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Review Article

Marine natural products: the new generation of pharmacotherapeutics

Rajeev Goel^{1*}, Binny Mahendru², Tushar Saini³

¹Department of Biophysics, Dr. Rajendra Prasad Government Medical College, Kangra, Himachal Pradesh, India

²Department of Pharmacology, Dr. Radhakrishnan Government Medical College, Hamirpur, Himachal Pradesh, India

³Department of Forensic Medicine, Dr. Rajendra Prasad Government Medical College, Kangra, Himachal Pradesh, India

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***Correspondence:**

Dr. Rajeev Goel,

Email: rgoel302@yahoo.com

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ABSTRACT

The biomedical potential of the sea has gone largely unexplored so far, despite the fact that it covers three quarters of the planet surface and the fact that life on Earth originated from the sea. However, with the arrival of the professional deep sea divers, the marine researchers have gained access to all sorts of marine creatures like sponges, corals, sea urchins, sea squirts, hydroids, sea anemones, fishes and mollusks as well as to varied types of sea plants including algae and the other micro-organisms embedded in the sea bed. The biomedical scientists are exploiting these all to extract marine natural products (MNPs) having pharmacological properties that may one day cure long list of illnesses varying from bacterial infections to cancer, Alzheimer's and AIDS and is the focus of this review article.

Keywords: Marine organisms, Marine natural products, Therapeutics and human diseases

INTRODUCTION

Scientists so far have been purely dependent on the tropical forests and terrestrial ecosystem for unusual substances having medicinal properties which have been in use either as direct extracts or synthetic redesigns of the plant molecules. Anti-malarial drug quinine from the bark of cinchona tree, aspirin from the willow bark, morphine from opium poppies and taxol to treat cancer from the yew tree of rain forests are a few such examples. The quest to find novel sources of medicines to fight developing antibiotic resistance and the diseases of the industrialized world has forced researchers to explore marine animals and plants also.

The recent researches on marine biota have proved that it, in fact, is a great store house of useful bio-chemicals and lifesaving medicines which otherwise are not found in terrestrial natural products.¹ Marine organisms need these bioactive compounds for purposes such as reproduction,

communication and for their own protection against predation, infection and competition.² The biologically active chemical diversity from the vast plethora of marine organisms is now under translation into novel biomedicines having therapeutic potential.

Marine natural products from the incredible sponges

The marine sponges are the simplest of multi-cellular organisms and are collections of loosely organized single cells with no apparent true organs or tissues. The scientific term for sea sponges is *Porifera* which literally means pore bearing. Sponges being static organisms produce deadly toxins, to protect themselves from their predators, that are known to have medicinal properties beneficial to humans.

The sponges are thought to be a goldmine containing many bioactive molecules that can fight cancer and inflammation without minimal side effects which are associated with the nowadays available anti-cancerous and anti-inflammatory

drugs. Several sponge species produce compounds that show great promise as drugs to combat malaria, tuberculosis, carcinomas and other infectious diseases.

Consequently, sponges are finding a niche in medical research.³ Many compounds isolated from different types of sea sponges are now in human clinical trials against cancer and other diseases.⁴

