MARINE BIOPHARMACEUTICALS:
SCOPE AND PROSPECTS

Santhanam Ramesh
Ramasamy Santhanam
Veintramuthu Sankar

Bentham Books

Marine Biopharmaceuticals: Scope and Prospects

Authored by

Santhanam Ramesh
Karuna College of Pharmacy
Kerala University of Health Sciences, Palakkad
Kerala, India

Ramasamy Santhanam
Fisheries College and Research Institute
Tamil Nadu Veterinary and Animal Sciences University
Thoothukudi, India

&

Veintramuthu Sankar
P.S.G. College of Pharmacy
Coimbatore, Tamil Nadu
India

Marine Biopharmaceuticals: Scope and Prospects

Authors: Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

ISBN (Online): 978-981-5196-47-4

ISBN (Print): 978-981-5196-48-1

ISBN (Paperback): 978-981-5196-49-8

First published in 2024.

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Pte. Ltd.
80 Robinson Road #02-00
Singapore 068898
Singapore
Email: subscriptions@benthamscience.net

BENTHAM SCIENCE

CONTENTS

FOREWORD

I am delighted to write this foreword, not only because Prof. Ramasamy Santhanam, one of the authors, has been my teacher and colleague for more than 30 years, but also because I believe deeply in the educative value of the contents of this book for all the stakeholders in Fisheries and pharmaceutical Education.

Nature is considered to be an ancient pharmacy serving as the solitary source of therapeutics for thousands of years. Almost all of the current natural product-derived therapeutics have their terrestrial origins. The marine environment has also become a promising source of bioactive molecules and drugs of therapeutic use. Recent research findings have shown that marine organisms possess a higher incidence of significant bioactivity compared with terrestrial organisms. In a National Cancer Institute preclinical cytotoxicity screening, 1% of the examined marine samples exhibited anti-cancer potential versus 0.1% of the tested terrestrial samples. The number of new marine bioactive compounds reported each year is also increasing considerably, and more than 1000 new such compounds have been reported each year. However, the path to drug discovery from marine organisms faces several challenges. Lack of advancements in sampling techniques, taxonomic identification of therapeutically important marine species, compound structure determination strategies, etc. represent crucial steps in marine drug discovery.

The present volume titled “Marine Biopharmaceuticals: Scope and Prospects” the first of its kind is written by both the experts of pharmaceutical and fisheries disciplines and it deals with the pharmaceutically important marine organisms; and their bioactive compounds, chemical classes and modes of action. It also deals with the techniques in the development of marine biota-derived drugs; and the constraints and remedial measures. The chapter on the introduction of an inter-disciplinary PG degree program on the hitherto unknown but productivity course viz. Marine Bio-Pharmacy will help drug companies acquire trained personnel in the development of new marine drugs.

I congratulate the authors for their timely publication for the benefit of the Fisheries and Pharmaceutical sector.

Dr. G. Sugumar
Vice-Chancellor, Tamil Nadu Dr. J. Jayalalithaa Fisheries University
Tamil Nadu
India

PREFACE

Our marine ecosystems including the seas and oceans cover about 70% of the earth's surface and contain over 80% of the world's biodiversity. Unfortunately, only 5% of these ecosystems have so far been explored and only 9% (about 200,000) of the total species have been adequately researched. The marine biodiversity is an exceptional reservoir of natural products (bioactive compounds or secondary metabolites) owing to their different structural features from those of terrestrial natural products. During the last 50 years, about 15,000 bioactive compounds with potential applications as medical drugs have been isolated from these species. However, only less than 1% of these compounds have so far been examined for their pharmacological activities. The study of marine organisms for their bioactive potential has therefore increased in recent years. As there is a great demand for the discovery of new medicines, researchers are nowadays increasingly looking towards these marine ecosystems

for the isolation and development of novel compounds, treatments, and solutions to combat human disease.

Though some books are presently available on marine natural products, a comprehensive book on marine biopharmaceuticals and their scope and prospects is still needed. Further, a book dealing with the most promising pharmaceutical compounds derived from the major groups of marine organisms with an aim of utilizing them in the development of new drugs is the need of the hour. Keeping these in consideration, this publication is being brought out for the first time by bringing together the experts in Pharmaceutical Sciences, Marine Biology, and Marine Biochemistry disciplines. Aspects relating to Marine Bioprospecting; Promising Pharmaceutical Compounds of Marine Biota with their Therapeutic Applications; Marine Biopharmaceuticals in the Pipeline; and Scope and Career Prospects of Marine Bio-Pharmacy (= Marine Biopharmaceutical Sciences) and Pharmaceutical Marine Biology courses are dealt with .It is strongly hoped that this title would largely help the researchers and students of disciplines like Marine Bio-Pharmacy, Marine Biology, Marine Microbiology, Marine Biochemistry and Marine Biotechnology; as a standard Reference for all Libraries of Colleges and Universities; and as a guide for the drug companies involved in the development of new drugs from marine biopharmaceuticals.

Santhanam Ramesh
Karuna College of Pharmacy
Kerala University of Health Sciences, Palakkad
Kerala, India

Ramasamy Santhanam
Fisheries College and Research Institute
Tamil Nadu Veterinary and Animal Sciences University
Thoothukudi, India

&

Veintramuthu Sankar
P.S.G. College of Pharmacy
Coimbatore, Tamil Nadu
India

CHAPTER 1

Introduction

Abstract: This chapter deals with the role of seas and oceans in human life; marine biodiversity; marine drugs and their origin; groups of marine biota as sources of drugs; importance and advantages of the production of marine drugs; pharmaceutical marine biodiversity in the development of marine drugs; existing problems in the development of new marine drugs; and remedial measures for the adequate supply of bioactive compounds for the production of cost-effective new drugs for various diseases.

Keywords: Marine biodiversity, Marine organisms as drug sources, Origin of marine drugs, Pharmaceutical marine biodiversity, Problems in marine drug development.

INTRODUCTION

Although 71% of the earth's surface is covered in water, 97% of this is found in our seas and oceans. But, only 5% of our oceans have so far been explored. Further, the first marine organisms appeared about 3500 million years ago and even after 250 years of active marine research, only 9% of the species present have been adequately researched and the remaining 91% of the species present in the seas and oceans still lack a detailed description. The marine environment is the richest biosphere on earth and its living conditions differ significantly from those on the earth. The temperature range of this environment is huge as it varies from −1.5°C in ice sea to 350°C in deep hydrothermal systems; pressure from 1 to over 1,000 atmospheres; light from complete darkness to extensive photic zones; and nutritional conditions from nutrient-rich to nutrient-sparse.

Role of Seas and Oceans in Human Life

The seas and oceans play an important role in the human life. As per available reports, about one billion people depend on seafood as their primary source of animal protein. These water bodies are known to produce over half of the oxygen we breathe besides storing 50 times more carbon than the atmosphere. The coastal habitats adjoining the seas such as coral reefs and mangrove swamps provide protection from tsunamis and storms, while the ocean currents regulate largely our

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

climate and weather systems. The seas and oceans also provide humans with several unique recreational activities which include fishing, boating, and whale watching. These water bodies are also known to help largely in transportation and 76% of all US trade is done involving some form of marine transportation. Recent research on marine organisms has shown that these organisms are the reservoirs of several drug-producing natural products especially for the treatment of cancer, arthritis, Alzheimer's disease, and heart disease [1].

Marine Biodiversity

Only a fraction of the types of organisms that live in the sea are known today. As per the World Register of Marine Species, there are 240,000 known species (2016, http://www.marinespecies.org/) of which the highest number of species (about 33000) was found in the seas around Australia and Japan. Of the 36 animal phyla so far reported, about half are exclusive to the sea and among the marine animals, 60% belongs to the invertebrates [2].

Origin of Marine Drugs

Throughout history, nature and medicine have shown a strong relation, as highlighted by the wide use of therapeutic biomolecules in traditional medicines for thousands of years. During the ancient Greece and early Byzantium periods, the therapeutic applications of marine invertebrate organisms were deeply rooted in Mediterranean populations. Amazingly these invertebrates were used therapeutically in the forms of beverages, pulverized products, juices, broth, unguent, or eaten as fresh or dry flesh. The use of marine herbs and their formulas belongs to a thousand-year tradition. The Chinese Marine Materia Medica, a kind of encyclopedia is considered to be the best compendium about blue-green algae (cyanobacteria), seaweeds and marine animals. This encyclopedia is also considered the starting point in the development of new marketed drugs. This long tradition amply testifies that the interest in marine natural products developed in the ancient world, though the current research has been emphasizing the beneficial effects of these natural products and their molecules [3].

