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THE FIFTH FOOD-DRUGS FROM THE SEA CONFERENCE

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DRUG SECTION

SESSION I

STRUCTURE OF A COMPLEX METABOLITE ISOLATED FROM THE MARINE SPONGE PHAKELLIA FLABELLATA, G. M. Sharma, New York Ocean Science Laboratory, Montauk, New York, 11954.

A yellow compound having molecular formula C₁₂H₉N₅O₄.HCl has been isolated from the marine sponge <u>Phakellia flabellata</u>. This compound exhibits interesting changes in spectroscopic properties upon going from hydrochloride to the free base and vice versa. A structure will be proposed for the yellow compound which explains all its physical and chemical characteristics.

ADENOSINE AS THE CAUSATIVE ASYSTOLIC FACTOR FROM A MARINE SPONGE, A. J. Weinheimer¹, C. W. J. Chang², J. A. Matson¹ and P. N. Kaul, Departments of Chemistry and Pharmacology, The University of Oklahoma, Norman. [1.Department of Medicinal Chemistry and Pharmacognosy, University of Houston, Texas. 2. Department of Chemistry, University of West Florida, Pensacola, Florida.]

The cardioactive compound reported from the sponge, Dasychalina cyanthina (Zelenski, S.G, Weinheimer, A.J. and Kaul, P.N., Proc. Fourth Food-Drugs from the Sea Conference-1974, Marine Technology Society, Washington, D.C., 1976, pp. 288-296) has been identified as adenosine. Also isolated and identified are 2'-deoxyadenosine and thymidine. To our knowledge this represents the first report of the isolation of these compounds as the free nucleosides from a marine sponge. While adenosine has been demonstrated to be the causative factor of cessation of heart beat in the Langendorff heart, 2'-deoxyadenosine showed marginal activity and thymidine was inactive. The isolation of the nucleosides and the pharmacological properties of the common nucleosides will be discussed.

NOVEL ANTIMICROBIAL AND ANTINEOPLASTIC COMPOUNDS FROM SPONGES OF THE GULF OF CALIFORNIA, Kenneth L. Rinehart, Jr., Guy T. Carter, Yang M. Goo and Michael T. Cheng, Department of Chemistry, University of Illinois, Urbana, Illinois, 61801.

At the most recent Food-Drugs from the Sea Conference we described preliminary results from our Alpha Helix Baja Expedition 1974 which indicated that approximately 19% of the 670 animal species analyzed had either antibacterial or antifungal activity. A number of the most promising sponge species have subsequently been examined for their antimicrobial components. The procedure followed involves characterization of individual chromatographic fractions by antimicrobial assay and identification of their components by gas chromatography-mass spectrometry (GCMS) for volatile compounds and by field desorption mass spectrometry (FDMS) for non-volatile compounds. Biological activity is thus correlated early with chemical composition and is used in following purifications of active compounds. Examples will

be discussed of the use of these techniques in identifying active compounds from the sponges AHBE 3-III-74-3-2, AHBE 16-III-74-1-6, AHBE 19-III-74-1-1 and AHBE 22-III-74-1-1. Structure assignments have been made largely by the GCMS and FDMS methods noted above, including high resolution for both techniques.

EXPLANATION OF THE LOW BASICITIES OF PHAKELLINS, G. M. Sharma, New York Ocean Science Laboratory, Montauk, New York, 11954.

A few years ago we reported the structures of two guanidine derivatives, monobromo- and dibromophakellin, isolated from the marine sponge Phakellia flabellata. These compounds showed pka values of <8 which were rather low when compared with the pka values of <12 reported for all other guanidines. Because of the anomaly in the base strengths of phakellins the structures proposed for them have been questioned by nearly all marine chemists. In this paper we will emphasize that the structures are correct and the low basicities of phakellins may be attributed to the twisted conformation of the imidazoline ring.

GAS CHROMATOGRAPHY-MASS SPECTROMETRY OF <u>LAURENCIA</u> SPECIES, Salvatore Caccamese, Institute of Industrial Chemistry, University of Catania, Italy, and Kenneth L. Rinehart, Jr., Department of Chemistry, University of Illinois, Urbana, Illinois, 61801.

The combined technique of gas chromatography-mass spectrometry (GC-MS) has been employed in studying a number of Laurencia (Rhodophyta) species. As expected for red algae, n-heptadecane was the predominant n-alkane. On the basis of their GC-MS traces it is possible to divide Laurencia species into different groups containing related compounds. A careful study of Laurencia decidua (AHBE 18-111-74-2-106) using GC-MS as a guide to novel compounds has been especially productive. Several new terpenes containing the laurane skeleton have been identified and characterized by physical techniques (mass spectrometry, IH and 13C NMR spectroscopy) and biological activities (antimicrobial, antitumor). Two of the new terpenes have been synthesized and preliminary evidence has been obtained for a brominating enzyme. These techniques (GC-MS, antimicrobial and antitumor testing) have also been applied to other algae, allowing identification of compounds with antibacterial and antitumor activity.

STUDIES ON MARINE STEROLS USING CHEMICAL IONIZATION MASS SPECTRAL TECHNIQUES, Ajay K. Bose, B. N. Pramanik, B. G. Pujar, H. Fujiwara, Department of Chemistry and Chemical Engineering, Stevens Institute of Technology, Hoboken, New Jersey, 07030.

Chemical Ionization Mass Spectrometry is a powerful tool for the study of sterols. When ammonia is used as the reagent gas, the sensitivity of this mass spectral method is increased and strong pseudo-molecular ions are observed for multifunctional sterols and many of their derivatives. Sterols in marine species often occur together as several members of a homologous series that are usually difficult to separate by gas chromatography or thin layer chromatography. We have found convenient methods for derivatizing such mixtures in a way suitable for Cl mass spectrometry so that all the members of a whole family of steroids can be detected from a single spectral determination. We have developed an oxidation method (with RuO₄) which followed by CI-MS (NH₃) analysis can be used on sub-nanogram size samples for the location of double bonds in the chain of sterols. Negative CI-MS is a new technique for increasing the sensitivity of detection of compounds with appropriate functional groups. A derivatizing agent for sterols that is particularly useful is trichloroacetyl isocyanate. The chlorine containing urethanes from sterols provide strong M-1 peaks in negative Cl spectra. The application of these techniques and C.I. mass spectrometry to the study of sterols in some marine species will be described and the biomedical implications of the observations will be discussed.

