurotoxic effects of NPs remains poorly understood in marine bivalve species. Therefore, in order to gain a better understanding of the physiological effects of NPs, the impact of acute (96h) TiO₂ NP exposure on the in vivo concentrations of three major neurotransmitters, the activity of AChE, and the expression of neurotransmitter-related genes was investigated in the blood clam, *Tegillarca granosa*. The obtained results showed that the in vivo concentrations of the three tested

neurotransmitters (DA, GABA, and ACh) were significantly increased when exposed to relatively high doses of TiO₂ NPs (1mg/L for DA and 10mg/L for ACh and GABA). Additionally, clams exposed to seawater contaminated with TiO₂ NP had significantly lower AChE activity. In addition, the expression of genes encoding modulatory enzymes (AChE, GABAT, and MAO) and receptors (mAChR3, GABAD, and DRD3) for the neurotransmitters tested were all significantly down-regulated after TiO₂ NP exposure. Therefore, this study has demonstrated the evident neurotoxic impact of TiO₂ NPs in *T. granosa*, which may have significant consequences for a number of the organism's physiological processes.

Haynes, V. N., Ward, J. E., Russell, B. J., & Agrios, A. G. (2017). Photocatalytic Effects of Titanium Dioxide Nanoparticles on Aquatic Organisms-Current Knowledge and Suggestions for Future Research. *Aquatic Toxicology*, 185, 138-148 <https://doi.org/10.1016/j.aquatox.2017.02.012>

Nanoparticles are entering natural systems through product usage, industrial waste and post-consumer material degradation. As the production of nanoparticles is expected to increase in the next decade, so too are predicted environmental loads. Engineered metal-oxide nanomaterials, such as titanium dioxide, are known for their photocatalytic capabilities. When these nanoparticles are exposed to ultraviolet radiation in the environment, however, they can produce radicals that are harmful to aquatic organisms. There have been a number of studies that have reported the toxicity of titanium dioxide nanoparticles in the absence of light. An increasing number of studies are assessing the interactive effects of nanoparticles and ultraviolet light. However, most of these studies neglect environmentally-relevant experimental conditions. For example, researchers are using nanoparticle concentrations and light intensities that are too high for natural systems, and are ignoring water constituents that can alter the light field. The purpose of this review is to summarize the current knowledge of the photocatalytic effects of TiO₂ nanoparticles on aquatic organisms, discuss the limitations of these studies, and outline environmentally-relevant factors that need to be considered in future experiments.

Horricks, R. A., Tabin, S. K., Edwards, J. J., Lumsden, J. S., & Marancik, D. P. (2019). Organic Ultraviolet Filters in Nearshore Waters and in the Invasive Lionfish (*Pterois Volitans*) in Grenada, West Indies. *Plos One*, 14(7), 11 <https://doi.org/10.1371/journal.pone.0220280>

Sunscreens and other personal care products use organic ultraviolet (UV) filters such as oxybenzone, 4-methylbenzylidene camphor, Padimate-O, and octyl methoxycinnamate to prevent damage to human skin. While these compounds are effective at preventing sunburn, they have a demonstrated negative effect on cells and tissues across taxonomic levels. These compounds have a relatively short half-life in seawater but are continuously reintroduced via recreational activities and wastewater discharge, making them environmentally persistent. Because of this, testing seawater samples for the presence of these compounds may not be reflective of their abundance in the environment. Bioaccumulation of organic ultraviolet filters in a high-trophic level predator may provide greater insight to the presence and persistence of these compounds. To address this, the present study collected seawater samples as well as muscle and stomach content samples from the invasive Pacific lionfish (*Pterois volitans*) in the nearshore waters of Grenada, West Indies to examine the use of lionfish as potential bioindicator species. Seawater and lionfish samples were collected at four sites that are near point sources of wastewater discharge and that receive a high number of visitors each year. Samples were tested for the presence and concentrations of oxybenzone, 4-methylbenzylidene camphor (4-MBC), Padimate-O, and octyl methoxycinnamate (OMC) using liquid chromatography-mass spectrometry. Oxybenzone residues were detected in 60% of seawater samples and OMC residues were detected in 20% of seawater samples. Seawater samples collected in the surface waters near Grenada's main beach had oxybenzone

concentrations more than ten times higher than seawater samples collected in less frequently visited areas and the highest prevalence of UV filters in lionfish. Residues of oxybenzone were detected in 35% of lionfish muscle and 4-MBC residues were detected in 12% of lionfish muscle. Padimate-O was not detected in either seawater or lion fish samples. No organic UV filters were detected in lionfish stomach contents. Histopathologic examination of lionfish demonstrated no significant findings attributed to UV filter toxicity. These findings report UV filter residue levels for the first time in inshore waters in Grenada. Results indicate that lionfish may be bioaccumulating residues and may be a useful sentinel model for monitoring organic ultraviolet filters in the Caribbean Sea.

Liu, H., Sun, P., Liu, H., Yang, S., Wang, L., & Wang, Z. (2015). Hepatic Oxidative Stress Biomarker Responses in Freshwater Fish *Carassius Auratus* Exposed to Four Benzophenone UV Filters. *Ecotoxicology and Environmental Safety*, 119, 116-122
<https://doi.org/10.1016/j.ecoenv.2015.05.017>

Benzophenone (BP) type UV filters are widely used in many personal care products to protect human from UV irradiation. Despite the estrogenic potencies to fish and the environmental occurrences of BP derivatives in aquatic systems, little information is available regarding their effects on the antioxidant defense system in fish. In this work, the oxidative stress induced in livers of *Carassius auratus* was assessed using four biomarkers. The integrated biomarker response (IBR) was applied to assess the overall antioxidant status in fish. Moreover, liver tissues were also studied histologically. The changes in the activities of antioxidant enzymes and glutathione levels suggested that BPs generates oxidative stress in fish. The IBR index revealed that the hepatic oxidative toxicity followed the order BP-1>BP-2>BP-4>BP-3. The histopathological analysis revealed lesions caused by BPs. This investigation provides essential information for assessing the potential ecological risk of BP-type UV filters.

Lu, J., Tian, S., Lv, X., Chen, Z., Chen, B., Zhu, X., & Cai, Z. (2018). TiO₂ Nanoparticles in the Marine Environment: Impact on the Toxicity of Phenanthrene and Cd(2+) to Marine Zooplankton *Artemia Salina*. *Science of The Total Environment*, 615, 375-380
<https://doi.org/10.1016/j.scitotenv.2017.09.292>

The impact of manufactured nanoparticles on the toxicity of co-existing pollutants in aquatic environments has raised increasing concerns. However, the toxicity of polycyclic aromatic hydrocarbons or metal ions in the presence of titanium dioxide nanoparticles (nTiO₂) to marine zooplankton has been rarely reported. In the present study, the impacts of nTiO₂ on the toxicity of phenanthrene (Phe) and cadmium (Cd(2+)) to *Artemia salina*, a model marine zooplankton, were investigated. Although nTiO₂ alone exerted a limited toxicity to *A. salina* within 48h of exposure, nTiO₂ strongly altered the toxicity of Phe and Cd(2+) to *A. salina*. Compared with the individual toxicities of pollutants to *A. salina*, the toxicities of Phe and Cd(2+) increased by 2.0% and 12.2%, respectively, in the presence of 5mg/L nTiO₂, but decreased by 24.5% and 57.1%, respectively, in the presence of 400mg/L nTiO₂. These concentration-dependent impacts of nTiO₂ on the toxicity of Phe or Cd(2+) might be attributed to the concurrent functions of several interrelated factors including the adsorption of pollutants on nTiO₂, the nTiO₂-facilitated bioaccumulation of pollutants, the limited gut volume in organisms, and the aggregation and sedimentation behaviors of nTiO₂. These results presented in the study could help understand the effects of manufactured nanomaterials in marine environments.

Molins-Delgado, D., Manez, M., Andreu, A., Hiraldo, F., Eljarrat, E., Barcelo, D., & Diaz-Cruz, M. S. (2017). A Potential New Threat to Wild Life: Presence of UV Filters in Bird Eggs from a Preserved Area.

Environmental Science & Technology, 51(19), 10983-10990
<https://doi.org/10.1021/acs.est.7b03300>

The present study uses bird eggs of seven wild species as a biomonitoring tool for sunscreens occurrence. Seven UV filters (UV-Fs), including 3 hydroxy-metabolites of oxybenzone (benzophenone 3, BP3) were characterized in unhatched eggs from Donana Natural Space (Spain). High frequency of detection was observed for all UV-Fs, ranging from 95% to 100%. The oxybenzone metabolite 4-hydroxybenzophenone (4HB) was ubiquitous at concentrations in the range 12.0-3348 ng g⁻¹ dry weight (dw). The parent compound, oxybenzone, was also present in all samples at lower concentrations (16.9-49.3 ng g⁻¹ dw). Due to the three BP3's metabolites, benzophenone 1 (BP1), 4HB, and 4,4'-dihydroxybenzophenone (4DHB) presence in unhatched eggs, it can be inferred that parent compounds are absorbed into the bird through the upper gut and the OH-derivatives formed are transferred by the mother to the egg before the laying. White stork (*Ciconia ciconia*) and western marsh harrier (*Circus aeruginosus*) were the most contaminated species, with mean total UV-Fs concentrations of 834 and 985 ng g⁻¹ dw, respectively. Results evidenced that biomagnification process across the bird species studied cannot be ruled out.

Muñiz-González, A.-B., & Martínez-Guitarte, J.-L. (2020). Combined Effects of Benzophenone-3 and Temperature on Gene Expression and Enzymatic Activity in the Aquatic Larvae *Chironomus Riparius*. *Science of the Total Environment*, 698, 134292
<https://doi.org/10.1016/j.scitotenv.2019.134292>

Climate change and pollution are two of the main environmental problems living organisms currently face. Temperature can modify a toxicant's effects and the organism's response to it. Global warming is expected to increase the temperature of freshwater ecosystems. In this work, we analyzed the effect of a mild temperature increase on the acute response of the aquatic larvae *Chironomus riparius* to the ultraviolet filter benzophenone-3 (BP3). This substance is commonly used in sunscreens and other commercial products and can reach the environment in different ways. We exposed larvae to BP3 at 18.5 or 23 °C for 8 or 24 h and analyzed the acute response at the molecular level. By quantitative real-time polymerase chain reaction (q-PCR), we studied altered messenger RNA (mRNA) levels of genes related to the endocrine system (EcR, InR and Met), detoxification mechanisms (Cyp4d2, Cyp6b7, GST d6, GST o1 and MRP-1) and stress response (Hsp22, Hsp27, Hsp70, HYOU and Gp93). Moreover, enzyme activity was evaluated, with a focus on glutathione-S-transferase (GST), phenoloxidase (PO) and acetylcholinesterase (AChE). Results showed that temperature affected the acute response of this organism by modifying the expression of EcR, Cyp6b7, GST d6, GST o1, MRP-1, Hsp22, Hsp27 and Hsp70 genes. These results suggest that even mild temperature change can affect the response of this organism to BP3 influencing short-term progress of the population. Although longer exposures are required to determine the ability of *C. riparius* to manage the pollutants in this novel environmental conditions, in order to know the possible mechanisms of detoxification or adaptation that may develop. This research represents a first step in the analysis of multi-stress response in this animal, and opens new possibilities in the toxicity evaluation of this organism in line with the real scenario that organisms face today.

Siller, A., Blaszkak, S. C., Lazar, M., & Olasz Harken, E. (2018). Update About the Effects of the Sunscreen Ingredients Oxybenzone and Octinoxate on Humans and the Environment. *Plastic Surgical Nursing*, 38(4), 158-161 <https://doi.org/10.1097/PSN.000000000000244>

As skin cancer prevalence continues to rise, the importance of sun protection, including sunscreen use, has become accepted in the public. Sunscreens are divided into two main categories based on the type of their active ingredient, organic and inorganic ultraviolet (UV) filters. It has been shown that inorganic filters are more effective at blocking forms of UV light, both UVA and UVB, as compared with organic filters because organic sunscreens absorb and convert radiation whereas inorganic sunscreens reflect radiation. The use of the two most common organic filters, oxybenzone and octinoxate, has recently been restricted in Hawaii due to their harmful effect on the coral reefs. Here, we discuss recent studies about these specific filters related to the adverse health risks they pose for humans and other organisms, as well as environmental repercussions.

Tang, Z., Zhong, F., Cheng, J., Nie, Z., Han, X., Han, Y., & Yang, Y. (2019). Concentrations and Tissue-Specific Distributions of Organic Ultraviolet Absorbents in Wild Fish from a Large Subtropical Lake in China. *Science of The Total Environment*, 647, 1305-1313
<https://doi.org/10.1016/j.scitotenv.2018.08.117>

Organic ultraviolet absorbents (UVAs) have been detected in various materials and biota, but little is known about the distributions of UVAs in the tissues of biota. In this study, tissue-specific UVA accumulation in six fish species from Lake Chaohu, China, was investigated. The sums of 12 UVA concentrations in muscles, gills, and livers were 7.65-120, 10.1-281, and 26.4-359ng/g dry weight, respectively. Ethylhexyl methoxycinnamate, 4-methylbenzylidene-camphor, and 2-(2'-hydroxy-3',5'-di-tert-butylphenyl)-5-chlorobenzotriazole were the dominant UVAs. Ethylhexyl salicylate and homosalate have been found in the aquatic species firstly. UVAs were taken up to different degrees by different fish species. The UVA muscle bioconcentration factors were lower than predicted by the Estimation Programs Interface Suite model, suggesting that such models may overestimate UVA accumulation in fish. The tissue distribution patterns indicated that UVAs are easily transferred to the muscles after being absorbed through the gills. The liver was found to preferentially accumulate UVAs and have a high UVA accumulation capacity, implying liver damage may be caused by UVAs. This is the first time the partitioning of UVAs between the liver, muscle, and gills of freshwater fish has been studied. The data acquired will improve our understanding of the pharmacokinetics and toxicities of UVAs in aquatic organisms.

Tsui, M. M. P., Chen, L., He, T., Wang, Q., Hu, C., Lam, J. C. W., & Lam, P. K. S. (2019). Organic Ultraviolet (UV) Filters in the South China Sea Coastal Region: Environmental Occurrence, Toxicological Effects and Risk Assessment. *Ecotoxicology and Environmental Safety*, 181, 26-33
<https://doi.org/10.1016/j.ecoenv.2019.05.075>

Organic ultraviolet (UV) filters are common ingredients of personal care products and occur ubiquitously in the aquatic environment; however, little is known about their distribution in and potential effects to the marine environment. This study reports the occurrence, toxicological effects and risk assessment of eleven commonly consumed UV filters in marine surface water collected from the South China Sea (SCS) coastal region. The concentrations of UV filters ranged from <MDL to 145ng/L in the SCS, in which benzophenone-3, octocrylene and butyl methoxydibenzoylmethane were the most dominant compounds with their detection frequencies over 97%. Relatively higher levels of total UV filters were found near the highly industrialized and urbanized Pearl River Estuary (PRE) and the concentrations gradually decreased towards the SCS. In general, the environmental levels of UV filters were higher at the western marine waters in Hong Kong than the eastern marine waters. Significant negative correlations were observed between benzophenone-4 and water temperature, as well as ethylhexyl

methoxycinnamate and salinity ($P < 0.001$; $r < -0.5$). Immobilization test of barnacle nauplius larvae (*Balanus amphitrite*) was conducted to assess the acute toxicity of organic UV filters to marine organisms. Benzophenone-8 and 4-methylbenzylidene camphor showed relatively higher toxicity with the 50% effect concentrations (EC50) of 2.2 and 3.9 mg/L, respectively. A preliminary risk assessment was conducted by the results obtained from our field and laboratory studies. Results showed that the risk to cause immobilization in barnacle nauplius larvae is associated with exposure to current levels of organic UV filters in the SCS was minimal.

Wang, J., Pan, L., Wu, S., Lu, L., Xu, Y., Zhu, Y., . . . Zhuang, S. (2016). Recent Advances on Endocrine Disrupting Effects of UV Filters. *International Journal of Environmental Research and Public Health*, 13(8) <https://doi.org/10.3390/ijerph13080782>

Ultraviolet (UV) filters are used widely in cosmetics, plastics, adhesives and other industrial products to protect human skin or products against direct exposure to deleterious UV radiation. With growing usage and mis-disposition of UV filters, they currently represent a new class of contaminants of emerging concern with increasingly reported adverse effects to humans and other organisms. Exposure to UV filters induce various endocrine disrupting effects, as revealed by increasing number of toxicological studies performed in recent years. It is necessary to compile a systematic review on the current research status on endocrine disrupting effects of UV filters toward different organisms. We therefore summarized the recent advances on the evaluation of the potential endocrine disruptors and the mechanism of toxicity for many kinds of UV filters such as benzophenones, camphor derivatives and cinnamate derivatives.

WHO/UNEP. (2013). *State of the Science of Endocrine Disrupting Chemicals - 2012: An Assessment of the State of the Science of Endocrine Disruptors Prepared by a Group of Experts for the United Nations Environment Programme (UNEP) and WHO*. Retrieved from <https://www.who.int/ceh/publications/endocrine/en/>

This document provides the global status of scientific knowledge on exposure to and effects of endocrine disrupting chemicals (EDCs). The work is based on the fact that endocrine systems are very similar across vertebrate species and that endocrine effects manifest themselves independently of species. The effects are endocrine system related and not necessarily species dependent. Effects shown in wildlife or experimental animals may also occur in humans if they are exposed to EDCs at a vulnerable time and at concentrations leading to alterations of endocrine regulation. Of special concern are effects on early development of both humans and wildlife, as these effects are often irreversible and may not become evident until later in life. The third and final chapter of this document discusses exposure of humans and wildlife to EDCs and potential EDCs.

Zhong, X., Downs, C. A., Che, X., Zhang, Z., Li, Y., Liu, B., . . . Gao, H. (2019). The Toxicological Effects of Oxybenzone, an Active Ingredient in Suncream Personal Care Products, on Prokaryotic Alga *Arthrospira* Sp. And Eukaryotic Alga *Chlorella* Sp. *Aquatic Toxicology*, 216, 105295 <https://doi.org/10.1016/j.aquatox.2019.105295>

Oxybenzone (OBZ; benzophenone-3, CAS# 131-57-7) is a known pollutant of aquatic and marine ecosystems, and is an ingredient in over 3000 personal care products, as well as many types of plastics. The aim of this study is to explore the different toxicities of OBZ on an eukaryotic (*Chlorella* sp.) and a prokaryotic algae (*Arthrospira* sp.). OBZ is a photo-toxicant, with all observed toxicities more severe in the

light than in the dark. Cell growth and chlorophyll inhibition were positively correlated with increasing OBZ concentrations over time. Twenty days treatment with OBZ, as low as 22.8 ng L⁻¹, significantly inhibited the growth and chlorophyll synthesis of both algae. Both algae were noticeably photo-bleached after 7 days of exposure to OBZ concentrations higher than 2.28 mg L⁻¹. Relatively low OBZ concentrations (0.228 mg L⁻¹) statistically constrained photosynthetic and respiratory rates via directly inhibiting photosynthetic electron transport (PET) and respiration electron transport (RET) mechanisms, resulting in over production of reactive oxygen species (ROS). Transmission and scanning electron microscopy showed that the photosynthetic and respiratory membrane structures were damaged by OBZ exposure in both algae. Additionally, PET inhibition suppressed ATP production for CO₂ assimilation via the Calvin-Benson cycle, further limiting synthesis of other biomacromolecules. RET restriction limited ATP generation, restricting the energy supply used for various life activities in the cell. These processes further impacted on photosynthesis, respiration and algal growth, representing secondary OBZ-induced algal damages. The data contained herein, as well as other studies, supports the argument that global pelagic and aquatic phytoplankton could be negatively influenced by OBZ pollution.

Section III: Environmental Fate and Life Cycle of UV Filters in Marine Environments

Ahmadi, F., Sparham, C., & Pawliszyn, J. (2017). A Flow-through Aqueous Standard Generation System for Thin Film Microextraction Investigations of UV Filters and Biocides Partitioning to Different Environmental Compartments. *Environmental Pollution*, 230, 663-673
<https://doi.org/10.1016/j.envpol.2017.06.092>

In this paper problems associated with preparation of aqueous standard of highly hydrophobic compounds such as partial precipitation, being lost on the surfaces, low solubility in water and limited sample volume for accurate determination of their distribution coefficients are addressed. The following work presents two approaches that utilize blade thin film microextraction (TFME) to investigate partitioning of UV filters and biocides to humic acid (dissolved organic carbon) and sediment. A steady-state concentration of target analytes in water was generated using a flow-through aqueous standard generation (ASG) system. Dialysis membranes, a polytetrafluoroethylene permeation tube, and a frit porous (0.5 µm) coated by epoxy glue were basic elements used for preparation of the ASG system. In the currently presented study, negligible depletion TFME using hydrophilic-lipophilic balance (HLB) and octadecyl silica-based (C18) sorbents was employed towards the attainment of free concentration values of target analytes in the studied matrices. Thin film geometry provided a large volume of extraction phase, which improved the sensitivity of the method towards highly matrix-bound analytes. Extractions were performed in the equilibrium regime so as to prevent matrix effects and with aims to reach maximum method sensitivity for all analytes under study. Partitioning of analytes on dissolved organic carbon (DOC) was investigated in ASG to facilitate large sample volume conditions. Binding percentages and DOC distribution coefficients (Log KDOC) ranged from 20 to 98% and 3.71-6.72, respectively. Furthermore, sediment-water partition coefficients (K_d), organic-carbon normalized partition coefficients (Log KOC), and DOC distribution coefficients (Log KDOC) were investigated in slurry

sediment, and ranged from 33 to 2860, 3.31-5.24 and 4.52-5.75 Lkg(-1), respectively. The obtained results demonstrated that investigations utilizing ASG and TFME can yield reliable binding information for compounds with high log KOW values. This information is useful for study of fate, transport, and ecotoxicological effects of UV filters and biocides in aquatic environment.

Ahmed, M. B., Johir, M. A. H., Zhou, J. L., Ngo, H. H., Guo, W., & Sornalingam, K. (2017). Photolytic and Photocatalytic Degradation of Organic UV Filters in Contaminated Water. *Current Opinion in Green and Sustainable Chemistry*, 6, 85-92 <https://doi.org/10.1016/j.cogsc.2017.06.010>

UV filters as emerging contaminants are of great concern and their wide detection in aquatic environments indicates their chemical stability and persistence. This review summarized the photolytic and photocatalytic degradation of UV filters in contaminated water. The findings indicated that limited research has been conducted on the photolysis and photocatalysis of UV filters. Photolysis of UV filters through UV irradiation in natural water was a slow process, which was accelerated by the presence of photosensitisers e.g. triplet state of chromaphoric dissolved organic matter (3CDOM*) and nutrients but reduced by salinity, dissolved organic matter (DOM) and divalent cations. UV Photocatalysis of 4-methylbenzylidene camphor and 2-phenylbenzimidazole-5-sulfonic acid was very effective with 100% removal within 30 min and 90 min using medicated TiO₂/H₂O₂ and TiO₂, respectively. The radiation source, type of catalyst and oxygen content were key factors. Future research should focus on improved understanding of photodegradation pathways and by-products of UV filters.

Benvenuti, N. Z. (2012). How Does Octinoxate Degrade Avobenzone? Retrieved from <https://www.futurederm.com/how-does-octinoxate-degrade-avobenzone/>

In the past, I've briefly touched on the subject that octinoxate degrades avobenzone. Specifically, in Are Inorganic Sunscreens Better Than Organic Ones? Part III: Toxicity and Spotlight On: Vitamin B3 (Niacinamide and Nicotinic Acid), readers have seen the phrase "2 + 2 addition of cinnamates and alkenes" repeatedly used to explain this phenomenon. And in subsequent weeks, I've received many comments and messages inquiring about what exactly does this math mean? Therefore, this post will document what happens when octinoxate and avobenzone come together.

Botta, C., Labille, J., Auffan, M., Borschneck, D., Miche, H., Cabie, M., . . . Bottero, J. Y. (2011). TiO₂-Based Nanoparticles Released in Water from Commercialized Sunscreens in a Life-Cycle Perspective: Structures and Quantities. *Environmental Pollution*, 159(6), 1543-1550 <https://doi.org/10.1016/j.envpol.2011.03.003>

This work investigates the physical-chemical evolution during artificial aging in water of four commercialized sunscreens containing TiO₂-based nanocomposites. Sunscreens were analyzed in terms of mineralogy and TiO₂ concentration. The residues formed after aging were characterized in size, shape, chemistry and surface properties. The results showed that a significant fraction of nano-TiO₂ residues was released from all sunscreens, despite their heterogeneous behaviors. A stable dispersion of submicronic aggregates of nanoparticles was generated, representing up to 38 w/w% of the amount of sunscreen, and containing up to 30% of the total nano-TiO₂ initially present in the creams. The stability of the dispersion was tested as a function of salt concentration, revealing that in seawater conditions, a major part of these nano-TiO₂ residues will aggregate and sediment. These results were put in perspective with consumption and life cycle of sunscreens to estimate the amount of nano-TiO₂ potentially released into AQUATIC environment.

Careghini, A., Mastorgio, A. F., Saponaro, S., & Sezenna, E. (2015). Bisphenol a, Nonylphenols, Benzophenones, and Benzotriazoles in Soils, Groundwater, Surface Water, Sediments, and Food: A Review. *Environmental Science and Pollution Research*, 22(8), 5711-5741
<https://doi.org/10.1007/s11356-014-3974-5>

Contaminants of emerging concern (CECs) are not commonly monitored in the environment, but they can enter the environment from a variety of sources. The most worrying consequence of their wide use and environmental diffusion is the increase in the possible exposure pathways for humans. Moreover, knowledge of their behavior in the environment, toxicity, and biological effects is limited or not available for most CECs. The aim of this work is to edit the state of the art on few selected CECs having the potential to enter the soil and aquatic systems and cause adverse effects in humans, wildlife, and the environment: bisphenol A (BPA), nonylphenol (NP), benzophenones (BPs), and benzotriazole (BT). Some reviews are already available on BPA and NP, reporting about their behavior in surface water and sediments, but scarce and scattered information is available about their presence in soil and groundwater. Only a few studies are available about BPs and BT in the environment, in particular in soil and groundwater. This work summarizes the information available in the literature about the incidence and behavior of these compounds in the different environmental matrices and food. In particular, the review focuses on the physical-chemical properties, the environmental fate, the major degradation byproducts, and the environmental evidence of the selected CECs.

Chen, F., Huber, C., May, R., & Schroder, P. (2016). Metabolism of Oxybenzone in a Hairy Root Culture: Perspectives for Phytoremediation of a Widely Used Sunscreen Agent. *Journal of Hazardous Materials*, 306, 230-236 <https://doi.org/10.1016/j.jhazmat.2015.12.022>

Oxybenzone (OBZ), known as Benzophenone-3, is a commonly used UV filter in sun tans and skin protectants, entering aquatic systems either directly during recreational activities or indirectly through wastewater treatment plants discharge. To study the potential degradation capacity of plants for OBZ in phytotreatment, a well-established hairy root culture (*Armoracia rusticana*) was treated with OBZ. More than 20% of spiked OBZ (100µM) was eliminated from the medium by hairy roots after 3h of exposure. Two metabolites were identified as oxybenzone-glucoside (OBZ-Glu) and oxybenzone-(6-O-malonyl)-glucoside (OBZ-Mal-Glu) by LC-MS/MS and TOF-MS. Formation of these metabolites was confirmed by enzymatic synthesis, as well as enzymatic and alkaline hydrolysis. Incubation with O-glucosyltransferase (O-GT) extracted from roots formed OBZ-Glu; whereas beta-d-Glucosidase hydrolyzed OBZ-Glu. However, alkaline hydrolysis led to cleavage of OBZ-Mal-Glu and yielded OBZ-Glu. In the hairy root culture, an excretion of OBZ-Glu into the growth medium was observed while the corresponding OBZ-Mal-Glu remained stored in root cells over the incubation time. We propose that metabolism of oxybenzone in plants involves initial conjugation with glucose to form OBZ-Glu followed by malonylation to yield OBZ-Mal-Glu. To our best knowledge this first finding presenting the potential of plants to degrade benzophenone type UV filters by phytoremediation.

Chen, F., Huber, C., & Schroder, P. (2017). Fate of the Sunscreen Compound Oxybenzone in *Cyperus Alternifolius* Based Hydroponic Culture: Uptake, Biotransformation and Phytotoxicity. *Chemosphere*, 182, 638-646 <https://doi.org/10.1016/j.chemosphere.2017.05.072>

Oxybenzone (OBZ), a common ingredient in sunscreens and personal care products, has been frequently detected in effluents from municipal wastewater treatment plants and also in surface waters. OBZ is an emerging contaminant due to its adverse impacts on marine/aquatic ecosystems. To investigate the

removal and degradation capacity of phytotreatment for OBZ, the common wetland plant species *Cyperus alternifolius* L. was exposed to this compound at 5, 25 and 50 μM for 120 h, respectively. Continuous uptake by roots and accumulation in plant tissues was observed over the exposure time, and depletion of spiked OBZ from the aqueous medium exceeded 73.9 \pm 9.1% after 120 h. Similar to its fate in mammalian cells, OBZ is activated in a phase I reaction resulting in the hydroxylated metabolite 2,4-dihydroxybenzophenone (DHB). Independently, two phase II metabolites were identified as oxybenzone-glucoside (OBZ-Glu) and oxybenzone-(6-O-malonyl)-glucoside (OBZ-Mal-Glu) by LC-MS/MS. Formation of these metabolites increased over the experimental period. To our knowledge this is the first time that DHB, OBZ-Glu and OBZ-Mal-Glu are shown to be formed in higher plant tissues. Furthermore, plant defense systems-antioxidative enzymes (SOD, CAT, APOX and POX) were found to be elevated to counteract stress caused by exposure to OBZ. This study presents the huge potential of aquatic plants to cope with benzophenone type UV filters in contaminated water bodies.

Chen, F., Schnick, S., & Schroder, P. (2018). Concentration Effects of the UV Filter Oxybenzone in *Cyperus Alternifolius*: Assessment of Tolerance by Stress-Related Response. *Environmental Science and Pollution Research*, 25(16), 16080-16090 <https://doi.org/10.1007/s11356-018-1839-z>

Phytoremediation has been proposed to reduce the load of the sunscreen oxybenzone (OBZ) in the aquatic environment. Despite the proven removal efficiency of this compound, little is known about its influence, particularly oxidative stress on plants. In this study, a short-term incubation of macrophytic *Cyperus alternifolius* was performed to prove the plant's ability to withstand the stress. Detached shoots were immersed in medium spiked with different concentrations of OBZ (50, 100, and 500 μM) for 2, 4, and 7 days, respectively. Increased formation of O_2^- and H_2O_2 in *Cyperus* treated with OBZ was characterized by intense colorization following histochemical staining. Alterations of enzyme activities involved in the antioxidative defense system indicate an adaptive response of *C. alternifolius* to this xenobiotic stress. Quantification of lipid peroxidation reveals that no significant membrane damage occurred during incubation with OBZ. Overall, 50 μM OBZ (tenfold higher than the amount frequently detected in the environment) exhibited low toxic effects. Accordingly, this pilot study provides information on the potential use of *Cyperus* to remove emerging sunscreen contaminants from water bodies.

Chen, X., Wang, J., Chen, J., Zhou, C., Cui, F., & Sun, G. (2019). Photodegradation of 2-(2-Hydroxy-5-Methylphenyl)Benzotriazole (UV-P) in Coastal Seawaters: Important Role of Dom. *Journal of Environmental Sciences*, 85, 129-137 <https://doi.org/10.1016/j.jes.2019.05.017>

Benzotriazole UV stabilizers (BT-UVs) have attracted concerns due to their ubiquitous occurrence in the aquatic environment, and their bioaccumulative and toxic properties. However, little is known about their aquatic environmental degradation behavior. In this study, photodegradation of a representative of BT-UVs, 2-(2-hydroxy-5-methylphenyl) benzotriazole (UV-P), was investigated under simulated sunlight irradiation. Results show that UV-P photodegrades slower under neutral conditions (neutral form) than under acidic or alkaline conditions (cationic and anionic forms). Indirect photodegradation is a dominant elimination pathway of UV-P in coastal seawaters. Dissolved organic matter (DOM) from seawaters accelerate the photodegradation rates mainly through excited triplet DOM (3DOM^*), and the roles of singlet oxygen and hydroxyl radical are negligible in the matrixes. DOM from seawaters impacted by mariculture exhibits higher steady-state concentration of 3DOM^* ($[3\text{DOM}^*]$) relative to those from pristine seawaters, leading to higher photosensitizing effects on the photodegradation. Halide ions inhibit the DOM-sensitized photodegradation of UV-P by decreasing $[3\text{DOM}^*]$.

photodegradation half-lives of UV-P are estimated to range from 24.38 to 49.66 hr in field water bodies of the Yellow River estuary. These results are of importance for assessing environmental fate and risk UV-P in coastal water bodies.

Dondi, D., Albini, A., & Serpone, N. (2006). Interactions between Different Solar UVB/UVa Filters Contained in Commercial Suncreams and Consequent Loss of UV Protection. *Photochemical and Photobiological Sciences*, 5(9), 835-843 <https://doi.org/10.1039/b606768a>

A systematic investigation of two well-known and popular commercial suncreams reveals significant degradation when exposed to simulated UV sunlight at an irradiance corresponding to natural sunlight. We have examined the photochemistry of two widely used sunscreen active agents in pure solvents separately and together (in solution), and in neat form, as well as their photochemistry when present in the actual suncream emulsion (as thin films on a glass substrate) since their combination typically produces suncreams with high sun protection factors (SPF): (1a) octyl methoxycinnamate (OMC; octinoxate) and (2a) 4-tert-butyl-4'-methoxydibenzoylmethane (also known as avobenzone and Parsol 1789), present in the two suncream formulations in combination with others (one also contained TiO₂). Intermediates and/or photoproducts were identified by UV/visible spectroscopy, HPLC and liquid chromatographic/mass spectral methods, and by both ¹H and ¹³C-NMR techniques. Structural assignments of the substrates produced were aided by examining model systems {viz. ethyl cinnamate (1b) and dibenzoylmethane (2b)} of the two sunscreen active agents. Irradiation of the cinnamates and the diketones together led to a [2 + 2] photocycloaddition process yielding cinnamate dimers and cyclobutylketone photoadducts that subsequently fragmented into substituted oxopentanoates and oxobutanoates. Similar findings were observed when the two active agents were simultaneously present in the same suncream emulsion.

Du, J., Zhang, Y., Guo, R., Meng, F., Gao, Y., Ma, C., & Zhang, H. (2019). Harmful Effect of Nanoparticles on the Functions of Freshwater Ecosystems: Insight into Nanozno-Polluted Stream. *Chemosphere*, 214, 830-838 <https://doi.org/10.1016/j.chemosphere.2018.09.171>

ZnO nanoparticle toxicity on aquatic organisms has been extensively studied, but its concentration- and time-dependent effects on ecosystem functioning are remain uncertain. Here we assessed the harmful effects of nano-ZnO (10, 100, 1000mgL⁻¹) on the stream functioning by using a microcosm system simulating poplar leaf decomposition for 50 days. The 100mgL⁻¹ ZnO nanoparticles had significantly and stably inhibitory effect on the litter decomposition during the exposure period. The inhibition was not detected in the 10mgL⁻¹ treatment until 43d. In contrast, the significant and continuous inhibition started to disappear from 43d in the 1000mgL⁻¹ treatment. The varied consequences on litter decomposition might be directly affected by the different ZnO nanoparticle homogeneity of the different treatments. ZnO nanoparticles led to significant decreases in pH value of the decomposition environment, which had significant and positive relationships to the activities of dehydrogenase, glycine-aminopeptidase, N-acetylglucosaminidase, and acid phosphatase. Besides, 10 and 1000mgL⁻¹ ZnO nanoparticles led to lower fungal diversity, which was negatively related to the variability of decomposition. In conclusion, fungal decomposers showed different responses to the different concentrations of ZnO nanoparticle, and ultimately affected the stability of ecosystem functions.

Farré, M. I., Pérez, S., Kantiani, L., & Barceló, D. (2008). Fate and Toxicity of Emerging Pollutants, Their Metabolites and Transformation Products in the Aquatic Environment. *TrAC Trends in Analytical Chemistry*, 27(11), 991-1007 <https://doi.org/10.1016/j.trac.2008.09.010>

There has been a great effort to study the fate, the occurrence and the ecotoxicology of emerging pollutants in the aquatic environment. Recently, several articles have focused on degradation products of emerging pollutants and the study of their toxicological effects. We review the fate and the ecotoxicology of emerging pollutants, especially focusing on their metabolites and transformation products (TPs) in the aquatic environment, including pharmaceuticals, hormones, perfluorinated compounds, by-products of drinking-water disinfection, sunscreens or UV filters, benzotriazoles and naphthalenic acids. We describe analytical methodologies for the quantitative analysis of emerging pollutants, their metabolites, and their TPs in sewage and surface waters, and we give the results of monitoring surveys obtained from the application of these analytical methodologies.

Gackowska, A., Studzinski, W., Kudlek, E., Dudziak, M., & Gaca, J. (2018). Estimation of Physicochemical Properties of 2-Ethylhexyl-4-Methoxycinnamate (EHMC) Degradation Products and Their Toxicological Evaluation. *Environmental Science and Pollution Research*, 25(16), 16037-16049
<https://doi.org/10.1007/s11356-018-1796-6>

The organic UV filters, commonly used in personal protection products, are of concern because of their potential risk to aquatic ecosystems and living organisms. One of UV filters is ethylhexyl-4-methoxycinnamate (EHMC) acid. Studies have shown that, in the presence of oxidizing and chlorinating factors, EHMC forms a series of products with different properties than the substrate. In this study, the toxicities of EHMC and its transformation/degradation products formed under the influence of NaOCl/UV and H₂O₂/UV systems in the water medium were tested using Microtox(R) bioassay and by observation of mortality of juvenile crustaceans *Daphnia magna* and *Artemia Salina*. We have observed that oxidation and chlorination products of EHMC show significantly higher toxicity than EHMC alone. The toxicity of chemicals is related to their physicochemical characteristic such as lipophilicity and substituent groups. With the increase in lipophilicity of products, expressed as log KOW, the toxicity (EC₅₀) increases. On the basis of physicochemical properties such as vapour pressure (VP), solubility (S), octanol-water partition coefficient (KOW), bioconcentration factor (BCF) and half-lives, the overall persistence (POV) and long-range transport potential (LRTP) of all the products and EHMC were calculated. It was shown that the most persistent and traveling on the long distances in environment are methoxyphenol chloroderivatives, then methoxybenzene chloroderivatives, EHMC chloroderivatives, methoxybenzaldehyde chloroderivatives and methoxycinnamate acid chloroderivatives. These compounds are also characterised by high toxicity.

Gago-Ferrero, P., Badia-Fabregat, M., Olivares, A., Pina, B., Blanquez, P., Vicent, T., . . . Barcelo, D. (2012). Evaluation of Fungal- and Photo-Degradation as Potential Treatments for the Removal of Sunscreens Bp3 and Bp1. *Science of The Total Environment*, 427-428, 355-363
<https://doi.org/10.1016/j.scitotenv.2012.03.089>

Photodecomposition might be regarded as one of the most important abiotic factors affecting the fate of UV absorbing compounds in the environment and photocatalysis has been suggested as an effective method to degrade organic pollutants. However, UV filters transformation appears to be a complex process, barely addressed to date. The white rot fungus *Trametes versicolor* is considered as a promising alternative to conventional aerobic bacterial degradation, as it is able to metabolise a wide range of xenobiotics. This study focused on both degradation processes of two widely used UV filters, benzophenone-3 (BP3) and benzophenone-1 (BP1). Fungal treatment resulted in the degradation of more than 99% for both sunscreens in less than 24 h, whereas photodegradation was very inefficient, especially for BP3, which remained unaltered upon 24 h of simulated sunlight irradiation. Analysis of

metabolic compounds generated showed BP1 as a minor by-product of BP3 degradation by *T. versicolor* while the main intermediate metabolites were glycoconjugate derivatives. BP1 and BP3 showed a weak, but significant estrogenic activity (EC50 values of 0.058 mg/L and 12.5 mg/L, respectively) when tested by recombinant yeast assay (RYA), being BP1 200-folds more estrogenic than BP3. Estrogenic activity was eliminated during *T. versicolor* degradation of both compounds, showing that none of the resulting metabolites possessed significant estrogenic activity at the concentrations produced. These results demonstrate the suitability of this method to degrade both sunscreen agents and to eliminate estrogenic activity.

Gasparro, F. P. (1993). The Molecular Basis of UV-Induced Mutagenicity of Sunscreens. *Federation of European Biochemical Societies (FEBS)*, 336(1), 184-185 [https://doi.org/10.1016/0014-5793\(93\)81637-F](https://doi.org/10.1016/0014-5793(93)81637-F)

Knowland et al. recently described sunlight induced mutagenicity of a common sunscreen ingredient (padimate-0) [1]. In addition, they showed direct evidence for DNA damage using alkaline agarose gel electrophoresis of DNA which had been irradiated in vitro in the presence of Padimate-0. Earlier we [2] and others [3] demonstrated that the prototypical sunscreen, paraaminobenzoic acid, underwent several different photochemical reactions. Photoproducts resulting from dimerization as well as photoaddition to the common DNA bases have been characterized after exposure to ultraviolet B radiation. Although the photochemical reactions of other sunscreens have not been as well characterized, the in vitro formation of similar photoadducts in cells exposed to sunscreens and ultraviolet radiation could explain the observed mutagenic effects of these agents.

Ge, J., Huang, D., Han, Z., Wang, X., Wang, X., & Wang, Z. (2019). Photochemical Behavior of Benzophenone Sunscreens Induced by Nitrate in Aquatic Environments. *Water Research*, 153, 178-186 <https://doi.org/10.1016/j.watres.2019.01.023>

Benzophenones (BPs), which are widely used UV filters, have aroused considerable public concern owing to their potential endocrine-disrupting activities. Herein, we systematically investigated their photochemical behavior and fate, which is mediated by nitrate in aquatic environments. The results showed that 10 μM of 3 BPs can be completely degraded within 4h of simulated sunlight irradiation in a 10mM nitrate solution at pH 8.0, and 2,4-dihydroxybenzophenone (BP-1) has a 31.6% mineralization rate after 12h irradiation. Their photolytic rates (k_{obs}) presented a significant linear correlation with the logarithmic values of the nitrate concentration for 0.1-10mM (R²>0.98), and in three actual waters, the rates of BP-1 were also positively related to the intrinsic nitrate concentration. Furthermore, higher transformation rates under alkaline condition were observed, especially for BP-1, with its k_{obs} at pH 10 being 8.3-fold higher than that at pH 6.0. Moreover, dissolved oxygen (DO) also has an impact on the reaction kinetics to some degree. According to the quenching experiments, we found that three reactive oxygen species (ROS), namely, *OH, *NO, and *NO₂, participated in this photolysis of BPs, and the contribution of *OH accounted for 32.1%. Furthermore, we selected BP-1 as the model molecule to study the transformation pathways and toxicity changes in this system. Four main transformation pathways including hydroxylation, nitrosylation, nitration, and dimerization were proposed, based on liquid chromatography quadrupole time-of-flight mass spectrometry (LC-Q-TOF-MS) analysis and density functional theory (DFT). According to the toxicity test, the formed intermediates were more toxic to *Photobacterium phosphoreum* than the parent BP-1. Therefore, these results can help reveal primary phototransformation mechanisms and evaluate the potential ecological risks of BPs in aquatic environments.

Hao, Z., Yin, Y., Wang, J., Cao, D., & Liu, J. (2018). Formation of Organobromine and Organoiodine Compounds by Engineered TiO₂ Nanoparticle-Induced Photohalogenation of Dissolved Organic Matter in Environmental Waters. *Science of The Total Environment*, 631-632, 158-168
<https://doi.org/10.1016/j.scitotenv.2018.03.027>

There are increasing concerns about the adverse effects of released engineered nanoparticles and photochemically formed organohalogen compounds (OHCs) on human health and the environment. Herein, we report that titanium dioxide nanoparticles (TiO₂ NPs) can photocatalytically halogenate dissolved organic matter (DOM) to form a large number of organobromine compounds (OBCs) and organoiodine compounds (OICs), as characterized by negative ion electrospray ionization coupled with Fourier transform ion cyclotron resonance mass spectrometry. Compared with no OHCs produced in control samples in darkness and/or without TiO₂ NPs under sunlight irradiation, various OBCs and OICs were detected in freshwater and seawater under sunlight irradiation for 12h and 24h even in the presence of 1mgL⁻¹ TiO₂ NPs, indicating the photocatalytic roles TiO₂ NPs played in DOM halogenation. Furthermore, TiO₂ NPs could result in the photodegradation of newly formed OHCs, as evidenced by the intensity and the number of some OHCs decreased with reaction time. In addition, many TiO₂ NP-induced OBCs contained two or three bromine atoms, and/or nitrogen and sulfur elements, belonging to lignin-like, tannin-like, unsaturated hydrocarbon and aliphatic compounds. While the OICs were primarily contained one iodine, and very few consisted of nitrogen and sulfur elements, most were lignin-like and tannin-like compounds. Finally, the OBCs in freshwater were found to be formed mainly via a substitution reaction or addition reaction and were accompanied by other reactions such as photooxidation, while the OBCs in seawater and OICs were formed primarily via substitution reactions. Given the abundance of produced OHCs and their toxicity, our findings call for further studies on the exact structure and toxicity of the formed OHCs, taking account the TiO₂ NP-induced DOM photohalogenation in aquatic environments during the evaluation of the environmental effects of engineered TiO₂ NPs.

Jentsch, F., Olsson, O., Westphal, J., Reich, M., Leder, C., & Kummerer, K. (2016). Photodegradation of the UV Filter Ethylhexyl Methoxycinnamate under Ultraviolet Light: Identification and in Silico Assessment of Photo-Transformation Products in the Context of Grey Water Reuse. *Science of The Total Environment*, 572, 1092-1100 <https://doi.org/10.1016/j.scitotenv.2016.08.017>

To prevent water shortages in the future and to reduce domestic water consumption, decentralized grey water (GW) reuse has become increasingly important. This water has, however, to be free of pollutants. Conventional treatment of GW does not fully eliminate micropollutants such as the UV filter substance ethylhexyl methoxycinnamate (EHMC). EHMC, which is commonly used in sunscreens and personal care products, is an endocrine disruptor and shows potential to bioaccumulation, which is also reflected in its low water solubility. Photolysis has been proposed as an alternative treatment method for other micropollutants, but it is not clear yet whether it can also be used to eliminate EHMC. One goal of this study was to better understand the basic pathways involved in this process. It aimed to identify photo-transformation products (photo-TPs) by using, in the test conditions, an initial concentration of EHMC higher than those expected in the environment. Acetonitrile (ACN) was added in low concentrations to the aqueous solution to overcome the low aquatic solubility of EHMC. The influence of this co-solvent on the degradation kinetics was studied. The photolysis experiments were carried out using a medium pressure mercury lamp, which emits UV light in the range of 200-400 nm. The quantum yield of the photolysis of EHMC was 0.0042 and 0.0023 mol.Einstein⁻¹ (for 0.2 and 0.5% ACN (v/v), respectively),

and the relative and absolute UV photon fluxes were determined. HPLC was used to monitor the elimination kinetics of EHMC, which followed first-order kinetics. The results of LC-MSn analyses revealed that beside others, several oxidized and hydroxylized EHMC isomers were formed as photo-TPs in aqueous solution. Using a set of in silico quantitative structure-activity relationship (QSAR) models, this study also offered new insights concerning the environmental fate and toxicity of the TPs of EHMC.

Jurado, A., Gago-Ferrero, P., Vazquez-Sune, E., Carrera, J., Pujades, E., Diaz-Cruz, M. S., & Barcelo, D. (2014). Urban Groundwater Contamination by Residues of UV Filters. *Journal of Hazardous Materials*, 271, 141-149 <https://doi.org/10.1016/j.jhazmat.2014.01.036>

The occurrence and fate of UV filters (UV F) in an urban aquifer in correlation with (1) the spatial distribution of UV F in Barcelona's groundwater, (2) the depth of the groundwater sample, (3) the physicochemical properties of the target compounds, (4) the recharge sources, and (5) the redox conditions of the Barcelona aquifers, were studied for the first time. The highest groundwater concentrations and the largest number of detected UV F were observed in an aquifer recharged by a polluted river (around 55 ng/L in SAP-4). In contrast, the urbanized areas had lower concentrations (around 20 ng/L in MPSP-1). Two pathways can be identified for UV F to enter the aquifers: (1) leakage of raw sewage from the sewage network in urbanized areas and (2) wastewater treatment plant (WWTP) effluents discharged into the river. Measured concentrations of UV F were significantly much lower than those estimated from the waste water proportion in groundwater samples suggesting that UV F might undergo transformation processes in both reducing and oxidizing conditions.

Jurado, A., Walther, M., & Diaz-Cruz, M. S. (2019). Occurrence, Fate and Environmental Risk Assessment of the Organic Microcontaminants Included in the Watch Lists Set by Eu Decisions 2015/495 and 2018/840 in the Groundwater of Spain. *Science of The Total Environment*, 663, 285-296 <https://doi.org/10.1016/j.scitotenv.2019.01.270>

This paper aims to review the existing occurrence data in Spanish groundwater (GW) for the emerging organic contaminants (EOCs) defined in the surface water Watch Lists of Decisions 2015/495/EU and 2018/840/EU since these contaminants are likely to reach GW bodies because surface waters show close interaction with GW. These two lists include 20 substances: 9 pesticides (5 neonicotinoids, 2 carbamates, 1 oxadiazole and 1 semicarbazone), 6 pharmaceuticals (diclofenac and 5 antibiotics), 3 estrogens, 1 UV filter (2-ethylhexyl-4-methoxycinnamate, EHMC) and 1 antioxidant (2,6-di-tert-butyl-4-methylphenol, BHT). Most of these substances are usually detected at low ng/L concentration range or not detected in the GW bodies of Spain. However, eventually they are reported at concentrations >100ng/L (e.g., imidacloprid, methiocarb, diclofenac, macrolide antibiotics, ciprofloxacin, EHMC and BHT). Consequently, it is required to set up drinking water standards, and/or GW threshold quality values because GW is a valuable water resource worldwide. Overall, GW is less contaminated than other water bodies, such as rivers, suggesting that aquifers possess a natural attenuation capacity and/or are less vulnerable than rivers to contamination. Nevertheless, the natural hydrogeochemical processes that control the fate and transformation of these substances during infiltration and in the aquifer have been barely investigated so far. The concentrations of the target EOCs are used to calculate hazard quotients (HQs) in the Spanish GW bodies as an estimation of their ecotoxicity and in order to compare somehow their chemical quality with respect to those of surface water. Due to the limited ecotoxicity data for most EOCs, HQs can only be calculated for few substances. The results pointed out the risk posed by the anti-inflammatory diclofenac towards *Ceriodaphnia dubia* (HQ=21) and the medium risk associated to the antibiotic erythromycin for *Brachionus calyciflorus* (HQ=0.46).

Knowland, J., McKenzie, E. A., McHugh, P. J., & Cridland, N. A. (1993). Sunlight-Induced Mutagenicity of a Common Sunscreen Ingredient. *Federation of European Biochemical Societies (FEBS)*, 324(3), 309-313 [https://doi.org/10.1016/0014-5793\(93\)80141-G](https://doi.org/10.1016/0014-5793(93)80141-G)

We have tested the mutagenicity of a UV-B sunscreen ingredient called Padimate-O or octyl dimethyl PABA, which, chemically speaking, is identical to an industrial chemical that generates free radicals when illuminated. It is harmless in the dark but mutagenic in sunlight, attacking DNA directly. A commercial sunscreen containing Padimate-O behaves in the same way. UV-A in sunlight also excites Padimate-O, although less than UV-B. Some related compounds, including a known carcinogen, behave similarly. As mutagens may be carcinogenic, our results suggest that some sunscreens could, while preventing sunburn, contribute to sunlight-related cancers.

Kotnik, K., Kosjek, T., Zegura, B., Filipic, M., & Heath, E. (2016). Photolytic Fate and Genotoxicity of Benzophenone-Derived Compounds and Their Photodegradation Mixtures in the Aqueous Environment. *Chemosphere*, 147, 114-123 <https://doi.org/10.1016/j.chemosphere.2015.12.068>

This study investigates the environmental fate of eight benzophenone derivatives (the pharmaceutical ketoprofen, its phototransformation products 3-ethylbenzophenone and 3-acetylbenzophenone, and five benzophenone-type UV filters) by evaluating their photolytic behaviour. In addition, the genotoxicity of these compounds and the produced photodegradation mixtures was studied. Laboratory-scale irradiation experiments using a medium pressure UV lamp revealed that photodegradation of benzophenones follows pseudo-first-order kinetics. Ketoprofen was the most photolabile ($t_{1/2} = 0.8$ min), while UV filters were more resistant to UV light with $t_{1/2}$ between 17 and 99 h. The compounds were also exposed to irradiation by natural sunlight and showed similar photostability as predicted under laboratory conditions. Solar photodegradation experiments were performed in distilled water, lake and seawater, and revealed that photosensitizers present in natural waters significantly affect the photolytic behaviour of the investigated compounds. In this case, the presence of lake water resulted in accelerated photodecomposition, while seawater showed different effects on photodegradation, depending on a compound. Further, it was shown that the transformation products of ketoprofen 3-ethylbenzophenone and 3-acetylbenzophenone were formed under environmental conditions when ketoprofen was exposed to natural sunlight. Genotoxicity testing of parent benzophenone compounds using the SOS/umuC assay revealed that UV filters exhibited weak genotoxic activity in the presence of a metabolic activation system, however the concentrations tested were much higher than found in the environment (≥ 125 $\mu\text{g mL}^{-1}$). After irradiation of benzophenones, the produced photodegradation mixtures showed that, with the exception of benzophenone that exhibited weak genotoxic activity, all the other compounds tested did not elicit any activity when exposed to UV light.

Li, A. J., Sang, Z., Chow, C. H., Law, J. C., Guo, Y., & Leung, K. S. (2017). Environmental Behavior of 12 UV Filters and Photocatalytic Profile of Ethyl-4-Aminobenzoate. *Journal of Hazardous Materials*, 337, 115-125 <https://doi.org/10.1016/j.jhazmat.2017.04.067>

Ethyl-4-aminobenzoate (Et-PABA) is currently used as a substitute for 4-aminobenzoate (PABA) in sunscreens and anesthetic ointments. Despite its widespread use and hydrophilicity, Et-PABA has never been found in environmental waters. This study, probed the occurrence of Et-PABA in both seawater and drinking water sources in Hong Kong, and evaluated its transformation products (TPs) and environmental fate via cumulative potency and photocatalytic profile analyses. Another 11 UV filters

used in skin-care products were also studied. Et-PABA was not detected in any water sample. Four other UV filters were dominant at ng/L level in both seawater and drinking water sources. UHPLC-QTOF-MS was used to elucidate the structure of TPs. With high resolution accurate mass data and fragment rationalization, 11 Et-PABA TPs were characterized, including seven intermediates firstly proposed as TPs; two compounds were reported for the first time. It is proposed that photocatalysis induces transformation pathways of (de)hydroxylation, demethylation and molecular rearrangement. Luminescent bacteria tests showed decreasing toxicity with increasing irradiation of Et-PABA, suggesting that irradiation TPs are less toxic than the parent compound. Transformation of Et-PABA appears to explain why Et-PABA has not been detected in the natural environment.

Li, J., Ma, L. Y., & Xu, L. (2016). Transformation of Benzophenone-Type UV Filters by Chlorine: Kinetics, Products Identification and Toxicity Assessments. *Journal of Hazardous Materials*, 311, 263-272 <https://doi.org/10.1016/j.jhazmat.2016.02.059>

The present study focused on the kinetics, transformation pathways and toxicity of several benzophenone-type ultraviolet filters (BPs) during the water chlorination disinfection process. The transformation kinetics of the studied three BPs was found to be second-order reaction, which was dependent on the concentration of BPs and chlorine. The second-order rate constants increased from 86.7 to 975 M⁽⁻¹⁾ s⁽⁻¹⁾ for oxybenzone, 49.6-261.7 M⁽⁻¹⁾ s⁽⁻¹⁾ for 4-hydroxybenzophenone and 51.7-540 M⁽⁻¹⁾ s⁽⁻¹⁾ for 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid with the increasing pH value from 6 to 8 of the chlorination disinfection condition. Then the transformation products (TPs) of these BPs were identified by HPLC-QTOF analysis. Several transformation pathways, including electrophilic substitution, methoxyl substitution, ketone groups oxidation, hydrolysis, decarboxylation and ring cleavage reaction, were speculated to participate in the chlorination transformation process. Finally, according to the toxicity experiment on luminescent bacteria, *Photobacterium phosphoreum*, enhanced toxicity was observed for almost all the TPs of the studied BPs except for 2,2'-dihydroxy-4,4'-dimethoxybenzophenone; it suggested the formation of TPs with more toxic than the parent compounds during the chlorination process. The present study provided a foundation to understand the transformation of BPs during chlorination disinfection process, and was of great significance to the drinking water safety.

Li, Y., Qiao, X., Zhou, C., Zhang, Y. N., Fu, Z., & Chen, J. (2016). Photochemical Transformation of Sunscreen Agent Benzophenone-3 and Its Metabolite in Surface Freshwater and Seawater. *Chemosphere*, 153, 494-499 <https://doi.org/10.1016/j.chemosphere.2016.03.080>

The occurrence of sunscreen agents and their metabolites in surface waters gives rise to public concerns. However, little is known about the environmental fate of these pollutants at present, especially for their metabolites. In this study, we investigated the photochemical of sunscreen agents and their metabolites in natural waters, adopting benzophenone-3 (BP-3) and its human metabolite 4-hydroxybenzophenone (4-OH-BP3) as examples. Results show that only anionic forms of both BP-3 and 4-OH-BP3 can undergo direct photodegradation. The photolytic rates of both compounds in natural waters are faster as compared to those in pure water. Radical scavenging experiments revealed that triplet-excited dissolved organic matter ((3)DOM(*)) was responsible for the indirect photodegradation of BP-3 and 4-OH-BP3 in seawater, whereas in freshwater, the indirect photodegradation of these two compounds was attributed to (3)DOM(*) and .OH. (1)O₂ plays a negligible role in their photodegradation because of the weak (1)O₂ reactivity. Furthermore, we probed the contribution of .OH and (3)DOM(*) to the photodegradation of both compounds in freshwater, and the results revealed

that .OH accounted for 56% and 59% of the observed photodegradation for BP-3 and 4-OH-BP3, respectively, whereas (3)DOM(*) accounted for 43% and 12% of the observed photodegradation for BP-3 and 4-OH-BP3, respectively. These results are helpful in assessing the ecological risk of BP-3 and its metabolite in the aquatic environment.

Liu, Q., Chen, Z., Wei, D., & Du, Y. (2014). Acute Toxicity Formation Potential of Benzophenone-Type UV Filters in Chlorination Disinfection Process. *Journal of Environmental Sciences*, 26(2), 440-447
[https://doi.org/10.1016/s1001-0742\(13\)60411-8](https://doi.org/10.1016/s1001-0742(13)60411-8)

Benzophenones (BPs) are a class of widely used UV filters, which have been frequently detected within multiple environmental matrices. Disinfection is a necessary process in water treatment processes. The transformation behaviors and toxicity changes of 14 BP-type UV filters during chlorination disinfection treatment were investigated in this study. A new index, the acute toxicity formation potential, was proposed to evaluate the toxicity changes and potential risks of BP-type UV filters during chlorination treatment. It was found that 13 of 14 BP-type UV filters exhibited toxicity decreases in the chlorination disinfection process, more or less, while one showed a toxicity increase. The toxicity changes were dependent on substitution effects, such that 2,4-di-hydroxylated or 3-hydroxylated BPs exhibited significant toxicity decreases after chlorination treatment due to the ready cleavage of the aromatic ring. Importantly, the acute toxicity changes could be duplicated in an ambient water matrix.

Loosli, F., Wang, J. J., Rothenberg, S., Bizimis, M., Winkler, C., Borovinskaya, O., . . . Baalousha, M. (2019). Sewage Spills Are a Major Source of Titanium Dioxide Engineered (Nano)-Particle Release into the Environment. *Environmental Science-Nano*, 6(3), 763-777
<https://doi.org/10.1039/c8en01376d>

Sanitary sewer overflows (SSOs) are a common problem across the United States. An estimated number of 23000-75000 SSOs occurred in 2004, discharging between 11 and 38 billion liters of untreated wastewater to receiving waters. SSOs release many contaminants, including engineered nanomaterials (ENMs), to receiving water bodies. Measuring ENM concentrations in environmental samples remains a key challenge in environmental nanotechnology and requires the distinction between natural and engineered particles. This distinction between natural and engineered particles is often hampered by the similarities in the intrinsic properties of natural and engineered particles, such as particle size, composition, density, and surface chemistry, and by the limitations of the available nanometrology tools. To overcome these challenges, we applied a multi-method approach to measure the concentrations and properties of TiO₂ engineered particles (e.g., ENMs and pigments) including: 1) multi element-single particle-inductively coupled plasma-mass spectrometry (ME-SP-ICP-MS) to identify elemental associations and to determine elemental ratios in natural particles, 2) calculation of total elemental concentrations and ratios from total metal concentrations measured following total sample digestion to estimate engineered particle concentrations, and 3) transmission electron microscopy (TEM) to characterize engineered particle size and morphology. ME-SP-ICP-MS analysis revealed that natural TiO₂ particles are often associated with at least one of the following elements: Al, Fe, Ce, Si, La, Zr, Nb, Pb, Ba, Th, Ta, W and U, and that elemental ratios of Ti to these elements, except Pb, are typical of riverine particulates and the average crustal ratios. High TiO₂ engineered particle concentrations up to 100 µg L⁻¹ were found in SSO-impacted surface waters. TEM analysis demonstrated the presence of regular-shape TiO₂ particles in SSO-impacted surface waters. This study provides a comprehensive approach for measuring TiO₂ engineered particle concentrations in surface waters. The quantitative data produced in this work can be used as input for modeling studies and pave the way for routine

monitoring of ENMs in environmental systems, validation of ENM fate models, and more accurate ENM exposure and risk assessment.

Lu, Z., Smyth, S. A., Peart, T. E., & De Silva, A. O. (2017). Occurrence and Fate of Substituted Diphenylamine Antioxidants and Benzotriazole UV Stabilizers in Various Canadian Wastewater Treatment Processes. *Water Research*, 124, 158-166
<https://doi.org/10.1016/j.watres.2017.07.055>

Substituted diphenylamine antioxidants (SDPAs) and benzotriazole UV stabilizers (BZT-UVs) are additives used in industrial and consumer products to prevent degradation or color change of materials, but their environmental fate and disposition are not well characterized. In this study, SDPAs and BZT-UVs were analyzed in 68 liquid and 39 solid samples collected from 9 wastewater treatment plants (WWTPs) in Canada to investigate the occurrence and fate of these contaminants. The median concentrations of Sigma SDPAs and Sigma BZT-UVs was 483 and 76.2 ng L⁻¹ in influent, 28.4 and 4.84 ng L⁻¹ in effluent, and 2750 and 457 ng g⁻¹ in biosolids (dry weight), respectively. Dinonyl-diphenylamine (C9C9) was the predominant congener of SDPAs in all matrices (>40%). For target BZT-UVs, the major components were 2-(2H-benzotriazol-2-yl)-4,6-bis(1-methyl-1-phenylethyl)phenol (UV234) and 2-(2H-benzotriazol-2-yl)-4,6-di-tert-pentylphenol (UV328). SDPAs and BZT-UVs were effectively removed (>90%) from the liquid stream in most WWTPs mainly through sludge sorption and separation, but biotransformation, UV treatment and filtration may also contribute to removal of some contaminants in advanced treatment plants. In contrast, the removal efficiency of target contaminants using chemically assisted primary treatment was low, likely due to the short hydraulic retention time of this site. Our results suggest that wastewater effluent is a vector of SDPAs and BZT-UVs to the aquatic environment. The results also highlight the high concentrations of SDPAs and BZT-UVs associated with the solid stream in WWTPs, which could affect the beneficial use of biosolids (e.g., compost or land applications).

Luo, J. M., Liu, T. C., Zhang, D. Y., Yin, K., Wang, D., Zhang, W. Q., . . . Crittenden, J. C. (2019). The Individual and Co-Exposure Degradation of Benzophenone Derivatives by UV/H₂O₂ and UV/PDS in Different Water Matrices. *Water Research*, 159, 102-110
<https://doi.org/10.1016/j.watres.2019.05.019>

Benzophenone derivatives, including benzophenone-1 (C₁₃H₁₀O₃, BP1), benzophenone-3 (C₁₄H₁₂O₃, BP3) and benzophenone-8 (C₁₄H₁₂O₄, BP8), that used as UV filters are currently viewed as emerging contaminants. Degradation behaviors on co-exposure benzophenone derivatives using UV-driven advanced oxidation processes under different aqueous environments are still unknown. In this study, the degradation behavior of mixed benzophenone derivatives via UV/H₂O₂ and UV/peroxydisulfate (PDS), in different water matrices (surface water, hydrolyzed urine and seawater) were systematically examined. In surface water, the attack of BP3 by hydroxyl radicals (HO center dot) or carbonate radicals (CO₃ center dot-) in IN/H₂O₂ can generate BP8, which was responsible for the relatively high degradation rate of BP3. Intermediates from BP3 and BP8 in UV/PDS were susceptible to CO₃ center dot-, bringing inhibition of BP1 degradation. In hydrolyzed urine, Cl⁻ was shown the negligible effect for benzophenone derivatives degradation due to low concentration of reactive chlorine species (RCS). Meanwhile, BP3 abatement was excessively inhibited during co-exposure pattern. In seawater, non-first-order kinetic behavior for BP3 and BP8 was found during UV/PDS treatment. Based on modeling, Br⁻ was the sink for HO center dot, and the co-existence of Br⁻ and Cl⁻ was the sink for SO₄ center dot-. The cost-effective treatment toward target compounds removal in different water matrices was further

evaluated using EE/O. In most cases, UV/H₂O₂ process is more economically competitive than UV/PDS process.

MacManus-Spencer, L. A., Tse, M. L., Klein, J. L., & Kracunas, A. E. (2011). Aqueous Photolysis of the Organic Ultraviolet Filter Chemical Octyl Methoxycinnamate. *Environmental Science and Technology*, 45(9), 3931-3937 <https://doi.org/10.1021/es103682a>

Organic UV filter chemicals are the active ingredients in personal care products designed to protect the skin from UV radiation, and hundreds of tons are estimated to be produced annually. Despite their entrance into the aquatic environment by both direct and indirect routes and their detection in surface waters and fish, little is known about their environmental fate. UV filter chemicals are designed to be photostable, but some undergo transformation upon exposure to UV light. Octyl methoxycinnamate (OMC), a commonly used UV filter chemical, degrades rapidly by direct photolysis; previous studies have focused on its photoisomerization, and a few investigators have reported the formation of cyclodimers. Here, we present the kinetics and quantum efficiency of the direct photolysis of OMC and confirm that dimerization occurs as a result of direct photolysis in aqueous solution. Likely identities of the dimers are offered based on comparison to reported results for other cinnamate derivatives. We have identified additional products of direct photolysis that have not been previously reported and investigated their photostability, as well as the mechanism of product formation. There is also some evidence of indirect photolysis in the presence of dissolved natural organic matter.

Manasfi, T., Coulomb, B., Ravier, S., & Boudenne, J. L. (2017). Degradation of Organic UV Filters in Chlorinated Seawater Swimming Pools: Transformation Pathways and Bromoform Formation. *Environmental Science and Technology*, 51(23), 13580-13591 <https://doi.org/10.1021/acs.est.7b02624>

Organic ultraviolet (UV) filters are used in sunscreens and other personal-care products to protect against harmful effects of exposure to UV solar radiation. Little is known about the fate of UV filters in seawater swimming pools disinfected with chlorine. The present study investigated the occurrence and fate of five commonly used organic UV filters, namely dioxybenzone, oxybenzone, avobenzone, 2-ethylhexyl-4-methoxycinnamate, and octocrylene, in chlorinated seawater swimming pools. Pool samples were collected to monitor the variation of UV filter concentrations during pool opening hours. Furthermore, laboratory-controlled chlorination experiments were conducted in seawater spiked with UV filters to investigate the reactivity of UV filters. Extracts of chlorination reaction samples were analyzed using high-resolution mass spectrometry and electron-capture detection to identify the potentially formed byproducts. In the collected pool samples, all the UV filters except dioxybenzone were detected. Chlorination reactions showed that only octocrylene was stable in chlorinated seawater. The four reactive UV filters generated brominated transformation products and disinfection byproducts. This formation of brominated products resulted from reactions between the reactive UV filters and bromine, which is formed rapidly when chlorine is added to seawater. Based on the identified byproducts, the transformation pathways of the reactive UV filters were proposed for the first time. Bromoform was generated by all the reactive UV filters at different yields. Bromal hydrate was also detected as one of the byproducts generated by oxybenzone and dioxybenzone.

Manasfi, T., De Meo, M., Coulomb, B., Di Giorgio, C., Ravier, S., & Boudenne, J. L. (2019). Development of Transient Mutagenic Activity Following the Chlorination of the Sunscreen UV Filter

Dioxybenzone (Benzophenone-8) in Bromide-Rich Water. *International Journal of Hygiene and Environmental Health* <https://doi.org/10.1016/j.ijheh.2019.04.003>

The mutagenicity of four organic UV filters namely oxybenzone (benzophenone-3), dioxybenzone (benzophenone-8), avobenzone, and octyl methoxycinnamate, in chlorinated bromide-rich water (artificial seawater) was investigated. Mutagenicity was evaluated using Ames test in *Salmonella typhimurium* TA98 without S9 mix. Chemical analysis using high-resolution mass spectrometry was carried out to elucidate the mutagenic transformation products. Among the studied UV filters, only dioxybenzone exhibited a clear mutagenic activity following chlorination in seawater at ratio 1:10 (UV filter:chlorine). In contrast, no mutagenic activity was detected when chlorine was added at higher doses (ratio 1:1000). High-resolution mass spectrometry analysis showed that mutagenic extracts contained several brominated transformation products of dioxybenzone. Time course analysis of the transformation products at increasing chlorine doses showed that they were unstable and disappeared more quickly at higher chlorine doses. This instability explained the absence of mutagenic activity of dioxybenzone when 1000-fold excess chlorine was added, as no transformation products were detected. Relevance of these findings to the context of swimming pool is discussed. Further investigations taking into consideration the mutagenicity of not only the intermediate transformation products but also the final disinfection byproducts are needed to determine the overall impact of high levels of chlorine on the overall mutagenicity. This study highlights the importance of considering the reactivity of organic UV filters and their transformation products in disinfected recreational waters when sunscreen formulations are prepared.

Mao, F., You, L., Reinhard, M., He, Y., & Gin, K. Y. (2018). Occurrence and Fate of Benzophenone-Type UV Filters in a Tropical Urban Watershed. *Environmental Science and Technology*, 52(7), 3960-3967 <https://doi.org/10.1021/acs.est.7b05634>

The study investigated the occurrence and fate of seven benzophenone-type UV filters (i.e., 2,4-dihydroxybenzophenone (2,4OH-BP), 2,2',4,4'-tetrahydroxybenzophenone (2,2',4,4'OH-BP), 2-hydroxy-4-methoxybenzophenone (2OH-4MeO-BP), 2,2'-Dihydroxy-4,4'-dimethoxybenzophenone (2,2'OH-4,4'MeO-BP), 2,2'-dihydroxy-4-methoxybenzophenone (2,2'OH-4MeO-BP), 4-hydroxybenzophenone (4OH-BP), and 4,4'-dihydroxybenzophenone (4DHB)) in a tropical urban watershed consisting of five major tributaries that discharge into a well-managed basin. Total benzophenone concentrations (summation operatorCBPs) varied from 19-230.8 ng L(-1) in overlying bulk water, 48-115 ng L(-1) in pore water, 295-5813 ng g(-1) dry weight (d.w.) in suspended solids, and 6-37 ng g(-1) d.w. in surficial sediments, respectively. The tributaries (summation operatorCBPs: 19-231 ng L(-1)) were the main source of benzophenone compounds entering the basin (summation operatorCBPs: 20-81 ng L(-1)). In the water column, the vertical concentration profile in the aqueous phase was uniform while concentrations in the suspended solids decreased with depth. Different distribution profiles were also identified for benzophenones in suspended solids and sediments. A preliminary risk assessment suggested that the seven BPs were unlikely to pose ecotoxicological risks to local aquatic organisms except for 2OH-4MeO-BP in the case of an intermittent release.

Mao, L., Meng, C., Zeng, C., Ji, Y., Yang, X., & Gao, S. (2011). The Effect of Nitrate, Bicarbonate and Natural Organic Matter on the Degradation of Sunscreen Agent P-Aminobenzoic Acid by Simulated Solar Irradiation. *Science of The Total Environment*, 409(24), 5376-5381 <https://doi.org/10.1016/j.scitotenv.2011.09.012>

Our experiments revealed that a model sunscreen agent, p-aminobenzoic acid (PABA), can be effectively transformed through reactions that are mediated by simulated solar irradiation. We systematically explored the effects of nitrate ions, bicarbonate and different types of natural organic matter (NOM) on the degradation of PABA by simulated solar irradiation. Experimental data suggest that these components ubiquitous in nature water have different influence on the rates of the photoinduced removal of PABA. Products were extracted and analyzed using LC/MS and a total of four products probably resulting from OH and NO₂ radicals attack were identified and the possible reaction pathways were proposed. The findings in this study provide useful information for understanding the environmental transformation of sunscreen agent in aquatic system.

Molins-Delgado, D., Diaz-Cruz, M. S., & Barcelo, D. (2016). Ecological Risk Assessment Associated to the Removal of Endocrine-Disrupting Parabens and Benzophenone-4 in Wastewater Treatment. *Journal of Hazardous Materials*, 310, 143-151 <https://doi.org/10.1016/j.jhazmat.2016.02.030>

The occurrence of four widely used and endocrine disrupting parabens (PBs) (methylparaben, propylparaben, butylparaben and benzylparaben) and a polar UV filter (benzophenone-4) were determined in influent and effluent wastewater from the 19 major wastewater treatment plants (WWTPs) of Catalonia, Spain. For their analysis an on-line solid-phase extraction-liquid chromatography-tandem mass spectrometry (SPE-HPLC-MS/MS) method was developed and validated. Laboratory analysis revealed high levels for both PBs and BP4, with maximum concentrations of 5700ngL⁻¹ and 1806ngL⁻¹, respectively, in influent samples, and 137ngL⁻¹ and 1080ngL⁻¹, respectively in effluent wastewaters. Removal rates (RE%) for the target compounds in each WWTPs were calculated. RE% for parabens were almost 100%, whereas for BP4 values were in the range 5-91%. The half-life time (t_{1/2}), hydraulic retention time (HRT), and annual mass load (ML) for each facility was estimated. Results indicated that there was no clear influence of HRT on the RE% of BP4. MLs for BP4 were in the range 0.9-110.1kg_y⁻¹, with the highest values in the most populated areas. Finally, a risk assessment, estimated in terms of hazard quotients (HQs), was carried out for aquatic biota. HQs for the target compounds in effluent wastewaters indicated a negligible effect, whereas for some influent wastewaters' HQs pointed out that some species are at risk.

Mturi, G. J., & Martincigh, B. S. (2008). Photostability of the Sunscreening Agent 4-Tert-Butyl-4'-Methoxydibenzoylmethane (Avobenzone) in Solvents of Different Polarity and Proticity. *Journal of Photochemistry and Photobiology A: Chemistry*, 200(2-3), 410-420 <https://doi.org/10.1016/j.jphotochem.2008.09.007>

The most widely used UVA absorber in broad-spectrum sunscreens is 4-tert-butyl-4'-methoxydibenzoylmethane (avobenzone). However, the photostability of avobenzone is solvent-dependent. The aim of this work was to investigate the photostability of avobenzone in solvents of different polarity and proticity. Four solvents were employed, namely, cyclohexane, ethyl acetate, dimethylsulfoxide and methanol. The cause of the instability of avobenzone in these solvents was determined by means of UV spectroscopy, high performance liquid chromatography, gas chromatography-mass spectrometry and nuclear magnetic resonance spectroscopy. The effect of oxygen on the photo-instability was also determined. Avobenzone was found to lose absorption efficacy as a result of photoisomerisation from the enol to the keto form and/or photodegradation to form photoproducts that absorb principally in the UVC region, depending on the solvent. It was found to be essentially photostable in the polar protic solvent methanol but photoisomerised in the polar aprotic solvent dimethylsulfoxide. In the nonpolar solvent cyclohexane, it photodegraded appreciably. Both

photoisomerisation and photodegradation occurred to a similar extent in the moderately polar aprotic solvent ethyl acetate. Photoisomerisation occurred only in the presence of oxygen whereas photodegradation occurred irrespective of oxygen. This knowledge is important in order to achieve the correct formulation for sunscreens incorporating avobenzone.

Necasova, A., Banyiova, K., Literak, J., & Cupr, P. (2016). New Probabilistic Risk Assessment of Ethylhexyl Methoxycinnamate: Comparing the Genotoxic Effects of Trans- and Cis-EHMC. *Environmental Toxicology* <https://doi.org/10.1002/tox.22260>

Ethylhexyl methoxycinnamate (EHMC) is a widely used UV filter present in a large number of personal care products (PCPs). Under normal conditions, EHMC occurs in a mixture of two isomers: trans-EHMC and cis-EHMC in a ratio of 99:1. When exposed to sunlight, the trans isomer is transformed to the less stable cis isomer and the efficiency of the UV filter is reduced. To date, the toxicological effects of the cis-EHMC isomer remain largely unknown. We developed a completely new method for preparing cis-EHMC. An EHMC technical mixture was irradiated using a UV lamp and 98% pure cis-EHMC was isolated from the irradiated solution using column chromatography. The genotoxic effects of the isolated cis-EHMC isomer and the nonirradiated trans-EHMC were subsequently measured using two bioassays (SOS chromotest and UmuC test). In the case of trans-EHMC, significant genotoxicity was observed using both bioassays at the highest concentrations (0.5 - 4 mg mL⁻¹). In the case of cis-EHMC, significant genotoxicity was only detected using the UmuC test at concentrations of 0.25 - 1 mg mL⁻¹. Based on these results, the NOEC was calculated for both cis- and trans-EHMC, 0.038 and 0.064 mg mL⁻¹, respectively. Risk assessment of dermal, oral and inhalation exposure to PCPs containing EHMC was carried out for a female population using probabilistic simulation and by using Quantitative in vitro to in vivo extrapolation (QIVIVE). The risk of cis-EHMC was found to be approximately 1.7 times greater than trans-EHMC. In the case of cis-EHMC, a hazard index of 1 was exceeded in the 92nd percentile. Based on the observed differences between the isomers, EHMC application in PCPs requires detailed reassessment. Further exploration of the toxicological effects and properties of cis-EHMC is needed in order to correctly predict risks posed to humans and the environment.