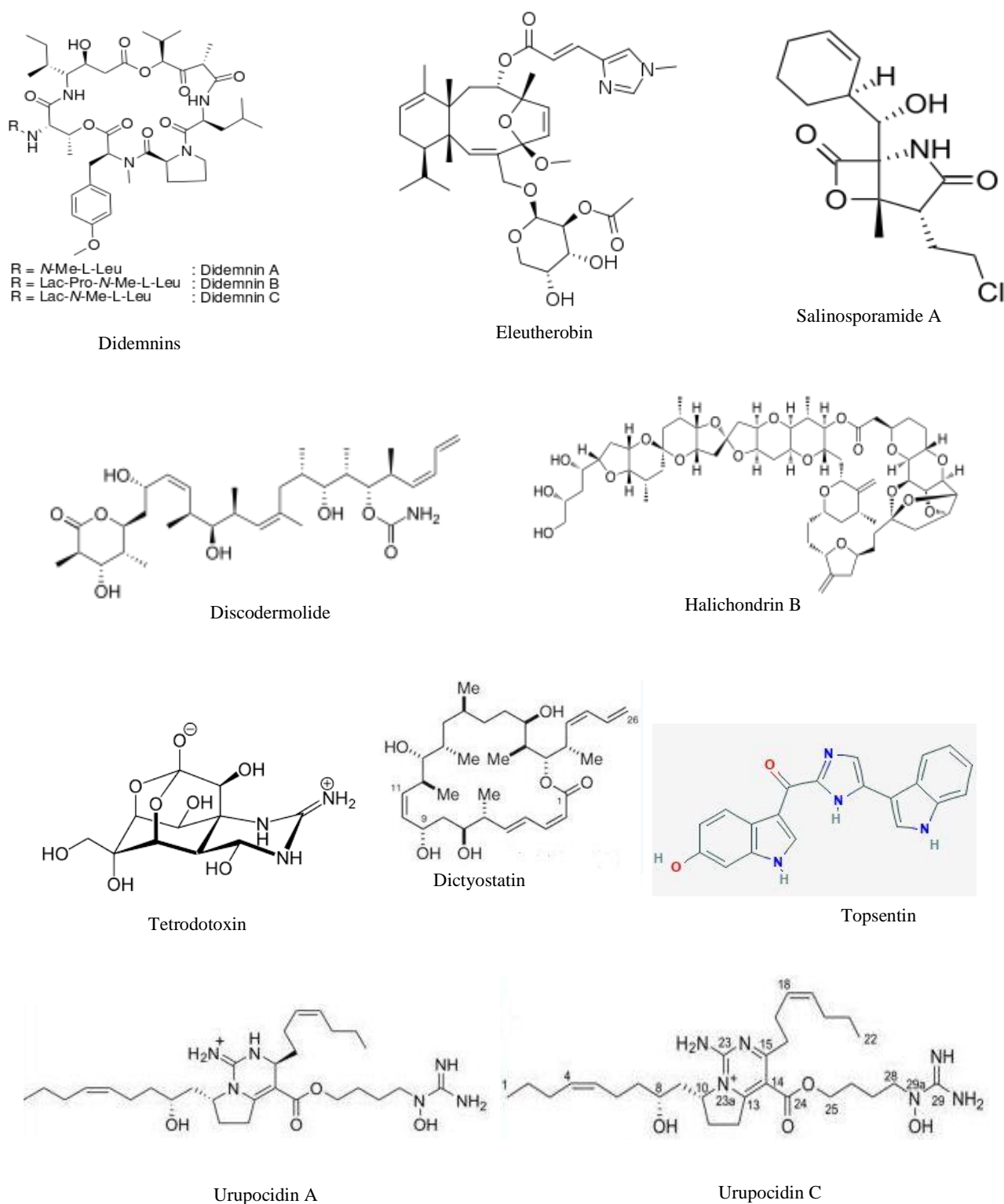


Figure 1: Chemical structures of marine natural products having promising therapeutic applications.

