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A REVIEW ON EXPLORATION OF ANCIENT MARINE DRUGS AND ITS FUTURE PROSPECTS

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ABSTRACT: The marine environment is a huge reservoir of biodiversity and represents an excellent source of chemical compound, some of which large economical values. Today the structures of around 1,40,000 secondary metabolites have been elucidated. Marine based drug discovery has progressed significantly over the past several decades. Recent advances in extraction and isolating techniques, and in state of the art technologies involved in organic synthesis and chemical structure elucidation, have accelerated the numbers of antimicrobial molecules originating from the ocean moving into clinical trials. These natural products have been categorized based on their chemical structures and the structure activity mediated relationships of some of these bioactive molecules have been discussed. Detailed accounts are also given on novel marine metabolites, were isolated from different (sponges, micro-organisms, seaweeds, fishes, cones) sources. (a part from that, we covered the role of natural products in disease, treatment and commercial utilization of the compound). This review article gives knowledge about the discovery, source, and future prospects of some of the marine drugs.

Key Words: Marine products, marine metabolites, Algae, Sponges, Globe fish, Ascidians, seaweed, Antineoplastic drugs, Antihypertensive drugs, Marine toxins, Antibiotics, Antimicrobial drugs, Antidiabetic drugs, Antiviral drugs. Alkaloids, polypeptides.

INTRODUCTION:

Ocean represents a source of a varied type of organisms due to the diversified environment offered by different oceanic zones [1]. The ecological resources of sea have been exploited since ancient times and included the use of marine animals like fish and preparations from algae as the sources of medicine [1].

The first record of aquatic medicine is nearly 5000 years old [2] and oceans contain nearly 3, 00, 000 described species [3], almost all forms of life in the marine environment.

Ex: Algae (Fig-4), Sponges (Fig-2), Globe fish (Fig-1), Ascidians (Fig-5), seaweed (Fig-3) have been investigated for their natural products content [(1)].

The therapeutic application of marine organisms was deeply rooted in Mediterranean populations [3]. A considerable contribution to marine drugs research was also given by traditional Chinese medicine [2]. The use of marine herbs and marine herbal formulas belongs to a thousand year tradition and in-depth knowledge of marine drugs and other organisms is published or stored in the form of local chronicles, monographs and dietary suggestions [2].

All these information and new discoveries by scientists were collected in the “Chinese marine Materia Medica” This helpful for the development of new market drugs.

Since beneficial effects are not related to the entire organism, but only to the presence of defined molecules, efficient extraction methods are necessary. Next steps refer to separation and isolation techniques which include many types of chromatography and micro and Nano filtration. Then the structure is usually analyzed using spectroscopic techniques and finally the compound is evaluated in terms of biological, toxicological and clinical effects.

Fig: 1 Globe fish

Fig: 2 Marine Sponge

Fig: 3 Sea weed

Fig: 4 Marine Algae

Fig: 5 Marine Ascidians

Classification of some of the marine drug categories:

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 Pharmacological actions [4].

There are some of the marine drugs categories listed below:

(A) Antineoplastic drugs

(B) Antihypertensive drugs

(C) Marine toxins

(D) Antibiotics

(E) Antimicrobial drugs

(F) Antidiabetic drugs

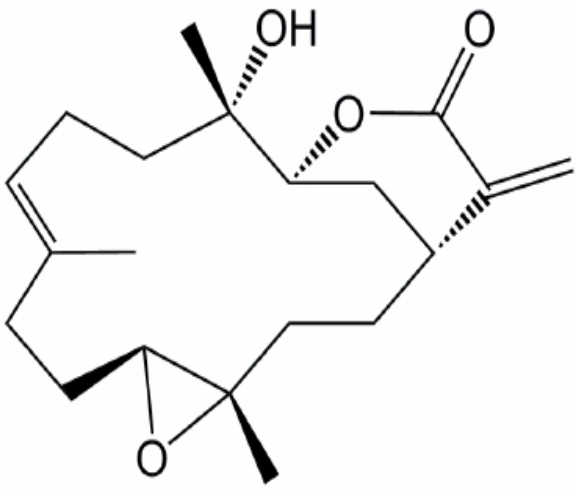
(G) Antiviral drugs

(A) ANTINEOPLASTIC MARINE DRUGS

1. Sinularin:

"Weinheimer" et al.in 1977 research about the anticancer activity against human epidermoid carcinoma cell line and the murine P388 lymphocytic leukemia cell line from the soft coral sinularia flexibilis [5].