Pan, X., Yan, L., Qu, R., & Wang, Z. (2018). Degradation of the UV-Filter Benzophenone-3 in Aqueous Solution Using Persulfate Activated by Heat, Metal Ions and Light. *Chemosphere*, 196, 95-104 <https://doi.org/10.1016/j.chemosphere.2017.12.152>

The goals of this study were to bring forward new data and insights into the effect of activation methods, operational variables and reaction pathways during sulfate radicals-based oxidation of benzophenone-3 (BP-3) in aqueous solution. Heat, transition metal ions (Fe(2+), Cu(2+), Co(2+)), UV and visible light irradiation were used to activate persulfate (PS) to degrade BP-3. The results showed that these three activation methods can remarkably enhance BP-3 removal efficiency. Under the conditions of [BP-3]: [PS]₀=1: 500, pH=7.0, and 40 degrees C, complete removal of BP-3 (1.31μM) was observed in 3h. In the pH range of 3.0-9.0, the degradation of BP-3 decreased with increasing pH. Increasing the PS dosage accelerated the reaction, while the presence of humic acid (HA) significantly inhibited the efficiency of BP-3 removal. Based on electron paramagnetic resonance (EPR) and radical quenching studies, sulfate and hydroxyl radicals contributed to the oxidation process. According to the evolution of BP-3 and its 7 by-products, as well as frontier electron densities (FED) calculation, two routes were proposed involving hydroxylation, demethylation and direct oxidation. On the whole, this work is a unique contribution to the systematic elucidation of BP-3 removal by PS.

Ramos, S., Homem, V., Alves, A., & Santos, L. (2016). A Review of Organic UV-Filters in Wastewater Treatment Plants. *Environment International*, 86, 24-44
<https://doi.org/10.1016/j.envint.2015.10.004>

UV-filters are a group of compounds which have been massively used in the past years due to the recent concerns with sunburns, premature skin ageing and the risk of developing skin cancer, related to sun exposure. At the moment, these compounds have been identified by the scientific community as emerging pollutants, due to their persistence in the environment, potential to accumulate in biota and potential threat as endocrine disruptors. At some point, the majority of sunscreens will find their way into wastewater (due to bathing and washing activities) and because wastewater treatment plants (WWTPs) are not able to remove and/or degrade them, consequently they find their way into rivers, lakes and ocean, so it is not surprising that UV-filters are found in the environment. Therefore, wastewater treatment plants should be the focus of the scientific community aiming to better understand the fate of the UV-filters and develop new technologies to remove them from wastewater and sludge. This review, aims to provide the current state of the art in the occurrence and fate of UV-filters in wastewater treatment plants and how the technologies that are being used are successfully removing these compounds from both wastewater and sludge.

Rodil, R., Moeder, M., Altenburger, R., & Schmitt-Jansen, M. (2009). Photostability and Phytotoxicity of Selected Sunscreen Agents and Their Degradation Mixtures in Water. *Analytical and Bioanalytical Chemistry*, 395(5), 1513-1524 <https://doi.org/10.1007/s00216-009-3113-1>

The study on the photostability of six UV filters in aqueous solution was combined with investigations on the phytotoxicity of the produced degradation mixtures. During the exposure to artificial sunlight over 72 h, the degradation of three of the UV filters evaluated was observed with half-lives between 20 and 59 h. The structural changes of iso-amylmethoxy-cinnamate (IAMC), ethylhexyl-methoxy-cinnamate (EHMC), and 4-methylbenzyliden camphor (4-MBC) occurred during irradiation were consistent with isomerisation and polymerization (IAMC and EHMC) whereas 2-ethylhexyl-4-(dimethylamino)benzoate (OD-PABA) was degraded. The analysis of the UV filters and their degradation products was performed by stir bar sorptive extraction (SBSE) followed by thermodesorption-gas chromatography-mass spectrometry (TD-GC-MS) or liquid desorption-liquid chromatography-mass spectrometry (LD-LC-MS). The phytotoxicological potential of the UV filters was examined in vitro by evaluating reproduction inhibition of the chlorophyte microalgae *Scenedesmus vacuolatus*. Excess toxicity was calculated by comparing experimental derived median efficiencies after log-logistic modeling to predict effects assuming narcotic mode of action. Benzophenone-3 (BP-3) showed 43-fold higher toxicity than theoretically predicted and a more specific mode of action was assumed. The other UV filters tested indicated toxicity in the range of modeled narcosis. For IAMC, EHMC, and OD-PABA the phytotoxicity of their photodegradation mixtures was followed over time. Phytotoxicity decreased directly with the reduction of the parent substance from the solution. Five of the tested UV filters do not represent a risk at least for algae. Octocrylen and 4-MBC were found to be photostable but few toxic to algae. EHMC, IAMC, and OD-PABA were fast degraded during UV radiation and the phytotoxicity of the corresponding degradation mixtures was low and decreased onward during exposure. Thus, for the UV filters studied, it could be confirmed that sunlight can account noticeably for decontamination and detoxification of contaminated water. However, due to its potential accumulation in combination with a specific mode of action, BP-3 may imply probable environmental risks at least to algae. This study emphasizes the need of a combined chemical and toxicological evaluation for a reliable risk assessment concerning degradation processes exemplified here for UV-protecting agents.

Santos, A. J., Miranda, M. S., & Esteves da Silva, J. C. (2012). The Degradation Products of UV Filters in Aqueous and Chlorinated Aqueous Solutions. *Water Research*, 46(10), 3167-3176
<https://doi.org/10.1016/j.watres.2012.03.057>

Ultraviolet (UV) filters are vital constituents of sunscreens and other personal care products since they absorb, reflect and/or scatter UV radiation, therefore protecting us from the sun's deleterious UV radiation and its effects. However, they suffer degradation, mainly through exposure towards sunlight and from reactions with disinfectant products such as chlorine. On the basis of their increasing production and use, UV filters and their degradation products have already been detected in the aquatic environment, especially in bathing waters. This paper presents a comprehensive review on the work done so far as to identify and determine the by-products of UV filter photodegradation in aqueous solutions and those subsequent to disinfection-induced degradation in chlorinated aqueous solutions, namely swimming pools.

Santos, A. J. M., & Esteves da Silva, J. C. G. (2019). Environmental Fate and Behaviour of Benzophenone-8 in Aqueous Solution. *Environmental Technology & Innovation*, 13, 48-61
<https://doi.org/10.1016/j.eti.2018.10.010>

The fate and behaviour of 2-hydroxy-4-methoxyphenyl)-(2-hydroxyphenyl)-methanone, ordinarily known as benzophenone-8 (BP8), in aqueous solution, is thoroughly addressed in this study. The reactions were followed by means of high-performance liquid chromatography coupled with ultraviolet, diode-array detection (HPLC-UV-DAD). Potential by-products of degradation were analysed and determined by liquid chromatography coupled with diode-array detection and mass spectrometry (LC-DAD-MS). BP8 displayed very significant reactivity towards free available chlorine, following a pseudo-first order kinetic profile with rate constant $k_{obs}=0.0036 \pm 0.0002 \text{ s}^{-1}$ and a half-life period of $t_{1/2}=194.12 \pm 7.90 \text{ s}$. Disinfection-induced degradation yielded only monochlorinated and dichlorinated disinfection by-products (DBPs). With or without dissolved organic matter (DOM) in solution, the pH and chlorine concentration were the only influential variables on degradation. Photo-induced degradation was assessed by means of exposure to artificial solar radiation. The compound proved to be extremely photo-stable, with a kinetic rate constant of $k=0.00083 \pm 0.00002 \text{ min}^{-1}$ and a half-life period of $t_{1/2}=835.12 \pm 20.12 \text{ min}$. Exposure to artificial solar radiation did not generate any meaningful alterations in the UV spectrum of BP8. There are indications of the possible formation of a photo-isomer, but its extremely low significance and intensity, even after pre-concentration, deemed it negligible.

Semones, M. C., Sharpless, C. M., MacKay, A. A., & Chin, Y.-P. (2017). Photodegradation of UV Filters Oxybenzone and Sulisobenzene in Wastewater Effluent and by Dissolved Organic Matter. *Applied Geochemistry*, 83, 150-157 <https://doi.org/10.1016/j.apgeochem.2017.02.008>

Organic UV-filters are key ingredients found in sunscreens, cosmetics and plastic goods. Concerns have been raised about potential ecological and human health effects of certain organic UV filters that are currently FDA approved for use in the United States. Here, we investigate the photochemical fate of two of these compounds, oxybenzone and sulisobenzene. Both oxybenzone and sulisobenzene have previously been detected in surface waters, seawater, and treated wastewater effluent. Direct photolysis is found to be unimportant for these compounds, however, enhanced photodegradation of oxybenzone and sulisobenzene was observed under simulated solar irradiation in solutions of

International Humic Substance Society standards (Pony Lake fulvic acid and Suwannee River natural organic matter), filtered wastewater effluent (Southerly Wastewater Treatment Plant in Lockbourne, OH), and Scioto River water (Columbus, OH) at pH 7. Quenching experiments with isopropanol revealed that the main pathway for degradation appears to be reaction with the hydroxyl radical (OH). Observed degradation rates were 2–3 times slower than estimates calculated using literature reported second-order rate constants and measured hydroxyl radical steady-state concentrations for Suwannee River natural organic matter, Pony Lake fulvic acid and Scioto waters. The Southerly sample, however, exhibited nearly identical expected and observed rate constants, which we take to indicate the presence of unidentified reactive species that can react with oxybenzone and sulisobenzene. Values obtained in this work were used to calculate second-order rate constants for oxybenzone and sulisobenzene with the hydroxyl radical, as well as to estimate environmental half-lives for these compounds. Near surface 24-h averaged half-lives of 3.0 and 4.0 days were calculated for oxybenzone and sulisobenzene, respectively. When extrapolated to an environmentally representative water column, these same 24-h averaged half-lives increased to 2.4 and 3.5 years, respectively.

Serra-Roig, M. P., Jurado, A., Diaz-Cruz, M. S., Vazquez-Sune, E., Pujades, E., & Barcelo, D. (2016). Occurrence, Fate and Risk Assessment of Personal Care Products in River-Groundwater Interface. *Science of The Total Environment*, 568, 829-837
<https://doi.org/10.1016/j.scitotenv.2016.06.006>

This work presents the occurrence and fate of selected personal care products (PCPs) in the urban river-groundwater interface. To this end, urban river and groundwater samples were collected in Sant Adria del Besos (NE of Spain) and a total of 16 PCPs were analyzed including benzophenone derivatives, camphor derivatives, p-aminobenzoic acid derivatives, triazoles and parabens in three different campaigns (from May 2010 to July 2014). These compounds reach the aquifer through the recharge of Besos River that receives large amounts of effluents from waste water treatment plants. Results have shown that most of the compounds were not or barely detected (maximum concentrations around 200 ng/L) in groundwater samples during the different sampling campaigns. Only two triazoles, namely benzotriazole (BZT) and methyl benzotriazol (MeBZT) were found at high concentrations in groundwater samples (maximum concentration around 2000 ng/L). The fate of PCPs in the aquifer was assessed using mixing analysis considering the seasonal variability of the Besos River. Overall, measured groundwater concentrations were significantly much lower than those estimated by the mixing of the river water. This observation suggested that most of the PCPs are naturally removed when river water infiltrates the aquifer. However, some compounds were more persistent in the aquifer. These compounds were in descending order: the triazoles BZT and MeBZT followed by the camphor derivative 4MBC and the paraben MePB. The measured concentrations allowed us to assess the environmental risk posed by the selected UV-filters and parabens in the river and groundwater samples. Hazard Quotients (HQs) for different aquatic species were calculated in order to characterize the ecotoxicity potential of the studied compounds in the river-groundwater interface. HQ values were always below 1 indicating that at the concentrations observed in the surface or aquifer water of Besos River these compounds pose no risk to the selected aquatic organisms.

Slomberg, D. L., Ollivier, P., Miche, H., Angeletti, B., Bruchet, A., Philibert, M., . . . Labille, J. (2019). Nanoparticle Stability in Lake Water Shaped by Natural Organic Matter Properties and Presence

of Particulate Matter. *Science of The Total Environment*, 656, 338-346
<https://doi.org/10.1016/j.scitotenv.2018.11.279>

Predicting nanoparticle (NP) fate in the environment continues to remain a challenge, especially for natural surface water systems, where NPs can hetero-aggregate with natural organic and mineral suspended matter. Here we present the interactions and aggregation behavior of TiO₂ NPs with natural organic matter (NOM) in a natural lake water. NP fate in a synthetic water of the same pH and ionic composition was also tested in the presence and absence of NOM analogs to gain insight into the different stabilizing effects of each NOM type. Several complementary analytical techniques were utilized to assess lake NOM composition, including pyrolysis-gas chromatography-mass spectrometry, gel permeation chromatography, the polarity rapid-assessment method, and Nanoparticle Tracking Analysis. In the natural lake water, the TiO₂ NPs preferentially interacted with mostly anionic NOM of high and medium molecular weight (~1200-1450 and 400-520Da). Specifically, strong interactions with proteins and polyhydroxy aromatics were observed. NP fate and stability were determined in both raw lake water containing mineral particulate matter and total NOM (NOM_{tot}) and filtered lake water containing only NOM <0.8µm (NOM<0.8), with different aggregation profiles observed over time. Additionally, three times the number of TiO₂ NPs remained in suspension when only NOM<0.8 was present compared to the unfiltered water containing mineral particulate matter and NOM_{tot}. These results demonstrate the contrasting NP fates in the aquatic environment according to the presence of NOM_{tot} vs. NOM<0.8 and further suggest that the use of pure NOM analogs may not accurately represent NP interactions and fate in the natural system.

Trebse, P., Polyakova, O. V., Baranova, M., Kralj, M. B., Dolenc, D., Sarakha, M., . . . Lebedev, A. T. (2016). Transformation of Avobenzone in Conditions of Aquatic Chlorination and UV-Irradiation. *Water Research*, 101, 95-102 <https://doi.org/10.1016/j.watres.2016.05.067>

Emerging contaminants represent a wide group of the most different compounds. They appear in the environment at trace levels due to human activity. Most of these compounds are not yet regulated. Sunscreen UV-filters play an important role among these emerging contaminants. In the present research the reactions of 4-tert-butyl-4'-methoxydibenzoylmethane (avobenzone), the most common UV filter in the formulation of sunscreens, were studied under the combined influence of active chlorine and UV-irradiation. Twenty five compounds were identified by GC/MS as transformation products of avobenzone in reactions of aquatic UV-irradiation and chlorination with sodium hypochlorite. A complete scheme of transformation of avobenzone covering all the semivolatile products is proposed. The identification of the two primary chlorination products (2-chloro-1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)-1,3-propanedione and 2,2-dichloro-1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)-1,3-propanedione) was confirmed by their synthesis and GC/MS and NMR analysis. Although the toxicities of the majority of these products remain unknown substituted chlorinated phenols and acetophenones are known to be rather toxic. Combined action of active chlorine and UV-irradiation results in the formation of some products (chloroanhydrides, chlorophenols) not forming in conditions of separate application of these disinfection methods. Therefore caring for people <<well-being>> it is of great importance to apply the most appropriate disinfection method. Since the primary transformation products partially resist powerful UV-C irradiation they may be treated as stable and persistent pollutants.

Vione, D., Calza, P., Galli, F., Fabbri, D., Santoro, V., & Medana, C. (2015). The Role of Direct Photolysis and Indirect Photochemistry in the Environmental Fate of Ethylhexyl Methoxy Cinnamate

(Ehmc) in Surface Waters. *Science of The Total Environment*, 537, 58-68
<https://doi.org/10.1016/j.scitotenv.2015.08.002>

The aquatic environmental fate of ethylhexyl methoxy cinnamate (EHMC), one of the most used UVB filters worldwide, was studied by assessing its environmental persistence and photoinduced transformations. The role of direct and indirect photolysis was evaluated. Direct photolysis was shown to play a key role, and this process is expected to be the main attenuation route of EHMC in sunlit surface waters. In contrast, the reaction with OH radicals would be negligible and that with (3)CDOM* would at most be a secondary process. The measurement of the quantum yield of direct photolysis and of the rate constants of reaction with photogenerated transient species (or, sometimes, the use of reasonable values for the latter) allowed the prediction of the EHMC half-life time in surface waters, by means of a validated photochemical model. The predicted EHMC lifetime is of the order of hours to a few days in fair-weather summertime, and the main factors controlling the EHMC phototransformation in sunlit surface waters would be the water depth and the dissolved organic carbon (DOC) content. The formation of transformation products (TPs) was followed as well via HPLC/HRMS. Three TPs were detected in the samples exposed to UVA radiation, while one additional TP was detected in the samples exposed to UVB radiation. The detected TPs comprised 4-methoxybenzaldehyde, a hydroxylated derivative and dimeric species. Through the use of heterogeneous photocatalysis with TiO₂, seven additional TPs were identified, most of them resulting from the further degradation of primary TPs formed through direct photolysis and that might be detected in aquatic systems as well. The photodegradation of EHMC in the presence of TiO₂ yielded more toxic TPs than the parent compound (as determined with the *Vibrio fischeri* Microtox assay). The increased toxicity is partially accounted for by the formation of 4-methoxybenzaldehyde.

Vione, D., Caringella, R., De Laurentiis, E., Pazzi, M., & Minero, C. (2013). Phototransformation of the Sunlight Filter Benzophenone-3 (2-Hydroxy-4-Methoxybenzophenone) under Conditions Relevant to Surface Waters. *Science of The Total Environment*, 463–464(0), 243-251
<https://doi.org/10.1016/j.scitotenv.2013.05.090>

The UV filter benzophenone-3 (BP3) has UV photolysis quantum yield $\Phi_{BP3} = (3.1 \pm 0.3) \cdot 10^{-5}$ and the following second-order reaction rate constants: with $\bullet OH$, $k_{BP3, \bullet OH} = (2.0 \pm 0.4) \cdot 10^{10} M^{-1} s^{-1}$; with the triplet states of chromophoric dissolved organic matter (3CDOM*), $k_{BP3, 3CDOM^*} = (1.1 \pm 0.1) \cdot 10^9 M^{-1} s^{-1}$; with 1O_2 , $k_{BP3, ^1O_2} = (2.0 \pm 0.1) \cdot 10^5 M^{-1} s^{-1}$, and with $CO_3^{\bullet-}$, $k_{BP3, CO_3^{\bullet-}} < 5 \cdot 10^7 M^{-1} s^{-1}$. These data allow the modelling of BP3 photochemical transformation, which helps filling the knowledge gap about the environmental persistence of this compound. Under typical surface-water conditions, direct photolysis and reactions with $\bullet OH$ and 3CDOM* would be the main processes of BP3 phototransformation. Reaction with $\bullet OH$ would prevail at low DOC, direct photolysis at intermediate DOC (around 5 mg C L⁻¹), and reaction with 3CDOM* at high DOC. If the reaction rate constant with $CO_3^{\bullet-}$ is near the upper limit of experimental measures ($5 \cdot 10^7 M^{-1} s^{-1}$), the $CO_3^{\bullet-}$ degradation process could be somewhat important for DOC < 1 mg C L⁻¹. The predicted half-life time of BP3 in surface waters under summertime conditions would be of some weeks, and it would increase with increasing depth and DOC. BP3 transformation intermediates were detected upon reaction with $\bullet OH$. Two methylated derivatives were tentatively identified, and they were probably produced by reaction between BP3 and fragments arising from photodegradation. The other intermediates were benzoic acid (maximum concentration ~ 10% of initial BP3) and benzaldehyde (1%).

Volpe, A., Pagano, M., Mascolo, G., Grenni, P., & Rossetti, S. (2017). Biodegradation of UV-Filters in Marine Sediments. *Science of The Total Environment*, 575, 448-457
<https://doi.org/10.1016/j.scitotenv.2016.10.001>

The degradation of two of the most frequently used UV-filters was investigated through microcosm studies. Marine sediments sampled from two sites in Italy (La Spezia harbour and Sarno river estuary, S1 and S2 respectively) were used to set up aerobic and anaerobic sets of reactors. The sediments were spiked with a methanol solution of 3-(4-methylbenzylidene)camphor (4-MBC) and 2-ethylhexyl 4-(dimethylamino)benzoate (EH-DPAB), at concentrations of either 25 or 50mgkg⁻¹ each. Methanol (6.3g/L) also served as an organic amendment and growth substrate for improving microbial activity. Monitoring of the biotic and abiotic degradation of the selected contaminants over 16months revealed that 4-MBC biodegradation was very slow and incomplete, whereas over 90% of EH-DPAB was degraded both in the aerobic and the anaerobic reactors by the natural microbial communities of both sediments. Repeated spikes of EH-DPAB were followed by complete decay, characterised by first-order kinetics. The calculated kinetic rate constants under aerobic and anaerobic conditions were similar. In reactors inoculated with the S1 sediment the degradation rate constants progressively increased after each spike, up to the value of 0.039d⁻¹. For the S2 sediment the rate constant was around 0.020d⁻¹ throughout the duration of the experiment. Mass spectrometry analysis of sediment extracts allowed detection of potential transformation products of EH-DPAB and 4-MBC. Moreover, the natural microbial community of the sediments was studied using the CAlyzed Reporter Deposition Fluorescence In Situ Hybridization (CARD-FISH) both in the initial sediments and after degradation under aerobic and anaerobic conditions.

Wang, C., Bavcon Kralj, M., Kosmrlj, B., Yao, J., Kosenina, S., Polyakova, O. V., . . . Trebse, P. (2017). Stability and Removal of Selected Avobenzene's Chlorination Products. *Chemosphere*, 182, 238-244 <https://doi.org/10.1016/j.chemosphere.2017.04.125>

Stability studies of two avobenzene transformation products: chloro-avobenzene [2-chloro-1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)-1,3-propanedione] and dichloro-avobenzene [2,2-dichloro-1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)-1,3-propanedione] have been performed at different pHs values as well as under UV A light and compared with the stability of avobenzene, one of the mostly used UV A filter present in sunscreens. We have additionally investigated the possibility of application of TiO₂ photocatalysis as a method for the removal of them. Results have shown the differences in pH stability of all three studied compounds with much slower degradation rate under neutral conditions in comparison to the acidic ones for all three studied compounds. In the case of photolytic experiment, performed under UV A light, dichloro-avobenzene exhibited the lowest UVA stability (half-life 22.4 +/- 0.7 min), while avobenzene and chloro-avobenzene are much more stable and have shown quite similar degradation pattern (half-lives 126 +/- 16 min and 128 +/- 25 min). Under the photocatalytic conditions the less stable was dichloro-avobenzene (half-life 14.1 +/- 0.6 min), while chloro-avobenzene and avobenzene were much more stable (half-lives 41 +/- 3 min and 79 +/- 13 min). Dichloroavobenzene is significantly more reactive than avobenzene and its monochloro-derivative. On the basis of the formation of various stable degradation products, including substituted acetophenones, benzoic acids and phenols, identified by GC-MS, the degradation pathway has been proposed.

Wang, Z., Deb, A., Srivastava, V., Iftexhar, S., Ambat, I., & Sillanpää, M. (2019). Investigation of Textural Properties and Photocatalytic Activity of Pbo/Tio₂ and Sb₂o₃/Tio₂ Towards the Photocatalytic

Benzophenone-3 (BP-3) is a widely used organic UV filter in sunscreen which has been detected in surface and groundwater. BP-3 can affect the aquatic environment and human health. In this study, PbO/TiO₂ and Sb₂O₃/TiO₂ photocatalyst were synthesized for the photocatalytic degradation of Benzophenone-3 (BP-3) and various degradation parameters such as initial pH value, initial concentration, and the dose of catalysts were optimized. Two different TiO₂ based catalysts PbO/TiO₂ and Sb₂O₃/TiO₂ were synthesized by hydrothermal method. Synthesized photocatalysts were characterized by X-ray diffraction pattern (XRD), scanning electron microscope (SEM), Energy Dispersive Spectroscopy (EDS), BET and UV-Vis DRS techniques. Molar ratio variation of PbO and Sb₂O₃ with respect to TiO₂ significantly affected the surface area, structure, and bandgap of photocatalyst and hence the variation in degradation efficiency of the photocatalyst was observed. The BP-3 can be completely degraded by using PbO/TiO₂ within 120 min under UV-C irradiation. The highest degradation of BP-3 was obtained for the 20 µM concentration at pH 7 when the dose was adjusted to be 0.75 g/L. However, negligible degradation of BP-3 was demonstrated in the absence of a catalyst. Moreover, with the catalysts PbO/TiO₂ and Sb₂O₃/TiO₂, BP-3 followed the pseudo-first-order kinetics with a rate constant of $3.58 \times 10^{-2} \text{ min}^{-1}$ and $0.92 \times 10^{-2} \text{ min}^{-1}$ respectively. Electron paramagnetic resonance (EPR) spectrum with three distinct peaks with an intensity of 1:1:1 showed the presence of TEMP-1O2 adduct which suggested the generation of ¹O₂ (singlet oxygen) in both catalysts. The plausible mechanism of BP-3 degradation was proposed by the Gas chromatography-mass spectrometry (GC-MS) analysis which showed the formation of pentamethyl- and 5-Hydroxy-7-methoxy-2-methyl-3-phenyl-4-chromenone byproducts on BP-3 photocatalytic degradation by the synthesized catalyst.

Wang, Z., Deb, A., Srivastava, V., Iftekhhar, S., Arnbhat, I., & Sillanpaa, M. (2019). Investigation of Textural Properties and Photocatalytic Activity of Pbo/Tio2 and Sb2o3/Tio2 Towards the Photocatalytic Degradation Benzophenone-3 UV Filter. *Separation and Purification Technology*, 228, 13
<https://doi.org/10.1016/j.seppur.2019.115763>

Benzophenone-3 (BP-3) is a widely used organic UV filter in sunscreen which has been detected in surface and groundwater. BP-3 can affect the aquatic environment and human health. In this study, PbO/TiO₂ and Sb₂O₃/TiO₂ photocatalyst were synthesized for the photocatalytic degradation of Benzophenone-3 (BP-3) and various degradation parameters such as initial pH value, initial concentration, and the dose of catalysts were optimized. Two different TiO₂ based catalysts PbO/TiO₂ and Sb₂O₃/TiO₂ were synthesized by hydrothermal method. Synthesized photocatalysts were characterized by X-ray diffraction pattern (XRD), scanning electron microscope (SEM), Energy Dispersive Spectroscopy (EDS), BET and UV-Vis DRS techniques. Molar ratio variation of PbO and Sb₂O₃ with respect to TiO₂ significantly affected the surface area, structure, and bandgap of photocatalyst and hence the variation in degradation efficiency of the photocatalyst was observed. The BP-3 can be completely degraded by using PbO/TiO₂ within 120 min under UV-C irradiation. The highest degradation of BP-3 was obtained for the 20 µM concentration at pH 7 when the dose was adjusted to be 0.75 g/L. However, negligible degradation of BP-3 was demonstrated in the absence of a catalyst. Moreover, with the catalysts PbO/TiO₂ and Sb₂O₃/TiO₂, BP-3 followed the pseudo-first-order kinetics with a rate constant of $3.58 \times 10^{-2} \text{ min}^{-1}$ and $0.92 \times 10^{-2} \text{ min}^{-1}$ respectively. Electron paramagnetic resonance (EPR) spectrum with three distinct peaks with an intensity of 1:1:1 showed the presence of TEMP-O-1(2) adduct which suggested the generation of ¹O₂ (singlet oxygen) in both catalysts. The plausible mechanism of BP-3 degradation was proposed by the Gas chromatography-mass spectrometry

(GC-MS) analysis which showed the formation of pentamethyl- and 5-Hydroxy-7-methoxy-2-methyl-3-phenyl-4-chromenone byproducts on BP-3 photocatalytic degradation by the synthesized catalyst.

Xiang, Q., Nomura, Y., Fukahori, S., Mizuno, T., Tanaka, H., & Fujiwara, T. (2019). Innovative Treatment of Organic Contaminants in Reverse Osmosis Concentrate from Water Reuse: A Mini Review. *Current Pollution Reports* <https://doi.org/10.1007/s40726-019-00119-2>

Reverse osmosis concentrate (ROC) from wastewater reclamation in water reuse retains concentrated toxic bio-refractory organics, and developing technologies for their removal is essential. This paper reviews innovative treatment technologies for organic contaminants in the ROC, and treatment options for applications are proposed. To adequately manage ROC, volume reduction and quality improvement are important. Forward osmosis (FO) can reduce the ROC volume. Advanced oxidation processes (AOPs) result in degrading organic contaminants and producing biodegradable organics, but the reduction of energy consumption is required. Coagulation is an effective option as a pre-treatment of AOPs and can improve the biodegradability of ROC. Partial use of short-time AOPs can transform high molecular weight organics into relatively biodegradable organics. Among AOPs, a rotating advanced oxidation contactor (RAOC) can be an energy-saving technique for removing bio-refractory organics from ROC using solar light irradiation. Post-biological treatment can significantly save energy and efficiently eliminate biodegradable organics that are produced by AOPs. Microalgae cultivation is also an effective option for resource recovery from ROC. Considering the techniques, an integrated process comprising FO, pre-coagulation, short-time and/or solar-driven AOPs (e.g., RAOC), and post-biological treatment is proposed as an energy-saving and cost-effective technology for ROC treatment.

Yang, P., Kong, D., Ji, Y., Lu, J., Yin, X., & Zhou, Q. (2018). Chlorination and Chloramination of Benzophenone-3 and Benzophenone-4 UV Filters. *Ecotoxicology and Environmental Safety*, 163, 528-535 <https://doi.org/10.1016/j.ecoenv.2018.07.111>

The objective of this research was to explore the fundamental reactions between chlorine/chloramine and 2-hydroxyl-4-methoxyl benzophenone (BP3)/2-hydroxyl-4-methoxyl benzophenone-sulfonic acid (BP4), which were the most common reactions in benzophenone-type UV filters during drinking water treatment processes. Both BP3 and BP4 could react with free chlorine and chloramine, with reactions following pseudo-first-order kinetics in excess of chlorine (HClO) and chloramine (NH₂Cl). Generally, chlorination was more rapid than chloramination. BP4 was less reactive than BP3 toward both chlorine and chloramine, due to the presence of an electron-accepting sulfonate group. Therefore, BP3 had a significantly higher disinfection by-products (DBP) formation potential than BP4. Chlorination of BP3 and BP4 generated remarkably higher levels of DBPs than chloramination, with high pH conditions facilitating the formation of chloroform but inhibiting the formation of haloacetic acid (HAAs). Comparison of the reaction behavior of two different BP-type UV filters, i.e., BP3 and BP4, revealed that certain functional groups significantly affected the reactivity of BP-type UV filters in chlorination and chloramination processes. This contribution may provide new insights into the reaction behavior of UV filters during drinking water disinfection process using chlorine and/or chloramine as disinfectant, and provide guidelines for drinking water safety management.

Yu, Q., Wei, D., Liu, W., & Du, Y. (2017). Acute Toxicity Variation of Hydroxyl Benzophenone UV Filters During Photoinduction-Chlorination Disinfection Processes. *Journal of Environmental Sciences*, 54, 48-55 <https://doi.org/10.1016/j.jes.2016.05.020>

Benzophenones (BPs), a group of widely used UV filters, exert multiple, significant toxicity effects. The 11 BPs were selected as target compounds, and the photobacterium acute toxicity test and an index for acute toxicity formation potential (ATFP) were used to evaluate the toxicity variation of BPs before and after a photoinduction-chlorination disinfection process. Orthogonal experiments were performed at different pH values and chlorine dosages. The characteristics of ATFP values for 11 BPs after a photoinduction-chlorination process can be summarized as follows: (1) The ATFPs decreased as the hydroxyl group number increased in BPs molecules. (2) For those BPs with the same hydroxyl group number, the ATFPs were higher when the hydroxyl groups were located at the 3- or 4-position than those at the 2-position; the BPs with hydroxyl groups distributed on two benzene rings had higher ATFPs than those on one ring. (3) Introducing a methoxyl group and sulfonic acid group into BP molecules increased the ATFP values. (4) The ATFPs were pH-dependent, the values of which were lowest at the neutral condition and highest at the acid condition. (5) The ATFPs increased and then decreased as the chlorine dosage increased. The results can be used as a reference to scientifically evaluate the environmental fate and potential risk of BPs in photoinduction-chlorination disinfection processes.

Zhang, S., Wang, X., Yang, H., & Xie, Y. F. (2016). Chlorination of Oxybenzone: Kinetics, Transformation, Disinfection Byproducts Formation, and Genotoxicity Changes. *Chemosphere*, 154, 521-527
<https://doi.org/10.1016/j.chemosphere.2016.03.116>

UV filters are a kind of emerging contaminant, and their transformation behavior in water treatment processes has aroused great concern. In particular, toxic products might be produced during reaction with disinfectants during the disinfection process. As one of the most widely used UV filters, oxybenzone has received significant attention, because its transformation and toxicity changes during chlorine oxidation are a concern. In our study, the reaction between oxybenzone and chlorine followed pseudo-first-order and second-order kinetics. Three transformation products were detected by LC-MS/MS, and the stability of products followed the order of tri-chloro-methoxyphenyl > di-chlorinated oxybenzone > mono-chlorinated oxybenzone. Disinfection byproducts (DBPs) including chloroform, trichloroacetic acid, dichloroacetic acid and chloral hydrate were quickly formed, and increased at a slower rate until their concentrations remained constant. The maximum DBP/oxybenzone molar yields for the four compounds were 12.02%, 6.28%, 0.90% and 0.23%, respectively. SOS/umu genotoxicity test indicated that genotoxicity was highly elevated after chlorination, and genotoxicity showed a significantly positive correlation with the response of tri-chloro-methoxyphenyl. Our results indicated that more genotoxic transformation products were produced in spite of the elimination of oxybenzone, posing potential threats to drinking water safety. This study shed light on the formation of DBPs and toxicity changes during the chlorination process of oxybenzone.

Zhou, C. Z., Wang, Y. P., Chen, J., & Niu, J. F. (2019). Electrochemical Degradation of Sunscreen Agent Benzophenone-3 and Its Metabolite by Ti/SnO₂-Sb/Ce-PbO₂ Anode: Kinetics, Mechanism, Toxicity and Energy Consumption. *Science of The Total Environment*, 688, 75-82
<https://doi.org/10.1016/j.scitotenv.2019.06.197>

Electrochemical degradation of sunscreen agent benzophenone-3 (BP-3) and its metabolite 4-hydroxybenzophenone (4-OH-BP) was investigated by using a Ti/SnO₂-Sb/Ce-PbO₂ anode. Results showed that the degradation of BP-3 and 4-OH-BP followed pseudo-first-order kinetics, and the rate constants were 0.083 and 0.113 min⁻¹ at a current density of 25 mA cm⁻², respectively. The electrochemical degradation of BP-3 and 4-OH-BP was efficient over a wide range of pH values, and the degradation was obviously accelerated in the presence of Cl⁻. Degradation intermediates were identified

during the electrochemical process, and the degradation pathways, mainly including hydroxylation, carbonyl group broken from aromatic ring, benzene ring opening and carboxylation, were proposed. Quantitative structure-activity relationship model indicated that the potential risks of BP-3 and 4-OH-BP to fish, daphnia and green algae were decreased with the increase of reaction time. The energy consumption for the degradation of 90% BP-3 and 4-OH-BP was 3.3-62.1 and 3.6-79.5 Wh L⁻¹, respectively. The results illustrate that the electrochemical technique with Ti/SnO₂-Sb/Ce-PbO₂ anode is expected to be an effective way for removing BP-3 and its metabolite 4-OH-BP from wastewater.

Zhuang, R., Zabar, R., Grbovic, G., Dolenc, D., Yao, J., Tisler, T., & Trebse, P. (2013). Stability and Toxicity of Selected Chlorinated Benzophenone-Type UV Filters in Waters. *Acta Chimica Slovaca*, 60, 826-832 Retrieved from <https://journals.matheo.si/index.php/ACSi/article/view/170/110>

In our study, the transformation of two most widely used UV filters, benzophenone-3 (BP3) and benzophenone-4 (BP4), in chlorinated water with disinfection reagents sodium hypochlorite (NaClO) and trichloroisocyanuric acid (TCCA) was studied. Based on the HPLC/MS and UV-Vis analysis the formation of two different chlorinated products (5-chloro-2-hydroxy-4-methoxybenzophenone and 3,5-dichloro-2-hydroxy-4-methoxybenzophenone) was established. Identity of chlorinated products was confirmed by means of comparison of retention times with independently synthesized standards. Photostability study showed that dichloro-derivative in water is less stable than parent compounds, which is not the case for monochloro-derivatives. Toxicity of chlorinated compounds tested by *Vibrio fischeri* was found to be in the same range as that of the starting compounds. Preliminary testing of real water samples from swimming pools and sea swimming areas confirmed the presence of BP3 and its 3,5-dichloro derivative.

Section IV: Concentrations of UV Filters in Marine Environments

Allinson, M., Kameda, Y., Kimura, K., & Allinson, G. (2018). Occurrence and Assessment of the Risk of Ultraviolet Filters and Light Stabilizers in Victorian Estuaries. *Environmental Science and Pollution Research*, 25(12), 12022-12033 <https://doi.org/10.1007/s11356-018-1386-7>

This reconnaissance study was undertaken to examine the occurrence of common ultraviolet filters (UVF) and light stabilizers (UVLS), and preservatives in four different estuaries in Port Philip Bay, Victoria, for the first time. In total, 11 UV filters, 10 UV stabilizers, 12 preservatives and a metabolite, and one fragrance were screened in grab samples of water and sediment using a combination of solid phase extraction and gas and liquid chromatography mass spectrometry measurement techniques. In that context, 16 of the UVF and UVLS and 5 of the preservatives screened were observed in water and/or sediment samples. There are no marine water quality guideline values for any of the fragrances, preservatives and UV filters and light stabilizers in Australia's current national water quality guidelines, so potential risk was assessed using the risk quotient (RQ) and toxic unit (TU) concepts. In that context, only two chemicals (OC and EHMC) had both an RQ above 1 and a log₁₀TU above - 3, suggesting that few of the screened chemicals would have posed an individual, short-term risk to organisms in the waters studied at the time of sampling. However, the detection of common UV filters, such as 4MBC, EHMC, OC and the common preservatives 2-PE, MP, and PB in these Victorian estuaries highlights that the existence of personal care products in the environment is not just an issue for more densely populated countries in the northern hemisphere, but also potentially of concern in Australia. And, in that context, more sampling campaigns in Port Philip Bay are of paramount importance to assess the potential risk posed by these compounds to aquatic ecosystems.

Aminot, Y., Sayfritz, S. J., Thomas, K. V., Godinho, L., Botteon, E., Ferrari, F., . . . Readman, J. W. (2019). Environmental Risks Associated with Contaminants of Legacy and Emerging Concern at European Aquaculture Areas. *Environmental Pollution*
<https://doi.org/10.1016/j.envpol.2019.05.133>

The contamination of marine ecosystems by contaminants of emerging concern such as personal care products or per- and polyfluoroalkyl substances is of increasing concern. This work assessed the concentrations of selected contaminants of emerging concern in water and sediment of European aquaculture areas, to evaluate their co-variation with legacy contaminants (polycyclic aromatic hydrocarbons) and faecal biomarkers, and estimate the risks associated with their occurrence. The 9 study sites were selected in 7 European countries to be representative of the aquaculture activities of their region: 4 sites in the Atlantic Ocean and 5 in the Mediterranean Sea. Musks, UV filters, preservatives, per- and polyfluoroalkyl substances and polycyclic aromatic hydrocarbons were detected in at least one of the sites with regional differences. While personal care products appear to be the main component of the water contamination, polycyclic aromatic hydrocarbons were mostly found in sediments. As expected, generally higher levels of personal care products were found in sewage impacted sites, urbanised coasts and estuaries. The risk assessment for water and sediment revealed a potential risk for the local aquatic environment from contaminants of both legacy and emerging concern, with a significant contribution of the UV filter octocrylene. Despite marginal contributions of per- and polyfluoroalkyl substances to the total concentrations, PFOS (perfluorooctane sulfonate) aqueous concentrations combined to its low ecotoxicity thresholds produced significant hazard quotients indicating a potential risk to the ecosystems.

Apel, C., Joerss, H., & Ebinghaus, R. (2018). Environmental Occurrence and Hazard of Organic UV Stabilizers and UV Filters in the Sediment of European North and Baltic Seas. *Chemosphere*, 212, 254-261 <https://doi.org/10.1016/j.chemosphere.2018.08.105>

UV absorbing compounds are of emerging concern due to their large production volumes, their persistence or pseudo-persistence, and their potential adverse effects. This is the first study investigating the environmental occurrence and potential hazard of organic UV stabilizers and UV filters in the North and Baltic Sea surface sediments, including the connecting Skagerrak and Kattegat straits. In total, nineteen substances were identified over the entire study area, including the rarely studied compounds ethylhexyl triazone (EHT) and bisoctrizole (UV-360). Octocrylene (OC) was the predominant compound in this study with regard to detection frequency (79%) and concentrations (up to 9.7ng/g dw). OC accounted for more than 65% of UV stabilizer contamination in the German Bight. The triazine derivative EHT was quantified in the Rhine-Meuse-Delta and the German Bight in concentrations up to 2.0ng/g dw. In the Baltic Sea, benzotriazole UV stabilizers accounted for 60% of the contamination, with UV-360 as the main substance. The estimated environmental hazard quotients indicated a negligible impact on benthic and sediment-dwelling organisms in the North and Baltic Seas. Region-specific contamination pattern and riverine influences were revealed. The results suggest that both direct and indirect sources contribute to the UV stabilizer and UV filter contamination in the study area.

Apel, C., Tang, J., & Ebinghaus, R. (2018). Environmental Occurrence and Distribution of Organic UV Stabilizers and UV Filters in the Sediment of Chinese Bohai and Yellow Seas. *Environmental Pollution*, 235, 85-94 <https://doi.org/10.1016/j.envpol.2017.12.051>

Organic UV stabilizers and UV filters are applied to industrial materials and cosmetics worldwide. In plastics they prevent photo-induced degradation, while in cosmetics they protect human skin against harmful effects of UV radiation. This study reports on the occurrence and distribution of organic UV stabilizers and UV filters in the surface sediment of the Chinese Bohai and Yellow Seas for the first time. In total, 16 out of 21 analyzed substances were positively detected. Concentrations ranged from sub-ng/g dw to low ng/g dw. The highest concentration of 25ng/g dw was found for octocrylene (OC) in the Laizhou Bay. In the study area, characteristic composition profiles could be identified. In Korea Bay, the dominating substances were OC and ethylhexyl salicylate (EHS). All other analytes were below their method quantification limit (MQL). Around the Shandong Peninsula, highest concentrations of benzotriazole derivatives were observed in this study with octrizole (UV-329) as the predominant compound, reaching concentrations of 6.09ng/g dw. The distribution pattern of UV-329 and bumetrizole (UV-326) were related (Pearson correlation coefficient $r > 0.98$, $p < 0.01$ around the Shandong Peninsula), indicating an identical input pathway and similar environmental behavior.

Arpin-Pont, L., Bueno, M. J., Gomez, E., & Fenet, H. (2016). Occurrence of PPCPs in the Marine Environment: A Review. *Environmental Science and Pollution Research*, 23(6), 4978-4991 <https://doi.org/10.1007/s11356-014-3617-x>

Little research has been conducted on the occurrence of pharmaceuticals and personal care products (PPCPs) in the marine environment despite being increasingly impacted by these contaminants. This article reviews data on the occurrence of PPCPs in seawater, sediment, and organisms in the marine environment. Data pertaining to 196 pharmaceuticals and 37 personal care products reported from more than 50 marine sites are analyzed while taking sampling strategies and analytical methods into account. Particular attention is focused on the most frequently detected substances at highest concentrations. A snapshot of the most impacted marine sites is provided by comparing the highest concentrations reported for quantified substances. The present review reveals that: (i) PPCPs are widespread in seawater, particularly at sites impacted by anthropogenic activities, and (ii) the most frequently investigated and detected molecules in seawater and sediments are antibiotics, such as erythromycin. Moreover, this review points out other PPCPs of concern, such as ultraviolet filters, and underlines the scarcity of data on those substances despite recent evidence on their occurrence in marine organisms. The exposure of marine organisms in regard to these insufficient data is discussed.

Asztemborska, M., Jakubiak, M., Stęborowski, R., Chajduk, E., & Bystrzejewska-Piotrowska, G. (2018). Titanium Dioxide Nanoparticle Circulation in an Aquatic Ecosystem. *Water, Air, & Soil Pollution*, 229(6), 208 <https://doi.org/10.1007/s11270-018-3852-8>

Nanotechnology is a dynamically developing field of scientific and industrial interest across the entire world, and the commercialization of nanoparticles (NPs) is rapidly expanding. Incorporation of nanotechnologies into a range of manufactured goods results in increasing concern regarding the subsequent release of engineered NPs into the environment. One of the biggest threats of using NPs is the transfer and magnification of these particles in the trophic chain. The aim of the studies was the evaluation of the distribution of TiO₂ NP contamination in the aquatic ecosystem under laboratory conditions. Bioaccumulation of TiO₂ NPs by plants (*Elodea canadensis*) and fish (*Danio rerio*) in the source of contamination was investigated. The studies were focused on the consequences of short-term water contamination with TiO₂ NPs and the secondary contamination of the components of the investigated model ecosystem (plants, sediments). It was found that in the fish and the plants exposed to NP contamination, the amount of Ti was higher than in the control, indicating an effective

bioaccumulation of NPs or ions originating from NPs. It was clearly shown that the NPs present in the sediments are available to plants and fish. Additionally, the aquatic plants, an important trophic level in the food chain, can accumulate NPs and be a source of NPs for higher organisms. It was concluded that even an incidental contamination of water by NPs may result in long-term consequences induced by the release of NPs.

Bachelot, M., Li, Z., Munaron, D., Le Gall, P., Casellas, C., Fenet, H., & Gomez, E. (2012). Organic UV Filter Concentrations in Marine Mussels from French Coastal Regions. *Science of The Total Environment*, 420, 273-279 <https://doi.org/10.1016/j.scitotenv.2011.12.051>

The accumulation of EHMC, OCT and OD-PABA, three common UV filter compounds, was investigated in marine mussels. Wild *Mytilus edulis* and *Mytilus galloprovincialis* were sampled in ten sites along the French Atlantic and Mediterranean coasts from June to November. In mussel tissues, 100% of the samples had quantifiable EHMC concentrations ranging from 3 to 256 ng g⁻¹ dry weight, while 55% of the samples had detectable OCT concentrations ranging from under 2 to 712 ng g⁻¹ dry weight. These concentrations significantly increased with the rising air temperature in summer, the recreational pressure and the geomorphological structure of the sampling sites (its lack of openness to the wide). This is the first study to report bioaccumulation of UV filters in marine mussels, thus highlighting the need for further monitoring and assessment.

Bakkerud, O. L. (2019). *Profiles of Bisphenols and Benzophenone-Type UV Filters Concentrations in Sediment from Trondheimsfjorden: Associations with Paks and Trace Elements*. (Master's Master's), Norwegian University of Science and Technology, Trondheim, Norway. Retrieved from [no URL available]

In this Master's project, 64 unique marine sediment samples from various locations in Trondheimsfjorden, Norway were acquired by sampling from a research vessel the 31st of May 2018. The aim of the project has been to determine occurrences and evaluate correlations between several organic and inorganic chemical contaminants in the sediment. The target chemicals of interest included nine bisphenol A analogues, five benzophenone analogues, sixteen EPA priority polycyclic aromatic hydrocarbons, and nine trace elements. Total organic matter content was also evaluated. Sediment samples were treated with various techniques and methods for extracting target chemicals, including liquid-solid extraction (LSE), solid phase extraction (SPE), accelerated solvent extraction (ASE) and microwave-assisted acid digestion. After treatment, the samples were analysed using liquid chromatography-tandem mass spectrometry (LCMS/MS), high performance liquid chromatography with ultraviolet and fluorescence detection (HPLC-UV/FLD), and inductively coupled plasma mass spectrometry (ICP-MS). The total concentration sum of bisphenols (PBPs), benzophenones (PBzPs) and polycyclic aromatic hydrocarbons (PPAHs) in sediment samples ranged from 0.67 - 12.1 ng/g dry weight (d.w.), 0.25 - 34.7 ng/g d.w. and 33.4 - 548 ng/g d.w., respectively. The concentration of elements ranged from 0.018 - 525 µg/g d.w. Percentage total organic matter content ranged from 1.97 - 4.80 %. BPA and BPF were the predominant bisphenol analogues and accounted for 52.5% and 41.9% of the total bisphenol concentration respectively. BzP-3 accounted for 57.6% of the total benzophenone concentration. Correlations among sediment samples were evaluated by the use of principal component analysis (PCA). Results from PCA analysis indicated variations between samples from different sampling locations based on levels of trace elements and polycyclic aromatic hydrocarbons, as well as correlations between some target analytes including BPA and BzP-3. To the authors knowledge, this is the first time

occurrences of bisphenols, benzophenones, polycyclic aromatic hydrocarbons and trace elements in marine sediment have been reported.

Balmer, M. E., Buser, H.-R., Müller, M. D., & Poiger, T. (2005). Occurrence of Some Organic UV Filters in Wastewater, in Surface Waters, and in Fish from Swiss Lakes. *Environmental Science & Technology*, 39(4), 953-962 <https://doi.org/10.1021/es040055r>

Organic UV filters are used in personal care products such as sunscreen products, and in cosmetics, beauty creams, skin lotions, lipsticks, hair sprays, hair dyes, shampoos, and so forth. The compounds enter the aquatic environment from showering, wash-off, washing (laundry), and so forth via wastewater treatment plants (WWTPs) (“indirect inputs”) and from recreational activities such as swimming and bathing in lakes and rivers (“direct inputs”). In this study, we investigated the occurrence of four important organic UV filter compounds (benzophenone-3, BP-3; 4-methylbenzylidene camphor, 4-MBC; ethylhexyl methoxy cinnamate, EHMC; octocrylene, OC) in wastewater, and in water and fish from various Swiss lakes, using gas chromatographic/mass spectrometric analyses. All four UV filters were present in untreated wastewater (WWTP influent) with a maximum concentration of 19 µg L⁻¹ for EHMC. The data indicate a seasonal variation with influent loads higher in the warmer season (June 2002) than in the colder one (April 2002). The influent loads were in the order EHMC > 4-MBC ~ BP-3 > OC. The concentrations in treated wastewater (WWTP effluent) were considerably lower, indicating substantial elimination in the plants. 4-MBC was usually the most prevalent compound (maximum concentration, 2.7 µg L⁻¹), followed by BP-3, EHMC, and OC. UV filters were also detected in Swiss midland lakes and a river (Limmat) receiving inputs from WWTPs and recreational activities. However, all concentrations were low (<2–35 ng L⁻¹); no UV filters (<2 ng L⁻¹) were detected in a remote mountain lake. Data from passive sampling using semipermeable membrane devices (SPMDs) supported the presence of these UV filters in the lakes and the river and suggested some potential for accumulation of these compounds in biota. SPMD-derived water concentrations increased in the order Greifensee < Zürichsee < Hüttnersee. This order is reversed from that observed for methyl triclosan, used as a chemical marker for WWTP-derived lipophilic contaminants in the lakes. This indicated inputs of UV filters from sources other than WWTPs to the lakes during summer, for example, inputs from recreational activities. Fish (white fish, *Coregonus* sp.; roach, *Rutilus rutilus*; perch, *Perca fluviatilis*) from these lakes contained low but detectable concentrations of UV filters, in particular, 4-MBC (up to 166 ng g⁻¹ on a lipid basis). 4-MBC concentrations relative to methyl triclosan were lower in fish than in SPMDs exposed in the same lakes, suggesting that 4-MBC is less bioaccumulated than expected or metabolized in fish. The lipid-based bioconcentration factor (BCFL) estimated from the fish (roach) data and SPMD-derived water concentrations was about 1–2.3 × 10⁴ and thus approximately 1 order of magnitude lower than expected from its K_{ow} value.

Barbosa, M. O., Moreira, N. F., Ribeiro, A. R., Pereira, M. F., & Silva, A. M. (2016). Occurrence and Removal of Organic Micropollutants: An Overview of the Watch List of Eu Decision 2015/495. *Water Research*, 94, 257-279 <https://doi.org/10.1016/j.watres.2016.02.047>

Although there are no legal discharge limits for micropollutants into the environment, some regulations have been published in the last few years. Recently, a watch list of substances for European Union-wide monitoring was reported in the Decision 2015/495/EU of 20 March 2015. Besides the substances previously recommended to be included by the Directive 39/2013/EU, namely two pharmaceuticals (diclofenac and the synthetic hormone 17-alpha-ethinylestradiol (EE2)) and a natural hormone (17-beta-estradiol (E2)), the first watch list of 10 substances/groups of substances also refers three macrolide

antibiotics (azithromycin, clarithromycin and erythromycin), other natural hormone (estrone (E1)), some pesticides (methiocarb, oxadiazon, imidacloprid, thiacloprid, thiamethoxam, clothianidin, acetamiprid and triallate), a UV filter (2-ethylhexyl-4-methoxycinnamate) and an antioxidant (2,6-di-tert-butyl-4-methylphenol) commonly used as food additive. Since little is known about the removal of most of the substances included in the Decision 2015/495/EU, particularly regarding realistic concentrations in aqueous environmental samples, this review aims to: (i) overview the European policy in the water field; (ii) briefly describe the most commonly used conventional and advanced treatment processes to remove micropollutants; (iii) summarize the relevant data published in the last decade, regarding occurrence and removal in aqueous matrices of the 10 substances/groups of substances that were recently included in the first watch list for European Union monitoring (Decision 2015/495/EU); and (iv) highlight the lack of reports concerning some substances of the watch list, the study of un-spiked aquatic matrices and the assessment of transformation by-products.

Barón, E., Gago-Ferrero, P., Gorga, M., Rudolph, I., Mendoza, G., Zapata, A. M., . . . Barceló, D. (2013). Occurrence of Hydrophobic Organic Pollutants (Bfrs and UV-Filters) in Sediments from South America. *Chemosphere*, 92(3), 309-316 <https://doi.org/10.1016/j.chemosphere.2013.03.032>

In the present study the occurrence of emerging hydrophobic organic pollutants in sediment samples from South America (Chile and Colombia) was investigated for the first time. Nineteen Chilean and thirteen Colombian sediment samples were analyzed in order to determine their content of brominated flame retardants (BFRs) (including PBDEs and emerging BFRs) as well as UV filters (UV-F). Samples were collected from neighboring aquatic ecosystems highly urbanized and industrialized in Colombia (Magdalena River area) and Chile (Biobio region). Different analytical procedures were applied depending on the selected analytes, based on chromatographic and mass spectrometric methodologies (GC-MS and LC-MS-MS). In general, concentration levels of both BFRs (up to 2.43 and 143 ng g⁻¹ dw of PBDEs in Chile and Colombia, respectively) and UV-F (nd-2.96 and nd-54.4 ng g⁻¹ dw in Chile and Colombia, respectively) were in the low range of published data, and the contribution of BFRs was higher than that of UV-F for almost all the sampled sediments.

Bell, L. J., Ucharm, G., Patris, S., Diaz-Cruz, M. S., Roig, M. P. S., & Dawson, M. N. (2017). *Sunscreen Pollution Analysis in Jellyfish Lake Coral Reef Research Foundation Palau*. Coral Reef Research Foundation. Retrieved from <https://coralreefpalau.org/wp-content/uploads/2017/10/CRRF-UNESCO-Sunscreen-in-Jellyfish-Lake-no.2732.pdf>

Jellyfish Lake in Palau is part of the Koror State Rock Island Southern Lagoon (RISL), a UNESCO World Heritage site and is famous for its Golden Jellyfish population. Palau has seen a dramatic increase in its visitors, now over 100,000 per year, and most of those visit Jellyfish Lake, causing concern for the continued health of the lake. Our preliminary sampling for sunscreen chemicals in 2014 indicated the presence of oxybenzone (BP-3), a compound that is extremely common in personal care products, including sunscreens. The present study builds on those results, using more rigorous sampling and analytical methods to look for sunscreen products in water, sediment and jellyfish samples in Jellyfish Lake (tourism site) and three other sites (non-tourism) for comparison. Our results showed that sunscreen compounds or their transformation products (such as metabolites) are wide spread in Jellyfish Lake. They were also present in the sites presumed to be 'pristine' with little human use. In general, water samples had low levels of sunscreen compounds, while jellyfish tissues and sediment had relatively higher levels of these compounds and metabolites. This is an indication of bioaccumulation of these chemicals. Comparing different lakes and ocean/lagoon sites, Jellyfish Lake had the highest levels

of sunscreen compound concentrations. The levels of sunscreen compounds and their metabolites in Jellyfish Lake indicates that: 1) personal care product pollution is entering the environment through tourist use, i.e. sunscreen washing off, and 2) jellyfish are absorbing and metabolizing BP3. Compounds were also detected in Ngermeuangel Lake, i.e. what should have been a control and uncontaminated lake. These may be from effluent/sewer leaking from the nearby population center into the adjacent watersheds, indicating that there are more widespread issues with marine pollution from different sources. The Golden Jellyfish medusa stage is relatively short lived, with a life span of about 6 months. The presence of sunscreen chemicals in the medusae and their presence in the sediment in Jellyfish Lake and other marine lakes is cause for concern. The medusae stage may not live long enough to be directly affected, but their benthic polyp stage, critical to their life cycle, could be. We feel in the short term the known presence of UV filters should be addressed in a practical manner to try to stabilize their levels in Jellyfish Lake and minimize additions of them to the system.

Bratkovics, S., Wirth, E., Sapozhnikova, Y., Pennington, P., & Sanger, D. (2015). Baseline Monitoring of Organic Sunscreen Compounds Along South Carolina's Coastal Marine Environment. *Marine Pollution Bulletin* <https://doi.org/10.1016/j.marpolbul.2015.10.015>

Organic ultraviolet filters (UV-F) are increasingly being used in personal care products to protect skin and other products from the damaging effects of UV radiation. In this study, marine water was collected monthly for approximately one year from six coastal South Carolina, USA sites and analyzed for the occurrence of seven organic chemicals used as UV filters (avobenzone, dioxybenzone, octocrylene, octinoxate, oxybenzone, padimate-o and sulisobenzene). The results were used to examine the relationship between beach use and the distribution of UV-F compounds along coastal South Carolina, USA. Five of the seven target analytes were detected in seawater along coastal South Carolina during this study. Dioxybenzone and sulisobenzene were not detected. The highest concentrations measured were >3700ng octocrylene/L and ~2200ng oxybenzone/L and beach use was greatest at this site; a local beach front park. Patterns in concentrations were assessed based on season and a measure of beach use.

Brausch, J. M., & Rand, G. M. (2011). A Review of Personal Care Products in the Aquatic Environment: Environmental Concentrations and Toxicity. *Chemosphere*, 82(11), 1518-1532
<https://doi.org/10.1016/j.chemosphere.2010.11.018>

Considerable research has been conducted examining occurrence and effects of human use pharmaceuticals in the aquatic environment; however, relatively little research has been conducted examining personal care products although they are found more often and in higher concentrations than pharmaceuticals. Personal care products are continually released into the aquatic environment and are biologically active and persistent. This article examines the acute and chronic toxicity data available for personal care products and highlights areas of concern. Toxicity and environmental data were synergized to develop a preliminary hazard assessment in which only triclosan and triclocarban presented any hazard. However, numerous PCPs including triclosan, paraben preservatives, and UV filters have evidence suggesting endocrine effects in aquatic organisms and thus need to be investigated and incorporated in definitive risk assessments. Additional data pertaining to environmental concentrations of UV filters and parabens, in vivo toxicity data for parabens, and potential for bioaccumulation of PCPs needs to be obtained to develop definitive aquatic risk assessments.

Buser, H. R., Balmer, M. E., Schmid, P., & Kohler, M. (2006). Occurrence of UV Filters 4-Methylbenzylidene Camphor and Octocrylene in Fish from Various Swiss Rivers with Inputs from Wastewater Treatment Plants. *Environmental Science & Technology*, 40(5), 1427-1431 <https://doi.org/10.1021/es052088s>

UV filters are widely used compounds in many personal care products and cosmetics, such as sunscreens. After use, UV filters are washed off from skin and clothes and enter the aquatic environment. Recent studies indicate that some lipophilic UV filters do accumulate in biota and act as endocrine disruptors. In this study, concentrations of 4-MBC (4-methylbenzylidene camphor) and OC (octocrylene), two widely used UV filters, were determined in the muscle tissue of fish (brown trout, *Salmo trutta fario*) from seven small Swiss rivers, all receiving inputs from wastewater treatment plants (WWTPs). Lipid-weight based concentrations of up to 1800 (4-MBC) and 2400 ng g⁻¹ (OC) were found. These levels were distinctly higher than those previously observed in white fish (*Coregonus* sp.) and roach (*Rutilus rutilus*) from Swiss lakes with inputs from WWTPs. This suggests a higher availability of these contaminants for fish in rivers than in lakes and identifies WWTPs as a major source for UV filters in the aquatic environment. As compared to lake fish, individual fish from a river showed much greater variation in 4-MBC and OC concentrations, likely as a result of a wider range of exposure in rivers than in lakes. 4-MBC concentrations correlated reasonably well with concentrations of methyl triclosan, a chemical marker for lipophilic WWTP-derived contaminants. The ratio P/Q of population (P) in a watershed to water throughflow (Q) is considered to be a measure of the domestic burden from WWTPs. A correlation of methyl triclosan with P/Q was previously observed with lake fish. However, such a correlation could not be confirmed with river fish. The higher average concentrations of OC as compared to 4-MBC in river fish, and the fact that OC was mostly absent in lake fish, suggests differences in bioaccumulation and availability of these two UV filters.

Camacho, M., Herrera, A., Gomez, M., Acosta-Dacal, A., Martinez, I., Henriquez-Hernandez, L. A., & Luzardo, O. P. (2019). Organic Pollutants in Marine Plastic Debris from Canary Islands Beaches. *Science of The Total Environment*, 662, 22-31 <https://doi.org/10.1016/j.scitotenv.2018.12.422>

Given their capacity to adsorb chemical pollutants, microplastics represent a growing environmental concern in the oceans. The levels of 81 chemical compounds in two types of beached microplastic (pellets and fragments) were monitored across the Canary Islands (Spain). The highest concentrations were found for polycyclic aromatic hydrocarbons (PAH) (52.1-17,023.6ng/g and 35.1-8725.8ng/g for pooled pellets and fragments, respectively). The polychlorinated biphenyl (PCB) concentrations were 0.9-2285.8 and 1.6-772.5ng/g for pooled pellets and fragments, respectively, whereas organochlorine pesticides (OCP) ranged from 0.4-13,488.7 and 0.4-3778.8ng/g, respectively. The sum of polychlorinated biphenyls and diphenyl-dichloro-ethane (DDT) metabolites was significantly higher in beaches on Gran Canaria, which is the most populated and industrialized island. The sum of ultraviolet filters (UV-filters) was higher in those beaches more frequented by tourists (Famara and Las Canteras), than in occasionally or very rarely visited beaches (Cuervitos and Lambra), with values ranging from 0 to 37,740.3ng/g and 3.7-2169.3ng/g for pellets and fragments, respectively. Furthermore, the sum of brominated diphenyl ethers (BDE) (0-180.58ng/g for pooled pellets and 0.06-3923.9ng/g for pooled fragments) and organophosphorus flame retardants (OPFR) (20.0-378.0ng/g for pooled pellets, and 22.6-7013.9ng/g for pooled fragments) was significantly higher in an urban beach (Las Canteras) than in the rest of the studied beaches. Finally, the concentrations of the pesticide chlorpyrifos were much higher on Gran Canaria beaches than in the rest. In this research we provide further evidence of the important role of plastic debris in the adsorption of a wide range of marine pollutants. The regional pattern of chemical contamination of plastics reveals that the sorption of many compounds probably

occurs in coastal waters. Further investigation is necessary to understand the relationship between plastic types and adsorption of different pollutants, especially for emerging pollutants.

Capela, D., Vila, M., Llompарт, M., Dagnac, T., Garcia-Jares, C., Alves, A., & Homem, V. (2019). Footprints in the Sand - Assessing the Seasonal Trends of Volatile Methylsiloxanes and UV-Filters. *Marine Pollution Bulletin*, 140, 9-16 <https://doi.org/10.1016/j.marpolbul.2019.01.021>

This study focused on the determination of seven volatile methylsiloxanes (VMSs) and eleven UV-filters (UVFs) in beach sand from the Oporto's region (Portugal). A QuEChERS methodology ("Quick, Easy, Cheap, Effective, Rugged, and Safe") was used to extract VMSs from the sand, which has never been employed before. To extract the UVFs, a solid-phase microextraction (SPME) was used. The analyses were performed by gas chromatography-mass spectrometry (GC-MS). Twenty-three beach sand samples were analysed, from two campaigns - summer/winter. VMSs were found in all the samples with concentrations ranging from 0.007+/-0.001 to 17.8+/-0.9ngg(-1)dw, while UVFs in summer samples from 0.030+/-0.001 to 373+/-17ngg(-1)dw. Cyclic VMSs and octocrylene (OC) were detected in higher concentrations. In general, higher levels were detected in summer than winter. Hazard quotients were determined and 3-(4'-methylbenzylidene) camphor (4-MBC), 2-ethylhexyl 4-methoxycinnamate (EMC) and benzophenone-3 (BP3) presented values >1, which may indicate that they may pose an ecotoxicological risk.

Cuderman, P., & Heath, E. (2007). Determination of UV Filters and Antimicrobial Agents in Environmental Water Samples. *Analytical and Bioanalytical Chemistry*, 387(4), 1343-1350 <https://doi.org/10.1007/s00216-006-0927-y>

Although there is increasing concern about residues from personal care products entering the aquatic environment and their potential to accumulate to levels that pose a health threat to humans and wildlife, we still know little about the extent and magnitude of their presence in the aquatic environment. In this study we describe a procedure for isolation, and subsequent determination, of compounds commonly added to personal care products. The compounds of interest include UV filters with the commercial name Eusolex (homosalate, 4-methylbenzylidenecamphor, benzophenone-3, octocrylene, butylmethoxydibenzoylmethane, ethylhexyl methoxycinnamate) and two common anti-microbial agents, clorophene and triclosan. Water samples were filtered, acidified, and extracted by use of solid-phase extraction. Extracted compounds were then derivatised before analysis by gas chromatography-mass spectroscopy. By use of our method we obtained limits of detection of 13-266 ng L-1 for UV filters, and 10-186 ng L-1 for triclosan and clorophene. Recoveries were 82-98% for deionised water and 50-98% for natural water (seawater, pool water, lake water, and river water). Samples collected in Slovenia included seventeen recreational waters (seawater, pool water, lake water, and river water; August 2004) and four wastewaters (January 2005). The most abundant UV filter was benzophenone-3 (11-400 ng L-1). Of the two anti-microbial agents studied, trace amounts, only, of triclosan were present in the river Kolpa (68 ng L-1) and in an hospital effluent (122 ng L-1).

Cunha, S. C., Trabalon, L., Jacobs, S., Castro, M., Fernandez-Tejedor, M., Granby, K., . . . Domingo, J. L. (2018). UV-Filters and Musk Fragrances in Seafood Commercialized in Europe Union: Occurrence, Risk and Exposure Assessment. *Environmental Research*, 161, 399-408 <https://doi.org/10.1016/j.envres.2017.11.015>

In the framework of the FP7 ECsafeSeafood project, 62 seafood samples commercialized in Europe Union from several representative species - mackerel, tuna, salmon, seabream, cod, monkfish, crab, shrimp, octopus, perch and plaice - were analysed for residues of 21 personal care products (PCPs), including 11 UV-filters (UV-Fs) and 10 musk fragrances (musks). PCPs analysis were performed by Quick, Easy, Cheap, Effective Rugged, Safe (QuEChERS), combined with liquid-liquid extraction (LLE) or dispersive solid-phase extraction (dSPE), followed by gas chromatography-tandem mass spectrometry (GC-MS/MS). The results showed the presence in a wide range of samples of nine out of eleven UV-Fs compounds analysed, namely 2-ethylhexyl salicylate (EHS), 2-ethylhexyl,4-methoxycinnamate (EHMC), 4-methylbenzylidenecamphor (4-MBC), benzophenone-1 (BP1), benzophenone-3 (BP3), isoamyl-4-methoxycinnamate (IMC), 2,2'-dihydroxy-4,4'-dimethoxybenzophenone (DHMB), homosalate (HS), and octocrylene (OC), whereas galaxolide (HHCB), galaxolide lactone (HHCB-lactone), and tonalide (AHTN) were the most found musks. The potential risks to human health associated with the exposure to eight of the more prevalent PCPs - EHS, EHMC, 4-MBC, BP1, BP3, IMC, HHCB, and AHTN - through seafood consumption were assessed for consumers from five European countries (Belgium, Ireland, Italy, Portugal and Spain). Results showed that the human exposure to UV-Fs and musks estimated from the concentration values found in seafood and the daily consumption of concerned seafood species, were far below toxicological reference values.

da Silva, C. P., Emídio, E. S., & de Marchi, M. R. R. (2015). The Occurrence of Uv Filters in Natural and Drinking Water in São Paulo State (Brazil). *Environmental Science and Pollution Research*, 22(24), 19706-19715 <https://doi.org/10.1007/s11356-015-5174-3>

Ultraviolet (UV) filters are widely used in the formulation of personal care products (PCPs) to prevent damage to the skin, lips, and hair caused by excessive UV radiation. Therefore, large amounts of these substances are released daily into the aquatic environment through either recreational activities or the release of domestic sewage. The concern regarding the presence of such substances in the environment and the exposure of aquatic organisms is based on their potential for bioaccumulation and their potential as endocrine disruptors. Although there are several reports regarding the occurrence and fate of UV filters in the aquatic environment, these compounds are still overlooked in tropical areas. In this study, we investigated the occurrence of the organic UV filters benzophenone-3 (BP-3), ethylhexyl salicylate (ES), ethylhexyl methoxycinnamate (EHMC), and octocrylene (OC) in six water treatment plants in various cities in Southeast Brazil over a period of 6 months to 1 year. All of the UV filters studied were detected at some time during the sampling period; however, only EHMC and BP-3 were found in quantifiable concentrations, ranging from 55 to 101 and 18 to 115 ng L⁻¹, respectively. Seasonal variation of BP-3 was most clearly noticed in the water treatment plant in Araraquara, São Paulo, where sampling was performed for 12 months. BP-3 was not quantifiable in winter but was quantifiable in summer. The levels of BP-3 were in the same range in raw, treated and chlorinated water, indicating that the compound was not removed by the water treatment process.

Diaz-Cruz, M. S., Gago-Ferrero, P., Llorca, M., & Barcelo, D. (2012). Analysis of UV Filters in Tap Water and Other Clean Waters in Spain. *Analytical and Bioanalytical Chemistry*, 402(7), 2325-2333 <https://doi.org/10.1007/s00216-011-5560-8>

The present paper describes the development of a method for the simultaneous determination of five hormonally active UV filters namely benzophenone-3 (BP3), 3-(4-methylbenzylidene) camphor (4MBC), 2-ethylhexyl 4-(dimethylamino) benzoate (OD-PABA), 2-ethylhexyl 4-methoxycinnamate (EHMC) and octocrylene (OC) by means of solid-phase extraction and gas chromatography-electron impact

ionization-mass spectrometry. Under optimized conditions, this methodology achieved low method limits of detection (needed for clean waters, especially drinking water analysis), between 0.02 and 8.42 ng/L, and quantitative recovery rates higher than 73% in all cases. Inter- and intraday precision for all compounds were lower than 7% and 11%, respectively. The optimized methodology was applied to perform the first survey of UV absorbing compounds in tap water from the metropolitan area and the city of Barcelona (Catalonia, Spain). In addition, other types of clean water matrices (mineral bottled water, well water and tap water treated with an ion-exchange resin) were investigated as well. Results evidenced that all the UV filters investigated were detected in the water samples analyzed. The compounds most frequently found were EHMC and OC. Maximum concentrations reached in tap water were 290 (BP3), 35 (4MBC), 110 (OD-PABA), 260 (EHMC), and 170 ng/L (OC). This study constitutes the first evidence of the presence of UV filter residues in tap water in Europe.

Diaz-Cruz, M. S., Molins-Delgado, D., Serra-Roig, M. P., Kalogianni, E., Skoulikidis, N. T., & Barcelo, D. (2019). Personal Care Products Reconnaissance in Evrotas River (Greece): Water-Sediment Partition and Bioaccumulation in Fish. *Science of The Total Environment*, 651(Pt 2), 3079-3089 <https://doi.org/10.1016/j.scitotenv.2018.10.008>

Twenty-six common ingredients of personal care products (PCPs) in water, sediment and fish from the Evrotas River (Greece) were investigated. Water sample analysis revealed the occurrence of twenty PCPs at concentrations ranging from 2.8 to 2031.0ngl(-1), the maximum corresponding to the endocrine disrupting UV filter benzophenone 3 (BP3). In sediment samples, six compounds were found to be adsorbed, the highest concentration being that of 4-methylbenzylidene camphor (4MBC, 1400.4ngg(-1) dw). Evrotas cyprinid fish (*Squalius keadicus*) showed a high accumulation potential for these chemicals, 100% detection frequency with maximum concentration that of benzophenone 2 (BP2, 41.9ngg(-1) dw). These data allowed estimating the distribution coefficients sediment-water (DCs-w) and the bioaccumulation factors (BAFs) of the pollutants investigated. Calculated rates revealed that benzophenone 1 (BP1), 4-hydroxybenzophenone (4HB) and ethyl-4-(dimethyl-amino)benzoate (EtPABA) have a strong tendency to adsorb onto the sediments, showing high DCs-w, i.e. $8.2E+4lg(-1)$, $6.7E+4lg(-1)$ and $5.7E+3lg(-1)$, respectively. BFAs were only estimated for 5-methyl benzotriazole (MeBT), the compound having paired data from fish and water. The obtained values (range $2.0E+2lg(-1)$ - $3.8E+3lg(-1)$), indicated MeBT's strong bioaccumulation. Risk assessment of the investigated compounds for several aquatic organisms indicated a high ecological risk ($HQ>1$) for BP3 and medium ecological risk ($HQ\sim 0.5$) for ODPABA.

Doughton, C. G., & Ternes, T. A. (1999). Pharmaceuticals and Personal Care Products in the Environment: Agents of Subtle Change? *Environmental Health Perspectives*, 107(Supplement 6), 907-938 <https://doi.org/10.2307/3434573>

During the last three decades, the impact of chemical pollution has focused almost exclusively on the conventional "priority" pollutants, especially those acutely toxic/carcinogenic pesticides and industrial intermediates displaying persistence in the environment. This spectrum of chemicals, however, is only one piece of the larger puzzle in "holistic" risk assessment. Another diverse group of bioactive chemicals receiving comparatively little attention as potential environmental pollutants includes the pharmaceuticals and active ingredients in personal care products (in this review collectively termed PPCPs), both human and veterinary, including not just prescription drugs and biologics, but also diagnostic agents, "nutraceuticals," fragrances, sun-screen agents, and numerous others. These compounds and their bioactive metabolites can be continually introduced to the aquatic environment as

complex mixtures via a number of routes but primarily by both untreated and treated sewage. Aquatic pollution is particularly troublesome because aquatic organisms are captive to continual life-cycle, multigenerational exposure. The possibility for continual but undetectable or unnoticed effects on aquatic organisms is particularly worrisome because effects could accumulate so slowly that major change goes undetected until the cumulative level of these effects finally cascades to irreversible change-change that would otherwise be attributed to natural adaptation or ecologic succession. As opposed to the conventional, persistent priority pollutants, PPCPs need not be persistent if they are continually introduced to surface waters, even at low parts-per-trillion/parts-per-billion concentrations (ng-µg/L). Even though some PPCPs are extremely persistent and introduced to the environment in very high quantities and perhaps have already gained ubiquity worldwide, others could act as if they were persistent, simply because their continual infusion into the aquatic environment serves to sustain perpetual life-cycle exposures for aquatic organisms. This review attempts to synthesize the literature on environmental origin, distribution/occurrence, and effects and to catalyze a more focused discussion in the environmental science community.

Ekowati, Y., Buttiglieri, G., Ferrero, G., Valle-Sistac, J., Diaz-Cruz, M. S., Barcelo, D., . . . Rodriguez-Roda, I. (2016). Occurrence of Pharmaceuticals and UV Filters in Swimming Pools and Spas. *Environmental Science and Pollution Research*, 23(14), 14431-14441
<https://doi.org/10.1007/s11356-016-6560-1>

The occurrence of 32 pharmaceuticals and 14 UV filters in swimming pools and spas was studied. Fifty-one water samples were collected from 17 pools located in sport centres and hotels in Catalonia, Spain. The samples were analysed by liquid chromatography-tandem mass spectrometry. The pharmaceuticals atenolol, carbamazepine, hydrochlorothiazide, metronidazole, ofloxacin, sulfamethoxazole, acetaminophen, ibuprofen, ketoprofen and phenazone were measured in water samples at concentrations higher than their limit of quantification (LOQ). The highest concentration of any individual pharmaceutical was measured for the diuretic hydrochlorothiazide (904 ng/L). The most frequently detected pharmaceutical was carbamazepine, as it was observed in more than half of all the water samples measured (53 %, 27/51). The UV filters at concentrations higher than LOQ in water samples were BP1, BP2, BP3, BP8, THB, 4DHB, 4MBC, OD-PABA, 1HBT, MeBT and DMeBT. The highest concentration of UV filter observed was 4MBC (69.3 ng/L) while the most frequent UV filters in the samples were 1HBT (59 %, 30/51). The results also showed that pharmaceuticals and UV filters were most frequently found in spas. Finally, from a water treatment technology perspective, the lowest occurrence of pharmaceuticals was in the pools applying sand filters followed by disinfection by sodium hypochlorite, while the lowest occurrence of UV filters was in the pools applying coagulation, sand filtration, UV and salt electrolysis.