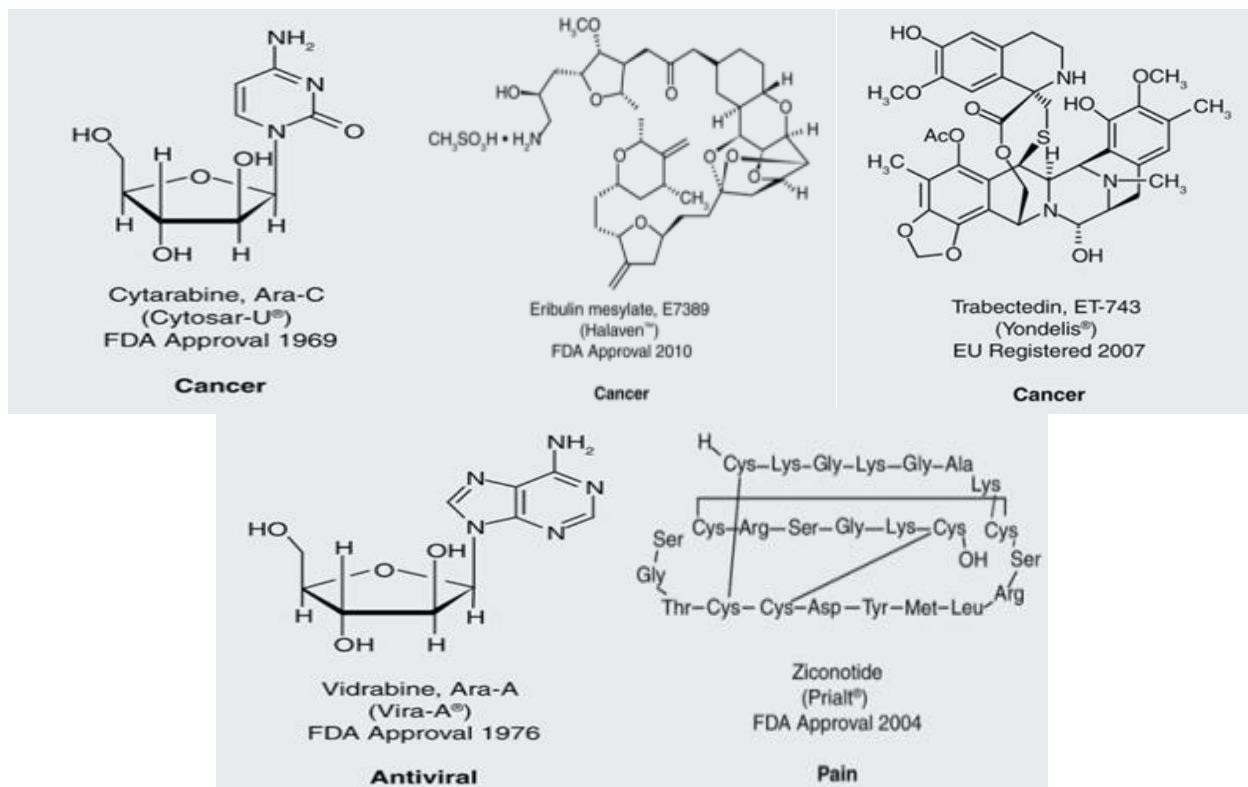


Figure 2: Marine drugs on the market and their therapeutic uses.

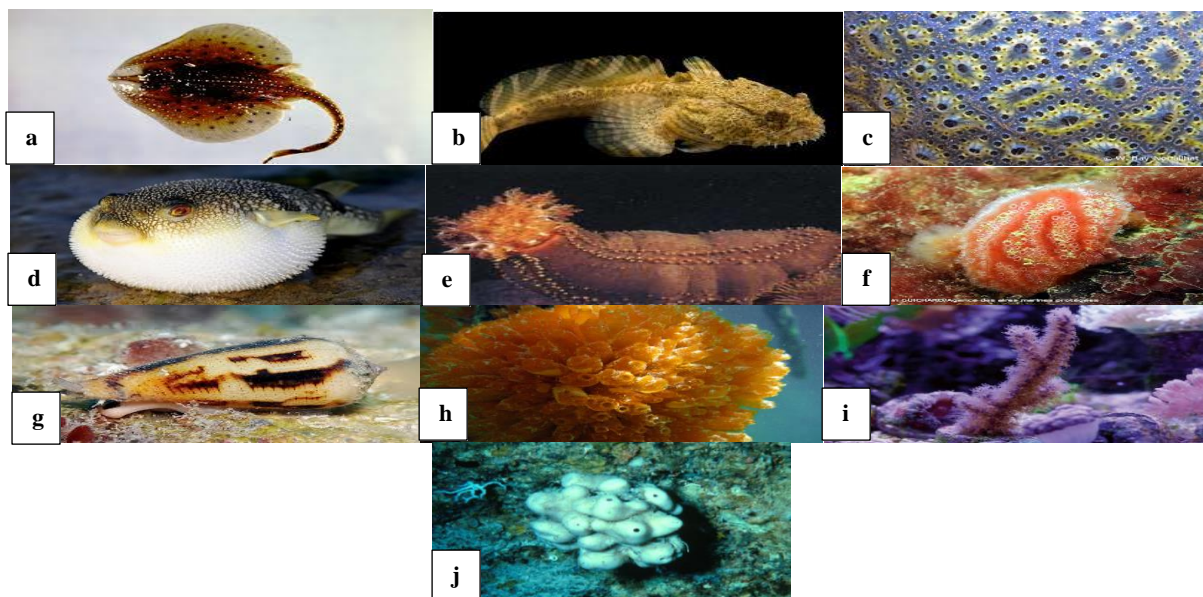


Figure3: Some marine vertebrates and invertebrates of therapeutic importance: (a) *Leucoraja erinacea* (little skate fish); (b) *Opsanus Tau* (toad fish); (c) *Botryllus schlosseri* (star tunicate); (d) *Tetraodontidae* (pufferfish); (e) *Cucumaria frondose* (sea cucumber); (f) *Aplidium albicans* (tunicate); (g) *Conus magus* (sea snail); (h) *Ecteinascidin turbinate* (sea squirt); (i) *Pseudopterogorgia* (sea fan); (j) *Discodermia dissolute* (sea sponge).

