# ADVANCES IN AQUATIC BIOLOGY AND FISHERIES

## PROF. N. BALAKRISHNAN NAIR FELICITATION VOLUME


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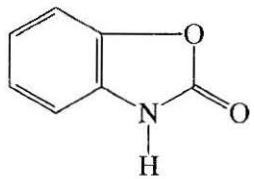
# 2.

# Pharmaceutical Potential of Marine Organisms

S. Z. QASIM

The use of extracts of plants and animals for medicinal purposes is a practice as old as the history of mankind. However, man's efforts have largely been confined to land plants and animals probably because of their easy accessibility. These represent only 20% of the earth's total plant and animal life. The oceans, which cover about 71% of the earth, support very rich plant and animal life, classified under more than 30 flora and fauna. Some of these are exclusively marine and thrive under extremely diverse environmental conditions. A large number of marine organisms are known to possess bioactive substances which have a tremendous pharmaceutical potential for the future. An outstanding example of how a traditional medical practice can lead to the isolation of a pharmaceutically active compound has been provided by the work on the mangrove plant *Acanthus illicifolius*. Bathing by the extract from this plant in the form of a decoction obtained by boiling the leaves and young shoots, has long been used in Goa to provide relief from rheumatic pain. Intrigued by this kind of usage, the scientists of the National Institute of Oceanography (NIO) and the Goa Medical College selected this plant for detailed pharmacological and chemical studies. The crude methanolic extract was found to exhibit analgesic and anti-inflammatory properties. It was found to be more effective in small doses than the standard analgesic pethidine hydrochloride and sodium salicylate. Its use also did not show addiction. The activity was found to be due to the occurrence of 2-benzoxazolinone with the following formula:



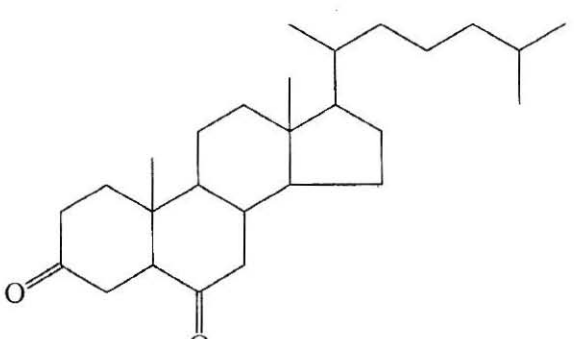

2-benzoxazolinone (analgesic, anti-inflammatory)

The anti-inflammatory activity could also be due to the presence of its precursors benzoxazinoids.

**Known Products of Marine Origin**

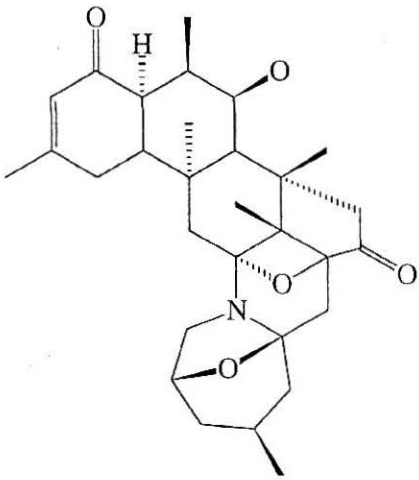
Substances like agar, alginates, carrageenan, cod-liver oil, sodium morrhulate, protamine sulphate, ichthammol etc. are being obtained from marine organisms since a long time. Cephalosporins, a new breed of antibiotic, which has helped make once-difficult surgery like the heart-transplant and the replacement of other body parts has become a matter of daily routine. It was first isolated from a marine organism. Likewise, some compounds have given very promising results for the development of antitumour drugs. The discovery of Ar-C (cytosine aralsinoside), a chemical not found in terrestrial organisms, but discovered in Caribbean sponges is worth mentioning here.

From the seaweed (red alga) *Acanthophora specifera*, an antibacterial compound has been isolated. It has the formula:



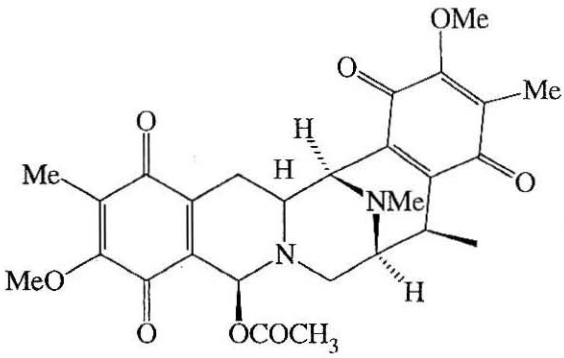

5 Chlostene-3, 6 dione (antibacterial)

A new class of alkaloids that possess anti-inflammatory and analgesic properties has been isolated from the zooanthid *Zooanthus* sp.




zooanthemine (analgesic, anti-inflammatory)

A new antibiotic which kills bacteria very fast has been obtained from a sponge *Kestospongia sp.* with a formula:




xestomycin (antibacterial) from *Kestospongia sp.*

**Active Substances from Marine Plants**

Predominant substances that can be obtained from marine plants include morphine, atropine, glycosides, carotenoids, algal lipids and certain en-

zymes and lipids. Cholesterol is widely distributed in trace amounts in algae. Phytoplankton are also known to be a rich source of vitamin D.