Fagervold, S. K., Rodrigues, A. S., Rohée, C., Roe, R., Bourrain, M., Stien, D., & Lebaron, P. (2019). Occurrence and Environmental Distribution of 5 UV Filters During the Summer Season in Different Water Bodies. *Water, Air, & Soil Pollution*, 230(7), 172
<https://doi.org/10.1007/s11270-019-4217-7>

Organic UV filters are used worldwide in various personal care products as well as textiles, paints, plastic, food, and adhesives. They are main ingredients in sunscreen lotions that are used heavily by beachgoers in the summer season. There is thus an increasing concern regarding the fate of organic UV filters in the environment and their impact on living organisms. Many of the UV filters in use are hydrophobic and are expected to accumulate in the sediment phase in aquatic systems, but this has yet

to be validated in situ. We targeted the UV filters benzophenone 3 (BP3), butyl methoxydibenzoylmethane (BMDBM), diethylhexyl butamido triazone (DBT), bis-ethylhexyloxyphenol methoxyphenyl triazine (BEMT), and methylene bis-benzotriazolyl tetramethylbutylphenol (MBBT) in a freshwater lake and in a coastal bay in order to understand their distribution during summer 2016. Further, we examined their environmental partitioning by collecting samples from the surface water, the sediment phase, and water surface microlayer (SML). We show for the first time the presence of DBT, BEMT, and MBBT in environmental matrices (water, SML, and sediment). Notably, these UV filters were detected at low amounts in surface waters with maximum concentrations of 9.9 ng/L for DBT, 18.4 ng/L for BEMT, and below detection limits for MBBT and somewhat higher concentrations in the SML, with maximum concentrations of 43.3 ng/L for DBT, 5625.4 ng/L for BEMT, and 45.6 ng/L for MBBT. These filters were detected at even greater concentrations in the sediments, with maximum concentrations of 652.6 ng/g for DBT, 115.0 ng/g for BEMT, and 75.2 ng/g for MBBT (dry weight sediment). We also performed controlled laboratory experiments to determine their partitioning behavior, and we verified the actual solubility of many of the filters. This will help in determining the environmental fate and finally lead to a better risk assessment of these compounds. Together, these results corroborate the hypothesis that hydrophobic UV filters accumulate in the sediment phase and highlight the importance of discerning whether these UV filters impact the benthic community and their potential for bioaccumulation.

Foltete, A. S., Masfaraud, J. F., Bigorgne, E., Nahmani, J., Chaurand, P., Botta, C., . . . Cotelle, S. (2011). Environmental Impact of Sunscreen Nanomaterials: Ecotoxicity and Genotoxicity of Altered TiO₂ Nanocomposites on *Vicia Faba*. *Environmental Pollution*, 159(10), 2515-2522
<https://doi.org/10.1016/j.envpol.2011.06.020>

Mineral sunscreen nanocomposites, based on a nano-TiO₂ core, coated with aluminium hydroxide and dimethicone films, were submitted to an artificial ageing process. The resulting Altered TiO₂ Nanocomposites (ATN) were then tested in the liquid phase on the plant model *Vicia faba*, which was exposed 48 h to three nominal concentrations: 5, 25 and 50 mg ATN/L. Plant growth, photosystem II maximum quantum yield, genotoxicity (micronucleus test) and phytochelatin levels showed no change compared to controls. Oxidative stress biomarkers remained unchanged in shoots while in roots, glutathione reductase activity decreased at 50 mg ATN/L and ascorbate peroxidase activity decreased for 5 and 25 mg ATN/L. Nevertheless, despite the weak response of biological endpoints, ICP-MS measurements revealed high Ti and Al concentrations in roots, and X-ray fluorescence micro-spectroscopy revealed titanium internalization in superficial root tissues. Eventual long-term effects on plants may occur.

Gago-Ferrero, P., Diaz-Cruz, M. S., & Barcelo, D. (2011). Occurrence of Multiclass UV Filters in Treated Sewage Sludge from Wastewater Treatment Plants. *Chemosphere*, 84(8), 1158-1165
<https://doi.org/10.1016/j.chemosphere.2011.04.003>

Many substances related to human activities end up in wastewater and accumulate in sewage sludge. So far, there is only one extensive survey on the occurrence of UV filter residues in sewage sludge. However, more data are required to draw a reliable picture of the fate and effects of these compounds in the environment. This study attempts to fill this gap through the determination of selected UV filters and derivatives namely 4-methylbenzylidenecamphor, benzophenone-3, octocrylene, ethylhexylmethoxycinnamate, ethylhexyldimethyl PABA, 4-hydroxybenzophenone, 2,4-dihydroxybenzophenone, and 4,4'-dihydroxybenzophenone in treated sewage sludge. The target

compounds were extracted using pressurized liquid extraction and after this, determined by ultra high resolution liquid chromatography-tandem mass spectrometry. The determination was fast and sensitive, affording limits of detection lower than 19 ng g(-1) dry weight (dw) except for 2,4-dihydroxybenzophenone (60 ng g(-1) dw). Good recovery rates, especially given the high complexity of sludge matrix (between 70% and 102% except for 2,4-dihydroxybenzophenone (30%)) were achieved. The application of developed method allowed reporting for the first time the occurrence of two major degradation products of benzophenone-3 that have estrogenic activity in sewage sludge: 4,4'-dihydroxybenzophenone (in 5/15 WWTPs) and 4-hydroxybenzophenone (in 1/15 WWTPs). Results revealed the presence of UV filters in 15 wastewater treatment plants in Catalonia (Spain) at concentrations ranging from 0.04 to 9.17 $\mu\text{g g}^{-1}$ dw.

Galindo-Miranda, J. M., Guízar-González, C., Becerril-Bravo, E. J., Moeller-Chávez, G., León-Becerril, E., & Vallejo-Rodríguez, R. (2019). Occurrence of Emerging Contaminants in Environmental Surface Waters and Their Analytical Methodology – a Review. *Water Supply*
<https://doi.org/10.2166/ws.2019.087>

A new concern about surface water quality is the occurrence of emerging contaminants that have being recognized as a new class of water contaminants such as antibiotics, hormones, pesticides, personal care products and pharmaceutical products. The occurrence of these contaminants in the aquatic environment and especially in surface water is a serious concern because this is usually the source of water for drinking water treatment plants (DWTP). This review provides a summary of the occurrence and the analytical methodology (extraction process, chromatography analysis, detection systems and ionization source) of emerging contaminant analysis in surface waters including rivers, lakes, creeks and wetlands for their analysis.

He, K., Hain, E., Timm, A., Tarnowski, M., & Blaney, L. (2019). Occurrence of Antibiotics, Estrogenic Hormones, and UV-Filters in Water, Sediment, and Oyster Tissue from the Chesapeake Bay. *Science of The Total Environment*, 650(Pt 2), 3101-3109
<https://doi.org/10.1016/j.scitotenv.2018.10.021>

Globally, the occurrence of contaminants of emerging concern (CECs) in the environment has raised critical questions on ecological and human health, but few efforts have focused on the Chesapeake Bay, the largest estuary in the United States. Here, 43 antibiotics, 3 estrogenic hormones, and 5 ultraviolet-filters (UV-filters), which are active ingredients in a variety of personal care products, were measured in water, sediment, and oyster tissue from 14 sites along the Eastern Shore of the Chesapeake Bay in Maryland. Fluoroquinolone, macrolide, and sulfonamide antibiotics were detected in water samples. As both human- and animal-labeled antibiotics were found, wastewater effluent and agricultural runoff were identified as potential sources. The highest aqueous-phase concentrations were recorded for norfloxacin (94.1ng/L), enrofloxacin (17.8ng/L), sulfamethoxazole (14.8ng/L), and clarithromycin (9.7ng/L). Estrone and four UV-filters, namely 2-ethylhexyl-4-methoxycinnamate, benzophenone-3, homosalate, and octocrylene, were frequently detected in Chesapeake Bay water (93-100%), sediment (100%), and oyster tissue (79-100%). High sediment-phase concentrations of estrone (58.4ng/g) and 17beta-estradiol (11.5ng/g) were detected at the mouth of the Manokin River. Homosalate and benzophenone-3 were present at concentrations as high as 187.9 and 113.7ng/L in water, 74.2 and 10.8ng/g in sediment, and 158.3 and 118.0ng/g in oyster tissue, respectively. These results demonstrate the ubiquitous presence of CECs in the Chesapeake Bay, confirm UV-filter bioaccumulation in oysters,

and suggest the need for improved CEC removal during municipal wastewater treatment and agricultural waste management within the Chesapeake Bay watershed.

Horricks, R. A., Tabin, S. K., Edwards, J. J., Lumsden, J. S., & Marancik, D. P. (2019). Organic Ultraviolet Filters in Nearshore Waters and in the Invasive Lionfish (*Pterois Volitans*) in Grenada, West Indies. *Plos One*, 14(7), 11 <https://doi.org/10.1371/journal.pone.0220280>

Sunscreens and other personal care products use organic ultraviolet (UV) filters such as oxybenzone, 4-methylbenzylidene camphor, Padimate-O, and octyl methoxycinnamate to prevent damage to human skin. While these compounds are effective at preventing sunburn, they have a demonstrated negative effect on cells and tissues across taxonomic levels. These compounds have a relatively short half-life in seawater but are continuously reintroduced via recreational activities and wastewater discharge, making them environmentally persistent. Because of this, testing seawater samples for the presence of these compounds may not be reflective of their abundance in the environment. Bioaccumulation of organic ultraviolet filters in a high-trophic level predator may provide greater insight to the presence and persistence of these compounds. To address this, the present study collected seawater samples as well as muscle and stomach content samples from the invasive Pacific lionfish (*Pterois volitans*) in the nearshore waters of Grenada, West Indies to examine the use of lionfish as potential bioindicator species. Seawater and lionfish samples were collected at four sites that are near point sources of wastewater discharge and that receive a high number of visitors each year. Samples were tested for the presence and concentrations of oxybenzone, 4-methylbenzylidene camphor (4-MBC), Padimate-O, and octyl methoxycinnamate (OMC) using liquid chromatography-mass spectrometry. Oxybenzone residues were detected in 60% of seawater samples and OMC residues were detected in 20% of seawater samples. Seawater samples collected in the surface waters near Grenada's main beach had oxybenzone concentrations more than ten times higher than seawater samples collected in less frequently visited areas and the highest prevalence of UV filters in lionfish. Residues of oxybenzone were detected in 35% of lionfish muscle and 4-MBC residues were detected in 12% of lionfish muscle. Padimate-O was not detected in either seawater or lion fish samples. No organic UV filters were detected in lionfish stomach contents. Histopathologic examination of lionfish demonstrated no significant findings attributed to UV filter toxicity. These findings report UV filter residue levels for the first time in inshore waters in Grenada. Results indicate that lionfish may be bioaccumulating residues and may be a useful sentinel model for monitoring organic ultraviolet filters in the Caribbean Sea.

Huang, W., Xie, Z., Yan, W., Mi, W., & Xu, W. (2016). Occurrence and Distribution of Synthetic Musks and Organic UV Filters from Riverine and Coastal Sediments in the Pearl River Estuary of China. *Marine Pollution Bulletin*, 111(1-2), 153-159 <https://doi.org/10.1016/j.marpolbul.2016.07.018>

This study reports the occurrence and distribution of synthetic musks (SMs) and organic UV filters (UVFs) in sediment samples collected in 8 riverine runoffs from the Pearl River and Pearl River estuary (PRE). Here, 6 of the 8 target compounds were detected in all sediments with concentrations ranging from 0.35ngg(-1) to 456ngg(-1). Higher concentrations of SMs and UVFs were evident in the eastern outlets compared to the western suggesting greater input of these contaminants from the Pearl River Delta (PRD) region. All the compounds showed a decreasing trend toward the seaward side which confirming that riverine runoff was the most important source of SMs and UVFs to the coastal environment. Notably, high levels of SMs and UVFs were detected in two fishing harbors in the PRE area. In comparison to UVFs, the SM compounds exhibited a significant correlation with TOC content in the sediments.

Jeon, H. K., Chung, Y., & Ryu, J. C. (2006). Simultaneous Determination of Benzophenone-Type UV Filters in Water and Soil by Gas Chromatography-Mass Spectrometry. *Journal of Chromatography A*, 1131(1-2), 192-202 <https://doi.org/10.1016/j.chroma.2006.07.036>

A novel method has been developed to simultaneously determine and quantify seven organic UV filters employing liquid (solid)-liquid extraction, derivatization with N-methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA) and gas chromatography with mass spectrometric detection in various environmental matrices. The UV filters determined were: benzophenone (BP), benzhydrol (BH), 4-hydroxybenzophenone (HBP), 2-hydroxy-4-methoxybenzophenone (HMB), 2,4-dihydroxybenzophenone (DHB), 2,2'-dihydroxy-4-methoxybenzophenone (DHMB) and 2,3,4-trihydroxybenzophenone (THB). Under optimal conditions, the analysis required 23 min and good linearity over the range of 10-2500 ng/L in water and 100-25000 ng/kg in soil for each UV filter obtained. The high recovery (62-114% and 60-125% for water and soil samples, respectively) and the low RSD values (less than 13.9 and 17.2% for water and soil samples, respectively) indicated the high performance of this method. The method detection limits (MDLs) were relatively low, ranging from 5 to 100 ng/L or kg and quantification limits ranged between 25 and 500 ng/L or kg for all test compounds. This validated method was applied in the analysis of seven BP-type UV filters collecting water and soil samples in Korea, between April and May 2003. The overall concentration of UV filters in the soil sample (500-18380 ng/kg) was highly distributed in water sample (27-204 ng/L). The established method was successfully applied to monitor the residue measurement of the BP-type UV filters in environmental water and soil samples.

Jurado, A., Gago-Ferrero, P., Vazquez-Sune, E., Carrera, J., Pujades, E., Diaz-Cruz, M. S., & Barcelo, D. (2014). Urban Groundwater Contamination by Residues of UV Filters. *Journal of Hazardous Materials*, 271, 141-149 <https://doi.org/10.1016/j.jhazmat.2014.01.036>

The occurrence and fate of UV filters (UV F) in an urban aquifer in correlation with (1) the spatial distribution of UV F in Barcelona's groundwater, (2) the depth of the groundwater sample, (3) the physicochemical properties of the target compounds, (4) the recharge sources, and (5) the redox conditions of the Barcelona aquifers, were studied for the first time. The highest groundwater concentrations and the largest number of detected UV F were observed in an aquifer recharged by a polluted river (around 55 ng/L in SAP-4). In contrast, the urbanized areas had lower concentrations (around 20 ng/L in MPSP-1). Two pathways can be identified for UV F to enter the aquifers: (1) leakage of raw sewage from the sewage network in urbanized areas and (2) wastewater treatment plant (WWTP) effluents discharged into the river. Measured concentrations of UV F were significantly much lower than those estimated from the waste water proportion in groundwater samples suggesting that UV F might undergo transformation processes in both reducing and oxidizing conditions.

Kameda, Y., Kimura, K., & Miyazaki, M. (2011). Occurrence and Profiles of Organic Sun-Blocking Agents in Surface Waters and Sediments in Japanese Rivers and Lakes. *Environmental Pollution*, 159(6), 1570-1576 <https://doi.org/10.1016/j.envpol.2011.02.055>

Sun-blocking agents including eight UV filters (UVF) and 10 UV light stabilizers (UVLS) were measured in water and sediment collected from 22 rivers, four sewage treatment plant effluents (STPE) and three lakes in Japan. Total sun blocking agents levels ranged from N.D. to 4928 ng/L and from 2.0 to 3422 µg/kg dry wt in surface water and in sediment, respectively. Benzyl salicylate, benzophenone-3, 2-ethyl hexyl-4-methoxycinnamate (EHMC) and octyl salicylate were dominant in surface water receiving wastewater effluents and STPE, although UV-328, benzophenone and EHMC were dominant in other

surface water except background sites. Three UVF and nine UVLS were observed from all sediment and their compositions showed similar patterns with UV-328 and UV-234 as the most prevalent compounds. Homosalate, octocrylene, UV-326, UV-327, UV-328 and UV-234 were significantly correlated with Galaxolide (R) in sediments. Concentrations of UV-327 and UV-328 also had strong correlation between those of UV-326 in sediment.

Kim, K. Y., Ekpeghere, K. I., Jeong, H. J., & Oh, J. E. (2017). Effects of the Summer Holiday Season on UV Filter and Illicit Drug Concentrations in the Korean Wastewater System and Aquatic Environment. *Environmental Pollution*, 227, 587-595
<https://doi.org/10.1016/j.envpol.2017.04.055>

Seasonal variations in the concentrations of eight ultraviolet (UV) filters and 22 illicit drugs including their metabolites in the Korean aquatic environment were investigated. Seawater samples from three beaches, water samples from two rivers, and influents and effluents from three wastewater treatment plants were analyzed. The UV filter concentrations in the seawater, river water, and effluent samples were 39.4-296, 35.4-117, and 6.84-51.1 ng L⁻¹, respectively. The total UV filter concentrations in the seawater samples were 1.9-4.4 times higher at the peak of the holiday season than outside the peak holiday season. An environmental risk assessment showed that ethylhexyl methoxy cinnamate (EHMC) could cause adverse effects on aquatic organisms in the seawater at the three beaches during the holiday period. Seven of the 22 target illicit drugs including their metabolites were detected in the wastewater influent samples, and the total illicit drug concentrations in the influent samples were 0.08-65.4 ng L⁻¹. The estimated daily consumption rates for cis-tramadol (Cis-TRM), methamphetamine (MTP), meperidine (MEP), and codeine (COD) were 25.7-118.4, 13.8-36.1, 1.36-12.6, and 1.75-8.64 mg d⁻¹ (1000 people)⁻¹, respectively. In popular vacation area, the illicit drug consumption rates (Cis-TRM, MTP and MEP) were 1.6-2.6 times higher at the peak of the summer holiday season than at the beginning of the summer.

Kim, S., & Choi, K. (2014). Occurrences, Toxicities, and Ecological Risks of Benzophenone-3, a Common Component of Organic Sunscreen Products: A Mini-Review. *Environment International*, 70, 143-157 <https://doi.org/10.1016/j.envint.2014.05.015>

Benzophenone-3 (BP-3) has been widely used in sunscreens and many other consumer products, including cosmetics. The widespread use of BP-3 has resulted in its release into the water environment, and hence its potential impact on aquatic ecosystem is of concern. To better understand the risk associated with BP-3 in aquatic ecosystems, we conducted a thorough review of available articles regarding the physicochemical properties, toxicokinetics, environmental occurrence, and toxic effects of BP-3 and its suspected metabolites. BP-3 is lipophilic, photostable, and bioaccumulative, and can be rapidly absorbed via oral and dermal routes. BP-3 is reported to be transformed into three major metabolites in vivo, i.e., benzophenone-1 (BP-1), benzophenone-8 (BP-8), and 2,3,4-trihydroxybenzophenone (THB). BP-1 has a longer biological half-life than its parent compound and exhibits greater estrogenic potency in vitro. BP-3 has been detected in water, soil, sediments, sludge, and biota. The maximum detected level in ambient freshwater and seawater is 125ng/L and 577.5ng/L, respectively, and in wastewater influent is 10,400ng/L. The major sources of BP-3 are reported to be human recreational activities and wastewater treatment plant (WWTP) effluents. BP-3 and its derivatives have been also detected in fish lipid. In humans, BP-3 has been detected in urine, serum, and breast milk samples worldwide. BP-1 has also been detected in placental tissues of delivering women. While sunscreens and cosmetics are known to be major sources of exposure, the fact that BP-3 has been

detected frequently among young children and men suggests other sources. An increasing number of in vitro studies have indicated the endocrine disrupting capacity of BP-3. Based on a receptor binding assay, BP-3 has shown strong anti-androgenic and weak estrogenic activities but at the same time BP-3 displays anti-estrogenic activity as well. Predicted no effect concentration (PNEC) for BP-3 was derived at 1.32µg/L. The levels observed in ambient water are generally an order of magnitude lower than the PNEC, but in wastewater influents, hazard quotients (HQs) greater than 1 were noted. Considering limited ecotoxicological information and significant seasonal and spatial variations of BP-3 in water, further studies on environmental monitoring and potential consequences of long-term exposure in aquatic ecosystem are warranted.

Klotz, K., Hof, K., Hiller, J., Göen, T., & Drexler, H. (2019). Quantification of Prominent Organic UV Filters and Their Metabolites in Human Urine and Plasma Samples. *Journal of Chromatography B*, 1125, 121706 <https://doi.org/10.1016/j.jchromb.2019.06.033>

Monitoring human exposure to chemical UV filters is essential for an accurate assessment of the health risk caused by the resorbed compounds. We developed different procedures for the determination of the prominent UV filters octocrylene (OC), avobenzone (AVO) and 2-ethylhexyl salicylate (EHS) as well as for two OC and EHS metabolites in human urine and OC, AVO and 2-cyano-3,3-diphenylacrylic acid (CDAA) in plasma samples using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Since the development of a multi-method for all analytes proved to be difficult, three different procedures were established for the determination of AVO, OC and its metabolite CDAA in urine and plasma as well as for EHS and its metabolite 5-hydroxy-EHS in urine. The methods have been validated with good sensitivity, precision and accuracy. The procedures were satisfactorily applied to the determination of the target compounds in human samples collected from volunteers after sunscreen application. These new analytical procedures can provide information on the internal exposure to the UV filters OC, AVO and EHS, which has been little studied.

Kung, T. A., Lee, S. H., Yang, T. C., & Wang, W. H. (2018). Survey of Selected Personal Care Products in Surface Water of Coral Reefs in Kenting National Park, Taiwan. *Science of The Total Environment*, 635, 1302-1307 <https://doi.org/10.1016/j.scitotenv.2018.04.115>

Kenting National Park (KNP) located in the Hengchun Peninsula in southern Taiwan is a popular tourist spot, annually attracting millions of visitors, who engage in water sport and amusement activities. In this region, sewage is directly discharged into the marine environment. In this study, the concentrations of five organic UV filters [benzophenone (BP), 2,4-dihydroxy benzophenone (BP-1), 2-hydroxy-4-methoxy benzophenone (BP-3), 2,2'-dihydroxy-4-methoxy benzophenone (BP-8), and 4-methylbenzylidene camphor], five preservatives [methylparaben (MeP), ethylparaben, propylparaben (PrP), butylparaben, and benzylparaben], one disinfectant [triclosan (TCS)], and twenty-four detergent derivatives [nonylphenol (NP), nonylphenol ethoxylates (NP2EO-NP12EO), octylphenol (OP) and octylphenol ethoxylates OP2EO-OP12EO] were detected in seawater and river water samples collected from eight beaches in KNP and two major river estuaries in the Hengchun Peninsula. BP-3 was detected at all sampling sites and was higher in concentration than the other organic UV filters. The highest concentration of BP-3 was 1233ng/L collected from Wanlitong Beach. MeP and PrP were the main preservative components in seawater. The highest total content of preservative agents was 164ng/L collected from Houwan Beach. Moreover, NP was detected at all sampling sites, with the highest concentration found at Sail Rock Beach (26.5ng/L). The highest concentration of OP was 113ng/L in the Boli River estuary. The widespread use of personal care products (PCPs) has resulted in the release of

their major ingredients into natural ecosystems. Therefore, the potential long-term effects of multi-PCPs at low concentration exposure to on the coral reef ecosystem in KNP must be considered and monitored.

Langford, K. H., Reid, M. J., Fjeld, E., Oxnevad, S., & Thomas, K. V. (2015). Environmental Occurrence and Risk of Organic UV Filters and Stabilizers in Multiple Matrices in Norway. *Environment International*, 80, 1-7 <https://doi.org/10.1016/j.envint.2015.03.012>

Eight organic UV filters and stabilizers were quantitatively determined in wastewater sludge and effluent, landfill leachate, sediments, and marine and freshwater biota. Crab, prawn and cod from Oslofjord, and perch, whitefish and burbot from Lake Mjosa were selected in order to evaluate the potential for trophic accumulation. All of the cod livers analysed were contaminated with at least 1 UV filter, and a maximum concentration of almost 12 µg/g wet weight for octocrylene (OC) was measured in one individual. 80% of the cod livers contained OC, and approximately 50% of cod liver and prawn samples contained benzophenone (BP3). Lower concentrations and detection frequencies were observed in freshwater species and the data of most interest is the 4 individual whitefish that contained both BP3 and ethylhexylmethoxycinnamate (EHMC) with maximum concentrations of almost 200 ng/g wet weight. The data shows a difference in the loads of UV filters entering receiving water dependent on the extent of wastewater treatment. Primary screening alone is insufficient for the removal of selected UV filters (BP3, Padimate, EHMC, OC, UV-234, UV-327, UV-328, UV-329). Likely due in part to the hydrophobic nature of the majority of the UV filters studied, particulate loading and organic carbon content appear to be related to concentrations of UV filters in landfill leachate and an order of magnitude difference in these parameters correlates with an order of magnitude difference in the effluent concentrations of selected UV filters (Fig. 2). From the data, it is possible that under certain low flow conditions selected organic UV filters may pose a risk to surface waters but under the present conditions the risk is low, but some UV filters will potentially accumulate through the trophic food chain.

Liao, C., & Kannan, K. (2019). Species-Specific Accumulation and Temporal Trends of Bisphenols and Benzophenones in Mollusks from the Chinese Bohai Sea During 2006-2015. *Science of The Total Environment*, 653, 168-175 <https://doi.org/10.1016/j.scitotenv.2018.10.271>

Information on the occurrence and bioaccumulation of bisphenols and benzophenones in coastal marine invertebrates is limited. In this study, concentrations of eight bisphenol and five benzophenone analogues were determined in 186 mollusks collected from coastal areas of the Chinese Bohai Sea during the period 2006-2015. Total concentrations of bisphenols and benzophenones were in range of not detected (nd)-58 (geometric mean: 13.0ng/g) and nd-59.1 (2.06ng/g) on a dry-weight basis, respectively. BPA and BPF were the major bisphenols, collectively accounting for >90% of the total concentrations. BP-3 was the predominant benzophenone, representing 74% of the total concentrations. The mollusk species, *Meretrix meretrix*, accumulated high concentrations of both bisphenols and benzophenones. A steady increase in bisphenol concentrations in mollusks was observed in recent years, whereas no obvious temporal trend was found for benzophenones. The estimated daily intakes of bisphenols through consumption of mollusks were lower than the current reference dose. This study establishes a baseline concentration for bisphenols and benzophenones in mollusks in Chinese coastal waters.

Lindo-Atichati, D., Montero, P., Rodil, R., Quintana, J. B., & Miro, M. (2019). Modeling Dispersal of UV Filters in Estuaries. *Environmental Science & Technology*, 53(3), 1353-1363
<https://doi.org/10.1021/acs.est.8b03725>

Lagrangian ocean analysis, where virtual parcels of water are tracked through hydrodynamic fields, provides an increasingly popular framework to predict the dispersal of water parcels carrying particles and chemicals. We conduct the first direct test of Lagrangian predictions for emerging contaminants using (1) the latitude, longitude, depth, sampling date, and concentrations of UV filters in raft cultured mussel (*Mytilus galloprovincialis*) of the estuary Ria de Arousa, Spain (42.5 degrees N, 8.9 degrees W); (2) a hydrodynamic numerical model at 300 m spatial resolution; and (3) a Lagrangian dispersion scheme to trace polluted water parcels back to pollution sources. The expected dispersal distances (mean +/- SD) are 2 +/- 1 km and the expected dispersal times (mean +/- SD) are 6 +/- 2 h. Remarkably, the probability of dispersal of UV filters from potential sources to rafts decreases 5-fold over 5 km. In addition to predicting dispersal pathways and times, this study also provides a framework for quantitative investigations of concentrations of emerging contaminants and source apportionment using turbulent diffusion. In the coastline, the ranges of predicted concentrations of the UV-filters 4-methylbenzylidene-camphor, octocrylene, and benzophenone-4 are 3.2×10^{-4} to 0.023 ng/mL, 2.3×10^{-5} to 0.009 ng/mL, and 5.6×10^{-4} to 0.013 ng/mL, respectively. At the outfalls of urban wastewater treatment plants these respective ranges increase to 8.9×10^{-4} to 0.07 ng/mL, 6.2×10^{-5} to 0.027 ng/mL, and 1.6×10^{-3} to 0.040 ng/mL.

Liu, Y. Y., Lin, Y. S., Yen, C. H., Miaw, C. L., Chen, T. C., Wu, M. C., & Hsieh, C. Y. (2018). Identification, Contribution, and Estrogenic Activity of Potential Edcs in a River Receiving Concentrated Livestock Effluent in Southern Taiwan. *Science of The Total Environment*, 636, 464-476
<https://doi.org/10.1016/j.scitotenv.2018.04.031>

We assessed 22 selected endocrine-disrupting compounds (EDCs) and other emerging, potentially endocrine-active compounds with estrogenic activity from the waters of the Wuluo River, southern Taiwan. This watershed receives high amounts of livestock and untreated household wastewaters. The river is surrounded by concentrated animal feedlot operations (CAFOs). River water samples were analyzed for selected compounds by liquid chromatography-tandem mass spectrometry (LC-MS/MS), T47D-KBluc reporter gene assay, and E-screen cell proliferation in vitro bioassay. Total concentrations of summation operatoralkylphenolic compounds (bisphenol A, 4-nonylphenol, t-nonylphenol, octylphenol, nonylphenol mono-ethoxylate, nonylphenol di-ethoxylate) were much higher than summation operatorestrogens (estrone, 17 beta-estradiol, estriol, 17ss-ethynylestradiol, diethylstilbestrol), summation operatorpreservatives (methyl paraben, ethyl paraben, propyl paraben, butyl paraben), summation operatorUV-filters (benzophenone, methyl benzylidene camphor, benzophenone-3), summation operatorantimicrobials (triclocarben, triclosan, chloroxylenol), and an insect repellent (diethyltoluamide) over four seasonal sampling periods. The highest concentration was found for bisphenol A with a mean of 302ng/L. However, its contribution to estrogenic activity was not significant due to its relatively low estrogenic potency. Lower detection rates were found for BP, EE2, TCS, and PCMX, while DES and EP were not detected. E1 and E2 levels in raw water samples were 50% higher than the predicted no-effect concentrations (PNEC) for aquatic organisms of 6 and 2ng/L, respectively. The potency of estrogenic activity ranged from 11.7 to 190.1ng/L E2T47D-Kbluc and 6.63 to 84.5ng/L E2E-Screen for extracted samples. Importantly, estrone contributed 50% of the overall activity in 60% and 44% of the samples based on T47D-KBluc and MCF-7 bioassays, followed by 17 ss-estradiol,

highlighting the importance of total steroid estrogen loading. This study demonstrates that the estrogenic activity of target chemicals was comparable to levels found in different countries worldwide. More intense wastewater treatment is required in areas of intensive agriculture in order to prevent adverse impacts on the ambient environment and aquatic ecosystems.

Loosli, F., Wang, J. J., Rothenberg, S., Bizimis, M., Winkler, C., Borovinskaya, O., . . . Baalousha, M. (2019). Sewage Spills Are a Major Source of Titanium Dioxide Engineered (Nano)-Particle Release into the Environment. *Environmental Science-Nano*, 6(3), 763-777
<https://doi.org/10.1039/c8en01376d>

Sanitary sewer overflows (SSOs) are a common problem across the United States. An estimated number of 23000-75000 SSOs occurred in 2004, discharging between 11 and 38 billion liters of untreated wastewater to receiving waters. SSOs release many contaminants, including engineered nanomaterials (ENMs), to receiving water bodies. Measuring ENM concentrations in environmental samples remains a key challenge in environmental nanotechnology and requires the distinction between natural and engineered particles. This distinction between natural and engineered particles is often hampered by the similarities in the intrinsic properties of natural and engineered particles, such as particle size, composition, density, and surface chemistry, and by the limitations of the available nanometrology tools. To overcome these challenges, we applied a multi-method approach to measure the concentrations and properties of TiO₂ engineered particles (e.g., ENMs and pigments) including: 1) multi element-single particle-inductively coupled plasma-mass spectrometry (ME-SP-ICP-MS) to identify elemental associations and to determine elemental ratios in natural particles, 2) calculation of total elemental concentrations and ratios from total metal concentrations measured following total sample digestion to estimate engineered particle concentrations, and 3) transmission electron microscopy (TEM) to characterize engineered particle size and morphology. ME-SP-ICP-MS analysis revealed that natural TiO₂ particles are often associated with at least one of the following elements: Al, Fe, Ce, Si, La, Zr, Nb, Pb, Ba, Th, Ta, W and U, and that elemental ratios of Ti to these elements, except Pb, are typical of riverine particulates and the average crustal ratios. High TiO₂ engineered particle concentrations up to 100 µg L⁻¹ were found in SSO-impacted surface waters. TEM analysis demonstrated the presence of regular-shape TiO₂ particles in SSO-impacted surface waters. This study provides a comprehensive approach for measuring TiO₂ engineered particle concentrations in surface waters. The quantitative data produced in this work can be used as input for modeling studies and pave the way for routine monitoring of ENMs in environmental systems, validation of ENM fate models, and more accurate ENM exposure and risk assessment.

Lopardo, L., Adams, D., Cummins, A., & Kasprzyk-Hordern, B. (2018). Verifying Community-Wide Exposure to Endocrine Disruptors in Personal Care Products - in Quest for Metabolic Biomarkers of Exposure Via in Vitro Studies and Wastewater-Based Epidemiology. *Water Research*, 143, 117-126 <https://doi.org/10.1016/j.watres.2018.06.028>

This study aimed to identify human specific metabolites of selected known or suspected endocrine disruptors (EDCs), mainly UV filters, used in personal care and consumer products whose metabolism has hardly been explored and to select suitable candidate biomarkers for human exposure studies using wastewater based epidemiology (WBE). The analysis of metabolic biomarkers of target chemicals is crucial in order to distinguish between internal and external exposure, since many sources contribute to chemicals being discharged into wastewater. This was achieved through the employment of a new analytical framework for verification of biomarkers of exposure to chemicals combining human

biomonitoring and water fingerprinting. Eight EDCs with unknown metabolic pathways (benzophenone-1 (BP-1); benzophenone-2 (BP-2); 4,4'-dihydroxybenzophenone (4,4'-DHBP); 4-benzylphenol (4-BenzPh); homosalate (HO); octocrylene (OC); 3-benzylidene camphor (3-BC), and two EDCs with known metabolism (bisphenol A (BPA) and benzophenone-3 (BP-3)) were tested. The biotransformation observed consisted mainly of phase I processes such as hydrolysis and hydroxylation together with phase II conjugation reactions such as sulphation and glucuronidation. Only two chemicals (BP-1, BP-3) were identified in urine and three chemicals (BPA, BP-1, BP-3) in wastewater. Five newly discovered metabolites (HO-Met1, OC-Met1, 4-BenzPh-Met4, 4-BenzPh-Met5 and 4-BenzPh-Met6) and one previously known metabolite (BPA-Met3) were detected in tested urine/wastewater samples from five WWTPs serving large communities ranging between 17 and 100 thousand inhabitants. The presence of metabolic biotransformation products of OC, 4-BenzPh, BPA and HO in wastewater provides evidence for internal exposure of studied populations to these chemicals.

Ma, X., Wan, Y., Wu, M., Xu, Y., Xu, Q., He, Z., & Xia, W. (2018). Occurrence of Benzophenones, Parabens and Triclosan in the Yangtze River of China, and the Implications for Human Exposure. *Chemosphere*, 213, 517-525 <https://doi.org/10.1016/j.chemosphere.2018.09.084>

Humans could be exposed to ingredients in personal care products (PCPs) via ingestion of water originated from contaminated water source, yet little attention has been focused on the distribution of benzophenones, parabens and triclosan in the Yangtze River water from China so far. Benzophenones, parabens and triclosan were analyzed in the water samples from 20 various sites in the middle reach of the Yangtze River, China from March to July, and September during 2015. Among the targeted compounds, p-hydroxybenzoic acid (PHBA, a paraben metabolite) was found with the highest concentration (median: 510ng/L), followed by benzophenone-1 (2.79ng/L), methylparaben (MeP, median 2.72ng/L) and triclosan (median: 1.85ng/L). Significant differences were observed in seasonal variations for most observed compounds. Parabens and benzophenones showed higher concentrations in spring while triclosan and PHBA showed higher concentration in summer. Spatial variations of benzophenone-1 were observed among 20 sampling sites, whereas other benzophenones, parabens and triclosan distributed evenly comparatively. Human exposure assessment showed higher estimated daily intake of the detected compounds for infants and toddlers from water than adults, implicating that infants may experience a higher exposed risk than adults. This study provides evidence that parabens, benzophenones and triclosan commonly occurred in the Yangtze River.

Mitchelmore, C. L., He, K., Gonsior, M., Hain, E., Heyes, A., Clark, C., . . . Blaney, L. (2019). Occurrence and Distribution of UV-Filters and Other Anthropogenic Contaminants in Coastal Surface Water, Sediment, and Coral Tissue from Hawaii. *Science of The Total Environment*, 670, 398-410 <https://doi.org/10.1016/j.scitotenv.2019.03.034>

The occurrence of UV-filters in the environment has raised concerns over potentially adverse impacts on corals. In this study, the concentrations of 13 UV-filters and 11 hormones were measured in surface seawater, sediment, and coral tissue from 19 sites in Oahu, Hawaii. At least eight UV-filters were detected in seawater, sediment, and coral tissue and total mass concentrations of all UV-filters were <750ngL(-1), <70ngg(-1) dry weight (dw), and <995ngg(-1) dw, respectively. Four UV-filters were detected in water, sediment, and coral tissue at detection frequencies of 63-100%, 56-91%, and 82-100%, respectively. These UV-filter concentrations generally varied as follows: water, homosalate (HMS)>octisalate (OS)>benzophenone-3 (BP-3, also known as oxybenzone)>octocrylene (OC); sediment, HMS>OS > OC>BP-3; coral, OS approximately HMS>OC approximately BP-3. BP-3 concentrations in

surface seawater were <10ngL(-1) at 12 of 19 sites and highest at Waikiki beach (e.g., 10.9-136ngL(-1)). While BP-3 levels were minimal in sediment (e.g., <1ngg(-1) dw at 18 of 19 sites), and ranged from 6.6 to 241ngg(-1) dw in coral tissue. No quantifiable levels of 2-ethylhexyl 4-methoxycinnamate (also known as octinoxate) were recorded in surface seawater or coral tissues, but 5-12.7ngg(-1) dw was measured for sediment at 5 of 19 sites. No hormones were detected in seawater or sediment, but 17alpha-ethinylestradiol was present in three corals from Kaneohe Bay. Surfactant degradation products were present in seawater, especially at Waikiki beach. These results demonstrate ubiquitous parts-per-trillion concentrations of UV-filters in surface seawater and is the first report of UV-filters in coral tissue from U.S.A. coastal waters. These data inform the range of environmentally-relevant concentrations for future risk assessments on the potential impacts of UV-filters on coral reefs in Oahu, Hawaii.

Mizukawa, A., Molins-Delgado, D., de Azevedo, J. C. R., Fernandes, C. V. S., Diaz-Cruz, S., & Barcelo, D. (2017). Sediments as a Sink for UV Filters and Benzotriazoles: The Case Study of Upper Iguacu Watershed, Curitiba (Brazil). *Environmental Science and Pollution Research*
<https://doi.org/10.1007/s11356-017-9472-9>

Ingredients in home and personal care products, including UV filters and benzotriazoles, are high production volume chemicals extensively used in our daily life, despite several studies revealed their potential eco-toxicity and endocrine-disrupting capacity. Due to some features, such as high lipophilicity, low degradability, and persistence of many of these compounds, sediments can be considered a sink for them in the aquatic environment. In the present study, nine organic UV filters and three benzotriazoles were investigated for the first time in sediments from four urban rivers in Brazil. The contaminants were analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS). The results revealed that octocrylene (OC), ethylhexyl-methoxycinnamate (EHMC), benzophenone-3 (oxybenzone, BP3), and benzotriazole (BZT) were the predominant compounds adsorbed on the sediments, with concentrations ranging from 5.6 to 322.2 ng g-1 dry weight. The results reported in this work constitute the first data on the accumulation of polar benzotriazoles and lipophilic organic UV filters in sediments from Brazil.

Molins-Delgado, D., Munoz, R., Nogueira, S., Alonso, M. B., Torres, J. P., Malm, O., . . . Diaz-Cruz, M. S. (2018). Occurrence of Organic UV Filters and Metabolites in Lebranche Mullet (Mugil Liza) from Brazil. *Science of The Total Environment*, 618, 451-459
<https://doi.org/10.1016/j.scitotenv.2017.11.033>

UV filters (UV-Fs) constitute a heterogeneous group of chemicals used as protection against the effects of UV radiation, widely used in all sort of goods and ubiquitous in the environment. The presence of these chemicals in fish is a matter of concern, because many UV-Fs display hormonal activity. In this study, muscle, gills, and liver from 11 Mugil liza individuals from the highly urbanized Guanabara Bay (Rio de Janeiro, Brazil) were analysed in order to detect eight UV-Fs and metabolites (4-dihydroxybenzophenone [BP1] (2-hydroxy-4-methoxybenzophenone [BP3], 4-methylbenzylidene camphor [4MBC], ethylhexyl methoxycinnamate [EHMC], ethylhexyl dimethyl p-aminobenzoic acid [ODPABA], octocrylene [OC], 4-hydroxybenzophenone [4HB], and 4,4'-dihydroxybenzophenone [4DHB]) using liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Results showed that both target UV-Fs and metabolites were ubiquitous in the analysed tissues. Lower concentrations were observed in muscle and gills (3.07-31.6ngg(-1) dry weight (dw)), whereas in liver significant amounts of metabolites (5.47-451ngg(-1) dw) were present. With the concentrations determined in the fish, an estimation of the daily intake revealed that consumption of muscle in the diet represent from 0.3 to

15.2ng UV-Fs (kg body weight⁻¹) d⁻¹), higher than those reported in fish for selected persistent organic pollutants (POPs).

Molins-Delgado, D., Tavora, J., Silvia Diaz-Cruz, M., & Barcelo, D. (2017). UV Filters and Benzotriazoles in Urban Aquatic Ecosystems: The Footprint of Daily Use Products. *Science of The Total Environment*, 601-602, 975-986 <https://doi.org/10.1016/j.scitotenv.2017.05.176>

The increased use of beauty and other daily use products, in particular those containing UV filters (UV-Fs) and benzotriazoles, results in their introduction in significant amounts into the aquatic environment. In this study, we aim to assess the occurrence and impact of UV-Fs and benzotriazoles in aquatic ecosystems in the metropolitan area of Barcelona, Spain. River water samples from the Llobregat and Besos Rivers were analysed together with sediment, suspended particulate matter, and wastewater samples from 6 wastewater treatment plants (WWTPs) along their basins. The analysis of 6 UV-Fs and 2 benzotriazoles in water samples was performed using an automatized on-line solid phase extraction coupled to liquid chromatography tandem mass spectrometry (SPE-HPLC-MS/MS) method. The analysis of the target compounds in the suspended solids and in the sediments was performed by HPLC-MS/MS. The analysis of the water samples showed the ubiquitous presence of UV-Fs. Benzotriazole (BZT; partition coefficient octanol-water Log Kow=1.23) and methylbenzotriazole (MeBZT; Log Kow=1.89) had the highest levels in both river water and wastewater. Removal rates in the selected WWTPs were highly variable (4-100%). Concentrations of lipophilic UV-Fs (Log Kow 4.95-7.53) in suspended particulate matter from wastewaters were high (up to 1,031,868.2ngg⁻¹dry weight (dw)), whereas in sediment the concentrations were always below 300ng g⁻¹ dw. The risk assessment expressed in terms of hazard quotients (HQs) revealed that most UV-Fs were not likely to produce adverse ecotoxicological effects against the living organisms assayed in river waters and influent wastewaters at the concentrations observed. However, HQs above 1 were obtained for BZT and MeBZT in effluent wastewaters discharged to the river.

Montes-Grajales, D., Fennix-Agudelo, M., & Miranda-Castro, W. (2017). Occurrence of Personal Care Products as Emerging Chemicals of Concern in Water Resources: A Review. *Science of The Total Environment*, 595, 601-614 <https://doi.org/10.1016/j.scitotenv.2017.03.286>

Personal care products (PCPs) are a diverse group of common household substances used for health, beauty and cleaning purposes. These include disinfectants, fragrances, insect repellents, preservatives and UV filters, among others. Some of them are considered chemicals of emerging concern due to their presence and negative impact on aquatic ecosystems, specially related to endocrine disruption and reproductive disorders. The entry of those chemicals to water bodies occurs mainly through the sewage effluents from wastewater treatment plants due to their incomplete or inefficient removal. The purpose of this review was to collect and analyze data about the incidence and concentrations of PCPs reported as emerging pollutants in different water matrices, including wastewater influents and effluents. Our database is composed of 141 articles with information about 72 PCPs recorded as emerging pollutants in 30 countries, in concentrations ranging from 0.029ng/L to 7.811x10⁶ng/L. Fragrances, antiseptics and sunscreens were the most reported groups. As expected, the largest number of PCPs documented as emerging pollutants were found in wastewater treatment plant effluents with a total of 64 compounds, compared to 43 in surface water and 23 in groundwater, which evidence the anthropological contribution of PCPs to water bodies. These molecules were found in all the continents, however, there is a lack of information regarding the presence of emerging pollutants from PCPs in developing

countries. Therefore, we suggest further efforts in assessing the occurrence and concentrations of these chemicals in those areas.

Montesdeoca-Esponda, S., Checchini, L., Del Bubba, M., Sosa-Ferrera, Z., & Santana-Rodriguez, J. J. (2018). Analytical Approaches for the Determination of Personal Care Products and Evaluation of Their Occurrence in Marine Organisms. *Science of The Total Environment*, 633, 405-425 <https://doi.org/10.1016/j.scitotenv.2018.03.182>

Contamination of the aquatic environment caused by multiple human activities may exert a negative impact on all living organisms. Several contaminants of emerging concern such as personal care products (PCPs) are continuously released into the aquatic environment where they are biologically active and persistent. This work reviews the current knowledge, provided by papers published after 2010 and indexed by SciFinder, Scopus, and Google search engines, about the determination and occurrence of PCPs in marine biota. Analytical methodologies have been critically reviewed, emphasizing the importance of green and high-throughput approaches and focusing the discussion on the complexity of the solute-matrix interaction in the extraction step, as well as the matrix effect in the instrumental determination. Finally, the worldwide distribution of PCPs is surveyed, taking into account the concentrations found in the same organism in different marine environments. Differences among various world areas have been highlighted, evidencing some critical aspects from an environmental point of view.

Moschino, V., Schintu, M., Marrucci, A., Marras, B., Nesto, N., & Da Ros, L. (2017). An Ecotoxicological Approach to Evaluate the Effects of Tourism Impacts in the Marine Protected Area of La Maddalena (Sardinia, Italy). *Marine Pollution Bulletin*, 122(1-2), 306-315 <https://doi.org/10.1016/j.marpolbul.2017.06.062>

In the Marine Protected Area of La Maddalena Archipelago, environmental protection rules and safeguard measures for nautical activities have helped in reducing anthropogenic pressure; however, tourism related activities remain particularly significant in summer. With the aim of evaluating their impacts, the biomarker approach using transplanted *Mytilus galloprovincialis* as sentinel organisms coupled with POCIS deployment was applied. Mussels, translocated to four marine areas differently impacted by tourism activities, were sampled before, during and after the tourist season. Moreover, endocrine disruptors in passive samplers POCIS and the cellular toxicity of whole POCIS extracts on mussel haemocytes were evaluated to integrate ecotoxicological information. Lysosomal biomarkers, condition index and mortality rate, as well as metals in tissues suggested an alteration of the health status of mussels transplanted to the most impacted sites. The cellular toxicity of POCIS extracts was pointed out, notwithstanding the concentrations of the examined compounds were always below the detection limits.

Nakata, H., Murata, S., & Filatreau, J. (2009). Occurrence and Concentrations of Benzotriazole UV Stabilizers in Marine Organisms and Sediments from the Ariake Sea, Japan. *Environmental Science and Technology*, 43, 6920-6926 <https://doi.org/10.1021/es900939j>

The benzotriazole UV stabilizers, which are used in a variety of plastic products, were analyzed in marine organisms and sediments collected from the Ariake Sea, Japan. The UV stabilizers, such as UV-320, UV-326, UV-327, and UV-328 were detected in all of the samples analyzed, suggesting the production and use of these compounds in Japan. High concentrations of UV stabilizers were found in clams, oysters,

and gastropods collected from the tidal flat, at concentrations on the order of several hundreds of ng/g on a lipid weight (wt.) basis. The higher trophic species, such as hammerhead sharks and coastal birds, accumulated UV stabilizers, with mean concentrations of 190 ng/g and 74 ng/g (lipid wt.), respectively. These results indicate that benzotriazole UV stabilizers are persistent and bioaccumulative in the marine food-chains. The benzotriazole UV stabilizers were also detected in coastal and river sediments around the Ariake Sea, at concentrations in the range of 7.9–720 ng/g (dry weight basis). Significant correlations were found between concentrations of UV stabilizers and organic carbon content in sediments, implying adsorption of these compounds to organic matter. To our knowledge, this is the first report of ubiquitous contamination and bioaccumulation of benzotriazole UV stabilizers in the marine environment.

Nguyen, K. T., Scapolla, C., Di Carro, M., & Magi, E. (2011). Rapid and Selective Determination of UV Filters in Seawater by Liquid Chromatography-Tandem Mass Spectrometry Combined with Stir Bar Sorptive Extraction. *Talanta*, 85(5), 2375-2384
<https://doi.org/10.1016/j.talanta.2011.07.085>

Fast liquid chromatography coupled to triple-quadrupole tandem mass spectrometry was employed for the determination of six UV filters in seawater. The separation of the analytes was achieved in less than 5 min; polarity switching was used as four of the analytes were ionized in positive mode and the remaining two in negative mode. Two ionization sources were employed and compared: atmospheric pressure chemical ionization (APCI) gave better results than electrospray ionization (ESI) for all analytes, with higher reproducibility and lower detection limits. Therefore APCI was chosen for the determination of the analytes in seawater samples using stir bar sorptive extraction-liquid desorption (SBSE-LD). Quantitative analysis was performed in multiple reaction monitoring (MRM) mode; fragmentation pathways of the analytes with regard to the formation of the MRM ions were also proposed. For the analysis of seawater samples, calibration curves were drawn using SBSE in spiked seawater. All figures of merit of the method were satisfactory; limits of detection were particularly low for the four analytes ionized in positive mode, being in the range 8-31 ng/L. The method was applied to the determination of the six UV filters in seawater samples from Liguria, Italy. Only benzophenone-3 (BP-3) and ethylhexyl methoxycinnamate (EHMC) were measured in the analyzed samples; some of the remaining analytes were also detected but always below the limit of quantitation.

O'Malley, E., O'Brien, J. W., Tschärke, B., Thomas, K. V., & Mueller, J. F. (2019). Per Capita Loads of Organic UV Filters in Australian Wastewater Influent. *Science of The Total Environment*, 662, 134-140 <https://doi.org/10.1016/j.scitotenv.2019.01.140>

Per capita loads of six UV filters were estimated in wastewater influent samples from 36 wastewater treatment plants in Australia collected over a weekend period during the 2016 Australian Census. Of the analysed samples, 99% contained at least one of the target compounds. Phenyl benzimidazole sulfonic acid (PBSA) was the most prevalent (99%), followed by benzophenone 4 (BP4) (97%), benzophenone 3 (BP3) (87%), benzophenone 1 (BP1) (84%), 4-methylbenzylidene camphor (4-MBC) (22%) and isoamyl 4-methoxycinnamate (IMC) (1.5%). The highest concentrations were 3780 and 5070 ng/L(-1) for PBSA and BP4, respectively. Total per capita UV filter loads in influent across all plants were calculated using population data from the Australian Census and ranged from 0.21 to 3.4 mg day(-1) person(-1). Notably, a relationship was found between latitude and total per capita daily mass load of UV filters with an increase in mass load from southern to northern catchments. Compared to international studies, mass loads were generally similar with higher loads of BP4 found in Australia. This study provides insight into

the occurrence of UV filters in influent wastewater from across Australia and provides the first comprehensive nationwide baseline of UV filter loads.

Paredes, E., Perez, S., Rodil, R., Quintana, J. B., & Beiras, R. (2014). Ecotoxicological Evaluation of Four UV Filters Using Marine Organisms from Different Trophic Levels *Isochrysis Galbana*, *Mytilus Galloprovincialis*, *Paracentrotus Lividus*, and *Siriella Armata*. *Chemosphere*, 104, 44-50
<https://doi.org/10.1016/j.chemosphere.2013.10.053>

Due to the concern about the negative effects of exposure to sunlight, combinations of UV filters like 4-Methylbenzylidene-camphor (4-MBC), Benzophenone-3 (BP-3), Benzophenone-4 (BP-4) and 2-Ethylhexyl-4-methoxycinnamate (EHMC) are being introduced in all kind of cosmetic formulas. These chemicals are acquiring a concerning status due to their increasingly common use and the potential risk for the environment. The aim of this study is to assess the behaviour of these compounds in seawater, the toxicity to marine organisms from three trophic levels including autotrophs (*Isochrysis galbana*), herbivores (*Mytilus galloprovincialis* and *Paracentrotus lividus*) and carnivores (*Siriella armata*), and set a preliminary assessment of potential ecological risk of UV filters in coastal ecosystems. In general, EC50 results show that both EHMC and 4-MBC are the most toxic for our test species, followed by BP-3 and finally BP-4. The most affected species by the presence of these UV filters are the microalgae *I. galbana*, which showed toxicity thresholds in the range of $\mu\text{g L}^{-1}$ units, followed by *S. armata* > *P. lividus* > *M. galloprovincialis*. The UV filter concentrations measured in the sampled beach water were in the range of tens or even hundreds of ng L^{-1} . The resulting risk quotients showed appreciable environmental risk in coastal environments for BP-3 and 4-MBC.

Pawlowski, S., Lanzinger, A. C., Dolich, T., Fussl, S., Salinas, E. R., Zok, S., . . . Petersen-Thiery, M. (2019). Evaluation of the Bioaccumulation of Octocrylene after Dietary and Aqueous Exposure. *Science of The Total Environment*, 672, 669-679 <https://doi.org/10.1016/j.scitotenv.2019.03.237>

Octocrylene is used as UV filter in personal care products with a high production volume and can be detected in surface water and biota. It is liquid at ambient temperature, highly lipophilic, has a high adsorption capacity to organic material and is considered as persistent in the environment. The very low water solubility complicates the evaluation of potential long-term effects in aquatic toxicity testing, since effect thresholds are often above the water solubility limit. Thus, the evaluation of the bioaccumulation potential becomes highly relevant for the assessment of long-term environmental effects. However, even the determination of the water solubility limit for a substance with such difficult properties is challenging. The following experiments are described, and results compared to available environmental monitoring data: A bioconcentration study with aqueous exposure (BCF) in zebrafish and a biomagnification study with dietary exposure (BMF) in rainbow trout, as well as supporting experiments to evaluate the water solubility. The growth and lipid corrected BCF determined by aqueous exposure was 858Lkg^{-1} while the corrected BMF was 0.0335. The model-based estimation of the BCF from BMF ($152\text{-}1182 \text{Lkg}^{-1}$) is in good agreement with the measured BCF value. Environmental monitoring data provide only limited information on the bioaccumulation potential of octocrylene, as only few investigations were made in biota and water in parallel and concentrations of octocrylene vary by several orders of magnitude during seasons. Based on the determined fish BCF data, we conclude that OCR is not bioaccumulative according to the criteria as laid down by ECHA, 2017. Furthermore, the low BMF value indicates no accumulation along the food chain.

Peng, X., Fan, Y., Jin, J., Xiong, S., Liu, J., & Tang, C. (2017). Bioaccumulation and Biomagnification of Ultraviolet Absorbents in Marine Wildlife of the Pearl River Estuarine, South China Sea. *Environmental Pollution*, 225, 55-65 <https://doi.org/10.1016/j.envpol.2017.03.035>

Bioaccumulation and trophic transfer in ecosystems is an important criterion for assessing environmental risks of contaminants. This study investigated bioaccumulation and biomagnification of 13 organic ultraviolet absorbents (UVAs) in marine wildlife organisms in the Pearl River Estuary, South China Sea. The UVAs could accumulate in the organisms with biota - sediment accumulation factors (BSAF) of 0.003-2.152. UV531 was the most abundant and showed the highest tendency to accumulate in the organisms with a median BSAF of 1.105. The UVAs demonstrated species - and compound-specific accumulation in the marine organism. Fishes showed significantly higher capability than the cephalopods and crustaceans in accumulation of the UVAs. Habitat did not demonstrate obvious impact on accumulation of the UVA. On the other hand, benzophenone-3, UV328, and UV234 showed significantly higher concentration in the detritus feeding fishes than carnivorous and planktivorous fishes, suggesting governing effect of dietary habits of the organisms on bioaccumulation of these UVAs. Direct uptake from growth media was a significant exposure pathway of the organisms to the UVAs. The estimated trophic magnification factors and biomagnification factors revealed that UV329, UV531, and octocrylene could potentially biomagnify in the marine food web.

Picot-Groz, M., Fenet, H., Martinez Bueno, M. J., Rosain, D., & Gomez, E. (2018). Diurnal Variations in Personal Care Products in Seawater and Mussels at Three Mediterranean Coastal Sites. *Environmental Science and Pollution Research* <https://doi.org/10.1007/s11356-017-1100-1>

The presence of personal care products (PCPs) in the marine environment is of major concern. PCPs, UV filters, and musks can enter the marine environment indirectly through wastewater or directly via recreational activities. We conducted this study to document patterns in the occurrence of seven PCPs at three coastal sites impacted by recreational activities during 1 day. The study focused on diurnal variations in these seven PCPs in seawater and indigenous mussels. In seawater, UV filters showed diurnal variations that mirrored variations in recreational activities at the sites. Ethylhexyl methoxycinnamate (EHMC) and octocrylene (OC) water concentrations increased from under the limit of quantification in the morning to 106 and 369 ng/L, respectively, when recreational activities were the highest. In mussels, diurnal variations in OC were observed, with the lowest concentrations recorded in the morning and then increasing throughout the day. As *Mytilus* spp. are widely used as sentinels in coastal pollution monitoring programs (mussel watch), our findings on diurnal variations could enhance sampling recommendations for recreational sites impacted by PCPs.

Picot Groz, M., Martinez Bueno, M. J., Rosain, D., Fenet, H., Casellas, C., Pereira, C., . . . Gomez, E. (2014). Detection of Emerging Contaminants (UV Filters, UV Stabilizers and Musks) in Marine Mussels from Portuguese Coast by QuEChERS Extraction and Gc-MS/MS. *Science of The Total Environment*, 493, 162-169 <https://doi.org/10.1016/j.scitotenv.2014.05.062>

The UV filters and musk fragrances have come into focus because these compounds are contained and increasingly used not only in sunscreen products but also in many products of daily use, such as cosmetics, skin creams, plastics or varnish. In view of this, the main objective of the present work was to develop and validate a method for the determination of three UV filters, two UV stabilizers and four musks in mussel samples (*Mytilus galloprovincialis*). The procedure combined a QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) extraction method with an analysis by gas chromatography-tandem mass spectrometry (GC-MS/MS). The methodology allowed the determination of target analytes at trace

concentration levels (ng/g), with mean recoveries ranging from 91 to 112%. A monitoring study was conducted in four beaches in the Portuguese coast which are impacted by recreational activities and outflow of treated waste water effluents in rivers. The results are used to assess the occurrence of UV filters in comparison with UV stabilizers and musk fragrances which indicate other activities than bathing.

Poiger, T., Buser, H. R., Balmer, M. E., Bergqvist, P. A., & Muller, M. D. (2004). Occurrence of UV Filter Compounds from Sunscreens in Surface Waters: Regional Mass Balance in Two Swiss Lakes. *Chemosphere*, 55(7), 951-963 <https://doi.org/10.1016/j.chemosphere.2004.01.012>

Consumer care products often contain UV filters, organic compounds which absorb ultraviolet light. These compounds may enter surface waters directly (when released from the skin during swimming and bathing) or indirectly via wastewater treatment plants (when released during showering or washed from textiles). Predicted and measured UV filter concentrations were compared in a regional mass balance study for two Swiss lakes: Lake Zurich, a typical midland lake which is also an important drinking water resource, and Huttnersee, a small bathing lake. Both lakes are extensively used for recreational activities and considerable direct input of UV filters is thus expected. This input was estimated from the number of visitors at swimming areas around the lakes and a survey of the usage of sunscreen products among these visitors. Possible additional indirect input via wastewater treatment plants was not considered in this study. The quantitatively most important UV filters, as indicated by the survey data, ethylhexyl methoxycinnamate, octocrylene, 4-methylbenzylidene camphor, butyl methoxydibenzoylmethane, and benzophenone-3, all lipophilic compounds, were selected for analysis by gas chromatography-mass spectrometry. Concentrations of individual UV filters in water from Lake Zurich were low, ranging from <2 ng l⁻¹ (detection limit) to 29 ng l⁻¹, and somewhat higher at Huttnersee, ranging from <2 to 125 ng l⁻¹, with the highest concentrations found in summer, consistent with direct inputs to the lakes during this time. The concentrations were clearly lower than predicted from input estimates based on the surveys. This may be in part due to (i) an overestimation of these inputs (e.g. less than the 50% wash-off of UV filters assumed to occur during swimming), and (ii) some removal of these compounds from the lakes by degradation and/or sorption/sedimentation. UV filters were also detected in semipermeable membrane devices (SPMDs) deployed at Lake Zurich and Greifensee, another midland lake, at concentrations of 80-950 ng SPMD⁻¹, confirming the presence of the compounds in surface waters and indicating a certain potential for bioaccumulation. SPMD-derived water concentrations were in the range of 1-10 ng l⁻¹ and thus corresponded well with those determined in water directly. No UV filters were detected above blank levels in SPMDs deployed at a remote mountain lake used for background measurements.

Ramos, S., Homem, V., Alves, A., & Santos, L. (2015). Advances in Analytical Methods and Occurrence of Organic UV-Filters in the Environment--a Review. *Science of The Total Environment*, 526, 278-311 <https://doi.org/10.1016/j.scitotenv.2015.04.055>

UV-filters are a group of compounds designed mainly to protect skin against UVA and UVB radiation, but they are also included in plastics, furniture, etc., to protect products from light damage. Their massive use in sunscreens for skin protection has been increasing due to the awareness of the chronic and acute effects of UV radiation. Some organic UV-filters have raised significant concerns in the past few years for their continuous usage, persistent input and potential threat to ecological environment and human health. UV-filters end up in wastewater and because wastewater treatment plants are not efficient in removing them, lipophilic compounds tend to sorb onto sludge and hydrophilics end up in river water,

contaminating the existing biota. To better understand the risk associated with UV-filters in the environment a thorough review regarding their physicochemical properties, toxicity and environmental degradation, analytical methods and their occurrence was conducted. Higher UV-filter concentrations were found in rivers, reaching 0.3mg/L for the most studied family, the benzophenone derivatives. Concentrations in the ng to mug/L range were also detected for the p-aminobenzoic acid, cinnamate, crylene and benzoyl methane derivatives in lake and sea water. Although at lower levels (few ng/L), UV-filters were also found in tap and groundwater. Swimming pool water is also a sink for UV-filters and its chlorine by-products, at the mug/L range, highlighting the benzophenone and benzimidazole derivatives. Soils and sediments are not frequently studied, but concentrations in the mug/L range have already been found especially for the benzophenone and crylene derivatives. Aquatic biota is frequently studied and UV-filters are found in the ng/g-dw range with higher values for fish and mussels. It has been concluded that more information regarding UV-filter degradation studies both in water and sediments is necessary and environmental occurrences should be monitored more frequently and deeply.

Ribeiro, H., Ramos, S., Homem, V., & Santos, L. (2017). Can Coastline Plant Species Be Used as Biosamplers of Emerging Contaminants? - UV-Filters and Synthetic Musks as Case Studies. *Chemosphere*, 184, 1134-1140 <https://doi.org/10.1016/j.chemosphere.2017.06.084>

Personal care products, an important class of emerging contaminants, have been frequently detected in different environmental matrices. Included in this category are synthetic musks compounds (SMCs) and UV-filters. Their occurrence in the coastal environment has been poorly studied. Therefore, this work aimed to verify whether five coastline plant species (*Carpobrotus edulis*, *Cakile maritima*, *Medicago marina*, *Elymus farctus borealis-atlanticus* and *Euphorbia paralias*) have the ability to accumulate 11 SMCs (cashmeran, celestolide, phantolide, galaxolide, tonalide, exaltolide, musk moskene, tibetene, ambrette, xylene and ketone) and 2 organic UVB filters (3-(4'-methylbenzylidene) camphor and octocrylene), functioning as biosamplers. To accomplish this task, a QuEChERS technique ("Quick, Easy, Cheap, Effective, Rugged, and Safe") was employed to extract the target compounds from the plant material collected in 15 beaches of Matosinhos and Vila Nova de Gaia (Portugal). The resulting extracts were analysed by gas chromatography-mass spectrometry. Limits of detection ranged from 0.02 ng g(-1) for celestolide and tonalide to 1.32 ng g(-1) for musk ambrette. The obtained recoveries were around 93% and relative standard deviation was generally less than 15%. SMCs were detected at levels ranging from 1.56 to 350 ng g(-1) dw and UV-filters from 2.9 to 264 ng g(-1) dw. Galaxolide and 3-(4'-methylbenzylidene) camphor were the synthetic musk and UV-filter detected in higher concentrations, respectively. Plants with higher water content accumulate better SMCs (hottentot-fig), while those with higher lipid content retain better the UV-filters (sea spurge).

Richardson, S. (2006). Environmental Mass Spectrometry: Emerging Contaminants and Current Issues. *Analytical Chemistry*, 78, 4021-4046 <https://doi.org/10.1021/ac202903d>

This biennial review covers developments in environmental mass spectrometry over the period of 2004-2005. A few significant references that appeared between January and February 2006 are also included. Analytical Chemistry's current policy is to limit reviews to include 100-200 significant references and to mainly focus on new trends. As a result, as was done in the previous 2004 Environmental Mass Spectrometry review (1), this 2006 review will be limited in its focus to new, emerging contaminants and environmental issues that are driving most of the current research. Even with a more narrow focus, only a small fraction of the quality research publications could be discussed. Thus, this review will not be

comprehensive, but will highlight new areas and discuss representative papers in the areas of focus. I welcome any comments you have, in particular regarding this more narrow focus, whether you find it more (or less) useful than a broader approach (richardson.susan@epa.gov). Numerous abstracts were consulted before choosing the best ones to present here. Abstract searches were carried out using Current Contents, and in many cases, full articles were obtained.

Rocha, F., Homem, V., Castro-Jimenez, J., & Ratola, N. (2019). Marine Vegetation Analysis for the Determination of Volatile Methylsiloxanes in Coastal Areas. *Science of The Total Environment*, 650(Pt 2), 2364-2373 <https://doi.org/10.1016/j.scitotenv.2018.10.012>

Volatile methylsiloxanes (VMSs) are massively produced chemicals that comprise a wide range of industrial and household applications. The presence of cyclic and linear VMSs in several environmental matrices and ecosystems indicates persistence associated with a potential of (bio)accumulation and food web transfer with possible toxicological effects. Due to the high anthropogenic pressure in its vicinities particularly in summer, coastal areas in Southern European countries are potential hotspots for the presence of VMSs. The massive afflux of tourists and consequent increase of the use of personal care products (PCPs) with VMSs in their formulations highlight the importance of VMSs assessment in such areas. In this study, different species of marine vegetation (algae and seaweed) were collected in three different geographical areas, covering the Atlantic Ocean (North coast of Portugal), as well as the Mediterranean Sea (coasts of the Region of Murcia, Spain and of the city of Marseille, France). Samples were analysed for the determination of 4 cyclic (D3, D4, D5, D6) and 3 linear (L3, L4, L5) VMSs employing a QuEChERS extraction methodology, followed by gas chromatography/mass spectrometry (GC/MS) quantification. VMSs were detected in 92% of the 74 samples analysed, with the sum of the concentrations per sample ranging from below the limit of detection (LOD) to 458+/-26ng.g(-1)dw (dry weight). A strong predominance of cyclic VMSs over linear ones was verified in almost all samples studied, with D5 and D6 found at higher concentrations. Seasonal variation was also assessed and despite higher levels of VMSs being identified mostly in summer months, clear seasonal trends were not perceived. It was also noted that generally the higher incidence of VMSs occurred in samples from urban and industrialized areas or in the vicinities of WWTPs, suggesting a direct input from these sources in the levels of siloxanes observed.

Rodil, R., Quintana, J. B., Concha-Grana, E., Lopez-Mahia, P., Muniategui-Lorenzo, S., & Prada-Rodriguez, D. (2012). Emerging Pollutants in Sewage, Surface and Drinking Water in Galicia (Nw Spain). *Chemosphere*, 86(10), 1040-1049 <https://doi.org/10.1016/j.chemosphere.2011.11.053>

A monitoring programme was carried out on wastewater, surface and drinking water on the NW area of Spain during the four seasons of a year period (November 2007-September 2008). This study covered a series of emerging pollutants of different classes, including pharmaceuticals, neutral and acidic organophosphorus flame retardant/plasticizers (OPs), triclosan, phenoxy-herbicides, insect repellents and UV filters. From the total set of 53 compounds, 19 were found in raw wastewater with median concentrations higher than 0.1 mug L(-1). Among them, salicylic acid, ibuprofen and the UV filter benzophenone-4 (BP-4) were the most concentrated, exceeding the 1 mug L(-1) median value. Subsequently, 11 of these contaminants are not efficiently enough removed in the small WWTPs tested and their median concentrations in effluents still surpassed the 0.1 mug L(-1), so that they can spread through surface water. These chemicals are the pharmaceuticals naproxen, diclofenac and atenolol; the OPs tri(2-chloroethyl) phosphate (TCEP), tri(chloropropyl) phosphate (TCPP), tri-n-butyl phosphate (TnBP), diphenyl phosphate (DPHP) and diethylhexyl phosphate (DEHP); and the sulphonate UV filters

BP-4 and 2-phenylbenzimidazole-5-sulphonic acid (PBSA). These OPs were then the dominant emerging pollutants occurring in surface and drinking water, where they are detected in the 20-200 ng L⁻¹ range. Pharmaceuticals and UV filters are typically below the 10 ng L⁻¹ level. Finally, herbicides were only detected in the last sampling campaign under the 100 ng L⁻¹ drinking water European Union limit.

Rodríguez-Romero, A., Ruiz-Gutiérrez, G., Viguri, J. R., & Tovar-Sánchez, A. (2019). Sunscreens as a New Source of Metals and Nutrients to Coastal Waters. *Environmental Science & Technology*
<https://doi.org/10.1021/acs.est.9b02739>

Studies detailing the environmental impact of sunscreen products on coastal ecosystems are considered a high priority. In the present study, we have determined the release rate of dissolved trace metals (Al, Cd, Cu, Co, Mn, Mo, Ni, Pb, and Ti) and inorganic nutrients (SiO₂, P-PO₄³⁻, and N-NO₃⁻) from a commercial sunscreen in seawater, and the role of UV radiation in the mobilization of these compounds. Our results indicate that release rates are higher under UV light conditions for all compounds and trace metals except Pb. We have developed a kinetic model to establish the release pattern and the contribution to marine coastal waters of dissolved trace metals and inorganic nutrients from sunscreen products. We conservatively estimate that sunscreen from bathers is responsible for an increase of dissolved metals and nutrients ranging from 7.54 × 10⁻⁴ % for Ni up to 19.8% for Ti. Our results demonstrate that sunscreen products are a significant source of metals and inorganic nutrients to coastal waters. The normally low environmental concentrations of some elements (e.g., P) and the toxicity of others (e.g., Pb) could be having a serious adverse effect on marine ecology in the Mediterranean Sea. This risk must not be ignored.

Rainieri, S., Barranco, A., Primec, M., and Langerholc, T. (2017). Occurrence and Toxicity of Musks and UV Filters in the Marine Environment. *Food and Chemical Toxicology*, 104, 57-68
<https://doi.org/10.1016/j.fct.2016.11.012>

Emerging chemical contaminants in the marine ecosystem represent a threat to the environment and also to human health due to insufficient knowledge about their toxicity and bioaccumulation in the food chain. Consequently, many of them are not regulated. In this review we focus on musks and organic UV filters. For both groups of compounds we describe occurrence in the marine environment, toxic effects identified so far and methods used to identify such effects. The final objective of this work is to identify gaps in the understanding of their toxicology.

Sanchez-Quiles, D., & Tovar-Sanchez, A. (2015). Are Sunscreens a New Environmental Risk Associated with Coastal Tourism? *Environment International*, 83, 158-170
<https://doi.org/10.1016/j.envint.2015.06.007>

The world coastal-zone population and coastal tourism are expected to grow during this century. Associated with that, there will be an increase in the use of sunscreens and cosmetics with UV-filters in their formulation, which will make coastal regions worldwide susceptible to the impact of these cosmetics. Recent investigations indicate that organic and inorganic UV-filters, as well as many other components that are constituents of the sunscreens, reach the marine environment--directly as a consequence of water recreational activities and/or indirectly from wastewater treatment plants (WWTP) effluents. Toxicity of organic and inorganic UV filters has been demonstrated in aquatic organism. UV-filters inhibit growth in marine phytoplankton and tend to bioaccumulate in the food webs. These findings together with coastal tourism data records highlight the potential risk that the

increasing use of these cosmetics would have in coastal marine areas. Nevertheless, future investigations into distribution, residence time, aging, partitioning and speciation of their main components and by-products in the water column, persistence, accumulation and toxicity in the trophic chain, are needed to understand the magnitude and real impact of these emerging pollutants in the marine system.

Sanchez Rodriguez, A., Rodrigo Sanz, M., & Betancort Rodriguez, J. R. (2015). Occurrence of Eight UV Filters in Beaches of Gran Canaria (Canary Islands). An Approach to Environmental Risk Assessment. *Chemosphere*, 131, 85-90 <https://doi.org/10.1016/j.chemosphere.2015.02.054>

Due to the growing concern about human health effects of ultraviolet (UV) radiation, the use of UV filters has increased in recent decades. Unfortunately, some common UV filters are bioaccumulated in aquatic organisms and show a potential for estrogenic activity. The aim of the present study is to determine the presence of some UV filters in the coastal waters of six beaches around Gran Canaria Island as consequence of recreational seaside activities. Eight commonly used UV filters: benzophenone-3 (BP-3), octocrylene (OC), octyl-dimethyl-PABA (OD-PABA), ethylhexyl methoxy cinnamate (EHMC), homosalate (HMS), butyl methoxydibenzoyl methane (BMDBM), 4-methylbenzylidene camphor (4-MBC) and diethylamino hydroxybenzoyl hexyl benzoate (DHHB), were monitored and, with the exception of OD-PABA, all were detected in the samples collected. 99% of the samples showed some UV filters and concentration levels reached up to 3316.7 ng/L for BP-3. Environmental risk assessment (ERA) approach showed risk quotients (RQ) higher than 10, which means that there is a significant potential for adverse effects, for 4-MBC and EHMC for those samples with highest levels of UV filters.

Sang, Z., & Leung, K. S. (2016). Environmental Occurrence and Ecological Risk Assessment of Organic UV Filters in Marine Organisms from Hong Kong Coastal Waters. *Science of The Total Environment*, 566-567, 489-498 <https://doi.org/10.1016/j.scitotenv.2016.05.120>

Organic UV filters, now considered to be emerging contaminants in aquatic ecosystems, are being intensively tracked in environmental waters worldwide. However, their environmental fate and impact of these contaminants on marine organisms remains largely unknown, especially in Asia. This work elucidates the occurrence and the ecological risks of seven UV filters detected in farmed fish, wild mussels and some other wild organisms collected from local mariculture farms in Hong Kong. For all of the organisms, ethylhexyl methoxycinnamate (EHMC) and octyl dimethyl p-aminobenzoic acid (OD-PABA) were the predominant contaminants with the highest concentrations up to 51.3 and 24.1ng/g (dw), respectively; lower levels were found for benzophenone-8 (BP-8), octocrylene (OC) and benzophenone-3 (BP-3) from <LOQ to <14.4ng/g (dw); 4-methylbenzylidene camphor (4-MBC) and 3-benzylidene camphor (3-BC) were rarely detected. Additionally, the detection frequencies and measured concentrations of all targets were clearly higher in mussels than in fish. Spatial distribution of studied UV filters indicated a positive correlation between their measured concentrations and the anthropogenic activities responsible for their direct emission. The ecological risk assessment specific to the marine aquatic environment was carried out. The risk quotient (RQ) values of EHMC and BP-3 were calculated as 3.29 and 2.60, respectively, indicating these two UV filters may pose significant risks to the marine aquatic environment.

Schaap, I., & Slijkerman, D. M. E. (2018). An Environmental Risk Assessment of Three Organic UV-Filters at Lac Bay, Bonaire, Southern Caribbean. *Marine Pollution Bulletin*, 135, 490-495 <https://doi.org/10.1016/j.marpolbul.2018.07.054>

Although organic UV filters (OUVFs) benefit human health by preventing skin burns and cancer, several studies revealed that organic UV filters can induce developmental and reproductive toxicity to aquatic organisms. Discharge of OUVFs occurs predominantly at marine recreational hotspots, such as Lac Bay, Bonaire, and is predicted to increase significantly due to growing tourism worldwide. Unfortunately, there is no insight what the current and future discharge of OUVF at Lac Bay is. Therefore, this study aimed to 1) measure concentrations and estimate the risk of specific OUVFs to different nursery habitats at Lac Bay, and 2) compare measured and predicted concentration based risk assessment outcome. Results showed that at least one of the three nurseries at Lac Bay had a potential for adverse effects. Furthermore, predicted environmental concentrations of UV filter discharge can be applied to gain more insight in the order of extent of OUVF discharge by marine tourism.

Schlenk, D., Sapozhnikova, Y., Irwin, M. A., Xie, L., Hwang, W., Reddy, S., . . . Snyder, S. (2005). In Vivo Bioassay-Guided Fractionation of Marine Sediment Extracts from the Southern California Bight, USA, for Estrogenic Activity. *Environmental Toxicology and Chemistry*, 24(11), 2820-2826
<https://doi.org/10.1897/05-116R.1>

The exposure and uptake of environmental estrogenic compounds have been reported in previous studies of demersal flatfish species in the central Southern California Bight (SCB), USA. The objective of this study was to evaluate the estrogenic or feminizing activity of marine sediments from the SCB by using in vivo vitellogenin (VTG) assays in male or juvenile fish. In 2003, sediments were collected near wastewater outfalls serving the counties of Los Angeles (LACSD) and Orange (OCSD), and the city of San Diego (SD), California, USA. Cultured male California halibut (CH; *Paralichthys californicus*) were either directly exposed to sediments for 7 d or treated with two intraperitoneal injections of sediment extract over 7 d. The 17 β -estradiol (E2) equivalent values ranged from 1 to 90 μ g/kg with LACSD > SD > OCSD. Measurable concentrations of E2 were observed in all sediment extracts and ranged from 0.16 to 0.45 ng/g. Estrone (E1) was only observed in sediments near the LACSD outfall (0.6 ng/g). Alkylphenols and alkylphenol ethoxylates were observed in all sediment samples, but were highest near the OCSD outfall, where concentrations of nonylphenol were 3,200 ng/g. Fractionation studies of the LACSD sediment extract collected in 2004 failed to demonstrate relationships between VTG expression and 62 analytes, including E2, which was observed in the whole extract (2.9 ng/g). Oxybenzone (1.6 ng/g) was identified in bioactive fractions as well as unknown compounds of relatively high polarity. These results indicate that estrogen receptor-based assays may underestimate environmental estrogenic activity and estrogenic compounds other than classic natural and xenoestrogens may contribute to estrogenic activity of sediments from the SCB.