Marine Organisms as Sources of Drugs

Nowadays, most drugs in use come from nature. For example, while aspirin was first discovered from the willow tree, penicillin was isolated from the common bread mold. Further, the majority of drugs derived from natural sources have their origin from land-dwelling organisms. However, as there is a great demand for the discovery of new medicines, researchers are nowadays increasingly looking towards the ocean. Systematic and continuous searches for new drugs have shown that marine invertebrate organisms are capable of producing several anticancer, antibiotic, and anti-inflammatory substances than any group of terrestrial organisms. Such promising invertebrates include sponges (Porifera), corals and jellies (Cnidaria), flatworms (Platyhelminthes), polychaetes (Annelida), moss animals (Bryozoa), lamp shells (Brachiopoda), crustaceans (Arthropoda), mollusks (Mollusca), sea stars and other echinoderms, (Echinodermata), acorn worms and relatives (Hemichordata), tunicates, (Urochordata) and elasmobranchs and teleost fishes (Chordata). Across these animals, the marine sponges (Porifera) account for almost half of new natural products since 1990. An interesting feature of the habitats of these drug-producing organisms (except the cone snail) is more or less sessile (non-moving) invertebrates. The possible reasons for this phenomenon are: these sessile invertebrates use these chemicals to repel predators because they cannot escape from their habitat easily; and since many of these sessile species are filter feeders, they may use these powerful chemicals to repel parasites or as antibiotics against disease-causing organisms. [2, 4].

Need for the Production of Marine Drugs

Of late, diseases, such as Alzheimer's and Arthritis have been reported to create greater threats to the quality of human life. Heart disease, on the other hand, has become a major threat, while cures for cancer and AIDS continue to be challenging. Unfortunately, many of the drugs formulated over the past several decades have now become less useful due to the development of drug resistance. Some forms of cancer have evolved multiple drug resistance which has made all drug treatments ineffective. In this context, the organisms of the seas and oceans could be a new source of biodiversity and novel drugs. Unlike the terrestrial environment, ethnomedicinal information to guide marine research is very much limited. It is interesting to know that about one-half of all cancer drug discovery focuses now on marine organisms. It was only after the 1950s, scientists began to explore the seas and oceans for useful therapeutics and this was largely due to the advent of scuba diving and new sampling technologies. Marine drug discovery, however, began in the late 1970s, and programs were formulated in the 1980s in the USA, Japan, and Australia. These programs have led to the development of novel new drug leads. Significant progress in the clinical development of marine-derived drugs has been achieved during the last 20 years and during this period, six out of nine currently used drugs of marine origin have been approved [5].

Pharmaceutical Marine Biodiversity and Drug Development

The high diversity of marine species and associated high competition for survival make their compounds unique in chemical structures and biological activities compared to terrestrial natural products. The marine life yielding bioactive compounds includes mainly microorganisms such as microalgae, cyanobacteria,

CHAPTER 2

Marine Bioprospecting

Abstract: This chapter deals with the types of marine ecosystems and their pharmaceutical biodiversity; the present status of marine bioactive compounds and their chemical classes; therapeutic activities of marine bioactive compounds**;** level of contribution of bioactive compounds by different groups of marine organisms; green processing methods of marine drug development; and measures to tackle supply problems of bioactive compounds.

Keywords: Contribution of bioactive compounds by marine biota, Green processing methods, Marine ecosystems, Meeting supply problems, Status of bioactive compounds, Therapeutic activities of bioactive compounds.

INTRODUCTION

Bioprospecting or biodiversity prospecting is defined as the "process of collecting or surveying of a large set of flora (or fauna) for the purpose of biological evaluation and isolation of lead compounds" [7]. Marine bioprospecting is a process involving the collection of microorganisms like bacteria and fungi and microalgae and larger organisms (marine plants, invertebrates, and fishes) from the sea; categorization into species through valid taxonomical identification; and analysis in research and development. The result of such bioprospecting may be a purified molecule that is produced biologically or synthetically or the entire organism. From a business perspective, the purpose of marine bioprospecting is to find components, and compounds that may be included as components in products or processes. In other words, marine bioprospecting is not an industry but it may procure different compounds that may be used in many different industries. Due to its importance, marine bioprospecting is now lying at the forefront of industrial production as it is also considered as doing something new in order to create future wealth. Companies possessing high profile in the field of marine bioprospecting in recent decades include Diverse and New England Biolabs. In regards to the development of new biopharmaceuticals, the marine bioprospecting (also known as Marine biodiversity prospecting) can be described as a targeted and systematic search for bioactive compounds (secondary metabolites/natural products/ ectocrines) from marine organisms. This unique venture in fact started

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

in geographic territories with long coast-line with warm temperatures. Prominent countries where large-scale samplings were done for pharmaceutically important invertebrates (and probably also other groups of marine organisms) include Asia followed by Oceania, America, Africa, and Europe [2]. Further, the bioprospecting approach is not new, as more than 10,000 pharmaceutically important compounds have already been reported from marine sources, although very few of them have been put on the market.

Marine Ecosystems and their Pharmaceutical Biodiversity

The marine ecosystem is the largest ecosystem of our blue planet. Its biotic and abiotic components play an important role in maintaining proper balance in this ecosystem. Compared to other ecosystems of the planet, the marine ecosystem supports great biodiversity. The different types of marine ecosystems are open deep sea, salt water wetland, coral reefs, estuaries, mangroves, sandy beach, kelp forests, polar marine and rocky marine ecosystems [8]. The salient features of the different types of marine ecosystems are given below.

Open Marine Ecosystem

This is the upper layer of the ocean with adequate light penetration and the sun rays reach quite easily in this ecosystem. This open marine ecosystem which extends up to 150 m from the ocean surface provides habitat to a variety of sea creatures such as plankton, algae, whales, jellyfish, *etc*.

Deep-Sea Ecosystem

The deep-sea marine ecosystem inhabits various animal species up to its 1000 m depth. As there is poor light penetration at the seafloor of this ecosystem, its inhabiting species possess several adaptations. The important animals of this ecosystem include squids, fishes, elephant seals, sperm whales, crabs, worms, some sharks, *etc*.

Sandy Beach Ecosystem

Compared to other marine ecosystems, the biodiversity is quite poor in this ecosystem. However, the species of this sandy beach ecosystem such as mollusks, crustaceans, and polychaetes are very much adapted to a constantly variable environment.

Rocky Marine Ecosystem

The rock shores, rock cliffs, boulders, tide pools, *etc*. are the different constituents of this rocky marine ecosystem. The biodiversity of this ecosystem includes lichens, birds, and invertebrates such as lobsters, urchins, barnacles, sea stars, sea squirts, *etc*.

Coral Reef Ecosystem

It is a special type of marine ecosystem and is mostly found in tropical waters forming the most productive ecosystem of the earth. This ecosystem has been reported to provide food and shelter to about ¼ of marine species. Further, this ecosystem attracts exotic color fishes like sponges, snails, and seahorses; and occasionally large animals like sharks, dolphins, *etc*.

Kelp Forest Ecosystem

Kelp forests are underwater areas with a high density of kelp, (large brown algae) which has been reported to cover a large part of the world's coastlines. This ecosystem supports various animal species such as seabirds, shorebirds, invertebrates (like crabs, sea stars, snails, *etc*.), fishes, and mammals (like sea lions, seals, whales, sea otters, *etc*.).

Estuarine Ecosystem

The region around the river mouth where it connects with the sea is usually termed an estuarine ecosystem. The characteristic feature of this ecosystem is its salinity which largely depends on the influence of tides and it varies between 0 and 35 ppt. This ecosystem does not normally support a variety of species and it plays an important role as nurseries for various kinds of fishes, shrimps, *etc*.

Saltwater Wetland Ecosystem

The coastal regions of oceans and seas are commonly known as the saltwater wetland ecosystem which is classified into two types *viz.* saltwater swamps and salt marshes. While the saltwater swamps are dominated by trees, salt marshes are often covered with grasses. The most common animals of this ecosystem are shellfish, fishes, amphibians, reptiles, migratory birds, *etc*.

Mangrove Ecosystem

It is a special type of saltwater swamp found in some tropical and sub-tropical coastal regions. These mangrove swamps are home to special types of plants such as *Avicennia* and *Rhizophora*. This mangrove ecosystem provides shelter to various species such as shrimps, jellyfish, birds, sponges, crabs, fish, crocodiles, *etc*.

CHAPTER 3

Promising Pharmaceutical Compounds of Marine Plants: Their Chemistry and Therapeutic Applications

Abstract: This chapter deals with the promising marine bioactive compounds of marine plants such as, seaweeds, seagrasses, mangroves, and halophytes; and their chemistry and therapeutic applications. Among the different constituents, the seaweeds in general and brown and red algae exhibited a variety of bioactivities followed by mangroves, seagrasses, and halophytes in that order.

Keywords: Halophytes chemical classes of bioactive compounds, Marine plants, Mangroves, Pharmaceutical marine biodiversity, Seaweeds, Seagrasses, Therapeutic activities.

INTRODUCTION

Several types of secondary metabolites have been isolated from plant sources of terrestrial origin and many of them are presently in preclinical trials or clinical trials or they are undergoing further investigation. However, the derivation of bioactive compounds as therapeutic agents from marine plants such as seaweeds. seagrasses, mangroves and halophytes is still in an infant stage due to the absence of an analogous ethno-medical history as compared to that of terrestrial environments; and the relative technical difficulties associated with the collection of the marine plant samples. In the past few decades, considerable efforts have been made, by both academic institutions and pharmaceutical companies to isolate new marine-derived secondary metabolites especially from marine invertebrates. However, marine plants are largely unexplored, and further research is therefore urgently needed in this field.