Halichondrin B

A compound halichondrin B belonging to a chemical family known as macrolides isolated from the Japanese

sponge, *Halicondria okadai*, shows antitumor activity in melanoma, leukemia, breast and esophagus cell lines (Figure 1). It binds tubulin and alters the tubulin depolymerisation in the cells.⁵ A halichondrin B analog,

eribulin mesylate also known as E7389-a synthetic compound developed by a Massachusetts based Eisai pharmaceutical is currently in the first phase of clinical trial for treatment of non-small cell lung cancer (Figure 2).⁶ Eribulin mesylate (Halaven®) has been approved for treatment of metastatic breast cancer.⁷ It exhibits therapeutic effect by binding to the plus ends of the microtubules and stops their growth with no effect on microtubule shortening by forming non-productive tubulin aggregates.⁸

Discodermolide

Discodermolide, a poly hydroxylated lactone is a promising natural product discovered to date to have an anti-cancerous properties against the solid tumors (Figure 1).⁹ It has been isolated from the deep sea sponge, *Discodermia dissolute* (Figure 3). Discodermolide exhibits better water solubility, facilitating patient delivery. It stabilizes microtubules in the cells and is believed to be more potent than Taxol®, a widely used anti-cancer drug extracted from the bark of Pacific yew tree. It also exhibits activity against the multi drugs and Taxol® resistant tumors. Discodermolide has been licensed for further development and the compound has completed phase I clinical trials.¹⁰

Topsentin

The compound topsentin (Fig.1) from the deep water sponge, *Spongosporites ruetzleri* (from the family *Halichondriidae*, genus *sponogosorites*) displays great promise as an anti-inflammatory agent to treat arthritis and skin irritations.¹¹ Topsentin is a novel indole alkaloid also having anti-tumor and anti-viral properties and is under investigation for the treatment of colon cancer and even alzheimer's disease. The compound is currently under pre-clinical development stage.¹¹

Dictyostatin

Dictyostatin-1 (Fig.1) originally isolated from a shallow water sponge in the *Spongia* genus, which is found off the coast of Republic of Maldives, is an anticancer compound in preclinical development. The compound appears to be a great promise in lab and more potent than Taxol® in action.¹²

Nucleosides

The nucleosides, spongo-thymidine and spongo-uridine isolated from the Caribbean sponge *Tectitethya crypta* (family *Tethylidae*) contain an unusual and rare sugar-arabinose instead of the ribose, a ubiquitous sugar in nucleosides which forms the building blocks of nucleic acids. It was rather the discovery of these novel nucleosides spongo-thymidine and spongo-uridine, which ushered the era of marine derived drugs in 1950s.¹³ These nucleosides were discovered to possess the antiviral properties via inhibition of reverse transcriptase activity. The analogues

such as Ara-A (3, Vidarabine®) and Ara-C (4, Cytarabine) with improved anti-viral activities have been synthesized on the basis of these marine nucleosides (Figure 2).¹³ The isolation of C-nucleosides from the Caribbean sponge, *Cryptotethya crypta*, provided the basis for the synthesis of cytarabine (Cytosar®), a FDA approved drug in 1969 to be used in patients with leukemia and lymphoma particularly.¹⁴

Other compounds

A black sponge from *Plakinastrella* species, collected by U. S. marine scientists from the west of the Felicite Island in the Indian Ocean possesses potent anti-fungal activity. This black sponge produces cyclic peroxy acids which inhibit growth of *Candida albicans* comparable to amphotericin B, the anti-fungal gold standard.¹⁵

Many compounds from the sponges induce apoptosis and act as anti-cancer agents. Renieramycin isolated from the sponge genera *Reniera* induces apoptosis in lung cancer cells. A lectin from the sponge *Cinachyrella apion* also causes cell death in tumor cells.¹⁶

The marine biotech company by the name porifarma is farming two sponge species *Dysidea avara* and *Chondrosia reniformis*. The former produces a compound avarol, a cyto-statically active compound shown to have antitumor, antibacterial and anti-fungal properties and the latter is a good source of collagen that can be converted into nano-particles to be used for drug delivery to the target locations.¹⁷

Bioactive compounds from novel marine microbes

The discovery of the group of marine microbes from the coral reef sponges and from the marine sediments has provided an opportunity to microbiologists to look for novel antibiotics. The studies have revealed an elevated microbial population that is exceptionally bioactive in many sponges. Marine invertebrates such as corals and sponges are hosts to a multitude of microorganisms. The nature of relationship between the microbes and the host organisms is not yet fully understood. The presence of micro-organisms in the marine invertebrates seems to play a role in keeping them healthy and nourished besides producing defense chemicals to protect them from their predators.¹⁸