Biological source: Sinularin (1) obtained from soft coral "sinularia f flexibles"

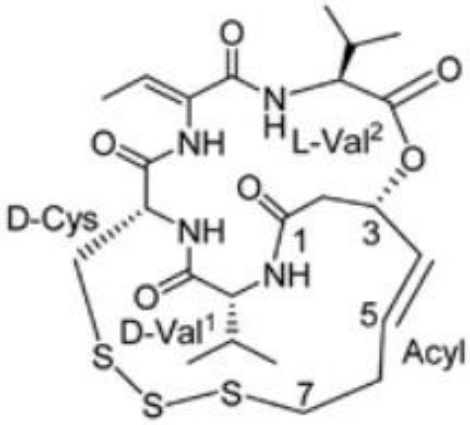


Sinularin Structure (1)

2. CHROMOPEPTIDE-A:

ZHOU et al. also research about the anticancer drug from marine animals that is chromopeptide-A It is a class of a bicyclic depsipeptide.

Biological source: Chromopeptide –A (2) is obtained from the marine bacteria called chromobacterium.



Chromopeptide-A (2)

3. Preussin:

Malha .et al research about anticancer drug preussin belonging to the class hydroxyl pyrolidine derivative.

Biological source: Preussin obtained from the marine sponge "Asperigillus candidus"

(B) ANTIHYPERTENSIVE MARINE DRUGS:

1. Laminin:

Lynnyap et al. perform in vitro differentiation of pluripotent embryonic stem cells to cardiovascular progenitors using laminin.use of these cells for in vivo cardiac regeneration and to generate human heart muscle bundles results in improved heart function [6].

Biological source: Laminin is obtained from a marine algae "Laminaria Angustata".

Uses: It shows hypotensive effect. It also exhibits diverse biological activities.

(C) MARINE TOXINS:

1. Tetrodotoxin:

In July 1894 Dr.Yoshizumi Tahara presented the use of poison isolated from the ovaries and liver of a large number of tetraodontidae; especially the spheroids rubripes globe fish (puffer fish) species [7].

- It causes neurological problems and cause cardiovascular and gastrointestinal problems.
- It is used as anti-inflammatory.
- It has analgesic effect.
- It also acts as muscle relaxant

(D) ANTIBIOTIC MARINE DRUGS:

1 .Nor-Halichondrin:

K.C.Nicolaou research about the Nor-Halichondrin-A and several other halichondrin structural analogues have been obtained from sponge "Halichondria Okadai"[8].

(E)ANTIMICROBIAL MARINE DRUGS:

1. Streptopertusacin A:

Zhang et al. researched about the antimicrobial drug streptoper tusacin- A.

Biological source: Streptopertusacin-A is obtained from the culture of sea weed derived from the Streptomyces species[9].

(F) ANTIDIABETIC MARINE DRUGS:

(1).Asperchalasine-I:

QUI et al research about the antidiabetic marine drug Asperchalasine.

Biological source: Asperchalasine obtained from the mangrove fungus "Mycospharella"

It exhibits inhibitory activity against alpha-glucosidase.

(G) ANTIVIRAL MARINE DRUGS:

(1).Neoabyssomicin-A:

Song et al. research about the antiviral marine drug Neoabyssomicin – A.

Biological source: Neoabyssomicin is obtained from the strain "Streptomyces koyangensis".

HIV-I virus replication in human lymphocyte model[11].

(2).Aspergillipeptides:

Ma et al. also done research about the antiviral marine drug asperigillipeptides.

Biological Source: Aspergillipeptides obtained from marine gorgonian derived fungus "Asperigillus" species [10].

FUTURE PROSPECTS OF MARINE DRUGS:

In the same context, marine discovery is a new trend for searching of marine natural products with potential economic and medicinal uses including agrochemicals, cosmetics, nutraceuticals and pharmaceuticals[12].

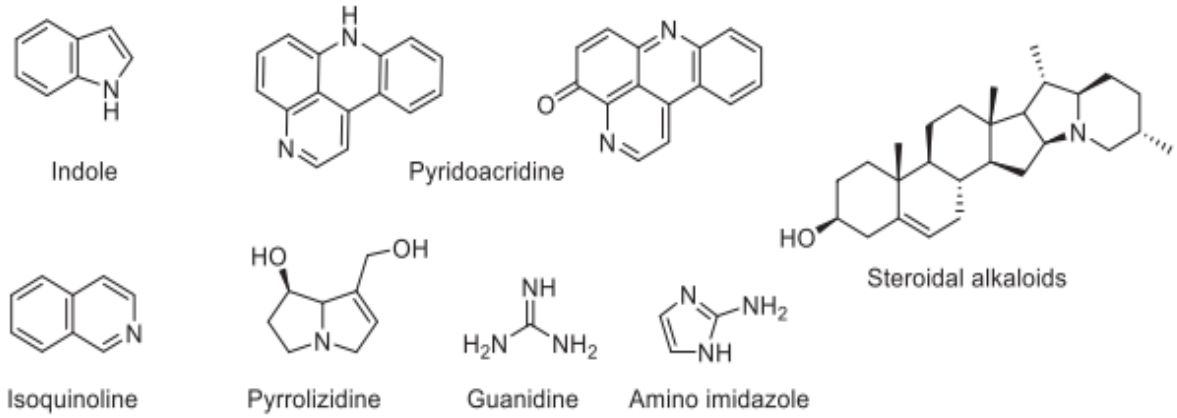
Recent investigations in structural elucidation, synthesis and bioassays have resulted in the separation and clinical assessments of diverse new bioactive compound from different marine sources like sponges, algae, microbes, tunicates, corals, seaweeds, and sea cucumbers.