Schneider, S. L., & Lim, H. W. (2019). Review of Environmental Effects of Oxybenzone and Other Sunscreen Active Ingredients. *Journal of the American Academy of Dermatology*, 80(1), 266-271
<https://doi.org/10.1016/j.jaad.2018.06.033>

With increasing awareness regarding the risks of sunburn, photoaging, and skin cancer, the use of sunscreens has increased. Organic and inorganic filters are used in sunscreen products worldwide. Concerns have been raised regarding the environmental effects of commonly used organic ultraviolet (UV) filters, including oxybenzone (benzophenone-3), 4-methylbenzylidene camphor, octocrylene, and octinoxate (ethylhexyl methoxycinnamate). Studies have identified UV filters such as oxybenzone, octocrylene, octinoxate, and ethylhexyl salicylate in almost all water sources around the world and have commented that these filters are not easily removed by common wastewater treatment plant techniques. Additionally, in laboratory settings, oxybenzone has been implicated specifically as a

possible contributor to coral reef bleaching. Furthermore, UV filters such as 4-methylbenzylidene camphor, oxybenzone, octocrylene, and octinoxate have been identified in various species of fish worldwide, which has possible consequences for the food chain. As dermatologists, it is important for us to continue to emphasize the public health impact of excessive sun exposure and advise our patients about proper photoprotection practice, which consists of seeking shade, wearing photoprotective clothing (including hats and sunglasses), and applying appropriate sunscreens.

Sharifan, H., Klein, D., & Morse, A. N. (2016). UV Filters Are an Environmental Threat in the Gulf of Mexico: A Case Study of Texas Coastal Zones. *Oceanologia*, 58(4), 327-335
<https://doi.org/10.1016/j.oceano.2016.07.002>

UV filters are the main ingredients in many cosmetics and personal care products. A significant amount of lipophilic UV filters annually enters the surface water due to large numbers of swimmers and sunbathers. The nature of these compounds cause bioaccumulation in commercial fish, particularly in estuarine areas. Consequently, biomagnification in the food chain will occur. This study estimated the amount of four common UV filters (ethylhexyl methoxycinnamate, EHMC; octocrylene, OC; butyl methoxydibenzoylmethane, BM-DBM; and benzophenone-3, BP3), which may enter surface water in the Gulf of Mexico. Our data analysis was based on the available research data and EPA standards (age classification/human body parts). The results indicated that among the 14 counties in Texas coastal zones, Nueces, with 43 beaches, has a high potential of water contamination through UV filters; EHMC: 477 kg year⁻¹; OC: 318 kg year⁻¹; BM-DBM: 258 kg year⁻¹; and BP by 159 kg year⁻¹. Refugio County, with a minimum number of beaches, indicated the lowest potential of UV filter contamination. The sensitive estuarine areas of Galveston receive a significant amount of UV filters. This article suggests action for protecting Texas estuarine areas and controlling the number of tourists and ecotourism that occurs in sensitive areas of the Gulf of Mexico.

Sharma, V. K. (2009). Aggregation and Toxicity of Titanium Dioxide Nanoparticles in Aquatic Environment--a Review. *Journal of Environmental Science and Health Part A*, 44(14), 1485-1495
<https://doi.org/10.1080/10934520903263231>

The use of nanoparticles--particles with size approximately 1-100 nm is increasing worldwide. This is particularly the case for applications of titanium dioxide nanoparticles (nano-TiO₂) in consumer products, which have expanded at a fast rate in the last decade. The properties of nano-TiO₂ differ significantly from bulk-TiO₂ of the same composition because of an increase in surface area. A release of nano-TiO₂ from application sources to the aquatic environment may pose possible risks due to their bioavailability and toxicity. The aggregation of nano-TiO₂ plays an important role in the environmental effects of nanoparticles because the size and shape of nanoparticles will determine the magnitude of any potentially toxic effect. Aggregation is affected by pH, ionic strength, and ionic identity (inorganic and organic) of aqueous suspensions and is reviewed in this paper. The current information on the evaluation of ecotoxicological hazards of nano-TiO₂ to bacteria, algae, invertebrates, nematodes, and rainbow trout is also given.

Shoeib, M., Schuster, J., Rauert, C., Su, K., Smyth, S. A., & Harner, T. (2016). Emission of Poly and Perfluoroalkyl Substances, UV-Filters and Siloxanes to Air from Wastewater Treatment Plants. *Environmental Pollution*, 218, 595-604 <https://doi.org/10.1016/j.envpol.2016.07.043>

The potential of wastewater treatment plants (WWTPs) to act as sources of poly and perfluoroalkyl substances (PFASs), volatile methyl siloxanes (VMSs) and organic UV-filters to the atmosphere was investigated. Target compounds included: PFASs (fluorotelomer alcohols (FTOHs), perfluorooctane sulfonamides/sulfonamidoethanols (FOSAs/FOSEs), perfluoroalkyl sulfonic acids (PFASs) and perfluoroalkyl carboxylic acids (PFCAs)), cyclic VMSs (D3 to D6), linear VMSs (L3 to L5) and eight UV-filters. Emissions to air were assessed at eight WWTPs using paired sorbent-impregnated polyurethane foam passive air samplers, deployed during summer 2013 and winter 2014. Samplers were deployed on-site above the active tank and off-site as a reference. Several types of WWTPs were investigated: secondary activated sludge in urban areas (UR-AS), secondary extended aeration in towns (TW-EA) and facultative lagoons in rural areas (RU-LG). The concentrations of target compounds in air were approximately 1.7-35 times higher on-site compared to the corresponding off-site location. Highest concentrations in air were observed at UR-AS sites while the lowest were at RU-LG. Higher air concentrations (approximately 2-9 times) were observed on-site during summer compared to winter, possibly reflecting enhanced volatilization due to higher wastewater temperatures or differences in influent wastewater concentrations. A significant positive correlation was obtained between concentrations in air and WWTP characteristics (influent flow rate and population in the catchment of the WWTP); whereas a weak negative correlation was obtained with hydraulic retention time. Emissions to air were estimated using a simplified dispersion model. Highest emissions to air were seen at the UR-AS locations. Emissions to air (g/year/tank) were highest for VMSs (5000-112,000) followed by UV-filters (16-2000) then SigmaPFASs (10-110).

Silvia Díaz-Cruz, M., Llorca, M., Barceló, D., & Barceló, D. (2008). Organic UV Filters and Their Photodegradates, Metabolites and Disinfection by-Products in the Aquatic Environment. *TrAC Trends in Analytical Chemistry*, 27(10), 873-887 <https://doi.org/10.1016/j.trac.2008.08.012>

Organic ultraviolet (UV) filters are compounds used to absorb UV radiation and are increasingly being used as a result of growing concern about UV radiation and skin cancer. Their growing use may increase environmental contamination and exposure through the food chain. There is therefore major concern about the environmental fate and potential effect of organic UV filters used in beauty creams, hair sprays, shampoos, and other personal-care products, as well as those added to plastics and other materials to prevent degradation of polymers and pigments. This review describes the processes undergone by these compounds once released into the environment and the instrumental methods based on chromatography and mass spectrometry reported in the literature for their determination in environmental samples. We include concentrations found in the environment (e.g., water, soil, sediments, sludge and biota). The main focus is on metabolites, photodegradates and by-products of wastewater treatment.

Tang, Z., Han, X., Li, G., Tian, S., Yang, Y., Zhong, F., . . . Yang, J. (2018). Occurrence, Distribution and Ecological Risk of Ultraviolet Absorbents in Water and Sediment from Lake Chaohu and Its Inflowing Rivers, China. *Ecotoxicology and Environmental Safety*, 164, 540-547 <https://doi.org/10.1016/j.ecoenv.2018.08.045>

The available information is insufficient to enable a reliable understanding of the global distribution and effect of organic ultraviolet absorbents (UVAs) on ecosystems. Little is known about the pollution of China's lakes by these chemicals. We conducted a survey of UVAs in water and sediment from Lake Chaohu and its inflowing rivers. The UVAs were widely present in this area and the concentrations of total 12 UVAs (Sigma12 UVAs) ranged between 162 and 587ng/L in water and 9.70-178ng/g in sediment.

Benzophenone and benzophenone-3 were dominant in water, and benzophenone and octocrylene dominated in sediment. Higher concentrations of benzophenone were detected in the investigated water samples, although the contamination levels of UVAs in this study were comparable to those investigated in other areas. In addition to the inputs from the UVAs used as filters in cosmetics, the discharge from industries using UVAs as stabilizers also contributed much to the pollution in the study waters. Generally, the risk to aquatic organisms from exposure to UVAs in this area was low, but further research is needed to elucidate the fate of UVAs and to understand bioaccumulation and associated risks.

Tashiro, Y., & Kameda, Y. (2013). Concentration of Organic Sun-Blocking Agents in Seawater of Beaches and Coral Reefs of Okinawa Island, Japan. *Marine Pollution Bulletin*, 77(1–2), 333-340
<https://doi.org/10.1016/j.marpolbul.2013.09.013>

The concentration of UV filters (UVFs) and UV light stabilizers (UVLSs) were measured in seawater and river water collected from sites at four beaches, two reefs, and one river on Okinawa Island, Japan. UVFs and/or UVLSs of 8–10 types were detected in beaches samples and 6–9 types were detected in reef samples. The total UVF concentrations at the beach sites were highest either in July or August with a maximum of 1.4 lgL^{-1} . The concentrations at the reef sites did not show peaks in summer and the maximum values were close to 10 ng L^{-1} . The detected UVF profiles reflected the ingredients of sunscreens used in each region. The highest UVLS concentrations at the reefs were observed not only in summer but also in June and September. The UVLS concentrations at the reefs were similar to or even higher than that at the beaches or in the river.

Tovar-Sanchez, A., Sanchez-Quiles, D., Basterretxea, G., Benede, J. L., Chisvert, A., Salvador, A., . . . Blasco, J. (2013). Sunscreen Products as Emerging Pollutants to Coastal Waters. *Plos One*, 8(6)
<https://doi.org/10.1371/journal.pone.0065451>

A growing awareness of the risks associated with skin exposure to ultraviolet (UV) radiation over the past decades has led to increased use of sunscreen cosmetic products leading the introduction of new chemical compounds in the marine environment. Although coastal tourism and recreation are the largest and most rapidly growing activities in the world, the evaluation of sunscreen as source of chemicals to the coastal marine system has not been addressed. Concentrations of chemical UV filters included in the formulation of sunscreens, such as benzophenone 3 (BZ-3), 4-methylbenzylidene camphor (4-MBC), TiO_2 and ZnO, are detected in nearshore waters with variable concentrations along the day and mainly concentrated in the surface microlayer (i.e. 53.6-577.5 ng L^{-1} BZ-3; 51.4-113.4 ng L^{-1} 4-MBC; 6.9-37.6 microg L^{-1} Ti; 1.0-3.3 microg L^{-1} Zn). The presence of these compounds in seawater suggests relevant effects on phytoplankton. Indeed, we provide evidences of the negative effect of sunblocks on the growth of the commonly found marine diatom *Chaetoceros gracilis* (mean $\text{EC}_{50} = 125 \pm 71 \text{ mg L}^{-1}$). Dissolution of sunscreens in seawater also releases inorganic nutrients (N, P and Si forms) that can fuel algal growth. In particular, PO_4^{3-} is released by these products in notable amounts (up to 17 $\text{micromol PO}_4^{3-} \text{g}^{-1}$). We conservatively estimate an increase of up to 100% background PO_4^{3-} concentrations (0.12 micromol L^{-1}) over a background level of 0.06 micromol L^{-1}) in nearshore waters during low water renewal conditions in a populated beach in Majorca island. Our results show that sunscreen products are a significant source of organic and inorganic chemicals that reach the sea with potential ecological consequences on the coastal marine ecosystem.

Tsui, M. M., Leung, H. W., Lam, P. K., & Murphy, M. B. (2014). Seasonal Occurrence, Removal Efficiencies and Preliminary Risk Assessment of Multiple Classes of Organic UV Filters in Wastewater Treatment Plants. *Water Research*, 53, 58-67 <https://doi.org/10.1016/j.watres.2014.01.014>

Organic ultraviolet (UV) filters are applied widely in personal care products (PCPs), but the distribution and risks of these compounds in the marine environment are not well known. In this study, the occurrence and removal efficiencies of 12 organic UV filters in five wastewater treatment plants (WWTPs) equipped with different treatment levels in Hong Kong, South China, were investigated during one year and a preliminary environmental risk assessment was carried out. Using a newly developed simultaneous multiclass quantification liquid chromatography-tandem mass spectrometry (LC-MS/MS) method, butyl methoxydibenzoylmethane (BMDM), 2,4-dihydroxybenzophenone (BP-1), benzophenone-3 (BP-3), benzophenone-4 (BP-4) and 2-ethyl-hexyl-4-trimethoxycinnamate (EHMC) were frequently ($\geq 80\%$) detected in both influent and effluent with mean concentrations ranging from 23 to 1290 ng/L and 18-1018 ng/L, respectively; less than 2% of samples contained levels greater than 1000 ng/L. Higher concentrations of these frequently detected compounds were found during the wet/summer season, except for BP-4, which was the most abundant compound detected in all samples in terms of total mass. The target compounds behaved differently depending on the treatment level in WWTPs; overall, removal efficiencies were greater after secondary treatment when compared to primary treatment with $>55\%$ and $<20\%$ of compounds showing high removal (defined as $>70\%$ removal), respectively. Reverse osmosis was found to effectively eliminate UV filters from effluent ($>99\%$ removal). A preliminary risk assessment indicated that BP-3 and EHMC discharged from WWTPs may pose high risk to fishes in the local environment.

Tsui, M. M., Leung, H. W., Wai, T. C., Yamashita, N., Taniyasu, S., Liu, W., . . . Murphy, M. B. (2014). Occurrence, Distribution and Ecological Risk Assessment of Multiple Classes of UV Filters in Surface Waters from Different Countries. *Water Research*, 67C, 55-65 <https://doi.org/10.1016/j.watres.2014.09.013>

Organic UV filters are common ingredients of personal care products (PCPs), but little is known about their distribution in and potential impacts to the marine environment. This study reports the occurrence and risk assessment of twelve widely used organic UV filters in surface water collected in eight cities in four countries (China, the United States, Japan, and Thailand) and the North American Arctic. The number of compounds detected, Hong Kong (12), Tokyo (9), Bangkok (9), New York (8), Los Angeles (8), Arctic (6), Shantou (5) and Chaozhou (5), generally increased with population density. Median concentrations of all detectable UV filters were <250 ng/L. The presence of these compounds in the Arctic is likely due to a combination of inadequate wastewater treatment and long-range oceanic transport. Principal component analysis (PCA) and two-way analysis of variance (ANOVA) were conducted to explore spatiotemporal patterns and difference in organic UV filter levels in Hong Kong. In general, spatial patterns varied with sampling month and all compounds showed higher concentrations in the wet season except benzophenone-4 (BP-4). Probabilistic risk assessment showed that 4-methylbenzylidene camphor (4-MBC) posed greater risk to algae, while benzophenone-3 (BP-3) and ethylhexyl methoxycinnamate (EHMC) were more likely to pose a risk to fishes and also posed high risk of bleaching in hard corals in aquatic recreational areas in Hong Kong. This study is the first to report the occurrence of organic UV filters in the Arctic and provides a wider assessment of their potential negative impacts in the marine environment.

Tsui, M. M. P., Chen, L., He, T., Wang, Q., Hu, C., Lam, J. C. W., & Lam, P. K. S. (2019). Organic Ultraviolet (UV) Filters in the South China Sea Coastal Region: Environmental Occurrence, Toxicological Effects and Risk Assessment. *Ecotoxicology and Environmental Safety*, 181, 26-33
<https://doi.org/10.1016/j.ecoenv.2019.05.075>

Organic ultraviolet (UV) filters are common ingredients of personal care products and occur ubiquitously in the aquatic environment; however, little is known about their distribution in and potential effects to the marine environment. This study reports the occurrence, toxicological effects and risk assessment of eleven commonly consumed UV filters in marine surface water collected from the South China Sea (SCS) coastal region. The concentrations of UV filters ranged from <MDL to 145ng/L in the SCS, in which benzophenone-3, octocrylene and butyl methoxydibenzoylmethane were the most dominant compounds with their detection frequencies over 97%. Relatively higher levels of total UV filters were found near the highly industrialized and urbanized Pearl River Estuary (PRE) and the concentrations gradually decreased towards the SCS. In general, the environmental levels of UV filters were higher at the western marine waters in Hong Kong than the eastern marine waters. Significant negative correlations were observed between benzophenone-4 and water temperature, as well as ethylhexyl methoxycinnamate and salinity ($P < 0.001$; $r < -0.5$). Immobilization test of barnacle nauplius larvae (*Balanus amphitrite*) was conducted to assess the acute toxicity of organic UV filters to marine organisms. Benzophenone-8 and 4-methylbenzylidene camphor showed relatively higher toxicity with the 50% effect concentrations (EC50) of 2.2 and 3.9mg/L, respectively. A preliminary risk assessment was conducted by the results obtained from our field and laboratory studies. Results showed that the risk to cause immobilization in barnacle nauplius larvae is associated with exposure to current levels of organic UV filters in the SCS was minimal.

Vicente-Cera, I., Moreno-Andres, J., Amaya-Vias, D., Biel-Maeso, M., Pintado-Herrera, M. G., Lara-Martin, P. A., . . . Nebot, E. (2019). Chemical and Microbiological Characterization of Cruise Vessel Wastewater Discharges under Repair Conditions. *Ecotoxicology and Environmental Safety*, 169, 68-75 <https://doi.org/10.1016/j.ecoenv.2018.11.008>

Cruise ship wastewater discharges are pollution sources towards the marine environment that are poorly characterized. In this study, wastewater samples from cruise ships have been obtained during repair works in a shipyard. Different organic pollutants have been analyzed and their concentrations were similar to those in urban wastewaters for pharmaceuticals and fragrances, but higher for UV filters and PAHs. For the first time, cypermethrin, a pesticide highly toxic towards aquatic species, was found at relevant concentrations ($>1 \mu\text{g L}^{-1}$). The faecal microorganisms were for all parameters higher than $10^4 \text{ CFU } 100 \text{ mL}^{-1}$, which together with the presence of antibiotic compounds in wastewater (e.g., triclosan), could potentially lead to the generation of antibiotic resistance bacteria (ARB). The historical position of cruise ships, determined from the Automatic Identification System (AIS), were used to define the time ships were underway, at port, or in repair. From ship's passenger and crew load, and from estimates of discharges the total volume of wastewater produced by these ships ($371,000 \text{ m}^3 \text{ year}^{-1}$) and the average flow ($0.15 \pm 0.03 \text{ m}^3 \text{ crew}^{-1} \text{ day}^{-1}$) were calculated.

Vidal-Linan, L., Villaverde-de-Saa, E., Rodil, R., Quintana, J. B., & Beiras, R. (2018). Bioaccumulation of UV Filters in *Mytilus Galloprovincialis* Mussel. *Chemosphere*, 190, 267-271
<https://doi.org/10.1016/j.chemosphere.2017.09.144>

In this study the bioaccumulation kinetics of organic UV filters, such as 4-MBC, BP-3, BP-4, OC and OD-PABA in wild *Mytilus galloprovincialis* mussels was investigated. The uptake and accumulation of

waterborne 4-MBC, BP-4 and OC was very rapid, and after only 24 h of exposure to 1 µg L⁻¹, the tissular concentrations were 418, 263 and 327 µg kg⁻¹d.w., respectively. The kinetics of bioaccumulation of BP-4 and OC significantly fitted to an asymptotic model with BCF values of 905 L kg⁻¹ and 2210 L kg⁻¹, respectively. Measured bioaccumulation of the hydrophilic chemical BP-4 was much higher than predicted by Kow-based bioconcentration models, which would lead to a marked underestimation of actual risk. On the other hand, the patterns of uptake found for BP-3 and OD-PABA suggest biotransformation ability of mussels for these two chemicals.

Vita, N. A., Brohem, C. A., Canavez, A., Oliveira, C. F. S., Kruger, O., Lorencini, M., & Carvalho, C. M. (2018). Parameters for Assessing the Aquatic Environmental Impact of Cosmetic Products. *Toxicology Letters*, 287, 70-82 <https://doi.org/10.1016/j.toxlet.2018.01.015>

The cosmetic industry's growing concern about the impact of its supply chain on the environment, sustainability of raw materials, and biodiversity increases the need to ensure that the final product has a lower environmental impact. The objective of this review is to summarize and compare the information available from international organizations and legislation regarding the main criteria used to assess raw materials for aquatic toxicity, as well as the most suitable alternative methods for obtaining assessment parameters. Using the literature available in databases, a review of the scientific literature and international legislation, this work discusses and compares the parameters established by international organizations such as the Environmental Protection Agency (EPA) and Cradle to Cradle (C2C), as well as European legislation, namely, European Regulation 1272/2008, for assessing environmental impact. Defining the ecotoxicity parameters of the main classes of raw materials in rinse-off cosmetic products can enable the development of products that are more environmentally sustainable, prioritizing substances with less environmental impact.

Wang, W., & Kannan, K. (2017). Mass Loading and Emission of Benzophenone-3 (Bp-3) and Its Derivatives in Wastewater Treatment Plants in New York State, USA. *Science of The Total Environment*, 579, 1316-1322 <https://doi.org/10.1016/j.scitotenv.2016.11.124>

The occurrence of benzophenone type ultra-violet (UV) light filters, especially 2-hydroxy-4-methoxy benzophenone (2OH-4MeO-BP; BP-3), in aquatic ecosystems is a concern due to the endocrine disruption potential of these chemicals. In this study, mass loading, emission and fate of BP-3 and its derivatives were investigated in two wastewater treatment plants (WWTPs) in the Albany area of New York State, USA. The median concentrations of BP-3 and sum of its four derivatives (SigmaBPderivatives) in influents were 35.6-49.1 and 124-145ng/L, respectively. The highest concentrations found for BP-3 and SigmaBPderivatives in sludge (n=10) were 426-5770 and 856-5910ng/g, dry wt, respectively. Sorption to sludge explained for 13.2-15.7% of SigmaBPs mass reduction, whereas predominant pathway of BPs removal was biodegradation. The mass loadings (25.7-81.4 and 76.1-194mg/d/1000 people) and environmental emissions (10.5-17.5 and 44.5-76.2mg/d/1000 people) for BP-3 and SigmaBPderivatives in WWTPs were estimated. Approximately 11% and 20% of the total production of BP-3 and 2,4-diOH-BP (BP-1) in the U.S. reach WWTPs, while 3% and 15% of the loaded amounts were emitted through WWTP discharges.

Wu, H., Long, K., Lu, D., Mo, Y., Yang, Q., & Wei, X. (2019). Occurrence and Formation of Halobenzoquinones in Indoor and Outdoor Swimming Pool Waters of Nanning City, Southwest

Disinfection byproducts (DBPs) in swimming pool have elicited increasing worldwide concern due to their potential health risks. However, only trihalomethanes (THMs) are regulated by several local governing bodies. Studies indicated that specific unregulated DBP classes would drive disinfected water toxicity in addition to THMs. Halobenzoquinones (HBQs), a type of emerging unregulated DBPs, have been shown to be possible bladder cancer carcinogens. This study aimed to determine the distribution and formation of HBQs in indoor and outdoor swimming pool waters of Nanning City, Southwest China. Seven HBQs in water from seven public indoor and outdoor swimming pools were examined using an effective ultra-performance liquid chromatography–tandem mass spectrometry method. Results suggest the presence of 2,6-dichloro-1,4-benzoquinone in all the swimming pool waters in the range of 4.56–45.30 ng/L. Furthermore, 2,6-dibromo-1,4-benzoquinone and 3,4,5,6-tetrachloro-1,2-benzoquinone (TetraC-1,2-BQ) were detected in two pools at concentrations of < 0.38–14.20 and < 0.54–2.60 ng/L, respectively. The swimming pool water featured higher HBQs than input tap water, and TetraC-1,2-BQ was only detected in pool water. Higher HBQ levels were observed in the indoor pools than in the outdoor pools. These findings demonstrate that low NH₃-N, high chloride, humic acid, chemical oxygen demand, and UV₂₅₄ in the indoor pools increased the HBQ formation. This study is the first to reveal the occurrence and formation of HBQs in water from Chinese indoor and outdoor swimming pools. The findings should be useful in the management of these governing factors and HBQ controls in swimming pools.

Wu, M. H., Li, J., Xu, G., Ma, L. D., Li, J. J., Li, J. S., & Tang, L. (2018). Pollution Patterns and Underlying Relationships of Benzophenone-Type UV-Filters in Wastewater Treatment Plants and Their Receiving Surface Water. *Ecotoxicology and Environmental Safety*, 152, 98-103
<https://doi.org/10.1016/j.ecoenv.2018.01.036>

The environmental behaviors of emerging pollutants, benzophenone-type UV filters (BP-UV filters) and their derivatives were investigated in four wastewater treatment plants (WWTPs), and their receiving surface waters in Shanghai. The concentration level of selected BP-UV filters in the WWTPs was detected from ngL(-1) to µg(-1). BP (621-951ngL(-1)) and BP-3 (841-1.32 x 10(3)ngL(-1)) were the most abundant and highest detection frequency individuals among the target BP-UV filters in influents, whereas BP (198-400ngL(-1)), BP-4 (93.3-288ngL(-1)) and BP-3 (146-258ngL(-1)) were predominant in effluents. BP-UV filters cannot be completely removed and the total removal efficiency varied widely (-456% to 100%) during the treatment process. It can be inferred that the usage of BP and BP-3 are higher than other BP-UV filters in the study area. The lowest and highest levels were BP-2 (ND-7.66ngL(-1)) and BP-3 (68.5-5.01 x 10(3)ng L(-1)) in the receiving surface water, respectively. Interestingly, the seasonal variation of BP-3 is larger than those of other BP-UV filters in surface water from Shanghai. There is no obvious pollution pattern of BP-UV filters in the surface water from the cosmetic factory area. The correlation analysis of BP-UV filters between WWTPs effluents and nearby downstream water samples suggested that BP-UV filters emitted from some WWTPs might be the main source of receiving surface water. Preliminary risk assessment indicated that the levels of BP-UV filters detected by the effluent posed medium to high risk to fish as well as other aquatic organisms.

Wu, M. H., Xie, D. G., Xu, G., Sun, R., Xia, X. Y., Liu, W. L., & Tang, L. (2017). Benzophenone-Type UV Filters in Surface Waters: An Assessment of Profiles and Ecological Risks in Shanghai, China.

Benzophenone-type UV filters (BP-UV filters) are frequently introduced into aquatic environment from several sources. The occurrence and fate of select BP-UV filters and their metabolites were investigated in this study. All target compounds were detected in water samples, except for 2, 3, 4-trihydroxybenzophenone (2, 3, 4-OH-BP). The concentration reached up to 131 ng/L for 5-benzoyl-4-hydroxy-2-ethoxybenzenesulfonic acid (BP-4), 30.0 ng/L for 2-hydroxy-4-methoxybenzophenone (BP-3), and mean value of 158 ng/L for benzophenone (BP). Concentrations of BP-UV filters were not related to recreational waters but with high population frequencies. In addition, five BP-UV filters, namely 2,2',4,4'-tetrahydroxybenzophenone (BP-2), 2,3,4-OH-BP, 2,4-dihydroxybenzophenone (BP-1), 4-hydroxybenzophenone (4-OH-BP) and BP were investigated for probable sources, and found that they originate from BP-3 metabolism. There is a similar source for BP-3, BP-4, BP-1, 4-OH-BP and BP. Environmental risk assessment (ERA) showed that risk quotients (RQs) of BP-4, BP-3 and BP were 2.7, 0.8 and 0.5, respectively.

Zhang, N. S., Liu, Y. S., Van den Brink, P. J., Price, O. R., & Ying, G. G. (2015). Ecological Risks of Home and Personal Care Products in the Riverine Environment of a Rural Region in South China without Domestic Wastewater Treatment Facilities. *Ecotoxicology and Environmental Safety*, 122, 417-425 <https://doi.org/10.1016/j.ecoenv.2015.09.004>

Home and personal care products (HPCPs) including biocides, benzotriazoles (BTs) and ultraviolet (UV) filters are widely used in our daily life. After use, they are discharged with domestic wastewater into the receiving environment. This study investigated the occurrence of 29 representative HPCPs, including biocides, BTs and UV filters, in the riverine environment of a rural region of South China where no wastewater treatment plants were present, and assessed their potential ecological risks to aquatic organisms. The results showed the detection of 11 biocides and 4 BTs in surface water, and 9 biocides, 3 BTs and 4 UV filters in sediment. In surface water, methylparaben (MeP), triclocarban (TCC), and triclosan (TCS) were detected at all sites with median concentrations of 9.23 ng/L, 2.64 ng/L and 5.39 ng/L, respectively. However, the highest median concentrations were found for clotrimazole (CLOT), 5-methyl-1H-benzotriazole (MBT) and carbendazim (CARB) at 55.6 ng/L, 33.7 ng/L and 13.8 ng/L, respectively. In sediment, TCC, TCS, and UV-326 were detected with their maximum concentrations up to 353 ng/g, 155 ng/g, and 133 ng/g, respectively. The concentrations for those detected HPCPs in surface water and sediment were generally lower in the upper reach (rural area) of Sha River than in the lower reach of Sha River with close proximity to Dongjiang River (Pt-test < 0.05), indicating other input sources of HPCPs in the lower reach. Biocides showed significantly higher levels in surface water in the wet season than in the dry and intermediate seasons. Preliminary risk assessment demonstrated that the majority of HPCPs monitored represented low risk in surface waters. There are potentially greater risks to aquatic organisms from the use of TCS and TCC in the wet season than in dry and intermediate seasons in surface waters. This preliminary assessment also indicates potential concerns associated with TCC, TCS, DEET, CARB, and CLOT in sediments, although additional data should be generated to assess this fully. Thus future research is needed to investigate ecological effects of these HPCPs on benthic organisms in sediment of rural rivers receiving untreated wastewater discharge.

Zhang, Z., Ren, N., Li, Y. F., Kunisue, T., Gao, D., & Kannan, K. (2011). Determination of Benzotriazole and Benzophenone UV Filters in Sediment and Sewage Sludge. *Environmental Science & Technology*, 45(9), 3909-3916 <https://doi.org/10.1021/es2004057>

Benzophenones and benzotriazoles are widely used as ultraviolet (UV) light filters and stabilizers in cosmetics, skin creams, and body lotions and as corrosion inhibitors in building materials, automobile components, and automotive antifreeze cooling systems. Benzophenones and benzotriazoles have been reported to occur in the environment. Some of these UV filters have been reported to possess significant estrogenic activity. Despite this, very few studies have examined their occurrence and profiles in the environment. In this work, we determined five benzophenone-type UV filters and two benzotriazole-type corrosion inhibitors, namely, 2-hydroxy-4-methoxybenzophenone (2OH-4MeO-BP), 2,4-dihydroxybenzophenone (2,4OH-BP), 2,2'-dihydroxy-4-methoxybenzophenone (2,2'OH-4MeO-BP), 2,2',4,4'-tetrahydroxybenzophenone (2,2',4,4'OH-BP), 4-hydroxybenzophenone (4OH-BP), 1H-benzotriazole (1H-BT), and 5-methyl-1H-benzotriazole (5Me-1H-BT), in sediment and sewage sludge samples, using liquid-liquid extraction and liquid chromatography-tandem mass spectrometry (LC-MS/MS). In addition, four benzotriazole-type UV stabilizers, namely, 2-(3-t-butyl-2-hydroxy-5-methylphenyl)-5-chlorobenzotriazole (UV-326), 2,4-di-t-butyl-6-(5-chloro-2H-benzotriazole-2-yl) phenol (UV-327), 2-(2H-benzotriazole-2-yl)-4,6-di-t-pentylphenol (UV-328), and 2-(5-t-butyl-2-hydroxyphenyl) benzotriazole (TBHPBT) were determined by gas chromatography (GC)-mass spectrometry (MS). The limits of quantitation (LOQ) were in the ranges of 0.06-0.33 ng g⁻¹(1) dry weight (dw) and 0.1-1.65 ng g⁻¹(1) dw for sediment and sludge samples, respectively. Recoveries of target compounds spiked into sample matrices and passed through the entire analytical procedure ranged from 70% to 116% (RSD: 3.32-13.8%) and from 82% to 106% (RSD: 2.89-8.09%) for the compounds analyzed by LC-MS/MS and GC-MS, respectively. The methods were applied to the analysis of sediment samples from the Songhua, Saginaw, and Detroit Rivers; the sum concentrations of target compounds were 3.29-9.93, 5.81-22.5, and 190-389 ng g⁻¹(1) dw, respectively. Five sludge samples collected from five wastewater treatment plants in northeastern China contained the sum concentrations of target compounds in the range of 104-6370 ng g⁻¹(1) dw. The concentration of UV-328 in sludge was the highest (mean: 1300 ng g⁻¹(1) dw) among the target compounds. To our knowledge, this is the first work to report the occurrence of 2OH-4MeO-BP, 2,4OH-BP, 2,2'OH-4MeO-BP, 2,2',4,4'OH-BP, and 4OH-BP in sediment and sludge samples.

Ziarrusta, H., Mijangos, L., Montes, R., Rodil, R., Anakabe, E., Izagirre, U., . . . Zuloaga, O. (2018). Study of Bioconcentration of Oxybenzone in Gilt-Head Bream and Characterization of Its by-Products. *Chemosphere*, 208, 399-407 <https://doi.org/10.1016/j.chemosphere.2018.05.154>

The widespread occurrence of UV filters such as oxybenzone (OXY) in the aquatic ecosystems has raised social and scientific concern due to their high bioaccumulation potential and possible adverse effects in organisms. Within this context, the aim of the present work was to study the uptake, distribution, metabolization and elimination of OXY in different tissues (liver, gill and muscle) and biofluids (bile and plasma) of gilt-head bream (*Sparus aurata*) in a controlled seawater ecosystem (50ng/mL OXY) within a 14-day exposure. The highest OXY concentrations in all the tissue/biofluids were found at the end of the experiment. The highest OXY levels were found in bile (1.8-17µg/mL). In the case of liver, the concentrations found (9-160ng/g) were lower than those expected for a lipidic matrix, which could be explained by a high OXY metabolization. Up to 20 Phase I and Phase II by-products of OXY were annotated by means of liquid chromatography-high resolution mass spectrometry, of which 12 were reported for the first time. In addition to OXY, its by-products might also cause adverse effects and their biomonitoring is advisable in order to fully characterize OXY exposure.

Section V: Laboratory Studies on the Toxicity and Endocrine Disruption Effects of UV Filters

Ahn, S., An, S., Lee, M., Lee, E., Pyo, J. J., Kim, J. H., . . . Noh, M. (2019). A Long-Wave UVA Filter Avobenzone Induces Obesogenic Phenotypes in Normal Human Epidermal Keratinocytes and Mesenchymal Stem Cells. *Archives of Toxicology* <https://doi.org/10.1007/s00204-019-02462-1>

Avobenzone is the most commonly used ultraviolet (UV) A filter ingredient in sunscreen. To investigate the biological activity of avobenzone in normal human epidermal keratinocytes (NHEKs), the genome-scale transcriptional profile of NHEKs was performed. In this microarray study, we found 273 up-regulated and 274 down-regulated differentially expressed genes (DEGs) in NHEKs treated with avobenzone (10 μ M). Gene Ontology (GO) enrichment analysis showed that avobenzone significantly increased the DEGs associated with lipid metabolism in NHEKs. In addition, avobenzone increased the gene transcription of peroxisome proliferator-activated receptor gamma (PPAR γ) and fatty acid binding protein 4 in NHEKs, implicating that avobenzone may be one of the metabolic disrupting obesogens. To confirm the obesogenic potential, we examined the effect of avobenzone on adipogenesis in human bone marrow mesenchymal stem cells (hBM-MSCs). Avobenzone (EC₅₀, 14.1 μ M) significantly promoted adipogenesis in hBM-MSCs as its positive control obesogenic chemicals. Avobenzone (10 μ M) significantly up-regulated mRNA levels of PPAR γ during adipogenesis in hBM-MSCs. However, avobenzone did not directly bind to PPAR γ and the avobenzone-induced adipogenesis-promoting activity was not affected by PPAR γ antagonists T0070907 and GW9662. Therefore, avobenzone promoted adipogenesis in hBM-MSCs through a PPAR γ -independent mechanism. This study suggests that avobenzone functions as a metabolic disrupting obesogen.

Alamer, M., & Darbre, P. D. (2018). Effects of Exposure to Six Chemical Ultraviolet Filters Commonly Used in Personal Care Products on Motility of MCF-7 and Mda-Mb-231 Human Breast Cancer Cells in Vitro. *Journal of Applied Toxicology*, 38(2), 148-159 <https://doi.org/10.1002/jat.3525>

Benzophenone (BP)-1, BP-2, BP-3, octylmethoxycinnamate (OMC), 4-methylbenzilidenecamphor and homosalate are added to personal care products to absorb ultraviolet light. Their presence in human milk and their oestrogenic activity suggests a potential to influence breast cancer development. As metastatic tumour spread is the main cause of breast cancer mortality, we have investigated the effects of these compounds on migration and invasion of human breast cancer cell lines. Increased motility of oestrogen-responsive MCF-7 human breast cancer cells was observed after long-term exposure (>20 weeks) to each of the six compounds at $\geq 10^{-7}$ m concentrations using three independent assay systems (scratch assay, live cell imaging, xCELLigence technology) and increased invasive activity was observed through matrigel using the xCELLigence system. Increased motility of oestrogen-unresponsive MDA-MB-231 human breast cancer cells was observed after 15 weeks of exposure to each of the six compounds by live cell imaging and xCELLigence technology, implying the increased migratory activity was not confined to oestrogen-responsive cells. Molecular mechanisms varied between compounds and cell lines. Using MCF-7 cells, reduction in E-cadherin was observed following 24 weeks' exposure to 10^{-5} m BP-1 and 10^{-5} m homosalate, and reduction in beta-catenin was noted following 24 weeks' exposure to 10^{-5} m OMC. Using MDA-MB-231 cells, increased levels of matrix metalloproteinase 2 were observed after 15 weeks exposure to 10^{-7} m OMC and 10^{-7} m 4-methylbenzilidenecamphor. Although molecular mechanisms differ, these results demonstrate that exposure to any of these six compounds can increase migration and invasion of human breast cancer cells.

Amar, S. K., Goyal, S., Srivastav, A. K., Chopra, D., & Ray, R. S. (2018). Combined Effect of Benzophenone-2 and Ultraviolet Radiation Promote Photogenotoxicity and Photocytotoxicity in Human Keratinocytes. *Regulatory Toxicology and Pharmacology*, 95, 298-306
<https://doi.org/10.1016/j.vrtph.2018.04.003>

Benzophenone-2 (BP2), a common ingredient of sunscreens formulation is widely used as UV filter. We have assessed the photogenotoxic and photocytotoxic potential of BP2. Photostability test showed that BP2 is unstable under UV exposure. Cell proliferation assay revealed that viability of HaCaT cells significantly reduced under UVA, UVB and sunlight exposure. DCF fluorescence intensity proved intracellular ROS generation capacity of BP2 under sunlight, UVA and UVB irradiation. Photodynamic degradation of guanine base of DNA is promoted by BP2 under UV treatment. Genotoxicity assessed by comet assay, showed that photosensitized BP2 enhanced DNA damage, which is measured in term of % tail DNA and olive tail moment. Genotoxic potential of BP2 was further validated with photomicronuclei assay. Photogenotoxicity of BP2 was lastly confirmed by formation of CPDs (Cyclo butane pyrimidine dimmers). DNA damage induced by BP2 was irreversible and extended incubation periods (6-12h) not favored the recovery from damaged DNA. JC 1 staining showed significant reduction in mitochondrial membrane potential. Membrane integrity compromisation of HaCaT cells was established by AO (Acridine orange), EtBr (Ethidium bromide) staining and confirmed with sub G1 population of cell cycle. Thus, results suggest that BP2 should be avoided in topical application for safe sunscreen practices.

Ao, J., Yuan, T., Gao, L., Yu, X., Zhao, X., Tian, Y., . . . Shen, Z. (2018). Organic UV Filters Exposure Induces the Production of Inflammatory Cytokines in Human Macrophages. *Science of The Total Environment*, 635, 926-935 <https://doi.org/10.1016/j.scitotenv.2018.04.217>

Organic ultraviolet (UV) filters, found in many personal care products, are considered emerging contaminants due to growing concerns about potential long-term deleterious effects. We investigated the immunomodulatory effects of four commonly used organic UV filters (2-hydroxy-4-methoxybenzophenone, BP-3; 4-methylbenzylidene camphor, 4-MBC; 2-ethylhexyl 4-methoxycinnamate, EHMC; and butyl-methoxydibenzoylmethane, BDM) on human macrophages. Our results indicated that exposure to these four UV filters significantly increased the production of various inflammatory cytokines in macrophages, particular tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6). After exposure to the UV filters, a significant 1.1-1.5 fold increase were found in TNF-alpha and IL-6 mRNA expression. In addition, both the p38 MAPK and the NF-kappaB signaling pathways were enhanced 2 to 10 times in terms of phosphorylation after exposure to the UV filters, suggesting that these pathways are involved in the release of TNF-alpha and IL-6. Molecular docking analysis predicted that all four UV filter molecules would efficiently bind transforming growth factor beta-activated kinase 1 (TAK1), which is responsible for the activation of the p38 MAPK and NF-kappaB pathways. Our results therefore demonstrate that exposure to the four organic UV filters investigated may alter human immune system function. It provides new clue for the development of asthma or allergic diseases in terms of the environmental pollutants.

Ashby, J., Tinwell, H., Plautz, J., Twomey, K., & Lefevre, P. A. (2001). Lack of Binding to Isolated Estrogen or Androgen Receptors, and Inactivity in the Immature Rat Uterotrophic Assay, of the Ultraviolet Sunscreen Filters Tinosorb M-Active and Tinosorb S. *Regulatory Toxicology and Pharmacology*, 34(3), 287-291 <https://doi.org/10.1006/rtph.2001.1511>

The presence of structurally diverse chemicals as contaminants in the environment has led to concerns regarding their possible endocrine disturbing effects. Recently, some ultraviolet absorbing components

of sunscreen preparations have given positive responses in assays monitoring estrogen-like activity both in vitro and in vivo. Consequently, two recently developed sunscreen components, Tinosorb M-active and Tinosorb S, were evaluated using the in vitro estrogen and androgen receptor competitive binding assays. Neither compound gave a positive response in either of the assays, consistent with the large molecular dimensions of each chemical disfavoring binding to the hormone receptors. Both of the chemicals were inactive in immature rat uterotrophic assays conducted using the subcutaneous route of administration. It is concluded that neither of these agents possess intrinsic estrogenic/antiestrogenic or androgenic/antiandrogenic activity. The several positive control chemicals evaluated gave the expected positive responses in the assays used.

Axelstad, M., Boberg, J., Hougaard, K. S., Christiansen, S., Jacobsen, P. R., Mandrup, K. R., . . . Hass, U. (2011). Effects of Pre- and Postnatal Exposure to the UV-Filter Octyl Methoxycinnamate (OMC) on the Reproductive, Auditory and Neurological Development of Rat Offspring. *Toxicology and Applied Pharmacology*, 250(3), 278-290 <https://doi.org/10.1016/j.taap.2010.10.031>

Octyl Methoxycinnamate (OMC) is a frequently used UV-filter in sunscreens and other cosmetics. The aim of the present study was to address the potential endocrine disrupting properties of OMC, and to investigate how OMC induced changes in thyroid hormone levels would be related to the neurological development of treated offspring. Groups of 14-18 pregnant Wistar rats were dosed with 0, 500, 750 or 1000 mg OMC/kg bw/day during gestation and lactation. Serum thyroxine (T(4)), testosterone, estradiol and progesterone levels were measured in dams and offspring. Anogenital distance, nipple retention, postnatal growth and timing of sexual maturation were assessed. On postnatal day 16, gene expression in prostate and testes, and weight and histopathology of the thyroid gland, liver, adrenals, prostate, testes, epididymis and ovaries were measured. After weaning, offspring were evaluated in a battery of behavioral and neurophysiological tests, including tests of activity, startle response, cognitive and auditory function. In adult animals, reproductive organ weights and semen quality were investigated. Thyroxine (T(4)) levels showed a very marked decrease during the dosing period in all dosed dams, but were less severely affected in the offspring. On postnatal day 16, high dose male offspring showed reduced relative prostate and testis weights, and a dose-dependent decrease in testosterone levels. In OMC exposed female offspring, motor activity levels were decreased, while low and high dose males showed improved spatial learning abilities. The observed behavioral changes were probably not mediated solely by early T(4) deficiencies, as the observed effects differed from those seen in other studies of developmental hypothyroxinemia. At eight months of age, sperm counts were reduced in all three OMC-dosed groups, and prostate weights were reduced in the highest dose group. Taken together, these results indicate that perinatal OMC-exposure can affect both the reproductive and neurological development of rat offspring, which may be a cause of concern, as humans are systematically exposed to the compound through usage of sunscreens and other cosmetics.

Bae, J., Kim, S., Kannan, K., & Buck Louis, G. M. (2016). Couples' Urinary Concentrations of Benzophenone-Type Ultraviolet Filters and the Secondary Sex Ratio. *Science of The Total Environment*, 543(Pt A), 28-36 <https://doi.org/10.1016/j.scitotenv.2015.11.019>

The secondary sex ratio (SSR), defined as the ratio of males to females at birth, has been investigated in relation to endocrine disruptors to search for environmental toxicants perturbing human sex selection. Benzophenone (BP)-type ultraviolet (UV) filters, which are used in sunscreens and personal care products, have been reported to exert estrogenic and anti-androgenic activities. This study aimed to evaluate the association between maternal, paternal, and couple urinary concentrations of BP-type UV

filters and the SSR, given the absence of previous investigation. The study cohort comprised 220 couples who were enrolled in the Longitudinal Investigation of Fertility and the Environment (LIFE) Study between 2005 and 2009 prior to conception and who had a singleton birth during the follow-up period. Couples' urinary concentrations of five BP-type UV filters (ng/mL) were measured using triple-quadrupole tandem mass spectrometry: 2,4-dihydroxybenzophenone (BP-1), 2,2',4,4'-tetrahydroxybenzophenone (BP-2), 2-hydroxy-4-methoxybenzophenone (BP-3), 2,2'-dihydroxy-4-methoxybenzophenone (BP-8), and 4-hydroxybenzophenone (4-OH-BP). Modified Poisson regression models were used to estimate the relative risks (RRs) of a male birth for each BP-type UV filter, after adjusting for potential confounders. When maternal and paternal urinary BP-type UV filter concentrations were modeled jointly, both maternal BP-2 (2nd vs 1st tertile, RR, 0.62, 95% confidence interval [CI], 0.43-0.91) and paternal BP-2 (3rd vs 1st tertile, RR, 0.67, 95% CI, 0.45-0.99; p-trend, 0.04) were significantly associated with an excess of female births. Contrarily, maternal 4-OH-BP was significantly associated with an excess of male births (2nd vs 1st tertile, RR, 1.87, 95% CI, 1.27-2.74; 3rd vs 1st tertile, RR, 1.80, 95% CI, 1.13-2.87; p-trend, 0.02). Our findings provide the first evidence suggesting that BP-type UV filters may affect the SSR. However, future corroboration is needed, given the exploratory design of this study.

Bain, J. (2018). Sunscreen Safety. Retrieved from <https://skincancer.org/blog/sunscreen-safety/>

There's a lot of information out there about sunscreen safety, and not all of it is reliable. We asked a top expert, Elizabeth Buzney, MD, outpatient clinical director of the Department of Dermatology at Brigham and Women's Hospital and assistant professor of dermatology at Harvard Medical School, to address some common questions about sunscreens. She also serves on The Skin Cancer Foundation's Photobiology Committee.

Balazs, A., Krifaton, C., Orosz, I., Szoboszlay, S., Kovacs, R., Csenki, Z., . . . Kriszt, B. (2016). Hormonal Activity, Cytotoxicity and Developmental Toxicity of UV Filters. *Ecotoxicology and Environmental Safety*, 131, 45-53 <https://doi.org/10.1016/j.ecoenv.2016.04.037>

Ultraviolet (UV) filters are commonly used compounds in personal care products and polymer based materials, as they can absorb solar energy in the UVA and UVB spectrum. However, they are able to bind to hormone receptors and have several and different types of hormonal activities determined by in vitro assays. One of the aims of this work was to measure the hormonal and cytotoxic activities of four frequently used UV filters using bioluminescence based yeast test organisms. Using *Saccharomyces cerevisiae* BLYES and BLYAS strains allowed the rapid and reliable detection of agonist and antagonist hormonal activities, whereas BLYR strain served to measure cytotoxicity. Results confirmed that all tested UV filters show multiple hormonal activities. Cytotoxicity is detected only in the case of benzophenone-3. Research data on the toxic effects of benzophenone-3, especially on aquatic organisms are scarce, so further investigations were carried out regarding its cytotoxic and teratogenic effects on bacteria and zebrafish (*Danio rerio*) embryos, respectively. Results revealed the cytotoxicity of benzophenone-3 not only to yeasts but to bacteria, as well as its ability to influence zebrafish embryo hatching and development.

Bluthgen, N., Meili, N., Chew, G., Odermatt, A., & Fent, K. (2014). Accumulation and Effects of the UV-Filter Octocrylene in Adult and Embryonic Zebrafish (*Danio rerio*). *Science of The Total Environment*, 476-477, 207-217 <https://doi.org/10.1016/j.scitotenv.2014.01.015>

Wide application of the UV-filter octocrylene (OC) in cosmetics leads to contamination of the aquatic environment, but effects of OC remain unclear. Here we determine bioaccumulation and molecular effects of OC. Adult male zebrafish were exposed to 22, 209 and 383 µg/L and embryos to 69, 293 and 925 µg/L OC. OC accumulated in fish up to 17 µg/g. Calculated BCF varied between 41 and 136. Microarray analysis in brain and liver following exposure to 383 µg/L OC revealed alteration of 628 and 136 transcripts, respectively. Most prominent GO processes included developmental processes, organ development, hematopoiesis, formation of blood vessels, blood circulation, fat cell differentiation and metabolism. Validation by RT-qPCR in brain and liver of adult fish and embryos included a series of genes. Blood levels of 11-ketotestosterone were not altered. The transcriptomics data suggest that OC mainly affects transcription of genes related to developmental processes in the brain and liver as well as metabolic processes in the liver.

Blüthgen, N., Zucchi, S., & Fent, K. (2012). Effects of the UV Filter Benzophenone-3 (Oxybenzone) at Low Concentrations in Zebrafish (*Danio rerio*). *Toxicology and Applied Pharmacology*, 263(2), 184-194 <https://doi.org/10.1016/j.taap.2012.06.008>

Organic UV filters including benzophenone-3 (BP-3) are widely used to protect humans and materials from damage by UV irradiation. Despite the environmental occurrence of BP-3 in the aquatic environment, little is known about its effects and modes of action. In the present study we assess molecular and physiological effects of BP-3 in adult male zebrafish (*Danio rerio*) and in eleuthero-embryos by a targeted gene expression approach focusing on the sex hormone system. Fish and embryos are exposed for 14 days and 120 hours post fertilization, respectively, to 2.4–312 µg/L and 8.2–438 µg/L BP-3. Chemical analysis of water and fish demonstrates that BP-3 is partly transformed to benzophenone-1 (BP-1) and both compounds are accumulated in adult fish. Biotransformation to BP-1 is absent in eleuthero-embryos. BP-3 exposure leads to similar alterations of gene expression in both adult fish and eleuthero-embryos. In the brain of adult males *esr1*, *ar* and *cyp19b* are down-regulated at 84 µg/L BP-3. There is no induction of vitellogenin expression by BP-3, both at the transcriptional and protein level. An overall down-regulation of the *hsd3b*, *hsd17b3*, *hsd11b2* and *cyp11b2* transcripts is observed in the testes, suggesting an antiandrogenic activity. No histological changes were observed in the testes after BP-3 treatment. The study leads to the conclusion that low concentrations of BP-3 exhibit similar multiple hormonal activities at the transcription level in two different life stages of zebrafish. Forthcoming studies should show whether this translates to additional physiological effects.

Broniowska, Z., Pomierny, B., Smaga, I., Filip, M., & Budziszewska, B. (2016). The Effect of UV-Filters on the Viability of Neuroblastoma (SH-SY5Y) Cell Line. *Neurotoxicology*, 54, 44-52 <https://doi.org/10.1016/j.neuro.2016.03.003>

Topical application of cosmetic products, containing ultraviolet filters (UV filters) are recommended as a protection against sunburns and in order to reduce the risk of skin cancer. However, some UV filters can be absorbed through skin and by consuming contaminated food. Among the chemical UV filters, benzophenone-3 (BP-3), 3-(4-methylbenzylidene)camphor (4-MBC) and 2-ethylhexyl-4-methoxycinnamate (OMC) are absorbed through the skin to the greatest extent. So far, these lipophilic compounds were demonstrated to influence the gonadal and thyroid hormone function, but their effect on central nervous system cells has not been investigated, yet. In the present study, we investigated the effect of some UV filters on cell viability and caspase-3 activity in SH-SY5Y cells. It has been found that benzophenone-2 (BP-2), BP-3, 4-methylbenzophenone (4-MBP) and OMC present in the culture medium for 72h in high concentration (10^{-5} and 10^{-4} M) and 4-MBC only 10^{-4} M produced a significant

cytotoxic effect, as determined both by the MTT reduction test and LDH release assay. In contrast to necrotic changes, all tested UV filters increased caspase-3 activity in much lower concentrations (from 10^{-8} to 10^{-7} M). Proapoptotic properties of the test compounds were positively verified by Hoechst staining. The obtained results indicated that UV filters adversely affected the viability of nerve cells, most likely by enhancing the process of apoptosis. The most potent effect was exerted by BP-3 and 4-MBC and at concentrations that may be reached in vivo. Since human exposure to UV filters is significant these compound should be taken into consideration as one of the possible factors involved in pathogenesis of neurodegenerative diseases.

Bury, D., Modick-Biermann, H., Leibold, E., Bruning, T., & Koch, H. M. (2019). Urinary Metabolites of the UV Filter Octocrylene in Humans as Biomarkers of Exposure. *Archives of Toxicology*
<https://doi.org/10.1007/s00204-019-02408-7>

Octocrylene (OC) is a UV filter used in sun screens and other personal care products, but also in polymers and food contact materials for stabilization. In this study, we investigate human OC metabolism and urinary excretion after oral dosage of approx. 5 mg OC [wedge 61.8-89.5 microg/(kg body weight)] in three male volunteers. In a screening approach, we tentatively identified six urinary OC metabolites. For three, renal elimination kinetics was quantitatively investigated using authentic standards: the sidechain oxidation product 2-ethyl-5-hydroxyhexyl 2-cyano-3,3-diphenyl acrylate (5OH-OC), the beta-oxidation product 2-(carboxymethyl)butyl 2-cyano-3,3-diphenyl acrylate (dinor OC carboxylic acid; DOCCA), and the ester hydrolysis product 2-cyano-3,3-diphenylacrylic acid (CPAA). CPAA was the major urinary metabolite, representing 45% (range 40-50%) of the OC dose. 5OH-OC and DOCCA were only minor metabolites with low, but highly consistent renal conversion factors of 0.008% (0.005-0.011%) and 0.13% (0.11-0.16%), respectively. Peak urinary metabolite concentrations were observed between 3.2 h and 4.2 h postdose. All three metabolites were excreted with biphasic elimination kinetics, with considerably longer elimination half-lives for DOCCA (1st phase: 3.0 h; 2nd phase: 16 h) and CPAA (5.7 h and 16 h) compared to 5OH-OC (1.3 h and 6.4 h). 99% of all 5OH-OC was excreted within 24 h compared to 82% of DOCCA and 77% of CPAA. After dermal exposure, we detected the same metabolites with similar ratios in urine, however, at much lower concentrations and with considerably delayed elimination.

Butt, S. T., & Christensen, T. (2000). Toxicity and Phototoxicity of Chemical Sun Filters. *Radiation Protection Dosimetry*, 91(1-3), 283-286 <https://doi.org/10.1093/oxfordjournals.rpd.a033219>

Two chemical sun filters that are ingredients in sunscreen products have been tested for their dark toxicity and possible toxicity to mouse cells after UV irradiation. Increased toxicity as a result of breakdown of a UVB filter, octyl methoxycinnamate, was observed. UV radiation absorbed by the pure chemical sunscreen may lead to breakdown to more reactive chemical compounds than the unexposed sunscreen filter. The UVA filter included in our tests, butyl methoxydibenzoylmethane, was also toxic in the dark, however, it was the more photostable of the two and no additional significant toxicity was induced by UV irradiation. It can be concluded that the two sun filters are toxic to cells in the dark, but the biological role of this dark toxicity in the skin is not clear. Unstable sun filters may be broken down by UV to form photoproducts that are potentially toxic.

Calafat Antonia, M., Wong, L.-Y., Ye, X., Reidy John, A., & Needham Larry, L. (2008). Concentrations of the Sunscreen Agent Benzophenone-3 in Residents of the United States: National Health and

Nutrition Examination Survey 2003–2004. *Environmental Health Perspectives*, 116(7), 893-897
<https://doi.org/10.1289/ehp.11269>

Background: The capability of benzophenone-3 (BP-3) to absorb and dissipate ultraviolet radiation facilitates its use as a sunscreen agent. BP-3 has other uses in many consumer products (e.g., as fragrance and flavor enhancer, photoinitiator, ultraviolet curing agent, polymerization inhibitor). **Objectives:** Our goal was to assess exposure to BP-3 in a representative sample of the U.S. general population ≥ 6 years of age. **Methods:** Using automated solid-phase extraction coupled to high-performance liquid chromatography–tandem mass spectrometry, we analyzed 2,517 urine samples collected as part of the 2003–2004 National Health and Nutrition Examination Survey. **Results:** We detected BP-3 in 96.8% of the samples. The geometric mean and 95th percentile concentrations were 22.9 $\mu\text{g/L}$ (22.2 $\mu\text{g/g}$ creatinine) and 1,040 $\mu\text{g/L}$ (1,070 $\mu\text{g/g}$ creatinine), respectively. Least-square geometric mean (LSGM) concentrations were significantly higher ($p \leq 0.04$) for females than for males, regardless of age. LSGM concentrations were significantly higher for non-Hispanic whites than for non-Hispanic blacks ($p \leq 0.01$), regardless of age. Females were more likely than males [adjusted odds ratio (OR) = 3.5; 95% confidence interval (95% CI), 1.9–6.5], and non-Hispanic whites were more likely than non-Hispanic blacks (adjusted OR = 6.8; 95% CI, 2.9–16.2) to have concentrations above the 95th percentile. **Conclusions:** Exposure to BP-3 was prevalent in the general U.S. population during 2003–2004. Differences by sex and race/ethnicity probably reflect differences in use of personal care products containing BP-3.

Campos, D., Gravato, C., Fedorova, G., Burkina, V., Soares, A., & Pestana, J. L. T. (2017). Ecotoxicity of Two Organic UV-Filters to the Freshwater Caddisfly *Sericostoma vittatum*. *Environmental Pollution*, 228, 370-377 <https://doi.org/10.1016/j.envpol.2017.05.021>

Organic ultraviolet filters (UV-filters) used for protection against radiation in personal care products and other materials (e.g. textiles, plastic products) are considered emerging contaminants of aquatic ecosystem. Benzophenone-3 (BP3) and 3-(4-methylbenzylidene)camphor (4-MBC) are the most commonly used organic UV-filters and have been reported in freshwater environments due to contamination through discharges from wastewater treatment plants and swimming pools or by direct contamination from recreational activities. Our aim was to evaluate the ecotoxicological effects of these UV-filters using the freshwater caddisfly *Sericostoma vittatum*' biochemical biomarkers and energy processing related endpoints (feeding behaviour, energy reserves and cellular metabolism). In laboratory trials, both compounds induced feeding inhibition of *S. vittatum* at 3.55 mg/kg of BP3 and at concentrations ≥ 2.57 mg/kg of 4-MBC, decreased carbohydrates content at 3.55 and 6.95 mg/kg of BP3 and 4-MBC respectively, and increased total glutathione levels at concentrations ≥ 1.45 and 1.35 mg/kg of BP3 and 4-MBC respectively. No significant effects were observed on endpoints associated with oxidative stress, antioxidant defences, phase II biotransformation or neurotoxicity after exposure to the two UV-filters. Our results show that environmental relevant concentrations of BP3 and 4-MBC, can negatively impact freshwater insects and demonstrate the importance of monitoring the ecological effects of organic UV-filters using non-model invertebrate species.

Campos, D., Gravato, C., Quintaneiro, C., Golovko, O., Zlabek, V., Soares, A., & Pestana, J. L. T. (2017). Toxicity of Organic UV-Filters to the Aquatic Midge *Chironomus riparius*. *Ecotoxicology and Environmental Safety*, 143, 210-216 <https://doi.org/10.1016/j.ecoenv.2017.05.005>

Despite the frequent detection of organic ultraviolet-filters (UV-filters) in freshwater sediments, there is a lack of ecotoxicological data undermining a correct risk assessment for these emerging contaminants.

The present study assessed the effects of three of the most commonly used UV-filters (benzophenone-3 - BP3; 3-(4-methylbenzylidene)camphor - 4-MBC and octocrylene - OC) on *Chironomus riparius* life history and biochemical responses. Standard ecotoxicological assays confirmed that all compounds impaired growth of *C. riparius* larvae and induced developmental effects such as delayed emergence and a reduction of imagoes weight. Concerning the biochemical responses analysed no evidences of oxidative damage in lipids or neurotoxicity (tested assessing acetylcholinesterase activity) were observed for any of the tested compounds. However, 4-MBC exposure induced a decrease in catalase activity and an increase in glutathione-S-transferase activity at 14.13mg/Kg while OC exposure caused an increase in total glutathione levels at 0.23 and 18.23mg/Kg. Exposure to all UV-filters tested, increased energy consumption on *C. riparius* with significant differences above 1.00mg/Kg for BP3, 0.09mg/Kg for 4-MBC and 2.13mg/Kg for OC. These results suggest that environmental relevant concentrations of UV-filters can cause deleterious effects to aquatic benthic species, such as *C. riparius*, and call for further research concerning effects of organic UV-filters on natural invertebrate communities and ecosystem functioning.

Campos, D., Silva, A. R. R., Loureiro, S., Grabicova, K., Stanova, A. V., Soares, A., & Pestana, J. L. T. (2019). Two-Generational Effects of Benzophenone-3 on the Aquatic Midge *Chironomus riparius*. *Science of The Total Environment*, 669, 983-990 <https://doi.org/10.1016/j.scitotenv.2019.03.023>

Organic UV-filters are emergent contaminants continuously released into the aquatic ecosystems. These compounds are persistent showing potential for bioaccumulation. Partial life-cycle tests may underestimate the toxicity of UV-filters especially since these compounds have shown to act as endocrine disruptors. In the present study, the benthic aquatic insect *Chironomus riparius* was exposed to a gradient of Benzophenone-3 (BP3) concentrations over two generations to assess effects over a full life cycle from the first-instar larvae in the parental (P) generation (emergence, fecundity and fertility) until emergence in the subsequent generation (filial - F1). Recovery from exposure was also assessed after one generational exposure. Our results showed that concentrations of up to 8mg BP3/kg, elicited no effects regarding emergence rate and development time of *C. riparius* in the P generation. Our results also showed that *C. riparius* fecundity was not affected by BP3 exposure, but a strong dose-response relationship was observed for fertility with none of the egg ropes hatching at 8mg BP3/kg. Regarding effects observed in the F1 generation, emergence and development time were impaired by continuous exposure to BP3. Moreover, reduced emergence and changes in development time were observed in the F1 generation maintained in control/clean conditions but whose parents were exposed to BP3. Results found in this two-generational study clearly show reproductive effects of BP3 on *C. riparius* that would not be detected using standard tests. Full life cycle and multigenerational assays are critical to properly evaluate the population level effects of endocrine disrupting compounds such as organic UV-filters.

Chapin, R., Gulati, D., & Mounce, R. (1997). 2-Hydroxy-4-Methoxybenzophenone. *Environmental Health Perspectives*, 105(Supplement 1), 313-314 <https://doi.org/10.1289/ehp.105-1470294>

2-Hydroxy-4-methoxybenzophenone (HMBP), a common ingredient in sunscreens and tanning agents, was found in a preliminary study in B6C3F1 mice to reduce epididymal sperm density by approximately 25%, and to slightly increase estrous cycle length. This stimulated a further evaluation of its potential to cause reproductive toxicity in Swiss CD-1 mice using the RACB protocol. Data on food and water consumption, body weights, and clinical signs during a 2-week dose-range-finding study (Task 1) were used to set exposure concentrations for the Task 2 continuous cohabitation phase at 0.0, 1.25, 2.5, and

5.0% in feed. Based on body weight and feed consumption data, the estimated average daily dose values were approximately 1.8, 4, and 9 g/kg body weight.

Chen, L., Hu, C., Guo, Y., Shi, Q., & Zhou, B. (2019). TiO₂ Nanoparticles and BPA are Combined to Impair the Development of Offspring Zebrafish after Parental Coexposure. *Chemosphere*, 217, 732-741 <https://doi.org/10.1016/j.chemosphere.2018.11.052>

Titanium dioxide (TiO₂) nanoparticles and bisphenol A (BPA) in aquatic environments interact reciprocally to enhance the maternal transfer of pollutants to offspring, thus varying the innate toxicities during early embryonic development. However, it remains unexplored regarding the molecular mechanisms of developmental toxicity in offspring after parental coexposure. In the present study, adult zebrafish were exposed to TiO₂ nanoparticles (100µg/L), BPA (20µg/L) or their binary mixture for four months. Then, eggs of F1 generation were collected and reared in clean water until 5 days post-fertilization. In characteristic of larval survival and growth, parental coexposure to TiO₂ particles and BPA caused a severer inhibition of F1 offspring larvae compared with single exposure. Mechanistic investigation by shotgun proteomics found that development of larval offspring from coexposed parents was impaired through a distinct mode of toxicity, that is, specifically altering the activity of phagosome and lysosome. Single exposure of adult zebrafish to TiO₂ mainly affected insulin-responsive compartment; and BPA parental exposure mainly affected carbohydrate metabolism and calcium signaling of larval offspring. Furthermore, considering the tight regulation of sex hormones in the expression of vitellogenin (VTG), addition of nanoparticles during parental exposure led to inconsistencies between VTG induction and endogenous levels of sex hormones (estradiol and testosterone) in F1 offspring fish. This implied that transfer of nanoparticles to offspring larvae may change the availability of hormonal molecules and BPA at target tissues. Overall, current results provided mechanistic clues into the multigenerational developmental toxicity by parental coexposure to TiO₂ particles and BPA.

Chen, L., Li, X., Hong, H., & Shi, D. (2018). Multigenerational Effects of 4-Methylbenzylidene Camphor (4-MBC) on the Survival, Development and Reproduction of the Marine Copepod *Tigriopus japonicus*. *Aquatic Toxicology*, 194, 94-102 <https://doi.org/10.1016/j.aquatox.2017.11.008>

One of the most widely used organic UV filters, 4-methylbenzylidene camphor (4-MBC), is present at high concentrations in offshore waters. The marine copepod *Tigriopus japonicus* was exposed to different concentrations of 4-MBC (i.e., 0, 0.5, 1, 5 and 10µg/L(-1)) for 4 consecutive generations (F0-F3) to evaluate the impact of 4-MBC on marine ecosystems. The results showed that in the F0 generation, 4-MBC caused significant lethal toxicity in *T. japonicus* at concentrations of 5 and 10µg/L(-1) and the nauplii were more sensitive to 4-MBC toxicity than the adults. However in the F1-F3 generations, 4-MBC exposure did not affect the survival rate. The hatching rate and the developmental duration from the nauplii to the copepodite (N-C) and from the nauplii to adult (N-A) decreased significantly in the F1-F2 generations and in the F2-F3 generations, respectively, even at the lowest exposure concentration (0.5µg/L(-1)). In the subsequent two generations (i.e., the F4-F5 generations) of recovery exposure in clean seawater, the growth rates of the original 4-MBC exposure groups were still faster than the control in both the N-C and N-A stages, suggesting possible transgenerational genetic and/or epigenetic changes upon chronic 4-MBC exposure. The expression of the ecdysone receptor gene was up-regulated by 4-MBC, which was consistent with the decrease of the N-C/N-A duration. In addition, 4-MBC may induce oxidative stress and trigger apoptosis in *T. japonicus*, resulting in developmental, reproductive and even lethal toxicity. A preliminary risk assessment suggested that

under environmentally realistic concentrations, 4-MBC had significant potential to pose a threat to marine crustaceans and marine ecosystems.

Chen, T. H., Hsieh, C. Y., Ko, F. C., & Cheng, J. O. (2018). Effect of the UV-Filter Benzophenone-3 on Intra-Colonial Social Behaviors of the False Clown Anemonefish (*Amphiprion ocellaris*). *Science of The Total Environment*, 644, 1625-1629 <https://doi.org/10.1016/j.scitotenv.2018.07.203>

The UV-filter benzophenone-3 (BP-3) is widely used and is environmentally stable, lipophilic, and bioaccumulative. Previous in vitro and in vivo studies have shown that BP-3 can cause endocrine disrupting effects. However, little information is available on its ecotoxicity on coral reef fish. Agonistic behavior, which is regulated by the endocrine system, is crucial to the social structure of some coral reef fish species. Endocrine disruptors may disturb fish agonistic behavior and social interactions. In this study, we tested whether chronic BP-3 exposure can affect social behaviors in coral reef fish. Juvenile false clown anemonefish (*Amphiprion ocellaris*) were exposed to BP-3 via diet (0 and 1000ng/g food) for 90d. Through the experiment, each tank was videotaped and behavioral indicators of social status, including threatening, attacking, and submissive behaviors were quantitatively analyzed from the videos. Survival and growth were not affected by the BP-3 exposure except that the body weight of the dominant fish was higher in the BP-3 group. Social rankings were not changed by BP-3. Intra-colonial social behaviors were significantly affected only by rank but not by the BP-3 exposure. Our results suggest that BP-3 at environmental levels may not cause significant harm to social behavior of coral reef fish. However, more research is needed to better understand the behavioral effects of BP-3 in fish.

Chen, X., Chen, M., Xu, B., Tang, R., Han, X., Qin, Y., . . . Wang, X. (2013). Parental Phenols Exposure and Spontaneous Abortion in Chinese Population Residing in the Middle and Lower Reaches of the Yangtze River. *Chemosphere*, 93(2), 217-222 <https://doi.org/10.1016/j.chemosphere.2013.04.067>

Widespread use of phenols has led to ubiquitous exposure to phenols. In experimental animals, phenols increased resorptions, reduced live litter size and fetal body weights. However, there are limited epidemiological evidences of the relationships between exposure to phenols and pregnancy outcomes. We evaluated the associations between parental urinary levels of various phenols and spontaneous abortion in a Chinese population residing in the middle and lower reaches of the Yangtze River. A case-control study was conducted that included 70 case couples with medically unexplained spontaneous abortion and 180 control couples who did not have a history of spontaneous abortion and had at least one living child. Both parental urinary phenols were measured by ultra-high performance liquid chromatography-tandem mass spectrometry including bisphenol A (BPA), benzophenone-3 (BP-3), 2,3,4-trichlorophenol (2,3,4-TCP), pentachlorophenol (PCP), 4-n-octylphenol (4-n-OP) and 4-n-nonylphenol (4-n-NP). Compared with the low exposure group, there was an increased risk of spontaneous abortion with high paternal urinary PCP concentration [odds ratio (OR)=2.09, 95% Confidence Interval (CI), 1.05-4.14], and maternal exposure to 4-n-OP and alkylphenol(s) also significantly increased the risk of spontaneous abortion (OR=2.21, 95% CI, 1.02-4.80; OR=2.81, 95% CI, 1.39-5.65, respectively). Our study firstly provides the evidence that paternal PCP exposure, maternal 4-n-OP and alkylphenol(s) exposure are associated with spontaneous abortion in humans.

Christen, V., Zucchi, S., & Fent, K. (2011). Effects of the Uv-Filter 2-Ethyl-Hexyl-4-Trimethoxycinnamate (EHMC) on Expression of Genes Involved in Hormonal Pathways in Fathead Minnows

(*Pimephales promelas*) and Link to Vitellogenin Induction and Histology. *Aquatic Toxicology*, 102, 167-176 <https://doi.org/10.1016/j.aquatox.2011.01.013>

UV-filters are increasingly used in cosmetics and in the protection of materials against UV-irradiation, and ultimately they reach aquatic systems. The lipophilic UV-filter 2-ethyl-hexyl-4-trimethoxycinnamate (EHMC) belongs to one of the most frequently used UV-filters and accumulates in aquatic animals. Despite its ubiquitous presence in water and biota, very little is known about its potential hormonal effects on aquatic organisms. In our study, we evaluated the effects of measured water concentration of 5.4, 37.5, 244.5 and 394 µg/L EHMC on the expression of genes involved in hormonal pathways in the liver, testis and brain of male and female fathead minnows (*Pimephales promelas*). We compare the transcription profile with the plasma vitellogenin (VTG) content, secondary sex characteristics, and gonad histology. Transcripts of the androgen receptor (*ar*) were significantly down-regulated in the liver of females at 37.5, 244.5 µg/L and 394 µg/L EHMC. Additionally, the 3β-hydroxysteroid dehydrogenase (3β-HSD) transcript was significantly decreased in the liver of males at 37.5, 244.5 and 394 µg/L EHMC, and at 244.5 and 394 µg/L EHMC in females. The expressional changes were tissue-specific in most cases, being most significant in the liver. Vitellogenin plasma concentration was significantly increased at 244.5 µg/L EHMC in males. EHMC induced significant histological changes in testes and ovaries at 394 µg/L. Testes displayed a decrease in spermatocytes, and ovaries a decrease in previtellogenic oocytes. The induction of VTG plasma concentration and the histological changes in gonads suggest an estrogenic and/or antiandrogenic activity of EHMC. On the other hand, the gene expression profile shows an antiestrogenic (e.g.: down-regulation of *esr1*) activity of EHMC. In conclusion, our data demonstrate that EHMC displays low but multiple hormonal activities in fish.

Christiansen, S., Kortenkamp, A., Axelstad, M., Boberg, J., Scholze, M., Jacobsen, P. R., . . . Hass, U. (2012). Mixtures of Endocrine Disrupting Contaminants Modelled on Human High End Exposures: An Exploratory Study in Rats. *International Journal of Andrology*, 35(3), 303-316 <https://doi.org/10.1111/j.1365-2605.2011.01242.x>

By diminishing the action of androgens during gestation, certain chemicals can induce irreversible demasculinization and malformations of sex organs in the male rat after gestational exposure. Studies with mixtures of such anti-androgens have shown that substantial combined effects occur even though each individual chemical is present at low, ineffective doses, but the effects of mixtures modelled based on human intakes have not previously been investigated. To address this issue for the first time, we selected 13 chemicals for a developmental mixture toxicity study in rats where data about in vivo endocrine disrupting effects and information about human exposures was available, including phthalates, pesticides, UV-filters, bisphenol A, parabens and the drug paracetamol. The mixture ratio was chosen to reflect high end human intakes. To make decisions about the dose levels for studies in the rat, we employed the point of departure index (PODI) approach, which sums up ratios between estimated exposure levels and no-observed-adverse-effect-level (NOAEL) values of individual substances. For high end human exposures to the 13 selected chemicals, we calculated a PODI of 0.016. As only a PODI exceeding 1 is expected to lead to effects in the rat, a total dose more than 62 times higher than human exposures should lead to responses. Considering the high uncertainty of this estimate, experience on lowest-observed-adverse-effect-level (LOAEL)/NOAEL ratios and statistical power of rat studies, we expected that combined doses 150 times higher than high end human intake estimates should give no, or only borderline effects, whereas doses 450 times higher should produce significant responses. Experiments indeed showed clear developmental toxicity of the 450-fold dose in terms of increased nipple retention (NR) and reduced ventral prostate weight. The 150-fold dose group

exhibited significantly increased NR. These observations suggest that highly exposed population groups, especially women of reproductive age, may not be protected sufficiently against the combined effects of chemicals that affect the hormonal milieu required for normal male sexual differentiation.

Coelho, S. G., Rua, D., Miller, S. A., & Agrawal, A. (2019). Suboptimal Uva Attenuation by Broad Spectrum Sunscreens under Outdoor Solar Conditions Contributes to Lifetime Uva Burden. *Photodermatology, Photoimmunology & Photomedicine*, n/a(n/a) <https://doi.org/10.1111/phpp.12503>

Abstract Background Broad spectrum sunscreens with a sun protection factor (SPF) of 15 or greater are indicated to decrease the risk of skin cancer and early skin aging caused by the sun if used as directed with other sun protection measures. To determine whether sunscreen product performance is compromised under solar exposure and to test spectral uniformity of protection across the UVA spectrum, we tested broad spectrum sunscreens with a variety of active pharmaceutical ingredients (APIs) and in a variety of dosage forms. **Methods** A cross-sectional market survey of 32 sunscreen drug products containing either organic or inorganic APIs with SPF of 15, 30, 50, and 70 was tested. UV doses were delivered via natural sun in Silver Spring, Maryland between June and September of 2017. **Results** Of the 32 sunscreen drug products, 6 products failed to meet their broad spectrum claim under solar exposure. Using FDA's new proposal to strengthen sunscreen broad spectrum requirements, spectral uniformity based on the mean sunscreen absorbance of UVA1(340-400 nm)/UV (290-400 nm) indicated that ~40% of sunscreen drug products tested had suboptimal UVA protection. **Conclusion** US consumers may unknowingly be receiving up to 36% more transmitted UVA when selecting between similarly labeled broad spectrum sunscreen drug products with equivalent SPF values. FDA's new proposal may help decrease consumers' overall lifetime UVA burden. Spectral absorbance data on sunscreen performance can be used to further improve the coupling of broad spectrum protection to a product's SPF value so that consumers have improved proportional increases in UV protection.