SEAWEEDS

Seaweeds (also known as macroalgae), which form one of the main ingredients used in East Asian food are multicellular, photoautotrophic organisms and are mainly inhabiting the seas or brackish water environments. Unlike terrestrial

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

plants, these seaweeds are without vascular differentiations, and are distinguished by their coloration present in thallus, *i.e.* red (Rhodophyta), green (Chlorophyta), and brown (Phaeophyceae). Seaweeds are known for their rich health promoting molecules and minerals *viz.* sulphated polysaccharides, polyphenolics, terpenoids, flavonoids, pigments, MUFAs (monounsaturated fatty acids), PUFAs (polyunsaturated fatty acids), and HUFAs (highly unsaturated fatty acids), essential amino acids, vitamins (A, B1, B2, B9, B12, C, D, E, and K), and essential minerals (calcium, iron, iodine, magnesium, phosphorus, potassium, zinc, copper, manganese, selenium, and fluoride). These compounds have been reported to be of great value in the development of novel food products,nutraceuticals and pharmaceuticals. While the nutraceutical products might help prevent health problems, such as cancer, arthritis, diabetes, autoimmune diseases, ocular diseases, and cardiovascular diseases, the bioactive compounds of these organisms possess: anti-cancer, anti-fungal, anti-inflammatory, anti-cholesterol, anti-pruritic, anti-allergic, anti-viral, anti-bacterial, antioxidant, neuroprotective, chemoprotective, immunomodulatory, and hepatoprotective properties [14].

Fig. (1). *Bryopsis* sp.

Fig. (2). *Caulerpa racemosa*.

Fig. (3). *Caulerpa scalpelliformis*.

Fig. (4). *Codium decorticatum*.

Fig. (5). *Ulva fasciata*.

CHAPTER 4

Promising Pharmaceutical Compounds of Marine Sponges: Their Chemistry and Therapeutic Applications

Abstract: This chapter deals with the promising bioactive compounds of the marine sponge species belonging to the classes Calcarea and Demospongiae. Further, the chemical classes and the bioactivities of these secondary metabolites are dealt with.

Keywords: Ara-C, Bioactivities, Calcarea, Demospongiae, Marine sponges, Secondary metabpolites, Vira-A.

INTRODUCTION

Marine invertebrates, due to their high genetic richness, have been reported to be an important and major source of bioactive compounds that can find applications in various fields like pharmaceutics, nutraceuticals, cosmetics, *etc.* Among the most studied marine invertebrates for pharmaceutically important compounds, the marine sponges with their 8500 species ranked first in both diversity and number of compounds [11]. These sponges are also well known for harboring substantial amounts of symbiotic microorganisms, including bacteria, fungi, and microalgae. For example, many of the structurally diverse and bioactive secondary metabolites originally derived from sponge extracts are known to be produced by such microorganisms [40]. Thus the sponge holobiome is considered as the source of the rich chemical diversity. As a source of various secondary metabolites, they possess significant applicability in biomedical research. Though considerable research has been done on this promising biopharmaceutical potential, it is still vastly unexplored.

MARINE SPONGE SPECIES YIELDING PROMISING BIOACTIVE COMPOUNDS

1. Leucetta chagosensis; 2. Agelas sp.; *3. Axinella* sp.; *4. Cymbastela* sp.; *5. Chondrosia* sp.; *6. Spirastrella* sp.*; 7. Aplysilla* sp.; *8. Cacospongia* sp.; *9. Dactylospongia elegans; 10. Dysidea* sp.; *11. Hyrtios erectus; 12. Ircinia* sp.; *13. Lendenfeldia* sp.*; 14. Psammocinia* sp.; *15. Scalarispongia scalaris; 16*. Smenos-

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

pongia aurea; 17. *Spongia* sp.*; 18. Arenosclera brasiliensis;.19. Callyspongia (Callyspongia) siphonella; 20. Haliclona* sp.; *21. Neopetrosia* sp.; *22. Niphates olemda.*

Class: Calcarea: *Leucetta chagosensis* (Fig. **1**) and *Leucetta microraphis.*

Fig. (1). *Leucetta chagosensis*.

Class: Demospongiae:

Order: Agelasida: *Agelas oxeata (= Agelas mauritiana)* (Fig. **2**)

Fig. (2). *Agelas* sp.

Order: Axinellida: *Axinella brevistyla, Axinella infundibuliformis, Axinella* sp. (Fig. **3**), *Cymbastela cantharella, Cymbastela* sp. (Fig. **4**), and *Lithoplocamia lithistoides*.

Fig. (3). *Axinella* sp.

Fig. (4). *Cymbastela* sp.

Order: Bubarida: *Lipastrotethya* sp.

Order: Chondrosiida: *Chondrosia corticata.* (Fig. **5**)

Fig. (5). *Chondrosia* sp.

CHAPTER 5

Promising Pharmaceutical Compounds of Marine Cnidarians: Their Chemistry and Therapeutic Applications

Abstract: This chapter deals with the promising secondary metabolites of the different constituents of marine cnidarians *viz.* hydrozoan medusae, scyphozoan medusae and soft corals and their bioactivities. Among the chemical classes of compounds, terpenoids ranked first and cytotoxicity of these compounds was the major activity.

Keywords: Bioactivities, Hydrozoan medusae, Marine cnidarians, Scyphozoan medusae, Soft corals, Secondary metabolites.

INTRODUCTION

Marine invertebrates are known to be potential sources of secondary metabolites and their pharmaceutical and therapeutical applications attract scientific and economic interest worldwide. Among these organisms, cnidarians are ranked second in the chemical diversity and quantity of marine bioactive compounds. The phylum Cnidaria has about 11,000 described species including the classes Hydrozoa (hydroids), Scyphozoa (jellyfish), Cubozoa (box jellies), and Anthozoa (sea anemones, corals, sea pens).

Among these classes of Cnidaria, the class Anthozoa has the maximum number of species over 7500 valid species (about two-thirds of all known cnidarian species) in its 10 orders [68]. However, the order Alcyonacea (soft corals) and Gorgonacea (sea fans) have been reported to contribute with the maximum number of promising bioactive secondary metabolites although other orders, such as Scleractinia (hard corals), and Actiniaria (sea anemones) have also yielded substantial number of promising compounds [69]. Asian countries such as Taiwan, Japan, and China, have been reported to possess more number of cnidarian species for the extraction of marine natural products.

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

Hydroids (Hydrozoa)

The marine hydroids of the phylum Cnidaria inhabit mostly marine environments, though some have invaded freshwater habitats. These organisms are either solitary or colonial, and there are about 3,700 described species. It is also reported that through evolution, many hydroids have suppressed the medusa and retained their sessile hydroid colonies. Studies relating to the bioactive compounds of marine hydroids are still in the infant stage and very few reports are available on anticancer properties of these animals.

Biopharmaceutically Important Marine Hydrozoans

Abylopsis sp. (Fig. **1**), *Aegina citrea* (Fig. **2**), *Aeginura grimaldii* (Fig. **3**), *Arctapodema* sp, *Colobonema sericeum* (Fig. **4**), *Crossota* sp. (Fig. **5**), *Halecium beanie, Halecium muricatum* (Fig. **6**), *Halicreas minimum* (Fig. **7**), *Macrorhynchia philippina* (Fig. **8**), *Pantachogon haeckeli,* and *Thuiaria* sp. (Fig. **9**).

Fig. (1). *Abylopsis* sp.

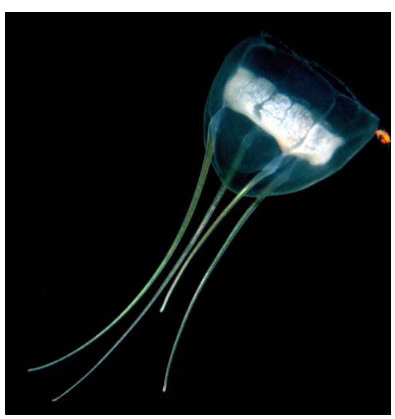

Fig. (2). *Aegina citrea*.

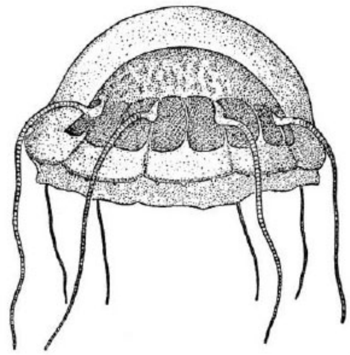

Fig. (3). *Aeginura grimaldii*.

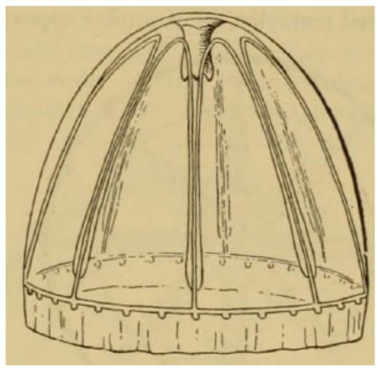

Fig. (4). *Colobonema sericeum*.

Fig. (5). .*Crossota* sp.