Microorganisms such as bacteria, cyanobacteria and fungi contribute to as much as 50% to 60% of sponges' biomass. The 50% of the cellular volume of the Australian tropical sponge, *Dysidea herbacea*, for example is composed of the *Cyanobacterium*, *Oscillatoria spongeliae*.¹⁹ The bacterial population in sponges could be very diverse and efforts are on to culture them in the lab to procure new antibiotics. It is believed that some of the bioactive molecules are likely to come from these bacteria rather than the sponges themselves. For example, an extract from a common Chesapeake Bay sponge, *Microciona porlifera*, contains

around 150 bacterial isolates which inhibit the growth of H37Rv strain of *Mycobacterium tuberculosis* responsible for tuberculosis, a leading cause of death after HIV/AIDS.²⁰

The ocean floor itself is a next major potential source of bioactive compounds. It is estimated that there are one billion living cells per cubic centimeters of seafloor sediment. The micro-organisms diversity in the deep ocean is boundless. These microbes can be used more quickly, efficiently, cost effectively and sustainably as compared to other marine organisms and can be harvested with little impact on the natural environment, in case they can be cultured in large quantities in lab.

It is worth noticing that 70% of the naturally occurring antibiotics such as actinomycin, streptomycin, novobiocin are produced by soil based actinomycetes family. However, the discovery of many novel marine actinomycetes from the marine environment such as sea floor sediments, algae and sponges may lead to the availability of novel antibiotics which may overcome the menace of antibiotic resistance in future.²¹

Actinomycetes are responsible for the production of about half of the discovered bioactive secondary metabolites mainly antibiotics, antitumor agents, immunosuppressive agents and enzymes. Many new chemical compounds from the marine actinomycetes now stands isolated and ten new genera of microbes have been remarkably characterized including the genus *Salinispora* from which 2,500 new strains have been discovered.²²

Marine bacteria *Salinispora tropica* isolated from the marine sediments produce a compound salinosporamide-A (NPI-0052, Fig.1), a novel β -lactone- γ -lactam, that exhibits cytotoxicity against breast cancer, colon cancer, non-small cell lung cancer and melanoma (Figure 1).²³ NPI-0052 is an orally active proteasome inhibitor that induces apoptosis in multiple myeloma cells with mechanisms distinct from the commercial proteasome inhibitor anticancer drug bortezomib.²³

A novel metabolite diazepinomicin (ECO-4601), a unique farnesylated dibenzodiazepinone produced by marine actinomycetes (*Micromonospora* species) possesses anti-bacterial, anti-inflammatory and antitumor activities.²⁴ It has broad spectrum of in vitro cytotoxicity and has demonstrated in vivo, activity against glioma, breast and prostate cancer in mouse models.²⁴

Several bacterial and fungal isolates from the seawater sample were similarly assayed for the antibiotic potential. One of these isolates, the marine derived fungi *Cephalosporium acremonium* contains significant inhibitory activity against a number of bacterial strains. The finding rather marked the discovery of the first of the cephalosporin family of antibiotics, an important addition to fight against the range of bacterial infections.²⁵

Marine natural products from the exotic corals

Corals, the beautiful red, pink or white creatures found in different shapes, sizes and texture which were earlier familiar only for their exotic structures are now known for new medicines. Corals are the group of marine invertebrate animals that deposit a mineral skeleton as they grow eventually producing coral reefs. The coral reefs contain a diverse assemblage of invertebrates such as corals, tunicates, mollusks, bryozoans, sponges and echinoderms that are absent from terrestrial ecosystems. Coral reefs are also home to sessile plants and fungi similar to those found on land.

A Mediterranean soft coral *Sarcodictyon roseum* produces a bioactive compound sarcodictyin and a similar compound named eleutherobin from a shallow water *Eleutherobia* species in Western Australia (Figure 1). It possesses paclitaxel (Taxol ®) like anti cancerous activity and is in pre-clinical developmental stages.²⁶

Certain corals particularly the tropical ones belonging to genera *Porites*, *Alveopora*, *Acropora* and *Goniopora* have the structure almost identical to human bone, outer hard sheath and a spongy inner core with correct pore diameter and ability to connect properly with the bone. As a result tropical coral bone substitutes are nowadays used as bone grafts to heal fractures in orthopedic, dental, craniofacial trauma and neurosurgeries.²⁷

The natural coral structure has been successfully used to synthesize bone analogs. Coral is not implanted in its natural state although the structure and mineral composition of coral is very similar to that of bone. Following its harvest, coral is treated chemically under heat and high pressure to convert the calcium carbonate matrix to hydroxyapatite (calcium phosphate hydroxide), the normal mineral portion of the bone. It is the three-dimensional structure, porosity, pore interconnections and composition of commonly used corals that confer its osteo-conductive capacity. It consequently allows cell attachment and growth through the scaffold of the material, characteristic of a good support of cells.²⁸ The initial invasion of coral by blood and bone marrow cells with subsequent vascularization is a determinant factor for bone regeneration. The coral is only osteo-conductive and is not an osteo-inductive material.²⁹