Corinaldesi, C., Damiani, E., Marcellini, F., Falugi, C., Tiano, L., Bruge, F., & Danovaro, R. (2017). Sunscreen Products Impair the Early Developmental Stages of the Sea Urchin *Paracentrotus lividus*. *Scientific Reports*, 7(1), 7815 <https://doi.org/10.1038/s41598-017-08013-x>

Marine ecosystems are increasingly threatened by the release of personal care products. Among them, sunscreens are causing concern either for the effects on skin protection from UV radiation and for the potential impacts on marine life. Here, we assessed the UVA protective efficacy of three sunscreens on human dermal fibroblasts, including two common products in Europe and USA, and an eco-friendly product. The sunscreens' effects were also tested on *Paracentrotus lividus*, a marine species possibly threatened by these contaminants. We found that all tested sunscreens had similar efficacy in protecting human fibroblasts from UVA radiation. Conversely, the sunscreens' effects on embryo-larval development of *P. lividus* were dependent on the product tested. In particular, the USA sunscreen, containing benzophenone-3, homosalate and preservatives, caused the strongest impact on the sea urchin development, whereas the eco-friendly sunscreen determined the weakest effects. These results suggest that although the tested products protected human skin cells from UVA-induced damage, they might severely affect the success of recruitment and survival of the sea urchin. Our findings underline the importance of developing eco-friendly sunscreens for minimising or avoiding the impact on marine life while protecting human skin from UV damage.

Coronado, M., De Haro, H., Deng, X., Rempel, M. A., Lavado, R., & Schlenk, D. (2008). Estrogenic Activity and Reproductive Effects of the UV-Filter Oxybenzone (2-Hydroxy-4-Methoxyphenyl-Methanone) in Fish. *Aquatic Toxicology*, *90*(3), 182-187
<https://doi.org/10.1016/j.aquatox.2008.08.018>

Previous studies in extracts of sediments surrounding municipal outfalls off the coast of California, USA and effluents of New York City, NY, USA indicated the UV-filtering agent, oxybenzone (CAS# 131-57-7; benzophenone-3) as a potential estrogen. The effects of oxybenzone on estrogenic activity and reproduction were evaluated using a 14-day juvenile rainbow trout assay for plasma vitellogenin and a subsequent 21-day Japanese medaka reproduction assay. Significant induction of vitellogenin was observed in the rainbow trout at the 1000 microg/L nominal concentration (749 microg/L median measured value) of oxybenzone which was approximately 75 times greater than the concentrations observed in previous wastewater effluent. Vitellogenin induction was also observed in the 1000 microg/L nominal concentration (620 microg/L median measured) of oxybenzone in male Japanese medaka (*Oryzias latipes*) after 21 days of exposure. The number of eggs produced per female per day exposed to the same concentration (620 microg/L) were significantly lower after 7 days, but returned to control values after 21 days. Fertilized eggs were then monitored for 20 days to assess hatching success. The overall percentage of fertilized eggs collected during the 21-day exposure that hatched was significantly lower in the 620 microg/L oxybenzone concentration. There was also a temporal effect at this concentration as egg viability (percentage of fertilized eggs that hatched) was diminished 13-15 days after eggs were collected. All three oxybenzone concentrations (16, 132, and 620 microg/L) and the 50 ng/L estradiol positive control showed reduced hatching of eggs at day 15, and the 132 and 620 microg/L oxybenzone concentrations diminished the percentage of eggs that hatched on days 13-15. These data indicate that the UV-filter oxybenzone alters endocrine or reproduction endpoints in two fish species, but at concentrations significantly higher than those measured in the environment.

Danovaro, R., & Corinaldesi, C. (2003). Sunscreen Products Increase Virus Production through Prophage Induction in Marine Bacterioplankton. *Microbial Ecology*, *45*(2), 109-118
<https://doi.org/10.1007/s00248-002-1033-0>

Classical pollutants (e.g., hydrocarbon, pesticides) have been recently recognized to induce lytic cycle in lysogenic bacteria, but information on micro-pollutants is almost completely lacking. We investigated the effects of cosmetic sun products (sunscreen and solar oil) on viral abundance and bacterial activity. We found that both sunscreen and solar oil acted as pollutants, inducing viral development and controlling bacterial abundance and production, thus leading to an increase of the virus to bacterium ratio. Short-term experiments revealed that sunscreen supplementation induced the lytic cycle in a large fraction of total bacterial abundance (13-24% of bacteria, at low and high concentrations, respectively), whereas solar oil had a lower impact (6-9%). A synchronized development of the phage-host system was observed only after sunscreen addition. The addition of sunscreen, even at low concentrations, had a significant impact on all enzymatic activities (aminopeptidase, glucosidase, and phosphatase), which increased significantly. However, when enzymatic activities were normalized per cell, a selective enhancement was observed for certain enzymes (e.g., aminopeptidase) and inhibition for others (e.g., glucosidase). These results indicate that sunscreen products can modify C, N, and P biogeochemical cycling in seawater and increase virus abundance through prophage induction in marine bacterioplankton.

Darbre, P. D. (2019). The Potential for Estrogen Disrupting Chemicals to Contribute to Migration, Invasion and Metastasis of Human Breast Cancer Cells. *Journal of Cancer Metastasis and Treatment*, 5, 58 <https://doi.org/10.20517/2394-4722.2019.22>

Estrogen disrupting chemicals are environmental compounds which mimic, antagonize or interfere in the action of physiological estrogens. They occur naturally (plant phytoestrogens) but the majority are man-made compounds, which, through their use in agricultural, industrial and consumer products, have become widely present in human tissues including breast tissue. Since exposure to estrogen is a risk factor for breast cancer, estrogen disrupting chemicals may also contribute to breast cancer development. This review discusses evidence implicating estrogen disrupting chemicals in increasing migratory and invasive activity of breast epithelial cells, in epithelial-to-mesenchymal transition, and in growth of breast tumours at metastatic sites as well as the primary site. Mechanisms may be through the ability of such chemicals to bind to estrogen receptors, but unlike for proliferation, effects on cell migration and invasion are not limited to estrogen receptor-mediated mechanisms. Furthermore, whilst effects on proliferation can be measured within hours/days of adding an estrogen disrupting chemical to estrogen-responsive breast cancer cells, effects on cell migration occur after longer times (weeks). Most studies have focused on individual chemicals, but there is now a need to consider the environmentally relevant effects of long-term, low-dose exposure to complex mixtures of estrogen disrupting chemicals on mechanisms of metastasis.

de Souza, J. M., Mendes, B. O., Guimaraes, A. T. B., Rodrigues, A. S. L., Chagas, T. Q., Rocha, T. L., & Malafaia, G. (2018). Zinc Oxide Nanoparticles in Predicted Environmentally Relevant Concentrations Leading to Behavioral Impairments in Male Swiss Mice. *Science of The Total Environment*, 613-614, 653-662 <https://doi.org/10.1016/j.scitotenv.2017.09.051> [Two page numbers?](#)

Although the potential neurotoxic effects from the exposure to zinc oxide nanoparticles (ZnO NPs) on humans and on experimental models have been reported in previous studies, the effects from the exposure to environmentally relevant concentrations of them remain unclear. Thus, the aim of the present study is to investigate the effects from the exposure to environmentally relevant concentrations of ZnO NPs on the behavior of male Swiss mice. The animals were daily exposed to environmentally relevant concentrations of ZnO NPs (5.625×10^{-5} mg/kg(-1)) at toxic level (300 mg/kg(-1)) through intraperitoneal injection for five days; a control group was set for comparison purposes. Positive control groups (clonazepam and fluoxetine) and a baseline group were included in the experimental design to help analyzing the behavioral tests (open field, elevated plus maze and forced swim tests). Although we did not observe any behavioral change in the animals subjected to the elevated plus maze and forced swim tests, our data evidence the anxiogenic behavior of animals exposed to the two herein tested ZnO NPs concentrations in the open field test. The animals stayed in the central part of the apparatus and presented lower locomotion ratio in the central quadrants/total of locomotion during this test. It indicates that the anxiogenic behavior was induced by ZnO NP exposure, because it leads to Zn accumulation in the brain. Thus, the current study is the first to demonstrate that the predicted environmentally relevant ZnO NPs concentration induces behavioral changes in mammalian experimental models. Our results corroborate previous studies that have indicated the biological risks related to the water surface contamination by metal-based nanomaterials.

Dean, S. W. D., R.H; Ruddock, S.P.; Dean, J.C.; Martin, C.N. and Kirkland, D.J. (1992). Development of Assays for the Detection of Photomutagenicity of Chemicals During Exposure to UV Light. II.

Results of Testing Three Sunscreen Ingredients. *Mutagenesis*, 7(3), 179-182

<https://doi.org/10.1093/mutage/7.3.179>

Three sunscreen ingredients, derivatives of benzylidene camphor, were tested for photomutagenic potential. These were benzenesulfonic acid, 4-[(4,7,7-trimethyl-3-oxo-bicyclo [2.2.1] hept-2-ylidene) methyl] (Mexoryl SL), 4-(2-oxo 3-bornylidenemethyl) phenyl trimethylammonium methyl sulphate (Mexoryl SO) and 3,3'-(1,4-phenylenedimethylidene) bis [7,7-dimethyl-2-oxo-bicyclo [2.2.1] heptane-1-methane-sulfonic acid] (Mexoryl SX). Two complementary assay systems were used, one involving the induction of reverse mutations in *Escherichia coli* strain WP2, the other measuring the induction of reverse mutations in *Escherichia coli* strain WP2, the other measuring the induction of chromosome damage in Chinese hamster ovary (CHO) cells. Irradiation with UVA and/or UVB was provided by an Osram Ultra-Vitalux sunlamp. None of the three sunscreens, tested either to the limit of solubility or toxicity, gave any indication of photomutagenicity in either assay, under conditions in which the positive control compound, 8-methoxypsoralen, was extremely photomutagenic. It is concluded that Mexoryls SL, SO and SX can be exposed to UV light without producing photomutagenicity measurable using a bacterial reverse mutation or a mammalian chromosome aberration assay.

Diaz-Gil, C., Cotgrove, L., Smee, S. L., Simon-Otegui, D., Hinz, H., Grau, A., . . . Catalan, I. A. (2017). Anthropogenic Chemical Cues Can Alter the Swimming Behaviour of Juvenile Stages of a Temperate Fish. *Marine Environmental Research*, 125, 34-41
<https://doi.org/10.1016/j.marenvres.2016.11.009>

Human pressure on coastal areas is affecting essential ecosystems including fish nursery habitats. Among these anthropogenic uses, the seasonal increment in the pressure due to leisure activities such as coastal tourism and yachting is an important environmental stressor in many coastal zones. These pressures may elicit understudied impacts due to, for example, sunscreens or other seasonal pollutants. The island of Majorca, northwest Mediterranean Sea, experiences one of the highest number of tourist visits per capita in the world, thus the surrounding coastal habitat is subject to high anthropogenic seasonal stress. Studies on early stages of fishes have observed responses to coastal chemical cues for the selection or avoidance of habitats. However, the potential interferences of human impacts on these signals are largely unknown. A choice chamber was used to determine water type preference and behaviour in naive settled juvenile gilt-head sea bream (*Sparus aurata*), a temperate species of commercial interest. Fish were tested individually for behavioural changes with respect to water types from potential beneficial habitats, such as seawater with extract of the endemic seagrass *Posidonia oceanica*, anthropogenically influenced habitats such as water extracted from a commercial and recreational harbour and seawater mixed with sunscreen at concentrations observed in coastal waters. Using a Bayesian approach, we investigated a) water type preference; b) mean speed; and c) variance in the movement (as an indicator of burst swimming activity, or "sprint" behaviour) as behavioural descriptors with respect to water type. Fish spent similar percentage of time in treatment and control water types. However, movement descriptors showed that fish in sunscreen water moved slower (98.43% probability of being slower) and performed fewer sprints (90.1% probability of having less burst in speed) compared to control water. Less evident increases in sprints were observed in harbour water (73.56% more sprints), and seagrass (79.03% more) in comparison to control water. When seagrass water was tested against harbour water, the latter elicited a higher number of sprints (91.66% increase). We show that juvenile gilt-head seabream are able to react to a selection of naturally occurring chemically different odours, including the increasingly important presence of sunscreen products, and provide a plausible interpretation of the observed behavioural patterns.

Diffey, B. L., Tanner, P. R., Matts, P. J., & Nash, J. F. (2000). In Vitro Assessment of the Broad-Spectrum Ultraviolet Protection of Sunscreen Products. *Journal of the American Academy of Dermatology*, 43(6), 1024-1035 <https://doi.org/10.1067/mjd.2000.109291>

Background: There are considerable data to suggest that protection from solar ultraviolet (UV) radiation will reduce the risk of acute and chronic skin damage in humans. Whereas the sun protection factor (SPF) provides an index of protection against erythemally effective solar UV, largely confined to the UVB (290-320 nm) and short-wavelength UVA (320-340 nm) region, there is currently no agreed-upon method to measure broad-spectrum protection against long-wavelength UVA (340-400 nm). Objective: The objective of these studies was to assess the potential of in vitro UV substrate spectrophotometry and subsequent calculation of the "critical wavelength" value as a measure of broad-spectrum UV protection and as a routine, practical procedure for classification of sunscreen products. Methods: The spectral absorption of 59 commercially available sunscreen products and multiple experimental formulas with one or more UV filters was measured. Sunscreen product, 1 mg/cm², was applied to a hydrated synthetic collagen substrate, preirradiated with a solar simulator, and then subjected to UV substrate spectrophotometry. Multiple determinations from 5 independent samples per product were used to calculate the critical wavelength value, defined as the wavelength at which the integral of the spectral absorbance curve reached 90% of the integral from 290 to 400 nm. Results: We found that a recognized long-wave UVA active ingredient such as titanium dioxide, zinc oxide, or avobenzone is a necessary but insufficient product requirement for achieving the highest proposed broad-spectrum classification, that is, critical wavelength of 370 nm or more. Although SPF and critical wavelength are largely independent of each other, UVA absorbance must increase commensurate with SPF to maintain the same critical wavelength value. Substrate spectrophotometry and the calculation of critical wavelength can readily account for sunscreen photostability by UV preirradiation. Finally, there is also a strong positive relationship between critical wavelength and a currently available in vivo measure of UVA protection. Conclusion: Determination of critical wavelength by means of UV substrate spectrophotometry provides a rapid, inexpensive, and reliable measure of broad-spectrum protection, which is largely independent of SPF, yet ensures long-wavelength UVA protection commensurate with SPF. The procedure provides a routine, sensitive means of differentiating and classifying sunscreen products and, importantly, obviates the need to subject volunteers to acute exposures of high-dose, nonterrestrial UV, the health risks of which are still poorly understood.

DiNardo, J. C., & Downs, C. A. (2018). Dermatological and Environmental Toxicological Impact of the Sunscreen Ingredient Oxybenzone/Benzophenone-3. *Journal of Cosmetic Dermatology*, 17(1), 15-19 <https://doi.org/10.1111/jocd.12449>

Oxybenzone (Benzophenone-3) is an emerging human and environmental contaminant used in sunscreens and personal care products to help minimize the damaging effects of ultraviolet radiation. The Center for Disease Control fourth national report on human exposure to environmental chemicals demonstrated that approximately 97% of the people tested have oxybenzone present in their urine, and independent scientists have reported various concentrations in waterways and fish worldwide. Oxybenzone can also react with chlorine, producing hazardous by-products that can concentrate in swimming pools and wastewater treatment plants. Moreover, adverse reactions could very well be increased by the closed loop of ingesting fish contaminated with oxybenzone and/or washing the ingredient off our bodies and having it return in drinking water as treatment plants do not effectively remove the chemical as part of their processing protocols. In humans, oxybenzone has been reported to

produce contact and photocontact allergy reactions, implemented as a possible endocrine disruptor and has been linked to Hirschsprung's disease. Environmentally, oxybenzone has been shown to produce a variety of toxic reactions in coral and fish ranging from reef bleaching to mortality. Lastly, with the rise in skin cancer rates and the availability of more effective sunscreen actives such as micronized zinc oxide and titanium dioxide, serious doubts about the relative prevention benefit of personal care products containing oxybenzone must be raised and compared with the potential negative health and environmental effects caused by the accumulation of this and other chemicals in the ecosystem.

DiNardo, J. C., & Downs, C. A. (2019). Can Oxybenzone Cause Hirschsprung's Disease? *Reproductive Toxicology*, 86, 98-100 <https://doi.org/10.1016/j.reprotox.2019.02.014>

Oxybenzone is a ultraviolet (UV) absorber used in 70% of sunscreen products, is a recognized endocrine disrupting chemical (EDC) and is small enough to pass through skin and placenta barriers. Numerous studies have identified this chemical in the urine/blood of pregnant women as well as in fetal and umbilical cord blood. A recent study demonstrated that women with medium to high levels of oxybenzone in their urine was associated with giving birth to neonates with Hirschsprung's Disease (HSCR). Testing in human cell lines confirmed that low levels of oxybenzone has the potential to disrupt cell migration and function in a manner similar to what is associated with HSCR. Analysis of human exposure levels to oxybenzone from sunscreen use, under normal conditions, demonstrates that enough chemical can cross into the mother's blood making it available to the fetus at high enough levels that can indeed inhibit migration of neural crest cells during critical embryonic development.

Du, J., Qv, M., Li, K., Yin, X., Meng, F., Yang, J., & Ma, C. (2018). Impacts of Benzophenone-Type UV Filters on Cladoceran *Daphnia carinata*. *Limnology*, 20(2), 173-179 <https://doi.org/10.1007/s10201-018-0563-1>

The impacts of three commonly used benzophenone-type UV filters including benzophenone (BP), 2-hydroxy-4-methoxy-benzophenone (BP3), and 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid (BP4) were assayed in vitro using a cladoceran *Daphnia carinata*. The 24-h LC50 on *D. carinata* calculated for BP, BP3, and BP4 was 8.37, 2.18, and 82.27 mg l⁻¹, respectively. BP3 and BP4 significantly impacted on the time of *D. carinata* first molting at a concentration of 0.1 µg l⁻¹. BP4 had an inhibitory effect on *D. carinata* molting and BP3 had an inhibitory effect on *D. carinata* pregnancy at a concentration of 1 µg l⁻¹. Furthermore, BP4 significantly inhibited the number of *D. carinata* first brood per female at a concentration of 10 µg l⁻¹. All of the endpoints from acute and chronic toxicity demonstrated that the hydroxy group in BP3 and BP4 significantly enhanced the toxic effect compared to BP. Therefore, the toxicity of BP-type UV filters is related to their molecular structure.

Dunford, R., Salinaro, A., Cai, L. Z., Serpone, N., Horikoshi, S., Hidaka, H., & Knowland, J. (1997). Chemical Oxidation and DNA Damage Catalysed by Inorganic Sunscreen Ingredients. *FEBS Letters*, 418(1-2), 87-90 [https://doi.org/10.1016/S0014-5793\(97\)01356-2](https://doi.org/10.1016/S0014-5793(97)01356-2)

Titanium dioxide (TiO₂) has been noted (US Federal Register, 43FR38206, 25 August 1978) to be a safe physical sunscreen because it reflects and scatters UVB and UVA in sunlight. However, TiO₂ absorbs about 70% of incident UV, and in aqueous environments this leads to the generation of hydroxyl radicals which can initiate oxidations, Using chemical methods, we show that all sunscreen TiO₂ samples tested catalyse the photo-oxidation of a representative organic substrate (phenol), We also show that sunlight-

illuminated TiO₂ catalyses DNA damage both in vitro and in human cells, These results may be relevant to the overall effects of sunscreens.

Esperanza, M., Seoane, M., Rioboo, C., Herrero, C., & Cid, A. (2019). Differential Toxicity of the UV-Filters BP-3 and BP-4 in *Chlamydomonas reinhardtii*: A Flow Cytometric Approach. *Science of The Total Environment*, 669, 412-420 <https://doi.org/10.1016/j.scitotenv.2019.03.116>

Due to the concern about the negative effects of exposure to sunlight, UV-filters are being introduced in all kind of cosmetic formulas. Wastewater treatment plants are not able to remove and/or degrade them; consequently they find their way into rivers, lakes and oceans. These chemicals are acquiring a concerning status due to their increasingly common use and the potential risk for the environment. Benzophenone-3 (BP-3) and Benzophenone-4 (BP-4) are broad-spectrum UV-filters used for the same purpose in personal care products, insecticides and plastic bags; however, after 96h of exposure to several concentrations of these UV-filters, the growth of *C. reinhardtii* was more affected by BP-3 than by BP-4, being the 96h-EC₅₀ for growth 5mgL⁽⁻¹⁾ and 38mgL⁽⁻¹⁾, respectively. Based on these values *Chlamydomonas reinhardtii* cultures were exposed during 24h to 2.5, 5 and 10mgL⁽⁻¹⁾ of BP-3 and 19, 38 and 76mgL⁽⁻¹⁾ of BP-4. A cytometric panel was carried out to evaluate the effect of sublethal concentrations of these UV-filters, thus several cytotoxicity biomarkers were analysed, including chlorophyll a fluorescence, viability, metabolic activity, oxidative stress, cytoplasmic and mitochondrial membrane potentials, and intracellular pH. BP-3 and BP-4 affect *C. reinhardtii* cells in a different way, showing differences for three of the examined parameters. Chlorophyll a fluorescence and mitochondrial membrane potential showed a significant increase ($p < 0.05$) in BP-3 and a significant decrease in BP-4, whereas viability only decreased significantly in the highest concentrations of BP-3. Regarding to the other parameters analysed, a similar pattern of cytotoxicity was observed. Growth rate, vital population and metabolic activity (esterase activity) and intracellular pH decreased significantly and cytoplasmic membrane potential and ROS levels increased significantly in cultures exposed to both pollutants.

Falfushynska, H., Gnatyshyna, L., Horyn, O., Sokolova, I., & Stoliar, O. (2017). Endocrine and Cellular Stress Effects of Zinc Oxide Nanoparticles and Nifedipine in Marsh Frogs *Pelophylax ridibundus*. *Aquatic Toxicology*, 185, 171-182 <https://doi.org/10.1016/j.aquatox.2017.02.009>

Freshwater organisms including amphibians experience increasing exposures to emerging pollutants such as nanoparticles and pharmaceuticals, which can affect their fitness and performance. We studied the effects of two common pollutants extensively used in industry, pharmaceutical and personal care products, nano-zinc oxide (nZnO) and a Ca-channel blocker nifedipine (Nfd), on endocrine status and cellular stress markers of the marsh frog *Pelophylax ridibundus*. Males were exposed for 14days to nZnO (3.1μM), Zn(2+) (3.1μM, as a positive control for nZnO exposures), Nfd (10μM), and combination of nZnO and Nfd (nZnO+Nfd). Exposure to nZnO and Zn(2+) led to an increase in Zn burdens, elevated concentrations of the metal-bound metallothioneins (MT-Me) in the liver and increased vitellogenin in the serum, whereas exposures to Nfd and nZnO+Nfd resulted in the metal release from MTs and a significant increase in the ratio of total to metal-bound MTs. This likely reflects oxidative stress caused by Nfd exposures as manifested in the elevated levels of oxyradical production, upregulation of superoxide dismutase activity (SOD) and increase in the total and oxidized glutathione concentrations in Nfd-exposed frogs. Zn-containing exposures upregulated activity of deiodinase (in nZnO and nZnO+Nfd exposures) and serum thyrotropin level (in the case of Zn(2+)). All exposures caused an increase in DNA fragmentation, lipofuscin accumulation as well as upregulation of caspase-3 and CYP450 levels reflecting

cytotoxicity of the studied compounds in the liver. Across all experimental treatments, nZnO exposures in the absence of Nfd had the least impact on the cellular stress traits or redox status in frogs. This indicates that at the low environmentally relevant levels of pollution, pharmaceuticals such as Nfd and free metals (such as Zn(2+)) may represent a stronger threat to the health of the frogs than nZnO particles.

Farner, J. M., Cheong, R. S., Mahé, E., Anand, H., & Tufenkji, N. (2019). Comparing TiO₂ Nanoparticle Formulations: Stability and Photoreactivity Are Key Factors in Acute Toxicity to *Daphnia Magna*. *Environmental Science: Nano*, 6(8), 2532-2543 <https://doi.org/10.1039/C9EN00666D>

Given their widespread manufacture and use, it is anticipated that titanium dioxide nanoparticles (TiO₂ NPs) will make their way into environmental surface waters where they may adversely impact biota. Characteristics of both the NPs themselves and the aquatic environment will determine the potential risks associated with release. While multiple water chemistries are often considered in the same study, differences in TiO₂ NPs themselves have been overlooked. Photocatalytic reactive oxygen species generation will be governed by the intrinsic reactivity of a NP, the extent of aggregation in suspension, and the aquatic chemistry of the solution. Here, two different commercial formulations of TiO₂ NPs are investigated in terms of aggregate stability, photoreactivity, and toxicity to the freshwater crustacean *Daphnia magna*. *D. magna* neonates were exposed to TiO₂ NPs in 48 h acute toxicity tests under either visible or UV illumination, in either the presence or absence of natural organic matter (NOM). Negligible lethal toxicity was observed by either TiO₂ formulation when illuminated by visible light, although swimming performance was significantly affected. For both NPs, the presence of UV light dramatically increased hydroxyl radical ([•]OH) generation and toxicity. This toxicity was partially mitigated by the presence of NOM acting as a quenching agent for [•]OH. Differences in both aggregate stability and photoreactivity between the two TiO₂ NPs are shown to influence toxicity. These results highlight that not all TiO₂ should be treated equally, and that the particle stability and photoreactivity of an individual formulation must be taken into account when predicting risk.

Fennell, T. R., Mathews, J. M., Snyder, R. W., Hong, Y., Watson, S. L., Black, S. R., . . . Waidyanatha, S. (2017). Metabolism and Disposition of 2-Ethylhexyl-P-Methoxycinnamate Following Oral Gavage and Dermal Exposure in Harlan Sprague Dawley Rats and B631/N Mice and in Hepatocytes in Vitro. *Xenobiotica*, 1-15 <https://doi.org/10.1080/00498254.2017.1400129>

1. 2-Ethylhexyl-p-methoxycinnamate (EHMC) is commonly used as an ingredient in sunscreens, resulting in potential oral and dermal exposure in humans. 2. Clearance and metabolism of EHMC in hepatocytes and disposition and metabolism of EHMC in rodents following oral (8-800 mg/kg) intravenous (IV) (8 mg/kg) or dermal (0.8-80 mg/kg representing 0.1-10% formulation concentration) exposure to [(14)C]EHMC were investigated in rats and mice. 3. EHMC was rapidly cleared from rat and mouse hepatocytes (half-life \leq 3.16 min) and less rapidly (half-life \leq 48 min) from human hepatocytes. 4. [(14)C]EHMC was extensively absorbed and excreted primarily in urine by 72 h after oral administration to rats (65-80%) and mice (63-72%). Oral doses to rats were excreted to a lesser extent (3-8%) in feces and as CO₂ (1-4%). Radioactive residues in tissues were $<$ 1% of the dose. There were no sex or species differences in disposition in rats. 5. Following dermal application, 34-42% of an 8-mg/kg dose was absorbed in rats, and 54-62% in mice in 72-h. 6. Among numerous urinary metabolites associated with hydrolysis of the ester, two potential reproductive and developmental toxicants, 2-ethylhexanol and 2-ethylhexanoic acid were produced by metabolism of EHMC.

Fent, K., Kunz, P. Y., & Gomez, E. (2008). UV Filters in the Aquatic Environment Induce Hormonal Effects and Affect Fertility and Reproduction in Fish. *CHIMIA International Journal for Chemistry*, 62(5), 368-375 <https://doi.org/10.2533/chimia.2008.368>

UV-absorbing organic chemicals (UV filters) are being increasingly used in sunscreens, personal care products and in the protection of materials against UV irradiation. Environmental contamination originates from direct input from recreational activities and wastewaters. Concentrations in treated wastewaters are in the lower $\mu\text{g/l}$ range, whereas in rivers and lakes they are in the range of a few up to hundreds of ng/l . It is known that lipophilic UV filters accumulate in aquatic biota, but only little is known about their environmental fate. A large number of UV filters elicit hormonal effects in vitro. Estrogenic activity has also been demonstrated for some UV filters in fish in vivo. Benzophenone-1 (BP1), benzophenone-2 (BP2), 3-benzylidene camphor (3BC) and ethyl-4-aminobenzoate (Et-PABA) lead to induction of vitellogenin. 3BC and BP2 cause feminization in secondary sex characteristics of male fish, alteration of gonads in male and female fish and decrease in fertility and reproduction. The lowest observed effect concentrations for 3BC and BP2 were 3 $\mu\text{g/l}$ and 1.2 mg/l , respectively. UV filter mixtures show mainly a synergistic activity in vitro, whether this is also reflected by the in vivo activity is under investigation. In conclusion, a hazard and risk for aquatic ecosystems cannot be ruled out for the UV filter 3BC, where histological and reproductive effects occurred in fish at low concentrations. However for BP1, BP2 and Et-PABA an environmental risk is rather low based on current knowledge.

Fent, K., Kunz, P. Y., Zenker, A., & Rapp, M. (2010). A Tentative Environmental Risk Assessment of the Uv-Filters 3-(4-Methylbenzylidene-Camphor), 2-Ethyl-Hexyl-4-Trimethoxycinnamate, Benzophenone-3, Benzophenone-4 and 3-Benzylidene Camphor. *Marine Environmental Research*, 69, S4-S6 <https://doi.org/10.1016/j.marenvres.2009.10.010>

UV-filters are increasingly used in cosmetics and in the protection of materials against UV-irradiation. The widespread occurrence of UV-filter residues in aquatic systems has been reported, but still little is known about their environmental effects. Some of these compounds negatively interact with the hormone system of fish, resulting in decreased fecundity and reproduction. Here we report on acute and chronic effects of UV-filters 3-(4-methylbenzylidene-camphor) (4MBC), 2-ethyl-hexyl-4-trimethoxycinnamate (EHMC), benzophenone-3 (BP3) and benzophenone-4 (BP4) on *Daphnia magna*. The acute toxicity increased with log Pow of the compound. The LC50 values (48 h) of 4MBC, EHMC, BP3 and BP4 were 0.56, 0.29, 1.9 and 50 mg/L , respectively. A tentative preliminary environmental risk assessment (ERA) based on a limited set of data indicates that individual UV-filters should undergo further ecotoxicological analysis, as an environmental risk cannot be ruled out. Consequently new data on the environmental occurrence and the effects of UV-filters are needed for a more accurate ERA. When regarded as a mixture occurring in surface waters they may pose a risk for sensitive aquatic organisms.

Fong, H. C., Ho, J. C., Cheung, A. H., Lai, K. P., & Tse, W. K. (2016). Developmental Toxicity of the Common UV Filter, Benophenone-2, in Zebrafish Embryos. *Chemosphere*, 164, 413-420 <https://doi.org/10.1016/j.chemosphere.2016.08.073>

Benzophenone (BP) type UV filters are extensively used in the personal care products to provide protection against the harmful effects of UV radiation. BPs are one of the primary components in the UV filter family, in which benzophenone-2 (BP2) is widely used as a UV filter reagent in the sunscreen. Humans used these personal care products directly on skin and the chemicals will be washed away to

the water system. BP2 has been identified as one of the endocrine disruptor chemicals, which can interfere the synthesis, metabolism, and action of endogenous hormones. Environmentally, it has been found to contaminate water worldwide. In this study, we aimed to unfold the possible developmental toxicology of this chemical. Zebrafish are used as the screening model to perform in situ hybridization staining to investigate the effects of BP2 on segmentation, brain regionalization, and facial formation at four developmental stages (10-12 somite, prim-5, 2 and 5 days post-fertilization). Results showed 40 µM (9.85 mg L⁻¹) or above BP2 exposure in zebrafish embryos for 5 days resulted in lipid accumulation in the yolk sac and facial malformation via affecting the lipid processing and the expression of cranial neural crest cells respectively. To conclude, the study alarmed its potential developmental toxicities at high dosage exposure.

French, J. E. (1992). Ntp Technical Report on the Toxicity Studies of 2-Hydroxy-4-Methoxybenzophenone (Cas No. 131-57-7) Administered Topically and in Dosed Feed to F344/N Rats and B6C3F1 Mice. *Toxicity Report Series, 21*, 1-E14 Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/12209185>

2-Hydroxy-4-methoxybenzophenone (HMB) occurs naturally in flower pigments and is synthesized for use in sunscreens, as a UV stabilizer in various cosmetic products, and in plastic surface coatings and polymers. Toxicity studies of HMB were performed in F344/N rats and B6C3F1 mice, by administering HMB in feed and by topical application, in studies of 2 weeks' (5 animals/sex, dose and species) and 13 weeks' (10 animals/sex, dose and species) duration. Assessments included hematology, clinical chemistry, urinalysis, reproductive toxicity, and histopathologic evaluations. In both 2- and 13-week dosed feed studies, rats received diets containing 0, 3125, 6250, 12500, 25000, or 50000 ppm HMB. One high-dose female rat died during the 2-week study. Body weight gains of high-dose male and female rats were reduced in the 13-week study. Liver and kidney weights were increased in dosed rats in both studies. In the 2-week studies, enlarged livers were associated with a marked hepatocyte cytoplasmic vacuolization in rats receiving diets containing concentrations of 6250 ppm HMB or higher; renal lesions, consisting of dilated tubules and regeneration of tubular epithelial cells, were found primarily in high-dose rats. In the 13-week studies, kidney lesions progressed to include papillary degeneration, or necrosis, and inflammation, while the liver lesion appeared to regress; liver enzymes in serum remained elevated. Rats receiving a diet with 50000 ppm HMB showed markedly lower epididymal sperm density and an increase in the length of the estrous cycle at the end of the 13-week studies. In 2-week dermal studies, rats received topical applications of 1.25 to 20 mg of HMB in an acetone or lotion vehicle. The only effects noted were small and variable increases in liver and kidney weights, reaching statistical significance primarily in the higher dose groups. In 13-week studies, rats received topical doses from 12.5 to 200 mg/kg HMB in acetone. Kidney weights were elevated in dosed groups of female rats. No other findings were attributed to HMB treatment. In 2- and 13-week dosed feed studies, mice received feed containing 0, 3125, 6250, 12500, 25000, or 50000 ppm HMB. A dose-related increase in liver weight associated with hepatocyte cytoplasmic vacuolization was the only finding in mice in the 2-week studies. Decreased body weight gains were dose-related in mice in the 13-week studies; mild increases in liver weights were seen in dosed mice of both sexes. Kidney weights were increased variably in dosed females. Microscopic lesions were noted only in the kidneys of males receiving 50000 ppm HMB; these included eosinophilic protein casts in dilated renal tubules and a mild inflammation associated with the dilated tubules. Mice in the highest dose group exhibited a decrease in epididymal sperm density and an increase in length of the estrous cycle. In 2-week dermal studies, mice received topical applications from 0.5 to 8 mg HMB in an acetone or lotion vehicle. The only effects noted were minimal, variable increases in liver and kidney weights, primarily in the higher dose groups. In 13-week studies, mice received topical doses of 22.75 to 364 mg/kg in acetone. Kidney weights were increased variably in dosed male

mice. Epididymal sperm density was decreased at all 3 dose levels evaluated (22.75, 91, and 200 mg/kg). The genetic toxicity of HMB also was evaluated in mutagenicity studies with *Salmonella typhimurium*, in cytogenetic studies with Chinese hamster ovary (CHO) cells, and by evaluation of micronucleated erythrocytes in peripheral blood smears from mice in the 13-week studies. HMB was weakly mutagenic in *Salmonella* with metabolic activation, and induced sister-chromatid exchanges and chromosomal aberrations in CHO cells in the presence of a metabolic activation system. There was no increase in the frequency of micronucleated erythrocytes in the blood of mice receiving HMB. In summary, HMB produced generally similar effects following topical and oral administration to rats and mice. Consistent findings included decreases in epididymal sperm density, lengthened estrous cycle, and increased liver and kidney weights. Mice in the dosed feed studies exhibited microscopic changes in the kidneys, comprising tubular dilatation with eosinophilic protein casts. Dilatation, tubular regeneration, papillary degeneration, and inflammation were noted in the kidneys of rats; and liver lesions consisting of an apparently reversible hepatocyte cytoplasmic vacuolization occurred in both rats and mice. A no-observed-adverse-effect level (NOAEL) for microscopic lesions was 6250 ppm HMB in the diet for rats and mice. A NOAEL was not reached for decreased epididymal sperm density in the 13-week dermal study in mice (<23 mg/kg/day). Synonyms: Oxybenzone; 4-Methoxy-2-hydroxy-benzophenone; Cyasorb UV; Uvinul M 40; (2-hydroxy-4-methoxyphenyl)phenyl-methanone; NSC-7778; Spectra-sorb UV; Syntase 62; UF 3; USAF CY-9; NCI-C60957.

Frenzilli, G., Bernardeschi, M., Guidi, P., Scarcelli, V., Lucchesi, P., Marsili, L., . . . Nigro, M. (2014). Effects of In Vitro Exposure to Titanium Dioxide on DNA Integrity of Bottlenose Dolphin (*Tursiops truncatus*) Fibroblasts and Leukocytes. *Marine Environmental Research*, 100, 68-73
<https://doi.org/10.1016/j.marenvres.2014.01.002>

In the present study, the genotoxic potential of nanosized TiO₂ anatase and micro-sized rutile on bottlenose dolphin (*Tursiops truncatus*) fibroblasts and leukocytes was investigated. Human and mouse cells were also studied in order to compare susceptibility to TiO₂ in different mammalian species. Cell lines were exposed for 4, 24, and 48 h to different concentrations of TiO₂ (20, 50, 100, 150 µg/ml) and DNA damage was investigated by single cell gel electrophoresis (Comet assay). Both anatase and rutile induced increased DNA damage, even though statistically significant effects were scattered according to species and cell lines. Bottlenose dolphin leukocytes and murine fibroblasts exhibited increased DNA damage after rutile exposure at some doses/times, while human fibroblasts showed a significant dose-response effect after a 4 h exposure to anatase. Human leukocytes were tolerant to both anatase and rutile. Ultrastructural investigation showed that TiO₂ particles entered the cell and were compartmentalized within membrane-bound vesicles.

Frikeche, J., Couteau, C., Roussakis, C., & Coiffard, L. J. (2015). Research on the Immunosuppressive Activity of Ingredients Contained in Sunscreens. *Archives of Dermatological Research*, 307(3), 211-218 <https://doi.org/10.1007/s00403-014-1528-9>

The immunosuppressive properties of Benzophenone-4, an UV-filter and three ingredients, Allantoin, Bisabolol and Enoxolon used in sunscreen formulation, previously characterized as anti-inflammatory compounds, are studied. The results of this study demonstrate that four tested molecules have effects on DCs and T cells which are the most important cells of the immune system. The impact is also visible on keratinocyte cells which are in the direct contact with skin sunscreens. Each ingredient should be used with caution at reduced doses or even removed from some cosmetic preparations, such as sunscreens.

Gago-Ferrero, P., Díaz-Cruz, M. S., & Barceló, D. (2013). Multi-Residue Method for Trace Level Determination of UV Filters in Fish Based on Pressurized Liquid Extraction and Liquid Chromatography–Quadrupole-Linear Ion Trap-Mass Spectrometry. *Journal of Chromatography A*, 1286(0), 93-101 <https://doi.org/10.1016/j.chroma.2013.02.056>

So far, the very few studies addressing the occurrence of UV filters (UV F) in biota showed important limitations in the analysis of the so complex biological matrices. In order to improve the knowledge on the bioaccumulation of UV F by fish, a simple and highly sensitive method was successfully developed and validated for the simultaneous determination of eight extensively used UV F and transformation products with a wide range of physicochemical properties. The present study demonstrated that liquid chromatography coupled to tandem mass spectrometry (LC–MS/MS) using a QqLIT mass analyser was applicable to the simultaneous analysis of UV F in fish. Pressurized liquid extraction (PLE) was chosen for the sample pretreatment due to the good extraction efficiency provided. An additional SPE clean-up step was added in order to minimize matrix effects and to improve the sensitivity. The method allowed recovery efficiencies in the range 70–112% for most compounds at the three spike levels. The low limits of detection (MLOD) achieved (0.1–6.0 ng/g dw) allowed the reliable quantification of UV F residues in fish samples. The developed methodology was applied to assess the occurrence of UV F in different fish species from the Guadalquivir river basin (Spain). Results confirmed the bioaccumulation of benzophenone-3 (BP3), ethylhexyl methoxycinnamate (EHMC) and octocrylene (OC) in the fish samples. The maximum concentration of 240 ng/g dw corresponded to EHMC, which was also the most ubiquitous compound. The reported concentrations constitute the first occurrence data of UV F residues in fish from Iberian rivers.

Gao, L., Yuan, T., Zhou, C., Cheng, P., Bai, Q., Ao, J., . . . Zhang, H. (2013). Effects of Four Commonly Used UV Filters on the Growth, Cell Viability and Oxidative Stress Responses of the *Tetrahymena thermophila*. *Chemosphere*, 93(10), 2507-2513 <https://doi.org/10.1016/j.chemosphere.2013.09.041>

UV filters are increasingly used in sunscreens and other personal care products. Although their residues have been widely identified in aquatic environment, little is known about the influences of UV filters to protozoan. The growth inhibition effects, cell viability and oxidative stress responses of four commonly used UV filters, 2-ethylhexyl 4-methoxycinnamate (EHMC), benzophenone-3 (BP-3), 4-methyl-benzylidene camphor (4-MBC) and octocrylene (OC), to protozoan *Tetrahymena thermophila* were investigated in this study. The 24-h EC50 values with 95% confidence intervals for BP-3 and 4-MBC were 7.544 (6.561-8.675) mg L⁻¹ and 5.125 (4.874-5.388) mg L⁻¹, respectively. EHMC and OC did not inhibit the growth of *T. thermophila* after 24h exposure at the tested concentrations. The results of cell viability assays with propidium iodide (PI) staining were consistent with that of the growth inhibition tests. As for BP-3 and 4-MBC, the relatively higher concentrations, i.e. of 10.0 and 15.0 mg L⁻¹, could lead to the cell membranes impairment after 4h exposure. With the increase of the exposure time to 6h, their adverse effects on cell viability of *T. thermophila* were observed at the relatively lower concentration groups (1.0 mg L⁻¹ and 5.0 mg L⁻¹). In addition, it is noticeable that at environmentally relevant concentration (1.0 µg L⁻¹), BP-3 and 4-MBC could lead to the significant increase of catalase (CAT) activities of the *T. thermophila* cells. Especially for the BP-3, the oxidative injuries were further confirmed by the reduction of glutathione (GSH) content. It is imperative to further investigate the additive action of UV filters and seek other sensitive endpoint, especially at environmentally relevant concentration.

Gaspar, L. R., Tharmann, J., Maia Campos, P. M., & Liebsch, M. (2013). Skin Phototoxicity of Cosmetic Formulations Containing Photounstable and Photostable UV-Filters and Vitamin A Palmitate. *Toxicology in Vitro*, 27(1), 418-425 <https://doi.org/10.1016/j.tiv.2012.08.006>

The aim of this study was to evaluate the in vitro skin phototoxicity of cosmetic formulations containing photounstable and photostable UV-filters and vitamin A palmitate, assessed by two in vitro techniques: 3T3 Neutral Red Uptake Phototoxicity Test and Human 3-D Skin Model In Vitro Phototoxicity Test. For this, four different formulations containing vitamin A palmitate and different UV-filters combinations, two of them considered photostable and two of them considered photounstable, were prepared. Solutions of each UV-filter and vitamin under study and solutions of four different combinations under study were also prepared. The phototoxicity was assessed in vitro by the 3T3 NRU phototoxicity test (3T3-NRU-PT) and subsequently in a phototoxicity test on reconstructed human skin model (H3D-PT). Avobenzone presented a pronounced phototoxicity and vitamin A presented a tendency to a weak phototoxic potential. A synergistic effect of vitamin A palmitate on the phototoxicity of combinations containing avobenzone was observed. H3D-PT results did not confirm the positive 3T3-NRU-PT results. However, despite the four formulations studied did not present any acute phototoxicity potential, the combination 2 containing octyl methoxycinnamate (OMC), avobenzone (AVB) and 4-methylbenzilidene camphor (MBC) presented an indication of phototoxicity that should be better investigated in terms of the frequency of photoallergic or chronic phototoxicity in humans, once these tests are scientifically validated only to detect phototoxic potential with the aim of preventing phototoxic reactions in the general population, and positive results cannot predict the exact incidence of phototoxic reactions in humans.

Ghazipura, M., McGowan, R., Arslan, A., & Hossain, T. (2017). Exposure to Benzophenone-3 and Reproductive Toxicity: A Systematic Review of Human and Animal Studies. *Reproductive Toxicology*, 73, 175-183 <https://doi.org/10.1016/j.reprotox.2017.08.015>

Hydroxy-4-methoxybenzophenone, also known as benzophenone-3 (BP-3), is a commonly used ultraviolet filter in skincare and as a food additive. Large concentrations of similar phenolic compounds have been detected in urine, amniotic fluid, and placental tissue, thereby raising questions about its impact on reproduction. The objective of this paper was to investigate the reproductive toxicity of BP-3 in humans and animals. In humans, studies showed that high levels of BP-3 exposure could be linked to an increase in male birth weight but a decline in female birth weight and male gestational age. In fish, BP-3 exposure resulted in a decline in egg production, hatching, and testosterone, along with a down-regulation of steroidogenic genes. In rats, a decrease in epididymal sperm density and a prolonged estrous cycle for females was observed. These positive associations may be attributed to an altered estrogen and testosterone balance as a result of endocrine disrupting effects of BP-3. However, the current body of literature is limited by non-uniform exposure and outcome measurements in studies both across and within species and future studies will need to be conducted in a standardized fashion to allow for a more significant contribution to the literature that allows for better comparison across studies.

Giokas, D. L., Salvador, A., & Chisvert, A. (2007). UV Filters: From Sunscreens to Human Body and the Environment. *TrAC Trends in Analytical Chemistry*, 26(5), 360-374 <https://doi.org/10.1016/j.trac.2007.02.012>

Recognition of the harmful effects of ultraviolet (UV) radiation on the skin has triggered development of organic chemicals (commonly referred as UV filters) that can absorb UV radiation and attenuate the negative effects of sunlight exposure. Depending on the properties and the intended degree of protection, a wide array of combinations is being marketed as delivering protection against most kinds of UV-induced skin damage. However, some UV filters have dermatological implications, so maximum applicable concentrations have been established. To monitor to what extent commercial products comply with the mandatory limits, several analytical methods have been used for their determination in cosmetics and related products. Further research on the efficacy of UV filters applied on the skin surface has brought to light a gradual attenuation of their UV-protective capacity that cannot solely be attributed to photo-induced decomposition. Investigations carried out to elucidate the reasons underlying this behaviour concluded that UV filters may be systematically absorbed through the skin surface or even released during bathing and washing activities. These observations gave rise to numerous studies aiming to investigate the magnitude and effects of skin penetration as well as accumulation in the water environment. Because of the need for more in-depth investigation into the behavior of UV filters, the initial demand for product certification has been extended to include reliable analytical methods to determine these substances at low concentration levels and in complex matrices (e.g., biological and environmental samples). Until now, most of the available methods, although designed to cover a large variety of substances, quantify them at only high-mg/L levels; however, recently, researchers have paid special attention to developing more sensitive procedures able to determine these substances in biological tissues and fluids or environmental samples at ng/L levels without matrix interferences. This article gives a comprehensive outline of the accumulated knowledge on UV-filter determination in biological and environmental samples and encourages further research in this new, challenging field of analytical, health and environmental science.

Giraldo, A., Montes, R., Rodil, R., Quintana, J. B., Vidal-Linan, L., & Beiras, R. (2017). Ecotoxicological Evaluation of the Uv Filters Ethylhexyl Dimethyl P-Aminobenzoic Acid and Octocrylene Using Marine Organisms *Isochrysis Galbana*, *Mytilus Galloprovincialis* and *Paracentrotus Lividus*. *Archives of Environmental Contamination & Toxicology*, 72(4), 606-611
<https://doi.org/10.1007/s00244-017-0399-4>

The growing concern regarding the negative effects of solar radiation on the skin has led to a drastic increase in the use of sunscreens containing in its composition up to 10% of aromatic chemicals, such as ethylhexyl dimethyl p-aminobenzoic acid (OD-PABA) and octocrylene (OC). The objective of this study was to evaluate the toxicity and to assess the environmental risk posed by these two ultraviolet filters, widely used in cosmetics and as plastic additives, in the marine environment. Several ecotoxicological bioassays were performed with three model organisms belonging to different trophic levels: the microalgae *Isochrysis galbana*, the mussel *Mytilus galloprovincialis*, and the sea urchin *Paracentrotus lividus*. The results show remarkable toxicity to marine species for both OD-PABA (EC10 values range 26,5-127 microg L(-1)) and OC (EC10 range 103-511 microg L(-1)). The cell division in the microalgae *I. galbana* was the most sensitive endpoint tested. To determine the environmental risk of these substances, the risk coefficient (RQ) was calculated. Due to the higher concentrations reported, OC showed remarkable risk (RQ = 0.27), whereas for OD-PABA the risk was low (RQ = 0.007).

Gomez, E., Bachelot, M., Boillot, C., Munaron, D., Chiron, S., Casellas, C., & Fenet, H. (2012). Bioconcentration of Two Pharmaceuticals (Benzodiazepines) and Two Personal Care Products (UV Filters) in Marine Mussels (*Mytilus galloprovincialis*) under Controlled Laboratory

Bioaccumulation is essential for gaining insight into the impact of exposure to organic micropollutants in aquatic fauna. Data are currently available on the bioaccumulation of persistent organic pollutants, but there is very little documentation on the bioaccumulation of pharmaceuticals and personal care products (PPCPs). The bioconcentration of selected PPCPs was studied in marine mussels (*Mytilus galloprovincialis*). The selected PPCPs were two organic UV filters, i.e., 2-ethylhexyl-4-trimethoxycinnamate (EHMC) and octocrylene (OC), and two benzodiazepines (BZP), i.e., diazepam (DZP) and tetrazepam (TZP). Laboratory experiments were performed in which *M. galloprovincialis* was exposed to these compounds either directly from water, for the less lipophilic substances (BZP) or via spiked food for lipophilic UV filters. *M. galloprovincialis* uptook and eliminated BZP following first-order kinetics. The biological half-life ($t_{1/2}$) of TZP was 1.4 days, resulting in a bioconcentration factor of 64 and 99 mL g⁻¹ dry weight (dw), respectively, for 2.3 and 14.5 µg L⁻¹ of exposure, while the biological half-life ($t_{1/2}$) of DZP was 0.4 days, resulting in a bioconcentration factor of 51 mL g⁻¹ dw for 13.2 µg L⁻¹ of exposure. The uptake of UV filter was rapid in mussels, followed by elimination within 24 h. EHMC increased from 15 to 138 ng g⁻¹ dw in 1 h and decreased to 25 ng g⁻¹ after 24 h for 11.9 µg L⁻¹ exposure. OC reached 839 ng g⁻¹ dw after 1 h and decreased to 33 ng g⁻¹ after 24 h for 11.6 µg L⁻¹ exposure. However, EHMC and OC were slightly accumulated in 48 h, i.e., 38 and 60 ng g⁻¹ dw, respectively.

Gonzalez, H. (2006). *Studies of Sunscreens: Percutaneous Absorption of Benzophenone-3 and Photostability*. (Doctor of Philosophy (Medicine)), Göteborg University. Sahlgrenska Academy, Göteborg, Sweden. Retrieved from <http://hdl.handle.net/2077/721>

Aim: To learn more about percutaneous absorption of the photoactive compound benzophenone-3 (BZ-3) and to study the excretion pattern of BZ-3 and its metabolite dihydroxy benzophenone (DHB). We also got the opportunity to develop a reverse-phase HPLC method to analyze BZ-3 and DHB. The photostability of seven commercial sunscreens was also studied. Material and methods: Paper I: 11 participants applied a sunscreen, 2 mg/cm², containing 4% BZ-3. They collected urine for 48 hours after the application. Paper II: 26 participants applied a sunscreen, 2 mg/cm², containing 4% BZ-3 morning and night for five days. Half of the participants were exposed to UV radiation (UVR). They collected urine for the five days the sunscreen was applied and an additional five days after the last application. Paper III: The assay uses: solid-phase extraction with C8 columns; a Genesis C18 column (4.6 mm x 150 mm); a gradient acetonitrile-water mobile phase; a UV-detector set at 287 nm. Paper IV: Seven commercial sunscreens were studied with absorption spectrophotometry. Sunscreen product, 0.5 mg/cm², was placed between plates of silica. The area under the curve (AUC) in the spectrum was calculated for the different UV regions. AUC before (AUC_{before}) and after (AUC_{after}) artificial UV exposure and before and after natural UV exposure were calculated. If the AUC Index (AUCI), defined as $UCI = AUC_{after} / AUC_{before}$, was > 0.80, the sunscreen was considered photostable. Results: Paper I: The average total amount excreted was 11 mg, median 9.8 mg, which is approximately 0.4% of the applied amount BZ-3. Paper II: The volunteers excreted 1.2-8.7% BZ-3 of the total applied amount. The mean value found was 3.7%. There was no significant difference between the two groups; $p < 0.99$. Paper III: The assay was linear $r^2 > 0.99$, with detection limits for BZ-3 and DHB of 0.01 µmol/l and 0.16 µmol/l respectively. Relative standard deviation was less than 10% for BZ-3 and less than 13% for DHB. The excretion pattern varied among the human volunteers, different patterns were discerned among the individuals. Paper IV: Three sunscreens were unstable after 90 min of natural UV, in the UVA range the

AUCI was between 0.41 and 0.76. In the UVB range, one of these sunscreens was unstable with an AUCI of 0.75 after 90 min. Three sunscreens were photostable after 120 min of natural UV, in the UVA range the AUCI was between 0.85 and 0.99 and in the UVB range between 0.92 and 1.0. Conclusions: Paper I: BZ-3 is absorbed by the skin and excreted in the urine after one topical application of a sunscreen containing 4% BZ-3. There are individual differences in the amount excreted and in the excretion pattern. Paper II: Repeated topical applications of a sunscreen containing 4% BZ-3 lead to a higher excretion of BZ-3. There was no statistical difference after exposure to UVR. Paper III: The developed reverse-phase HPLC-method was reliable and suitable to handle a large number of samples. BZ-3 and DHB were excreted in a similar pattern. Paper IV: Three of the seven investigated sunscreens were photounstable in the UVA region. The combination ethylhexyl methoxycinnamate and butyl methoxydibenzoylmethane was unstable regardless of which other photoactive compound that was included in the sunscreen.

Gonzalez, H., Farbrot, A., Larko, O., & Wennberg, A. M. (2006). Percutaneous Absorption of the Sunscreen Benzophenone-3 after Repeated Whole-Body Applications, with and without Ultraviolet Irradiation. *British Journal of Dermatology*, 154(2), 337-340
<https://doi.org/10.1111/j.1365-2133.2005.07007.x>

Background: Benzophenone-3 (BZ-3; 2-hydroxy-4-methoxybenzophenone, oxybenzone) is commonly used to absorb ultraviolet (UV) radiation. BZ-3 penetrates the skin and can be found in the urine. The amount varies between 0.4% and 2%. This seems to be the main metabolic pathway in rats. Objectives: To investigate the total amount of BZ-3 excreted in the urine after repeated topical whole-body applications of a sunscreen and to see if UV radiation has any effect on the amount excreted. Methods: Twenty-five volunteers applied a commercially available sunscreen containing 4% BZ-3 morning and night for 5 days. Their urine was measured during those 5 days and during a further 5 days after the last application. They were divided into groups A (unirradiated) and B. Group B received UV radiation according to skin type: UVA between 400 and 707 J cm⁻², and UVB between 0.46 and 2.0 J cm⁻². BZ-3 in urine was analysed with a high-performance liquid chromatography method. Results: The volunteers excreted 1.2-8.7% (mean 3.7%) of the total amount of BZ-3 applied. There was no significant difference between the two groups (P < 0.99, t-test). Conclusions: We show that a large amount of BZ-3 is absorbed. BZ-3 is accumulated in the body as the volunteers excreted BZ-3 5 days after the last application.

Gonzalez, H. G., Farbrot, A., & Larko, O. (2002). Percutaneous Absorption of Benzophenone-3, a Common Component of Topical Sunscreens. *Clinical and Experimental Dermatology*, 27, 691-694
<https://doi.org/10.1046/j.1365-2230.2002.01095.x>

Benzophenone-3 (BZ-3) is a commonly used, chemical UV-absorber. It has been used for many years to protect against UV-radiation. Previous studies have shown that BZ-3 penetrates the skin, and it can be found in urine, faeces, and blood. In this study we examined the percutaneous absorption of BZ-3. The amount of BZ-3 absorbed was measured in urine, as experimental studies in the rat have shown that urine is the major route of excretion. Eleven volunteers applied the recommended amount of a commercially available sunscreen and urine samples were collected during a 48-h period after application. The average total amount excreted was 11 mg, median 9.8 mg, which is approximately 0.4% of the applied amount of BZ-3. Some of the volunteers still excreted BZ-3 48 h after application. It is evident that BZ-3 undergoes conjugation in the body to make it water soluble. However, we do not know at what age the ability to conjugate is fully developed, and therefore for children physical filters

such as titanium dioxide and/or zinc oxide might still be considered a more appropriate sunscreen component.

Gorman, S. G., & MacManus-Spencer, L. A. (2008). ANYL 129-Bioaccumulation of Ultraviolet Filter Chemicals in *Lumbriculus Variegatus*. *Abstracts of Papers of the American Chemical Society*, 235, 1 Retrieved from <http://oasys2.confex.com/acs/235nm/techprogram/P1126543.HTM>

Ultraviolet (UV) filter chemicals, such as those found in sunscreens, cosmetics, and other personal care products, have been detected in wastewater and surface waters. Previous work has shown that they sorb strongly to sediment due to their hydrophobicity. There is concern that they also may accumulate in organisms that live in the sediment, which is a potential environmental health hazard due to evidence of the endocrine disrupting activity of some of these chemicals. The bioaccumulation of two commonly used UV filter chemicals, benzophenone-3 and octyl methoxycinnamate, has been examined using laboratory-spiked sediments and the freshwater oligochaete *Lumbriculus variegatus*. Methods have been developed for the extraction of UV filter chemicals from the worms and their analysis by HPLC. Results from 28-day bioaccumulation experiments will be presented.

Gulson, B., Wong, H., Korsch, M., Gomez, L., Casey, P., McCall, M., . . . Greenoak, G. (2012). Comparison of Dermal Absorption of Zinc from Different Sunscreen Formulations and Differing UV Exposure Based on Stable Isotope Tracing. *Science of The Total Environment*, 420, 313-318
<https://doi.org/10.1016/j.scitotenv.2011.12.046>

In a pilot study to determine if zinc (Zn) from zinc oxide nanoparticles in sunscreen can penetrate human skin in vivo, nanoparticles (~30nm) of a stable isotope (52% (68)Zn enrichment) were incorporated into an essentially phytochemical-based formulation and applied to the backs of 3 human subjects twice daily for 5 days during the Southern Hemisphere winter. Blood and urine were collected prior to application and at regular intervals and up to 50 days. As observed in a larger outdoor trial following this pilot study but with a different formulation and with UV exposure: values of (68)Zn in blood continued to increase beyond the 5 day application phase with the highest measurement at 14 days after the first application; variable amounts of the (68)Zn tracer were observed in urine; and the amounts of extra Zn added to blood were small and indicate very low levels of absorption (minimal estimate <0.01% of the applied dose) through the skin. Reasons for differences in absorption detected in the stable isotope trials and previous investigations include: the sensitivity of the stable isotope method; the duration of the investigations; the number of applications of sunscreen formulation; in vitro methods with excised skin; lack of measurement of blood and urine; no skin flexing; and lack of UV exposure.

Guo, Y., Chen, L., Wu, J., Hua, J., Yang, L., Wang, Q., . . . Zhou, B. (2019). Parental Co-Exposure to Bisphenol A and Nano-TiO₂ Causes Thyroid Endocrine Disruption and Developmental Neurotoxicity in Zebrafish Offspring. *Science of The Total Environment*, 650(Pt 1), 557-565
<https://doi.org/10.1016/j.scitotenv.2018.09.007>

The coexistence of organic toxicants and nanoparticles in the environment influences pollutant bioavailability and toxicity. Using chronic co-exposure to an adult zebrafish model, this study investigated the transfer kinetics and transgenerational effects of bisphenol A (BPA) and titanium dioxide nanoparticles (n-TiO₂) exposure in F1 offspring. When single and combined exposure to BPA (0, 2, and 20µg/L) and n-TiO₂ (100µg/L) were compared, combined exposure was found to reciprocally facilitate bioaccumulation in adult fish while enhancing maternal transfer to offspring. Thyroid

endocrine disruption and developmental neurotoxicity were observed in larval offspring by parental exposure to BPA alone or in combination with n-TiO₂. Exposure to 20µg/L BPA significantly decreased the thyroxine (T₄) concentration in adult plasma, leading to less transfer into the eggs. The presence of 20µg/L BPA with n-TiO₂ further decreased the level of T₄ compared to BPA exposure alone. Additionally, offspring larvae derived from exposed parents exhibited lethargic swimming behavior. Overall, this study examined the interactions of BPA and n-TiO₂ with regard to their bioaccumulation, maternal transfer, and developmental effects, which highlighted that co-exposure dynamics are important and need to be considered for accurate environmental risk assessment.

Guyon, A., Smith, K. F., Charry, M. P., Champeau, O., & Tremblay, L. A. (2018). Effects of Chronic Exposure to Benzophenone and Diclofenac on DNA Methylation Levels and Reproductive Success in a Marine Copepod. *Journal of Xenobiotics*, 8(1), 7674
<https://doi.org/10.4081/xeno.2018.7674>

The UV-filter benzophenone and the anti-inflammatory diclofenac are commonly detected in the environment. The aim of this study was to assess the multigenerational effects of chronic exposure to low concentrations of these chemicals on toxicity and DNA methylation levels in the copepod *Gladioferens pectinatus*. Acute toxicity tests were conducted to determine the sensitivity of *G. pectinatus* to the chemicals. All chemicals impacted breeding, hatching and egg viability. Diclofenac (1 mg.L⁻¹) reduced the number of eggs per gravid female. Benzophenone (0.5 mg.L⁻¹) decreased egg hatching success. Exposure to the reference toxicant copper (0.02 mg.L⁻¹) led to unsuccessful hatching. Effects on DNA methylation was estimated by the percentage of 5- methylcytosine. The treatments resulted in strong differences in DNA methylation with increased methylation in the exposed animals. The two chemicals impacted both egg viability and the induction of differential DNA methylation, suggesting potential intra- and trans-generational evolutionary effects.

Hanigan, D., Truong, L., Schoepf, J., Nosaka, T., Mulchandani, A., Tanguay, R. L., & Westerhoff, P. (2018). Trade-Offs in Ecosystem Impacts from Nanomaterial Versus Organic Chemical Ultraviolet Filters in Sunscreens. *Water Research*, 139, 281-290 <https://doi.org/10.1016/j.watres.2018.03.062>

Both nanoparticulate (nZnO and nTiO₂) and organic chemical ultraviolet (UV) filters are active ingredients in sunscreen and protect against skin cancer, but limited research exists on the environmental effects of sunscreen release into aquatic systems. To examine the trade-offs of incorporating nanoparticles (NPs) into sunscreens over the past two decades, we targeted endpoints sensitive to the potential risks of different UV filters: solar reactive oxygen production in water and disruption of zebrafish embryo development. First, we developed methodology to extract nanoparticles from sunscreens with organic solvents. Zebrafish embryos exposed to parts-per-million NPs used in sunscreens displayed limited toxicological effects; nZnO particles appeared to be slightly more toxic than nTiO₂ at the highest concentrations. In contrast, seven organic UV filters did not affect zebrafish embryogenesis at or near aqueous solubility. Second, to simulate potent photo-initiated reactions upon release into water, we examined methylene blue (MB) degradation under UV light. nTiO₂ from sunscreen caused 10 times faster MB loss than nZnO and approached the photocatalytic degradation rate of a commercial nTiO₂ photocatalysts (P25). Organic UV filters did not cause measurable MB degradation. Finally, we estimated that between 1 and 10ppm of sunscreen NPs in surface waters could produce similar steady state hydroxyl radical concentrations as naturally occurring fluvic acids under sunlight irradiation. Incorporation of NPs into sunscreen may increase environmental concentrations of

reactive oxygen, albeit to a limited extent, which can influence transformation of dissolved substances and potentially affect ecosystem processes.

Hannan, K. D., Zuckerman, Z. C., Haak, C. R., & Shultz, A. D. (2015). Impacts of Sun Protection on Feeding Behavior and Mucus Removal of Bonefish, *Albula Vulpes*. *Environmental Biology of Fishes*, 98(11), 2297-2304 <https://doi.org/10.1007/s10641-015-0457-6>

Catch-and-release angling is growing as a tool for the conservation of fish stocks because it assumes that the impacts of angling are negligible. However, many studies have shown that catch-and-release can be stressful to the fish and even result in mortality. Bonefishing represents a popular catch-and-release fishery in the tropics and subtropics, with most anglers spending 6+ hours per day in full sunlight. To protect themselves, anglers typically employ sun protection in the form of liquid sunscreen and UV-blocking clothing. Exposure to chemicals contained in sunscreens may impose additional stressors on fish that are handled and subsequently released. In this study we conducted two separate experiments in the lab facilities in Cape Eleuthera, Bahamas. The first examined bonefish feeding behaviors in response to bait handled with zinc-based sunscreen, oxybenzone-based sunscreen, and no coating on the researcher's hands. The second experiment quantified the effects of sunscreens and UV blocking gloves on the removal of fish's protective mucus layer as a result of handling. We did not observe evidence of a change in feeding behavior when bait was handled with hands covered in sunscreen compared to wet hands. However, there was an increase in removal of protective mucus of bonefish when researcher's hands were coated in oxybenzone containing sunscreen compared to researchers handling fish with wet hands. The results of this study indicate wet hands are the best way to handle fish when participating in catch-and-release angling.

Hanson, K. M., Gratton, E., & Bardeen, C. J. (2006). Sunscreen Enhancement of UV-Induced Reactive Oxygen Species in the Skin. *Free Radical Biology and Medicine*, 41(8), 1205-1212 <https://doi.org/10.1016/j.freeradbiomed.2006.06.011>

The number of UV-induced (20 mJ cm⁻²) reactive oxygen species (ROS) generated in nucleated epidermis is dependent upon the length of time the UV filter octocrylene, octylmethoxycinnamate, or benzophenone-3 remains on the skin surface. Two-photon fluorescence images acquired immediately after application of each formulation (2 mg cm⁻²) to the skin surface show that the number of ROS produced is dramatically reduced relative to the skin-UV filter control. After each UV filter remains on the skin surface for t = 20 min, the number of ROS generated increases, although it remains below the number generated in the control. By t = 60 min, the filters generate ROS above the control. The data show that when all three of the UV filters penetrate into the nucleated layers, the level of ROS increases above that produced naturally by epidermal chromophores under UV illumination.

He, T. T., Zhang, T., Liu, S. B., Shi, J. C., Huang, Y. S., Zheng, H. P., & Liu, W. H. (2019). Toxicological Effects Benzotriazole to the Marine Scallop *Chlamys nobilis*: A 2-Month Exposure Study. *Environmental Science and Pollution Research*, 26(10), 10306-10318 <https://doi.org/10.1007/s11356-019-04201-6>

Benzotriazole and its associated derivatives (BTs) are widely used as ultraviolet stabilizers and corrosion inhibitors. They have been extensively found in marine environments and are bioaccumulative through the food chain. However, the toxicities of BTs to marine organisms are seldom identified and no assessment has been conducted for filter-feeding bivalves. In this study, a marine scallop *Chlamys*

nobilis was exposed to 0, 0.01, 0.1, and 1.0 mg/L of BT for 60 days. Effects of BT on endocrine system, cytochrome P450 activity, antioxidant activity, and neural activity of *C. nobilis* were examined. The results showed that BT exerted significant estrogenic effects on both male and female scallops and inhibited EROD activities of *C. nobilis* even at 0.01 mg/L level. BT at ≥ 0.01 mg/L levels also caused significant oxidative stress on *C. nobilis*. Moreover, most of the adverse effects of BT to *C. nobilis* were found from day 35 and 0.01 mg/L was the lowest concentration with observed effects, showing the long-term toxic effects of BT to *C. nobilis*. Thus, the adverse effects of BT and its derivatives to marine benthic communities deserve more attention in future research.

Holbech, H., Norum, U., Korsgaard, B., & Bjerregaard, P. (2002). The Chemical UV-Filter 3-Benzylidene Camphor Causes an Oestrogenic Effect in an *In Vivo* Fish Assay. *Pharmacology & Toxicology*, 91, 204-208 <https://doi.org/10.1034/j.1600-0773.2002.t01-3-910403.x>

Chemical UV-filters are used in sun protection products and various kinds of cosmetics. The lipophilic chemical UV-filter 3-benzylidene camphor was investigated for its capability to cause vitellogenin induction, possibly via oestrogen receptor binding, in a well-established *in vivo* fish assay (juvenile rainbow trout, *Oncorhynchus mykiss*, vitellogenin ELISA). A clear relationship was demonstrated between the dose of injected 3-benzylidene camphor and the concentration of plasma vitellogenin with a 105-times induction from 68 mg 3-benzylidene camphor /kg/injection and above compared to the control vitellogenin level. The relationship between the injected dose of 3-benzylidene camphor and the percent of responding fish (vitellogenin) was evaluated by logistic regression analysis and effective dose-values (ED-values) were determined. ED10, ED50 and ED90 of 3-benzylidene camphor after 6 days (2 injections) were 6.4, 16 and 26 mg/kg/ injection, respectively. These ED-values place 3-benzylidene camphor among the more potent xenoestrogens discovered to date and necessitates investigations on the distribution, concentration, persistence and bioaccumulation of 3-benzylidene camphor and other UV-filters in nature.

Hou, J., Li, T., Miao, L., You, G., Xu, Y., & Liu, S. (2019). Effects of Titanium Dioxide Nanoparticles on Algal and Bacterial Communities in Periphytic Biofilms. *Environmental Pollution*, 251, 407-414 <https://doi.org/10.1016/j.envpol.2019.04.136>

The widespread application of commercial TiO₂ NPs inevitably leads to their release into environmental waters through various ways. TiO₂ NPs released into water might be absorbed by and react with periphytic biofilms, which are a kind of aquatic environmental media of important ecological significance, and influence the physiological activity and ecological function of periphytic biofilms. This study investigated the effects of exposure to 1mg/L and 5mg/L of TiO₂ NPs on periphytic biofilms cultured indoors. After a 10-day exposure to TiO₂ NPs, the growth (measured by chlorophyll-a content) of microalgal community was inhibited greatly (more than 60%); however, the primary production (indicated by quantum yield) of periphytic biofilms maintained changeless. As for bacteria, TiO₂ NP-exposure increased the bacterial diversity and altered the composition structure. Significant changes were observed in the bacterial communities at the class level, mainly including Alphaproteobacteria, Gammaproteobacteria, Cytophagia, Flavobacteriia, Sphingobacteriia, Synechococcophycideae and Oscillatoriothycideae. The enhancement of metabolic activities (the production of extracellular polymeric substances, especially proteins content increased by 48.51%) of periphytic biofilms was a resistance mechanism to toxicity of NPs. As for extracellular enzyme activities of periphytic biofilms, alkaline phosphatase activity was inhibited (22.43%) after exposed to 5mg/L of TiO₂ NPs, which posed a threat to phosphorus metabolism of periphytic biofilms. Overall, this study demonstrated that 1mg/L

and 5mg/L of TiO₂ NPs negatively influenced physiological activities and ecological functions of periphytic biofilms, highlighting that the ecological risks of TiO₂ NPs should be paid attention to.

Huang, Y., Luo, L., Ma, X. Y., & Wang, X. C. (2018). Effect of Elevated Benzophenone-4 (Bp4) Concentration on *Chlorella vulgaris* Growth and Cellular Metabolisms. *Environmental Science and Pollution Research*, 25(32), 32549-32561 <https://doi.org/10.1007/s11356-018-3171-z>

Benzophenone-4 (BP4), as the raw material of common sunscreen products, usually shows strong ecotoxicity and endocrine-disrupting activity in aquatic animals. However, the potential adverse effect of BP4 on aquatic vegetation is still unclear. In order to evaluate the inhibitory effect of BP4 on phytoplankton, wild and acclimated *Chlorella vulgaris* was used as representative aquatic plant cells and experimental studies were conducted on the characteristics of its growth and cellular metabolisms upon exposure to elevated BP4 concentrations (1, 5, 10, 20, 50, and 100 mg L⁻¹). *C. vulgaris* basically appeared low sensitivity to BP4 exposure because the 96-h EC₅₀ was measured as 65.16 mg L⁻¹ for its wild type. The 96-h EC₅₀ of the acclimated type, which was pre-exposed to 10 mg L⁻¹ of BP4 and transferred twice, was 140.76 mg L⁻¹. By cellular response tests regarding non-enzymatic antioxidants carotenoid content, malondialdehyde (MDA), enzyme antioxidant superoxide dismutase (SOD) activity, and the photosynthetic efficiency, it was clarified that increasing exposure concentration elevated the hindrance to cellular metabolism. However, the rate of BP4 utilization as substrates for *C. vulgaris* growth showed a trend of decreasing with increasing BP4 concentration. The higher 96-h EC₅₀ value of the acclimated *C. vulgaris* to BP4 inhibition than the wild *C. vulgaris* showed the enhanced tolerance capability; however, the continuous stress response of acclimated type should be taken into account when using microalgae species for toxicity assessment.

Huo, W., Cai, P., Chen, M., Li, H., Tang, J., Xu, C., . . . Xia, Y. (2016). The Relationship between Prenatal Exposure to BP-3 and Hirschsprung's Disease. *Chemosphere*, 144, 1091-1097 <https://doi.org/10.1016/j.chemosphere.2015.09.019>

Hirschsprung's disease (HSCR) is neonatal intestinal abnormality which derived from the failure of enteric neural crest cells migration to hindgut during embryogenesis from 5 to 12 weeks. Currently, the knowledge of environmental factors contributing to HSCR is still scarce. Benzophenone-3 (BP-3) is one of the most widely used UV filters, and has weak estrogen and strong anti-androgenic effects. In order to examine the effect of maternal BP-3 exposure on development of offspring and explore the potential mechanism, we conducted case and control study and in vitro study. In this work, BP-3 concentrations in maternal urine was detected by ultra-high performance liquid chromatography. Besides, we investigated the cytotoxicity and receptor tyrosine kinase (RET) expression in cells exposed to BP-3. The results showed that maternal BP-3 exposure was associated with offspring's HSCR in the population as well as inhibited migration of 293T and SH-SY5Y cells. What's more, we discovered dose-response relationship between RET expression and BP-3 exposure dose, and miR-218 and some other genes involved in SLIT2/ROBO1-miR-218-RET/PLAG1 pathway were also related to BP-3 exposure. Therefore, we deduced that BP-3 influenced cell migration via SLIT2/ROBO1-miR-218-RET/PLAG1 pathway. Our study firstly revealed the relationship between maternal BP-3 exposure and HSCR as well as its potential mechanism.

Husain, W. M., Araak, J. K., & Ibrahim, O. M. S. (2019). Effect of Different Doses from ZnONPS on the Pituitary-Testes Axis Function in Adult Male Rats. *Advances in Animal and Veterinary Sciences*, 7(7) <https://doi.org/10.17582/journal.aavs/2019/7.7.550.556>

In our study, ZnONPs was prepared and characterized for investigation of pituitary-testes axis function in adult male rats. Fifty healthy adult male rats selected, weighted 300 ± 50 gm, randomly divided to five group each group have ten animals. One of them group consider as control group and other four group designed as (G1, G2, G3 and G4) group which receive oral dose of ZnONPs in different concentration (5, 10, 20 and 40 mg/kg- B.W) respectively for 56 day. Blood samples were collected via cardiac puncture for serum collection in (zero time, 28 and 56 day of experiment). The results showed significant ($P < 0.05$) elevation of testosterone and FSH hormones concentration in G3 and G4 after 56 day of experimental period as a compared with zero time and 28 day of experiment, whereas LH and inhibin B hormones concentration showed a significant ($P < 0.05$) decrement in all group at 56 day as a compared with control group and other period time. Histological study of testes and pituitary gland showed different pathological changes on these two gland's tissue and cells as mild to severe effects especially at dose (20 and 40 mg/kg B.W). Histometric study of seminiferous tubules illustrated a significant ($P < 0.05$) elevation of seminiferous tubules diameters in G4 group, whereas showed non-significant ($P > 0.05$) differences in number of interstitial cells in treated groups.

Inui, M. (2003). Effect of UV Screens and Preservatives on Vitellogenin and Choriogenin Production in Male Medaka (*Oryzias latipes*). *Toxicology*, 194(1-2), 43-50 [https://doi.org/10.1016/s0300-483x\(03\)00340-8](https://doi.org/10.1016/s0300-483x(03)00340-8)

Ultra violet (UV) screens and preservatives are widely and increasingly used in cosmetics and pharmaceuticals. In the present study, we examined the estrogenicity of 4-methyl-benzylidene camphor (4-MBC), octyl-methoxycinnamate (OMC), and propyl paraben (n-propyl-p-hydroxy-benzoate; PP), among UV screens and preservatives, using male medaka (*Oryzias latipes*), in regard to production of vitellogenin (VTG) and choriogenin (CHG) which are known to be estrogen-responsive gene products. First, using a VTG enzyme-linked immunosorbent assay (ELISA) system, we determined the increase in VTG plasma concentration in medaka due to exposure to 4-MBC, OMC, and PP, and compared this concentration to the non-treated control. Next, we found increases in mRNA expression levels of VTG subtypes VTG-1 and VTG-2, and CHG subtypes CHG-L and CHG-H, in liver due to exposure to 4-MBC, OMC, and PP compared to the non-treated control. In addition, we also found increased mRNA expression levels of estrogen receptor (ER) α , among sex hormone receptors in the liver, due to exposure to 4-MBC, OMC, and PP compared to the non-treated control. In this study, we showed that 4-MBC, OMC, and PP have estrogenic activity in fish.

Jain, A., Kumar, S., & Seena, S. (2019). Can Low Concentrations of Metal Oxide and Ag Loaded Metal Oxide Nanoparticles Pose a Risk to Stream Plant Litter Microbial Decomposers? *Science of The Total Environment*, 653, 930-937 <https://doi.org/10.1016/j.scitotenv.2018.10.376>

Nanoparticles (NPs) continue to be extensively produced by many industries, which ultimately leads to its release into the aquatic environment. It is crucial to estimate the impact of low concentrations of NPs which are environmentally relevant. Litter decomposition is a key ecological process in forested streams; microbes like fungi and bacteria are recognised to play a vital role in litter decomposition. In this study, zinc oxide (ZnO), titanium dioxide (TiO₂), silver loaded ZnO (Ag/ZnO) and silver loaded TiO₂ (Ag/TiO₂) NPs were synthesized, and impacts of low concentrations (0, 2.5, 25, 50 μ M) on leaf litter decomposition, fungal sporulation and bacterial growth were assessed. Fungal assemblages consisting of *Articulospora tetracladia*, *Neonectria lugdunensis*, *Tricladium splendens* and *Varicosporium elodeae* were used to study litter decomposition in microcosms exposed to NPs for 21 days. Two freshwater bacterial species belonging to the family Enterobacteriaceae were used to assess growth after 12h of

exposure to NPs. Types and concentrations of NPs affected litter decomposition and sporulation but not growth of bacteria. Leaf mass loss was significantly different between all concentrations but not between 25 and 50µM. Fungal sporulation was significantly different among all concentrations of NPs. Fungal sporulation decreased with increase in concentration of NPs whereas a particular trend was not observed with mass loss except for Ag/ZnO. A 50µM of Ag/ZnO had the highest impact on litter decomposition while 50µM of ZnO on sporulation. The impact of Ag loaded metal oxides were not strikingly different from those of bare metal oxides except for the more pronounced impact on the mass loss accomplished by Ag/ZnO than by ZnO. Overall our study highlights that very low concentrations of NPs in freshwaters can impact freshwater ecosystem functioning.

