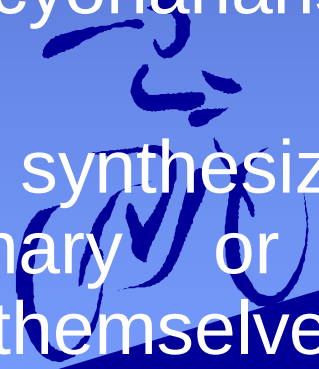
BIOACTIVE COMPOUNDS FROM MARINE ORGANISMS

BY
Dr N Manoharan
Assistant Proffessor
Department Of Marine Science
Bharathidasan University
Tiruchirapalli -24

- Marine bioactive compounds are organic compounds produced by microbes, sponges, gorgonians, soft and hard corals seaweeds, and other marine organisms.
- These products are the current interest of industry for new drugs and chemicals.
- Marine microorganisms form highly specific and symbiotic relationships with filter-feeding organisms like sponges, alcyonarians, ascidians and marine plants.
- The host organism synthesizes these compounds as non-primary or secondary metabolites to protect themselves and to maintain homeostasis in their environment.



- A diverse array of bioactive compounds can be isolated from the extracts of marine organisms.
- Many of them have novel chemical structures which may lead to the development of entirely new drugs and therapeutic agents.
- Anti-cancer agents have been isolated from algae, sponges, jellyfish, corals, shark cartilage and shellfish.
- The Pacific oyster contains a substance which may help diabetics by promoting the secretion of insulin.
- Chemicals found in sponges may be used to treat yeast and fungi.
- A poison emitted by the cone snail has been found to prevent brain damage in animals after a head injury or stroke, and offers great promise in future applications in humans.

1. Marine bacteria

- It has been demonstrated that marine bacteria produce anti-microbial substances.
- The first documented identification of a bioactive marine bacterial metabolite was the highly brominated pyrrole antibiotic, isolated from a bacterium obtained from the surface of the Caribbean Sea grass *Thalassia*.
- This metabolite was identified by x-ray crystallographic methods, which composed of more than 70% bromine by weight.
- The metabolite exhibited impressive *in vitro* antibiotic properties against Gram-positive bacteria, with minimum inhibitory concentration (MIC) ranging from 0.0063 to 0.2 g/ml.
- However, it was inactive for Gram-negative bacteria and animal assays.

- It is becoming abundantly clear that bacteria form highly specific, symbiotic relationships with marine plants and animals.
- Experience in this area arose from a study of the pathogen resistance of the estuarine shrimp *Palaemon macrodactylus*.
- The eggs of *P. dactylus* possess significant bacterial epibionts, which, when removed by treatment with antibiotics, leads to the rapid infestation of the eggs by pathogenic fungi, especially of *Lagenidium callinectes*.
- It could be due to the anti-fungal agents produced by bacteria.

2. Marine fungi

- Although terrestrial fungi have represented a major biomedicinal resource (e.g., penicillin from *Penicillium*), studies to develop the biomedicinal potential of marine fungi were less.
- The isolation of a small lactone, leptosphaerin from *Leptosphaeria oraemaris* demonstrated that marine fungi may form important resource for unique metabolites.
- Later, the useful chemical, Gliovictin was isolated from marine fungus, *Asteromyces cruciatus*.
- Since then more than twenty useful bioactive compounds have been derived from marine fungi.

3. Marine microalgae

- Marine microalgae are relatively unexploited but rich resources for bioactive compounds.
- Toxins initially isolated from fish or shellfish were found to originate from microalgae, especially dinoflagellates.
- These toxins are useful tools to investigate the structure and function of ion channels on cell membranes or to elucidate the mechanism of tumor promotion based on their specific inhibitory action against protein phosphatases.
- The number of antifungal or antitumoral substances of microalgal origin is rapidly increasing.

- More importantly, structural similarities have been found between many bioactives found in marine invertebrates and those in freshwater blue-green algae.
- The similarities point to a great potential of marine blue-greens, the least explored resource, for producing bioactive compounds of medicinal value.
- Microalgae are significant resource for bioactive metabolites, particularly cytotoxic agents with applications in cancer chemotherapy.
- From the marine microalgae such as from the blooms of *Phaeocystis sp*., antibiotic substances were listed.
- *P. pouchetii* is reported to produce chemicals such as Acrylic acid, which constitutes about 7.0% of the dry weight.

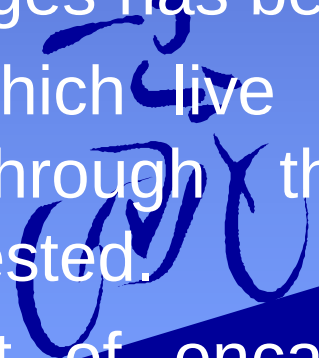
4. Marine macroalgae

- Of the total marine algae so far evaluated, about 25% showed one or the other biological activity.
- The metabolites of green algae were reported to contain 1,4 –diacetoxic butadiene moiety, which exhibited icthyotoxic property.
- Among the red algae, halogenated lipids have been isolated, particularly from the *Laurencia sp.*
- The rare chemical prostaglandin was also reported to occur in *Gracilaria pichenoids*.

