IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

STUDY OF MARINE DRUGS

Tejswini Devidas Navgire

Shivajirao Pawar College of Pharmacy, Pachegaon

Abstract

Disease ailments are changing the patterns, and **t**he new diseases are emerging due to changing environments. The enormous growth of world population has overburdened the existing resources for the drugs. And hence, the drug manufacturers are always on the lookout for new resources to develop effective and safe drugs for the increasing demands of the world population. Marine pharmacology offers the scope for research on these drugs of marine origin. Few institutes in India offer such opportunities which can help us in the quest for new drugs. This is an extensive review of the drugs developed and the potential new drug candidates from marine origin along with the opportunities for research on marine derived products. It also gives the information about the institutes in India which offer marine pharmacology related courses.

Key Words: Marine agents, Pharmacology of marine sources, Natural Agents, under water study.

Introduction:

Over 70% of the earth's surface is covered by oceans which contain 95% of the earth's biosphere. It was over 3500 million years ago that organisms first appeared in the sea. Over time, they have evolved many different mechanisms to survive the various harsh environments which include extreme temperatures, salinity, pressure, different levels of aeration and radiation, overcoming effects of mutation, and combating infection, fouling and overgrowth by other organisms. Adaptations to survive the different environments could be by physical or chemical adaptation. Organisms with no apparent physical defense, like sessile organisms, are believed to have evolved chemical defenses to protect themselves. It is also believed that the compounds would have to be extremely potent due to the dilution effect of seawater. This has been described to be analogues to pheromones but with the purpose of repelling instead of attracting. As well, predators have evolved chemical weapons in order to paralyze or kill prey. Conus magus is an example of a cone snail that has a poisoned harpoon-like projectile which

it uses to paralyze prey like small fish. Some organisms, like the Viperfish, are believed to attract small fish or prey by using its photosphere.

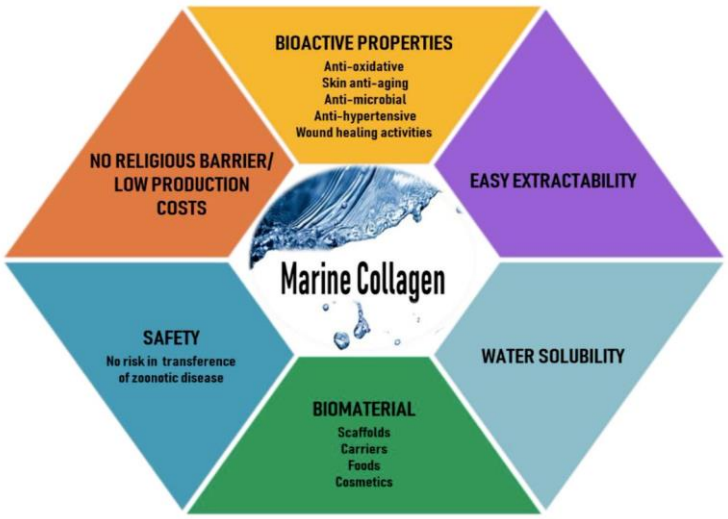
Definition:

Marine drugs:

Marine pharmacognosy is a sub branch of pharmacognosy which is mainly concerned with the naturally occurring substances of medicinal value from marine. Generally the drugs are obtained from the marine species of bacteria, virus, algae, fungi and sponge

Marine source:

Marine organisms such as sponges, tunicates, fishes, soft corals, nudibranchs, sea hares, opisthobranch Molluscs, echinoderms, bryozoans, prawns, shells, sea slugs, and marine microorganisms are sources of bioactive compounds.



CLASSIFICATION OF DRUG MOLECULES OF MARINE ORGANISMS

The enormous quantum of newer and potent drug molecule derived from the wide spectrum of marine organism across the world may be judiciously and logically classified based on their specific pharmacologic actions as stated below.

- ❖ Antibacterial
- ❖ Anti-inflammatory
- ❖ Neuroprotective
- ❖ Antiparasitic
- ❖ Antiviral agent
- ❖ Anticancer
- ❖ Analgesic
- ❖ Antimicrobial

Antibacterial

Eicosapentaenoic acid, a polyunsaturated fatty acid, isolated from a diatom of marine origin Phaeodactylum tricornutum which has shown activity against an array of Gram-positive and Gram-negative bacteria, which also includes a multidrug-resistant variety of Staphylococcus aureus.

Anti-inflammatory

The anti-inflammatory function of extracts and other parts of a Mediterranean sponge species Spongia officinalis in the in vivo study on rat model of carrageenan-induced paw edema assay.

Neuroprotective

The extracts of South Indian green seaweed Ulva reticulata has shown neuroprotection by inhibiting acetyl-and butyryl-cholinesterases, efficacy comparable to agents currently approved for Alzheimer's disease treatment.

