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Novel Natural Products from Marine Sea Stars

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Abstract

Marine invertebrates specifically echinoderms have been the subject of researchers in recent times. Quite a few metabolites have been elucidated from echinoderms which have gained a demand in the fields of pharmacology and pharmaceutics. The sea star which belongs to the Echinoderms produces unique natural products which have gained a demand in the fields of medicine The aim of this review is to provide current analysis on varied species of starfish and its bioactive compounds possessing cytotoxic, hemolytic, antibacterial, antifungal, antiparasitic, itcthyotoxic and antifouling activity. The major compounds isolated from marine sea stars include steroids, steroidal glycosides, anthraquinones, alkaloids, phospholipids and peptides.

Introduction

Natural products obtained from marine sources have provided useful resource having medicinal values. On comparison with the natural products obtained from terrestrial sources, marine origin equally produces mammoth resources of novel compounds with possible pharmaceutical importance. These marine products from the marine invertebrates namely the echinoderms (sea stars) have been evolved over millions of years. The secondary metabolites which are produced by the sea stars is an integral part of their survival tactic. The secondary metabolites are nothing but the chemical defenses produced by the marine sea star in order to protect them from the predators during attack. These chemical metabolites serve as a sole source of compounds having medicinal value for mankind.

Characteristics of Sea Stars

Sea stars predominantly have gained their name due to their protruded arms resembling star which arises from the central disc; some of sea stars have more than five arms. Sea stars belong to the phylum Echinoderms and class Asteroidea. They however are classified under invertebrates owing to the fact that they lack spinal column. Sea stars have a tough skin which acts as a solid shield over them giving them a protective covering. Sea stars are protected by a calcareous plate which serves as an external skeleton. These plates are connected by muscles and tissues to give flexibility. The locomotion of the sea stars is mainly through the tubular feet which is located at the ventral side of the body. They are otherwise called as water vascular system which functions with the hydraulic pressure and they are not only used for locomotion but also for respiration and feeding. The most remarkable character of star fish is their ability to regenerate their body evidently the arms which has been damaged during their attack. The sea stars reproduce both sexually and asexually. Asexual reproduction is division of the whole body by the regeneration mechanism. Sexual reproduction occurs by the fusion of the sperm and the egg which is released in the water forming an adult.

Novel Products from Sea Stars with Cytotoxic and Hemolytic Activity

Echinoderms represent an exceptional source of polar steroids of immense structural diversity, showing a range of biological activities. Steroids are organic compounds which act as an integral part of the cell membrane of echinoderms. The steroidal components namely saponins, asterosaponins, and astropectenol are the major source of compounds abundantly found in sea stars [1-3]. A basic study has revealed facts about the search for "Drugs from the Sea". This has progressed at the rate of a ten percent increase in new compound per year [4]. The isolation and characterization of bioactive compounds from the sea stars in the marine ecosystem serves a good resource for

the human population to fight against the deadly diseases like cancer.

Elucidation of novel compounds from far eastern sea star *Leptasterias ochotensis* illustrated cytotoxic activity towards cancer cell lines RPMI-7951 and T-47D [1]. Steroidal compounds and asterosaponins were isolated from cold water star fish *Ctenodiscus crispatus* and starfish *Culcita novaeguineae* respectively showing cytotoxicity against human carcinoma cell lines HepG2 and U87MG ensuing the apoptosis of the cells hence playing a significant role in the anti tumor chemotherapy [2,3]. Steroidal compounds were elucidated from one another species of sea star *Astropecten polyacanthus* which showed cytotoxic activity against the Human cancer cell lines HL-60,PC-3 and SNU- C5 [4]. The crude extracts of same species starfish *Astropecten polyacanthus* possessing inhibitory effects against the inflammatory components (TNF-α and IL-6) [5].

A polysaccharide compound was reported to be extracted from the sea star *Asterina pectinifera* possessing a chemo preventive activity initiating the enzymes which stages a key role in carcinogenesis against Human colon cancer (HT-29) and Human breast cancer cell lines [6,7]. Few new compounds were reported as a metabolite of asterosaponins from sea star *Archaster typicus* showing cytotoxic activity against human cervical cell line and mouse epidermal cell line [8]. Glycolipids secluded from the sea star *Narcissia canariensis* from the coast of Africa indicated the presences of cyotoxic activity against various adherent human cancerous cell lines (multiple myloma, colarectal adenocarcinoma and glioblastoma multiforme) [9]. A comparative study was reported with the crude extract from *Acanthaster planci* starfish was compared with the conventional drug tamoifen, the crude extract demonstrated effective apoptotic activity than the conventional drug against human breast cancer cell line [10].