5. Marine sponges

- Chemicals found in sponges may be used to treat yeast and fungi.
- The wider biosynthetic capability of sponges could be attributed to their biological association with other symbionts.
- About 38% of the sponge body comprises of microorganisms.
- A wide variety of secondary metabolites were isolated from sponges and these have been associated with antibacterial, antimicrobial, antiviral, antifouling, HIV-protease inhibitory, HIV reverse transcriptase inhibitory, immuno-suppressent and cytotoxic activities.
- In addition to potential anticancer applications, the bioactive compounds of sponges have a myriad of activities ranging from antibiotic activity including anticoagulant, antithrombin, anti-inflammatory, as well as imunomodulatory activities.

- The fact that the psammaplins have been isolated from a diversity of sponge “sources” and that brominated aromatic amino acid derivatives are common in marine bacteria suggests that these metabolites may actually derive from biosynthetic pathways of microorganisms living in association with sponges.
- Presence of specific symbiont morphologies of bacteria within specific sponges has been reported.
- These specific bacteria, which live symbiotically with sponges, passed through their feeding chambers without being digested.
- This suggested some sort of encapsulation or recognition process.



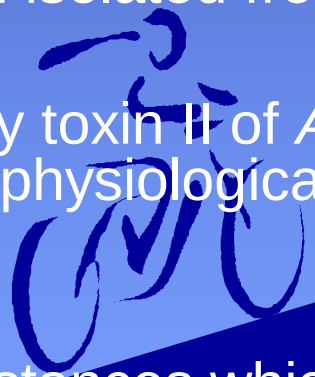
6. Sea Anemones

- In a 1977 conference on “Drugs and Food from the Sea : Myth or Reality,” “researchers described cardiotonic polypeptides from sea anemones .

- The sea anemone, *Anemonia sulcata* is a well-known natural source of supply of biologically active polypeptides.

- So far, five toxins, ATX I, II, III, IV and AS V, several polyvalent protease inhibitors, an elastase inhibitor, two blood pressure-depressive polypeptides have been isolated from it.

- The sea anemone toxins (especially toxin II of *A*. *sulcata*, ATX II) are very important tools in neurophysiological and pharmacological research.



7. Ascidians

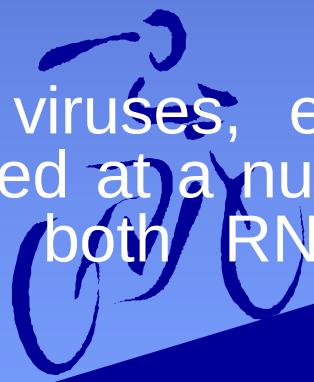
- Ascidians synthesize bioactive substances which are cytotoxic.

8. Tunicates

- Rinehart *et al*. (1981) have described antiviral and antitumor depsipeptides from a Caribbean tunicate.

- The tunicate of the *Tridemnum* genus, when extracted with methanol-tolulene (3:1), showed activity against herpes simplex virus, type I, grown in CV-1 cells (monkey kidney tissue), indicating that the extract inhibited the growth of the virus.

- When tested against other viruses, essentially all extracts of the tunicate collected at a number of sites showed activity in inhibiting both RNA and DNA viruses.



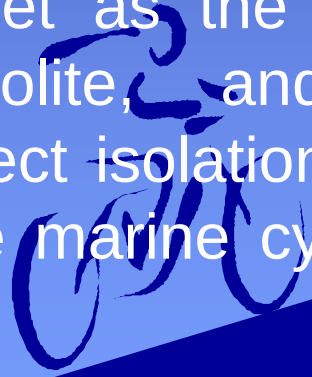
- Didemnin B, a cyclic antiproliferative depsipeptide isolated from the Caribbean tunicate *Tridemnum solidum*, was the first marine natural product to enter clinical trial as an antitumor agent.

- Didemnin B inhibits the synthesis of RNA, DNA, and proteins and binds noncompetitively to palmitoyl protein thioesterase.

9. Sea Hares

- In the early 1970s, the extremely potent anticancer properties were reported from the extracts of sea hare *Dolabella auricularia*.

- The low concentrations of dolastatin 10 in sea hares implicates a cyanobacterial diet as the origin of this bioactive secondary metabolite, and this was subsequently confirmed by direct isolation of dolastatin 10 from field collections of the marine cyanobacterium *Symploca*.

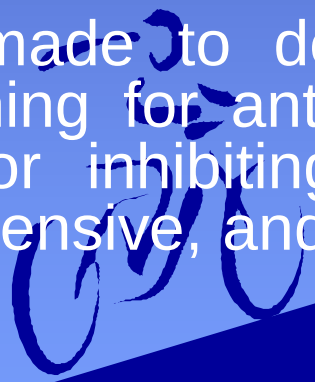


Marine Toxins

- A toxin is a substance possessing a specific functional group arranged in the molecule (s) and showing strong physiological activity.

- Even if direct use as a drug is not feasible because of potent of harmful side effects, the toxin can serve as a model for synthesis or improvement of other drugs.

- Many attempts have been made to develop useful drugs from the sea by screening for anticarcinogenic, antibiotic, growth-promoting (or inhibiting), hemolytic, analgetic, antispasmodic, hypotensive, and hypertensive agents.



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