CHAPTER 6

Promising Pharmaceutical Compounds of Marine Bryozoans: Their Chemistry and Therapeutic Applications

Abstract: This chapter deals with the pharmaceutically important marine bryozoans, their promising secondary metabolites, and bioactivities. All the bioactive compounds of this marine invertebrate group are dealt with as per their chemical classes.

Keywords: Bryostatins, *Bugula neritina*, Cheilostomatida, Gymnolaemata, Marine bryozoans.

INTRODUCTION

The phylum Bryozoa is one of the excellent marine invertebrate sources of pharmacologically interesting substances. The bryozoans are found distributed from tropical to polar regions particularly in New Zealand, Antarctica, the North Pacific around Japan, the northern Mediterranean and the Adriatic and North Sea. While many marine bryozoans are colonial, they are also benthic or epibiotic on algae, seagrass, and marine animals. There are more than 6000 species of marine bryozoans and the species of the class Gymnolaemata are considered to be important sources of marine drug leads. Bryostatins of Bugula neritina with remarkable antineoplastic activity have attracted researchers' interests worldwide. However, this phylum has so far received little attention and most studied species belong to the order Cheilostomatida, the species of which possess erect, foliose, and large colonies. The major reason for these scarce studies is believed to be the insufficient biomass of bryozoan samples for the use of the isolation of bioactive compounds. Further, many species of bryozoans are heavily calcified with encrusting growth and difficulty in taxonomical identifications. The origin of the bioactive compounds in marine invertebrates is said to be either from de novo biosynthesis, from the diet, or from symbiotic microorganisms. In bryozoans, the origin of the most important bioactive compounds *viz.* bryostatins has been traced to bacterial symbiont *Endobugula sertula* but it is still unknown for many such compounds. Intensive and coordinated research is therefore required to isolate and

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

characterize the secondary metabolites of bryozoans with pharmaceutical applications [79].

MARINE BRYOZOANS WITH PROMISING BIOACTIVE COMPOUNDS

Amathia convoluta, Amathia tortusa, Amathia verticillata (= Zoobotryon verticillatum) Amathia wilsoni, Biflustra grandicella, Aspidostoma giganteum, Bidenkapia spitzbergensis (= Tegella spitzbergensis), Biflustra perfragilis (= Membranipora perfragilis), Bugula longissima, Bugula neritina, Caulibugula intermis, Chartella papyracea, Cryptosula pallasiana, Dendrobeania murrayana, Euthyroides episcopalis, Flustra foliacea, Hincksinoflustra denticulate, Myriapora truncata, Paracribricellina cribraria (= Cribricellina cribraria), Pentapora fascialis, Pterocella vesiculosa, Securiflustra securifrons, Sessibugula translucens, Terminoflustra membranaceotruncata Virididentula dentata (= Bugula dentata), Wateripora subtorquata, and Watersipora cucullaa (Figs. **1 - 15**).

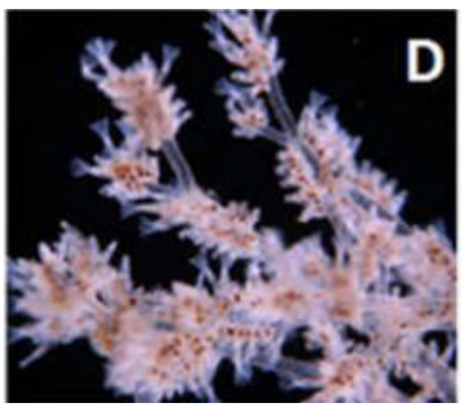

Fig. (1). *Amathia verticillata*.

Fig. (2). *Biflustra* sp.

Fig. (3). *Bidenkapia spitzbergensis*.

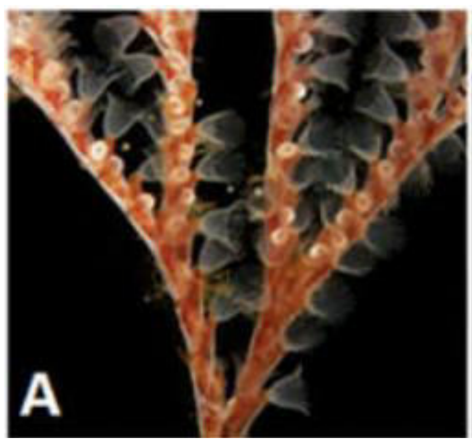

Fig. (4). *Bugula neritina*.

Fig. (5). *Caulibugula* sp.

CHAPTER 7

Promising Pharmaceutical Compounds of Marine Worms: Their Chemistry and Therapeutic Applications

Abstract: This chapter deals with the promising bioactive compounds of marine worms such as nemertines, sipunculids, and annelids. Further, the chemical classes and the bioactivities of these secondary metabolites are dealtwith.

Keywords: Marine polychaete annelids, Nemertine worms, Peanut worm, Sipunculid worm, Spatial learning and memory, Wound healing.

INTRODUCTION

Recent investigations have demonstrated that the bioactive compounds of marine worms nemertines, sipunculids and polychaete annelids) such as peptides and polysaccharides have several health promoting functions, namely, anti-cancer, anti-inflammatory, anti-oxidant, anti-hypertensive, immunomodulatory, wound healing, and anti-hypoxia activities. While the bioactive potential of marine nemertines has been fairly studied, sipunculids and marine polychaete annelids are not at all explored for this aspect even though marine environment is rich in polychaete fauna compared to nemertines and sipunculids.

Marine Nemertine Worms

The phylum Nemertini (Nemertina, Rhyncocoeles or Nemertea) includes “ribbon worms” which are found closely related to flatworms comprising about 1300 species. While most species are found in marine environments, 22 species have been reported to occur in freshwater. These ribbon worms are poorly known to the general public and only little information is available on the biology and ecology of this group. Recent research conducted on these worms has reported that certain nemertean species are known to possess potent toxins including pyridine alkaloids, tetrodotoxin, and cytolytic or neurotoxic peptides. A few of these compounds have been found to be pharmacologically important and are of potential medicinal use or for application in biotechnology.

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

Pharmaceutically Important Species of Marine Nemertine Worms: *Amphiporus lactifloreus* and *Notospermus geniculatus*

Fig. (1). *Amphiporus lactifloreus*. Image credit: Wikipedia.

Fig. (2). *Notospermus geniculatus*. Image credit: Wikipedia.

Bioactivities of Marine Nemertine Worms

Amphiporus lactifloreus

Anti-Alzheimer's Activity

The toxin of this species *viz.* GTS21 (DMXB), 3- (2, 4- dimethoxy benzylidene)-anabaseine, has been reported to be a selective α7 nAChR partial agonist. This compound showed improvement in learning performance and memory retention in passive avoidance models in nucleus basalis magnocellularis (NbM)-lesioned rats. It has also been found to reduce neo- cortical cell loss in NbM lesioned rats and cell death induced by β-amyloid or glutamate in cultures of neuronal cells. This compound is currently in clinical trials for possible treatment of Alzheimer's dementia [82].

Notospermus geniculatus

Bioactivities

The toxins Q7T3S7, P0C929 and Q38L02 of this nemertine species inhibited platelet aggregation. Further, its toxins P0DN10 and C1 IC_{50} served as serine protease inhibitors which possess therapeutic benefits in treating cancer, blood coagulation disorders and viral infections [83].

Fig. (3). *Phascolosoma sp.*. Image credit: Wikimedia commons.

Sipunculids

Sipunculid or peanut worm is a member of the invertebrate phylum Sipuncula, a group of unsegmented worms. Its common name is due to its general shape of shelled peanut. There are about 320 described species of sipunculids which are all marine and mostly from shallow waters. These worms have been reported to be a good source of several bioactive compounds which are of great use in food and pharmaceutical industries. For instance, the peptides and polysaccharides derived from these worms have been reported to possess anti-cancer, anti-hypertensive, anti-oxidant, immunomodulatory, anti-inflammatory, anti-hypoxia and wound healing activities by modulating various molecular mechanisms. However, studies of these compounds in humans have not been performed considerably. Therefore, it is important to undertake active research on this aspect.

Pharmaceutically Important Species of Sipunculids: *Phascolosoma esculenta, Phascolosoma* sp. and *Sipunculus (Sipunculus) nudus*

Fig. (4). *Sipunculus (Sipunculus) nudus (Mass)*. Image credit: Wikimedia commons.

CHAPTER 8

Promising Pharmaceutical Compounds of Marine Shellfish: Their Chemistry and Therapeutic Applications

Abstract: This chapter deals with the promising bioactive compounds of marine shellfish *viz.* crustaceans, molluscs, and echinoderms. Among the marine crustaceans, the extracts of shrimps and crabs containing astaxanthin showed major bioactivities. On the other hand, among molluscs, gastropods possessed the maximum number of secondary metabolites and associated bioactivities compared to the bivalves and cephalopods. Further, among echinoderms, the asteroids and holothurians showed maximum number of secondary metabolites compared to their counterparts *viz.* echinoids and crinoids.

Keywords: Bioactivities, Cephalopod ink, Echinoderms, Marine crustaceans, Marine molluscs, Secondary metabolites.