SESSION II

A DUAL ADRENERGIC COMPOUND FROM THE SPONGE VERONGIA FISTULARIS, K. H. Hollenbeak and F. J. Schmitz, Department of Chemistry, University of Öklahoma, Norman, OK, P. N. Kaul and S. K. Kulkarni, University of Oklahoma Health Sciences Center, College of Pharmacy, Oklahoma City, OK.

Bioassay-guided fractionation of extracts of the sponge Verongia fistularis has led to the isolation of a dibromotyramine derivative possessing a dual adrenergic activity. Isolation was guided by measuring the effect of the fractions on the blood pressure of anesthetized dogs. The pure isolate exhibited both pressor and depressor activities attributable to its alpha and beta adrenergic activities which could be blocked by the appropriate blockers. The structure of the compound has been confirmed by synthesis.

AN INHIBITOR OF DRUG METABOLISM ISOLATED FROM SEA HARE <u>APLYSIA</u> DACTYLOMELA, P. N. Kaul, S. K. Kulkarni, F. J. Schmitz and K. Hollenbeak, College of Pharmacy and Department of Chemistry, University of Oklahoma.

In our ongoing program aimed at evaluating and isolating pharmacologically active substances of marine origin, the extracts of the sea hare, Aplysia dactylomela, exhibited an ability to potentiate pentobarbital hypnosis. The extracts also decreased the spontaneous and locomotor activities of laboratory animals. A bioassay guided fractionation, using a sequence of solvent partitioning followed by LH-20 and adsorption chromatography, led to the isolation of an acetylenic dibromochloroether, dactylyne. It did not have any effect on the cardiovascular, respiratory and central nervous systems of mice, rats and guinea pigs. However, in 25 mg/kg doses it prolonged the pentobarbital hypnosis in mice by more than 20 hours. The mechanism of this potentiation appears to be the inhibition of pentobarbital metabolism.

IMMUNOMODULATION BY EXTRACT OF ECTEINASCIDIA TURBINATA (ETE) SUPPRESSIVE EFFECTS OF LYMPHOCYTES, Wolf Lichter, Abdul Ghaffar, Larry L. Wellham and M. Michael Sigel.

We have previously reported that Ete can exert a number of profound immunosuppressive effects. Thus the extracts have inhibited antibody production in vivo; prolonged skin graft survival of allogeneic skin transplants in mice; diminished graft versus host (GVH) reaction; suppressed the appearance of antibody plaque forming cells and ablated the mitogenic response of lymphocytes to lectins. In the last mentioned activity Ete was able to inhibit tritiated thymidine uptake, not only when administered at the time of mitogen stimulation but also when given as late as 24 hours (and even partly when given 48 hours) after stimulation. We are presently reporting that the suppressive activity has the following characteristics: 1) it is dependent on route of administration (the 1.P. route is more efficient than the 1.V. route), 2) the activity is mediated principally through T cells, and 3) there are indications that some of the suppression is brought about by suppressor cells and/or suppressor molecules.

IMMUNOMODULATION BY EXTRACT OF ECTEINASCIDIA TURBINATA, ACTIVATION OF THE RE SYSTEM, Abdul Ghaffar, Wolf Lichter, Larry L. Wellham and M. Michael Sigel.

It has been observed that Ete can potentiate humoral immune response to SRBC under certain conditions. This agent also caused splenomegaly in mice. The possibility that Ete might be a potential activator of the reticuloendothelial system was explored. The results indicate that Ete treatment causes an accelerated clearance of colloidal material in vivo and activates in vivo macrophages cytotoxic to tumor target in vitro. This may be one of the mechanisms by which Ete exerts its antitumor effect in vivo.

SESSION III

MECHANISM OF ACTION OF PALYTOXIN, S. K. Kulkarni and P. N. Kaul, College of Pharmacy, University of Oklahoma Health Sciences Center, Oklahoma City, OK.

Palytoxin (PTX) obtained from the coelenterate zoanthids of genus Palythoa, was previously shown to produce acute coronary constriction in the isolated perfusing guinea pig heart and produce EKG changes in anesthetized animals similar to those observed in variant angina. The present study has revealed that the coronary vasculature is the primary site of cardiotoxic action of PTX. When PTX was administered in intracerebroventricular (icv) doses of 1-50 ng, the pressor response and the EKG changes occurred between 1 and 15 minutes of injection. These changes occurred much faster with i.v. doses of PTX. The vasoconstriction produced by PTX could be counteracted by papaverine, verapamil and to some extent by phenoxybenzamine. However, lanthanum (10⁻⁵M) did not prevent the constrictor action of PTX in aortic strip preparations. Also, low Ca and added lanthanum in the perfusion fluid did not block the coronary constrictor action of PTX in the isolated perfusing guinea pig heart. All these data suggest that PTX may have a direct effect on the coronary vasculature which is at least partially independent.

ISOLATION AND CHARACTERIZATION OF BIOLOGICALLY ACTIVE POLYPEPTIDES (TOXINS AND PROTEINASE INHIBITORS) FROM SEA ANEMONES (ANEMONIA SULCATA AND CONDYLACTIS AURANTIACA), 1. Beress*, G. Wunderer**, R. Beress*, and M. Fritz**, *Institut fur Meereskunde an der Universität Kiel, **Abteilung für Klinische Chemie and Klinische Biochemie in der Chirurgischen Klinische Biochemie in der Chirurgischen Klinische Biochemie

Sea anemones contain toxic polypeptides utilized for the capture of prey or for defense. They are also the first marine animals in which proteinase inhibitors could be detected. Like the toxins, the proteinase inhibitors are also polypeptides. The isolation of the sea anemone toxins and proteinase inhibitors was accomplished by alcoholic extraction of the homogenized animals, batchwise adsorption on cation exchangers (CM-Cellulose, SP-Sephadex C25), gel-filtration on Sephadex (G50, G25, G10) and Biogel P-2, and ion exchange chromatography on SP-Sephadex and QAE-Sephadex. All toxins were tested on the shore crab Carcinus maenas by intramuscular injection. The lethalities (LD100) of the toxins for the Anemonia sulcata (ATX I and ATX II) and for that of the Condylactis aurantiaca (CTX I, II, III and IV) range between 2 and 6 ug/kg Carcinus maenas. The LD100 for ATX III is 50 ug/kg Carcinus maenas. All proteinase inhibitors isolated from the sea anemones inhibit trypsin, chymotrypsin, kallikreins and plasmin.