Antiparasitic

Extracts of Sarcotragus sp. known as Tunisian sponge prepared in dichloromethane has demonstrated in-vitro anti-leishmanial activity by demonstrating the associated morphological alterations in promastigotes of leishmania major.

Antiviral agents

Anti-herpes simplex virus-1 (HSV) activity found in high molecular weight exo-polysaccharides extracted from the Celtodoryx girardae (French marine sponge) and its associated symbiotic bacteria has been reported.

Anticancer

Bryostatin, primarily obtained from the Bryozoan, Bugula neritina, although some forms have been extracted from sponges and tunicates. Sorbicillin-derived alkaloids sorbicillactone A and its 2', 3'-dihydro analog sorbicillactone-B has shown activity against leukemia cells free from any noteworthy cytotoxicity. Sorbicillactone-B has been derived from a salt-water culture of a bacterial strain Penicillium chrysogenum which has been isolated from a sponge Ircinia fasciculata, a Mediterranean sponge specimen.

Another promising anticancer drug used as an immunotherapeutic agent is keyhole limpet hemocyanin (KLH). KLH is a copper containing extracellular respiratory protein present in Megathura crenulata, a marine Gastropod species found in large numbers at the Pacific coast of California and Mexico. KLH is found in two isoforms KLH1 and KLH2. KLH is reported to possess remarkable immunostimulatory properties in experimental animals and

human, used in experimental immunology and also clinically as an immunotherapeutic agent. KLH is specifically used in clinical setup for the treatment of bladder carcinoma, and its efficacy is perhaps due to a cross-reacting carbohydrate epitope. KLH may also have significant potential for the treatment of other types of cancers, particularly the adenocarciomas derived from the epithelium, by using it as a carrier for gangliosides of carcinoma and mucin-like epitopes.

KLH is intravesically administered to patients with bladder carcinoma. Its clinical success in carcinoma patients is attributed to the presence of the disaccharide epitope Gal (β1-3), Ga1NAc.This epitope of KLH is believed to be cross-reactive with an equivalent epitope on the urinary bladder tumor cell surface. The cumulative cellular and humoral immunological responses to KLH can result in a cytolytic reduction of tumor growth.

In addition to tumor immunotherapy, KLH is also prescribed in the following conditions:

- As a generalized vaccine component for antigen presentation, alone or in adjuvant cocktail
- For diagnosis of schistosomiasis because of cross-reactivity to one of the epitopes on larval schistosomes
- In drug assays
- Treatment of drug addiction by immunoassay for abused drugs
- For immune competence testing
- Assessment of stress and inflammation.

Analgesic

Ziconotide was the first drug of marine origin to obtain approval from the U.S. Food and Drug Administration (USFDA) in 2004 to treat pain. It is also known as Prialt, and it was originally extracted from the marine snail Conus magus. Results from animal studies suggested the role of ziconotide in blocking of N-type calcium channels on the primary nociceptive nerves of the spinal cord.

Antimicrobial

The cephalosporins are well-known antimicrobial agents with a marine source of origin. Cephalosporin C was firstly extracted and purified from a marine fungus, Cephalosporium acremonium.

Marine drugs:

Cytarabine (cytosine arabinoside or arabinosyl cytosine, ara-C)

Cytarabine is a synthetic pyrimidine nucleoside derived from spongothymidine and primarily isolated from a Caribbean sponge species Tethya crypta. It is FDA approved and mainly used in different types of leukemia, including acute myelocytic leukemia, lymphocytic leukemia, meningeal leukemia, and blast crisis phase of chronic myelogenous leukemia.

Vidarabine (adenine arabinoside, ara-A or arabinofuranosyladenine)

Vidarabine is a synthetic purine nucleoside isolated from the Caribbean sponge T. crypta and developed from spongouridine is currently obtained from Streptomyces antibioticus. It is approved by FDA for use in recurrent epithelial keratitis caused by HSV) type 1 and 2, acute kerato-conjunctivitis, and also for superficial keratitis.

Ziconotide

Ziconotide is a synthetic molecule, equivalent to a natural 25-amino acid peptide, v-conotoxin MVIIA.

It is originally extracted and purified from the venom of marine snail C. magus, which is a fish-hunting species. Ziconotide has shown potential as an analgesic with a novel mechanism of action. It is approved as an analgesic by FDA.

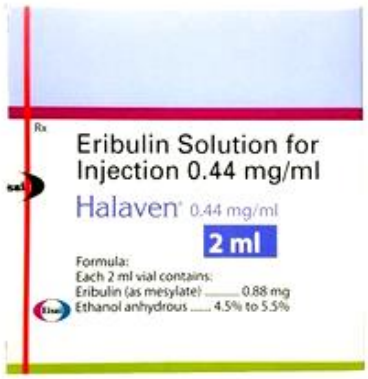
Trabectedin

A marine natural product extracted from a tunicate species Ecteinascidia turbinata generally inhabitant of Mediterranean and Caribbean Sea.