Jang, G. H., Park, C. B., Kang, B. J., Kim, Y. J., & Lee, K. H. (2016). Sequential Assessment Via Daphnia and Zebrafish for Systematic Toxicity Screening of Heterogeneous Substances. *Environmental Pollution*, 216, 292-303 <https://doi.org/10.1016/j.envpol.2016.06.001>

Environment and organisms are persistently exposed by a mixture of various substances. However, the current evaluation method is mostly based on an individual substance's toxicity. A systematic toxicity evaluation of heterogeneous substances needs to be established. To demonstrate toxicity assessment of mixture, we chose a group of three typical ingredients in cosmetic sunscreen products that frequently enters ecosystems: benzophenone-3 (BP-3), ethylhexyl methoxycinnamate (EHMC), and titanium dioxide nanoparticle (TiO₂ NP). We first determined a range of nominal toxic concentration of each ingredient or substance using *Daphnia magna*, and then for the subsequent organismal level phenotypic assessment, chose the wild-type zebrafish embryos. Any phenotype change, such as body deformation, led to further examinations on the specific organs of transgenic zebrafish embryos. Based on the systematic toxicity assessments of the heterogeneous substances, we offer a sequential environmental toxicity assessment protocol that starts off by utilizing *Daphnia magna* to determine a nominal concentration range of each substance and finishes by utilizing the zebrafish embryos to detect defects on the embryos caused by the heterogeneous substances. The protocol showed additive toxic effects of the mixtures. We propose a sequential environmental toxicity assessment protocol for the systematic toxicity screening of heterogeneous substances from *Daphnia magna* to zebrafish embryo in-vivo models.

Janjua, N. R., Kongshoj, B., Andersson, A. M., & Wulf, H. C. (2008). Sunscreens in Human Plasma and Urine after Repeated Whole-Body Topical Application. *Journal of the European Academy of Dermatology and Venerology*, 22(4), 456-461 <https://doi.org/10.1111/j.1468-3083.2007.02492.x>

BACKGROUND: The three chemical ultraviolet absorbers benzophenone-3 (BP-3), octyl-methoxycinnamate (OMC) and 3-(4-methylbenzylidene) camphor (4-MBC) are commercially used in sunscreens worldwide. Apart from sun protection, they may possess endocrine-disrupting effects in animals and in vitro. For all three compounds, only sporadic measurements of percutaneous absorption and excretion after topical application in humans have been described. **METHODS:** In this study, 32 healthy volunteers, 15 young males and 17 postmenopausal females, were exposed to daily whole-body topical application of 2 mg/cm² of sunscreen formulation at 10% (w/w) of each for 4 days. Blood concentrations were measured at 0, 1, 2, 3, 4, 24 and 96 h and urine concentrations at 0, 24, 48, 72 and 96 h. **RESULTS:** Almost all three sunscreens were undetectable in plasma and urine before the first application. One to 2 h after the first application, all three sunscreens were detectable in plasma. The maximum median plasma concentrations were 187 ng/mL BP-3, 16 ng/mL 4-MBC and 7 ng/mL OMC for females and 238 ng/mL BP-3, 18 ng/mL 4-MBC and 16 ng/mL OMC for men. In the females, urine levels

of 44 ng/mL BP-3 and 4 ng/mL of 4-MBC and 6 ng/mL OMC were found, and in the males, urine levels of 81 ng/mL BP-3, 4 ng/mL of 4-MBC and OMC were found. In plasma, the 96-h median concentrations were higher compared with the 24-h concentrations for 4-MBC and OMC in men and for BP-3 and 4-MBC in females.

Jannesson, L., Birkhed, D., Scherl, D., Gaffar, A., & Renvert, S. (2004). Effect of Oxybenzone on PGE₂ Production In Vitro and on Plaque and Gingivitis In Vivo. *Journal of Clinical Periodontology*, 31, 91-94 <https://doi.org/10.1111/j.0303-6979.2004.00453.x>

OBJECTIVES: To study the effect of oxybenzone on prostaglandin E2 (PGE2) production in cell culture and to evaluate the effect of an oxybenzone-containing dentifrice on plaque and gingivitis in a 6-week clinical trial. **MATERIAL AND METHODS:** Human embryo palatal mesenchyme (HEPM) cells were used for testing the inhibition of IL-1beta-stimulated PGE2-production in vitro by different concentrations of oxybenzone. For the in vivo study, a total of 66 individuals with a Quigley & Hein plaque index of at least 1.5 and an Ainamo & Bay gingival index of at least 0.2 were included in a double-blind clinical trial with two cells and a parallel design. Two compositions of fluoride dentifrice were used, one with the addition of 0.5% oxybenzone, and one without. Plaque and gingival index were obtained at three time points: (1) at baseline, (2) after 3 weeks, and (3) after 6 weeks. **RESULTS:** A dose-dependent inhibition of PGE2-production was found in the HEPM cell culture following oxybenzone exposure. In the clinical trial, a 25% reduction of gingival index was observed in the oxybenzone group (p<0.001) after 6 weeks as compared with 2% for the placebo group. **CONCLUSIONS:** These findings indicate that PGE2-production is reduced by oxybenzone in vitro and that the use of oxybenzone in a dentifrice reduces gingivitis in vivo.

Jeon, H. K., Sarma, S. N., Kim, Y. J., & Ryu, J. C. (2008). Toxicokinetics and Metabolisms of Benzophenone-Type UV Filters in Rats. *Toxicology*, 248(2-3), 89-95 <https://doi.org/10.1016/j.tox.2008.02.009>

Sunscreens containing UV filters are recommended to reduce damage caused by solar UV radiation. Recently, benzophenone (BP)-type UV filters have become widely used as UV stabilizers in skin-moisturizing products and sunscreen lotions; however, very little information is available regarding the potential harmful effects of prolonged exposure to these compounds. Therefore, we investigated the toxicokinetics and metabolism of BP-type UV filters in rats using gas chromatography-mass spectrometry (GC-MS). To examine the metabolism of BP-type UV filters, we analyzed the parent compounds BP and 2-hydroxy-4-methoxybenzophenone (HMB). In rats, BP was mainly converted to benzhydrol (BH) and 4-hydroxybenzophenone (HBP) (i.e., type A UV filters). In contrast, HMB was converted into at least three intermediates, including 2,4-dihydroxybenzophenone (DHB), which was formed via o-demethylation and subsequently converted into 2,3,4-trihydroxybenzophenone (THB), and 2,2'-dihydroxy-4-methoxybenzophenone (DHMB), which formed via the aromatic hydroxylation of HMB (i.e., type B UV filters). Next, the toxicokinetic curve for BP showed a peak concentration (C_{max}) of 2.06±0.46 microg/ml at approximately 4h after BP administration. After a single oral dose of HMB, the C_{max} of HMB reached 21.21±11.61 microg/ml within 3h (T_{max}), and then declined rapidly compared to the kinetic curve of BP. The concentration of these metabolites in rat blood decreased much more slowly over time compared to the parent compounds. Thus, our results indicate that such metabolites might have more significant adverse effects than the parent compounds over the long term.

Jomini, S., Labille, J., Bauda, P., & Pagnout, C. (2012). Modifications of the Bacterial Reverse Mutation Test Reveals Mutagenicity of TiO₂ Nanoparticles and Byproducts from a Sunscreen TiO₂-Based Nanocomposite. *Toxicology Letters*, 215(1), 54-61 <https://doi.org/10.1016/j.toxlet.2012.09.012>

The bacterial reverse mutation test, recommended by the Organization for Economic Co-operation and Development (OECD) to determine genotoxicity of chemical compounds, has been recently used by several authors to investigate nanoparticles. Surprisingly, test results have been negative, whereas in vitro mammalian cell tests often give positive genotoxic responses. In the present study, we used the fluctuation test procedure with the *Salmonella typhimurium* strains TA97a, TA98, TA100 and TA102 to determine the mutagenic potential of TiO₂ nanoparticles (NP-TiO₂) and showed that, when it is used conventionally, this test is not suitable for nanoparticle genotoxicity assessment. Indeed, the medium used during exposure prevents electrostatic interactions between bacterial cells and nanoparticles, leading to false-negative responses. We showed that a simple pre-exposure of bacteria to NP-TiO₂ in a low ionic strength solution (NaCl 10 mM) at a pH below the nanoparticle isoelectric points (pH 5.5) can strongly improve the accuracy of the test. Thus, based on these improvements, we have demonstrated the genotoxicity of the engineered NP-TiO₂ tested and a NP-TiO₂ byproduct from a sunscreen nanocomposite. It was also shown that strain TA102 is more sensitive than the other strains, suggesting an oxidative stress-mediated mechanism of genotoxicity.

Kaiser, D., Sieratowicz, A., Zielke, H., Oetken, M., Hollert, H., & Oehlmann, J. (2012). Ecotoxicological Effect Characterisation of Widely Used Organic UV Filters. *Environmental Pollution*, 163, 84-90 <https://doi.org/10.1016/j.envpol.2011.12.014>

Chemical UV filters are used in sun protection and personal care products in order to protect consumers from skin cancer induced by ultraviolet (UV) radiation. The present study aims to evaluate the effects of three common UV filters butyl-methoxydibenzoylmethane (B-MDM) ethylhexyl-methoxycinnamate (EHMC) and octocrylene (OCR) on aquatic organism, focussing particularly on infaunal and epibenthic invertebrates (*Chironomus riparius*, *Lumbriculus variegatus*, *Melanoides tuberculata* and *Potamopyrgus antipodarum*). Due to their life habits, these organism are especially affected by lipophilic substances. Additionally, two direct sediment contact assays utilising zebra fish (*Danio rerio*) embryos and bacteria (*Arthrobacter globiformis*) were conducted. EHMC caused a toxic effect on reproduction in both snails with lowest observed effect concentrations (LOEC) of 0.4 mg/kg (*Potamopyrgus antipodarum*) and 10 mg/kg (*Melanoides tuberculata*). At high concentrations sublethal effects could be observed for *D. rerio* after exposure to EHMC (NOEC 100 mg/kg). B-MDM and OCR showed no effects on any of the tested organism.

Kang, H., Kim, S., Lee, G., Lee, I., Lee, J. P., Lee, J., . . . Choi, K. (2019). Urinary Metabolites of Dibutyl Phthalate and Benzophenone-3 Are Potential Chemical Risk Factors of Chronic Kidney Function Markers Among Healthy Women. *Environment International*, 124, 354-360 <https://doi.org/10.1016/j.envint.2019.01.028>

Chronic kidney disease (CKD) is a global health threat of growing concern. Recently, exposure to endocrine disrupting compounds (EDCs) such as phthalates and bisphenol A has been suggested as a risk factor for CKD. However, most epidemiological studies have focused on a limited number of urinary chemicals. This study aimed to identify chemical determinants of the urinary albumin-to-creatinine ratio (ACR), which is a kidney function marker, among multiple major EDCs including phthalate metabolites, bisphenols, and benzophenones in a Korean female population (20-45years old, n=441). First, the creatinine-adjusted urinary concentration of each urinary chemical was associated with ACR in a linear

regression model (single-pollutant model). Then, compounds with a significant association with ACR in the single-pollutant model were added in a multi-pollutant model and evaluated for their association with ACR. Moreover, to prevent potential reverse causality due to impaired kidney function, quartile analyses were performed for the subjects with healthy renal function ($ACR < 9.71 \text{ mg/g}$). In addition to creatinine adjustment, the statistical analysis was also conducted with specific gravity-adjusted concentrations of urinary chemicals, and the results were compared. Several compounds measured in the urine showed a significant association with ACR in the single-pollutant model. In the multi-pollutant model, however, only monobutyl phthalate and benzophenone-1, which are metabolites of dibutyl phthalate and benzophenone-3, respectively, showed significant positive associations. The association of these chemicals remained significant in a couple of the sensitivity analyses with a different adjustment of urine dilution and in a subpopulation with normal ACR. In conclusion, among dozens of urinary chemicals, monobutyl phthalate and benzophenone-1 consistently showed a strong association with urinary ACR. Confirmation of our observation in other human populations and experimental studies is warranted.

Kasichayanula, S., House, J. D., Wang, T., & Gu, X. (2007). Percutaneous Characterization of the Insect Repellent Deet and the Sunscreen Oxybenzone from Topical Skin Application. *Toxicology and Applied Pharmacology*, 223(2), 187-194 <https://doi.org/10.1016/j.taap.2007.05.016>

The synergistic percutaneous enhancement between insect repellent DEET and sunscreen oxybenzone has been proven in our laboratory using a series of in vitro diffusion studies. In this study, we carried out an in vivo study to characterize skin permeation profiles from topical skin application of three commercially available repellent and sunscreen preparations. The correlation between skin disposition and drug metabolism was attempted by using data collected. Both DEET and oxybenzone permeated across the skin after the application and achieved substantial systemic absorption. Combined use of DEET and oxybenzone significantly enhanced the percutaneous penetration percentages (ranging 36-108%) due to mutual enhancement effects. Skin disposition indicated that DEET produced a faster transdermal permeation rate and higher systemic absorption extent, but oxybenzone formed a concentrated depot within the skin and delivered the content slowly over the time. In vivo AUCP/MRT of DEET and oxybenzone was increased by 37%/17% and 63%/10% when the two compounds were used together. No DEET was detected from the urine samples 48 h after the application. Tape stripping seemed to be a satisfactory approach for quantitative assessment of DEET and oxybenzone penetration into the stratum corneum. It was also concluded that pharmacological and toxicological perspectives from concurrent application of insect repellent and sunscreen products require further evaluation to ensure use efficacy and safety of these common consumer healthcare products.

Kerdivel, G., Le Guevel, R., Habauzit, D., Brion, F., Ait-Aissa, S., & Pakdel, F. (2013). Estrogenic Potency of Benzophenone UV Filters in Breast Cancer Cells: Proliferative and Transcriptional Activity Substantiated by Docking Analysis. *Plos One*, 8(4), e60567 <https://doi.org/10.1371/journal.pone.0060567>

The results from recent studies show that some benzophenones (BPs) and their hydroxylated metabolites can function as weak estrogens (E2) in the environment. However, little is known about the structure-activity relationship of these molecules. We have examined the effects of exposure to ten different BPs on the proliferation of estrogen receptor (ER)-positive breast cancer cells and on the transcriptional activity of E2-target genes. We analyzed two genes that are tightly linked with estrogen-mediated proliferation, the CXCL12 and amphiregulin genes and two classical estrogen-responsive

genes, the pS2 and progesterone receptor. Significant differences in the BPs efficiency to induce cell proliferation and endogenous E2-target gene expressions were observed. Using ERE-, Sp1-, AP1- and C3-reporter genes that contain different ER-binding sites in their promoter, we also showed significant differences in the BPs efficiency in activation of the ER transactivation. Together, our analyzes showed that the most active molecule is 4-hydroxy-BP. Docking analysis of the interaction of BPs in the ligand-binding pocket of ERalpha suggests that the minimum structural requirement for the estrogenic activity of BPs is a hydroxyl (OH) group in the phenyl A-ring that allows interaction with Glu-353, Arg-394 or Phe-404, which enhances the stability between BPs and ERalpha. Our modeling also indicates a loss of interaction between the OH groups of the phenyl B-ring and His-524. In addition, the presence of some OH groups in the phenyl B-ring can create repulsion forces, which may constrain helix 12 in an unfavorable position, explaining the differential estrogenic effects of BPs. These results, together with our analysis of BPs for their potency in activation of cell proliferation and ER-mediated transcription, report an improved understanding of the mechanism and structure-activity relationship of BPs.

Kim, H. J., Lee, E., Lee, M., Ahn, S., Kim, J., Liu, J., . . . Noh, M. (2018). Phosphodiesterase 4B Plays a Role in Benzophenone-3-Induced Phototoxicity in Normal Human Keratinocytes. *Toxicology and Applied Pharmacology*, 338, 174-181 <https://doi.org/10.1016/j.taap.2017.11.021>

Benzophenone-3 (BP-3), which is extensively used in organic sunscreen, has phototoxic potential in human skin. Phosphodiesterase 4B (PDE4B) has a well-established role in inflammatory responses in immune cells. Currently, it is unknown if PDE4B is associated with BP-3-induced phototoxicity in normal human keratinocytes (NHKs). We found that BP-3 significantly increased PDE4B expression in ultraviolet B (UVB)-irradiated NHKs. Notably, BP-8, a sunscreen agent that shares the 2-hydroxy-4-methoxyphenyl methanone moiety with BP-3, also upregulated PDE4B expression in NHKs. Upon UVB irradiation, BP-3 upregulated the expression of pro-inflammatory factors, such as prostaglandin endoperoxide synthase 2, tumor necrosis factor alpha, interleukin 8, and S100A7, and downregulated the level of cornified envelope associated proteins, which are important in the development of the epidermal permeability barrier. The additive effects of UVB-activated BP-3 on the expression of both pro-inflammatory mediators and cornified envelope associated proteins were antagonized by treatment with the PDE4 inhibitor rolipram. The BP-3 and UVB co-stimulation-induced PDE4B upregulation and its association with the upregulation of pro-inflammatory mediators and the downregulation of epidermal differentiation markers were confirmed in a reconstituted three dimensional human epidermis model. Therefore, PDE4B has a role in the mechanism of BP-3-induced phototoxicity.

Kim, J., Lee, S., Kim, C. M., Seo, J., Park, Y., Kwon, D., . . . Choi, K. (2014). Non-Monotonic Concentration-Response Relationship of TiO₂ Nanoparticles in Freshwater Cladocerans under Environmentally Relevant UV-A Light. *Ecotoxicology and Environmental Safety*, 101, 240-247 <https://doi.org/10.1016/j.ecoenv.2014.01.002>

The effects of UV-A on the toxicity of TiO₂ nano-particles (NPs) were evaluated using *Moina macrocopa* and *Daphnia magna* under environmentally relevant level of UV-A. The waterfleas were exposed to TiO₂ NPs with different sizes of ~298nm, ~132nm, or ~72nm for up to 48h, with or without UV-A light. Whole body reactive oxygen species and transcription of antioxidant enzyme genes were measured, as well as the survival of the waterflea. In the presence of UV-A, the survival rates of *M. macrocopa* significantly decreased in concentration dependent way until ~1mg/L TiO₂ NPs, but the survivals were reversed at greater concentrations. This peculiar non-monotonic trend of concentration-response relationship might be explained by changes of particle size under different light conditions. TiO₂ NPs within a certain size

range could be trapped in the filter apparatus and exert toxicity, and the NPs of greater size were subject to either precipitation or ingestion leading to no or little toxicity. Observed TiO₂ toxicity was associated with oxidative stress in the filter apparatus. The results of this study showed that the size change due to UV-A irradiation should be considered in evaluation of ecological risks of TiO₂ NP.

Kim, S., Jung, D., Kho, Y., & Choi, K. (2014). Effects of Benzophenone-3 Exposure on Endocrine Disruption and Reproduction of Japanese Medaka (*Oryzias latipes*)--a Two Generation Exposure Study. *Aquatic Toxicology*, 155, 244-252 <https://doi.org/10.1016/j.aquatox.2014.07.004>

Benzophenone-3 (BP-3) has been widely used in sunscreens and cosmetics to protect human skin from the harmful effects of UV irradiation. While BP-3 has been frequently detected in surface waters, sediments and biota, only limited information is available on its in vivo toxicity, particularly in fish. In the present study the endocrine disrupting capacity of BP-3 and its underlying mechanisms were investigated using Japanese medaka (*Oryzias latipes*). Adult Japanese medaka pairs (F0) were exposed to 0, 4.7, 8.4, 26, or 90 µg/L (or 0, 15, 50, 150, or 500 µg/L of BP-3 based on nominal concentration) for 14 d and its effects on sex steroid hormones, and transcription of various associated genes were determined. Following additional 14 d of exposure, the F1 eggs reproduced were counted and were further exposed to 0, 5.4, 12, or 30 µg/L of BP-3 (or 0, 15, 50, or 150 µg/L based on nominal concentrations) until 30 d after hatching. Chemical analysis of the exposed media confirmed transformation of BP-3 to benzophenone-1 (BP-1), a more potent estrogen agonist. After 14 d of the adult fish exposure, plasma concentrations of testosterone (T) significantly increased in male fish. The 17β-estradiol (E2) to T (E2/T) ratio showed significant decreases in both male and female fish. Overall down-regulation of gonadal steroidogenic genes such as *star*, *cyp11a*, *cyp17*, *hsd3b*, *hsd17b3*, and *cyp19a* was also observed. After 28 d of exposure, the daily average egg reproduction per female was significantly reduced at 26 µg/L of BP-3. However, hatchability of F1 eggs was not affected by continuous exposure. After continued exposure until 30 dph, juvenile fish showed concentration-dependent decrease of condition factor, but mortality was not affected. Our observation clearly indicates that endocrine balance and reproduction performance in fish could be affected by µg/L level exposure to BP-3. Consequences of longer term exposure over multi-generations warrant further investigation.

Kim, S. Y., Lamichhane, S., Ju, J. H., & Yun, J. (2018). Protective Effect of Octylmethoxycinnamate against Uv-Induced Photoaging in Hairless Mouse Via the Regulation of Matrix Metalloproteinases. *International Journal of Molecular Sciences*, 19(7) <https://doi.org/10.3390/ijms19071836>

Ultraviolet (UV) irradiation damages skin and produces symptoms of photoaging, such as thickening, rough texture, wrinkles, and pigmentation. However, the cellular and molecular mechanisms underlying photoaging induced by chronic UV irradiation are not yet fully understood. Matrix metalloproteinases (MMPs) have been reported to be involved in the response to UV irradiation. In this study, we examined the effects of the sunscreen agent Octylmethoxycinnamate (OMC) on photoaging of the skin induced by chronic UV exposure in hairless albino Crl:SKH1-Hrhr (SKH-1) mice. We demonstrated that the expression of MMPs was elevated by UV irradiation, whereas the topical application of OMC inhibited the upregulation of MMPs. Furthermore, UV-induced wrinkle formation was decreased by OMC treatment. These results suggest that OMC is a potential agent for the prevention and treatment of skin photoaging.

Kim, T. H., Shin, B. S., Kim, K. B., Shin, S. W., Seok, S. H., Kim, M. K., . . . Yoo, S. D. (2014). Percutaneous Absorption, Disposition, and Exposure Assessment of Homosalate, a UV Filtering Agent, in Rats. *Journal of Toxicology and Environmental Health, Part A*, 77(4), 202-213
<https://doi.org/10.1080/15287394.2013.861376>

Homosalate (HMS) is an ultraviolet (UV) filtering agent used in sunscreens and other cosmetics for skin protection purposes. Despite the widespread use of these products, absorption, disposition, and in vivo endocrine disrupting potential of HMS have not been characterized. Thus, the aim of this study was to examine the percutaneous absorption, disposition, and exposure assessment of HMS in rats. Initially, sunscreen preparations of petrolatum jelly, oily solution, lotion, and gel were prepared and evaluated for in vitro permeation of HMS across excised rat skin. Dermal permeability was greatest for gel, and this preparation was used in subsequent in vivo topical application investigations. After iv injection (0.5, 2, or 5 mg/kg), the pharmacokinetics of HMS was linear and was characterized by a large Vd(ss) (13.2-17 L/kg), high Cl(s) (4.5-6.1 L/h/kg), and long t(1/2) (6.1-8.4 h). After topical application of gel, the bioavailability of HMS was 5.4 +/- 1.1 and 4.2 +/- 0.6% for high and low doses (10 and 20 mg), respectively. Consistent with the prolonged absorption (Tmax 11.2 +/- 1.8 and 12 +/- 0 h for low and high doses, respectively), the terminal t(1/2) was longer after topical application (23.6-26.1 h) compared to iv injection. A population pharmacokinetic model was further developed to simultaneously fit the time courses of plasma concentrations and dermal content data after iv injection and topical application. Findings of this study may be useful to further examine the relationship between exposure and endocrine disrupting potential of HMS in risk assessment.

Kinnberg, K. L., Petersen, G. I., Albrektsen, M., Minghlani, M., Awad, S. M., Holbech, B. F., . . . Holbech, H. (2015). Endocrine-Disrupting Effect of the Ultraviolet Filter Benzophenone-3 in Zebrafish, *Danio Rerio*. *Environmental Toxicology and Chemistry*, 34(12), 2833-2840
<https://doi.org/10.1002/etc.3129>

The chemical ultraviolet (UV) filter benzophenone-3 (BP-3) is suspected to be an endocrine disruptor based on results from in vitro and in vivo testing. However, studies including endpoints of endocrine adversity are lacking. The present study investigated the potential endocrine-disrupting effects of BP-3 in zebrafish (*Danio rerio*) in the Fish Sexual Development Test (Organisation for Economic Co-operation and Development TG 234) and a 12-d adult male zebrafish study. In TG 234, exposure from 0 d to 60 d posthatch caused a monotone dose-dependent skewing of the phenotypic sex ratio toward fewer males and more female zebrafish (no observed effect concentration [NOEC]: 191 µg/L, lowest observed effect concentration [LOEC]: 388 µg/L). Besides, gonad maturation was affected in both female fish (NOEC 191 µg/L, LOEC 388 µg/L) and male fish (NOEC 388 µg/L, LOEC 470 µg/L). Exposure to BP-3 did not affect the vitellogenin concentration in TG 234. After 12 d exposure of adult male zebrafish, a slight yet significant increase in the vitellogenin concentration was observed at 268 µg/L but not at 63 µg/L and 437 µg/L BP-3. Skewing of the sex ratio is a marker of an endocrine-mediated mechanism as well as a marker of adversity, and therefore the conclusion of the present study is that BP-3 is an endocrine-disrupting chemical in accordance with the World Health Organization's definition.

Klammer, H., Schlecht, C., Wuttke, W., Schmutzler, C., Gotthardt, I., Kohrle, J., & Jarry, H. (2007). Effects of a 5-Day Treatment with the UV-Filter Octyl-Methoxycinnamate (OMC) on the Function of the Hypothalamo-Pituitary-Thyroid Function in Rats. *Toxicology*, 238(2-3), 192-199
<https://doi.org/10.1016/j.tox.2007.06.088>

Octyl-methoxycinnamate (OMC) is one of the most frequently used UV-filters in sunscreens to protect the skin against the noxious influence of UV radiation. Recently, OMC was suspected to act as an "endocrine active chemical" (EAC) with estrogenic actions. While EACs have been investigated thoroughly for interference with reproductive function in mammals, surprisingly little efforts have been made to investigate an interference of EACs with the hypothalamo-pituitary-thyroid (HPT) axis despite the expression of estrogen receptors in all parts of this axis. Therefore, we conducted an in vivo study with ovariectomised rats treated for 5 days with different doses of OMC or 17beta-estradiol (E2) as a control. Determined parameters comprised serum levels of TSH, T4 and T3, hypothalamic TRH mRNA expression, protein-expression of the sodium-iodide-symporter (NIS) and the TSH receptor and the activities of thyroid peroxidase (TPO) in the thyroid and the T3-responsive hepatic type I 5'deiodinase (Dio1) in the liver. While E2 did not affect TSH-, T4- or T3-levels, OMC caused a dose-dependent decrease of serum concentrations of all of these hormones. TRH expression remained unaffected, while in the thyroid, expression of the TSH receptor but not of NIS was stimulated by OMC. TPO activity was unaltered but Dio1 activity was reduced by OMC. Thus, our results demonstrate a non-estrogenic interference of OMC within the rodent HPT axis with inadequate feedback response to impaired thyroid hormone status, indicated by decreased serum thyroid hormone and hepatic Dio1 levels.

Klingelfus, T., Disner, G. R., Voigt, C. L., Alle, L. F., Cestari, M. M., & Leme, D. M. (2019). Nanomaterials Induce DNA-Protein Crosslink and DNA Oxidation: A Mechanistic Study with RTG-2 Fish Cell Line and Comet Assay Modifications. *Chemosphere*, 215, 703-709
<https://doi.org/10.1016/j.chemosphere.2018.10.118>

Genotoxic effects of nanomaterials (NMs) have been controversially reported in literature, and the mode of action (MoA) via DNA oxidation is cited as the main damage caused by them. Evidence of nano-silver as a crosslinker has been previously reported by the present research team in an in vivo fish genotoxicity study. Thus, aiming to confirm the evidence about NMs as crosslinker agent, the present investigation elucidated the genotoxic potential of NMs and their genotoxic MoA through in vitro assay with RTG-2cells line (rainbow trout gonadal) by exposure to nano-silver (PVP-coated) and nano-titanium. The types and levels of DNA damage were assessed by the Comet assay (standard alkaline, hOGG1-modified alkaline, and two crosslink-modified alkaline versions). It was demonstrated that the use of the standard alkaline Comet assay alone may inaccurately predict the genotoxicity of NMs since oxidative and crosslink DNA damages were also verified in RTG-2cells when assessed by the modified versions of the alkaline protocol. More importantly, it was confirmed that both nano-silver and nano-titanium acted as DNA-protein crosslinkers through the Comet assay version with proteinase K. As both nano-silver and nano-titanium present a great risk to aquatic life, these findings reinforce the need of genotoxicity testing strategies that encompass the assessment of different types of DNA damage, in order to ensure an accurate prediction of the genotoxic potential of NMs.

Klotz, K., Hof, K., Hiller, J., Göen, T., & Drexler, H. (2019). Quantification of Prominent Organic Uv Filters and Their Metabolites in Human Urine and Plasma Samples. *Journal of Chromatography B*, 1125, 121706 <https://doi.org/10.1016/j.jchromb.2019.06.033>

Monitoring human exposure to chemical UV filters is essential for an accurate assessment of the health risk caused by the resorbed compounds. We developed different procedures for the determination of the prominent UV filters octocrylene (OC), avobenzone (AVO) and 2-ethylhexyl salicylate (EHS) as well as for two OC and EHS metabolites in human urine and OC, AVO and 2-cyano-3,3-diphenylacrylic acid

(CDAA) in plasma samples using liquid chromatography-tandem mass spectrometry (LC–MS/MS). Since the development of a multi-method for all analytes proved to be difficult, three different procedures were established for the determination of AVO, OC and its metabolite CDAA in urine and plasma as well as for EHS and its metabolite 5-hydroxy-EHS in urine. The methods have been validated with good sensitivity, precision and accuracy. The procedures were satisfactorily applied to the determination of the target compounds in human samples collected from volunteers after sunscreen application. These new analytical procedures can provide information on the internal exposure to the UV filters OC, AVO and EHS, which has been little studied.

Krause, M., Klit, A., Blomberg Jensen, M., Sjøberg, T., Frederiksen, H., Schlumpf, M., . . . Drzewiecki, K. T. (2012). Sunscreens: Are They Beneficial for Health? An Overview of Endocrine Disrupting Properties of UV-Filters. *International Journal of Andrology*, 35(3), 424-436
<https://doi.org/10.1111/j.1365-2605.2012.01280.x>

Today, topical application of sunscreens, containing ultraviolet-filters (UV-filters), is preferred protection against adverse effects of ultraviolet radiation. Evidently, use of sunscreens is effective in prevention of sunburns in various models. However, evidence for their protective effects against melanoma skin cancer is less conclusive. Three important observations prompted us to review the animal data and human studies on possible side effects of selected chemical UV-filters in cosmetics. (1) the utilization of sunscreens with UV-filters is increasing worldwide; (2) the incidence of the malignant disorder for which sunscreens should protect, malignant melanoma, is rapidly increasing and (3) an increasing number of experimental studies indicating that several UV-filters might have endocrine disruptive effects. The selected UV-filters we review in this article are benzophenone-3 (BP-3), 3-benzylidene camphor (3-BC), 3-(4-methyl-benzylidene) camphor (4-MBC), 2-ethylhexyl 4-methoxy cinnamate (OMC), Homosalate (HMS), 2-ethylhexyl 4-dimethylaminobenzoate (OD-PABA) and 4-aminobenzoic acid (PABA). The potential adverse effects induced by UV-filters in experimental animals include reproductive/developmental toxicity and disturbance of hypothalamic–pituitary–thyroid axis (HPT). Few human studies have investigated potential side effects of UV-filters, although human exposure is high as UV-filters in sunscreens are rapidly absorbed from the skin. One of the UV-filters, BP-3, has been found in 96% of urine samples in the US and several UV-filters in 85% of Swiss breast milk samples. It seems pertinent to evaluate whether exposure to UV-filters contribute to possible adverse effects on the developing organs of fetuses and children.

Krzyzanowska, W., Pomierny, B., Starek-Swiechowicz, B., Broniowska, Z., Strach, B., & Budziszewska, B. (2018). The Effects of Benzophenone-3 on Apoptosis and the Expression of Sex Hormone Receptors in the Frontal Cortex and Hippocampus of Rats. *Toxicology Letters*, 296, 63-72
<https://doi.org/10.1016/j.toxlet.2018.08.006>

Benzophenone-3 (BP-3) is the most commonly used chemical UV filter. This compound can easily be absorbed through the skin and the gastrointestinal tract and can disturb sex hormone receptor function. BP-3 is lipophilic and should cross the blood-brain barrier and it may reduce the survival of neurons, although so far, its effects on nerve cells have been studied in only in vitro cultures. The aim of the present study was to determine the effects of BP-3 on apoptosis and the expression of oestrogen, androgen and arylhydrocarbon receptors (AhR) in the rat frontal cortex and hippocampus. This compound was administered dermally to female rats during pregnancy and next to their male offspring through 6 and 7 weeks of age. BP-3 in the frontal cortex induced the mitochondrial apoptosis pathway by increasing the active forms of caspase-3 and caspase-9, inducing the pro-apoptotic proteins Bax and

Bak and increasing the number of cells with apoptotic DNA fragmentation. In the hippocampus, an increase in the caspase-9 level and a downward trend in the level of anti-apoptotic proteins were observed. In both brain regions, the contents of ERbeta in the nuclear fraction and GPR30 in the membrane fraction were significantly reduced. BP-3 significantly increased AhR in the cytosol of the frontal cortex but had no effect on the content of this receptor in the hippocampus. This is the first study showing that exposure to BP-3 induces the mitochondrial apoptosis pathway in the rat frontal cortex and this effect may result from a weakening of the neuroprotective effects of oestrogen and/or an intensification of AhR-mediated apoptosis.

Kunz, P. Y., & Fent, K. (2006). Estrogenic Activity of UV Filter Mixtures. *Toxicology and Applied Pharmacology*, 217(1), 86-99 <https://doi.org/10.1016/j.taap.2006.07.014>

UV-absorbing chemicals (UV filters) are widely used for protection against UV radiation in sunscreens and in a variety of cosmetic products and materials. Depending on the breadth and factor of UV protection, they are added as single compounds or as a combination thereof. Some UV filters have estrogenic activity, but their activity and interactions in mixtures are largely unknown. In this work, we analyzed 8 commonly used UV filters, which are pure or partial hER α agonists, for their estrogenic activity in equieffective mixtures in a recombinant yeast assay carrying the human estrogen receptor alpha (hER α). Mixtures of two, four and eight UV filters alone, or in combination with 17 β estradiol (E2), were assessed at different effect levels and no-observed-effect-concentrations (NOEC). Predictions of the joint effects of these mixtures were calculated by employing the concentration addition (CA) and independent action (IA) model. Most binary mixtures comprising of pure hER α agonists showed a synergistic activity at all mixture combinations. Only in combination with benzophenone-1, antagonistic activity was observed at some effect levels. All mixtures of four or eight, pure or pure and partial hER α agonists, alone or including E2, showed synergistic activity at concentrations giving an increase of 10% of basal activity (BC10). This occurred even at concentrations that were at the NOEC level of each single compound. Hence, there were substantial mixture effects even though each UV filter was present at its NOEC level. These results show that significant interactions occur in UV filter mixtures, which is important for the hazard and risk assessments of these personal care products.

Kunz, P. Y., & Fent, K. (2006a). Multiple Hormonal Activities of UV Filters and Comparison of In Vivo and In Vitro Estrogenic Activity of Ethyl-4-Aminobenzoate in Fish. *Aquatic Toxicology*, 79(4), 305-324 <https://doi.org/10.1016/j.aquatox.2006.06.016>

UV filters have been detected in surface water, wastewater and fish, and some of them are estrogenic in fish. At present, little is known about their additional hormonal activities in different hormonal receptor systems despite their increasing use and environmental persistence. Besides estrogenic activity, UV filters may have additional activities, both agonistic and antagonistic in aquatic organisms. In our study, we investigate a series of UV filters for multiple hormonal activities in vitro in human receptor systems and evaluate the predictive value of these findings for the activity in fish in vitro and in vivo. First we systematically analysed the estrogenic, antiestrogenic, androgenic, and antiandrogenic activity of 18 UV filters and one metabolite in vitro at non-cytotoxic concentrations with recombinant yeast systems carrying either a human estrogen (hERalpha) or androgen receptor (hAR). All 19 compounds elicited hormonal activities, surprisingly most of them multiple activities. We found 10 UV-filters having agonistic effects towards the hERalpha. Surprisingly, we identified for the first time six UV filters with androgenic activities and many of them having pronounced antiestrogenic and antiandrogenic activities. As much as 17 compounds inhibited 4,5-dihydrotestosterone activity in the hAR assay, while 14

compounds inhibited estradiol activity in the hERalpha assay, indicating antiandrogenic and antiestrogenic activity, respectively. In particular, the antiandrogenic activities of phenyl- and benzyl salicylate, benzophenone-1 and -2, and of 4-hydroxybenzophenone were higher than that of flutamide, a known hAR antagonist. In a second series of experiments, we investigated the predictive power of the hERalpha assay for aquatic organisms by further investigating the estrogenic UV filter ethyl 4-aminobenzoate (Et-PABA) in vitro and in vivo in fish. Et-PABA showed estrogenic activity in a recombinant yeast system carrying the rainbow trout estrogen receptor (rtERalpha) with higher activity than in the hERalpha assay. In addition, Et-PABA induced vitellogenin after 14 days of exposure in juvenile fathead minnows at 4394µg/L. Our study shows estrogenic activity of this UV filter in fish both in vitro and in vivo. In conjunction with in vitro human receptor-based systems our results give a more detailed picture about distinct hormonal activities of UV filters occurring in aquatic systems. We conclude that receptor-based assays are important for in vitro assessment of UV-filters prior to or concurrently with in vivo assays, which ultimately provide data for the environmental risk assessment of these important personal care products.

Kunz, P. Y., & Fent, K. (2009). Estrogenic Activity of Ternary UV Filter Mixtures in Fish (*Pimephales promelas*) — an Analysis with Nonlinear Isobolograms. *Toxicology and Applied Pharmacology*, 234(1), 77-88 <https://doi.org/10.1016/j.taap.2008.09.032>

Numerous estrogenic compounds are present in aquatic environments, but currently it is not well understood how compounds that differ in maxima and slope of their individual dose–response curves contribute to the overall mixture effect. In order to better understand such interactions we investigated 3 commonly used UV filters, for their estrogenic mixture activity and analysed their joint effects by using the concentration addition (CA) concept. Thereby, we extended the method of isoboles for analysis of 3 compounds that differ in maxima and slopes of their dose–response curves. 3-Benzylidene camphor (3BC), benzophenone-1 (BP1) and benzophenone-2 (BP2) are estrogenic in fish and act as pure- or partial estrogen receptor α agonists. First we exposed juvenile fathead minnows for 14 days to six concentrations of each UV filter alone to determine vitellogenin (VTG) induction curves, calculate equi-effective mixture concentrations and predict mixture effects. For 3BC, BP1 and BP2 significant VTG-induction occurred at 420, 2668, and 4715 µg/L, respectively. BP2 displayed a full dose–response curve, whereas 3BC and BP1 showed submaximal activity of 70 and 78%, respectively. Second, we exposed fish to 6 equi-effective mixtures (EC-NOEC, EC1, EC5, EC10, EC20, EC30) of these UV filters. Significant VTG-induction occurred at EC5 and higher. Submaximal activity of 67% as compared to the control EE2 (100 ng/L) was reached. The curves for the observed and predicted mixture activity agreed for mixture levels (EC10 to EC30), however, at EC-NOEC, EC1 and EC5, lower activity was observed than predicted by CA. Detailed isobolographic analysis indicate additivity at EC10 to EC30, and antagonism at low levels (EC-NOEC to EC5). Our data show for the first time, that for compounds with differences in maxima and slope, considerably more mixture combinations are additive than previously thought. This should be taken into account for hazard and risk assessment of UV filters and xenoestrogens.

Kunz, P. Y., Galicia, H. F., & Fent, K. (2006). Comparison of *In Vitro* and *In Vivo* Estrogenic Activity of UV Filters in Fish. *Toxicological Sciences*, 90(2), 349-361 <https://doi.org/10.1093/toxsci/kfj082>

In this work, we evaluate whether in vitro systems are good predictors for in vivo estrogenic activity in fish. We focus on UV filters being used in sunscreens and in UV stabilization of materials. First, we determined the estrogenic activity of 23 UV filters and one UV filter metabolite employing a recombinant yeast carrying the estrogen receptor of rainbow trout (rtER alpha) and made comparisons

with yeast carrying the human hER alpha for receptor specificity. Benzophenone-1 (BP1), benzophenone-2 (BP2), 4,4-dihydroxybenzophenone, 4-hydroxybenzophenone, 2,4,4-trihydroxybenzophenone, and phenylsalicylate showed full dose-response curves with maximal responses of 81-115%, whereas 3-benzylidene camphor (3BC), octylsalicylate, benzylsalicylate, benzophenone-3, and benzophenone-4 displayed lower maximal responses of 15-74%. Whereas the activity of 17 beta-estradiol was lower in the rtER alpha than the hER alpha assay, the activities of UV filters were similar or relatively higher in rtER alpha, indicating different relative binding activities of both ER. Subsequently, we analyzed whether the in vitro estrogenicity of eight UV filters is also displayed in vivo in fathead minnows by the induction potential of vitellogenin after 14 days of aqueous exposure. Of the three active compounds in vivo, 3BC induced vitellogenin at lower concentrations (435 $\mu\text{g/l}$) than BP1 (4919 $\mu\text{g/l}$) and BP2 (8783 $\mu\text{g/l}$). The study shows, for the first time, estrogenic activities of UV filters in fish both in vitro and in vivo. Thus we propose that receptor-based assays should be used for in vitro screening prior to in vivo testing, leading to environmental risk assessments based on combined, complementary, and appropriate species-related assays for hormonal activity.

Kunz, P. Y., Gries, T., & Fent, K. (2006). The Ultraviolet Filter 3-Benzylidene Camphor Adversely Affects Reproduction in Fathead Minnow (*Pimephales promelas*). *Toxicological Sciences*, 93(2), 311-321
<https://doi.org/10.1093/toxsci/kfl070>

The ultraviolet (UV) filter 3-benzylidene camphor (3BC) is used in personal care products and in a number of materials for UV protection. 3BC has been shown in vitro and in vivo in fish to be estrogenic, but possible effects on fertility and reproduction are unknown. In this study we evaluate whether 3BC affects reproduction of fish *Pimephales promelas*. After a preexposure period of 21 days, reproductively mature fathead minnows were exposed to increasing concentrations of 3BC for 21 days in a static-renewal procedure. Actual 3BC concentrations decreased to 23% of initial levels and median concentrations were 0.5, 3, 33, 74, and 285 $\mu\text{g/l}$. 3BC affected reproduction in a dose-dependent manner with weak effects on fecundity at 3 $\mu\text{g/l}$, a significant decrease at 74 $\mu\text{g/l}$, and a cessation of reproduction at 285 $\mu\text{g/l}$. 3BC was accumulated in fish with an average bioconcentration factor of 313 \pm 151. Dose-dependent demasculinization in secondary sex characteristics of male fish and dose-dependent induction of plasma vitellogenin occurred, which was significant at 74 $\mu\text{g/l}$ and higher. 3BC had a profound and dose-dependent effect on the histology of gonads of male and female fish at 3 $\mu\text{g/l}$ and higher. At 74 and 285 $\mu\text{g/l}$, oocyte and spermatocyte development was inhibited in male and female gonads. Testes of exposed males had much fewer spermatogenic cysts, and ovaries of exposed females had much fewer mature but more atretic, follicles. This study shows significant effects of the UV filter 3BC on fertility, gonadal development, and reproduction of fish after short-term exposure that may have negative consequences on the population level.

Lee, H., Lee, J., Brown, M. T., Park, J., Vieira, C., & Han, T. (2019). Toxicity Testing of Cosmetic Ingredients Using Gametophyte Beads of the Brown Alga *Undaria pinnatifida* (Laminariales, Phaeophyta). *Journal of Applied Phycology* <https://doi.org/10.1007/s10811-018-1669-x>

A 6-h toxicity test of cosmetic ingredients (methylparaben, 2-phenoxyethanol, sodium dodecyl sulfate, triethanolamine) was developed, based on the photosynthetic maximum quantum yield (Fv/Fm) of immobilized gametophytes of the brown macroalga *Undaria pinnatifida*. From calculated EC50 values, the toxicity ranking of the tested ingredients is: SDS (0.0060%) > MP (0.0634%) > 2-PE (0.2418%) > TEA (3.7023%). Compared to the results from conventional endpoints with other ecotoxicity test organisms, measurements of Fv/Fm is a more sensitive indicator of the toxic effects of cosmetic ingredients. The

present technique is simple, rapid, practical, accurate, and requires little space to carry out. This novel method will be a useful tool for assessing the toxicity of a wide range of cosmetic ingredients once the respective sensitivities are fully established.

Lee, I., Lee, J., Jung, D., Kim, S., & Choi, K. (2019). Two-Generation Exposure to 2-Ethylhexyl 4-Methoxycinnamate (EHMC) in Japanese Medaka (*Oryzias latipes*) and its Reproduction and Endocrine Related Effects. *Chemosphere*, 228, 478-484
<https://doi.org/10.1016/j.chemosphere.2019.04.123>

2-Ethylhexyl 4-methoxycinnamate (EHMC) is one of the most widely used UV-filters, and hence has been frequently detected in water environment. EHMC has been reported to induce short-term reproductive toxicity in fish, and thyroid disrupting effects in other animal studies. However, limited information is available for its long-term effects on fecundity, and thyroid disrupting effects in fish. In the present study, effects of EHMC on fecundity, measured as number of eggs, were evaluated in Japanese medaka (*Oryzias latipes*), and its underlying mechanisms on sex and thyroid hormone disruption were explored. For this purpose, a five-month long (154 d) exposure to F0 generation was conducted on fertilized eggs (<24 h post-fertilization (hpf)), with nominal concentration of 0, 0.05, 0.158, 0.5, 1.58, or 5 mg/L EHMC, followed by a 3-8-d exposure of F1 generation. After >3 months exposure, significant decreases in reproductive performances were observed at all test concentrations as low as 0.05 mg/L. Reproduction effects were not accompanied with sex hormone changes, but up-regulation of vitellogenin gene was observed. Thyroid hormones were decreased by EHMC exposure in F1 fish at -38 day post-fertilization (dpf). In addition, down-regulation of type II iodothyronine deiodinase (dio2) and up-regulation of thyrotropin releasing hormone (trh) were observed in both F0 and F1 juvenile fish, suggesting thyroid disruption potential of EHMC. Our observation suggests that EHMC at the levels one to two orders of magnitude higher than those detected in ambient water may affect reproduction and thyroid hormonal balance of fish.

Lee, J., Kim, S., Park, Y. J., Moon, H. B., & Choi, K. (2018). Thyroid Hormone-Disrupting Potentials of Major Benzophenones in Two Cell Lines (GH3 and FRTL-5) and Embryo-Larval Zebrafish. *Environmental Science and Technology*, 52(15), 8858-8865
<https://doi.org/10.1021/acs.est.8b01796>

Benzophenones (BPs) have been widely used in personal care products (PCPs) such as UV protectants. Sex endocrine-disrupting effects have been documented for some BPs, but, significant knowledge gaps are present for their thyroid-disrupting effects. To investigate the thyroid-disrupting potential of BPs, a rat pituitary (GH3) and thyroid follicle (FRTL-5) cell line were employed on six BPs, i.e., benzophenone (BP), benzophenone-1 (BP-1), benzophenone-2 (BP-2), benzophenone-3 (BP-3), benzophenone-4 (BP-4), and benzophenone-8 (BP-8). Subsequently, zebrafish (*Danio rerio*) embryo exposure was conducted for three potent BPs that were identified based on the transcriptional changes observed in the cells. In GH3 cells, all BPs except BP-4 down-regulated the Tshbeta, Trhr, and Trbeta genes. In addition, some BPs significantly up-regulated the Nis and Tg genes while down-regulating the Tpo gene in FRTL-5 cells. In zebrafish embryo assay conducted for BP-1, BP-3, and BP-8, significant decreases in whole-body T4 and T3 level were observed at 6 day postfertilization (dpf). The up-regulation of the dio1 and ugt1ab genes in the fish suggests that decreased thyroid hormones are caused by changing metabolism of the

hormones. Our results show that these frequently used BPs can alter thyroid hormone balances by influencing the central regulation and metabolism of the hormones.

Lee, J. K., Kim, K. B., Lee, J. D., Shin, C. Y., Kwack, S. J., Lee, B. M., & Lee, J. Y. (2019). Risk Assessment of Drometrizole, a Cosmetic Ingredient Used as an Ultraviolet Light Absorber. *Toxicological Research*, 35(2), 119-129 <https://doi.org/10.5487/TR.2019.35.2.119>

As the use of cosmetics has greatly increased in a daily life, safety issues with cosmetic ingredients have drawn an attention. Drometrizole [2-(2'-hydroxy-5'-methylphenyl)benzotriazole] is categorized as a sunscreen ingredient and is used in cosmetics and non-cosmetics as a UV light absorber. No significant toxicity has been observed in acute oral, inhalation, or dermal toxicity studies. In a 13-week oral toxicity study in beagle dogs, No observed adverse effect level (NOAEL) was determined as 31.75 mg/kg bw/day in males and 34.6 mg/kg bw/day in females, based on increased serum alanine aminotransferase activity. Although drometrizole was negative for skin sensitization in two Magnusson-Kligman maximization tests in guinea pigs, there were two case reports of consumers presenting with allergic contact dermatitis. Drometrizole showed no teratogenicity in reproductive and developmental toxicity studies in which rats and mice were treated for 6 to 15 days of the gestation period. Ames tests showed that drometrizole was not mutagenic. A long-term carcinogenicity study using mice and rats showed no significant carcinogenic effect. A nail product containing 0.03% drometrizole was nonirritating, non-sensitizing and non-photosensitizing in a test with 147 human subjects. For risk assessment, the NOAEL chosen was 31.75 mg/kg bw/day in a 13-week oral toxicity study. Systemic exposure dosages were 0.27228 mg/kg bw/day and 1.90598 mg/kg bw/day for 1% and 7% drometrizole in cosmetics, respectively. Risk characterization studies demonstrated that when cosmetic products contain 1.0% of drometrizole, the margin of safety was greater than 100. Based on the risk assessment data, the MFDS revised the regulatory concentration of drometrizole from 7% to 1% in 2015. Under current regulation, drometrizole is considered to be safe for use in cosmetics. If new toxicological data are obtained in the future, the risk assessment should be carried out to update the appropriate guidelines.

Lewis, J. A., DiNardo, J. C., & McDaniel, D. M. (2009). Oxidative Stress, the Damage Accumulation Theory of Skin Aging, and the Role of Antioxidants in the Future of Topical Skin Protection. *Cosmetic Dermatology*, 22(11), 576-582 Retrieved from <https://mdedge-files-live.s3.us-east-2.amazonaws.com/files/s3fs-public/Document/September-2017/022110576.pdf>

The major cause of skin aging is a lifetime of damage accumulation from oxidative stress. This scientific review looks at the effects of both internal and external sources of oxidative stress: intrinsic oxidative stress from toxic free radicals produced as a result of cellular metabolic energy production, and extrinsic oxidative stress as a result of continuous exposure to a toxic environment and poor lifestyle choices. In this article, the most toxic free radicals are reviewed, and understanding of the role of molecular oxygen as a toxic, pollutant, mutagenic, biradical, dangerous, poisonous gas is discussed. The importance of antioxidants, their capacity to inhibit skin aging, and an in-depth look at various quantitative methods (eg, oxygen radical absorbance capacity, environmental protection factor, Trolox) for determining topical antioxidant skin protection capacity are reviewed.

Li, A. J., Law, J. C., Chow, C. H., Huang, Y., Li, K., & Leung, K. S. (2018). Joint Effects of Multiple UV Filters on Zebrafish Embryo Development. *Environmental Science and Technology*, 52(16), 9460-9467 <https://doi.org/10.1021/acs.est.8b02418>

The widespread use of UV filters has resulted in significant amounts of these chemicals appearing not only in the environment but also in organisms. This study first assessed the levels of nine UV filters in waters along the coast of Shenzhen, China, in tapwater, and in a nearby reservoir. UV filters were found to be high, in both winter and summer at most locations. Then, using zebrafish as a model, the influence of a UV filter mixture after dietary and aqueous exposure was assessed. After exposing artemia to three dominant UV filters at two levels and then feeding these artemia to zebrafish adults, concentrations in both were up to 4 times higher when exposed to the mixtures than when exposed to only a single UV filter. A short-term 25-day dietary exposure to the zebrafish adults did not appear to significantly influence early life stage development of the second generation; however, relatively long exposure over 47 days had significant adverse effects on embryo development. Aqueous exposure of fish embryos to mixtures of the three UV filters demonstrated a general trend of decreased heart/hatching rate as doses increased, coupled with significant changes in activities of catalase and malate dehydrogenase.

Li, M.-H. (2012). Acute Toxicity of Benzophenone-Type UV Filters and Paraben Preservatives to Freshwater Planarian, *Dugesia japonica*. *Toxicological & Environmental Chemistry*, 94(3), 566-573 <https://doi.org/10.1080/02772248.2012.655695>

Fourteen benzophenone-type UV filters and four paraben preservatives were selected to examine their acute toxicities on *Dugesia japonica*. The 48-h LC50 values for planarians exposed to benzophenone-type UV filters can be ranked as oxybenzone > mexenone > 5-chloro-2-hydroxybenzophenone > 2,4-dihydroxybenzophenone > 2-hydroxybenzophenone > dioxybenzone > benzophenone > 2,2',4,4'-tetrahydroxybenzophenone > 4-hydroxybenzophenone > 3-hydroxybenzophenone > 4,4'-dihydroxybenzophenone > 2,2'-dihydroxy-4,4'-dimethoxybenzophenone > 2,3,4-trihydroxybenzophenone > sulisobenzone with a range from 0.9 to 145 mg L⁻¹ with a similar sequence for the 96 h LC50 values, ranging from 0.5 to 77 mg L⁻¹. The 48 and 96 LC50 values for planarians exposed to paraben preservatives can be ranked as butylparaben > propylparaben > ethylparaben > methylparaben. Among all the tested chemicals, oxybenzone was the most toxic and sulisobenzone the least toxic chemical to planarian at each exposure period. Most benzophenone-type UV filters are toxic to aquatic animals with 48 h LC50 values less than 10 mg L⁻¹, except for 2,2'-dihydroxy-4,4'-dimethoxybenzophenone, 2,3,4-trihydroxybenzophenone, and sulisobenzone. Because of their common occurrence in aquatic environment, more studies on aquatic toxicities of benzophenone-type UV filters and paraben preservatives are needed to provide important information to adequately assess their ecological risk.

Li, M., Jiang, Y., Chuang, C. Y., Zhou, J., Zhu, X., & Chen, D. (2019). Recovery of *Alexandrium tamarensense* under Chronic Exposure of TiO₂ Nanoparticles and Possible Mechanisms. *Aquatic Toxicology*, 208, 98-108 <https://doi.org/10.1016/j.aquatox.2019.01.007>

Harmful algal blooms (HAB), heavily influenced by human activities, pose serious hazard to aquatic ecology and human health. In this study, we monitored the physiological responses and paralytic shellfish poisoning toxins (PSTs) of the toxin-producing HAB species *Alexandrium tamarensense* under titanium dioxide nanoparticles (nTiO₂) exposure in the concentration range of 2-320 mg L⁻¹ over a period of 13 days. The results showed the acute inhibition of nTiO₂ on the algal growth, photosynthetic efficiency and esterase activity at all concentrations except 2 mg L⁻¹. Nonetheless, they recovered

after 13 days nTiO₂ exposure from 20 to 80 mg L⁻¹). The EC₅₀ value increased from 85.1 mg L⁻¹ in Day 4 to 140.9 mg L⁻¹ in Day 13. The physiological recovery after prolonged exposure may result from the elimination of excess reactive oxygen species (ROS), a combined outcome of increased nTiO₂ aggregation and algal antioxidant defense mechanisms. This observation is supported by the immediately increased antioxidant enzyme activities, including the superoxide dismutase (SOD) and catalase (CAT) activities upon nTiO₂ exposure. Moreover, the production of PSTs in *A. tamarensis* significantly increased by 1.41-1.76 folds after chronic nTiO₂ exposure at all tested concentrations ($p < 0.05$), which might also be an adaptive response for the microalgae to overcome the stresses. In particular, the proportions of highly-toxic PSTs analogues GTX_{2/3}, STX and dcSTX were significantly increased upon nTiO₂ exposure ($p < 0.05$). Hence, the chronic nTiO₂ exposure might aggravate the ecological impact of HABs. Furthermore investigations on different HAB species, especially those toxin-producing ones, and detail physiological responses are obviously needed.

Li, M., Wu, Q., Wang, Q., Xiang, D., & Zhu, G. (2018). Effect of Titanium Dioxide Nanoparticles on the Bioavailability and Neurotoxicity of Cypermethrin in Zebrafish Larvae. *Aquatic Toxicology*, 199, 212-219 <https://doi.org/10.1016/j.aquatox.2018.03.022>

In aquatic environment, the presence of nanoparticles (NPs) has been reported to modify the bioavailability and toxicity of the organic toxicants. Nevertheless, the combined toxicity of NPs and the pesticides that were used world-widely still remains unclear. Cypermethrin (CYP), a synthetic pyrethroid insecticide, is commonly used for controlling agricultural and indoor pests. Therefore, the effects of titanium dioxide NPs (nTiO₂) on CYP bioconcentration and its effects on the neuronal development in zebrafish were investigated in our study. Zebrafish embryos (2-hour-post-fertilization, hpf) were exposed to CYP (0, 0.4, 2 and 10µg/L) alone or co-exposed with nTiO₂ (1mg/L) until 120-hpf. nTiO₂ is taken up by zebrafish larvae and also it can adsorb CYP. The zebrafish body burdens of CYP was observed and CYP uptake was increased by nTiO₂, indicating that the nTiO₂ could accelerate the bioaccumulation of CYP in larvae. Co-exposure of nTiO₂ and CYP induced the generation of reactive oxygen species. Exposure to CYP alone significantly decreased the mRNA expression of genes, including glial fibrillary acidic protein (gfap), alpha1-tubulin, myelin basic protein (mbp) and growth associated protein (gap-43). Besides, reductions of serotonin, dopamine and GABA concentrations were observed in zebrafish and the larval locomotion was significantly decreased in response to the lower level of the neurotransmitters. Moreover, co-exposure of nTiO₂ and CYP caused further significantly decreased in the locomotion activity, and enhanced the down-regulation of the mRNA expression of specific genes and the neurotransmitters levels. The results demonstrated that nTiO₂ increased CYP accumulation and enhanced CYP-induced developmental neurotoxicity in zebrafish.

Li, V. W., Tsui, M. P., Chen, X., Hui, M. N., Jin, L., Lam, R. H., . . . Cheng, S. H. (2016). Effects of 4-Methylbenzylidene Camphor (4-MBC) on Neuronal and Muscular Development in Zebrafish (*Danio Rerio*) Embryos. *Environmental Science and Pollution Research*, 23(9), 8275-8285 <https://doi.org/10.1007/s11356-016-6180-9>

The negative effects of overexposure to ultraviolet (UV) radiation in humans, including sunburn and light-induced cellular injury, are of increasing public concern. 4-Methylbenzylidene camphor (4-MBC), an organic chemical UV filter, is an active ingredient in sunscreen products. To date, little information is available about its neurotoxicity during early vertebrate development. Zebrafish embryos were exposed to various concentrations of 4-MBC in embryo medium for 3 days. In this study, a high concentration of 4-MBC, which is not being expected at the current environmental concentrations in the environment,

was used for the purpose of phenotypic screening. Embryos exposed to 15 μM of 4-MBC displayed abnormal axial curvature and exhibited impaired motility. Exposure effects were found to be greatest during the segmentation period, when somite formation and innervation occur. Immunostaining of the muscle and axon markers F59, znp1, and zn5 revealed that 4-MBC exposure leads to a disorganized pattern of slow muscle fibers and axon pathfinding errors during the innervation of both primary and secondary motor neurons. Our results also showed reduction in AChE activity upon 4-MBC exposure both in vivo in the embryos (15 μM) and in vitro in mammalian Neuro-2A cells (0.1 μM), providing a possible mechanism for 4-MBC-induced muscular and neuronal defects. Taken together, our results have shown that 4-MBC is a teratogen and influences muscular and neuronal development, which may result in developmental defects.

Liang, X., Li, J., Martyniuk, C. J., Wang, J., Mao, Y., Lu, H., & Zha, J. (2017). Benzotriazole Ultraviolet Stabilizers Alter the Expression of the Thyroid Hormone Pathway in Zebrafish (*Danio rerio*) Embryos. *Chemosphere*, 182, 22-30 <https://doi.org/10.1016/j.chemosphere.2017.05.015>

Benzotriazole ultraviolet stabilizers (BUVSs) are widely used in industrial products as well as personal-hygiene products to protect the material or skin from harmful UV-radiation. Due to their persistence and bioaccumulation, BUVSs have been ubiquitously detected in aquatic environments. Although the toxicological effects of BUVSs in aquatic organisms have been previously examined, the effects of BUVSs on the thyroid system have not been adequately addressed. In this study, we assessed putative thyroid disrupting effects of BUVSs (UV-234, UV-326, UV-329 and UV-P) in zebrafish embryos at 1, 10 and 100 $\mu\text{g/L}$ for 96 h. The heart rate was assessed in zebrafish and was observed to be decreased by 6.9%-21.4% in exposure of tested BUVSs. We also observed that the transcript levels of HPT axis-related genes were affected by the 4 BUVSs tested in different ways. Specifically, mRNA levels of thyroid hormone receptors (*thraa* and *thrb*) in zebrafish embryos were differentially expressed and the direction of change in these transcripts was isoform and BUVSs dependent. Pathway analysis of the targeted genes measured indicated that cellular processes putatively affected by BUVSs included response to organic substance, regulation of transcription from RNA polymerase II promoter, intracellular receptor signaling pathway, and hypothyroidism. Upon expansion of the network, novel genes involved in this predicted gene network may provide insight into the mechanisms of thyroid disrupting mechanisms of BUVSs. Taken together, our results indicate that BUVSs can potentially impact the thyroid system, and that this is dependent upon the type or structure of BUVSs.

Liu, H., Sun, P., Liu, H., Yang, S., Wang, L., & Wang, Z. (2015). Acute Toxicity of Benzophenone-Type UV Filters for *Photobacterium phosphoreum* and *Daphnia magna*: QSAR Analysis, Interspecies Relationship and Integrated Assessment. *Chemosphere*, 135, 182-188 <https://doi.org/10.1016/j.chemosphere.2015.04.036>

The hazardous potential of benzophenone (BP)-type UV filters is becoming an issue of great concern due to the wide application of these compounds in many personal care products. In the present study, the toxicities of BPs to *Photobacterium phosphoreum* and *Daphnia magna* were determined. Next, density functional theory (DFT) and comparative molecular field analysis (CoMFA) descriptors were used to obtain more detailed insight into the structure - activity relationships and to preliminarily discuss the toxicity mechanism. Additionally, the sensitivities of the two organisms to BPs and the interspecies toxicity relationship were compared. Moreover, an approach for providing a global index of the environmental risk of BPs to aquatic organisms is proposed. The results demonstrated that the mechanism underlying the toxicity of BPs to *P. phosphoreum* is primarily related to their electronic

properties, and the mechanism of toxicity to *D. magna* is hydrophobicity. Additionally, *D. magna* was more sensitive than *P. phosphoreum* to most of the BPs, with the exceptions of the polyhydric BPs. Moreover, comparisons with published data revealed a high interspecies correlation coefficient among the experimental toxicity values for *D. magna* and *Dugesia japonica*. Furthermore, hydrophobicity was also found to be the most important descriptor of integrated toxicity. This investigation will provide insight into the toxicity mechanisms and useful information for assessing the potential ecological risk of BP-type UV filters.

Lorigo, M., Mariana, M., & Cairrao, E. (2018). Photoprotection of Ultraviolet-B Filters: Updated Review of Endocrine Disrupting Properties. *Steroids*, 131, 46-58
<https://doi.org/10.1016/j.steroids.2018.01.006>

The Ultraviolet (UV) radiation is emitted by the sun and is part of the electromagnetic spectrum. There are three types of UV rays (UV-A, UV-B and UV-C), however only UV-A and UV-B have biologic effects in humans, with UV-B radiation being primarily responsible for these effects. Among the measures of photoprotection advised by the health authorities, the topical application of sunscreens (containing UV-B filters) is the preferred worldwide. Currently, octylmethoxycinnamate (OMC) is the most commonly used UV-B filter in sunscreens. Their application has proven to be effective in preventing burns, but its efficiency against melanoma continues under intense controversy. Studies have shown that OMC behaves like an endocrine disruptor, altering the normal functioning of organisms. However, few studies have evaluated their multiple hormonal activities. Some studies suggest that the OMC exerts an estrogenic, anti-androgenic, anti-progestenic and anti-thyroid activity. But, through what mechanisms? In humans, few studies were performed, and some questions remain unclear. Thus, the purpose of this review is to present the multiple hormonal activities established for the OMC, making a critical analysis and relationship between the effects in cells, animals and humans.

Lorigo, M., Quintaneiro, C., Lemos, M. C., Martinez-de-Oliveira, J., Breitenfeld, L., & Cairrao, E. (2019). UV-B Filter Octylmethoxycinnamate Induces Vasorelaxation by Ca²⁺ Channel Inhibition and Guanylyl Cyclase Activation in Human Umbilical Arteries. *International Journal of Molecular Sciences*, 20(6) <https://doi.org/10.3390/ijms20061376>

Ultraviolet (UV) filters are chemicals widely used in personal care products (PCPs). Due to their effect as endocrine disruptor compounds (EDCs), the toxicity of UV filters is a current concern for human health. EDC exposure may be correlated to cardiovascular diseases (CVD), but to our knowledge, no studies assessed the UV filters effects as human EDCs at the vascular level. Octylmethoxycinnamate (OMC) is the world's most widely used UV-B filter, present in more than 90% of PCPs. Due to its demonstrated multiple hormonal activities in animal models, this substance is also suspected to be a human EDC. The purpose of this study was to assess the rapid/short-term effects of OMC on arterial tonus and analyse its mode of action (MOA). Using human umbilical arteries, the endocrine effects of OMC were evaluated in *in vitro* (cellular and organ) experiments by planar cell surface area (PCSA) and organ bath, respectively. Our data show that OMC induces a rapid/short-term smooth muscle relaxation acting through an endothelium-independent MOA, which seems to be shared with oestrogens, involving an activation of soluble guanylyl cyclase (sGC) that increases the cyclic guanosine monophosphate (cGMP) intracellular levels and an inhibition of L-type voltage-operated Ca²⁺ channels (L-Type VOCC).

Louro, H., Saruga, A., Santos, J., Pinhao, M., & Silva, M. J. (2019). Biological Impact of Metal Nanomaterials in Relation to Their Physicochemical Characteristics. *Toxicology in Vitro*, 56, 172-183 <https://doi.org/10.1016/j.tiv.2019.01.018>

To contribute to the comprehensive investigation of the toxicological effects of metallic NMs, we have used cytotoxicity and genotoxicity assessment in human respiratory cells with a two-fold purpose: i) to compare the genotoxicity of cerium, barium and titanium benchmark NMs in an alveolar cell line and ii) to correlate the effects observed for a set of nanosized TiO₂ with their physicochemical characteristics. Human alveolar epithelial cells, A549 cells, were selected as in vitro model to exploit respiratory effects of those NMs because they have been described to retain the endocytic ability of the pulmonary epithelium and the localization of cytochrome P450 systems, providing a type II pulmonary epithelial cell model (Foster et al., 1998).

Lu, G., Zhou, R. R., Li, S., Dang, T. J., & Liu, J. C. (2018). Bioaccumulation and Biomagnification of 2-Ethylhexyl-4-Dimethylaminobenzoate in Aquatic Animals. *International Journal of Environmental Research and Public Health*, 15(11), 11 <https://doi.org/10.3390/ijerph15112395>

2-Ethylhexyl-4-dimethylaminobenzoate (EHDAB) is a commonly used organic ultraviolet filter. The bioaccumulation and biomagnification of EHDAB were investigated in two aquatic animals, the larvae of midge (*Chironomus riparius*) and crucian carp (*Carassius carassius*), and the metabolic enzyme responses in fish liver were determined. EHDAB in the larvae of midge reached a steady state within 10 days of sediment exposure. The biota-sediment accumulation factors ranged from 0.10 to 0.54, and were inversely proportional to the exposure concentrations. The EHDAB-contaminated larvae were used to feed the crucian carp. Within 28 days of feeding exposure, the EHDAB levels in fish tissues gradually increased with the increase of the exposure concentration, exhibiting an apparent concentration-dependence and time-dependence. The liver and kidneys were the main organs of accumulation, and the biomagnification factors of EHDAB ranged from 8.97 to 11.0 and 6.44 to 10.8, respectively. In addition, EHDAB significantly increased the activities of cytochrome P450 (CYP) 1A, CYP3A and glutathione S-transferase in the fish liver. Our results indicate that EHDAB may pose a risk of biomagnification in an aquatic environment and influence the biological processes of exposed organisms.

Ma, B., Lu, G., Liu, J., Yan, Z., Yang, H., & Pan, T. (2017). Bioconcentration and Multi-Biomarkers of Organic UV Filters (BM-DBM and OD-PABA) in Crucian Carp. *Ecotoxicology and Environmental Safety*, 141, 178-187 <https://doi.org/10.1016/j.ecoenv.2017.03.034>

Organic UV filters (OUV-Fs) are increasingly used in sunscreens and personal care products. In the present work, the bioconcentration and multi-biomarker effects of butyl methoxydibenzoylmethane (BM-DBM) and ethylhexyl dimethyl p-aminobenzoate (OD-PABA) were investigated in crucian carp (*Carassius auratus*). The fish were exposed to various concentrations of BM-DBM (3.88, 35.61, 181.85 and 337.15µg/L), OD-PABA (4.66, 53.83, 264.22 and 459.32µg/L) and their mixture (2.31+2.79, 23.69+26.18, 97.37+134.81 and 193.93+246.08µg/L) for 28 days. The maximal concentrations of two OUV-Fs were detected in the fish liver, followed by the brain, kidney, gill and muscle in most cases. The maximal BCF values of OD-PABA calculated in various exposure concentrations were 0.37 - 101.21 in single exposure groups and 0.11 - 31.09 in mixed exposure groups. Acetylcholinesterase (AChE) activity was significantly inhibited by BM-DBM as well as the mixtures at all of the exposure concentrations and by OD-PABA at higher concentrations ($\geq 264.22\mu\text{g/L}$) during 28 days of exposure. The maximal inhibition rates of AChE activity reached 64.04% for BM-DBM, 41.05% for OD-PABA and 61.50% for the

mixtures at the highest concentration, which indicated that these two OUV-Fs might damage the central nervous system. Concerning oxidative stress status, BM-DBM and the mixtures significantly increased superoxide dismutase (SOD) and glutathione reductase (GR) activities and inhibited catalase (CAT) activity, while OD-PABA caused a significant increase of GR and CAT activities. AChE and GR activities seemed to be more sensitive biomarkers for BM-DBM and OD-PABA.

Manivannan, J., Banerjee, R., & Mukherjee, A. (2019). Genotoxicity Analysis of Rutile Titanium Dioxide Nanoparticles in Mice after 28 days of Repeated Oral Administration. *The Nucleus* <https://doi.org/10.1007/s13237-019-00277-0>

Titanium dioxide (TiO₂) or titania has demonstrated excellent potential for commercial use in various arenas, such as in the paint, in pharmaceuticals and food industry. However information on the genotoxic potential of rutile form of TiO₂-NP after repeated (28 days) low dose oral exposure in major organs of the reticuloendothelial system (liver, spleen, bone marrow, lymph nodes) is not known. In this study Swiss albino male mice were gavaged TiO₂-NP at sub-acute concentration (0.2, 0.4 and 0.8 mg/kg body weight) over a period of 28 days. Results revealed that TiO₂-NP administered was of rutile form with mean average size of 25 nm by transmission electron microscopy. The values of PDI and Zeta potential from DLS of TiO₂-NP in suspension specified that the nanomaterial was stable without much agglomeration. Chromosomal aberration assay showed that TiO₂-NP was genotoxic and cytotoxic. DNA damage evaluation by comet assay confirmed that long term exposure to TiO₂-NP at low concentrations can induce genotoxicity systemically in organs, such as liver, spleen, and thymus cells. Structural chromosomal aberration test from bone marrow cells revealed the clastogenicity of TiO₂-NP at sub chronic low concentrations. Further in vivo studies are needed to elucidate the underlying mechanisms at the molecular level.

Manová, E., von Goetz, N., & Hungerbuehler, K. (2015). Aggregate Consumer Exposure to Uv Filter Ethylhexyl Methoxycinnamate Via Personal Care Products. *Environment International*, 74, 249-257 <https://doi.org/10.1016/j.envint.2014.09.008>

Ultraviolet (UV) filters are substances designed to protect our skin from UV-induced damage and can be found in many categories of personal care products (PCPs). The potential endocrine-disrupting effects attributed to UV filter ethylhexyl methoxycinnamate (EHMC) are being debated. We evaluated the aggregate exposure of the Swiss-German population (N=1196; ages ≤1–97years) to EHMC via the use of PCPs; thus we provide the first comprehensive information about the current EHMC exposure sources and aggregate exposure levels. In our probabilistic modeling method performed at an individual level, PCP use data obtained by a postal questionnaire were linked to concentration data on EHMC gained from chemical analyses of PCPs used by the questionnaire respondents. The modeled median and 99.9th percentile of the internal aggregate exposure for the general population were 0.012 and 0.873mgday⁻¹kg⁻¹ and 0.008 and 0.122mgday⁻¹kg⁻¹ for the summer/autumn and winter/spring period, respectively. The major contributors to internal aggregate exposure were sunscreen products in summer/autumn (females: 64%; males: 85%; children aged ≤12years 93%). In winter/spring, lip care dominated for females (30%) and sunscreen for males (38%) and children aged ≤12years (50%). Overall, the internal aggregate exposure estimates for the studied population are shown to be below the Derived No Effect Level (DNEL) for EHMC i.e., the level of exposure above which humans should not be exposed; however, when an intense short-term exposure via sunscreen is accounted for during a sunbathing day, at the high-end percentiles (99.9th) the predicted aggregate exposure exceeds the DNEL for thyroid-disrupting effects such as for children aged ≤4years, who might be particularly

susceptible to endocrine disrupting events. It is nevertheless critical to acknowledge that quantitative data on transdermal penetration of EHMC from PCPs are currently insufficient. Since long-term effects of endocrine disruptors are not known, future studies are warranted to provide accurate quantitative data on transdermal penetration of EHMC and to determine its metabolic fate in humans.

Manzo, S., Schiavo, S., Oliviero, M., Toscano, A., Ciaravolo, M., & Cirino, P. (2017). Immune and Reproductive System Impairment in Adult Sea Urchin Exposed to Nanosized ZnO Via Food. *Science of The Total Environment*, 599-600, 9-13
<https://doi.org/10.1016/j.scitotenv.2017.04.173>

In marine environment the release and the consequent sedimentation of ZnO NPs, mainly used in sunscreens, could provoke toxic effects in particular in grazer organisms, like sea urchins. In this work, a first evaluation of DNA and cellular effects on adult sea urchins *Paracentrotus lividus* exposed through the diet to different sizes (100 and 14nm) ZnO NPs, was performed. Moreover, the consequent impact upon offspring quality was evaluated. Preliminary results showed that the assumption of food containing ZnO NPs 100nm provoked in adult echinoids damages to immune cells (33% of damaged nucleus) and transmissible effects to offspring (75.5% of malformed larvae). Instead food with ZnO NPs 14nm provoked 64% of damaged nucleus in immune cells and 84.7% of malformed larvae.

Mao, F., He, Y., & Gin, K. Y. (2018). Evaluating the Joint Toxicity of Two Benzophenone-Type UV Filters on the Green Alga *Chlamydomonas Reinhardtii* with Response Surface Methodology. *Toxics*, 6(1)
<https://doi.org/10.3390/toxics6010008>

The widespread occurrence of benzophenone-type ultraviolet (UV) filter has raised the public concerns over the ecotoxicological effects of these chemicals. The present study assessed the joint toxicity of two representative benzophenones, benzophenone-1 (BP-1) and benzophenone-3 (BP-3), on the green alga *Chlamydomonas reinhardtii* using response surface methodologies (RSM). Specific growth rate and photosynthetic pigments were used as endpoints to evaluate the toxic effects. Generally, exposure to the combined BP-1 and BP-3 negatively affected cell growth and pigments production, with higher inhibitions at higher exposure concentrations. The simultaneous reduction in growth rate and pigments contents indicated that BP-1 and BP-3 regulated the growth of the tested alga by affecting the photosynthesis process. Results also showed that second order polynomial regression models fitted well with experimental results for all endpoints. The obtained regression models further indicated that the effects of the combination stemmed significantly from the linear concentration of BP-1 and BP-3. The overall results demonstrated that RSM could be a useful tool in ecotoxicological studies.