Bamboo corals from the family *Isididae* (genera *Keratoisis* and *Isidella*) found at a depth of more than 1000 meters in the sea have a unique protein-based material called gorgonin that closely resembles human collagen, an important component of the bone and keratin. Gorgonin may one day substitute collagen which at present is mainly derived from cattle tissues to be used in many biomedical applications such as controlled release of medicines into the body, scaffolding for tissue engineering and other biomaterial applications.³⁰ The risk of transmission of diseases from the cattle tissue to human makes bamboo corals a safer alternative. There are attempts to cultivate

bamboo corals in the lab by using biotechnological approaches for the development of natural bone implants and analogs.³⁰

A gorgonian coral feathery sea fan, *Pseudopterogorgia elisabethae*, found in Caribbean sea contains a compound pseudopterosin a diterpene glycoside, that relieves swelling caused by arthritis, sunburn or chemical irritants and is believed to be more active than hydrocortisone and is commercially found in the skin creams as topical anti-inflammatory agent (Figure 3).³¹

Novel compounds from other marine creatures

Many other marine creatures are also under laboratory investigations to look for biochemical storehouse. A standardized liquid extract derived from shark cartilage is a promising marine based anti-angiogenic agent, neovastat (AE-941).³² It is the anti-angiogenic aspects of AE-941 that makes it extraordinary, though the substance exhibits multiple mechanisms of action. AE-941 essentially thwarts the demands of tumors for new capillaries, thereby, depriving them of oxygen and nutrition required for their growth. AE-941 is now in international phase three clinical trials for renal cell carcinomas and non-small cell lung cancer.³³ Another anti-angiogenic agent is the compound squalamine, an aminosterol obtained from the spiny dogfish *Squalus acanthias*, a common New England coastal shark.³²

A compound called ecteinascidin (Ecteinascidin-743 or ET-743, trade name Yondelis®) isolated from the sea squirt, *Ecteinascidin turbinata* (Fig.3), from the reefs in West Indies is a tetrahydro isoquinoline alkaloid and has anti-cancerous properties many times more than taxol (Figure 3).³⁴ ET-743 is presently used to treat liposarcoma and leiomyosarcoma (Figure 2).³⁵ Ecteinascidin uniqueness lies in preventing tumors from becoming drug resistant.³⁴ ET-743 is known to act by preventing the formation of a P-glycoprotein, a membrane protein, that transports chemotherapy agents out of the cancer cells thereby causing drug resistance. ET-743 is effective as inhibitor of DNA synthesis, capable of arresting the cell cycle and inducing p-53 independent apoptosis in target cells.³⁶ The compound also exhibits tubulin interactive bioactivity. Similarly, an anti-neoplastic drug PM605, developed by PharmaMar, by extracting bio-actives from an Indian Ocean tunicate is under preclinical trials.³⁷

The coral reefs off the Philippines host a cone snail whose venom is observed as a potent pain killer, many times more potent than morphine and find its use in patients with chronic pain. The compound, ziconotide, a synthetic form of peptide extracted from the venom of a predatory tropical cone snail *Conus magus*, has been approved by the U. S. food and drug administration (FDA) as a pain killer to be used in terminally ill patients and is marketed as Prialt® (Figure 2 and 3).³⁸ Prialt (ziconotide) is a 25 amino acid peptide which acts by binding to and inhibiting pre-synaptic calcium channels, thereby preventing

neurotransmitter release. This consequently blocks nerve impulses in the key region of the spinal cord.³⁹ The precisely targeted mode of action of ziconotide gives it an important advantage over presently available opioid drugs having side effects such as sedation and suppressed respiration.³⁹ A protein aequorin from jelly fish *Rhopilema esculentum* is neuro-protective and thought to be effective in treating various neuro-degenerative disease.⁴⁰

Many compounds such as didemnin and aplidine showing anti-cancerous properties have been derived from the marine ascidians or sea squirts (*Subphylum tunicata*) (Figure 1). Didemnim is a cyclic depsipeptide compound and is found in Caribbean tunicates of the *Didemnidae* family.⁴¹ It is of special significance as it has a variety of biological effects including potent antiviral and antitumor activities. Its mechanism of action has been attributed to the inhibition of DNA synthesis.⁴¹ Aplidine isolated from the tunicate *Aplidium albicans* is also a novel depsipeptide and is found to be cytotoxic for molt-4 leukemic cells at nanomolar concentration (Figure 3).⁴²