ACTION OF CEMBRANOLIDES DERIVED FROM OCTOCORALS ON LARVAE OF THE NUDIBRANCH PHESTILLA SIBOGAE, M. G. Hadfield, Kewalo Marine Laboratory, Pacific Biomedical Research Center, University of Hawaii, Honolulu, 96813 and Leon S. Ciereszko, Chemistry Department, the University of Oklahoma, Norman, 73019.

Gorgonians, or homy corals, are coelenterates of the Class Anthozoa, Subclass Octocorallia, or Alcyonaria, Order Gorgonacea. They are prominent members of the sessile shallow water coral reef fauna in the Caribbean. They have few predators and succeed in the competition for "space" on solid substrate in coral reef areas. We feel that the success of gorgonians against predation and against overgrowth by competing organisms is in part due to the secretion of defense substances. These include compounds related to cembrene, a diterpene with a 14-membered ring. The cembranolides are toxic to a variety of organisms and inhibit ciliary movement (Ciereszko, 1962; Perkins and Ciereszko, 1970, 1973, 1974). Larvae of the nudibranch Phestilla sibogae were used in this study because they are well equipped with cilia the activity of which is easily observed. The larvae were exposed to dilute solutions of cembranolides derived from garganians collected in the Caribbean area. Crassin acetate, eunicin, eupalmerin acetate, jeunicin and peunicin killed the larvae at concentrations of 1 part per million of sea water. The velar cilia of larvae in contact with eunicin at 10 ppm began to disappear immediately. After exposure of the larvae to eunicin at 10 ppm for as little as 15 minutes followed by transfer to clean sea water, the larvae died within the following 48 hours.

THE MARYLAND BLUE CRAB: AN EXPERIMENTAL ANIMAL FOR CARDIOTOXICOLOGICAL INVESTIGATIONS, Joseph W. Burnett*, Gary J. Calton*, and Leah M. Staling**, Division of Dermatology, University of Maryland School of Medicine* and the Department of Physiology, University of Maryland School of Dentistry**, Baltimore, Maryland, 21201.

A technique for electrocardiographic examination of blue crabs is described and the normal tracings are demonstrated. Toxins derived from the sea nettle, pokeberry and tadpole induce ventricular conduction and repolarization abnormalities in the crab heart. The electrocardiographic examination of the blue crab is a simple, inexpensive technique to employ when screening substances for cardiotoxic activity.

SESSION IV

FUNCTION OF TRACE ELEMENTS SILICON, BORON AND IODINE IN MARINE PLANTS, Dietrich Werner, University of Marburg, Germany.

Three species of diatoms, used as laboratory organisms in the studies on silicon and boron metabolism are described in some detail: Cyclotella cryptica, small cells with a high growth rate (k⁻¹=5h) and a high silicate content (12 pgSi/cell), Coscinodiscus asteromphalus, large cells with a low growth rate (k-1=24 h) and a high silicate content (40 ugSi/cell) and Bellerochea yucatanensis, medium sized cells with a high growth rate (k = 6 h) and a very low silicate content. The sequences of metabolic effects, following Si(OH)_A deficiency and resupply and following Ge(OH)_A inhibition are described and compared. The connection of silicon and boron metabolism in diatoms is demonstrated with special effects of silico-borates on growth. Some more general ideas on the function of silicates and silicate structures in biological systems are added, which could be useful for biotechnological developments (e.g. water purification), lodine metabolism is compared in Asparagopsis armata and Falkenbergia rufolanosa, representing different generations of the same species of red algae. Remarkable differences in the uptake and in the extraction of iodine of both generations are demonstrated. Three different low molecular weight iodine-metabolites were isolated from Falkenbergia, that were absent in the other generation of the same species. Some experiments in mammalian thyroid gland metabolism, using these iodine metabolites from Falkenbergia are proposed.

NEW METHODS FOR MEASURING THE CONCENTRATION OF TRACE ELEMENTS IN OCEAN WATERS, G. M. Sharma and Henry DuBois, New York Ocean Science Laboratory, Montauk, New York, 11954.

The growth of marine plants is of paramount importance because it provides the basis of marine food chain which culminates in fish and marine mammals. These plants require a number of trace elements (Fe, Cu, Co, Mn, Zn, Mo, etc.) for their healthy growth. The blooming of marine plants would lower the concentration of the essential elements appreciably if the rates of their regeneration are not high. For investigating the generation (or supply) and uptake of trace elements in the marine environment analytical methods are needed which would be simple and rapid in addition to being highly sensitive. In this paper we will report the development of radiometric methods for the direct determination of biologically essential trace elements in a small volume of ocean waters. These methods are simple and can be used on shipboard for the routine analysis of sea water.

BROMOPEROXIDASE FROM THE RED ALGAE <u>BONNEMAISONIA HAMIFERA</u>, Lowell Hagar, Richard Theiler, and Jerry Siuda, University of Illinois, Urbana, Illinois, 61801.

A powerful brominating activity has been detected in crude extracts of the red alage. Bonnemaisonia hamifera. High concentrations of halometabolites were ariginally detected in lipid extracts of this algae in the organic halogen screening program conducted on the R/V Alpha Helix Expedition. Brominated derivatives of 2-heptone were subsequently identified as major halometabolites in this organism. The brominating activity found in the Bonnemaisonia crude extracts has been partially purified and has been shown to be associated with a hemecontaining alycoprotein fraction. The bromination reaction requires hydrogen peroxide for activity and will utilize a wide variety of nucleophiles as halogen acceptors. In may respects the Bonnemaisonia bromoperoxidase activity is quite analogous to the fungal enzyme, chloroperoxidase. However, bromoperoxidase differs from chloroperoxidase in two important aspects. First, the pH optima for the halogenating activity of the two enzymes is quite different. Bromoperoxidase has a pH optimum of near pH 7 while chloroperoxidase is inactive above pH 4.5. Secondly, as their names imply, chloroperoxidase will oxidize chloride ion in addition to bromide and iodide whereas bromoperoxidase will not oxidize chloride but is quite active with bromide and iodide ions. When 2-ketooctanoic acid serves as a halogen acceptor for the bromoperoxidase reaction, brominated 2heptanones are formed. Bromoform can also be detected as a product of

the enzymatic bromination of 2-ketooctanoic acid. In addition to its utility in studies on the biosynthesis of marine algae halometabolites, bromoperoxidase has a practical import in nuclear medicine. Bromoperoxidase will catalyze the incorporation of carrier-free 78 Br into protein tyrosinyl residues under very mild conditions. This labeling procedure offers a very useful method for preparing stable radioactive proteins for use in diagnostic medicine.