INTRODUCTION

The Marine crustaceans such as shrimps and crabs; marine molluscs and echinoderms are known for their biodiversity as they possess a considerable number of species. While the crustaceans are largely exploited as fisheries resources for edible purposes, the molluscs and echinoderms are only important biologically. In recent years, considerable research has been made on the potential bioactive compounds of gastropod molluscs and echinoderms. Among echinoderms, the sea cucumbers possess novel compounds with several bioactivities.

Marine Crustaceans

Marine crustaceans such as shrimps, prawns, lobsters and crabs are considered a healthy diet choice as they are a good source of various nutrients such as proteins, chitin, chitosan, lipids, carotenoids (pigments), and minerals. About 15 million tons of these organisms are captured annually around the world and Asian countries rank first in this regard. The structurally diverse bioactive nitrogenous components (10–23% (w/w)) of these organisms serve not only as functional food

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

ingredients but they also possess several bioactivities including anti-cancer, anti-diabetic, antihypertensive, antioxidant, anti-microbial, anti-coagulant, immunostimulatory, calcium-binding, hypocholesterolemic and appetite suppression [86]. Among the compounds of these crustaceans, the carotenoid astaxanthin is of great interest to researchers and to the food, feed, pharmaceutical, and nutraceutical industries. Its potent antioxidant properties have been considered to be stronger than vitamin E, vitamin C, and β-carotene [87]. Further, its bioactivity has been found to be associated with beneficial health effects for humans, namely its anti-cardiovascular, anti-inflammatory, and antiaging potentials as well as other favorable cosmetic benefits, such as improvement of skin moisture and elasticity. In 2020, the global astaxanthin market size was estimated at USD 1371 million, and it is expected to grow. Although the production of astaxanthin by chemical synthesis is less expensive (about $1000 per kilo); this process does not yield a pure compound and the combination of different isoforms are believed to be 20 times lower antioxidant capacity than their natural counterpart. Further, this synthesized compound has not been approved for human consumption. Therefore, the demand for the naturally extracted astaxanthin products is expected to rise. At the industrial level, astaxanthin is presently extracted from krill and crustacean byproducts. As there is a continuous demand for natural astaxanthin, marine crustaceans and their byproducts present a great opportunity for the whole sector.

Pharmaceutically Important Shrimps, Prawns and Crabs

Shrimps and Prawns

Aristaeomorpha foliacea, Metapenaeus sp., *Mierspenaeopsis hardwickii (= Parapenaeopsis hardwickii), Mierspenaeopsis sculptilis (= Parapenaeopsis sculptilis), Pandalus borealis, Parapenaeus longirostris, Penaeus chinensis (= Fenneropenaeus chinensis), Penaeus japonicus, Penaeus merguiensis, Penaeus monodon, Penaeus subtilis (= Farfantepenaeus subtilis)* and *Penaeus vannamei (= Litopenaeus vannamei)* (Figs. **1-12**).

Crabs

Callinectes sapidus, Cancer pagurus., Portunus segnis, and *Scylla serrata* (Figs. **13-16**).

Fig. (1). *Aristaeomorpha foliacea.*

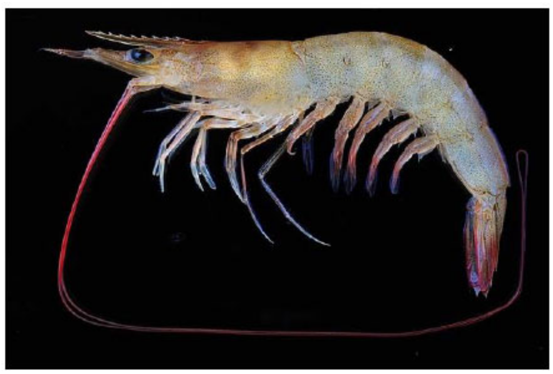

Fig. (2). *Metapenaeus* sp.

Fig. (3). *Mierspenaeopsis hardwickii.*

CHAPTER 9

Promising Pharmaceutical Compounds of Marine Tunicates: Their Chemistry and Therapeutic Applications

Abstract: This chapter deals with the pharmaceutically important species of the subphylum Tunicata of the phylum Chordata; their secondary metabolites and their bioactivities.

Keywords: Tunicates, Ascidians, Urochordates, Secondary metabolites, Bioactivities.

INTRODUCTION

Tunicates (Phylum: Chordata; Subphylum: Tunicata or Urochordates) are marine invertebrate chordates and are considered as the sister group of vertebrates. Their common name is due to the tunic, the external layer of the body. The test or tunic is secreted by the epidermis and is composed of collagen and tunicin (a form of cellulose) fibres. These tunicates include benthic and sessile species of the clade Ascidiacea (ascidians) and pelagic species of the clades Thaliacea and Larvacea or Appendicularia. There are about 3000 species of tunicates living in the seas and oceans of the world and about 2300 of them are represented by ascidians which is the largest and the most studied tunicate group. Among these tunicates, the ascidians possess a great variety of bioactive compounds with cytotoxic, antimitotic, antiviral, and antimicrobial activities and are of great interest to the biomedical field [116]. The most represented chemical class among the bioactive compounds isolated from the tunicates is alkaloids, (50%) followed by polyketides (37%) and peptides (13%). The compounds related to the cytotoxicity against human cancer cell lines and anti-proliferative activity account for 58% of the total number of bioactive compounds isolated from the ascidians and three of these compounds have entered clinical trials [111].

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

Biopharmaceutically Important Ascidians

Aplidium sp., *Ciona savignyi, Cystodytes* sp., *Diazona.*sp., *Didemnum* sp., *Eudistoma* sp., *Herdmania* sp., *Lissoclinum.* sp., *Phallusia nigra, Styela plicata,* and *Synoicum adareanum* (Figs. **1 - 11**).

Fig. (1). *Aplidium* sp.

Fig. (2). *Ciona savignyi*.

Fig. (3). *Cystodytes* sp.

Fig. (4). *Diazona* sp.

Fig. (5). *Didemnum* sp.

Fig. (6). *Eudistoma* sp.

CHAPTER 10

Promising Pharmaceutical Compounds of Marine Fishes: Their Chemistry and Therapeutic Applications

Abstract: This chapter deals with the bioactive potential of the different groups of marine fishes *viz.* cartilaginous, bony, and jawless fish species.

Keywords: Cartilaginous fish, Bony fish, Jawless fish, Eicosapentaenoic acid, Docosahexaenoic acid.

INTRODUCTION

According to available reports, the total number of fish species ranges is about 35000 and about 28,600 fish species have been found to be valid. Of these total fishes, 95% are bony fishes (mostly teleosts), about 50 species are agnathas (jawless fishes) and about 800 species are cartilaginous fishes. Further, 58% of fish species are marine; 41% are freshwater fish; and the remaining 1.0% are diadromous (travel between salt water and fresh water as part of their life cycle). Fish are nutritionally, medically and economically important owing to their rich protein and beneficial liver oils known as omega-3 fatty acids. The most vital omega-3 fatty acids present in fish oil are Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) which are seen in adequate quantities in fishes like mackerel, salmon, tuna, sturgeon, bluefish, mullet, sardines, anchovy, menhaden trout, and herring. All these fish are known to be rich in Omega-3 fatty acid and every 85 g of fish provide 1 gram of omega-3 fatty acids. Ullah and Ahmad [120] reported on the medicinal importance of fish as food and fish oil as detailed below.

i) Fish oil is used for a wide range of diseased conditions including ailments associated with the heart and blood system for which it truly lowers high triglyceride level.

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

ii) Fish is also considered “brain food” because they can treat Alzheimer's disease, psychosis, attention deficit-hyperactivity disorder (ADHD), and other cognitive problems.

iii) Fish oil may also be used for dry eyes glaucoma; and age-related macular degeneration (AMD).

iv) Women may use fish oil to prevent menstrual pain (dysmenorrheal), and breast pain. Fish oil is also beneficial for complications associated with pregnancy such as early delivery, miscarriage, and high blood pressure late in pregnancy.

v) Fish oil is used for diabetes, asthma, kidney disease, movement disorders, disorders, obesity, dyslexia, developmental coordination, certain diseases associated with pain and swelling including psoriasis, and avert weight loss caused by the use of some cancer drugs.

vi) It is also used for rheumatoid arthritis, weak bones (osteoporosis), stroke, and Raynaud's syndrome (Raynaud's (ray-NOSE) disease causes some areas of the body such as fingers and toes to feel numb and cold in response to cold temperatures or stress).

vii) Fish oil is used for complications arising due to surgery itself or some drugs *i.e.* after heart transplant surgery to preclude high blood pressure and kidney damage. It is also used to reduce the chances for the body to reject the new heart. Sometimes fish oil is used following coronary artery bypass surgery.

viii) Fish oil is known to assist hardening of the arteries (atherosclerosis), bipolar disorders, psychosis and kidney problems.

ix) Fish oil is believed to be handy for endometrial (uterus) cancer and weight loss. It reduces the risk of blood vessel re-blockage after heart bypass surgery or “balloon” catheterization (balloon angioplasty) and Age-related eye disease (age-related macular degeneration, abbreviated as AMD).

x) Fish oil has been reported to be efficient for recurrent miscarriage in pregnant women with high blood pressure, anti-phospholipid syndrome, and kidney problems after heart transplant. It also puts off damage to kidneys and high blood pressure caused by cyclosporine drugs.

xi) Fish oil is useful for movement disorders in children, known as dyspraxia. It is often used for preventing blockage of grafts used in kidney dialysis, developmental coordination disorder and psoriasis.

xii) It is extensively used to lower high cholesterol levels, coronary artery bypass surgery, asthma and cancer-related weight loss.