Hemolytic activity was also studied from various star fishes *Ophiocoma erinaceus, Acanthaster planci* (crown of thron), *Protoreaster linckii* (red knobbed), and *Holothuria polii* showed hemolysis when tested against human, chicken, goat and rabbit red blood cells having a natural secondary metabolite possessing hemolytic properties a naturally secondary metabolite possessing hemolytic properties [11-14].

Novel Products from Sea Stars with Antimicrobial Activity

Antibacterial and antifungal activity

Antimicrobial activity is a term coined as an agent that acts against the microbes confirming a cidal or a static activity against the pathogens. Continued existence of the sea stars depends on capable antimicrobial mechanisms to safeguard themselves against microbial infections and fouling. The potent secondary metabolite produced by the sea star shows a rich source of activity against the microbes. A study reported on the crude fractioned ethanolic, nbutanol and methanolic extracts from sea star *Luidia maculate, Stellaster equestris, Astropecten indicus, Protoreaster lincki, Pentaceraster regulus* showed an effective antibacterial and antifungal activity against human pathogens namely *Escherichia coli, Bacillus subtilus, Klebsiella sp, Shigella flexineri, Vibrio parahaemolyticus, Staphylococcus aureus, Salmonella paratyphi*, and the fungal pathogens like *Penicillium sp, Aspergillus sp* and *Trichophyton mentagropytes* respectively [15-18] (Table 1).

Table 1: Natural products of Sea stars and its activity.

S.No	Sea Star	Origin	Compounds/ Crude Extracts in Solvents	Activity	References
1.	*Leptasterias ocholensis*	Far east coast	Asterosaponins & Glycosides Methanolic extract	Cytotoxic activity	Malyarenko *et al.* [1]
2.	*Ctenodiscus crispatus*	Sea of Okhotsk	Steroidal compound (polyhydroxylated steroidal derivative) Methanolic extract	Cytotoxic activity & Antitumor against Hepatocellular carcinoma & Glioblastoma cells	Tranhong *et al.* [2]
3.	*Ophiocoma erinaceus*	Oeshn island Persian gulf	Saponins Ethanolic fractions	Hemolytic and cytotoxic activity	Elaheh Amini et al. [11]
4.	*Luidia maculata*	Center of Mandapam South East Tamilnadu	Partially purified compound Ethanolic extract	Antioxidant, Antifungal & Antibacterial	Suguna *et al.* [13]
5.	*Astropecten polyacanthus*	Coast of Vietnam	Asteropectinol (steroidal compound) Methanolic extract	Cytotoxic activity (potent compound against Leukemia)	Nguyen Phuong *et al.* [5]
6.	*Acanthaster planci*	Indo pacific region (Australia)	Glycoprotein (toxic veneom)	Cytotoxicity	Chi-Chiu Lee *et al.* [12]
7.	*Protoreaster linckii*	Center of Mandapam South East Tamilnadu	Crude Compound Methanolic extract	Antimicrobial, Hemolytic, Antinociceptive & Cytotoxic activity	Suguna *et al.* [13]