THE GEOGRAPHICAL DISTRIBUTION OF CIGUATOXIC FISH IN THE EASTERN HALF OF THE BRITISH VIRGIN ISLANDS, William T. Davin, Jr., Norman J. Doorenbos, and William D. Longest, Bitter End Field Station, Virgin Gorda, B.V.I., and the Departments of Pharmacognosy and Biology, University of Mississippi, University, Mississippi, 38677.

Waters of the eastern half of the British Virgin Islands were divided into quadrants of four square nautical miles and a random 30 of the resulting 54 quadrants were selected for capturing fish with native fish traps. A total of 1354 fish were collected of which 54 were found to be toxic and 94 marginally toxic in our brine shrimp assay. The most toxic areas were found along the 100 fathom dropoff at the south tip of Anagada Reef, Colisan Point on Virgin Gorda, and Seal Dog Rocks. Some species were found to be much more frequently toxic than others. This study is significant because the specimens trapped are similar to those most frequently eaten by local people. The procedures used and results obtained will be discussed.

TOXIN PRODUCING BACILLI ISOLATED FROM THE GUT OF SURGEONFISH, Norman J. Doorenbos, H. Ray Granade, Ned T. Barden, George A. Capiton, Eric Dahl, Norman O. Thomas, Edward J. Truemper and Samuel M. Tumey, Bitter End Field Station, Virgin Gorda, B.V.I., and Departments of Pharmacognosy and Biology, University of Mississippi, University, MS 38677.

Ciguatera toxins have been shown to be passed through the food chain but their source has not been established. In the belief that the source might be an intestinal microorganism, cultures were isolated from the intestines of three species of Surgeonfish, grown in liquid marine broth, and examined for the presence of toxins. Three of these cultures produced ciguatera-like toxins. These cultures were identified as <u>Bacilli</u>. They had been isolated from fish speared in waters known to contain many ciguatoxic fish. The isolation and culture of the bacteria and the properties of the toxins will be discussed.

INVERTEBRATE MUCUS: MODEL SYSTEMS FOR STUDYING DISEASES IN MAN?, Robert E. Hillman, Battelle, Columbus Laboratories, William F. Clapp Laboratories, Duxbury, Massachusetts, 02332.

Histochemical studies of mucopolysaccharides in the mantle of the quahog clam Mercenaria mercenaria indicate that the quahog has a variety of complex mucosubstances which may play very sophisticated roles in its physiology. The possibility that the formation and function of these materials in the clam and other invertebrates may be good model systems for the study of certain metabolic diseases in man is suggested. For example, a mucopolysaccharide in the shell-secreting tissue of the clam resembles, histochemically, chandroitin sulfate found associated with calcifying tissues in higher organisms, yet the molecular structure is different in certain respects. The differences in structure may be related to differences in how they function during calcification, and the possibility of similarities between normal clam shell deposition and abnormal calcification in arthritis and related diseases is speculated upon. In another portion of the mantle, the mucopolysaccharides appear to gain or lose sulfate and other acidic groups with changes in sodium and chloride levels in seawater. A possible similarity between this mechanism in the clam and those involved in cystic fibrosis in humans is also suggested.

FOOD SECTION

SESSION I

PACIFIC COAST SALMON INDUSTRY - STATUS OF NATURAL AND CURRENT PRODUCTION, Kenneth A. Henry, National Marine Fisheries Service, Washington, D.C.

The Pacific Coast salmon industry and the salmon resource are facing a period of great pressures. Following record high levels of natural production shortly after the turn of the century for most of the five species of Pacific salmon, many stocks experienced fairly severe declines in production and some stocks were even eliminated. These declines were due, in large part, to increased industrial development, pollution, urbanization, poor logging practices, overfishing, and particularly on the Columbia River, large scale hydroelectric development. Although some of the declines in population have been actually reversed through large scale hatchery production, particularly for chinook and coho salmon, this in itself has created additional problems in attempting to improve or even maintain production from the natural stocks. Nevertheless, artificial production and rearing of salmon is increasing dramatically along the Pacific Ocean. In addition to all these other problems, recent court decisions specifying certain fishing rights to Treaty Indians have been an additional concern to the salmon fishing industry.

PACIFIC SALMON MARICULTURE - ITS STATUS AND ITS PROBLEMS, Jon M. Lindbergh, Domsea Farms, Inc., 6720 Old Belfair Highway, Bremerton, Washington, 98310.

Pacific salmon mariculture had its inception in experiments carried out by the National Marine Fisheries Service in 1969 at Manchester, Washington. Subsequently in 1970 a joint pilot program was successfully completed by Domsea Farms and NMFS with assistance from the Sea Grant Office. In 1971 Domsea established a commercial scale venture with Pacific salmon which now provides significant harvests of plate sized salmon on a consistent basis. Nevertheless, problems still exist which restrict the development of a more healthy and profitable industry. Salmon culturists presently rear most of their stock from eggs taken from wild parents selected by nature for survival at sea. A domesticated salmon is needed which thrives efficiently under the high density conditions of controlled culture. Cultured salmon are fed primarily on prepared feed which is not yet as effective for growth and survivability as natural feed. Better nutrition would provide an important improvement in the economics of salmon mariculture. Disease still imposes a high attrition rate on salmon reared in the relatively dense conditions of commercial culture. The development of fish vaccines has progressed quite rapidly and has great promise for prevention of disease. Certain drugs and medications are presently available which are effective against some diseases. However, serious problems exist in completing and maintaining certification as required by regulatory agencies.