Pharmaceutically Important Bony Fishes

The therapeutically important marine teleost fish possessing promising bioactive compounds are: Bony fishes (Class: Osteichthyes): *Anguilla japonica, Cynoglossu semilaevis, Epinephelus coioides, Hippoglossus hippoglossus, Lagocephalus slatus, Lateolabrax japonicus, Limanda aspera, Miichthys miiuy, Pagru major, Pardachirus marmoratus, Pleuronectes latessa, Pseudopleuronectes ameri, Sarda orientalis, Seriola lalandi,* and *Tachysurus fulvidraco* (Figs. **1**-**14**).

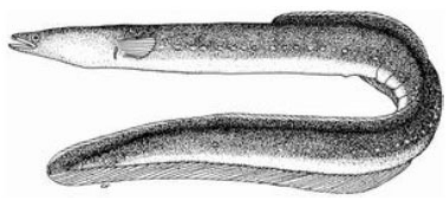

Fig. (1). *Anguilla japonica.*

Fig. (2). *Cynoglossus* sp.

Fig. (3). *Epinephelus coioides.*

CHAPTER 11

Marine Biopharmaceutical Compounds against SARS-CoV-2

Abstract: This chapter deals with the marine biopharmaceutical compounds acting against SARS-CoV-2. The promising compounds derived for anti-coronal activity were from marine plants such as cyanobacteria (blue-green algae), green algae, brown algae, and red algae. Among marine invertebrates, only sponges and soft corals contributed with their active bioactive compounds. The chemistry and mechanism of action of the different bioactive compounds have also been dealt with.

Keywords: SARS-CoV-2, Cyanobacteria, Seaweeds, Marine sponges, Marine soft corals, Bioactive compounds against SARS-CoV-2, Mechanism of action of anti-coronal compounds.

INTRODUCTION

Nowadays, among the several infections which threat people, viruses pose a very serious danger, with devastating global pandemics. The huge population growth, urbanization and local environments have been reported to be largely responsible for the emergence and spread of these viral diseases especially in many developing countries. The ongoing outbreak of pneumonia which was first identified in Wuhan, China at the end of 2019 was found to be caused by a novel virus known as 2019-novel coronavirus (2019-nCoV). As the International Committee on Taxonomy of Viruses related this virus with acute respiratory syndrome coronavirus 2, it was designated as SARS-CoV-2. Subsequently, on 11 February 2020, the WHO officially named it Coronavirus Disease 2019 (COVID 19) as it was caused by 2019-nCoV, and on 11 March 2020, this viral disease was announced as a pandemic [122]. Among all the SARS-CoV-2 variants, Omicron is the most recent one and it has been reported to harbor several mutations which yield the viral particles an improved ability to infect and transmit between hosts. Further, such viral particles may avoid immune protection even after vaccination. Newly developed therapeutics from different sources have started entering the market and many such therapeutics are still in preclinical phases only. Though considerable progress has been made in immunization and drug development, prophylactic vaccines and effective antiviral therapies for these coronavirus

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

infections are still wanting and therefore, the search for new antiviral substances is the need of the hour. The world experience of marine pharmacy has already testified the marine biota as sources of potential bioactive compounds for developing new and novel pharmaceutical substances and drugs for treating several diseases including cancer. In this connection, the bioactive compounds derived from marine invertebrates could be of great value with their ability to halt or treat corona viral infection. Metabolites derived from the marine biota capable of inhibiting coronaviruses include polysaccharides, terpenoids, steroids, alkaloids, peptides, *etc*. These compounds are not only environmentally friendly, metabolically compatible, and possess little (or no) toxins but are also able to prevent viral entry, viral replication, and protein synthesis, thus completely halting the viral life cycle [123, 124].

POTENTIAL MARINE BIOTA FOR THE PREVENTION/TREATMENT OF SARS-COV-2 VARIANTS

Seaweeds

Dictyosphaeria versluyii

The decalactone dictyospheric acid A, a compound of coumarin class derived from this green alga inhibits TMPRSS2, the priming agent of SARS-CoV-2 [124].

Dictyota pfaffii

New diterpenes dolabelladienols A–C derived from this Brazilian brown alga serve as promising protease inhibitors of SARS-Cov-2 Mpro [124].

Ecklonia cava

A total of 8 phlorotannins derived from this edible brown alga possess SARS-CoV3CLpro inhibitory properties in a dose-dependent and competitive manner. Of these phlorotannins, Dieckol and 6,6′-bieckol exhibited the most potent SARS-CoV3CLpro trans/cis-cleavage and Mpro inhibitory effects [124].

Saccharina japonica

The sulphated polysaccharide RPI-27 derived from this brown alga has been reported to strongly bind to the S-protein SARS-CoV-2 *in vitro*. This polysaccharide may be used *via* a nasal spray, metered dose inhaler, or oral delivery [124].

Sargassum spinuligerum

The phlorotannins and flavonoids, apigenin-7-O-neohesperidoside, and luteolin-7-rutinoside derived from this brown alga have been reported to be the most promising inhibitors of SARS-CoV-2Mpro [124].

Sargassum wightii

Two organic compounds *viz*. caffeic acid hexoside and phloretin isolated from this brown algal species have been reported to serve as inhibitors of the omicron variant. These compounds inhibited important residues necessary for ACE-2 interaction (ASN417, SER496, TYR501, and HIS505) [123].

Sargassum sp.

The drug-like compound, NPC163169 extracted from this brown alga inhibits the transmembrane protease serine 2 (TMPRSS2), the priming agent of SARS-CoV-2 [124].

Corallina officinalis

The cholesterol derivative cholestan-3-ol and 2-methylene derived from the red alga *Corallina officinalis* was found to serve as the inhibitor of the omicron variant. This compound inhibited the novel mutated residues, LEU452 and ALA484 on the RBD of the spike protein [123].

Chondrus crispus and Euchema cottonii

The polysaccharide, lambda-carrageenan derived from these red algae has been reported to possess inhibitory activity against influenza virus and SARS-CoV-2 viral replication dose-dependently [123].

Marine Sponges

The inorganic polyphosphate which is abundantly present in marine sponges has been reported to bind RBD of SARS-CoV-2 and prevent ACE-2 binding. Further, the alkaloids bromotyrosines derived from certain species of marine sponges have been reported to be promising compounds to investigate for SARS-CoV-2 infection blockade [123].

Agelas oroides

The alkaloid compound, (11R)-11-epi-Fistularin-3 isolated from the sponge *Agelas oroides* is a promising inhibitor of COVID-19 [124].

CHAPTER 12

Marine Biopharmaceuticals in Pipeline

Abstract: This chapter deals with the marine biopharmaceuticals in the pipeline *i.e*. year-wise number of approved marine drugs during the period 1969-2021 and their clinical uses; approved and marketed drugs up to 2021; marine biota-derived drug candidates under the different phases of clinical trials up to 2021; and marine biotaderived clinical level compounds against SARS-CoV-2.

Keywords: Marine biopharmaceuticals in the pipeline, Year-wise approved marine drugs, Clinical uses of approved marine drugs, Marketed marine drugs up to 2021, and clinically tested marine compounds against SARS-CoV-2.

INTRODUCTION

In the urgent need for new pharmaceuticals, the marine biota-based drug discovery has progressed significantly over the past several decades and we now largely benefit from a series of approved marine drugs (= biopharmaceuticals) to treat cancer and pain while a number of promising drug candidates are in clinical trials. However, the discovery of marine biota-based pharmaceuticals has always been challenging and this is due to several constraints including supply problems in pharmaceutically important biota; and lack of advanced technologies, collaboration between academics and pharmaceutical industries and adequate fund support. The development of new and improved organic synthesis methods made possible the synthesis of promising active compounds in the amounts required for further preclinical and clinical studies. Further, tremendous progress in the clinical development of marine-derived drugs has been achieved over the past 20 years. It is interesting to note that in the terrestrial environment, the plant kingdom is the main source of bioactive compounds. On the other hand, in the marine environment, the animals are the primary source of marketed drugs. Further, most of these animals, are heterotrophic, benthic invertebrates with little or no movement and living in symbiosis with microorganisms, which are believed to be the real producers of drug candidates with more relevance in drug discovery.

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

APPROVED AND MARKETED MARINE BIOTA - DERIVED DRUGS

Between 1969 and 2021, 19 marine-derived drugs have been approved. Among these compounds, 13 (68%) belong to cancer; 3 for hyperglyceridemia; 1 for virus; and 1 for chronic pain. The details relating to the year-wise approved marine drugs are given in Table **1**.

Table 1. Year-wise Number of Approved Marine Biota- derived Drugs and their Clinical Uses [126, 127].