Marine natural products are categorized according to their chemical structures into several chemical classes including alkaloids, terpenes, peptides, polysaccharides.

ALKALOIDS:

Alkaloid compounds are extremely varied category of broadly disseminated cyclic molecule including basic nitrogen in a negative oxidation state. Alkaloids have been obtained from marine creatures like sponges (Fig-2), tunicates, anemones, mollusks. Examples are Indole, pyridoacridine, Isoquinoline, Pyrrolizidine, Guanidine, AminoImidazole, Steroidal alkaloids(4).

These are some of the examples of alkaloids and structures are mentioned below.

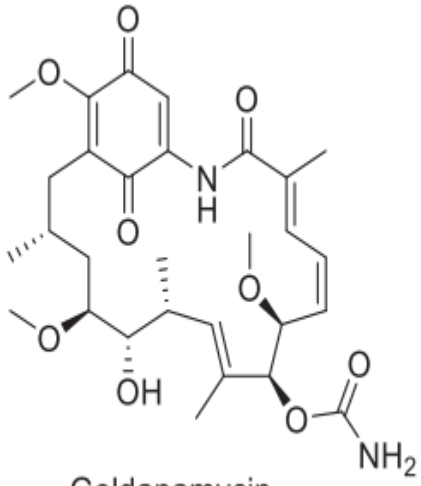


(4)

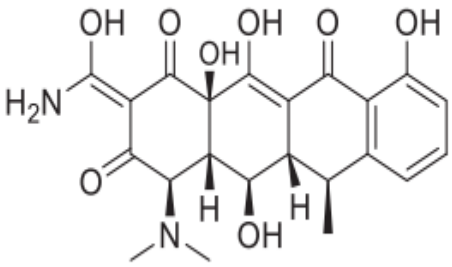
Polyketides:

Polyketides are naturally occurring molecules that includes extremely varied, chemical skeletons like macrolides polyethers and polyols.

Examples are: Geldanamycin (5); Doxycycline (6)



Geldanamycin

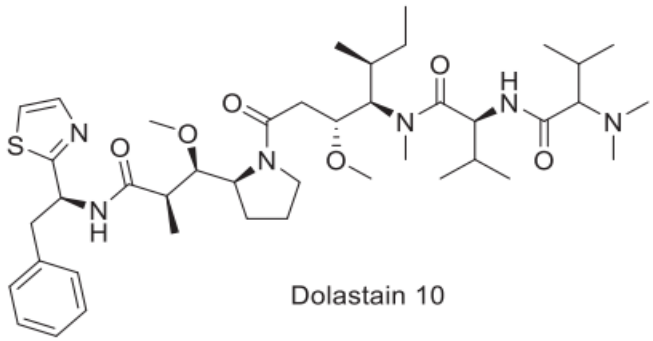


Doxycycline

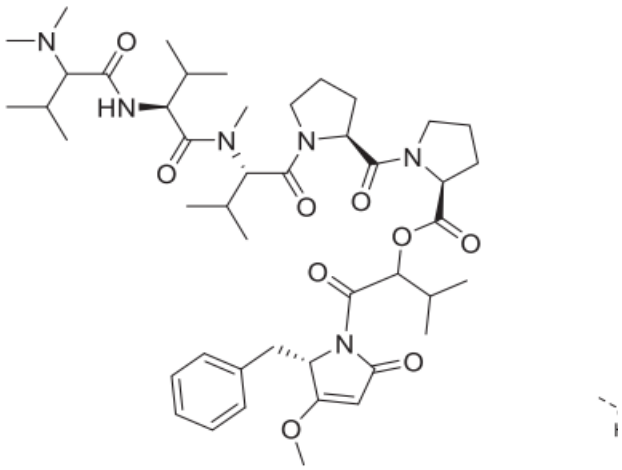
(5) **(6)**

Peptides:

Peptides are short change of amino acids linked via amide bonds and their size ranges from 2to 20 aminoacid resudies. That is Dolastatin 10, Dolastatin15 (7).