An enzyme, chitosanase which fights fungal infections has been isolated from shells of shrimps, crabs and lobsters.⁴³ An extract named paolin I from clams, oysters and abalone has antibacterial properties including against the streptococcal infections.⁴⁴ A related agent paolin II has anti-cancerous and anti-viral properties particularly against herpes virus.⁴⁵

Chitin, a substance found in shells of crabs and shrimps makes bonding with the red blood cells to form an artificial clot at the site of bleeding thereby sealing massive bleeding in 30 seconds. As a result, shrimp based bandages are now used by certain troops in the battlefield to stop excessive bleeding which is the main cause of death among soldiers in the field.⁴⁶

A common marine invertebrate named sea cucumber, *Cucumaria frondosa* (family *Holothuroidea*), found in Philippine coastal waters contains a lectin (lectins are proteins that bind specifically to sugars in the cell membrane), which stops the growing human cancer cells in vitro (Figure 3).⁴⁷

Many marine guanidinium toxins having high medical research value have also been isolated. These are tetrodotoxin (TTX) from *Tetraodontidae* (pufferfish), saxitoxin (STX) and its analog neosaxitoxin (NSTX) from shell fish and algae (Figure 1 and 3).⁴⁸ TTX is a selective sodium channel blocker non-protein toxin isolated from floral egg crab *Atergatis floridus*; blue-ringed octopus *Octopus maculosus*; starfish *Astropecten polyacanthus* and several other shellfish species. TTX-producing bacteria were also reported to have been isolated from marine or freshwater sediments. The consumption of an organism containing TTX can cause neurological and gastrointestinal symptoms. TTX is commonly used in many laboratories as a pharmacological agent because of its ability to selectively block the sodium channels on the

nerve membrane.⁴⁹ TTX can play an alternative role against opioid and can be used as painkiller in coming years as an alternative to opioid for pain management.^{49,50}

The guanidine group as such is of immense interest in pharmaceutical chemistry and has become a key element in many clinical drugs such as anti-diabetic drug dimethyldiguanide and the peptic ulcer drug cimetidine.^{51,52} The diversity and complexity of cyclic and linear guanidine marine natural products from sponges, mollusks and ascidians were recently observed as polyketide synthases (PKS) and nonribosomal peptide synthetases (NRPSs) derivatives, terpene and peptide conjugates.⁵³

Nonribosomal peptide synthetases synthesize nonribosomal peptides (NRP) which possess exceedingly broad range of biological activities, pharmacological properties and biotechnological applications. These are often siderophores (iron chelating compounds), pigments, toxins, cytostatics, antibiotics and immune-suppressants.⁵³

Marine bacteria, cyanobacteria and fungi have emerged as a source of these non-ribosomal peptides which initially were isolated from soil microorganisms such as actinomycetes, bacilli and eukaryotic filamentous microorganisms. Non-ribosomal peptides are also found in marine invertebrates such as soft bodied gastropod mollusks called as nudibranchs but are believed to be formed by bacteria inside these organisms.⁵⁴

The guanidine alkaloids isolated from the marine sponges of the *Monanchora* genus belonging to family *Crambeidae* possess wide range of biological activities such as cytotoxic, antimicrobial, antimalarial and anti-HIV properties.⁵⁵ For example, the guanidine alkaloid urupocidin A (Ur-A) has cytotoxic activity against different human cancer cell lines (Figure 1).⁵⁶ Ur-A inhibits an EGF-induced neoplastic transformation of epithelial cells. It induces a G2/M-phase cell cycle arrest and apoptosis of human cervical carcinoma HeLa cells.⁵⁷ A new bicyclic guanidine alkaloid, urupocidin C (Ur-C), along with the earlier known Ur-A, isolated from the rare deep-sea marine sponge *Monanchora pulchra* found in North-western Pacific waters exhibit acute selectivity for human prostate cancer cells and are believed to be a novel promising candidates as effective drugs against aggressive and drug resistant cancer of the prostate (Figure 1).⁵⁸