Year of Approval	Approved	Clinical Use
1969	1	Leukemia
1976	1	Virus
1992, 1994	1	Leukemia
2004, 2005	1	Chronic Pain
2004, 2005	1	Hypertriglyceridemia
2005,2007	1	Leukemia
2007, 2015	1	Ovarian Cancer
2010, 2011	1	Breast Cancer
2011, 2012	1	Lymphoma
2012	1	Hypertriglyceridemia
2014	1	Hypertriglyceridemia
2015	1	Cancer
2018	1	Cancer
2019, 2020	1	Breast Cancer
2020	1	Ovarian Cancer
2019, 2021	1	Urothelial Cancer
2020	1	Multiple Myeloma
2021	2	Cancer

ADC: Antibody Drug Conjugate; FDA: Food and Drug Administration; EMA: European Medicines Agency.

Approved Drugs

The approved and marketed marine drugs up to 2021 and their brand names, approved agencies, source species, chemical classes, and clinical uses are given in Table **2**.

Table 2. Approved and Marketed Marine Biota-derived Drugs up to 2021 [126, 127].

Generic Name	Brand Name (s)	Approved Yr/Agency	Source/Group	Chemical Class	Clinical Use
Cytarabine (Fig. **1**)	Cytosar-U Aracytin, C-Hospira	1969 (FDA)	*Tectitethya cripta* (Sponge)	Nucleoside	Leukemia
Vidarabine (Fig. **2**)	Vira-A	1976 (FDA)	*Tethya crypta.* (Sponge)	Nucleoside	Virus
Fludarabine (Fig. **3**)	Fludara	1992 (FDA); 1994 (EMA)	Sponge	Nucleoside	Leukemia
Ziconotide (Fig. **4**)	Prialt	2004 (FDA); 2005 (EMA)	*Conus magus* (Mollusk)	Peptide	Chronic pain
Omega-3 acid ethyl esters (Fig. **5**)	Lovaza (US) Eskim (EU) and others	2004 (FDA) ; 2005 (EMA)	Tuna, Salmon, Herring, Sardines, Mackeral (Fish)	PUFA	Hypertriglyceridemia
Omega-3 acid ethyl esters	Vascepa	2012 (FDA)	Tuna, Salmon, Herring, Sardines, Mackeral (Fish)	PUFA	Hypertriglyceridemia
Omega-3 acid ethyl esters	Epanova	2014 (FDA)	Tuna, Salmon, Herring, Sardines, Mackeral (Fish)	PUFA	Hypertriglyceridemia
Nelarabine (Fig. **6**)	Arranon (US) Atriance (EU)	2005 (FDA) ; 2007 (EMA)	Sponge	Nucleoside	Leukemia
Eribulin (Fig. **7)**	Halaven	2010 (FDA); 2011 (EMA)	*Lissodendoryx* sp. (Sponge)	Macrolide	Breast cancer
Trabectedin (Fig. **8**)	Yondelis	2007 (EMA) ; 2015 (FDA)	*Ecteinascidia turbinata* (Tunicate)	Alkaloid	Ovarian cancer, soft tissue sarcoma
Brentuximab vedotin)	Adcetris	2011 (FDA) 2012 (EMA)	*Dolabella auricularia* (Mollusk)/ *Lyngbya majuscuae, Symploca* spp. (Cyanobacteria)	ADC	Lymphomas
Panobinostat (Fig. **9**)	Farydak	2015 (FDA)	-	cinnamic hydroxamic acid analogue	Cancer (antineoplastic activity.)
Plitidepsin (Fig. **10**)	Aplidine	2018(Auistralia)	*Aplidium albicans* (Tunicate)	Depsipeptide	Cancer

CHAPTER 13

New PG Degree Course, Marine Bio-Pharmacy: Scope and Career Prospects

Abstract: This chapter deals with the importance and recent status of marine biopharmaceuticals and the need for popularizing this aspect; the introduction and scope of Marine Bio-Pharmacy as an interdisciplinary PG course; suggested syllabus for taught program and practicals in the event of its introduction; and career opportunities for the Marine Bio-Pharmacy graduates.

Keywords: Recent status of marine biopharmaceuticals, Marine bio-Pharmacy, Marine biopharmaceutical sciences, Suggested PG syllabus, Career opportunities for the marine bio-pharmacy graduates.

INTRODUCTION

The industry sector involved in land-based biopharmaceutical development, manufacture and marketing is about 25 years old (or several hundred years old, depending on the type of definition followed) with more than 350 marketed products (or thousands, depending on the definition followed). However, these biopharmaceuticals still remain a small and distinct subset (generally ~15%) of the pharmaceutical industry in terms of products, R&D, companies, revenue or other parameters. For example, the worldwide annual biotechnology-based biopharmaceutical revenues are now only about $100 billion, compared with $650+ billion for all pharmaceuticals [129].

Marine Biopharmaceuticals

Although marine biopharmaceuticals are very recent in their derivation, they have been reported to be very promising for disease control and prevention due to their characteristics and multiple advantages over chemical-based synthetic drugs. Apart from the approved marine biopharmaceuticals (so-called marine drugs), many novel marine biopharmaceuticals are under clinical trials and they may be applied for clinical application in the near future, though some scientific and regulatory issues are yet to be solved. More intensive research works including the discovery, production, applications, prospects, and challenges of marine

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

biopharmaceuticals are expected in the future to gain a fruitful outcome and have a great impact on humans. As land-based biopharmaceuticals, the marine biopharmaceutical industry which is an important part of the marine biological resources development has also not attained significant progress and this is largely due to the incomplete Industry-University-Research cooperation. It is worth mentioning here that the course Bachelor of Marine Pharmaceutical Science is presently offered only at the College of Food and Pharmaceutical Sciences at Ningbo University (Zhejiang, China) [130]. Considering the vast scope and career prospects of such academic programs there is an urgent need for starting PG degree programs in all universities worldwide. In this regard, a postgraduate degree program in Marine Bio-Pharmacy (= Marine Biopharmaceutical Sciences) would take care of this long felt need. Through innovative coursework and independent research opportunities, this interdisciplinary program may instill younger generations with skills in pharmaceutical sciences, medical product development business, marketing, *etc*.

Marine Bio-Pharmacy (=Marine Biopharmaceutical Sciences or Pharmaceutical Marine Biology, an Interdisciplinary PG Course)

The concept of Marine Bio-Pharmacy, Marine Pharmacology, or Marine Pharmacognosy is either new to the world or in an infant stage. Although the pharmaceutically important marine species diversity is enormous, no intensive research has been carried out on this aspect due to the absence of an inter-disciplinary approach. Although research papers on marine natural products and their bioactivities appear every now and then, there is no coordinated approach between Marine Biologists and Scientists of Pharmaceutical Sciences. As a result, the number of new marine bioactive compounds and drugs developed is almost nil in developing countries. This calls for an integrated approach among the concerned stakeholders so that the information and skills can be applied to novel and complex issues or challenges associated with the development of new marine drugs.

This applied course may involve disciplines such as, Marine Pharmacy, Marine Pharmaceutical Chemistry, Marine Pharmaceutical Biology, Marine Pharmaceutical Microbiology and Marine Pharmaceutical Biotechnology which are required to design and develop medicines from marine organisms. Courses focus on sub-disciplines of pharmaceutical sciences—including the study of the chemical and physical properties of drugs and their biological effects—and link these systems to the discovery, development and commercialization of pharmaceuticals for the advancement of human health. Courses also explore the business and marketing aspects of the pharmaceutical industry. In paramedical colleges, the master's degree program in Marine Bio-Pharmacy may be offered as a full-fledged course similar to the ongoing M.Pharm. course. As the newly designed course is of an interdisciplinary nature, it is advisable to include staff with other specializations like Marine Biology, Marine Biochemistry, Marine Microbiology and Marine Biotechnology apart from the regular Pharmacy Faculty.

Suggested Syllabus for the Master's Degree Program in "Marine Bio-Pharmacy (Marine Biopharmaceutical Sciences)"

Taught Program

i) Pharmaceutical Marine Life of World Seas and Oceans: Pharmaceutical Marine Biodiversity and its Ecology and Biology

ii) Pharmaceutical-yielding Marine Plant and Animal Sources: Collection, Taxonomy, and Storage

iii) Development of Chemical Processes/Technologies (Extraction, Isolation, Purification and Quantification for Pharmaceutical Compounds from Marine Organisms.

iv) Chemistry of Marine Pharmaceutical Compounds from Marine Life (Alkaloids, Peptides, Nucleosides, Prostaglandins, *etc*.): Chemistry, Medicinal Chemistry, Bioorganic Chemistry, Chemical Biology, Chemical Ecology and Synthesis.

v) Marine Microbial Pharmacognosy- Bacteria, Fungi, and Symbiotic Microbes; Pharmaceutical Compounds; and their Anticancer, Antimicrobial and Photoprotective Activities

vi) Pharmaceutical Compounds from the Different Groups of Marine Plants and Animals; and their Bioactivities such as Antimicrobial, Antiviral, Anti-tumor, Antioxidant, Antiprotozoal, Antihelmintic, Antidiabetic, Anti-inflammatory, Wound-healing, Lipid-lowering, Cytotoxic, Analgesic, Anticoagulant, Hypolipidemic, Antidiarrheal, Hepatoprotective, Neuroprotective, *etc*.

vii) Marine Biotoxins and their Therapeutic Activities

viii) Marine Drugs: Present status (Approved and under Clinical trials)

ix) Supply Problems in Marine Biopharmaceutical Compounds and Remedial Measures: Chemical Synthesis; Semisynthesis; Biotechnological Techniques; and Cultivation (Aquaculture) of need-based Marine Plants and Animals of Pharmaceutical Value.