Mao, F., He, Y., Kushmaro, A., & Gin, K. Y. (2017). Effects of Benzophenone-3 on the Green Alga *Chlamydomonas Reinhardtii* and the Cyanobacterium *Microcystis Aeruginosa*. *Aquatic Toxicology*, 193, 1-8 <https://doi.org/10.1016/j.aquatox.2017.09.029>

Effects of benzophenone-3 (BP-3) on the green alga, *Chlamydomonas reinhardtii*, and the cyanobacterium, *Microcystis aeruginosa*, were investigated. The tested organisms were exposed to environmental levels of BP-3 for 10 days, at nominal concentrations from 0.01 to 5000µg/L(-1). Specific growth rate and photosynthetic pigments were employed to evaluate the toxic responses. The two tested algae had distinct toxic responses towards BP-3 stress, with the green alga *C. reinhardtii* being more sensitive than the cyanobacterium *M. aeruginosa*, based on EC20 and EC50 values. Uptake of BP-3 from the medium occurred in both species, with *M. aeruginosa* showing greater overall uptake (27.2-

77.4%) compared to *C. reinhardtii* (1.1-58.4%). The effects of BP-3 on *C. reinhardtii* were variable at concentrations lower than 100µg/L(-1). At higher concentrations, the specific growth rate of *C. reinhardtii* decreased following a reduction in chlorophyll a (chl-a) content. Further experiments showed that BP-3 regulated the growth of *C. reinhardtii* by affecting the production of chl-a, chlorophyll b and carotenoids. In *M. aeruginosa*, specific growth rate was only moderately affected by BP-3. Additionally, the production of chl-a was significantly inhibited over the different exposure concentrations, while the production of carotenoids was stimulated. These results indicate a potential detrimental effect on prokaryotes and eukaryotes and that the mechanism of action varies with species.

Mao, Z., Guan, Y., Li, T., Zhang, L., Liu, M., Xing, B., . . . Chen, M. (2019). Up Regulation of miR-96-5p Is Responsible for TiO₂ NPs Induced Invasion Dysfunction of Human Trophoblastic Cells Via Disturbing Ezrin Mediated Cytoskeletons Arrangement. *Biomedicine & Pharmacotherapy*, 117, 109125 <https://doi.org/10.1016/j.biopha.2019.109125>

Titanium dioxide nanoparticles (TiO₂ NPs) are used extensively in our daily lives, and their toxic effects on the placenta have been reported. Animal studies indicated that placental development is impaired after maternal exposure of TiO₂ NPs, but the underlying mechanisms remain largely unknown. In the present study, we used a human trophoblast-derived cell, HTR8-SVneo, to determine how TiO₂ NPs affected placental functions, and found out potential reversal targets. TEM was employed for TiO₂ NPs morphology observation and uptake assessment. RT-PCR was used to detect the expression of both mRNA and miRNA, and western blotting was used for protein examination. Cell invasion ability was evaluated by Transwell assay, and cytoskeletons were observed by immunofluorescence combined with confocal microscope examination. We found that TiO₂ NPs disrupted cytoskeletons and impaired cell invasion ability. Further investigations showed that TiO₂ NPs increased the expression of a microRNA (miR-96-5p), which targeted and down-regulated the translation of EZR mRNA, a gene that encodes ezrin protein, and affected the cell cytoskeletons and ultimately cell invasion ability. When the expression of miR-96-5p was down-regulated, the expression level of ezrin protein was also reversed, and cell invasion ability was partially restored. Collectively, we determined how miR-96-5p mediates TiO₂ NP-induced placental dysfunction, and provided a potential rescue target for future therapy.

Martinez-Guitarte, J. L. (2018). Transcriptional Activity of Detoxification Genes Is Altered by Ultraviolet Filters in *Chironomus Riparius*. *Ecotoxicology and Environmental Safety*, 149, 64-71 <https://doi.org/10.1016/j.ecoenv.2017.11.017>

Ultraviolet (UV) filters are compounds used to prevent the damage produced by UV radiation in personal care products, plastics, etc. They have been associated with endocrine disruption, showing anti-estrogen activity in vertebrates and altering the ecdysone pathway in invertebrates. Although they have attracted the attention of multiple research teams there is a lack of data about how animals activate detoxification systems, especially in invertebrates. Here, analysis of the effects of two UV filters, benzophenone-3 (BP3) and 4-methylbenzylidene camphor (4MBC), on the transcriptional activity of nine genes covering the three steps of the detoxification process has been performed. Four cytochrome P450 genes belonging to different members of this family, five GST genes, and the multidrug resistance protein 1 (MRP1) gene were studied by RT-PCR to analyze their transcriptional activity in fourth instar larvae exposed to the UV filters for 8 and 24h. The obtained results show a differential response with downregulation of the different Cyp450s tested by 4MBC while BP3 seems not to modify their expression. On the other hand, some of the GST genes were affected by one or other of the filters, showing a less homogenous response. Finally, MRP1 was activated by both filters but at different times.

These results demonstrate for first time that UV filters alter the expression of genes involved in the different steps of the detoxification process and that they can be processed by phase I enzymes other than Cyp450s. They also suggest that UV filters affect biotransformation processes, compromising the ability of the individual to respond to chemical stress, so further research is needed to know the extent of the damage that they can produce in the resistance of the cell to chemicals.

Matouke, M. M., Elewa, D. T., & Abdullahi, K. (2018). Binary Effect of Titanium Dioxide Nanoparticles (nTiO₂) and Phosphorus on Microalgae (*Chlorella 'Ellipsoides* Gerneck, 1907). *Aquatic Toxicology*, 198, 40-48 <https://doi.org/10.1016/j.aquatox.2018.02.009>

The wide application of titanium dioxide nanoparticles and phosphorus in the manufacturing of many industrial products mainly used in agricultural sector has resulted in the release of considerable amounts of these compounds into freshwater aquatic ecosystem. These compounds may cause some unexpected effects to aquatic organisms. This study assessed the binary effects of Titanium nanoparticles (nTiO₂) and Phosphorus on *Chlorella ellipsoides*. Toxicological assay test of the compounds nTiO₂ (1.25µM) alone and the combination of Titanium dioxide (1.25µM) and Phosphorus (16, 32, 80, 160, 240µM) was assessed, after 96h exposures, for optical density (OD₆₈₀), specific growth rate, chlorophyll levels and lipid peroxidation via Malondialdehyde (MDA) activity. Superoxide dismutase (SOD), peroxidase (POD) and glutathione-s-transferase (GST) activities were also measured. Two-way ANOVA showed a significant interaction (P<0.05) between binary mixture. Co-exposure showed a decreased phosphorus bioconcentration in the microalgae with significant increase (P<0.05) in chlorophyll a/b and total chlorophyll contents. A significant decrease (P<0.05) in specific growth rate and optical density were recorded whereas, antioxidant enzymes (MDA, SOD, POD, GST) activities were significantly (P<0.05) increased. These results showed that the addition of nTiO₂ to Phosphorus affected the physiology of microalgae and should be of great concern for freshwater biodiversity.

Matouskova, K., Jerry, D. J., & Vandenberg, L. N. (2018). Exposure to Oxybenzone During the Perinatal Period Disrupts Development of the Male and Female Mouse Mammary Gland. *Reproductive Toxicology*, 80, 154 <https://doi.org/10.1016/j.reprotox.2018.07.060>

Introduction: The mammary gland is a structurally dynamic organ, with distinct growth and differentiation observed during five periods of life: embryonic development, puberty, pregnancy, lactation, and involution. Because of these periods are associated with rapid changes in proliferation, differentiation, and gene expression, it has been hypothesized that each stage is uniquely sensitive to environmental insults. Development of the mammary gland occurs under the influence of sex hormones, prolactin and growth hormones, and has been shown to be sensitive to compounds capable of mimicking those hormones as well as chemicals that interfere with their receptors (e.g. endocrine disrupting chemicals) In mice, growth of the gland is comparable in both sexes prior to embryonic day 13, and dissimilar towards the end of fetal period and postnatally. One compound that has recently received attention is oxybenzone (benzophenone 3, BP-3). a chemical absorbing UVA and UVB radiation that is widely used in personal care products, inks and plastic packaging. BP- 3 is a suspect endocrine disrupting chemical with estrogenic, antiestrogenic and antiandrogenic properties, and may mimic progesterone. Methods: In our study, we exposed Balb/c mice to three different, low doses of BP-3 in utero and during the perinatal period and quantified growth parameters in the mammary glands of male and female pups at three stages of life: prior to the onset of puberty, at the height of puberty, and in adulthood. Results: We found that male mice exposed to low doses of BP-3 during perinatal

development showed significant reduction in the area of mammary gland epithelium and the number of branching points, and exhibited lower potential for ductal extension and growth at the pre-pubertal age. In contrast, female mice displayed increased ductal extension at puberty. Conclusion: Our results are consistent with a strong potential of BP-3 altering normal mammary gland growth and development in both sexes of mice. Future studies will evaluate other endpoints including expression of hormone receptors, markers of proliferation, and hormone-dependent gene expression.

McCoshum, S. M., Schlarb, A. M., & Baum, K. A. (2016). Direct and Indirect Effects of Sunscreen Exposure for Reef Biota. *Hydrobiologia*, 776(1), 139-146 <https://doi.org/10.1007/s10750-016-2746-2>

Coral reefs are ecologically and economically important, contributing to both fishing and ecotourism economies around the world. Tourism and recreational activities have increased in coastal areas and so has the use of sunscreen. Sunscreen reduces human exposure to harmful UV rays, but washes off during aquatic recreational activities, which may negatively affect reef biota. To evaluate how sunscreen affects coral reef ecosystems, we added sunscreen at concentrations similar to previous studies to growing environments containing flatworms (*Convolutriloba macropyga*) with symbiotic algae, photosynthetic diatoms (*Nitzschia* sp.), Aiptasia anemones, and pulse corals (*Xenia* sp.). Using behavioral observations and estimates of population and colony growth, we show nominal concentrations of sunscreen negatively affect all of the studied species. Furthermore, we show that mobile flatworms do not avoid water which contains sunscreen and flatworms exposed to sunscreen prefer darker conditions. Based on our results, beachgoers should limit use of sunscreens when near coral reefs and consider alternative protective measures, such as the utilization of sun-protective clothing.

Minguez-Alarcon, L., Chiu, Y. H., Nassan, F. L., Williams, P. L., Petrozza, J., Ford, J. B., . . . Earth Study, T. (2019). Urinary Concentrations of Benzophenone-3 and Reproductive Outcomes among Women Undergoing Infertility Treatment with Assisted Reproductive Technologies. *Science of The Total Environment*, 678, 390-398 <https://doi.org/10.1016/j.scitotenv.2019.04.452>

Benzophenone-3 is used in a variety of cosmetic products as a sunscreen, and has shown weak estrogenic and antiandrogenic activity in animal and in vitro studies. Few studies have evaluated whether benzophenone-3 is associated with reproductive outcomes among women. We studied 304 women undergoing infertility treatment (2007-2017) in the prospective Environment and Reproductive Health cohort study and who underwent 449 treatment cycles (n=788 urines). Generalized linear mixed models were used with random intercepts to account for multiple cycles, and adjusting for confounders including physical activity. Analyses were also stratified by self-reported moderate/heavy outdoor work. The cycle-specific median (IQR) urinary benzophenone-3 concentration was 147 (58, 462) µg/L, and 98% samples had detectable concentrations. Self-reported sunscreen use, physical activity, and time spent on moderate/heavy outdoor work were positively associated with urinary benzophenone-3. Adjusted probabilities of implantation, clinical pregnancy and live birth were higher in increasing quartiles of benzophenone-3, but these associations were restricted to women who reported spending time outdoors performing moderate/heavy work. Specifically, among these women, those in the highest quartile of benzophenone-3 concentrations had 51% higher implantation (p,trend=0.02), 68% higher clinical pregnancy (p,trend=0.01) and 75% higher live birth (p,trend=0.02) adjusted probabilities than women in the lowest quartile. Benzophenone-3 was unrelated to these outcomes among women who did not report doing moderate/heavy work outdoors. These results confirm that sunscreen use is a source of benzophenone-3 exposure, and show positive associations between benzophenone-3 and

pregnancy outcomes, especially among women who reported engaging in outdoor work. Since these associations may be subject to important residual confounding by lifestyle factors, further research is needed to confirm these novel results in other populations, and to investigate whether other factors may be affecting the relation of benzophenone-3 with fertility and other health outcomes.

Molina-Molina, J.-M., Escande, A., Pillon, A., Gomez, E., Pakdel, F., Cavaillès, V., . . . Balaguer, P. (2008). Profiling of Benzophenone Derivatives Using Fish and Human Estrogen Receptor-Specific *In Vitro* Bioassays. *Toxicology and Applied Pharmacology*, 232(3), 384-395
<https://doi.org/10.1016/j.taap.2008.07.017>

Benzophenone (BP) derivatives, BP1 (2,4-dihydroxybenzophenone), BP2 (2,2',4,4'-tetrahydroxybenzophenone), BP3 (2-hydroxy-4-methoxybenzophenone), and THB (2,4,4'-trihydroxybenzophenone) are UV-absorbing chemicals widely used in pharmaceutical, cosmetics, and industrial applications, such as topical sunscreens in lotions and hair sprays to protect skin and hair from UV irradiation. Studies on their endocrine disrupting properties have mostly focused on their interaction with human estrogen receptor alpha (hER α), and there has been no comprehensive analysis of their potency in a system allowing comparison between hER α and hER β activities. The objective of this study was to provide a comprehensive ER activation profile of BP derivatives using ER from human and fish origin in a battery of in vitro tests, i.e., competitive binding, reporter gene based assays, vitellogenin (Vtg) induction in isolated rainbow trout hepatocytes, and proliferation based assays. The ability to induce human androgen receptor (hAR)-mediated reporter gene expression was also examined. All BP derivatives tested except BP3 were full hER α and hER β agonists (BP2>THB>BP1) and displayed a stronger activation of hER β compared with hER α , the opposite effect to that of estradiol (E2). Unlike E2, BPs were more active in rainbow trout ER α (rtER α) than in hER α assay. All four BP derivatives showed anti-androgenic activity (THB>BP2>BP1>BP3). Overall, the observed anti-androgenic potencies of BP derivatives, together with their proposed greater effect on ER β versus ER α activation, support further investigation of their role as endocrine disrupters in humans and wildlife.

Molins-Delgado, D., Gago-Ferrero, P., Diaz-Cruz, M. S., & Barcelo, D. (2016). Single and Joint Ecotoxicity Data Estimation of Organic UV Filters and Nanomaterials toward Selected Aquatic Organisms. Urban Groundwater Risk Assessment. *Environmental Research*, 145, 126-134
<https://doi.org/10.1016/j.envres.2015.11.026>

The hazardous potential of organic UV filters (UV-Fs) is becoming an issue of great concern due to the widespread application of these compounds in most daily-use goods, such as hygiene and beauty products. Nanomaterials (NMs) have also been used in personal care products (PCPs) for many years. Nowadays, both classes of chemicals are considered environmental emerging contaminants. Despite some studies performed in vitro and in vivo reported adverse effects of many UV-Fs on the normal development of organisms, there is scarce data regarding acute and chronic toxicity. The aim of the present study was to determine the EC50 values of selected UV-Fs using standardised toxicity assays on three aquatic species i.e. *Daphnia magna*, *Raphidocelis subcapitata* and *Vibrio fischeri*. EC50 values obtained were in the mg/l(-1) range for all the species. The estimated toxicity data allowed us to assess the environmental risk posed by selected UV-Fs in urban groundwater from Barcelona (Spain). The calculated ecological risk indicated a negligible impact on the aquifer. Giving the increasing importance of studying mixtures of pollutants and due to the widespread presence of nanomaterials (NMs) in the aquatic environment, other objective of this work was to explore the response on *D. magna* after

exposure to both binary combinations of UV-Fs among them and UV-F with NMs. In all cases but the nano-silver mixtures, joint toxicity was mitigated or even eradicated.

Monteiro, R., Costa, S., Coppola, F., Freitas, R., Vale, C., & Pereira, E. (2019). Toxicity Beyond Accumulation of Titanium after Exposure of *Mytilus galloprovincialis* to Spiked Seawater. *Environmental Pollution*, 244, 845-854 <https://doi.org/10.1016/j.envpol.2018.10.035>

Mytilus galloprovincialis was exposed to seawater spiked with 5, 50 and 100µg/L of Titanium (Ti) for 14 days. Seawater was renewed after 96h and new addition of Ti was done. A parallel experiment conducted in the absence of mussels showed that during the first 24h after spiking, Ti concentrations in seawater rapidly decreased to values below 2µg/L. For this reason, along the entire experimental period (14 days) mussels were exposed to Ti during two short periods, in the beginning of the experiment and after seawater renewal. At 96h, mussels exhibited low Ti concentrations (<2.5µg/g), close or not significantly different from a control condition (1.6µg/g) in the absence of Ti). Despite the low accumulated Ti in mussels' tissues after both experimental periods (96h and 14 days), biochemical markers indicated that mussels developed two main strategies: reduction of their metabolic capacity to avoid the uptake of Ti, and antioxidant and biotransformation defense mechanisms, such as the activation of SOD, CAT, GPx and GSTs enzymes that were triggered to prevent cellular damages. Nevertheless, oxidative stress occurred after 96h or 14 days. The current study highlights that alterations of biological activity of *M. galloprovincialis* exposed to Ti goes beyond its accumulation in tissues.

Morohoshi, K., Yamamoto, H., Kamata, R., Shiraishi, F., Koda, T., & Morita, M. (2005). Estrogenic Activity of 37 Components of Commercial Sunscreen Lotions Evaluated by *In Vitro* Assays. *Toxicology in Vitro*, 19(4), 457-469 <https://doi.org/10.1016/j.tiv.2005.01.004>

Thirty-seven chemical components of commercial sunscreen lotions were evaluated for estrogen agonistic and/or antagonistic activity using two in vitro assays, (1) an ELISA-based estrogen receptor competitive binding assay (ER-ELISA) and (2) a modified yeast two-hybrid estrogen assay, with and without addition of a rat liver preparation, S9 mix. Eleven compounds, most of which were benzophenone derivatives and parabens, showed binding affinity to ER by ER-ELISA without S9 mix. Although the activities of almost all of the compounds were attenuated by addition of S9 mix, 4-octylphenylsalicylate and 2,2'-dihydroxy-4,4'-dimethoxybenzophenone acquired estrogenic activity, suggesting metabolic activation of these compounds. Two benzophenones showed agonistic activity in the yeast two-hybrid assay without S9 mix. The activity of one of these was reduced by S9 treatment and a further two benzophenones was activated. Eight parabens were active in this assay without S9 exposure, but their activities were eliminated by S9 treatment. Benzophenones with para-phenolic hydroxyl groups and parabens with branched and/or longer linear chains were generally more potent in both bioassays. In addition, weak antagonistic activity of 4-t-butylphenyl-salicylate, 2-ethylhexyl 4-dimethylaminobenzoate and (+/-)-alpha-tocopherolacetate was observed with S9 treatment. In vivo testing of the compounds reported here to have estrogen agonistic and antagonistic activities is required to confirm their effects at an organismal level.

Nakamura, N., Vijay, V., Desai, V. G., Hansen, D. K., Han, T., Chang, C. W., . . . Inselman, A. L. (2018). Transcript Profiling in the Testes and Prostates of Postnatal Day 30 Sprague-Dawley Rats Exposed Prenatally and Lactationally to 2-Hydroxy-4-Methoxybenzophenone. *Reproductive Toxicology*, 82, 111-123 <https://doi.org/10.1016/j.reprotox.2018.10.001>

2-hydroxy-4-methoxybenzophenone (HMB) is an ultraviolet light-absorbing compound that is used in sunscreens, cosmetics and plastics. HMB has been reported to have weak estrogenic activity by in vivo and in vitro studies, making it a chemical with potential reproductive concern. To explore if prenatal and lactational HMB exposure alters gene expression profiles of the developing reproductive organs, we performed microarray analysis using the prostate and testis of postnatal day (PND) 30 male Sprague-Dawley rats offspring exposed to 0, 3000, or 30,000 ppm of HMB from gestational day 6 through PND 21. Gene expression profiles of the prostate and testis were differentially affected by HMB dose with significant alterations observed at the 30,000 ppm HMB group. Tissue-specific gene expression was also identified. These genes, whose expression was altered by HMB exposure, may be considered as candidate biomarker(s) for testicular or prostatic toxicity; however, further studies are necessary to explore this potential.

Novo, M., Muniz-Gonzalez, A. B., Trigo, D., Casquero, S., & Martinez Guitarte, J. L. (2019). Applying Sunscreens on Earthworms: Molecular Response of *Eisenia fetida* after Direct Contact with an Organic UV Filter. *Science of The Total Environment*, 676, 97-104
<https://doi.org/10.1016/j.scitotenv.2019.04.238>

The use of organic Ultraviolet (UV) filters has increased in the last years, either in sunscreens, other cosmetics, or even food packaging. These filters may end up in soil and water since the Wastewater Treatment Plants may not successfully remove them. Among them, benzophenones are known to act as endocrine disruptors. However, most of the studies are directed towards vertebrates and aquatic invertebrates, while there is a lack of information on the molecular mechanisms affected by these compounds on soil dwelling invertebrates. Here, we study the impact of direct acute (48h) contact of 4-hydroxybenzophenone (4-OHBP) at two sublethal concentrations (0.02 and 0.2mg/mL) on gene expression of the earthworm *Eisenia fetida*. Investigated genes were involved in endocrine pathways, stress response, detoxification mechanisms, genotoxicity, energy metabolism and epigenetics. Three of them were identified for the first time in earthworms. Our results suggest that exposure to 4-OHBP affected endocrine pathways, causing an increase in the Ecdysone receptor gene (EcR) expression. Moreover, the UV filter induced changes in the CuZn superoxide dismutase gene (CuZn SOD), indicating an effect in the stress response. Finally, significant changes were detected for glyceraldehyde-3-phosphate dehydrogenase gene (GAPDH) expression, indicating that energy metabolism is influenced by the 4-OHBP and highlighting the risks of using GAPDH as an internal reference for Real Time PCR.

O'Keefe, S. J., Feltis, B. N., Piva, T. J., Turney, T. W., & Wright, P. F. (2016). ZnO Nanoparticles and Organic Chemical UV-Filters Are Equally Well Tolerated by Human Immune Cells. *Nanotoxicology*, 10(9), 1287-1296 <https://doi.org/10.1080/17435390.2016.1206148>

An important part of assessing the toxic potential of nanoparticles for specific applications should be the direct comparison of biological activities with those of alternative materials for the same application. Nanoparticulate inorganic ultraviolet (UV) filters, such as zinc oxide (ZnO), are commonly incorporated into transparent sunscreen and cosmetic formulations. However, concerns have been raised about potential unwanted effects, despite their negligible skin penetration and inherent advantages over organic chemical UV-filters. To provide useful application-relevant assessments of their potential hazard with/without UVA co-exposure, we directly compared cytotoxic and immune response profiles of human THP-1 monocytic cells to ZnO nanoparticles (30 nm) with bulk ZnO particulates (200 nm) and five conventional organic chemical UV-filters - butylmethoxydibenzoylmethane (avobenzene), octylmethoxycinnamate, octylsalicylate, homosalate and 4-methylbenzylidene camphor. High exposure

concentrations of both organic and particulate UV-filters were required to cause cytotoxicity in monocyte and macrophage cultures after 24 h. Co-exposure with UVA (6.7 J/cm²) did not alter cytotoxicity profiles. Particle surface area-based dose responses showed that ZnO NPs were better tolerated than bulk ZnO. Organic and particulate UV-filters increased apoptosis at similar doses. Only particulates increased the generation of reactive oxygen species. Interleukin-8 (IL-8) release was increased by all particulates, avobenzone, homosalate and octylsalicylate. IL-1beta release was only increased in macrophages by exposure to avobenzone and homosalate. In conclusion, direct effects were caused in monocytes and macrophages at similar concentrations of both organic UV-filters and ZnO nanoparticulates - indicating that their intrinsic cytotoxicity is similar. With their lower skin penetration, ZnO nanoparticles are expected to have lower bioactivity when used in sunscreens.

Okereke, C. S., Barat, S. A., & Abdel-Rahman, M. S. (1995). Safety Evaluation of Benzophenone-3 after Dermal Administration in Rats. *Toxicology Letters*, 80(1–3), 61-67 [https://doi.org/10.1016/0378-4274\(95\)03334-H](https://doi.org/10.1016/0378-4274(95)03334-H)

Benzophenone-3 (BZ-3) is a category 1 (over-the-counter) product approved by the US Food and Drug Administration (FDA) for use as a sunscreen agent in medicine, cosmetics, industry, and agriculture. This is due to its ability to absorb and dissipate ultraviolet light in a harmless manner, thus protecting human skin and products from UV irradiation. This study investigated the safety of BZ-3 after repeated administration. BZ-3 in ointment base was applied at a dose of 100 mg/kg body wt. twice daily, for 4 weeks to the skin of male Sprague-Dawley rats. Body weight, organ to body weight ratios, hematological, and clinical chemistry parameters were not effected. Pathological examination revealed no significant changes between control and treated animals. No gross external abnormalities were observed. Both in vivo and in vitro blood glutathione (GSH) levels were effected by BZ-3 treatment. However, after 60 min of incubation, a reversal of this effect was observed in the treatment group as blood GSH levels approached normal levels. Furthermore, investigation of GSH-reductase and peroxidase with time indicated an increase in GSH-reductase activity at 60 and 90 min with no effect on GSH-peroxidase. Pre-treatment with phenobarbital modulated the metabolic disposition of BZ-3. There was an increase in the formation of the hydroxy metabolites but not the O-dealkylated form. This study suggests that BZ-3 is not toxic to rats when applied dermally at a dose of 100 mg/kg body wt. for 4 weeks.

Oliviero, M., Schiavo, S., Dumontet, S., & Manzo, S. (2019). DNA Damages and Offspring Quality in Sea Urchin *Paracentrotus lividus* Sperms Exposed to ZnO Nanoparticles. *Science of The Total Environment*, 651(Pt 1), 756-765 <https://doi.org/10.1016/j.scitotenv.2018.09.243>

The recent advances in nanotechnology lead to a potential increase of the release of nanoparticles (NPs) into marine environment through different routes, with possible toxic effects upon the living part of this ecosystem. One of the ways of NPs marine contamination gaining today increasing concern stems from the widespread use cosmetics containing ZnO NPs as UV-filter. Although the possible adverse effects on marine organisms have been already ascertained, the information about the possible genotoxicity of ZnO NPs is still scant. In this work the spermiotoxicity of ZnO particles of different sizes (ZnO Bulk>200nm, ZnO NPs 100nm and ZnO NPs 14nm) was assessed, using *Paracentrotus lividus* spermatozoa, by evaluating the DNA damage of the exposed sperm, fertilization capability and DNA damage transmission to progeny. Our results showed that ZnO NPs induced DNA damages in spermatozoa after 30min of exposure. While the sperm fertilization capability was not affected, morphological alterations (skeletal alterations) in offspring were observed and a positive correlation

between sperm DNA damage and offspring quality was reported. This study underlines that a possible spermiotoxic action of ZnO NPs at concentration close to those reported in marine coastal water could occur.

Oliviero, M., Schiavo, S., Rametta, G., Miglietta, M. L., & Manzo, S. (2017). Different Sizes of ZnO Diversely Affected the Cytogenesis of the Sea Urchin *Paracentrotus Lividus*. *Science of The Total Environment*, 607-608, 176-183 <https://doi.org/10.1016/j.scitotenv.2017.07.038>

Today nanoparticles (NPs) have many applications in commercial products due to their small size and peculiar properties that, conversely, make them potentially toxic for humans and the environment. ZnO NPs are largely used in many personal care products, such as sunscreens and cosmetics. In this study the cytotoxic effects of ZnO particles with different sizes (ZnO Bulk, >100nm; ZnO NPs, 100nm and ZnO NPs, 14nm) upon the first developmental stages of the sea urchin *Paracentrotus lividus*, are evaluated. Morphological alterations are also assessed by embryotoxicity tests. The cytogenetic analysis highlighted that ZnO NPs interfere with cell cycle inducing a dose-dependent decrease of mitotic activity and chromosomal aberrations at higher concentrations (30µM). Moreover, the larval development was affected by ZnO NPs 100nm (EC50=0.46 [0.30-0.63] µM [Zn]) in a dose-dependent way. Size-dependent toxicity was instead not obtained for ZnO NPs. From our results could be highlighted that the presence of embryos, blocked in pre-larval stage, could be due to the induction of chromosome aberrations by ZnO particles, confirming that cytogenetic analyses allow evaluating possible NPs action mechanisms.

Ozaez, I., Aquilino, M., Morcillo, G., & Martinez-Guitarte, J. L. (2016). UV Filters Induce Transcriptional Changes of Different Hormonal Receptors in *Chironomus riparius* Embryos and Larvae. *Environmental Pollution*, 214, 239-247 <https://doi.org/10.1016/j.envpol.2016.04.023>

Organic ultraviolet (UV) filters are emerging contaminants that are ubiquitous in fresh and marine aquatic systems due to their extensive use in cosmetics, plastics, paints, textiles, and many other industrial products. The estrogenic effects of organic UV filters have been long demonstrated in vertebrates, and other hormonal activities may be altered, according to more recent reports. The impact of UV filters on the endocrine system of invertebrates is largely unknown. We have previously reported that some UV filters may affect ecdysone-related genes in the aquatic insect *Chironomus riparius*, an ecotoxicologically important model organism. To further analyze other possible effects on endocrine pathways, we first characterized four pivotal genes related with hormonal pathways in insects; thereafter, these genes were assessed for alterations in transcriptional activity after exposure to 4-methylbenzylidene camphor (4MBC) or benzophenone-3 (BP-3), two extensively used sunscreens. We found that both chemicals disturbed the expression of all four genes analyzed: hormonal receptor 38 (HR38), methoprene-tolerant (Met), membrane-associated progesterone receptor (MAPR) and insulin-like receptor (INSR), measured by changes in mRNA levels by real-time PCR. An upregulatory effect at the genomic level was detected in different developmental stages. Interestingly, embryos appeared to be more sensitive to the action of the UV filters than larvae. Our results suggest that the risk of disruption through different endocrine routes is not negligible, considering the significant effects of UV filters on key hormonal receptor and regulatory genes. Further effort is needed to develop environmental risk assessment studies on these pollutants, particularly for aquatic invertebrate model organisms.

Ozaez, I., Martínez-Guitarte, J. L., & Morcillo, G. (2013). Effects of *In Vivo* Exposure to UV Filters (4-MBC, OMC, BP-3, 4-HB, OC, OD-PABA) on Endocrine Signaling Genes in the Insect *Chironomus riparius*. *Science of The Total Environment*, 456, 120-126 <https://doi.org/10.1016/j.scitotenv.2013.03.081>

There is increasing evidence indicating that several UV filters might have endocrine disruptive effects. Numerous studies have evaluated hormonal effects in vertebrates, mainly reporting estrogenic and androgenic activities in mammals and fishes. There is only limited knowledge about potential endocrine activity in invertebrate hormonal systems. In this work, the effects on endocrine signaling genes of six frequently used UV filters were investigated in *Chironomus riparius*, a reference organism in aquatic toxicology. The UV filters studied were: octyl-p-methoxycinnamate (OMC) also called 2-ethylhexyl-4-methoxycinnamate (EHMC); 4-methylbenzylidene camphor (4-MBC); benzophenone-3 (BP-3); 4-hydroxybenzophenone (4-HB); octocrylene (OC); and octyldimethyl-p-aminobenzoate (OD-PABA). After *in vivo* exposure at different dosages, expression levels of the genes coding for the ecdysone receptor (EcR), the ultraspiracle (*usp*, ortholog of the RXR) and the estrogen-related receptor (ERR) were quantified by Real Time PCR. The EcR gene was significantly upregulated by 4-MBC, OMC/EHMC and OD-PABA, with a dose-related response following 24 h exposure. In contrast, the benzophenones, BP-3 and 4-HB, as well as OC did not alter this gene at the same exposure conditions. The transcription profiles of the *usp* and ERR genes were not significantly affected, except for BP-3 that inhibited the *usp* gene at the highest concentration. To our knowledge, this is the first experimental evidence in invertebrates of a direct effect of UV filters on endocrine-related genes, and is consistent with the known effects on vertebrate hormonal receptor genes. The capability of 4-MBC, OMC/EHMC and OD-PABA to stimulate the expression of the ecdysone receptor, a key transcription factor for the ecdysone-genomic response in arthropods, suggests the possibility of a broad and long-term effect on this hormonal pathway. These findings strengthen the need for further research about the ecotoxicological implications of chronic exposure to these compounds in aquatic invertebrates.

Ozaez, I., Martínez-Guitarte, J. L., & Morcillo, G. (2014). The UV Filter Benzophenone 3 (BP-3) Activates Hormonal Genes Mimicking the Action of Ecdysone and Alters Embryo Development in the Insect *Chironomus riparius* (Diptera). *Environmental Pollution*, 192, 19-26 <https://doi.org/10.1016/j.envpol.2014.04.038>

Numerous studies have evaluated the endocrine effects of UV filters in vertebrates, but little attention has been paid to their possible hormonal activity in invertebrates. We examined the effects of benzophenone-3 (BP-3), one of the most common sunscreen agents, in *Chironomus riparius* (Insecta), a reference organism in aquatic toxicology. Salivary glands from larvae were treated with either the hormone ecdysone or BP-3 to compare the response of endocrine genes. It was found that BP-3 elicits the same effects as the natural hormone activating the expression of a set of ecdysone responsive genes. BP-3 also activated the stress gene *hsp70*. Interestingly, similar effects have been confirmed *in vivo* in embryos. Moreover, BP-3 also altered embryogenesis delaying hatching. This is the first demonstration of hormonal activity of UV filters in invertebrates, showing a mode of action similar to ecdysteroid hormones. This finding highlights the potential endocrine disruptive effects of these emergent pollutants.

Ozaez, I., Morcillo, G., & Martínez-Guitarte, J. L. (2016). The Effects of Binary UV Filter Mixtures on the Midge *Chironomus riparius*. *Science of The Total Environment*, 556, 154-162 <https://doi.org/10.1016/j.scitotenv.2016.02.210>

Organic ultraviolet (UV) filters are used in a wide variety of products, including cosmetics, to prevent damage from UV light in tissues and industrial materials. Their extensive use has raised concerns about potential adverse effects in human health and aquatic ecosystems that accumulate these pollutants. To increase sun radiation protection, UV filters are commonly used in mixtures. Here, we studied the toxicity of binary mixtures of 4-methylbenzylidene camphor (4MBC), octyl-methoxycinnamate (OMC), and benzophenone-3 (BP-3), by evaluating the larval mortality of *Chironomus riparius*. Also molecular endpoints have been analyzed, including alterations in the expression levels of a gene related with the endocrine system (EcR, ecdysone receptor) and a gene related with the stress response (hsp70, heat shock protein 70). The results showed that the mortality caused by binary mixtures was similar to that observed for each compound alone; however, some differences in LC50 were observed between groups. Gene expression analysis showed that EcR mRNA levels increased in the presence of 0.1mg/L 4MBC but returned to normal levels after exposure to mixtures of 4MBC with 0.1, 1, and 10mg/L of BP-3 or OMC. In contrast, the hsp70 mRNA levels increased after exposure to the combinations tested of 4MBC and BP-3 or OMC mixtures. These data suggest that 4MBC, BP-3, and OMC may have antagonist effects on EcR gene transcription and a synergistic effect on hsp70 gene activation. This is the first experimental study to show the complex patterned effects of UV filter mixtures on invertebrates. The data suggest that the interactions within these chemicals mixtures are complex and show diverse effects on various endpoints.

Ozaez, I., Morcillo, G., & Martinez-Guitarte, J. L. (2016). Ultraviolet Filters Differentially Impact the Expression of Key Endocrine and Stress Genes in Embryos and Larvae of *Chironomus riparius*. *Science of The Total Environment*, 557-558, 240-247
<https://doi.org/10.1016/j.scitotenv.2016.03.078>

Several organic UV filters have hormonal activity in vertebrates, as demonstrated in fishes, rodents and human cells. Despite the accumulation of filter contaminants in aquatic systems, research on their effects on the endocrine systems of freshwaters invertebrates is scarce. In this work, the effects of five frequently used UV filters were investigated in embryos and larvae of *Chironomus riparius*, which is a reference organism in ecotoxicology. LC50 values for larvae as well as the percentage of eclosion of eggs were determined following exposures to: octyl-p-methoxycinnamate (OMC) also known as 2-ethylhexyl-4-methoxycinnamate (EHMC); 4-methylbenzylidene camphor (4MBC); 4-hydroxybenzophenone (4HB); octocrylene (OC); and octyldimethyl-p-aminobenzoate (OD-PABA). To assess sublethal effects, expression levels of the genes coding for the ecdysone receptor (EcR) and heat shock protein HSP70 were investigated as biomarkers for endocrine and stress effects at the cellular level. Life-stage-dependent sensitivity was found. In embryos, all of the UV filters provoked a significant overexpression of EcR at 24h after exposure. OC, 4MBC and OD-PABA also triggered transcriptional activation of the hsp70 stress gene in embryos. In contrast, in larvae, only 4MBC and OMC/EHMC increased EcR and hsp70 mRNA levels and OD-PABA upregulated only the EcR gene. These results revealed that embryos are particularly sensitive to UV filters, which affect endocrine regulation during development. Most UV filters also triggered the cellular stress response, and thus exhibit proteotoxic effects. The differences observed between embryos and larvae and the higher sensitivity of embryos highlight the importance of considering different life stages when evaluating the environmental risks of pollutants, particularly when analyzing endocrine effects.

Pablos, M. V., Garcia-Hortiguera, P., & Fernandez, C. (2015). Acute and Chronic Toxicity of Emerging Contaminants, Alone or in Combination, in *Chlorella vulgaris* and *Daphnia magna*.

This work presents the toxicity results of different compounds classified as emerging contaminants on primary producers and primary consumers in the aquatic compartment. The objectives were to (1) obtain acute and chronic toxicity results for algae and *Daphnia magna* using standardised or currently used tests, (2) study the relationship between the effects on the impaired feeding rate for daphnia and the effects of reproduction and (3) examine the responses on daphnia and algae after binary combinations of environmentally relevant compounds and perfluorooctane sulfonate (PFOS). Toxicity data on personal care products (PCPs), not reported in the scientific literature up to now, are presented. The results confirmed that the *Daphnia* feeding bioassay can be a sensitive, ecologically relevant endpoint to detect sublethal effects and could complement the information obtained with the reproduction test on *Daphnia*. The results also suggested that the concomitant occurrence of PFOS and other emerging contaminants in the aquatic compartment could affect the toxicity of some compounds according to their lipophilicity.

Pablos, M. V., Rodriguez, J. A., Garcia-Hortiguera, P., Fernandez, A., Beltran, E. M., Torrijos, M., & Fernandez, C. (2018). Sublethal and Chronic Effects of Reclaimed Water on Aquatic Organisms. Looking for Relationships between Physico-Chemical Characterisation and Toxic Effects. *Science of The Total Environment*, 640-641, 1537-1547 <https://doi.org/10.1016/j.scitotenv.2018.05.349>

The use of reclaimed water for irrigation and aquaculture purposes is generally considered a reliable alternative for sustainable water management in regions with water scarcity. Many organic compounds, generally called compounds of emerging concern (CECs), have been detected in reclaimed water, which implies continuous exposure for aquatic organisms. To date no quality criteria have been proposed for this group of compounds. This work aims to assess the acute, sublethal and chronic effects of reclaimed water using two representative organisms of the aquatic compartment; the green alga *Chlorella vulgaris* and the microcrustacean *Daphnia magna*. The study comprises the 72h-algal growth inhibition test, the *D. magna* feeding bioassay and the *D. magna* reproduction test. The results highlighted, for the selected characterised compounds, no differences in the concentrations between the different tertiary WWTP treatments, except for the particular case of carbamazepine. Considering seasonality, no differences were observed between the two different sample collection campaigns. The sublethal and chronic effects observed for these samples could not be explained by the lower concentrations found in the chemical characterisation. However, in the majority of cases, dilution of raw reclaimed water reduced the toxic effects of these samples. Several interactions among compounds can affect the mixture's toxicity. Canonical correlation analyses (CCA) were included to explore the potential relationships between the physico-chemical characterisation of reclaimed water and effects on aquatic organisms. The results corroborated the toxic effect of some pharmaceuticals, in particular beta-blockers and antibiotics, on the growth and yield of green algae, as well as inhibition of *daphnia* reproduction. Thus the CCA methods could help to elucidate the potential relationships between the physico-chemical characterisation and toxic effects by considering all the potential interactions.

Park, C. B., Jang, J., Kim, S., & Kim, Y. J. (2017). Single- and Mixture Toxicity of Three Organic UV-Filters, Ethylhexyl Methoxycinnamate, Octocrylene, and Avobenzone on *Daphnia magna*. *Ecotoxicology and Environmental Safety*, 137, 57-63 <https://doi.org/10.1016/j.ecoenv.2016.11.017>

In freshwater environments, aquatic organisms are generally exposed to mixtures of various chemical substances. In this study, we tested the toxicity of three organic UV-filters (ethylhexyl

methoxycinnamate, octocrylene, and avobenzone) to *Daphnia magna* in order to evaluate the combined toxicity of these substances when they occur in a mixture. The values of effective concentrations (EC_x) for each UV-filter were calculated by concentration-response curves; concentration-combinations of three different UV-filters in a mixture were determined by the fraction of components based on EC₂₅ values predicted by concentration addition (CA) model. The interaction between the UV-filters were also assessed by model deviation ratio (MDR) using observed and predicted toxicity values obtained from mixture-exposure tests and CA model. The results from this study indicated that observed EC_x (e.g., EC₁₀mix, EC₂₅mix, or EC₅₀mix) values obtained from mixture-exposure tests were higher than predicted EC_x (e.g., EC₁₀mix, EC₂₅mix, or EC₅₀mix) values calculated by CA model. MDR values were also less than a factor of 1.0 in mixtures of three different UV-filters. Based on these results, we suggest for the first time a reduction of toxic effects in the mixtures of three UV-filters, caused by antagonistic action of the components. Our findings from this study will provide important information for hazard or risk assessment of organic UV-filters, when they existed together in the aquatic environment. To better understand the mixture toxicity and the interaction of components in a mixture, further studies for various combinations of mixture components are also required.

Pelclova, D., Navratil, T., Kacerova, T., Zamostna, B., Fenclova, Z., Vlckova, S., & Kacer, P. (2019). NanoTiO₂ Sunscreen Does Not Prevent Systemic Oxidative Stress Caused by UV Radiation and a Minor Amount of NanoTiO₂ Is Absorbed in Humans. *Nanomaterials*, 9(6) <https://doi.org/10.3390/nano9060888>

The present pilot study tested the efficiency of nanoTiO₂ sunscreen to prevent the oxidative stress/inflammation caused by ultraviolet (UV) radiation using biomarkers in subjects' blood, urine, and exhaled breath condensate (EBC). In addition, the skin absorption of nanoTiO₂ was studied. Six identical subjects participated in three tests: (A) nanoTiO₂ sunscreen, (B) UV radiation, and (C) sunscreen + UV. The first samples were collected before the test and the second after sunscreen application and/or UV exposure. On day 4, the third samples were collected, and the sunscreen was washed off, and the fourth samples were collected on day 11. The following biomarkers were measured: malondialdehyde, 4-hydroxy-trans-hexenal, 4-hydroxy-trans-nonanal, aldehydes C6-C12, 8-iso-Prostaglandin F₂alpha, o-tyrosine, 3-chlorotyrosine, 3-nitrotyrosine, 8-hydroxy-2-deoxyguanosine, 8-hydroxyguanosine, 5-hydroxymethyl uracil, and leukotrienes, using liquid chromatography-electrospray ionisation-tandem mass spectrometry. Titania was measured using inductively coupled plasma mass spectrometry and TiO₂ nanoparticles by transmission and scanning electron microscopy. Sunscreen alone did not elevate the markers, but UV increased the biomarkers in the plasma, urine, and EBC. The sunscreen prevented skin redness, however it did not inhibit the elevation of oxidative stress/inflammatory markers. Titania and nanoTiO₂ particles were found in the plasma and urine (but not in the EBC) in all sunscreen users, suggesting their skin absorption.

Pollack, A. Z., Mumford, S. L., Krall, J. R., Carmichael, A. E., Sjaarda, L. A., Perkins, N. J., . . . Schisterman, E. F. (2018). Exposure to Bisphenol a, Chlorophenols, Benzophenones, and Parabens in Relation to Reproductive Hormones in Healthy Women: A Chemical Mixture Approach. *Environment International*, 120, 137-144 <https://doi.org/10.1016/j.envint.2018.07.028>

BACKGROUND: Little is known about the associations of bisphenol A, chlorophenols, benzophenones, and parabens with reproductive hormone levels in women. Our goal was to evaluate the associations between repeated measures of these chemicals and their mixtures with reproductive hormones in women. METHODS: Longitudinal urine samples from healthy, premenopausal women (n=143 with 3-5

urine samples each) were measured for bisphenol A, five chlorophenols (2,4-dichlorophenol (2,4-DCP), 2,5-dichlorophenol, 2,4,5-trichlorophenol, 2,4,6-trichlorophenol, triclosan), two ultraviolet (UV) filters (benzophenone-1, benzophenone-3), and eight parabens and their metabolites (benzyl, butyl, ethyl, heptyl, methyl, propyl, 4-hydroxybenzoic acid (4-HB), 3,4-dihydroxybenzoic acid (3,4-DHB)) over two menstrual cycles. Estradiol, progesterone, luteinizing hormone (LH), and follicle stimulating hormone (FSH) were measured in blood up to 8 times each menstrual cycle. Linear mixed models were used for both single and multi-chemical exposures estimated using principal component analysis. Four factors were identified including: paraben; paraben metabolites and BPA, phenols, and UV filters. Models were adjusted for creatinine, age, race, and body mass index and weighted with inverse probability of exposure weights to account for time varying confounding. RESULTS: In single-chemical models, 3,4-DHB was associated with estradiol (0.06 (95% confidence interval (CI): 0.001, 0.12)), 2-4-DCP with increased progesterone 0.14 (0.06, 0.21) and decreased FSH -0.08 (-0.11, -0.04), and 4-HB was associated with increased FSH 0.07 (0.01, 0.13). In multi-chemical models, all factors were associated with increased progesterone (beta coefficient range: 0.15 for UV filter factor to 0.32 for paraben factor). The paraben factor and the paraben metabolite and BPA factor were associated with increased estradiol [0.21 (0.15, 0.28); 0.12 (0.07, 0.18)]. The phenol and UV filter factors were associated with decreased estradiol, FSH, and LH. The UV filter factor showed the strongest inverse association with estradiol -0.16 (-0.22, -0.10), FSH -0.12 (-0.17, -0.07), and LH -0.17 (-0.23, -0.10). CONCLUSION: Mixtures of phenols were associated with changes in reproductive hormones. Such changes could contribute to adverse health in women but additional research is necessary.

Pomierny, B., Krzyżanowska, W., Broniowska, Ż., Strach, B., Bystrowska, B., Starek-Świechowicz, B., . . . Budziszewska, B. (2019). Benzophenone-3 Passes through the Blood-Brain Barrier, Increases the Level of Extracellular Glutamate, and Induces Apoptotic Processes in the Hippocampus and Frontal Cortex of Rats. *Toxicological Sciences*, 171(2), 485-500
<https://doi.org/10.1093/toxsci/kfz160>

Benzophenone-3 is the most commonly used UV filter. It is well absorbed through the skin and gastrointestinal tract. Its best-known side effect is the impact on the function of sex hormones. Little is known about the influence of BP-3 on the brain. The aim of this study was to show whether BP-3 crosses the blood-brain barrier (BBB), to determine whether it induces nerve cell damage in susceptible brain structures, and to identify the mechanism of its action in the central nervous system. BP-3 was administered dermally during the prenatal period and adulthood to rats. BP-3 effect on short-term and spatial memory was determined by novel object and novel location recognition tests. BP-3 concentrations were assayed in the brain and peripheral tissues. In brain structures, selected markers of brain damage were measured. The study showed that BP-3 is absorbed through the rat skin, passes through the BBB. BP-3 raised oxidative stress and induced apoptosis in the brain. BP-3 increased the concentration of extracellular glutamate in examined brain structures and changed the expression of glutamate transporters. BP-3 had no effect on short-term memory but impaired spatial memory. The present study showed that dermal BP-3 exposure may cause damage to neurons what might be associated with the increase in the level of extracellular glutamate, most likely evoked by changes in the expression of GLT-1 and xCT glutamate transporters. Thus, exposure to BP-3 may be one of the causes that increase the risk of developing neurodegenerative diseases.

Pont, A. R., Charron, A. R., & Brand, R. M. (2004). Active Ingredients in Sunscreens Act as Topical Penetration Enhancers for the Herbicide 2,4-Dichlorophenoxyacetic Acid. *Toxicology and Applied Pharmacology*, 195(3), 348-354 <https://doi.org/10.1016/j.taap.2003.09.021>

Agricultural workers are encouraged to use sunscreen to decrease the risk of UV-related skin cancer. Our previous studies have shown certain commercial sunscreens to be penetration enhancers. The focus of this project is to determine whether active ingredients in sunscreen formulations (i.e., the UV absorbing components and insect repellants for the sunscreen/bug repellent combinations) also act as dermal penetration enhancers for herbicides in vitro. The total percentages of 2,4-dichlorophenoxyacetic acid (2,4-D) penetrating through hairless mouse skin in 24 h ranged from 54.9 +/- 4.7 for the no sunscreen control to 86.9 +/- 2.5 for padimate-o. Of the active ingredients tested (7.5% octyl methoxycinnamate, 7% octocrylene, 0.6% oxybenzone, 5% homosalate, 5% octyl salicylate, 8% padimate-o, 10% sulisobenzene, and 9.5% and 19% N,N-diethyl-m-toluamide [DEET]), all but octocrylene led to a significant increase in total 2,4-D penetration as compared to the control (P < 0.05), and only octocrylene and oxybenzone did not significantly decrease the corresponding lag time. Octyl salicylate (P < 0.01) and octyl methoxycinnamate (P < 0.05) significantly increased the 3H₂O penetration across mouse skin, indicating physical damage to the stratum corneum. Additional studies demonstrated that the penetration enhancement seen across hairless mouse skin also occurred with human skin. Thus, the active ingredients of sunscreen formulations enhance dermal penetration of the moderately lipophilic herbicide 2,4-D.

Ponzo, O. J., & Silvia, C. (2013). Evidence of Reproductive Disruption Associated with Neuroendocrine Changes Induced by UV-B Filters, Phthalates and Nonylphenol During Sexual Maturation in Rats of Both Gender. *Toxicology*, 311(1-2), 41-51 <https://doi.org/10.1016/j.tox.2013.05.014>

Endocrine disruptors (EDs) are exogenous substances or xenoestrogens natural or synthetic, capable of interacting with different systems and altering their normal hormonal regulation, being the reproductive system one of the most affected. EDs produce their effects not only by acting on nuclear steroid receptors, but also on membrane receptors, steroidal and non-steroidal synthetic enzymatic pathways and/or metabolism. The incorporation to the body depend on each EDs, which are liposoluble and easily deposited in the tissue; thus ensuring a prolonged accumulation and release, even when the exposure is not continuous. In addition to cross the placenta, EDs may act in the offspring during the reproductive system formation and maturation key stages and its regulatory mechanisms. The effects of EDs can be multiple, but most acts mediating estrogenic and/or antiandrogenic effect. Three groups of EDs are widely used: in plastics (phtalates), sunscreens (cinnamate and methylbenzylcamphor), and detergents (nonylphenol). In this paper we review the effects of the exposure to these environmental chemicals on the reproductive system and the possible mechanisms by which they occur, focusing in the hypothalamic-pituitary neuroendocrine mechanisms that regulate the reproductive system.

Prunk Zdravkovic, T., Zdravkovic, B., Zdravkovic, M., Daris, B., Lunder, M., & Ferk, P. (2017). In Vitro Study of the Influence of Octocrylene on a Selected Metastatic Melanoma Cell Line. *Giornale Italiano di Dermatologia e Venereologia* <https://doi.org/10.23736/S0392-0488.17.05616-4>

BACKGROUND: Octocrylene (OCT) is one of the most widespread chemical UV filters used in sunscreens and cosmetic products. Despite the use of sunscreens and personal care products over decades, melanoma as the most serious and aggressive form of skin cancer is still a cause of concern. Hence the aim of this study was to investigate any potential influence of OCT on metabolic activity, cytotoxicity and ABCB5 mRNA expression in melanoma cells. The ABCB5 transmembrane protein was tested due to its

well-known role in the initiation, invasion and metastatic spread of various cancers, including melanoma. METHODS: Metastatic melanoma cell line WM-266-4 (ATCC) was incubated with selected concentrations of OCT and for different time intervals. The MTT and LDH assays to measure the cells' metabolic activity and cytotoxicity were used respectively. Target gene (ABCB5) expression was detected by quantitative real-time PCR (qRT-PCR), using TaqMan(R) chemistry. RESULTS: Our results suggest decreased metastatic melanoma cells' metabolic activity, increased cytotoxicity and increased ABCB5 mRNA expression ($p < 0.05$) with longer time of exposure to OCT as compared to control cells. Accordingly, we suspect that the surviving cells are more invasive and aggressive, which might explain their microscopically observed cannibalistic activity. CONCLUSIONS: With this study, we elucidate a new promising field for further research to contribute to etiology and prevention of melanoma.

Quintaneiro, C., Teixeira, B., Benede, J. L., Chisvert, A., Soares, A., & Monteiro, M. S. (2019). Toxicity Effects of the Organic UV-Filter 4-Methylbenzylidene Camphor in Zebrafish Embryos. *Chemosphere*, 218, 273-281 <https://doi.org/10.1016/j.chemosphere.2018.11.096>

Ultraviolet (UV) filters are widely used in personal care products and due to their lipophilicity these chemicals tend to bioaccumulate in the aquatic biota. 4-Methylbenzylidene camphor (4-MBC) is one of the most used UV-filters, and it is commonly detected in freshwater fish tissues. This substance is suspected to be an endocrine disruptor due to its interaction with Hypothalamus-Pituitary-Gonadal (HPG) and HP-Thyroid (HPT)-axis. The main objective of this study was to evaluate the effects of 4-MBC on apical endpoints, biochemical markers and on genes involved in endocrine pathways in *Danio rerio*. Zebrafish embryos were exposed to 4-MBC (0.083-0.77mg/l) from 0 to 96h post-fertilization (hpf). Hatching, heart rate and malformations were the apical endpoints assessed. Alterations on neurotransmission and oxidative stress were evaluated through acetylcholinesterase (AChE), catalase (CAT) and glutathione S-transferase (GST) enzymatic activities. Endocrine effects were analysed by the expression of genes involved in HPG and HPT-axis of embryos exposed 96h to the EC10 of 4-MBC (0.19mg/l). Exposure to 4-MBC induced morphological abnormalities during embryonic development, including notochord curvature, delayed absorption of yolk sac and pericardial oedema. Concentration of 0.77mg/l 4-MBC decreased embryo heart rate at 48h. At neurotransmission level, an induction of AChE at concentrations above 0.15mg/l was observed. Malformations and decreased heart rate along with alterations observed at neurotransmission level might have compromised zebrafish larvae equilibrium. Glutathione S-transferase induction above 0.15mg/l 4-MBC suggests activation of detoxification processes. Furthermore, observed brain aromatase gene down-regulation by 4-MBC suggests impairment of normal functioning of HPG axis in zebrafish.

Rehfeld, A., Dissing, S., & Skakkebaek, N. E. (2016). Chemical UV Filters Mimic the Effect of Progesterone on Ca(2+) Signaling in Human Sperm Cells. *Endocrinology*, 157(11), 4297-4308 <https://doi.org/10.1210/en.2016-1473>

Progesterone released by cumulus cells surrounding the egg induces a Ca(2+) influx into human sperm cells via the cationic channel of sperm (CatSper) Ca(2+) channel and controls multiple Ca(2+)-dependent responses essential for fertilization. We hypothesized that chemical UV filters may mimic the physiological action of progesterone on CatSper, thus affecting Ca(2+) signaling in human sperm cells. We examined 29 UV filters allowed in sunscreens in the United States and/or the European Union for their ability to induce Ca(2+) signals in human sperm by applying measurements of the intracellular free Ca(2+) concentration. We found that 13 UV filters induced a significant Ca(2+) signal at 10 μ M. Nine UV filters induced Ca(2+) signals primarily by activating the CatSper channel. The UV filters 3-

benzylidene camphor (3-BC) and benzylidene camphor sulfonic acid competitively inhibited progesterone-induced Ca(2+) signals. Dose-response relations for the UV filters showed that the Ca(2+) signal-inducing effects began in the nanomolar-micromolar range. Single-cell Ca(2+) measurements showed a Ca(2+) signal-inducing effect of the most potent UV filter, 3-BC, at 10 nM. Finally, we demonstrated that the 13 UV filters acted additively in low-dose mixtures to induce Ca(2+) signals. In conclusion, 13 of 29 examined UV filters (44%) induced Ca(2+) signals in human sperm. Nine UV filters primarily activated CatSper and thereby mimicked the effect of progesterone. The UV filters 3-BC and benzylidene camphor sulfonic acid competitively inhibited progesterone-induced Ca(2+) signals. In vivo exposure studies are needed to investigate whether UV filter exposure affects human fertility.

Rodriguez-Fuentes, G., Sandoval-Gio, J. J., Arroyo-Silva, A., Norena-Barroso, E., Escalante-Herrera, K. S., & Olvera-Espinosa, F. (2015). Evaluation of the Estrogenic and Oxidative Stress Effects of the UV Filter 3-Benzophenone in Zebrafish (*Danio rerio*) Eleuthero-Embryos. *Ecotoxicology and Environmental Safety*, 115, 14-18 <https://doi.org/10.1016/j.ecoenv.2015.01.033>

Personal care products have been detected in superficial waters, representing an environmental risk to the biota. Some studies indicated that 3-benzophenone (3BP) alters hormones, inducing vitellogenesis and having adverse effects on fish reproduction. Other studies have reported generation of free radicals and changes in antioxidant enzymes. Therefore, the aim of the present study was to test acute exposure to 3BP at concentrations within and beyond that found environmentally to provide important toxicological information regarding this chemical. We evaluated the effect of 3BP on vitellogenin 1 (VTG1) gene expression and the transcription of the enzymes catalase (CAT), superoxide dismutase (SOD) or glutathione peroxidase (GPx), which are involved in cellular redox balance. Zebrafish eluthero-embryos (168hpf) were exposed to 1, 10, 100, 1000 microg/L 3BP, in addition to a negative control and a 0.1% ethanol control for 48h. The results of our study indicated a positive significant correlation between exposure concentrations and VTG1 expression ($r=0.986$, $p=0.0028$) but only 1000 microg/L 3BP produced a significant increase from control. Acute exposure showed no significant differences in transcription levels of CAT, SOD or GPx at the tested conditions. Nevertheless, a trend toward increase in GPx expression was observed as a positive significant correlation ($r=0.928$, $p=0.017$) was noted.

Ruszkiewicz, J. A., Pinkas, A., Ferrer, B., Peres, T. V., Tsatsakis, A., & Aschner, M. (2017). Neurotoxic Effect of Active Ingredients in Sunscreen Products, a Contemporary Review. *Toxicology Reports*, 4, 245-259 <https://doi.org/10.1016/j.toxrep.2017.05.006>

Sunscreen application is the main strategy used to prevent the maladies inflicted by ultraviolet (UV) radiation. Despite the continuously increasing frequency of sunscreen use worldwide, the prevalence of certain sun exposure-related pathologies, mainly malignant melanoma, is also on the rise. In the past century, a variety of protective agents against UV exposure have been developed. Physical filters scatter and reflect UV rays and chemical filters absorb those rays. Alongside the evidence for increasing levels of these agents in the environment, which leads to indirect exposure of wildlife and humans, recent studies suggest a toxicological nature for some of these agents. Reviews on the role of these agents in developmental and endocrine impairments (both pathology and related mechanisms) are based on both animal and human studies, yet information regarding the potential neurotoxicity of these agents is scant. In this review, data regarding the neurotoxicity of several organic filters: octyl methoxycinnamate, benzophenone-3 and -4, 4-methylbenzylidene camphor, 3-benzylidene camphor and octocrylene, and two allowed inorganic filters: zinc oxide and titanium dioxide, is presented and discussed. Taken

together, this review advocates revisiting the current safety and regulation of specific sunscreens and investing in alternative UV protection technologies.

Safety Assessment of Salicylic Acid, Butyloctyl Salicylate, Calcium Salicylate, C12-15 Alkyl Salicylate, Capryloyl Salicylic Acid, Hexyldodecyl Salicylate, Isocetyl Salicylate, Isodecyl Salicylate, Magnesium Salicylate, Mea-Salicylate, Ethylhexyl Salicylate, Potassium Salicylate, Methyl Salicylate, Myristyl Salicylate, Sodium Salicylate, Tea-Salicylate, and Tridecyl Salicylate. (2003). *International Journal of Toxicology*, 22 Suppl 3, 1-108 Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/14617432>

Salicylic Acid is an aromatic acid used in cosmetic formulations as a denaturant, hair-conditioning agent, and skin-conditioning agent--miscellaneous in a wide range of cosmetic products at concentrations ranging from 0.0008% to 3%. The Calcium, Magnesium, and MEA salts are preservatives, and Potassium Salicylate is a cosmetic biocide and preservative, not currently in use. Sodium Salicylate is used as a denaturant and preservative (0.09% to 2%). The TEA salt of Salicylic Acid is used as an ultraviolet (UV) light absorber (0.0001% to 0.75%). Several Salicylic Acid esters are used as skin conditioning agents--miscellaneous (Capryloyl, 0.1% to 1%; C12-15 Alkyl, no current use; Isocetyl, 3% to 5%; Isodecyl, no current use; and Tridecyl, no current use). Butyloctyl Salicylate (0.5% to 5%) and Hexyldodecyl Salicylate (no current use) are hair-conditioning agents and skin-conditioning agents--miscellaneous. Ethylhexyl Salicylate (formerly known as Octyl Salicylate) is used as a fragrance ingredient, sunscreen agent, and UV light absorber (0.001% to 8%), and Methyl Salicylate is used as a denaturant and flavoring agent (0.0001% to 0.6%). Myristyl Salicylate has no reported function. Isodecyl Salicylate is used in three formulations, but no concentration of use information was reported. Salicylates are absorbed percutaneously. Around 10% of applied salicylates can remain in the skin. Salicylic Acid is reported to enhance percutaneous penetration of some agents (e.g., vitamin A), but not others (e.g., hydrocortisone). Little acute toxicity (LD(50) in rats; >2 g/kg) via a dermal exposure route is seen for Salicylic Acid, Methyl Salicylate, Tridecyl Salicylate, and Butyloctyl Salicylate. Short-term oral, inhalation, and parenteral exposures to salicylates sufficient to produce high blood concentrations are associated primarily with liver and kidney damage. Subchronic dermal exposures to undiluted Methyl Salicylate were associated with kidney damage. Chronic oral exposure to Methyl Salicylate produced bone lesions as a function of the level of exposure in 2-year rat studies; liver damage was seen in dogs exposed to 0.15 g/kg/day in one study; kidney and liver weight increases in another study at the same exposure; but no liver or kidney abnormalities in a study at 0.167 g/kg/day. Applications of Isodecyl, Tridecyl, and Butyloctyl Salicylate were not irritating to rabbit skin, whereas undiluted Ethylhexyl Salicylate produced minimal to mild irritation. Methyl Salicylate at a 1% concentration with a 70% ethanol vehicle were irritating, whereas a 6% concentration in polyethylene glycol produced little or no irritation. Isodecyl Salicylate, Methyl Salicylate, Ethylhexyl (Octyl) Salicylate, Tridecyl Salicylate, and Butyloctyl Salicylate were not ocular irritants. Although Salicylic Acid at a concentration of 20% in acetone was positive in the local lymph node assay, a concentration of 20% in acetone/olive oil was not. Methyl Salicylate was negative at concentrations up to 25% in this assay, independent of vehicle. Maximization tests of Methyl Salicylate, Ethylhexyl Salicylate, and Butyloctyl Salicylate produced no sensitization in guinea pigs. Neither Salicylic Acid nor Tridecyl Salicylate were photosensitizers. Salicylic Acid, produced when aspirin is rapidly hydrolyzed after absorption from the gut, was reported to be the causative agent in aspirin teratogenesis in animals. Dermal exposures to Methyl Salicylate, oral exposures to Salicylic Acid, Sodium Salicylate, and Methyl Salicylate, and parenteral exposures to Salicylic Acid, Sodium Salicylate, and Methyl Salicylate are all associated with reproductive and developmental toxicity as a function of blood levels reached as a result of exposure. An exposure assessment of a representative cosmetic product

used on a daily basis estimated that the exposure from the cosmetic product would be only 20% of the level seen with ingestion of a "baby" aspirin (81 mg) on a daily basis. Studies of the genotoxic potential of Salicylic Acid, Sodium Salicylate, Isodecyl Salicylate, Methyl Salicylate, cosmetic product would be only 20% of the level seen with ingestion of a "baby" aspirin (81 mg) on a daily basis. Studies of the genotoxic potential of Salicylic Acid, Sodium Salicylate, Isodecyl Salicylate, Methyl Salicylate, Ethylhexyl (Octyl) Salicylate, Tridecyl Salicylate, and Butyloctyl Salicylate were generally negative. Methyl Salicylate, in a mouse skin-painting study, did not induce neoplasms. Likewise, Methyl Salicylate was negative in a mouse pulmonary tumor system. In clinical tests, Salicylic Acid (2%) produced minimal cumulative irritation and slight or no irritation (1.5%); TEA-Salicylate (8%) produced no irritation; Methyl Salicylate (>12%) produced pain and erythema, a 1% aerosol produced erythema, but an 8% solution was not irritating; Ethylhexyl Salicylate (4%) and undiluted Tridecyl Salicylate produced no irritation. In atopic patients, Methyl Salicylate caused irritation as a function of concentration (no irritation at concentrations of 15% or less). In normal skin, Salicylic Acid, Methyl Salicylate, and Ethylhexyl (Octyl) Salicylate are not sensitizers. Salicylic Acid is not a photosensitizer, nor is it phototoxic. Salicylic Acid and Ethylhexyl Salicylate are low-level photoprotective agents. Salicylic Acid is well-documented to have keratolytic action on normal human skin. Because of the possible use of these ingredients as exfoliating agents, a concern exists that repeated use may effectively increase exposure of the dermis and epidermis to UV radiation. It was concluded that the prudent course of action would be to advise the cosmetics industry that there is a risk of increased UV radiation damage with the use of any exfoliant, including Salicylic Acid and the listed salicylates, and that steps need to be taken to formulate cosmetic products with these ingredients as exfoliating agents so as not to increase sun sensitivity, or when increased sun sensitivity would be expected, to include directions for the daily use of sun protection. The available data were not sufficient to establish a limit on concentration of these ingredients, or to identify the minimum pH of formulations containing these ingredients, such that no skin irritation would occur, but it was recognized that it is possible to formulate cosmetic products in a way such that significant irritation would not be likely, and it was concluded that the cosmetics industry should formulate products containing these ingredients so as to be nonirritating. Although simultaneous use of several products containing Salicylic Acid could produce exposures greater than would be seen with use of baby aspirin (an exposure generally considered to not present a reproductive or developmental toxicity risk), it was not considered likely that consumers would simultaneously use multiple cosmetic products containing Salicylic Acid. Based on the available information, the Cosmetic Ingredient Review Expert Panel reached the conclusion that these ingredients are safe as used when formulated to avoid skin irritation and when formulated to avoid increasing the skin's sun sensitivity, or, when increased sun sensitivity would be expected, directions for use include the daily use of sun protection.

Saidani, W., Sellami, B., Khazri, A., Mezni, A., Dellali, M., Joubert, O., . . . Beyrem, H. (2019). Metal Accumulation, Biochemical and Behavioral Responses on the Mediterranean Clams *Ruditapes Decussatus* Exposed to Two Photocatalyst Nanocomposites (TiO₂ Nps and AuTiO₂NPS). *Aquatic Toxicology*, 208, 71-79 <https://doi.org/10.1016/j.aquatox.2019.01.003>

Nanoparticle decoration with noble metal represents a promising alternative to improve their photocatalytic and photovoltaic properties. However, toxicity can be influenced by such modification, as the bioavailability of these substances may be influenced. To understand how decoration influences the NP impacts in marine ecosystems, we exposed suspension-feeding clams, *Ruditapes decussatus*, to two photocatalyst nanocomposites, TiO₂ NPs and AuTiO₂ NPs, over 2 concentrations, 50 µg L⁻¹ and 100 µg L⁻¹, in a laboratory experiment. Accumulation of Au and Ti in gills and digestive gland was noted in clams after exposure to TiO₂ NPs and AuTiO₂ NPs using inductively coupled plasma optic emission spectroscopy (ICP-OES). TiO₂ and AuTiO₂ NPs alter the behavior of the clams *Ruditapes decussatus* by

reducing filtration and respiration rates. Furthermore, the highest concentration of TiO₂NPs induces an overproduction of H₂O₂ in gills and digestive gland and NO production only in gills. Superoxide dismutase (SOD), Catalase (CAT), Glutathione-S-transferase (GST) and acetylcholinesterase (AChE) activities were induced in gills and digestive gland in concentration and nanocomposite type dependent manner. Decorated form presented higher Malondialdehyde (MDA) levels in gills and digestive gland than the undecorated form, suggesting different mechanisms of action that may be mediated through oxidative stress. In conclusion, the considered parameters could represent reliable biomarkers for the assessment of NP toxicity on *R. decussatus* as biological biomonitoring model. In addition, based on the obtained results, nanoparticle decoration influences the toxicity of metal nanoparticles in marine organism.

Santamaria, C. G., Abud, J. E., Porporato, M. M., Meyer, N., Zenclussen, A. C., Kass, L., & Rodriguez, H. A. (2019). The UV Filter Benzophenone 3, Alters Early Follicular Assembly in Rat Whole Ovary Cultures. *Toxicology Letters*, 303, 48-54 <https://doi.org/10.1016/j.toxlet.2018.12.016>

Our goal was to study the effect of BP3 (benzophenone 3) in the follicular assembly and the potential involvement of Foxl2 pathway using whole ovary cultures. Ovaries were collected from Wistar rats at birth, treated in vitro with vehicle (0.01% DMSO), BP3 (5.8 nM, 276 nM, 576 nM and 876 nM) or ESR2 inhibitor (0.1 nM), and cultured for 7 days. Nest breakdown, follicular assembly and the expression of several regulators of these processes (p27, Foxl2, Sox9, Bmp2, Cyp19 and Fst) were evaluated. In vitro exposure to BP3 (5.8 nM) decreased the population of total oocytes, the number of nests per ovary and early primary follicles population. In addition, BP3 (5.8 nM) induced overexpression of Foxl2 mRNA levels through ESR2 but increased Fst mRNA levels independently from ESR2 or Foxl2. We also observed that the number of p27-positive oocytes was decreased after BP3 (5.8 nM). On the other hand, exposure to BP3-276 increased total oocytes, the number of nests per ovary and decreased primary follicles. In addition, BP3-276 induced no changes of Foxl2 mRNA levels through ESR2 but increased Fst mRNA levels independently from ESR2 or Foxl2. In conclusion, our study clearly shows that exposure to BP3 is to perturb the early events of germ cell development as showed here in whole ovary cultures.

Santovito, A., Ruberto, S., Galli, G., Menghi, C., Girotti, M., & Cervella, P. (2019). Induction of Chromosomal Aberrations and Micronuclei by 2-Hydroxy-4-Methoxybenzophenone (Oxybenzone) in Human Lymphocytes. *Drug and Chemical Toxicology*, 42(4), 378-385 <https://doi.org/10.1080/01480545.2018.1455206>

Oxybenzone or benzophenone-3 (2-hydroxy-4-methoxybenzophenone; BP-3) is a filter used in a variety of personal care products for protection of human skin and hair from damage by ultraviolet radiation. BP-3 is suspected to exhibit endocrine disruptive properties. Indeed, it was found to be able to interact with the endocrine system causing alteration of its homeostasis, with consequent adverse health effects. Moreover, it is ubiquitously present in the environment, mostly in aquatic ecosystems, with consequent risks to the health of aquatic organisms and humans. In the present study, we analyzed the cytogenetic effects of BP-3 on human lymphocytes using in vitro chromosomal aberrations and micronuclei assays. Blood samples were obtained from five healthy Italian subjects. Lymphocyte cultures were exposed to five concentrations of BP-3 (0.20, 0.10, 0.05, 0.025, and 0.0125 µg/mL) for 24 and 48 h (for chromosomal aberrations and micronuclei tests, respectively). The concentration of 0.10 µg/mL represents the acceptable/tolerable daily intake reference dose established by European Union, whereas 0.20, 0.05, 0.025, and 0.0125 µg/mL represent multiple and sub-multiple of this concentration value. Our results reported cytogenetic effects of BP-3 on cultured human lymphocytes in

terms of increased micronuclei and chromosomal aberrations' frequencies at all tested concentrations, including concentrations lower than those established by European Union. Vice versa, after 48-h exposure, a significant reduction of the cytokinesis-block proliferation index value in cultures treated with BP-3 was not observed, indicating that BP-3 does not seem to produce effects on the proliferation/mitotic index when its concentration is equal to or less than 0.20 µg/mL.

Saunders, L. J., Fontanay, S., Nichols, J. W., & Gobas, F. (2019). Concentration Dependence of in Vitro Biotransformation Rates of Hydrophobic Organic Sunscreen Agents in Rainbow Trout S9 Fractions: Implications for Bioaccumulation Assessment. *Environmental Toxicology and Chemistry*, 38(3), 548-560 <https://doi.org/10.1002/etc.4342>

In vitro biotransformation studies were performed to support the bioaccumulation assessment of 3 hydrophobic organic ultraviolet filters (UVFs), 4-methylbenzylidene camphor (4-MBC), 2-ethylhexyl-4-methoxycinnamate (EHMC), and octocrylene. In vitro depletion rate constants ($k(\text{dep})$) were determined for each UVF using rainbow trout liver S9 fractions. Incubations performed with and without added cofactors showed complete (4-MBC) or partial (EHMC and octocrylene) dependence of $k(\text{dep})$ on addition of the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH), suggesting that hydrolysis of EHMC and octocrylene by NADPH-independent enzymes (e.g., carboxylesterases) is an important metabolic route. The concentration dependence of $k(\text{dep})$ was then evaluated to estimate Michaelis-Menten parameters (K_M and V_{max}) for each UVF. Measured $k(\text{dep})$ values were then extrapolated to apparent whole-body biotransformation rate constants using an in vitro-in vivo extrapolation (IVIVE) model. Bioconcentration factors (BCFs) calculated from $k(\text{dep})$ values measured at concentrations well below K_M were closer to empirical BCFs than those calculated from $k(\text{dep})$ measured at higher test concentrations. Modeled BCFs were sensitive to in vitro binding assumptions employed in the IVIVE model, highlighting the need for further characterization of chemical binding effects on hepatic clearance. The results suggest that the tested UVFs are unlikely to accumulate to levels exceeding the European Union Registration, Evaluation, Authorisation, and Restriction regulation criterion for bioaccumulative substances ($\text{BCF} > 2000 \text{ L kg}^{-1}$). However, consideration of appropriate in vitro test concentrations and binding correction factors are important when IVIVE methods are used to refine modeled BCFs. *Environ Toxicol Chem* 2019;38:548-560.

Schlumpf, M., Durrer, S., Faass, O., Ehnes, C., Fuetsch, M., Gaille, C., . . . Lichtensteiger, W. (2008). Developmental Toxicity of UV Filters and Environmental Exposure: A Review. *International Journal of Andrology*, 31(2), 144-151 <https://doi.org/10.1111/j.1365-2605.2007.00856.x>

Several ultraviolet (UV) filters exhibit estrogenic, some also anti-androgenic activity. They are present in waste water treatment plants, surface waters and biosphere including human milk, suggesting potential exposure during development. Developmental toxicity was studied in rats for the UV filters 4-methylbenzylidene camphor (4-MBC, 0.7, 7, 24, 47 mg/kg/day) and 3-benzylidene camphor (3-BC, 0.07, 0.24, 0.7, 2.4, 7 mg/kg/day) administered in chow to the parent generation before mating, during pregnancy and lactation, and to the offspring until adulthood. Neonates exhibited enhanced prostate growth after 4-MBC and altered uterine gene expression after both chemicals. 4-MBC and 3-BC delayed male puberty and affected reproductive organ weights of adult offspring. Effects on the thyroid axis were also noted. Expression and oestrogen sensitivity of oestrogen-regulated genes and nuclear receptor coregulator levels were altered at mRNA and protein levels in adult uterus, prostate and brain regions involved in gonadal control and sexual behaviour. Female sexual behaviour was impaired by both filters; 3-benzylidene camphor caused irregular cycles. Classical endpoints exhibited lowest

observed adverse effect levels (LOAELs) and no observed adverse effect levels (NOAELs) of 7/0.7 mg/kg for 4-MBC and 0.24/0.07 mg/kg for 3-BC. Molecular endpoints were affected by the lowest doses studied. Our data indicate that the potential risk posed by endocrine active UV filters warrants further investigations.

Schlumpf, M., Schmid, P., Durrer, S., Conscience, M., Maerkel, K., Henseler, M., . . . Lichtensteiger, W. (2004). Endocrine Activity and Developmental Toxicity of Cosmetic UV Filters--an Update. *Toxicology*, 205(1-2), 113-122 <https://doi.org/10.1016/j.tox.2004.06.043>

UV filters represent a new class of endocrine active chemicals. In vitro, 8/9 chemicals showed estrogenic (MCF-7 cells), and 2/9 antiandrogenic activity (MDA-kb2 cells). Six/nine filters (benzophenone (Bp)-1, Bp-2, Bp-3, 3-benzylidene camphor (3-BC), 4-methylbenzylidene camphor (4-MBC), octyl-methoxycinnamate (OMC)) increased uterine weight in immature rats. 3-Benzylidene camphor and 4-MBC displaced 16alpha125I-estradiol from human estrogen receptor (ER)beta, not ERalpha. Developmental toxicity of 4-MBC (0.7-47 mg/kg body weight/day) and 3-BC (0.24-7 mg/kg), administered in chow was investigated in Long Evans (LE) rats. Weight gain of pregnant rats was reduced only by 3-BC, early postnatal survival rate and thymus weight by both compounds at higher doses. 4-Methylbenzylidene camphor and 3-BC delayed male puberty, and dose-dependently affected reproductive organ weights of adult male and female F1 offspring, with partly different effect patterns. Thyroid weight was increased by higher 4-MBC doses. Tissue-specific changes in mRNA levels of estrogen-regulated genes in prostate, uterus and brain regions, determined by real-time PCR, and in their response to acute estradiol challenge in adult gonadectomized offspring were observed. Lowest effective doses were 0.24 mg/kg/day for 3-BC and 7 mg/kg/day for 4-MBC. Fat tissue levels at 7 mg/kg 4-MBC (GC-MS) approached the range of UV filters in fish (Nagtegaal et al., 1997; Balmer et al., 2004).