Dolastain 10

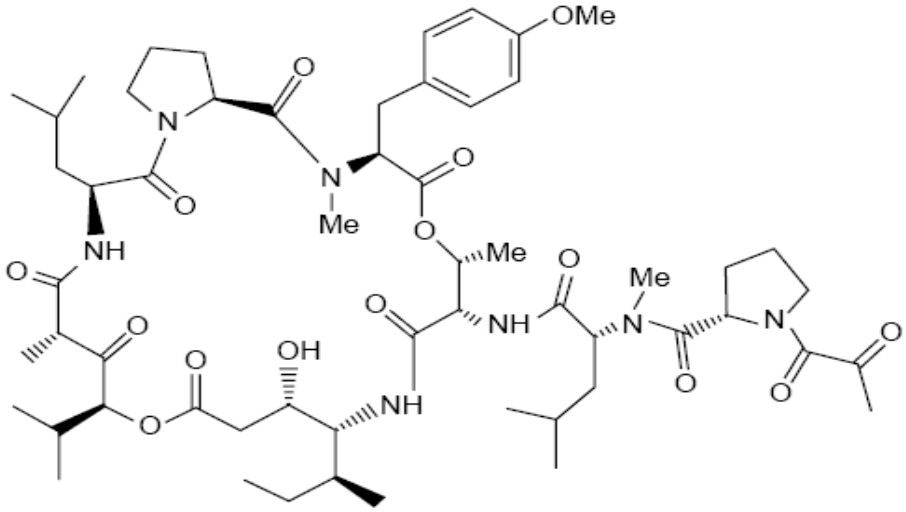


Dolastain 15

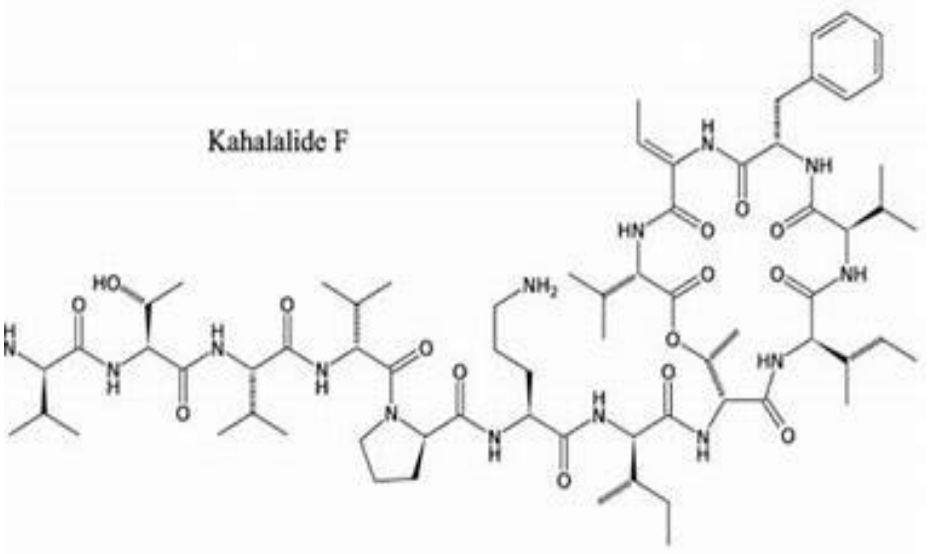
(7)

Marine Natural products under clinical trials {phase I-III}.

Several marine derived compounds have given auspicious outcomes in preclinical studies and have being promoted to clinical preliminaries or even confirmed by regulatory organization .The number lately approved drugs from marine source will keep on increasing, as of December 2018: Six marine derived compounds in phase-III, Ten compounds in phase-II, and atleast Nine compounds in phase-I including plidtepsin (Aplidin) (8), Kahalalide-F (9) [12].



Plidtepsin (8)



Kahahalide (9)

CONCLUSION:

The Marine system presents the biggest and the most divers eco-system on earth. Since 1950's, marine products have been emerged as potential and renewable resources for cosmetics and pharmacologically active compounds. In total, more than 32.000 marine-derived metabolites have been recorded from different marine organisms and their associated microorganisms. The curiosity of science and industry has established the oceans as a prospective source for new potential drug leads. Scientists have come up with drugs of various categories out of which anticancer, anti-inflammatory, analgesics, and antivirals are the most important to mention. These lead molecules are in different stages of preclinical and clinical testing stages around the world. Many drugs from marine sources have a promising effect on several chronic and unbeatable diseases like cancer. The review here demonstrate the past history of few marine products and drugs which are under clinical trials will continue development of new medicinal drugs.

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