Neutrophils play an important role in acute inflammatory responses and recent studies have expanded their role to modulate chronic inflammatory and autoimmune diseases. Several types of chemical drugs are in use to treat inflammatory disorders, but with adverse side effects. Marine natural products that inhibit neutrophil activation could therefore be used as alternative to these drugs for the treatment of inflammatory diseases. The biological and chemical diversity of marine habitats constitutes a sizeable reservoir of novel anti-inflammatory compounds such as sesquiterpenoids, diterpenes, steroids, polysaccharides,

alkaloids, fatty acids and proteins isolated from diverse marine organism.⁵⁹

The powdered shrimp shells are used in England as a treatment for allergies and hay fever. A product enzymol, developed from the enzymes in king crab shells helps in healing severe burns.⁶⁰ Certain compounds from crab wastes are used in cleansing lotions for burns, chilblains, gangrene and varicose sores. Studies have unveiled that sea urchin pigment is rich in antioxidants, anti-inflammatory and anti-bacterial activities and can be effective in the treatment of certain eye and heart ailments.⁶¹ Anti-cancerous substances from the anterior and posterior salivary glands extract of octopuses like *Octopus aegina* have been isolated. This octopus is used traditionally by the residents of the coastal areas to cure stomach ache, diarrhoea, scabies, toothache, measles and high blood pressure.⁶²

Marine organisms as model for human system

The different studies are in progress for gaining biomedical knowledge to understand how the marine creatures are living in extreme environmental conditions like high pressure under the sea, total darkness, acidic, salty or alkaline conditions and low temperature that otherwise would kill human beings. This will be of immense help to apply it to human system to understand and cure diseases. For example, the little skate fish, *Leucoraja erinacea*, can detect light in the darkest conditions using only rods, the light sensitive cells present in retina (Figure 3). It is believed that skates because of its ability to see in the darkest conditions can be a useful model for studying the human retina and may one day help in finding cure for retinitis pigmentosa, a disease that leads to total blindness in humans.⁶³

Toadfish having the toad like appearance has the unusual ability to regenerate its central nervous system unlike humans and the cues to regeneration in toadfish would be of importance in human neurodegenerative diseases.⁶⁴ The members of entire family of ray finned fish (order *Batrachoididae*) are usually called toadfish or frogfish (Figure 3). The toadfish also has the fastest twitching muscles (swim bladder muscle) in the vertebrate world. It is therefore supposed to be a good model for cardiomyopathy wherein the heart muscles lose their ability to relax normally and cannot pump blood properly.⁶⁵ The lab studies have shown that a myoplasmic protein called parvalbumin from common Atlantic oyster toadfish, *Opsanus tau*, when inserted in the muscles of the human heart helps to relax the cardiac muscle and may, therefore, find its use in patients suffering from cardiomyopathy. Parvalbumin is a Ca⁺⁺ binding protein of low molecular weight.⁶⁶

It is amazing to know that a starascidian or golden star tunicate *Botryllus schlosseri* found in the bays of Florida can re-grow or regenerate its entire body, the digestive system, heart and other tissues from its vasculature alone

likely by using stem cells (Figure 3). The researchers are studying the self-regenerating mechanisms operating in this star tunicate to apply it to humans, which will provide insights about the potential of cells and tissues to be reprogrammed and regenerate compromised human organs.⁶⁷

The studies are in progress on the molecules responsible for regulating egg and sperm interaction in sea urchin, *Echinus esculentus* and solitary sea squirt, *Ascidia mentula* (which have both types of reproductive organs) to unlock the mysteries of cell interaction in humans.⁶⁸ Moreover, understanding the mechanism of penetration of sperm into an egg will also give clues to find out how disease causing cells invade the normal cells. The list is in-exhaustive and many more marine species are on the bench top of bio-marine researchers.⁶⁹

CONCLUSION

Sea contains a big pharmacy for human benefits. Seafood once regarded as a dinner specialty is now getting increased respect among the medical scientists for medicines and future therapies. Marine natural products bio-prospecting has no doubt yielded a considerable number of drug candidates. Most of these molecules are still in pre-clinical or early clinical development but some are already in the market such as cytarabine and ET 743 (Yondelis™) as anticancer drugs, vidarabine as antiviral agent and ziconotide (Prialt®) for management of severe chronic pain. Hundreds of compounds exhibiting strong activities against a variety of infections (e.g. HIV, malaria, staphylococcal and fungal infections), carcinomas including solid human tumors and other disorders (e.g. asthma, atherosclerosis, epilepsy, osteoarthritis and inflammation) have been isolated. Some of these are in the advanced stages of new drugs development. The dozen of molecules have reached the stage of phase I and II of clinical evaluation. The need of the time is to fully identify the genes that produce the desired bioactive compounds with medicinal properties and to transfer those genes to the microorganisms such as *Escherichia coli* that are easy to culture in the lab. This is must to preserve the marine biota so that it may not get extinct by continuous harvesting from the sea for medical pursuits.

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