Schmitt, C., Oetken, M., Dittberner, O., Wagner, M., & Oehlmann, J. (2008). Endocrine Modulation and Toxic Effects of Two Commonly Used UV Screens on the Aquatic Invertebrates *Potamopyrgus Antipodarum* and *Lumbriculus Variegatus*. *Environmental Pollution*, 152(2), 322-329 <https://doi.org/10.1016/j.envpol.2007.06.031>

The two UV screens 3-benzylidene-camphor (3-BC) and 3-(4'-methylbenzylidene)-camphor (4-MBC) were tested regarding their toxicity and estrogenic activity. The Yeast Estrogen Screen (YES) and two sediment assays with the freshwater invertebrates *Lumbriculus variegatus* and *Potamopyrgus antipodarum* were performed. In the YES, both substances activated the human estrogen receptor alpha with EC50 values of 44.2 microM for 3-BC and 44.3 microM for 4-MBC, whereby 4-MBC attained only 8% of the maximal response of 17beta-estradiol. For *P. antipodarum* embryo production increased after exposure to both substances (EC50 of 4.60 microM 4-MBC=1.17 mg kg(-1)dw) while mortality increased at high concentrations. The reproduction of *L. variegatus* was decreased by 3-BC with an EC50 of 5.95 microM (=1.43 mg kg(-1)dw) and also by 4-MBC, where no EC50 could be calculated. While reproduction decreased, the worms' weight increased after exposure to 3-BC with an EC50 of 26.9 microM (=6.46 mg kg(-1) dw), hence the total biomass remained unaffected.

Schreurs, R., Lanser, P., Seinen, W., & van der Burg, B. (2002). Estrogenic Activity of UV Filters Determined by an In Vitro Reporter Gene Assay and an In Vivo Transgenic Zebrafish Assay. *Archives of Toxicology*, 76(5-6), 257-261 <https://doi.org/10.1007/s00204-002-0348-4>

In the past decade the list of chemicals in the environment that are able to mimic the natural hormone estrogen, thereby disrupting endocrine function, has grown rapidly. These chemicals are able to bind to estrogen receptors (ERs) and influence estrogen signalling pathways, although several of them have structures that differ substantially from the endogenous hormone 17beta-estradiol. In this study, six extensively used ultraviolet (UV) filters were assessed for transcriptional activation of estrogen receptors. Because of their high lipophilicity, these UV filters tend to bioaccumulate in the environment. They have been found in surface waters, fish, and in human milk fat. Using a sensitive in vitro reporter gene assay, we found that all six compounds induce estrogenic activity towards ERalpha, while four out of six compounds induced transcriptional activity of ERbeta. Zebrafish, in which an estrogen responsive luciferase reporter gene has been stably introduced, were used for in vivo testing. In this transgenic zebrafish assay none of the compounds showed estrogenic activity. Our findings suggest that one should be aware of over-interpretation when predicting in vivo effects from weak in vitro data. However, it can not be ruled out that these UV filters have long-term effects in the environment.

Sendra, M., Pintado-Herrera, M. G., Aguirre-Martinez, G. V., Moreno-Garrido, I., Martin-Diaz, L. M., Lara-Martin, P. A., & J, B. (2017). Are the TiO₂ NPS a "Trojan Horse" for Personal Care Products (PCPs) in the Clam *Ruditapes Philippinarum*? *Chemosphere*, 185, 192-204
<https://doi.org/10.1016/j.chemosphere.2017.07.009>

In recent years, increasing quantities of personal care products (PCPs) are being released into the environment. However, data about bioaccumulation and toxicity are scarce; and extraction and analytical approaches are not well developed. In this work, the marine clam *Ruditapes philippinarum*, selected as model organism, has been employed to investigate bioaccumulation, antioxidant enzyme activities and DNA damage due to exposure to TiO₂ nanoparticles and bulk TiO₂ (inorganic compounds that are frequent components of PCPs, plastics, paints and coatings, foods and disinfectant water treatments). We have also studied the joint effect of both forms of inorganic TiO₂ combined with four organic compounds (mixture exposures) commonly used in PCPs: an antimicrobial (triclosan), a fragrance (OTNE) and two UV filters (benzophenone-3 and octocrylene). Bioaccumulation of the inorganic compound, TiO₂, was almost immediate and constant over exposure time. With respect to the organic compounds in mixtures, they were mediated by TiO₂ and bioaccumulation is driven by reduced size of the particles. In fact, nanoparticles can be considered as a vector to organic compounds, such as triclosan and benzophenone-3. After a week of depuration, TiO₂ NPs and TiO₂ bulk in clams showed similar levels of concentration. Some organic compounds with bioactivity (Log Kow >3), like OTNE, showed low depuration after one week. The joint action of the organic compound mixture and either of the two forms of TiO₂ provoked changes in enzyme activity responses. However, for the mixtures, DNA damage was found only after the depuration period.

Sendra, M., Yeste, M. P., Gatica, J. M., Moreno-Garrido, I., & Blasco, J. (2017). Homoagglomeration and Heteroagglomeration of TiO₂, in Nanoparticle and Bulk Form, onto Freshwater and Marine Microalgae. *Science of The Total Environment*, 592, 403-411
<https://doi.org/10.1016/j.scitotenv.2017.03.127>

TiO₂ nanoparticles (TiO₂ NPs) are employed in many products (paints, personal care products, especially sunscreens, plastics, paper, water potabilization and food products) and are then released into the environment from these products. These nanoparticles present potential risk to freshwater and marine microalgae. The primary toxicity mechanism is adsorption between NPs and microalgae

(heteroagglomeration); however, studies of interactions of this kind are scarce. We investigated the heteroagglomeration process that occurs between two forms of TiO₂ material, nanoparticles and bulk, and three different microalgae species, and under different environmental conditions (freshwater and marine water), in order to assess the influence of pH and ionic strength (IS). The heteroagglomeration process was examined by means of co-settling experiments and the Derjaguin-Landau-Verwey-Overbeek (DLVO) approach. The homoagglomeration process (only NPs to NPs) did not show differences between culture media (freshwater and marine water). However, in the heteroagglomeration process between NPs and cells, IS played an important role. Ions can compress the electro-double layer between NPs and microalgae, allowing a heteroagglomeration process to take place, as shown by settling experiments. TiO₂ NPs presented a settling rate higher than bulk TiO₂. The DLVO theory could only partially explain heteroagglomeration because, in this model, it is not considered that NP-NP and Cell-Cell homoagglomeration co-occur. In this study neither the role of exopolymeric substances in the interaction between NPs and cells nor detoxification are considered. The authors suggest that the interaction between NPs and microalgae could be considered as the first stage in the process by which nanoparticles affect microalgae.

Seoane, M., Esperanza, M., Rioboo, C., Herrero, C., & Cid, A. (2017). Flow Cytometric Assay to Assess Short-Term Effects of Personal Care Products on the Marine Microalga *Tetraselmis Suecica*. *Chemosphere*, 171, 339-347 <https://doi.org/10.1016/j.chemosphere.2016.12.097>

Large quantities of personal care products (PCPs) are used daily and many of their chemical ingredients are subsequently released into marine environments. Cultures of the marine microalga *Tetraselmis suecica* were exposed for 24 h to three emerging compounds included in the main classes of PCPs: the UV filter benzophenone-3 (BP-3), the disinfectant triclosan (TCS) and the fragrance tonalide (AHTN). Concentrations tested, expressed as cellular quota (pg cell⁻¹), ranged from 5 to 40 for BP-3, from 2 to 16 for TCS and from 1.2 to 2.4 for AHTN. A small cytometric panel was carried out to evaluate key cytotoxicity biomarkers including inherent cell properties, growth and metabolic activity and cytoplasmic membrane properties. BP-3 caused a significant increase in growth rate, metabolic activity and chlorophyll a fluorescence from 10 pg cell⁻¹. However, growth and esterase activity decreased in cells exposed to all TCS and AHTN concentrations, except the lowest ones. Also these two compounds provoked a significant swelling of cells, more pronounced in the case of TCS-exposed cells. Although all treated cells remained viable, changes in membrane potential were observed. BP-3 and AHTN caused a significant depolarization of cells from 10 to 1.6 pg cell⁻¹, respectively; however all TCS concentrations assayed caused a noticeable hyperpolarization of cells. Metabolic activity and cytoplasmic membrane potential were the most sensitive parameters. It can be concluded that the toxicological model used and the toxicological parameters evaluated are suitable to assess the toxicity of these emerging contaminants.

Shioda, T., & Wakabayashi, M. (2000). Evaluation of Reproductivity of Medaka (*Oryzias Latipes*) Exposed to Chemicals Using a 2-Week Reproduction Test. *Water Science and Technology*, 42(5-6), 53-60 <https://doi.org/10.2166/wst.2000.0552>

Effects of endocrine disrupting chemicals on reproductive ability of medaka (*Oryzias latipes*) were investigated. Exposure of male medaka to estrogenic chemicals such as 17 β -estradiol (E2), p-nonylphenol (NP), 4-t-butylphenol (BP) and bisphenol-A (BPA) caused a decrease in the numbers of eggs hatched rather than those of eggs spawned, which seemed to be affected by estrogen-like effects of these chemicals. Exposure of female medaka to E2 and NP reduced the numbers of eggs spawned rather

than those of eggs hatched. The concentrations at which reproductivity of female decreased (E2:0.1 nmol/L, NP:0.03 µmol/L) were lower than those of male (E2:3 nmol/L, NP:>0.3 µmol/L). Diethylhexyl phthalate, benzophenone and tributyltin chloride did not affect reproductivity. In this study, adverse effects of estrogenic chemicals on reproductivity of medaka could be detected, so the materials and methods used in this study were considered to be able to be applied for a screening test method.

Sieratowicz, A., Kaiser, D., Behr, M., Oetken, M., & Oehlmann, J. (2011). Acute and Chronic Toxicity of Four Frequently Used UV Filter Substances for *Desmodesmus subspicatus* and *Daphnia magna*. *Journal of Environmental Science and Health, Part A*, 46(12), 1311-1319
<https://doi.org/10.1080/10934529.2011.602936>

As a consequence of growing public concern about UV radiation effects on human health chemical and physical UV filters are increasingly used in personal care and other products. The release of these lipophilic and often persistent compounds into surface waters may pose a risk for aquatic organisms. The aim of the study was to determine effects of four frequently used UV filters on primary aquatic producers and consumers, the green alga *Desmodesmus subspicatus* and the crustacean *Daphnia magna*. Exposure to benzophenone 3 (BP3), ethylhexyl methoxycinnamate (EHMC), 3-benzylidene camphor (3-BC) and 3-(4'-methylbenzylidene)-camphor (4-MBC) resulted in growth inhibition of *D. subspicatus* with 72 h IC(10) values of 0.56 mg/L (BP 3), 0.24 mg/L (EHMC), 0.27 mg/L (3-BC) and 0.21 mg/L (4-MBC). EC(50) concentrations in the acute test with *D. magna* were 1.67, 0.57, 3.61 and 0.80 mg/L for BP3, EHMC, 3-BC and 4-MBC, respectively. Chronic exposure of *D. magna* resulted in NOECs of 0.04 mg/L (EHMC) and 0.1 mg/L (3-BC and 4-MBC). BP 3 showed no effects on neonate production or the length of adults. Rapid dissipation of these substances from the water phase was observed indicating the need for more frequent test medium renewal in chronic tests or the use of flow-through test systems.

Srinivasan, M., Venkatesan, M., Arumugam, V., Natesan, G., Saravanan, N., Murugesan, S., . . . Pugazhendhi, A. (2019). Green Synthesis and Characterization of Titanium Dioxide Nanoparticles (TiO₂ NPs) Using *Sesbania grandiflora* and Evaluation of Toxicity in Zebrafish Embryos. *Process Biochemistry*, 80, 197-202 <https://doi.org/10.1016/j.procbio.2019.02.010>

Green synthesis of nanoparticles is becoming one of the robust techniques, which may be suitable alternatives for chemical and physical methods. This study reports a cost effective and environmental friendly green synthesis of titanium dioxide nanoparticles (TiO₂ NPs) using *Sesbania grandiflora*. The biosynthesized TiO₂ NPs were characterized by Fourier-transform infrared spectroscopy (FTIR), Scanning electron microscopy with energy dispersive X-ray spectroscopy (SEM-EDX) and Transmission Electron Microscopy (TEM), Ultraviolet–visible spectrophotometry (UV–Vis) and X-ray powder diffraction (XRD). FTIR spectrum confirmed the involvement of alkynes, alkanes, flavonoids and secondary alcohols in the capping and reduction of TiO₂ NPs while XRD characterized the crystallographic plane of the rutile phase of TiO₂. Size of TiO₂ NPs was in the range of 43–56 nm and EDX showed a strong TiO₂ signal. The phytosynthesised TiO₂ NPs were used for zebrafish embryo toxicity tests, which were performed to monitor the changes in the toxicological effects. Besides, the model adapted in this study was suitable to explore the toxicity in Zebrafish. TiO₂ NPs increased bioavailability and uptake into cells and organisms. In order to assess the TiO₂ NPs toxic level we employed the fish model as aquatic environment. This study demonstrates that TiO₂ NPs are lethal to zebrafish.

Starnes, D., Unrine, J., Chen, C., Lichtenberg, S., Starnes, C., Svendsen, C., . . . Tsyusko, O. (2019). Toxicogenomic Responses of *Caenorhabditis Elegans* to Pristine and Transformed Zinc Oxide Nanoparticles. *Environmental Pollution*, 247, 917-926
<https://doi.org/10.1016/j.envpol.2019.01.077>

Manufactured nanoparticles (MNPs) undergo transformation immediately after they enter wastewater treatment streams and during their partitioning to sewage sludge, which is applied to agricultural soils in form of biosolids. We examined toxicogenomic responses of the model nematode *Caenorhabditis elegans* to pristine and transformed ZnO-MNPs (phosphatized pZnO- and sulfidized sZnO-MNPs). To account for the toxicity due to dissolved Zn, a ZnSO₄ treatment was included. Transformation of ZnO-MNPs reduced their toxicity by nearly ten-fold, while there was almost no difference in the toxicity of pristine ZnO-MNPs and ZnSO₄. This combined with the fact that far more dissolved Zn was released from ZnO- compared to pZnO- or sZnO-MNPs, suggests that dissolution of pristine ZnO-MNPs is one of the main drivers of their toxicity. Transcriptomic responses at the EC₃₀ for reproduction resulted in a total of 1161 differentially expressed genes. Fifty percent of the genes differentially expressed in the ZnSO₄ treatment, including the three metal responsive genes (*mtl-1*, *mtl-2* and *numr-1*), were shared among all treatments, suggesting that responses to all forms of Zn could be partially attributed to dissolved Zn. However, the toxicity and transcriptomic responses in all MNP treatments cannot be fully explained by dissolved Zn. Two of the biological pathways identified, one essential for protein biosynthesis (Aminoacyl-tRNA biosynthesis) and another associated with detoxification (ABC transporters), were shared among pristine and one or both transformed ZnO-MNPs, but not ZnSO₄. When comparing pristine and transformed ZnO-MNPs, 66% and 40% of genes were shared between ZnO-MNPs and sZnO-MNPs or pZnO-MNPs, respectively. This suggests greater similarity in transcriptomic responses between ZnO-MNPs and sZnO-MNPs, while toxicity mechanisms are more distinct for pZnO-MNPs, where 13 unique biological pathways were identified. Based on these pathways, the toxicity of pZnO-MNPs is likely to be associated with their adverse effect on digestion and metabolism.

Stein, H. V., Berg, C. J., Maung, J. N., O'Connor, L. E., Pagano, A. E., MacManus-Spencer, L. A., & Paulick, M. G. (2017). Photolysis and Cellular Toxicities of the Organic Ultraviolet Filter Chemical Octyl Methoxycinnamate and Its Photoproducts. *Environmental Science Processes and Impacts*, 19(6), 851-860 <https://doi.org/10.1039/c7em00059f>

Organic ultraviolet filter chemicals (UVFCs) are the active ingredients used in many sunscreens to protect the skin from UV light; these chemicals have been detected in numerous aquatic environments leading to concerns about how they might affect aquatic organisms and humans. One commonly used organic UVFC is octyl methoxycinnamate (OMC), better known by its commercial name, octinoxate. Upon exposure to UV light, OMC degrades rapidly, forming numerous photoproducts, some of which have been previously identified. In this study, we isolated and completely characterized the major products of OMC photolysis, including the two major stable OMC cyclodimers. One of these cyclodimers is a delta-truxinate, resulting from a head-to-head dimerization of two OMC molecules, and the other cyclodimer is an alpha-truxillate, resulting from a head-to-tail dimerization of two OMC molecules. Additionally, the cellular toxicities of the individual photoproducts were determined; it was found that the parent UVFC, OMC, 4-methoxybenzaldehyde, and two cyclodimers are significantly toxic to cells. The photoproduct 2-ethylhexanol is not cytotoxic, demonstrating that different components of OMC photolysate contribute differently to its cellular toxicity. This study thus provides an enhanced understanding of OMC photolysis and gives toxicity data that can be used to better evaluate OMC as a sunscreen agent.

Subramaniam, V. D., Prasad, S. V., Banerjee, A., Gopinath, M., Murugesan, R., Marotta, F., . . . Pathak, S. (2019). Health Hazards of Nanoparticles: Understanding the Toxicity Mechanism of Nanosized ZnO in Cosmetic Products. *Drug and Chemical Toxicology*, 42(1), 84-93
<https://doi.org/10.1080/01480545.2018.1491987>

In recent years, nanoparticles are being used extensively in personal healthcare products such as cosmetics, sunscreens, soaps, and shampoos. Particularly, metal oxide nanoparticles are gaining competence as key industrial constituents, progressing toward a remarkable rise in their applications. Zinc oxide and titanium oxide nanoparticles are the most commonly employed metal oxide nanoparticles in sunscreens, ointments, foot care, and over the counter topical products. Dermal exposure to these metal oxides predominantly occurs through explicit use of cosmetic products and airway exposure to nanoparticle dusts is primarily mediated via occupational exposure. There is a compelling need to understand the toxicity effects of nanoparticles which can easily enter the cells and induce oxidative stress. Consequently, these products have become a direct source of pollution in the environment and thereby greatly impact our ecosystem. A complete understanding of the toxicity mechanism of nano-ZnO is intended to resolve whether and to what extent such nanoparticles may pose a threat to the environment and to human beings. In this review article, we have discussed the characteristics of metal oxide nanoparticles and its applications in the cosmetic industry. We have also highlighted about their toxicity effects and their impact on human health.

Sung, C. R., Kim, K. B., Lee, J. Y., Lee, B. M., & Kwack, S. J. (2019). Risk Assessment of Ethylhexyl Dimethyl PABA in Cosmetics. *Toxicological Research*, 35(2), 131-136
<https://doi.org/10.5487/TR.2019.35.2.131>

Ethylhexyl dimethyl para-aminobenzoic acid (PABA) is an oily yellow liquid derivative of water-soluble PABA commonly used in sunscreen. Ethylhexyl dimethyl PABA is widely used as an ingredient in many cosmetics at an average concentration of 1.25% (0.5-2.0%) in Korea. Previous studies, including those involving animals, have demonstrated that ethylhexyl dimethyl PABA is toxic to the following four organs: testis, epididymis, spleen, and liver. In addition, experiments using human keratinocytes found that ethylhexyl dimethyl PABA inhibits cell growth and DNA synthesis at low concentrations, and halted the cell cycle of MM96L cells (human melanoma cell line) at the G1 phase. Despite limited clinical data in humans, many studies have confirmed increased mutagenicity of ethylhexyl dimethyl PABA following exposure to sunlight, which suggests that this molecule is likely to contribute to onset of sun-induced cancer despite protecting the skin through absorption of UVB. For risk assessment, the no observed adverse effect level (NOAEL) chosen was 100 mg/kg bw/day in a 4 weeks oral toxicity study. Systemic exposure dosage (SED) was 0.588 mg/kg bw/day for maximum use of ethylhexyl dimethyl PABA in cosmetics. Based on the risk assessment and exposure scenarios conducted in this study, the margin of safety (MOS) was calculated to be 180.18 for a sunscreen containing 8% ethylhexyl dimethyl PABA, which is the maximum level allowed by the relevant domestic authorities.

Sureda, A., Capo, X., Busquets-Cortes, C., & Tejada, S. (2018). Acute Exposure to Sunscreen Containing Titanium Induces an Adaptive Response and Oxidative Stress in *Mytilus galloprovincialis*. *Ecotoxicology and Environmental Safety*, 149, 58-63
<https://doi.org/10.1016/j.ecoenv.2017.11.014>

The use of sunscreens to protect against ultraviolet radiation exposure progressively increases as result of a greater awareness of the people and the greater arrival of tourists. The components of these

creams can end up in the waters affecting coastal species. Mediterranean mussels (*Mytilus galloprovincialis*) were subjected to an acute exposure of a sunscreen with TiO₂ in their composition during 24h. The low and medium concentrations used in the assays contained a concentration of TiO₂ in the range of values found in coastal waters of the Balearic Islands. Titanium and metallothionein concentrations were progressively increasing in gills with the sunscreen concentration in a dose-dependent manner. The activities of the antioxidant enzymes and the detoxification glutathione s-transferase evidenced a hormetic shape response with increased activities at lower sunscreen concentrations, a response that was abolished at the highest concentration. In accordance with these enzyme activities, the levels of malondialdehyde, as a marker of lipid peroxidation, were significantly elevated by the higher sunscreen concentrations. Acetylcholinesterase activity maintained control activities except for the highest sunscreen concentration, where a significant decrease was evidenced. In conclusion, the treatment of mussels with a sunscreen containing TiO₂ in the range of Balearic coastal waters induces an adaptive response that is overcome by the highest concentration. Follow-up biomonitoring studies are necessary to control the concentration of sunscreen compound in coastal waters such as titanium since they can induce oxidative stress to affected organisms.

Suzuki, T., Kitamura, S., Khota, R., Sugihara, K., Fujimoto, N., & Ohta, S. (2005). Estrogenic and Antiandrogenic Activities of 17 Benzophenone Derivatives Used as UV Stabilizers and Sunscreens. *Toxicology and Applied Pharmacology*, 203(1), 9-17
<https://doi.org/10.1016/j.taap.2004.07.005>

Estrogenic and antiandrogenic activities of benzophenone and 16 of its derivatives, which are used as UV stabilizers, were comparatively examined with hormone-responsive reporter assay in various cell lines. Hydroxylated benzophenones exhibited estrogenic activity in human breast cancer cell line MCF-7, but their activities varied markedly. The highest activity was observed with 2,4,4'-trihydroxybenzophenone (2,4,4'-triOH-BP), followed by 2,3',4,4'-tetrahydroxybenzophenone, 4,4'-dihydroxybenzophenone, 2,2',4,4'-tetrahydroxybenzophenone, 4-hydroxybenzophenone and 2,4-dihydroxybenzophenone. Benzophenone itself showed little activity in the assay. In contrast, benzophenone and some related compounds showed significant inhibitory effects on the androgenic activity of dihydrotestosterone in rat fibroblast cell line NIH3T3. The highest activity was observed with 2,4,4'-triOH-BP, followed by 2,3',4,4'-tetrahydroxybenzophenone, 2,2',4,4'-tetrahydroxybenzophenone, 3-hydroxybenzophenone and 2,2'-dihydroxybenzophenone. However, 2,3,4,4'-tetrahydroxybenzophenone and 2,3,4-trihydroxybenzophenone showed little activity. 2,4-Dihydroxybenzophenone, 2,4,4'-triOH-BP and benzophenone gave positive responses in uterotrophic assay using ovariectomized rats, and 2,4,4'-triOH-BP was positive in the Hershberger assay using castrated rats. These results suggest that a 4-hydroxyl group on the phenyl ring of benzophenone derivatives is essential for high hormonal activities, and the presence of other hydroxyl groups markedly alters these activities.

Takemoto, K., Yamazaki, H., Nakajima, M., & Yokoi, T. (2002). Genotoxic Activation of Benzophenone and Its Two Metabolites by Human Cytochrome P450s in SOS/*Umu* Assay. *Mutation Research Genetic Toxicology and Environmental Mutagenesis*, 519, 199-204
[https://doi.org/10.1016/S1383-5718\(02\)00141-9](https://doi.org/10.1016/S1383-5718(02)00141-9)

The genotoxic potential of benzophenone and its metabolically related compounds, benzhydrol and p-benzoylphenol, was investigated using human cytochrome P450 (P450) enzymes. Benzophenone and its two metabolites (0.1–1 mM) showed a suppression of bacterial growth without any P450 system, but no

induction of umu gene expression was observed in *Salmonella typhimurium* TA1535/pSK1002. Human liver microsomes induced the bacterial cytotoxicity of these compounds without any umu gene expression. On the other hand, with the addition of *Escherichia coli* membranes expressing recombinant human P450 2A6 and NADPH-cytochrome P450 reductase (NPR), benzophenone showed umu gene expression (64 umu units/min/nmol) P450 2A6). Moderate activation of benzophenone by P450 1A1/NPR membranes, 1A2/NPR membranes, or 1B1/NPR membranes was also observed. Activation of benzhydrol and p-benzoylphenol by the P450/NPR system was similar to that of benzophenone. These results suggest that benzophenone and its metabolically related benzhydrol and p-benzoylphenol can be bioactivated by P450 2A6 and P450 family 1 enzymes. Until now, benzophenone has been investigated mainly in terms of estrogenic activity and cytotoxicity, however, the genotoxic activation of benzophenone by human cytochrome P450s should be examined in terms of the risks to humans.

Tamura, I., Yasuda, Y., Kagota, K. I., Yoneda, S., Nakada, N., Kumar, V., . . . Yamamoto, H. (2017). Contribution of Pharmaceuticals and Personal Care Products (PPCPs) to Whole Toxicity of Water Samples Collected in Effluent-Dominated Urban Streams. *Ecotoxicology and Environmental Safety*, 144, 338-350 <https://doi.org/10.1016/j.ecoenv.2017.06.032>

Water samples were collected from effluent-dominated urban streams in Tokushima, Kyoto, and Saitama in Japan to roughly determine the contribution of pharmaceuticals and personal care products (PPCPs) and surfactants to whole toxicity of the water. Approximately 100 PPCPs including anionic surfactants such as linear alkylbenzene sulfonate (LAS), were chemically analyzed. Using 14 water samples, chronic or sub-chronic toxicity tests were conducted on three aquatic species, the green alga *Raphidocelis subcapitata*, the cladoceran *Ceriodaphnia dubia*, and the zebrafish *Danio rerio*. Bioassays for the selected individual PPCPs were conducted using the three species. Assuming the concentration addition (CA) model, the contribution of each PPCP to the whole toxicity of the riverwater was estimated based on toxicity unit (TU). The contribution of PPCPs, which primarily consists of a few antibiotic agents such as triclosan and clarithromycin, ranged from 0.9% to 69% of the whole toxicity of the water samples for algae, whereas the selected LAS congeners accounted for at most 5.3%. In contrast, the contribution of LAS ranged from 0.067% to 86% and from 0.021% to 27% of the whole toxicity for cladoceran and zebrafish, respectively, whereas that of PPCPs for these species was at most 2.1% at all sampling points. Our results suggest a limited contribution of PPCPs except for antimicrobial agents and the possible substantial contribution of LAS to toxicity in cladocerans and zebrafish.

Tang, T., Zhang, Z., & Zhu, X. (2019). Toxic Effects of TiO₂NPs on Zebrafish. *International Journal of Environmental Research and Public Health*, 16(4) <https://doi.org/10.3390/ijerph16040523>

Titanium dioxide nanoparticles (TiO₂ NPs) have become a widely used nanomaterial due to the photocatalytic activity and absorption of ultraviolet light of specific wavelengths. This study investigated the toxic effects of rutile TiO₂ NPs on zebrafish by examining its embryos and adults. In the embryo acute toxicity test, exposure to 100 mg/L TiO₂ NPs didn't affect the hatching rate of zebrafish embryos, and there was no sign of deformity. In the adult toxicity test, the effects of TiO₂ NPs on oxidative damage in liver, intestine and gill tissue were studied. Enzyme linked immunosorbent assay (ELISA) and fluorescence-based quantitative real-time reverse transcription PCR (qRT-PCR) were used to detect the three antioxidant enzymes: superoxide dismutase (SOD), catalase (CAT) and glutathione S transferase (GSTs) in the above mentioned zebrafish organs at protein and gene levels. The results showed that long-term exposure to TiO₂ NPs can cause oxidative damage to organisms; and compared with the control group, the activity of the three kinds of enzyme declined somewhat at the protein level. In

addition, long-term exposure to TiO₂ NPs could cause high expression of CAT, SOD and GSTs in three organs of adult zebrafish in order to counter the adverse reaction. The effects of long-term exposure to TiO₂ NPs to adult zebrafish were more obvious in the liver and gill.

Thiagarajan, V., Iswarya, V., P, A. J., Seenivasan, R., Chandrasekaran, N., & Mukherjee, A. (2019). Influence of Differently Functionalized Polystyrene Microplastics on the Toxic Effects of P25 TiO₂ NPs Towards Marine Algae *Chlorella Sp.* *Aquatic Toxicology*, 207, 208-216
<https://doi.org/10.1016/j.aquatox.2018.12.014>

Increased utilization of titanium dioxide nanoparticles (TiO₂ NPs) for commercial as well as industrial purposes resulted in the accumulation of nanoparticles in the marine system. Microplastics being an emerging secondary pollutant in the marine ecosystem have an impact on the toxic effects of TiO₂ NPs which has not been evaluated up to date. So it is important to assess the toxic effects of both these pollutants on the marine environment. The present study examines the impact of differently functionalized microplastics on the toxic effects of P25 TiO₂ NPs to marine algae *Chlorella sp.* The tendency of nanoparticles to undergo aggregation in artificial seawater was observed with increase in time. The median effective concentration for TiO₂ NPs was found to be 81 µM which indicates higher toxic effects of NPs toward algae. In contrast, microplastics irrespective of their difference in functionalization had minimal toxic effect of about 15% at their higher concentration tested, 1000 mg L⁻¹. Plain and aminated polystyrene microplastics enhanced the TiO₂ NPs toxicity which was further validated with oxidative stress determination studies like reactive oxygen species and lipid peroxidation assays. Negatively charged carboxylated polystyrene microplastics decreased the TiO₂ NPs toxicity with possible hetero-aggregation between TiO₂ NPs and microplastics in the system. The toxicity data obtained for the mixture was further corroborated with Abbott's mathematical model.

Torres, T., Cunha, I., Martins, R., & Santos, M. M. (2016). Screening the Toxicity of Selected Personal Care Products Using Embryo Bioassays: 4-MBC, Propylparaben and Triclocarban. *International Journal of Molecular Sciences*, 17(10) <https://doi.org/10.3390/ijms17101762>

Recently, several emerging pollutants, including Personal Care Products (PCPs), have been detected in aquatic ecosystems, in the ng/L or microg/L range. Available toxicological data is limited, and, for certain PCPs, evidence indicates a potential risk for the environment. Hence, there is an urgent need to gather ecotoxicological data on PCPs as a proxy to improve risk assessment. Here, the toxicity of three different PCPs (4-Methylbenzylidene Camphor (4-MBC), propylparaben and triclocarban) was tested using embryo bioassays with *Danio rerio* (zebrafish) and *Paracentrotus lividus* (sea urchin). The No Observed Effect Concentration (NOEC) for triclocarban was 0.256 microg/L for sea urchin and 100 microg/L for zebrafish, whereas NOEC for 4-MBC was 0.32 microg/L for sea urchin and 50 microg/L for zebrafish. Both PCPs impacted embryo development at environmentally relevant concentrations. In comparison with triclocarban and 4-MBC, propylparaben was less toxic for both sea urchin (NOEC = 160 microg/L) and zebrafish (NOEC = 1000 microg/L). Overall, this study further demonstrates the sensitivity of embryo bioassays as a high-throughput approach for testing the toxicity of emerging pollutants.

Utsunomiya, H., Hiraishi, R., Kishimoto, K., Hamada, S., Abe, S., Bekki, Y., & Kamemura, N. (2019). Cytotoxicity of Benzophenone-3, an Organic Ultraviolet Filter, Caused by Increased Intracellular Zn(2+) Levels in Rat Thymocytes. *Chemico-Biological Interactions*, 298, 52-56
<https://doi.org/10.1016/j.cbi.2018.10.029>

Benzophenone-3 (BP-3) is often used as an ultraviolet (UV) light filter in sunscreen products. Although BP-3 protects the human skin and hair from damage caused by excessive UV radiation, it is reported to exhibit toxic effects in human. However, the cytotoxicity of BP-3 on various cells is still not well understood. In the present study, the cytotoxicity of BP-3 against rat thymocytes was evaluated using a flow cytometric technique with fluorescent probes. Cell mortality increased significantly after 3h of exposure to 300µM BP-3, whereas the mean intensity of 5-chloromethylfluorescein diacetate (5-CMF) fluorescence and cellular content of non-protein thiols decreased significantly. However, the membrane potential of thymocytes was not change by BP-3 treatment. Moreover, intracellular Zn(2+) levels increased significantly in a concentration-dependent manner in response to 30µM BP-3 or higher. The BP-3-induced changes in intracellular Zn(2+) levels and non-protein thiol content increased the vulnerability of thymocytes to oxidative stress. We concluded that BP-3-induced cytotoxicity may be caused by oxidative stress associated with an increase in intracellular Zn(2+) levels.

Vallabani, N. V. S., Sengupta, S., Shukla, R. K., & Kumar, A. (2019). ZnO Nanoparticles-Associated Mitochondrial Stress-Induced Apoptosis and G2/M Arrest in Hacat Cells: A Mechanistic Approach. *Mutagenesis* <https://doi.org/10.1093/mutage/gez017>

Zinc oxide nanoparticles (ZnO NPs) with their wide range of consumer applications in day-to-day life received great attention to evaluate their effects in humans. This study has been attempted to elucidate the DNA damage response mechanism in a dermal model exposed to ZnO NPs through Ataxia Telangiectasia Mutated (ATM)-mediated Chk1-dependent G2/M arrest. Further, viability parameters and mechanism involved in the cell death with special reference to the consequences arising due to DNA damage were explored. Our study showed that ZnO NPs at concentrations 5 and 10 µg/ml induced significant cytotoxic effect in skin cell line. Moreover, the results confirmed generation of reactive oxygen species (ROS) induces the cell death by genotoxic insult, leading to mitochondrial membrane depolarisation and cell cycle arrest. Subsequently, ZnO NPs treatment created DNA damage as confirmed via Comet assay (increase in olive tail moment), micronucleus assay (increase in micronucleus formation), double-strand breaks (increase in ATM and Ataxia Telangiectasia and Rad3 related (ATR) expression), DNA fragmentation and cell cycle (G2/M arrest) studies. Finally, marker proteins analysis concluded the mechanistic approach by demonstrating the key marker expressions HMOX1 and HSP60 (for oxidative stress), cytochrome c, APAF1, BAX, Caspase 9, Caspase 3 and decrease in BCL2 (for activating apoptotic pathway), pATM, ATR and gammaH2AX (for double-strand breaks), DNA-PK (involved in DNA repair) and decrease in cell cycle regulators. In together, our data revealed the mechanism of ROS generation that triggers apoptosis and DNA damage in HaCaT cell lines exposed to ZnO NPs.

Vicente, A., Sohm, B., Flayac, J., Rousselle, P., Bauda, P., & Pagnout, C. (2019). Toxicity Mechanisms of ZnO UV-Filters Used in Sunscreens toward the Model Cyanobacteria *Synechococcus Elongatus Pcc 7942*. *Environmental Science and Pollution Research*, 26(22), 22450-22463 <https://doi.org/10.1007/s11356-019-05057-6>

Zinc oxide (ZnO) nanoparticles are commonly used in sunscreens for their UV-filtering properties. Their growing use can lead to their release into ecosystems, raising question about their toxicity. Effects of these engineered nanomaterials (ENMs) on cyanobacteria, which are important primary producers involved in many biogeochemical cycles, are unknown. In this study, we investigated by several complementary approaches the toxicological effects of two marketed ZnO-ENMs (coated and uncoated) on the model cyanobacteria *Synechococcus elongatus PCC 7942*. It was shown that despite the rapid

adsorption of ENMs on cell surface, toxicity is mainly due to labile Zn released by ENMs. Zn dissipates cell membrane potential necessary for both photosynthesis and respiration, and induces oxidative stress leading to lipid peroxidation and DNA damages. It leads to global downregulation of photosystems, oxidative phosphorylation, and transcription/translation machineries. This also translates into significant decrease of intracellular ATP content and cell growth inhibition. However, there is no major loss of pigments and even rather an increase in exposed cells compared to controls. A proposed way to reduce the environmental impact of Zn would be the improvement of the coating stability to prevent solubility of ZnO-ENMs.

Wang, T., Huang, X., Jiang, X., Hu, M., Huang, W., & Wang, Y. (2019). Differential In Vivo Hemocyte Responses to Nano Titanium Dioxide in Mussels: Effects of Particle Size. *Aquatic Toxicology*, 212, 28-36 <https://doi.org/10.1016/j.aquatox.2019.04.012>

Titanium dioxide nanoparticles (TiO₂ NPs) are widely used in various products and inevitably released with different sizes and forms into aquatic environment. The purpose of this study was to assess the differential immune toxicity of TiO₂ NPs with size difference on mussel hemocytes using flow cytometry (FCM) assays. Hemocyte parameters, including total hemocyte count (THC), hemocyte mortality (HM), phagocytosis activity (PA), lysosomal content (LC), esterase activity (EA), mitochondrial number (MN), mitochondrial membrane potential (MMP) and reactive oxygen species content (ROS) were evaluated in the mussels *Mytilus coruscus* exposed to two types of TiO₂ NPs (25nm & 100nm: 0.1, 1, 10 mg/L, respectively). In general, size- and concentration-dependent toxicity was pronounced with 25nm-NP and highest concentration (10mg/L) being the most toxic. Although a slight recovery from the TiO₂ exposure was observed, significant carry-over effects were still detected. These results highlight the importance of differential size effects of metal oxide NPs on toxicity mechanisms in aquatic animals.

Wang, W. Q., Duan, H. X., Pei, Z. T., Xu, R. R., Qin, Z. T., Zhu, G. C., & Sun, L. W. (2018). Evaluation by the Ames Assay of the Mutagenicity of UV Filters Using Benzophenone and Benzophenone-1. *International Journal of Environmental Research and Public Health*, 15(9) <https://doi.org/10.3390/ijerph15091907>

Ultraviolet absorbing chemicals (UV filters) are widely used in personal care products for protecting human skin and hair from damage by UV radiation. Although these substances are released into the environment during production and consumption processes, little is known about their genotoxicity effects. Our previous studies have shown that benzophenone-type UV filters exhibited acute toxicity on three species of aquatic organisms. Mutagenesis by benzophenone (BP) and benzophenone-1 (BP-1) was tested in the present study by the *Salmonella typhimurium*/reverse mutation assay (Ames assay). All the positive reverse mutations occurred in the absence of the S9 liver extract system for both chemicals. From BP, positive mutation effects on the TA102 strain at doses of 0.05 mug/plate and 0.5 mug/plate were detected. From BP-1, positive mutation effects on the TA97 strain at doses of 0.05 mug/plate and 0.5 mug/plate, and on the TA100 strain at a dose of 0.5 mug/plate, were detected. A mixture of BP and BP-1 exhibited mutagenicity on the TA97 and TA100 strains. For the TA97 strain, the positive mutation results were detected at 10% and 50% of the mixture. For the TA100 strain, the results were detected when the mixture was at 5% and 10%. In the mixture at 5%, the concentrations of BP and BP-1 were 3.5 mug/plate and 14 mug/plate, respectively. In the 10% mixture, the doses of BP and BP-1 were 7 mug/plate and 28 mug/plate, respectively. In the 50% mixture, the doses of BP and BP-1 were 35 mug/plate and 140 mug/plate, respectively. The mixture test results suggested that there was antagonism in mutagenicity between BP and BP-1.

Wantanabe, Y., Hattori, S., Fujino, C., Tachibana, K., Kojima, H., Yoshinari, K., & Kitamura, S. (2019). Effects of Benzotriazole Ultraviolet Stabilizers on Rat PXR, CAR and PPAR α Transcriptional Activities. *Fundamental Toxicological Sciences*, 6(2), 57-63 <https://doi.org/10.2131/fts.6.57>

Benzotriazole ultraviolet stabilizers (BUVSs) are widely used as ultraviolet filters in various consumer and industrial products. For this purpose, we examined the effects of 10 BUVSs and benzotriazole itself on transcriptional activation mediated by nuclear receptors: pregnane X receptor (PXR), constitutive androstane receptor (CAR) and peroxisome proliferator-activated receptor alpha (PPAR α). UV-090 and UV-9 showed rat PXR-agonistic activity in the concentration range of 1-30 μ M in reporter gene assay using simian kidney COS-1 cells. UV-090 showed the highest activity (REC20 value: 3.85×10^{-6} M). UV-090 was also positive in rat CAR activation assay, while UV-P showed inverse agonistic activity towards CAR. In the presence of the CAR agonist artemisinin (10 μ M), UV-P also showed dose-dependent CAR-antagonistic activity in the concentration range of 10-30 μ M. UV-090 and UV-9 activated rat PPAR α . Overall, these results suggest that UV-090, UV-9 and UV-P modulate PXR, CAR and/or PPAR α activation.

Weisbrod, C. J., Kunz, P. Y., Zenker, A. K., & Fent, K. (2007). Effects of the UV Filter Benzophenone-2 on Reproduction in Fish. *Toxicology and Applied Pharmacology*, 225(3), 255-266 <https://doi.org/10.1016/j.taap.2007.08.004>

The UV filter benzophenone-2 (BP-2) is largely used in personal care products such as cosmetics and in numerous other materials for UV protection. Like other UV filters, BP-2 has been found to be estrogenic in vitro and in vivo, but potential effects on reproduction of fish are unknown. In this study, we evaluate whether BP-2 affects important reproductive parameters such as fecundity, gametogenesis and secondary sex characteristics. After a pre-exposure period of 19 days, reproductively mature fathead minnows (*Pimephales promelas*) were exposed to 0.002, 0.1, 1.2, 5.0 and 9.7 mg/L BP-2 for 15 days. BP-2 was accumulated in fish up to 3.1 μ g/g body weight. In males, a dose-dependent vitellogenin induction and decrease in the number of nuptial tubercles occurred. Moreover, significant dose-related effects on gonads of male and female fish were observed. At concentrations of 1.2 mg/L and higher, spermatocyte and oocyte development was significantly inhibited in male and female fish, respectively. Testes of exposed males had much fewer spermatocytes and ovaries of exposed females had much fewer mature and more atretic follicles. Reproduction was negatively affected in a dose-dependent manner with a decrease in egg production at 5.0 mg/L and a complete cessation of spawning activity at 9.7 mg/L BP-2. Our findings show significant estrogenic effects of the common UV filter BP-2 on vitellogenin induction, secondary sex characteristics, gonadal development, and reproduction in fish.

Williams, G. P., & Darbre, P. D. (2019). Low-Dose Environmental Endocrine Disruptors, Increase Aromatase Activity, Estradiol Biosynthesis and Cell Proliferation in Human Breast Cells. *Molecular and Cellular Endocrinology*, 486, 55-64 <https://doi.org/10.1016/j.mce.2019.02.016>

BACKGROUND: Phenolic endocrine-disrupting compounds (EDCs) have long been suspected of increasing human breast cancer risk, via aromatase up-regulation; however, the metabolic effects upon aromatase in human breast cells exposed to environmentally relevant concentrations of phenolic compounds, have not been addressed. OBJECTIVES: To examine the mechanistic responses of aromatase CYP19A1 mRNA, aromatase activity, estradiol biosynthesis and cellular proliferation, in three human breast cell lines, exposed to seven phenolic compounds, at environmentally relevant concentrations. METHODS: MCF-7 and ZR-75-1 breast cancer cells, and HMF3A breast fibroblasts were treated with specific concentrations of p,p'-DDT, methoxychlor, benzophenone-2, bisphenol A,

bisphenol S, 4-phenylphenol and n-butylparaben, with and without the presence of aromatase inhibitors and estrogen receptor inhibitors. RESULTS: All test EDCs up-regulated aromatase mRNA, increased aromatase activity, significantly increased the aromatase-induced biosynthesis of the breast carcinogen 17beta-estradiol, and increased ERalpha-positive breast cell proliferation. CONCLUSION: Inadvertent exposures to 'phenolic' EDCs, increase estradiol biosynthesis, and estrogen-sensitive breast cancer proliferation.

Williams, M. (2019). Rice Chemists: Sunscreen Essential, but Worth Fda Scrutiny [Press release].

Retrieved from <http://news.rice.edu/2019/02/26/rice-chemists-sunscreen-essential-but-worth-fda-scrutiny/>

The chemistry of sunscreen is under scrutiny by the U.S. Food and Drug Administration (FDA), which has proposed updated regulations for a product routinely used by American consumers. Two Rice University synthetic organic chemists are available to discuss the science behind sunscreen and the FDA's plan to bring those products up to date.

Wnuk, A., Rzemieniec, J., Lason, W., Krzeptowski, W., & Kajta, M. (2018). Apoptosis Induced by the UV Filter Benzophenone-3 in Mouse Neuronal Cells Is Mediated Via Attenuation of Er α /Pparg and Stimulation of Er β /Gpr30 Signaling. *Molecular Neurobiology*, 55(3), 2362-2383
<https://doi.org/10.1007/s12035-017-0480-z>

Although benzophenone-3 (BP-3) has frequently been reported to play a role in endocrine disruption, there is insufficient data regarding the impact of BP-3 on the nervous system, including its possible adverse effects on the developing brain. Our study demonstrated that BP-3 caused neurotoxicity and activated apoptosis via an intrinsic pathway involving the loss of mitochondrial membrane potential and the activation of caspases-9 and -3 and kinases p38/MAPK and Gsk3beta. These biochemical alterations were accompanied by ROS production, increased apoptotic body formation and impaired cell survival, and by an upregulation of the genes involved in apoptosis. The BP-3-induced effects were tissue-specific and age-dependent with the most pronounced effects observed in neocortical cells at 7 days in vitro. BP-3 changed the messenger RNA (mRNA) expression levels of Eralpha, Erbeta, Gpr30, and Ppargamma in a time-dependent manner. At 3 h of exposure, BP-3 downregulated estrogen receptor mRNAs but upregulated Ppargamma mRNA. After prolonged exposures, BP-3 downregulated the receptor mRNAs except for Erbeta mRNA that was upregulated. The BP-3-induced patterns of mRNA expression measured at 6 and 24 h of exposure reflected alterations in the protein levels of the receptors and paralleled their immunofluorescent labeling. Eralpha and Ppargamma agonists diminished, but Erbeta and Gpr30 agonists stimulated the BP-3-induced apoptotic and neurotoxic effects. Receptor antagonists caused the opposite effects, except for ICI 182,780. This is in line with a substantial reduction in the effects of BP-3 in cells with siRNA-silenced Erbeta/Gpr30 and the maintenance of BP-3 effects in Eralpha- and Ppargamma siRNA-transfected cells. We showed for the first time that BP-3-affected mRNA and protein expression levels of Eralpha, Erbeta, Gpr30, and Ppargamma, paralleled BP-3-induced apoptosis and neurotoxicity. Therefore, we suggest that BP-3-evoked apoptosis of neuronal cells is mediated via attenuation of Eralpha/Ppargamma and stimulation of Erbeta/Gpr30 signaling.

Wong, S. W., Leung, P. T., Djuricic, A. B., & Leung, K. M. (2010). Toxicities of Nano Zinc Oxide to Five Marine Organisms: Influences of Aggregate Size and Ion Solubility. *Analytical and Bioanalytical Chemistry*, 396(2), 609-618 <https://doi.org/10.1007/s00216-009-3249-z>

Nano zinc oxide (nZnO) is increasingly used in sunscreen products, with high potential of being released directly into marine environments. This study primarily aimed to characterize the aggregate size and solubility of nZnO and bulk ZnO, and to assess their toxicities towards five selected marine organisms. Chemical characterization showed that nZnO formed larger aggregates in seawater than ZnO, while nZnO had a higher solubility in seawater (3.7 mg L⁻¹) than that of ZnO (1.6 mg L⁻¹). Acute tests were conducted using the marine diatoms *Skeletonema costatum* and *Thalassiosira pseudonana*, the crustaceans *Tigriopus japonicus* and *Elasmopus rapax*, and the medaka fish *Oryzias melastigma*. In general, nZnO was more toxic towards algae than ZnO, but relatively less toxic towards crustaceans and fish. The toxicity of nZnO could be mainly attributed to dissolved Zn(2+) ions. Furthermore, molecular biomarkers including superoxide dismutase (SOD), metallothionein (MT) and heat shock protein 70 (HSP70) were employed to assess the sublethal toxicities of the test chemicals to *O. melastigma*. Although SOD and MT expressions were not significantly increased in nZnO-treated medaka compared to the controls, exposure to ZnO caused a significant up-regulation of SOD and MT. HSP70 was increased two to fourfold in all treatments indicating that there were probably other forms of stress in addition to oxidative stress such as cellular injury.

Xiong, L., Tang, J., Li, Y., & Li, L. (2019). Phototoxic Risk Assessment on Benzophenone UV Filters: In Vitro Assessment and a Theoretical Model. *Toxicology in Vitro*
<https://doi.org/10.1016/j.tiv.2019.05.021>

Benzophenones (BPs), filtering out both UVA and UVB rays, are widely used in a great variety of sunscreens and personal care products. However, they have not been extensively studied for the mechanisms of UV-absorbing toxicity. In this study, we used CPZ (chlorpromazine) as a positive control and SDS (sodium dodecyl sulfate) as a negative control, and the phototoxicity of BP-1, BP-3 and BP-4 were investigated in vitro assays using three cell types under different UV exposure conditions. This was followed by setting up a theoretical model, which was adopted to predict and compare the phototoxicity. It was found that Balb/c 3T3 (Balb/c 3T3 fibroblast cell lines) showed sensitivity to UVA+ and UVB+ exposure, while the HS68 (human HS68 fibroblast cell lines) to UVA+ and the HaCaT (human HaCaT keratinocyte cell lines) to UVB+. The test compound, BP-1, was detected to be phototoxic at UVA+ conditions, but BP-3 and BP-4 were discovered to be non-phototoxic at UVA+ conditions. This demonstrated that BP-1, BP-3 and BP-4 remained low-risk chemicals under UVB+ condition. The theoretical calculation of the energy gap (EGAP) showed BP-1(EGAP)>BP-3(EGAP)>BP-4(EGAP).

Yang, C., Lim, W., Bazer, F. W., & Song, G. (2018). Avobenzone Suppresses Proliferative Activity of Human Trophoblast Cells and Induces Apoptosis Mediated by Mitochondrial Disruption. *Reproductive Toxicology*, 81, 50-57 <https://doi.org/10.1016/j.reprotox.2018.07.003>

Avobenzone is widely used in various personal care products, is present in swimming pools, and is toxic to aquatic organisms. However, it is unclear how avobenzone affects human trophoblast cells. Results of the present study demonstrated that avobenzone inhibited the proliferation of HTR8/SVneo cells, the immortalized human trophoblast cell line, and inhibited the expression of PCNA. In addition, avobenzone increased the activity of AKT and ERK1/2 in HTR8/SVneo cells. When LY294002 (AKT inhibitor) and U0126 (ERK1/2 inhibitor) were treated with avobenzone, the anti-proliferative effect of avobenzone was alleviated. Moreover, avobenzone promoted Ca(2+) overload into the mitochondria and induced depolarization of the mitochondrial membrane. Expression of IFI27, which is located in the mitochondria, was elevated by avobenzone via inhibition of expression through siRNA transfection against IFI27, but did not alter cell properties. This study suggests that avobenzone induces

mitochondrial dysfunction-mediated apoptosis leading to abnormal placentation during early pregnancy.

Yazar, S., & GÖKÇEK, Y. (2018). Assessment of in Vitro Genotoxicity Effect of Homosalate in Cosmetics. *Journal of Research in Pharmacy*, 22(1), 109-115 <https://doi.org/10.12991/jrp.2018.84>

Many cosmetics contain UV filters as active ingredients for skin protection. Homosalate (HMS) is one of the most widely used organic UV filter. Despite the widespread use of these products, data about their genotoxic effects are lacking. Genotoxicity assessment is an important part of biosafety evaluation; therefore, we aimed to investigate genotoxic effects of homosalate as organic UV filter. The cytotoxicity effects of homosalate were assessed by trypan blue exclusion. Homosalate was incubated with four different concentrations for 30 min and 120 min. Our results revealed that HMS increased the DNA migration both the time and concentration manner. DNA damage was higher in cells that had been incubated with the greatest concentration of 200 µg mL⁻¹ (p<0.05). Results obtained by the present study indicate that homosalate would be genotoxic at higher concentration and incubation time. Further studies should be carried out with different test systems (in vivo and in vitro) related to its genotoxic effects and incubation time should be extended. This may be helpful for genotoxicity evaluation of compounds with similar characteristics and their impact of human population.

Yazar, S., & Kara Ertekin, S. (2019). Assessment of the Cytotoxicity and Genotoxicity of Homosalate in MCF-7. *Journal of Cosmetic Dermatology* <https://doi.org/10.1111/jocd.12973>

BACKGROUND: UV filters should be determined a strict toxicological safety prior to approval. Homosalate (HMS) is one of the most widely used organic UV filter. HMS accumulates in aquatic biota ecosystems and humans through the food chain; therefore, it is important to consider the effects on health and know its mechanisms of action. AIMS: The study aimed to evaluate the cytotoxic and genotoxic effects of HMS in MCF-7 cell line. METHODS: Cell viability was examined by the 3-(4,5-dimethylthiazol-2-yl)2,5-diphenyl tetrazolium bromide (MTT) and cell membrane integrity by the lactate dehydrogenase release assays (LDH), and genotoxicity by using the micronucleus test at 250, 500, 750, 1000, 1500, and 2000 microM concentrations with the human breast cell line MCF-7. RESULTS: Homosalate affected the cell viability dose-dependently at a concentrations of above 1000 microM. Micronucleus formation was significantly induced at 750 and 1000 microM within 24 hours due to an increase in cytostatic effect, the cell viability of HMS decreased to 57% at a concentration of 2000 microM, and a sufficient number of binucleated cells could not be obtained to count. Homosalate was also clastogenic when the cells were incubated at cytotoxic concentrations. CONCLUSION: These results suggest that homosalate can be considered as a cytotoxic and genotoxic substance.

Yazar, S., & Ortas, E. (2018). Activation of α , β Estrogen, p52 and AhR Receptors by UV Filters in MCF-7 Cell Line. *Fresenius Environmental Bulletin*, 27(4), 2110-2117 Retrieved from https://www.prt-parlar.de/download_feb_2018/

Endocrine disruptors chemicals including UV filters as cosmetic ingredients has been associated with developmental and reproductive abnormalities in wildlife and is suspected to interfere with human endocrine systems. Over the past few years, in vivo and in vitro investigations showed that some organic UV filters have potential effects as endocrine disruptors. In this study, three extensively used UV filters (4-Methylbenzylidene camphor (4-MBC), Benzo-phenone-3 (BP-3) and Homosalate (HMS)) were evaluated by gene expression levels of p52, aryl hydrocarbon receptor, estrogen receptor α , β in

MCF-7 cell line. In the MCF-7 cell proliferation assay, these UV filters exhibited estrogenic activity, comparable to 17- β -estradiol (E2) of 100 pM. The estrogenic po-tency was found as HMS>BP-3>4-MBC. The UV filters have been shown to increase the proliferative activity and alter estrogen-regulated gene expression in MCF-7 cell line. It was observed that 4-MBC and BP-3 have similar effects on gene expressions. HMS may display estrogenic activities through the classi-cal estrogen-response pathway via the ER α and AhR in MCF-7 cell line. Taken together with UV filters broad expression, results suggest that HMS was able to induce pS2 gene expression and the greatest re-sponse was observed as approximately 1-fold change at the both lowest and highest concentrations.

Zegura, B., Heath, E., Cernosa, A., & Filipic, M. (2009). Combination of in Vitro Bioassays for the Determination of Cytotoxic and Genotoxic Potential of Wastewater, Surface Water and Drinking Water Samples. *Chemosphere*, 75(11), 1453-1460
<https://doi.org/10.1016/j.chemosphere.2009.02.041>

In this study we evaluated genotoxicity and cytotoxicity of native samples of wastewaters (15 samples), surface waters (28 samples) and potable waters (8 samples) with the SOS/umuC assay with *Salmonella typhimurium* TA1535/pSK1002 and MTT assay with human hepatoma HepG2 cells. The genotoxicity of selected samples was confirmed with the comet assay with HepG2 cells. In the SOS/umuC assay 13 out of the 51 samples were genotoxic: two effluent samples from chemical industry; one sample of wastewater treatment plant effluent: two hospital wastewater samples; three river water samples and four lake water samples. Six samples were cytotoxic for HepG2 cells: both effluent samples of chemical industry, two wastewater treatment plant effluent samples, and two river water samples, however, only the chemical industry effluent samples were genotoxic and cytotoxic, indicating that different contaminants are responsible for genotoxic and toxic effects. Comparing genotoxicity of river and lake water samples with the chemical analytical data of the presence of the residues of pharmaceutical and personal care products (non-steroidal anti-inflammatory drugs, UV filters and disinfectants) in these samples, indicated that the presence of UV filters might be linked to the genotoxicity of these samples. The results showed that the application of the bacterial SOS/umuC assay and mammalian cell assays (MTT and comet assay) with HepG2 cells was suitably sensitive combination of assays to monitor genotoxicity and cytotoxicity of native samples of wastewaters and surface waters. With this study we also confirmed that the toxicity/genotoxicity bioassays should be an integral tool in the evaluation of toxicity of complex wastewaters before the release into environment, as well as for the monitoring of surface water quality, providing data useful in risk assessment.

Zhang, F., Zhang, J., Tong, C., Chen, Y., Zhuang, S., & Liu, W. (2013). Molecular Interactions of Benzophenone UV Filters with Human Serum Albumin Revealed by Spectroscopic Techniques and Molecular Modeling. *Journal of Hazardous Materials*, 263 Pt 2, 618-626
<https://doi.org/10.1016/j.jhazmat.2013.10.024>

Benzophenone (BP)-type UV filters have been widely used in many personal care products to protect human from UV exposure. Their dermal applications can cause direct human health risk following accumulation in bloodstream. Few studies have addressed whether BP-type UV filters could bind and alter the structure and function of human serum albumin (HSA), the major carrier protein in plasma. Four benzophenones, BP-1, BP-2, BP-3 and BP-8 were selected to investigate their potentially toxic interactions with HSA and the intrinsic binding mechanism using combined spectroscopies and molecular docking techniques. Four benzophenones significantly quench the intrinsic fluorescence of HSA via static mode. The competitive binding fluorescence assay and molecular docking both revealed

that the benzophenones bind at site II of HSA. Their binding constants range from $1.91 \times 10^4 \text{M}^{-1}$ to $12.96 \times 10^4 \text{M}^{-1}$ at 296 K. BP-8 interacts with HSA mainly through hydrogen bonding interactions and van der Waals interactions, while hydrophobic interactions and electrostatic interactions are dominant for interactions between BP-1, BP-2, BP-3 and HSA. Molecular docking revealed that the changes in structural moiety and hydrophobicity of four benzophenones account for their different binding affinities. As further revealed by circular dichroism and time-resolved fluorescence decay, these benzophenones cause global and local structural changes of HSA, which illustrates their potential toxicity to cause structural damage of HSA. Two degradation products of BP-3 have higher binding affinities to HSA, suggesting higher potencies in causing adverse effects on human health.

Zhang, Q., Ma, X., Dzakpasu, M., & Wang, X. C. (2017). Evaluation of Ecotoxicological Effects of Benzophenone UV Filters: Luminescent Bacteria Toxicity, Genotoxicity and Hormonal Activity. *Ecotoxicology and Environmental Safety*, 142, 338-347
<https://doi.org/10.1016/j.ecoenv.2017.04.027>

The widespread use of organic ultraviolet (UV) filters in personal care products raises concerns about their potentially hazardous effects on human and ecosystem health. In this study, the toxicities of four commonly used benzophenones (BPs) UV filters including benzophenone (BP), 2-Hydroxybenzophenone (2HB), 2-Hydroxy-4-methoxybenzophenone (BP3), and 2-Hydroxy-4-methoxybenzophenone-5-sulfonic acid (BP4) in water were assayed in vitro using *Vibrio fischeri*, SOS/umu assay, and yeast estrogen screen (YES) assay, as well as in vivo using zebrafish larvae. The results showed that the luminescent bacteria toxicity, expressed as logEC50, increased with the lipophilicity (logKow) of BPs UV filters. Especially, since 2HB, BP3 and BP4 had different substituent groups, namely -OH, -OCH3 and -SO3H, respectively, these substituent functional groups had a major contribution to the lipophilicity and acute toxicity of these BPs. Similar tendency was observed for the genotoxicity, expressed as the value of induction ratio=1.5. Moreover, all the target BPs UV filters showed estrogenic activity, but no significant influences of lipophilicity on the estrogenicity were observed, with BP3 having the weakest estrogenic efficiency in vitro. Although BP3 displayed no noticeable adverse effects in any in vitro assays, multiple hormonal activities were observed in zebrafish larvae including estrogenicity, anti-estrogenicity and anti-androgenicity by regulating the expression of target genes. The results indicated potential hazardous effects of BPs UV filters and the importance of the combination of toxicological evaluation methods including in vitro and in vivo assays.

Zhang, Q. Y., Ma, X. Y., Wang, X. C., & Ngo, H. H. (2016). Assessment of Multiple Hormone Activities of a UV-Filter (Octocrylene) in Zebrafish (*Danio rerio*). *Chemosphere*, 159, 433-441
<https://doi.org/10.1016/j.chemosphere.2016.06.037>

In this study, zebrafish (*Danio rerio*) were exposed to a UV-filter-octocrylene (OCT) with elevated concentrations for 28 d. The total body accumulation of OCT in zebrafish was found to reach 2321.01 ("L" level), 31,234.80 ("M" level), and 70,593.38 ng g⁻¹ ("H" level) when the average OCT exposure concentration was controlled at 28.61, 505.62, and 1248.70 µg L⁻¹, respectively. Gross and histological observations as well as RT-qPCR analysis were conducted to determine the effects of OCT accumulation on zebrafish. After exposure, the gonad-somatic index and percentage of vitellogenic oocytes were found to increase significantly in the ovaries of female zebrafish at the H accumulation level. Significant up-regulation of *esr1* and *cyp19b* were observed in the gonads, as well as *vtg1* in the livers for both female and male zebrafish. At M and H accumulation levels, apparent down-regulation of *ar* was observed in the ovaries and testis of the female and male zebrafish, respectively. Although the

extent of the effects on zebrafish differed at different accumulation levels, the induction of vtg1 and histological changes in the ovaries are indications of estrogenic activity and the inhibition of esr1 and ar showed antiestrogenic and antiandrogenic activity, respectively. Thus, as OCT could easily accumulate in aquatic life such as zebrafish, one of its most of concern hazards would be the disturbance of the histological development and its multiple hormonal activities.

Zhao, H., Chen, L., Zhong, G., Huang, Y., Zhang, X., Chu, C., . . . Wang, M. (2019). Titanium Dioxide Nanoparticles Induce Mitochondrial Dynamic Imbalance and Damage in HT22 Cells. *Journal of Nanomaterials*, 2019, 1-16 <https://doi.org/10.1155/2019/4607531>

Mitochondria, as dynamic organelles, are precisely regulated by fusion and fission. The dynamic balance of fusion and fission controls mitochondrial morphology and their subcellular location and function. Exposure to titanium dioxide nanoparticles (TiO₂ NPs) may cause serious health problems. However, how TiO₂ NPs affect the mitochondrial dynamics remains unclear. In the present study, we investigated the changes of mitochondrial dynamics in the TiO₂NPs-treated HT22 cells by confocal and stimulated emission depletion (STED) microscopy. The confocal images demonstrated obvious changes in the average length and density of the mitochondria after TiO₂ NPs treatment, while STED images further obtained the nanoscale submitochondrial structures of the mitochondria under TiO₂ NPs insult. The fluorescence intensity distributions suggested that mitochondria fragmented in the TiO₂ NPs-treated cells. TiO₂ NPs treatment caused mitochondrial dynamic imbalance due to the imbalanced expression of dynamin-related protein 1 (Drp1) and optic atrophy 1 (Opa1). Furthermore, we examined the levels of oxidative stress and mitochondrial membrane potential (MMP) and the generation of adenosine triphosphate (ATP), which revealed the damage of mitochondria under TiO₂ NPs exposure. Meanwhile, the significant changes of expressions of B-cell lymphoma 2-associated X protein (Bax), B-cell lymphoma 2 (Bcl-2), cytochrome c (Cyt C), and caspase 9 demonstrated that TiO₂ NPs treatment activated the mitochondrial-related apoptosis pathway. These cellular events can be largely prevented via cell incubation with mitoTEMPO, a mitochondria-targeted superoxide scavenger. Our results confirm that TiO₂ NPs targeted the mitochondria, inducing mitochondrial dynamic imbalance and damage in HT22 cells. Our study provides an insightful understanding of the mechanisms underlying TiO₂ NPs cytotoxicity.

Zhao, H., Wei, D., Li, M., & Du, Y. (2013). Substituent Contribution to the Genotoxicity of Benzophenone-Type UV Filters. *Ecotoxicology and Environmental Safety*, 95, 241-246 <https://doi.org/10.1016/j.ecoenv.2013.05.036>

Benzophenones (BPs) are widely used in UV filters, fragrance enhancers, and plastic additives. In this study, the genotoxicity of 14 BPs was tested using the SOS/umu assay, and the related substituent contribution was disclosed. The results of this study revealed that the major contributor to the genotoxicity of the BPs was the ortho,para-di-substitution, and the increasing hydroxy substitution on the benzene ring. In addition, the higher the dispersion of the substituent species on the two benzene rings, the lower the genotoxicity exhibited by the compound. Furthermore, 2 dimensional and 3 dimensional quantitative structure-activity relationships (2D- and 3D-QSAR) studies indicated that hydrogen-bond interactions and electrostatic effects were determinants for the genotoxicity of the BPs. The current results provide useful information for the assessment of the potential ecological risk and health effects of BP-type UV filters.

Zhao, J., Liu, S., Liu, N., Zhang, H., Zhou, Q., & Ge, F. (2019). Accelerated Productions and Physicochemical Characterizations of Different Extracellular Polymeric Substances from *Chlorella Vulgaris* with Nano-ZnO. *Science of The Total Environment*, 658, 582-589
<https://doi.org/10.1016/j.scitotenv.2018.12.019>

Extracellular polymeric substances (EPS) play significant roles in protecting cells against environmental stresses. However, little information is known about the roles of different EPS in these processes. In this study, the productions and physicochemical characterizations of soluble-EPS (S-EPS) and bound-EPS (B-EPS), the two different fractions of EPS from a green alga *Chlorella vulgaris* under the stress of ZnO nanoparticle (nano-ZnO) were investigated. The contents of S-EPS and B-EPS which described as dissolved organic carbon, polysaccharides and proteins, both increased with the addition of tested nano-ZnO (0.01 and 0.04mM) in a 72h cultivation. EPS-Free (EPS-F) cells produced more S-EPS and B-EPS than the EPS-Cover (EPS-C) cells did with the tested nano-ZnO, especially the contents of protein in the S-EPS of EPS-F cells increased by 45.5% with 0.04mM nano-ZnO compared to the control at 72h. Tryptophan-like substances of the protein in S-EPS exhibited a stronger chemical static quenching than tyrosine-like substances with nano-ZnO. In addition, the hydroxyl (OH) as well as carboxyl (CO) group, and CO of amide I, NH/CN of amide II groups in proteins were confirmed that involved in the reaction of S-EPS and B-EPS with nano-ZnO, meanwhile hemiacetal groups in saccharides were oxidized to carboxyl groups. This study could provide a better understanding of EPS in protecting against cells damage with nanoparticles.

Zhong, X., Li, Y., Che, X., Zhang, Z., Li, Y., Liu, B., . . . Gao, H. (2019). Significant Inhibition of Photosynthesis and Respiration in Leaves of *Cucumis sativus* L. By Oxybenzone, an Active Ingredient in Sunscreen. *Chemosphere*, 219, 456-462
<https://doi.org/10.1016/j.chemosphere.2018.12.019>

Oxybenzone (OBZ), an active ingredient in most sunscreens, was recently shown to be toxic to humans, corals and other animals. This study is the first to demonstrate that OBZ can significantly inhibit photosynthesis and respiration in the leaves of a higher plant, cucumber. An OBZ suspension content as low as 0.228mg/L obviously inhibited the photosynthesis and respiration of cucumber. OBZ instantly inhibits the electron transport of chloroplasts and mitochondria in cucumber leaves. Probit analysis demonstrated that the effective content for 20% inhibition of photosynthetic electron transport was 11.7mg/L (95% confidence level). The inhibition of photosynthesis and respiration restricts carbohydrate synthesis and ATP regeneration, respectively, limiting the energy available for metabolic processes including the synthesis of vital organic macromolecules such as proteins and nucleic acids in plant cells. The inhibition of photosynthesis also enhanced the excess excitation energy in chloroplasts, resulting in overproduction of reactive oxygen species (ROS), and the inhibition of respiration aggravated this process. ROS accumulation adversely affects the structure and function of proteins, DNA and membrane lipids in plant cells, interfering with normal metabolism and even leading to plant death. Therefore, reducing the use of OBZ is important for protecting global ecological security.

Zhou, R., Lu, G., Yan, Z., Bao, X., Zhang, P., & Jiang, R. (2019). Bioaccumulation and Biochemical Effects of Ethylhexyl Methoxy Cinnamate and Its Main Transformation Products in Zebra Fish. *Aquatic Toxicology*, 214, 105241 <https://doi.org/10.1016/j.aquatox.2019.105241>

The purpose of this study was to investigate the bioaccumulation and biochemical responses exposed to one of the main organic ultraviolet (UV) pollutants in the environment, ethylhexyl methoxy cinnamate (EHMC), and its main transformation product, either alone or in combination in zebra fish (*Danio rerio*).

Four-month-old zebrafish were exposed to EHMC (34.4, 344nmol/L) solution for 14 days, the species and contents of EHMC transformation products in zebrafish were determined and 3,5-dichloro-2-hydroxyacetophenone (3,5DCI2HAcP) was the one with the highest concentration in transformation products. Then, zebrafish were exposed to EHMC, 3,5DCI2HAcP alone and mixed solution for 21 days. At 7, 14 and 21 d, the related indexes of antioxidant defense system were determined. Results showed that both EHMC and 3,5DCI2HAcP can lead to the increase of malondialdehyde (MDA) and glutathione (GSH) contents, superoxide dismutase (SOD), catalase (CAT) and glutathione reductase (GR) activities in visceral mass compared with the corresponding control group, thus produced oxidative stress effect in organism and 3,5DCI2HAcP even showed stronger oxidative stress than EHMC. The effects of the two lower concentration co-exposure groups were similar and more significant to that of single exposure groups, while excessive oxidative stress occurred at the highest co-exposure group indicated by the decrease of GSH content, SOD, CAT, GR activities and the continued increase of MDA content. At 21 d, estradiol (E2), vitellogenin (Vtg) and testosterone (T) contents, estrogen receptor (Esr), progesterone receptor (Pgr), androgen receptor (Ar), Vtg1, P450 aromatase (Cyp19a1) and 17beta-hydroxysteroid dehydrogenase (Hsd17b3) expression were all significantly increased when exposed to 3,5DCI2HAcP alone, showing complex estrogen and androgen effects. When exposed to EHMC alone, E2 and Vtg contents, Esr, Pgr, Vtg1, Cyp19a1 and Hsd17b1 gene expression levels decreased significantly, and T content and Ar and Hsd17b3 expression increased significantly, indicated that EHMC can produce anti-estrogen and androgen effect. Last, the decrease of estrogen effect and increase of androgen effect in co-exposure group suggested that 3,5DCI2HAcP might weaken the estrogen effect and promote the androgen effect of EHMC.

Zhou, R., Lu, G., Yan, Z., Jiang, R., Shen, J., & Bao, X. (2019). Parental Transfer of Ethylhexyl Methoxy Cinnamate and Induced Biochemical Responses in Zebra Fish. *Aquatic Toxicology*, 206, 24-32
<https://doi.org/10.1016/j.aquatox.2018.11.001>

Ethylhexyl methoxy cinnamate (EHMC) is one of the major organic ultraviolet (UV) filter pollutants in the environment. The purpose of this study was to investigate the parental transfer of EHMC and induced biochemical responses in zebra fish (*Danio rerio*). Zebrafish embryos were exposed to EHMC solution (1, 10, and 100 µg/L) for 4 months until sexual maturation. Then male and female parents were paired to lay eggs. F1 generations were divided into 2 categories: with and without continued EHMC exposure. EHMC was detected in both F0 parents and F1 eggs, indicating that EHMC can accumulate in zebrafish and transfer to offspring through reproduction. The hatching rate decreased and malformation rate increased significantly among parents and progeny embryos in the high concentration exposure group. For 40 dpf (days post-fertilisation) F0 generations, estradiol hormone and vitellogenin (Vtg) contents, the expression levels of Vtg1, P450 aromatase (Cyp19a and Cyp19b), 17beta-hydroxysteroid dehydrogenase (Hsd17b1, Hsd17b3), estrogen receptor-alpha and progesterone receptor in all concentration groups decreased significantly, while androgen receptor increased significantly in 10 and 100 µg/L exposure groups compared with the corresponding control group, showing anti-estrogen and androgen effects. For 120 dpf F0 generations, acetylcholinesterase activity was significantly decreased and glutathione and malondialdehyde levels, superoxide dismutase, catalase and glutathione reductase activities were significantly increased in all treatment groups compared with the corresponding control group. In addition, F1 offspring with or without continued exposure to EHMC suffered similar or stronger oxidative stress compared with their parents. DNA breakage and apoptosis also occurred in 120 dpf parental liver cells in all treatment groups as a result of oxidative damage. Results suggested that EHMC have transfer effects between parents and offspring, which may cause negative effects on growth and development of zebrafish and induce biochemical responses in both parents and offspring.

Ziarrusta, H., Mijangos, L., Picart-Armada, S., Irazola, M., Perera-Lluna, A., Usobiaga, A., . . . Zuloaga, O. (2018). Non-Targeted Metabolomics Reveals Alterations in Liver and Plasma of Gilt-Head Bream Exposed to Oxybenzone. *Chemosphere*, 211, 624-631
<https://doi.org/10.1016/j.chemosphere.2018.08.013>

The extensive use of the organic UV filter oxybenzone has led to its ubiquitous occurrence in the aquatic environment, causing an ecotoxicological risk to biota. Although some studies reported adverse effects, such as reproductive toxicity, further research needs to be done in order to assess its molecular effects and mechanism of action. Therefore, in the present work, we investigated metabolic perturbations in juvenile gilt-head bream (*Sparus aurata*) exposed over 14 days via the water to oxybenzone (50mg/L). The non-targeted analysis of brain, liver and plasma extracts was performed by means of UHPLC-qOrbitrap MS in positive and negative modes with both C18 and HILIC separation. Although there was no mortality or alterations in general physiological parameters during the experiment, and the metabolic profile of brain was not affected, the results of this study showed that oxybenzone could perturb both liver and plasma metabolome. The pathway enrichment suggested that different pathways in lipid metabolism (fatty acid elongation, alpha-linolenic acid metabolism, biosynthesis of unsaturated fatty acids and fatty acid metabolism) were significantly altered, as well as metabolites involved in phenylalanine and tyrosine metabolism. Overall, these changes are signs of possible oxidative stress and energy metabolism modification. Therefore, this research indicates that oxybenzone has adverse effects beyond the commonly studied hormonal activity, and demonstrates the sensitivity of metabolomics to assess molecular-level effects of emerging contaminants.

Zucchi, S., Bluthgen, N., Ieronimo, A., & Fent, K. (2011). The UV-Absorber Benzophenone-4 Alters Transcripts of Genes Involved in Hormonal Pathways in Zebrafish (*Danio Rerio*) Eleuthero-Embryos and Adult Males. *Toxicology and Applied Pharmacology*, 250(2), 137-146
<https://doi.org/10.1016/j.taap.2010.10.001>

Benzophenone-4 (BP-4) is frequently used as UV-absorber in cosmetics and materials protection. Despite its frequent detection in the aquatic environment potential effects on aquatic life are unknown. In this study, we evaluate the effects of BP-4 in eleuthero-embryos and in the liver, testis and brain of adult male fish on the transcriptional level by focusing on target genes involved in hormonal pathways to provide a more complete toxicological profile of this important UV-absorber. Eleuthero-embryos and males of zebrafish were exposed up to 3 days after hatching and for 14 days, respectively, to BP-4 concentrations between 30 and 3000 µg/L. In eleuthero-embryos transcripts of *vtg1*, *vtg3*, *esr1*, *esr2b*, *hsd17ss3*, *cyp19b* *cyp19a*, *hhx* and *pax8* were induced at 3000 µg/L BP-4, which points to a low estrogenic activity and interference with early thyroid development, respectively. In adult males BP-4 displayed multiple effects on gene expression in different tissues. In the liver *vtg1*, *vtg3*, *esr1* and *esr2b* were down-regulated, while in the brain, *vtg1*, *vtg3* and *cyp19b* transcripts were up-regulated. In conclusion, the transcription profile revealed that BP-4 interferes with the expression of genes involved in hormonal pathways and steroidogenesis. The effects of BP-4 differ in life stages and adult tissues and point to an estrogenic activity in eleuthero-embryos and adult brain, and an antiestrogenic activity in the liver. The results indicate that BP-4 interferes with the sex hormone system of fish, which is important for the risk assessment of this UV-absorber.

Zucchi, S., Oggier, D. M., & Fent, K. (2011). Global Gene Expression Profile Induced by the UV-Filter 2-Ethyl-Hexyl-4-Trimethoxycinnamate (EHMC) in Zebrafish (*Danio Rerio*). *Environmental Pollution*, 159(10), 3086-3096 <https://doi.org/10.1016/j.envpol.2011.04.013>

Residues of the UV-filter 2-ethyl-hexyl-4-trimethoxycinnamate (EHMC) are ubiquitously found in aquatic biota but potential adverse effects in fish are fairly unknown. To identify molecular effects and modes of action of EHMC we applied a gene expression profiling in zebrafish using whole genome microarrays. Transcriptome analysis and validation of targeted genes were performed after 14 days of exposure of male zebrafish. Concentrations of 2.2 µg/L and 890 µg/L EHMC lead to alteration of 1096 and 1137 transcripts, respectively, belonging to many pathways. Genes involved in lipid metabolism and estrogenic pathway (*vtg1*), lipid biosynthesis (*ptgds*), vitamin A metabolic process (*rbp2a*), DNA damage and apoptosis (*gadd45b*), and regulation of cell growth (*igfbp1a*) were investigated by qRT-PCR analysis in whole body, liver, brain and testis. The analysis showed tissue-specific gene profiles and revealed that EHMC slightly affects the transcription of genes involved in hormonal pathways including *vtg1*, *esr1*, *esr2b*, *ar*, *cyp19b* and *hsd17beta3*.