A salmon mariculturist must often transport harvested fish and some times live fish across state and international boundaries. Health certification is required for such transport, but the services needed for certification are often very difficult to acquire. For salmon mariculture to thrive and expand, it will need new grow out sites in salt water. The intense competition for potential sites from other users coupled with complex permit proceedures makes the acquisition of new sites difficult.

OCEAN RANCHING - AN INDUSTRIAL MODEL, B. Allee, Weyerhaeuser Company, Tacoma, Washington.

Ocean ranching has been a traditional method of salmon enhancement for the common property fishery by publically funded state and federal hatcheries. An extension of the concept would satisfy the same objectives but also include private industry as the propagator of salmon smalts as well as a harvestor of adult salmon. In this connection, the state of Oregon has taken a bold lead in developing legislation to allow private ocean ranching. Weyerhaeuser Company will invest 10 million dollars to develop an ocean ranching business in Oregon State. This business is composed of a freshwater hatchery and two saltwater releaserecapture facilities. The former will temper river water with non-process cooling water from a Pulp mill and disenfect this water to achieve a "disease free" hatchery. The latter facility will pump saltwater to attract adult salmon into the fish ladder in the Fall and create a rearing pond for post smalt salmon during a period of osmotic acclimation to saltwater in the spring. Salmon smolts will be vaccinated in the freshwater hatchery and transported by truck to the Oregon coastal saltwater release site. Three species of salmon, chum (Oncorhynchus keta), coho (O. kisutch), and chinook (O. tshawytscha) will be managed to reduce biological risk and enhance product availability. The planned release strategy will eventually total 80 million smolts, over 90% of which by weight, will be coho and chinook salmon. The anticipated percentage of adult salmon returning to the saltwater recapture site will vary from 1-5%. A higher percentage of these fish will contribute to Oregon sport and commercial fishermen. This industrial model will serve to enhance the salmon resource in conjunction with state and federal programs in Oregon State.

SESSION II

ECONOMIC AND PRODUCTION ASPECTS OF THE GULF OF MEXICO SHRIMP FISHERY, John P. Nichols and Wade L. Griffin, Texas A & M, College Station, Texas.

Although total landings of shrimp from the Gulf of Mexico are twice what they were fifty years ago, little increase has been noted in the last 25 years. During this most recent period the general level of prices for shrimp has increased substantially, and the level of effort exerted in trawling for shrimp has also increased. The catch per unit of effort has declined in recent years and cost of operation increased (particularly related to increased cost of fuel). Since the U.S. market is dependent on foreign sources for more than 50 percent of its supply of shrimp, dislocations in the world market will greatly affect prices paid to U.S. fishermen. This periodically puts substantial pressure on vessel owners who are coping with rapidly escalating costs. Loss of opportunities to fish in Mexican waters will also affect the economic status of the U.S. shrimp fleet. The initiation of extended jurisdiction in the U.S. may provide some opportunities for improved management of the fishery, but action by the Regional Council regarding the shrimp industry is not likely in the near future. Data are presented in tables and graphs to support the discussion of trends in economic and production variables.

CONTROLLED ENVIRONMENT AQUACULTURE OF PENAEIDS, B. Salser, L. Mahler, D. Lightner, J. Ure, D. Danald, C. Brand, N. Stamp, D. Moore and B. Colvin, Environmental Research Laboratory, University of Arizona, Tucson, Arizona, 85706.

The Environmental Research Laboratory of the University of Arizona operates, in cooperation with the University of Sonora, a large intensive-culture research project at Puerto Penasco on the northern Gulf of California. The ERL's Controlled Environment Aquaculture (CEAq) system involves production of postlarvae in the station hatchery and subsequent rearing and growout in controlled environment. The flow-through raceways, which are completely enclosed in air-inflated plastic structures are inoculated with indigenous algal species for photosynthetic oxygen production and to assist in health maintenance and dietary supplementation. The CEAq system requires little and, but is relatively high in capital and operating costs. Because the system is independent of outside environmental influences, it maximizes growth rates and survival, controls disease, and eliminates predation, thereby circumventing some of the major problems which handicap extensive systems. In contrast to extensive systems, such high density cultivation requires a more nutrient-dense compounded feed and can generate circumstances which easily stress the animals increasing the predisposition to disease. Since its inception in 1973, CEAq at ERL has made considerable progress. Of approximately a dozen diseases and disease-like syndromes which may occur in dense, intensive-culture systems, only a few have caused major recurrent epizootics requiring chemotherapy,

e.g., filamentous-gil! disease, fusarium infection and Lagenidium infection. Others, e.g., "black-death syndrome" have been associated with nutritional deficiencies. The development of formulated feeds has resulted in a phase-feeding program beginning with early, postlarval animals greatly reducing the need for costly and often unavailable Artemia nauplii. Concurrently, the engineering staff has explored environmental and operational parameters so that manipulations are now possible in raceway configuration, temperature, water depth and flow rate, exchange rate, and work is in progress on nutrient recovery from feces. Using these tools, actual management systems have been developed which have resulted in increased harvest densities of < 1 kg/m² in 1975 to almost 3 kg/m² in 1977, and growth rates have been accelerated from <0.7g/wk in 1975 to >1.1g/wk in 1977. This data from the production research can be extrapolated to an anticipated harvest of 40,000 to 60,000 pounds of shrimp tails/acre/year compared to 1,500 to 2,500 pounds tails/acre/year from extensive systems. This data then supports the concept that the pilot scale operation is now ready to move on to the prototype production farm.

PENAEID SHRIMP CULTURE: PRESENT STATUS AND DIRECTION OF RESEARCH, F. S. Conte, Texas A&M University, College Station, Texas.

Penaeid shrimp culture as a viable and profitable enterprise is actively being pursued in many areas of the world. However, due to labor and operational cost it is not yet a reality in continental United States. Although interested investors have access to the same technology that has established shrimp culture in other areas of the world, a greater sophistication of this technology is necessary to reduce the cost of operating a shrimp farm in this country. Private, federal and state organizations are now establishing better avenues of technical exchange, and this increased communication is providing inroads to the solutions that will establish penaeid culture in the United States. In 1975 representatives of the various agencies conducting research in penaeid culture, hosted by the Oceanic Institute of Hawaii and the Office of Sea Grant of the Nation Oceanic and Atmospheric Administration, participated in a workshop to exchange information on the present status of penaeid culture and to define our most urgent priorities in research。 Since 1975 more intensive research has been directed towards disease identification, nutrition and life cycle control.