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8	*Stellaster equestris*	Center of Mandapam South East Tamilnadu	Crude and fractioned compound (steroidal compound)	Antibacterial	Bragadeeswaran *et al.* [13]
9.	*Acanthaster planci*	Indo pacific region coast of Pulau Redang (Malasia)	Homogenized crude extract	Potent Cytotoxic and apoptotic effect on Human breast cancer	Ahmed Faisal *et al.* [10]
10.	*Astropecten indicus*	Center of Mandapam South East Tamilnadu	Crude compound Methanolic extract	Antibacterial	Chamundeeswari *et al.* [17]
11.	*Archaster typicus*	Coast of Vietnam	Asterosaponins a. Archasterosides b. Regularosides	Cytotoxic activity against human and mouse myeloma	Kicha *et al.* [8]
12.	*Archaster typicus*	Queensland, Australia	Aqueous borne compound	Antifouling	Jana Guenther *et al.* [25]
13	*Linckia laevigata*	John Brewer Reef	Aqueous borne compound	Antifouling	Jana Guenther *et al.* [25]
14	*Fromia indica*	John Brewer Reef	Aqueous borne compound	Antifouling	Jana Guenther *et al.* [25]
15	*Cryptasterina pentagona*	Kissing Point in Townsville	Aqueous borne compound	Antifouling	Jana Guenther *et al.* [25]
16.	*Asterina pectinifera*	Coast of Pohang Korea	Polysaccharides	Antitumor against colon cancer	Kyung *et al.* [7]
17.	*Culcita novaeguineae*	Far east coast	Asterosaponins	Cytotoxic activity & Antitumor and chemotherapeutic agent	Guang *et al.* [3]
18.	*Asterias rubens*	Coast of Norway	Coelomocytes fluid (Antimicrobial peptides)	Antibacterial	Maltseva *et al.* [19]
19.	*Anasterias minuta*	Californian coast	Steroidal Glycosides	Antifungal	Chludi *et al.* [21]
20.	*Asterina pectinifera*	East coast of Korean Peninsula	Crude compound Methanolic extract	Antifungal	Choi *et al.* [23]
21	*Dermasterias imbricate*	Coast of North America	Saponins, Sulfated steroidal compound	Antifungal	Bruno *et al.* [24]

The celomic cavity is the internal structure of star fish which contains celomic fluid holding the cells of immunity and the antimicrobial peptides. Antimicrobial peptides form the first line of defenses and hence termed as the host defense peptides. They come under the innate defense response in both unicellular and multi cellular organisms [19]. They have a wide range of activity towards bacteria, fungi, viruses and parasites. Antimicrobial peptides (AMPs) are vital immune effect or molecules for invertebrates, including echinoderms, which lack a vertebrate-type adaptive immune system. The function of AMP binds to the bacterial surface and destructs the cell walls of the bacteria. A study conducted on sea star Asterias rubens illustrated the presence of two peptides and four antimicrobial peptides which was identified as actin and filamin which are known for its antimicrobial properties. [20,21]. Isolation of new sulfated steroidal compound ad crude compound holding similar chemical properties of steroidal oligoglycosides and polyhydroxy steroids extracted from the whole body of sea star using various solvents and water as a solvent from star fishes namely *Anasterias minuta, Asterias rubens, Asterina pectinifera* and *Dermasterias imbricate* had confirmed antifungal activity against pathogenic fungi namely *Cladosporium cucumerinum, Aspergillus sp, Cryptococus neoformans* and other fungal pathogens [22-24].

Novel Products from Sea Stars with Anti-Fouling Activity

Generally outer surface of sea star are hard hence mostly they are free from fouling organisms like bacteria and algae studies were conducted in sea stars like *Acanthaster Planci, Cryptasterina pentagona, Linckia laevigata, Formia Indica* and *Archaster typicus* which has indicated that both the physical and chemical barriers stages a key role in keeping away the fouling organisms. The physical barriers present on the epidermal surface of the sea stars like thron, pedicellariae and paxillae acts as a mechanical hindrance for the fouling micro and macro organism from settling on the surfaces. The natural products secreted by the sea star also acts the chemical barrier the surface associated compounds like hexadeconoic acid, cholesterol and lathosterol showed antifouling activity [25].

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Conclusion

Echinodermata is one of the most diverse phyla among the marine invertebrates, which include Sea stars, sea urchins, sea biscuits and sea cucumbers. The sea stars take part in several biological role and hence proved itself as a future untapped source of bioactive molecules. Among them, the sea stars have variety of chemical constituents such as steroids, glycosides consisting of asterosaponins,steroids,cyclic glycosides,steroid monoglycosides,diglycosides,saponins, asterosaponins and carotenoids. This proves that sea stars poses a great efficacy of echinoderm-derived molecules for therapeutic relevance in selected fields of cancer research, in the control of bacterial intensification as substances with new antibiotic properties, restrain the fungal growth as an essence with new antifungal properties, and lastly in the circumstance of industrial applications such as antifouling agents.

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