Trabectedin molecule is an alkaloid of tetrahydro isoquinoline class, and it was the first anticancer molecule of marine origin got approval in EU for use in the treatment of soft-tissue sarcoma and in relapsed cases of platinum-sensitive ovarian cancer.

Eribulin mesylate (E7389) or halichondrin B

It is a polyether macrolide natural molecule originally extracted from marine sponges, with potent anticancer activity reported in preclinical animal models. Eribulin is a potent molecule which produces irreversible antimitotic activity leading to cell death by apoptotic pathway.



On-going Phase III studies are evaluating the comparative clinical efficacy of eribulin versus capecitabine and eribulin versus other preferred treatment choice.

Soblidotin (auristatin PE or TZT-1027)

Is a synthetic derivative of the dolastatin backbone from dolastatin 10? It is a vascular disrupting agent causing the collapse of the vasculature inside the tumor, in addition to its tubulin inhibitory activity. This drug is undergoing trials in clinical Phases I, II, and III with different companies who are trying to use it as a weapon to specific monoclonal antibodies linked via customized peptides.

Tetrodotoxin

A very well known "marine toxin," and highly substituted guanidine-derivative. It is not an anti-tumor agent, currently in Phase III trials as analgesic against inadequately controlled pain related to the cancer. A Phase II trial is ongoing to assess the efficacy of tetrodotoxin against the neuropathic pain related to chemotherapy-induced peripheral neuropathy.

DMXBA (GTS-21) [3-(2,4-dimethoxybenzylidene)-anabaseine; GTS-21]

It is a synthetic imitative of anabaseine, which an alkaloid is found in many species of aquatic worms of phylum nemertea. DMXBA is reported to be beneficial for the central nervous system, improves cognition and sensory gating deficiency in a variety of laboratory animals. A recent clinical trial of the molecule in Phase II with schizophrenic patients has shown noteworthy improvement in cognitive functions.

Plitidepsin

It is a natural marine depsipeptide, currently obtained by total synthesis. It was primarily isolated from a tunicate Aplidium albicans found in the Mediterranean Sea. Plitidepsin is a highly potent apoptosis inducer with low nanomolar (nM) range of IC50 values. The major toxicity found with most schedules of plitidepsin were muscle toxicity, an increase of transaminases, general fatigue, diarrhea, and cutaneous rash.

Elisidepsin (PM02734)

It is a novel cyclic peptide derived from marine sources and belongs to the Kahalalide family of compounds. It is currently undergoing development in Phase II with primary evidence of antitumor potency with encouraging therapeutic index. It has shown potent in vitro cytotoxic action against diverse human tumor cell lines, which may be because of oncolytic cell death induction instead of apoptotic cell death.

PM00104 (Zalypsis)

It is a novel alkaloid with DNA-binding capacity. It is linked to jorumycin extracted from the Pacific nudibranch's (Jorunna funebris) skin and mucus as well as from renieramiycins extracted from varieties of sponges and tunicates. Preclinical in vivo studies done earlier with these molecules indicated considerably high antitumor activity in cells of breast, prostate and renal cancers with a modest antitumor action on colon cancer cells. Reversible hematological disorders or liver enzymes imbalance were the main toxicities found to be associated with Zalypsis treatment during the Phase I trials.

Uses:

- antibacterial
- immunomodulatory
- anti-fungal
- anti-inflammatory
- anticancer
- antimicrobial
- neuroprotective
- analgesic
- antimalarial properties

Advantages:

- ❖ Sources for developing potent drug candidates.
- ❖ As nutritional supplements.
- ❖ As molecular probes that can be supported to increase the healthy life span of human.
- ❖ Used in cosmetics.
- ❖ Unlimited supply of biomass

Disadvantages:

- ❖ Toxicity issues.
- ❖ Cultivating organisms for production, supply issue macro and microorganisms
- ❖ Expression of silent biosynthetic pathways.
- ❖ The marine ecosystem 8s not only productive to discover novel entities but it is also a tool to identify new cellular targets for therapeutic intervention.

REFERANCES:

1. Author1 LastnameA.F; Author3 LastnameA.F. Title. *Container* **2000**, *Volume*, pages Used.
2. Petit, C.; Sieffermann, J. Testing consumer preferences for iced-coffee: Does the drinking environment have any influence? **2007**, *18*, 161-172.
3. The Textbook of Pharmacognosy.
4. Mayer AM, Glaser KB, Cuevas C, Jacobs RS. The odyssey of marine pharmaceuticals: A Current pipeline perspective.