SESSION III

AQUACULTURE POTENTIALS IN THE GREAT LAKES AREA, George F. Greene, Jr., The Applied Research Center on Little Traverse Bay, Petoskey, Michigan, Wadsworth, Illinois.

The Great Lakes area is a complex combination of rural and urban populations. The former active commercial fishing industry is nearly gone due to a combination of natural and unnatural causes. When fishing is discussed today, it is sports fishing that everyone is talking about. The introduction of the Coho and Chinook Salmon into the system has created a huge recreational market. Still present, however, is a large demand for seafood products, in particular, for the Lake Perch (Perca flavacens), a most favored mid-west delicacy. With a reliable supply, this could easily be a national market. The answer may well be aquaculture and a plan for such an undertaking is discussed. The success of the big salmon in their adopted home is translated, into the commercial realm, by a suggestion to "ocean ranch" salmon in the Great Lakes, with a pilot project projected for the Little Traverse Bay in the 1978-79 season under the auspices of the Applied Research Center, (ARC). The establishment of bait minnow culture of walleyed pike, (Stizostedion vitreum vitreum), is also discussed.

IMPLICATIONS TO MARICULTURE OF THE STATUS OF FRESHWATER AQUACULTURE, Howard P. Clemens, The University of Oklahoma and Mayo Martin, Fish Farming Experimental Station, Stuttgart, Arkansas.

The development of such segments of freshwater aquaculture as the culture of catfish, minnows, goldfish, crayfish and trout is highlighted. Implications from these developments suggest patterns that may be applicable to mariculture.

SESSION IV

U.S. MOLLUSCAN SHELLFISH PRODUCTION, David M. Dressel, Industry and Consumer Services Division, National Marine Fisheries Service, Washington, D.C.

An historic review of the US molluscan shellfish production is given showing trends in oyster, clam, and mussel landings and changes resulting from resource availability and new technology. Attempts to offset declining resources resulting from pollution, disease, natural disasters, and overfishing are discussed in relation to the persistence of these problems.

SHELLFISH HATCHERIES: AN INDUSTRY VIEW, Stephen Henderson, President, International Shellfish Enterprises, Inc.

Introduction to Shellfish Mariculture

- A. Interest of Investors and Involvement of Governments
- B. Shellfish Hatchery Association

World Hatcheries - a State of the Art

Number, Location, Types & purposes of production

Commercially Feasible Sustained Production - a Myth?

- A. Historical Patterns and Current indications
- B. Operating Experience of ISE

Shellfish Culture: A glimpse at changing patterns

- A. Impact of pollution and "disease"
- B. Changes in the social order and economic pressures

The Market for Hatchery Products

- A. Displacement of Natural Seed
- B. Foundation for new business enterprises
- C. Re-building a public resource

The Commercial Challenge – Putting the pieces together

- A. Filling the needs of the grower
- B. Developing a production format
- C. Beating mother nature

A Glimpse into the future

- A. Short-term opportunities and liabilities
- B. The need, direction and benefits of research
- C. Competition from government-sponsored entities
- D. The need for a more-informed social environment
- E. Planning a solid base for the future

TRENDS IN CURRENT RESEARCH ON BIVALVE SHELLFISH MARICULTURE, Kent S. Price, University of Delaware, Lewes, Delaware, 19958.

The current status of research directed toward production of molluscan shellfish in the U.S.A. is reviewed. Key contributors and trends in research are identified. Special attention is given to research that has direct application to current production methods and to new industrial approaches for shellfish production.

SHELLFISH CULTURE IN JAPAN, William N. Shaw, U.S. Department of Commerce, National Oceanic and Atmospheric Administration, National Sea Grant Program, NOAA Advisory Service, Washington, D.C., 20235.

Japan is heavily involved in the extensive culture of shellfish. Principal species under cultivation include the Pacific oyster, Crassostrea gigas, the sea scallop, Patinopecten yessonensis, the abalone, Haliotis discus, and the pearl oyster Pinctada martensii. A variety of other molluscs and gastropods are mass reared for seeding. A variety of culturing techniques are utilized—these include hatcheries, rafts, racks, long lines, net enclosures, thermal heated raceways to mention a few. The Japanese have committed a major portion of their inland waterways for aquaculture of which a major portion of the area is devoted to off bottom culture. Slides depicting culturing techniques for the four principal species will be presented.

SESSION V

FOOD FROM THE SEA - MYTH OR REALITY, John P. Wise, National Marine Fisheries Service, Washington, D.C.

The most widely accepted estimate of potential annual yield of conventional species from the world ocean is well over 100 million metric tons. As of 1975 catches had increased to about 60 million tons. A total yield well in excess of 100 million tons may be possible if harvesting turns to less familiar types of marine animals. Production of food from the sea can be increased without increasing harvests. About 30 percent of world production now goes into fish meal. Total useful fish production could also be increased by some millions of tons by eliminating discards at sea and losses in handling, preservation, storage, and inefficient processing.

PUBLIC HEALTH CONSTRAINTS ON FOOD PRODUCTION FROM THE SEA, F. Raymond Fields, National Marine Fisheries Service, Pascagoula, Mississippi.

Public health hazards are limiting factors in seafood production. Among the hazards are toxins, metals, toxic organic substances, bacteria, viruses, and helminths. Examples of each, together with location and source are discussed. There are additional public health hazards involved in storage and transportation of food from the sea. Changes in procedures will be needed to remove limiting factors and hazards, and conclusions are drawn and recommendations made to remove public health constraints.

ECONOMIC CONSTRAINTS ON FOOD PRODUCTION FROM THE SEA, Daniel D. Huppert, National Marine Fisheries Service, La Jolla, California.