Because of the unique properties of marine plants, many products are becoming increasingly important in drug manufacturing industries and research units. From the blue-green and brown algae, four products namely carrageenan, algin, agar and agarose are extracted as gelling polysaccharides which are used as food additives and pharmacological phycocolloids. Carrageenan and algin can be used as cages for immobilising cells to be used in bioconversions. Bacteriologists have been using agar, agarose and alginic acid in tissue culture media and in electrophoresis and affinity chromatography.

## Substances from Marine Animals

Cardistonic peptides from sea anemones, an adrenergic compound from the sponge *Verongia fistularis* and an anti-cancer agent of high potential from the Caribbean gorgonians and soft corals have been isolated and are being intensively studied. More recently, a lot of attention has been focussed on antiviral and antitumour depsipeptides from the Caribbean tunicates. These depsipeptides from the Caribbean tunicates are also known to possess anticancer properties. Liver oil from the fish is an excellent source of vitamins A and D. Insulin is extracted from whales and tuna fish. Chitosan, a water soluble biopolymer, obtained from the shells of crustaceans, has varied functional properties. Currently, researches are being conducted on the use of chitoson globules to encapsulate microbial cells to be used in the production of enzymes and amino acids.

Of particular interest are toxins produced by marine organisms, which are compounds of high physiological activity and these can be used as drugs or pharmacological agents or as a base for the synthesis or improvement and screening of anticarcinogenic, antibiotic, haemolytic, analgesic and antispasmodic agents. Members of the phyla Coelenterata, Mollusca, Echinodermata and Protochordata are known to secrete toxins. Some of the very important toxins are ciguatoxin, palytoxin and halitoxin which are heat-stable-lipid-soluble compounds. Toxins are usually inhibitory in action. These usually act on peripheral nerves and have permeability through the nerve-membranes. They are most valuable in elucidating the excitation mechanisms. However, at present the application of toxins of marine origin is largely limited to the area of understanding the functions of body organs.

## 1. Chemistry of Marine Organisms

The chemistry of marine organism differs from that of their terrestrial counterparts in several respects. This is hardly surprising considering that the organisms are adapted to widely different environmental conditions. Also since many of the marine organisms are positioned much below the terrestrial organisms on the evolutionary ladder, they are expected to possess vastly different secondary metabolites. This is evident from the results obtained in several studies dealing with marine natural products. For example, halogenated compounds, seldom found in land plants and animals, occur frequently in marine organisms due to the high concentrations of chlorine and bromine present in sea water. These compounds are known to posses antimicrobial activities. Similarly, marine organisms are rich in sterols some of which are unique and have no equivalent when compared to their land derivatives. There has been a phenomenal increase in the use of steroids for the preparation of various drugs including antifertility agents and corticoids (sex hormones). These activities have led to a chronic shortage of steroid-producing materials. The steroids obtained from marine sources could serve as a large repository of steroid-generating organisms. Similarly, prostaglandins, which are produced in microscopic quantities in the human body to play an important role in the life processes, are present in large quantities in gorgonians (sea fans) and soft corals. Finally, there are numerous highly potent toxins produced by marine organisms with very unusual structures.

## 2. Research Activities in India

There was very little information available on the pharmaceutical potential of the Indian Ocean biota till 1978 when a project was initiated jointly by the National Institute of Oceanography (NIO), Goa and the Central Drug Research Institute (CDRI), Lucknow. This was initially promoted by the author during his tenure as Director, NIO, Goa (1974-81). Subsequently, the project was extended with a collaborative venture from the United States making use of the US-India fund (USIF). The project under the new title 'Bioactive Substances from the India Ocean' involved NIO, CDRI and the Bose Institute, Calcutta, as the three Indian participating institutions and the Stevens Institute of Technology, Hoboken, New Jersey, the University of Southern California, Los Angles, and the Osborn Laboratories, New York, as the three American collaborators. The project was initiated

in 1985. Much work has been carried out since then by the scientists of the various collaborating institutions. So far, it has not led to the development of a new drug as the development of a new drug is a very time-consuming process involving 10-20 years. Nevertheless, the results obtained have laid a solid foundation for further works to be undertaken in India. The project also helped in establishing the infrastructural facilities such as a "diving cell" with a team of trained divers for the underwater collections of plants and animals and a museum for maintaining taxonomical records of the organisms. The major funding agency in India is the Department of Ocean Development, New Delhi. We hope that the financial assistance from the Indian source will be continued and many more laboratories in the country will be involved in this work.

At first, a large number of extracts from marine plants and animals (collected from all along the coast including Laccadives and Andamans) were put through a broad biological screen. This included the tests for antibiotic (antibacterial and antifungal), antiviral, antifertility and anti-inflammatory activities and those which have an effect on the central nervous and cardiovascular systems. Of the 500 extracts screened, about 165 were found to be pharmacologically active. Perhaps the most significant activity observed is the antifertility (100% anti-implantation) activity displayed by 4 species of seaweeds, 6 species of sponges, 5 species of soft and hard corals and 1 species of amphineuran mollusc. Other notable activities include antimicrobial, diuretic, CNC stimulant, CNS depressant, hypotensive, spasmogenic, spasmolytic, hypoglycemic, oxytocic, analgesic and adrenergic blocking. These results raise the hope that the seas around India may provide very important therapeutic agents.

## 3. Conclusion

From the account presented above, it is obvious that marine organisms from the India Ocean, as diverse as those found anywhere else in the oceans, possess enormous potential for providing compounds that may be developed as useful drugs and drug intermediates. Considering that only a small fraction of the total organisms has been sampled so far (the collections have been made from limited geographical areas and depth ranges mostly intertidal), there is a vast scope for further researches. The next two decades are expected to witness rapid growth and important breakthroughs in the programme "Drugs from the Sea".