The potential supply of food from the sea is constrained more severely by economic than by biological or physical factors. Expansion of fish production requires that the average cost of production be maintained below the price at which consumers will demand additional quantities. In view of the continually expanding demand for meat products, the indirect consumption of fish meal through poultry and pork feed could conceivably expand several-fold. The economic constraint is that dense concentrations of fish must be found so that production costs are competitive with vegetable protein meals. Artificially synthesized potential sources of high quality protein could undercut the world market for fish protein. There is little evidence that aquaculture can seriously compete with either fisheries or agriculture in the mass production of protein foods.

PHYSICAL UPPER LIMITS ON FISHERIES PRODUCTION, Julien R. Goulet, Jr., National Marine Fisheries Service, Washington, D.C.

The marine fisheries production system may be considered as an "average" - or parameterized - trophic system. The system limits, as distinct from external limits such as economic or social constraints, are presented. These system limits are: (1) input to the system - i.e., primary production; (2) availability of production to man - i.e., fraction of the total that can be harvested; and (3) trophic level of the harvest. The impact of these limits on the system output - the harvest - is discussed, and preliminary estimates of the system limits and of fisheries production limits are presented. Time dependence of the system limits and of the system parameters is discussed. An environmental - fisheries synthesis approach to understanding the fisheries responses to variations in ocean properties and processes is presented.

CONSTRAINTS ON FOOD PRODUCTION FROM WILD PENAEID SHRIMP STOCKS IN THE GULF OF MEXICO, Edward F. Klima and Michael L. Parrack, National Marine Fisheries Service, Galveston, Texas.

Total U.S. shrimp production in the Gulf of Mexico from 1959-1975 has varied annually from a high of almost 150 million pounds heads-off in 1970 to a low of about 76 million pounds in 1961. During this period, fishing effort has increased and the trend in catch per boat decreased slightly. Biological, economic, social, and legal factors are examined to determine their impact on shrimp production in the Gulf of Mexico.

PROĢRAM

THE FIFTH FOOD-DRUGS FROM THE SEA CONFERENCE



Co-Chairmen

Pushkar N. Kaul The University of Oklahoma

Health Sciences Center. Oklahoma City, Ok

Carl J. Sindermann National Marine Fisheries Service

Sandy Hook Laboratory. Highlands, N.J.

Coordinator George F. Greene, Jr.

Applied Research Center, Wadsworth, III.

Host Committee Leon S. Ciereszko, chairman

Francis J. Schmitz Shriniyas K. Kulkarni Lucille Stellner Linda Stevens

Charlene Burns Assisted by: Phi Lambda Upsilon

The Committee wishes to thank the following Pharmaceutical Com-

(Michael Cleary, President)

panies for their financial support of the conference: The Upiohn Company G.D. Searle & Company **Abbott Laboratories**

Hoffmann-La Roche Inc.

CONFERENCE PROGRAM

ARRIVAL AND REGISTRATION Sept. 7. Afternoon Forum Room

2:00 - 8:00 Registration, OCCE Forum

8:00 - 10:00 Informal Mixer **OPENING SESSION** Co-Chairmen: Pushkar N. Kaul, Carl J. Sindermann

Sept. 8, Morning Forum Room

9:00 - 9:10 Opening of the Conference, Pushkar N. Kaul 9:10 - 9:15 Welcome by President Paul F. Sharp

9:15 - 9:25 Announcements, Local arrangements, Leon S. Ciereszko 9:30 - 10:30 Keynote Speech 1 "Contributions of the Sea to Medicine". Stewart Wolf, M.D. 10:30 - 11:00 Coffee Break

11:00 - 12:00 Keynote Speech 2 "Contributions of Aquaculture to Aquatic Food". John B. Glude. 12:00 Noon Adjourn for Lunch

DRUG SECTION

SESSION I Chairman: Kenneth L. Rinehart, Jr. Sept. 8. Afternoon Conference Room A 1:30 - 1:50 "Structure of a Complex

Marine Sponge Phakellia 1:50 - 2:10

"Adenosine as the Causative Asystolic Factor from a Marine Sponge", A.J. Weinheimer, C.W.J. Chang, J.A. Matson and P.N. Kaul. 2:10 - 2:30 "Novel Antimicrobial and Antineoplastic Compounds from Sponges of the Gulf of California", K.L. Rinehart, G.T. Carter, Y.M.

Metabolite isolated from the

flabellata", G.M. Sharma.

Goo and M.T. Cheng.

2:30 - 2:50	"Explanation of the Low Basicities of Phakellins", G.M. Sharma.	11:00 - 12:00	Lecture "Pharmacological Actions in Mammals and Therapeutic	
2:50 - 3:10	"Gas Chromatography-Mass Spectometry of Laurencia Species", S. Caccamese and K.L. Rinehart.		Potential of the Fish-urophysial Peptide Urotensin I'', Karl Lederis (introduced by N.J. Doorenbos).	
3:10 - 3:30	Coffee Break	12:00 Noon	Adjourn for Lunch	
3:30 - 3:50	"Studies on Marine Sterols Using Chemical Ionization Mass Spectral Techniques", A.K. Bose, B.N. Pramanik, B.G. Pujar and H. Fujiwara.	SESSION III	Chairman: George D. Ruggieri)
3:50 - 4:50	Lecture "A New Cardiotonic	Sept. 9, Afte		ζ.
	Substance from the Sea", Ted R.	, ,,,,,,		έ
	Norton (introduced by F.J. Schmitz).	1:30 - 1:50	"Mechanism of Action of Palytox- in", S.K. Kulkarni and P.N. Kaul.	1
6:30	Open Bar—Commons Restaurant	1:50 - 2:10		1
7:30	Banquet. Speaker: Harold H. Webber. (introduced by Earl H.Herron)		Biologically Active Polypeptides (Toxins and Proteinase-Inhibitors) from Sea Anemones (Anemonia sulcata and Condylactis aurantiaca)", L. Beress, G.	9
SESSION II	Chairman: James S.		Wunderer, R. Beress and H. Fritz.	
0	Kittredge	2:10 - 2:30	"Action of Cembranolides Derived	
9:00 - 9:20	ning "Some New Marine Anticancer	2.10 - 2.00	from Octocorals on Larvae of the Nudibranch <i>Phestilla Sibogae</i> ", M.G. Hadfield and L.S. Clereszko.	
	Agents", A.J. Weinhelmer, J.A. Matson, D. Van der Heim and M.B. Hossain.	2:30 - 2:50		#15.4
9:20 - 9:40	"A Dual Adrenergic Compound from the Sponge <i>Verongia</i> fistularis", K.H. Hollenbeak, F.J.		Burnett, G.J. Calton and L.M. Staling.	
	Schmitz, P.N. Kaul and S.K.		Coffee Break	ļ
9:40 - 10:00	Kulkarni. "An Inhibitor of Drug Metabolism Isolated from the Sea Hare Aplysia	3:30 - 4:30	Plenary Lecture "Overview from the National Sea Grant Office", David H. Attaway (introduced by L.S. Ciereszko) — Forum Room.	AND LAND
	dactylomela", P.N. Kaul, S.K. Kulkarni, F.J. Schmitz and K. Hollenbeak.	6:00 - 10:00		
10:00 - 10:20	"Immunomodulation by Extract of Ecteinascidia turbinata. Sup- pressive Effects of Lymphocytes", W. Lichter, A. Ghaffar, L.L.	SECCION IV	Chairman Ones P	THE PERSON NAMED IN
	Wellham and M. Michael Sigel.	SESSION IV	Chairman: George B.	
10:20 - 10:40	"Immunomodulation by Extract of Ecteinascidia turbinata, Activation of the RE System", A. Ghaffar, W. Lichter, L.L. Wellham and M.	Whitfield Sept. 10, Morning		
		9:00 - 9:20		
	Michael Sigel.	•	Silicon, Boron and Iodine in Marine	
10:40 - 11:00	Coffee Break		Plants", D. Werner.	
				_

	Ocean Waters", G.M. Sharma and H. DuBois.		Lindbergh.			
9:40 - 10:00	"Bromoperoxidase from the Red	2:30 - 2:50	"Ocean Ranching — An Industrial Model", B. Alee.			
	Alga <i>Bonnemaisonia hamilera</i> ", L. Hager, R. Theiler, J. Siuda.	3:10 - 3:30	Coffee Break			
10:00 - 10:20	"The Geographical Distribution of Ciguatoxic Fish in the Eastern Half of the British Virgin Islands", W.T. Davin, Jr., N.J. Doorenbos and W.D. Longest.					
10:20 - 10:40	Coffee Break	SESSION II	Marina Chrima Chairman			
10:40 - 11:00	"Bacteriology of the Hydrocoral Millepora Sp.", H.A.M. De Kruyf.		Marine Shrimp. Chairman: Carl J. Sindermann			
11:00 - 11:20	"Toxin Producing Bacilli Isolated	Sept. 8, Afte	rnoon			
	form the Gut of Surgeonfish", N.J. Doorenbos, H.R. Granade, N.T. Barden, G.A. Capiton, E. Dahl, N.O. Thomas, E.J. Truemper and	3:30 - 4:10	Lecture "Economic and Production Aspects of the Gulf of Mexico Shrimp Fishery", John P. Nichols.			
11:20 - 12:20	Model Systems for Studying Diseases in Man?", Robert H. Hillman (introduced by A.J.	4.10 - 4:30	"Controlled Environment Aquaculture of Penaeids", B. Salser, L. Mahler, D. Lightner, J. Ure, D. Danald, C. Brand, N. Stamp, D. Moore and B. Colvin.			
	Weinheimer).	4:30 - 4:50	"Penaeid Shrimp Culture: Present Status and Direction of Research, F.S. Conte.			
		6:30	Open Bar			
		7:30	Banquet			
	FOOD SECTION					
1	(Conference Room B)					
The overall theme of the conference in the Food Section is a realistic assessment of present status						
and potential production of principal marine food species, e.g., pacific salmon, marine shrimp and molluscan shellfish, for which significant fisheries		SESSION III	Diversified Aquaculture. Chairman: George F.			
and aquaculture	e facilities exist.	Sept. 9, Mor	Greene Jr.			
		00pt. 0, 11101	g			
SESSION I	Pacific Salmon. Chairman: Conrad Mahnken	9:00 - 10:00	Lecture "Implications of the Status of Freshwater Aquaculture to			
Sept. 8, Afternoon			Mariculture", Howard P. Clemens.			
		10:00 - 10:20	"Polyculture", R. Stickney.			
1:30 - 2:10	Lecture "Pacific Coast Salmon Industry — Status of Natural and	10:20 - 10:40	"Aquaculture Potentials in the Great Lakes Area", G.F. Greene.			
	Current Production," Kenneth A.	10:40 - 11:00	Coffee Break			
	Henry.	11:00 - 12:00	Voluntary Presentations			

2:10 - 2:30 "Pacific Salmon Mariculture — Its Status and Its Problems", J.M.

9:20 - 9:40 "New Methods for Measuring the Concentration of Trace Elements in

SESSION IV Molluscan Shellfish. Chairman: William N. Shaw

Sept. 9. Afternoon

- 1:30 2:10 Lecture "U.S. Molluscan Shellfish Production", D.M. Dressel.
- 2:10 2:30 "Shellfish Hatcheries: An Industry View", S. Henderson.
- 2:30 2:50 "Trends in Current Research on Bivalve Shellfish Mariculture", K.S. Price.
- 2:50 3:10 "Shellfish Culture in Japan", W.N. Shaw.
- 3:10 3:30 Coffee Break
- 3:30 4:30 Plenary Lecture "Overview from the National Sea Grant Office", David H. Attaway Forum Room.
 - 6:00 10:00 Outdoor Picnic, Fishing and Tour: Catfish Acres, Shawnee, Ok.

SESSION V Constraints on Production. Chairman: John P. Wise

Sept. 10, Morning

9:00 - 10:00 Lecture "Food from the Sea — Myth or Reality", John P. Wise.

F.R. Fields.

- 10:00 10:20 "Public Health Constraints on Food Production from the Sea",
- 10:20 10:40 "Economic Constraints on Food Production from the Sea", **D.D. Huppert**.
- 10:40 11:00 Coffee Break
- 11:00 11:20 "Physical Upper Limits on Fisheries Production", J.R. Goulet Jr.
- 11:20 11:40 "Contraints on Food Production from Wild Penaeid Shrimp Stocks in the Gulf of Mexico", E.F. Klima and M.L. Parrack.