REFERENCES

[1] Available From: https://www.fauna-flora.org/environments/marine/

[2] Lomartire S, Gonçalves AMM. An overview of potential seaweed-derived bioactive compounds for pharmaceutical applications. Mar Drugs 2022; 20(2): 141.
[http://dx.doi.org/10.3390/md20020141] [PMID: 35200670]

[3] Catanesi M, Caioni G, Castelli V, Benedetti E, d'Angelo M, Cimini A. Benefits under the Sea: The role of marine compounds in neurodegenerative disorders. Mar Drugs 2021; 19(1): 24.
[http://dx.doi.org/10.3390/md19010024] [PMID: 33430021]

[4] Available From: https://oceanexplorer.noaa.gov/facts/medicinesfromsea.html

[5] Sankar V, Ramesh S, Santhanam R. Marine bio-pharmacy: Scope and career prospects. Pharm Times 2022; 54: 14-6.

[6] Albini A. From sea bed to bedside: Tapping the cancer pharmacy beneath the waves. 2021. Available From: https://cancerworld. net/from -sea-bed-to-bedside-tapping-the-cancer- pharmacy-beneath- the-waves/

[7] Korsmo KA. Isolation and characterization of bioactive compounds from the marine hydrozoans *Halecium muricatum* and *Halecium beanie*. Master of Pharmacy Thesis 2012.

[8] Available From: https://www.earthreminder.com/marine-ecosystem-characteristics-types/

[9] Stonik VA. Marine natural products: A way to new drugs. Acta Nat 2009; 1(2): 15-25.
[http://dx.doi.org/10.32607/20758251-2009-1-2-15-25] [PMID: 22649599]

[10] Aguiar ACC, Parisi JR, Granito RN, de Sousa LRF, Renno ACM, Gazarini ML. Metabolites from marine sponges and their potential to treat malarial protozoan parasites infection: A systematic review. Mar Drugs 2021; 19(3): 134.
[http://dx.doi.org/10.3390/md19030134] [PMID: 33670878]

[11] Romano G, Almeida M, Varela Coelho A, *et al.* Biomaterials and bioactive natural products from marine invertebrates: from basic research to innovative applications. Mar Drugs 2022; 20(4): 219.
[http://dx.doi.org/10.3390/md20040219] [PMID: 35447892]

[12] Ghosh S, Sarkar T, Pati S, Kari ZA, Edinur HA, Chakraborty R. Novel bioactive compounds from marine sources as a tool for functional food development. Front Mar Sci 2022; 9: 832957.
[http://dx.doi.org/10.3389/fmars.2022.832957]

[13] Kesik-Brodacka M. Progress in biopharmaceutical development. Biotechnol Appl Biochem 2018; 65(3): 306-322 .
[http://dx.doi.org/10.1002/bab.1617] [PMID: 28972297]

[14] Santhanam R, Ramesh S, Suleria HAR. Biology and Ecology of Pharmaceutical Marine Plants CRC Press 2018; 504.
[http://dx.doi.org/10.1201/9781351187114]

[15] Cotas J, Pacheco D, Gonçalves AMM, Silva P, Carvalho LG, Pereira L. Seaweeds' nutraceutical and biomedical potential in cancer therapy: A concise review. J Cancer Metastasis Treat 2021; 2021: 13.
[http://dx.doi.org/10.20517/2394-4722.2020.134]

[16] Nho JA, Shin YS, Jeong H, *et al.* Neuroprotective effects of phlorotannin-rich extract from brown seaweed *ecklonia cava* on neuronal pc-12 and sh-sy5y cells with oxidative stress. J microbiol biotechnol 2020; 30(3): 359-67.
[PMID: 9728360]

[17] Jha R, Zi-rong X. Biomedical compounds from marine organisms. Mar Drugs 2004; 2(3): 123-46.
[http://dx.doi.org/10.3390/md203123]

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

[18] Vajiravelu S, Subbiah M, Sundaresan B, Natarajan TS. *In vitro* cytotoxic studies of red algae *Portieria hornemannii* and *Spyridia fusiformis* against Dalton's lymphoma ascite and Ehrlich ascite carcinoma cell lines. J Coastal Life Med 2016; 4: 949-52.
[http://dx.doi.org/10.12980/jclm.4.2016J6-208]

[19] Kang C, Jin YB, Lee H, *et al*. Brown alga *Ecklonia cava* attenuates type 1 diabetes by activating AMPK and Akt signaling pathways. Food Chem Toxicol 2010; 48(2): 509-16.
[http://dx.doi.org/10.1016/j.fct.2009.11.004] [PMID: 19913068]

[20] Iwai K. Antidiabetic and antioxidant effects of polyphenols in brown alga *Ecklonia stolonifera* in genetically diabetic KK-A(y) mice. Plant Foods Hum Nutr 2008; 63(4): 163-9.
[http://dx.doi.org/10.1007/s11130-008-0098-4] [PMID: 18958624]

[21] Yang HW, Fernando KHN, Oh JY, Li X, Jeon YJ, Ryu B. Anti-obesity and anti-diabetic effects of *Ishige okamurae*. Mar Drugs 2019; 17(4): 202.
[http://dx.doi.org/10.3390/md17040202] [PMID: 30934943]

[22] Choi JS, Haulader S, Karki S, Jung HJ, Kim HR, Jung HA. Acetyl- and butyryl-cholinesterase inhibitory activities of the edible brown alga *Eisenia bicyclis.* Arch Pharm Res 2015; 38(8): 1477-87.
[http://dx.doi.org/10.1007/s12272-014-0515-1] [PMID: 25370610]

[23] Cho CH, Lu YA, Kim MY, Jeon YJ, Lee SH. Therapeutic potential of seaweed-derived bioactive compounds for cardiovascular disease treatment. Appl Sci 2022; 12(3): 1025.
[http://dx.doi.org/10.3390/app12031025]

[24] García Delgado N, Frías Vázquez AI, Cabrera Sánchez H, Soto del Valle RM, Sierra Gómez Y, Suárez Alfonso AM. Anti-inflammatory and antinociceptive activities of methanolic extract from red seaweed *Dichotomaria obtusata.* Braz J Pharm Sci 2013; 49(1): 65-74.
[http://dx.doi.org/10.1590/S1984-82502013000100008]

[25] Hannan MA, Dash R, Haque MN, *et al.* Neuroprotective potentials of marine algae and their bioactive metabolites: pharmacological insights and therapeutic advances. Mar Drugs 2020; 18(7): 347.
[http://dx.doi.org/10.3390/md18070347] [PMID: 32630301]

[26] Senthil KA, Murugan A. Antiulcer, wound healing and hepatoprotective activities of the seaweeds *Gracilaria crassa, Turbinaria ornata* and *Laurencia papillosa* from the southeast coast of India. Braz J Pharm Sci 2013; 49(4): 669-78.
[http://dx.doi.org/10.1590/S1984-82502013000400006]

[27] Apostolova E, Lukova P, Baldzhieva A, *et al.* Immunomodulatory and anti-inflammatory effects of fucoidan: A review. Polymers 2020; 12(10): 2338.
[http://dx.doi.org/10.3390/polym12102338] [PMID: 33066186]

[28] Khongthong S, Theapparat Y, Roekngam N, Tantisuwanno C, Otto M, Piewngam P. Characterization and immunomodulatory activity of sulfated galactan from the red seaweed *Gracilaria fisheri.* Int J Biol Macromol 2021; 189: 705-14.
[http://dx.doi.org/10.1016/j.ijbiomac.2021.08.182] [PMID: 34474051]

[29] Gono CMP, Ahmadi P, Hertiani T, Septiana E, Putra MY, Chianese G. A comprehensive update on the bioactive compounds from seagrasses. Mar Drugs 2022; 20(7): 406.
[http://dx.doi.org/10.3390/md20070406] [PMID: 35877699]

[30] Wang L, Mu M, Li X, Lin P, Wang W. Differentiation between true mangroves and mangrove associates based on leaf traits and salt contents. J Plant Ecol 2011; 4(4): 292-301.
[http://dx.doi.org/10.1093/jpe/rtq008]

[31] Mitra S, Naskar N, Chaudhuri P. A review on potential bioactive phytochemicals for novel therapeutic applications with special emphasis on mangrove species. Phytomedicine Plus 2021; 1(4): 100107.
[http://dx.doi.org/10.1016/j.phyplu.2021.100107]

[32] Dahibhate NL, Saddhe AA, Kumar K. Mangrove plants as a source of bioactive compounds. Nat Prod J 2018; 9(2): 86-97.

[http://dx.doi.org/10.2174/2210315508666180910125328]

[33] Costa CSB, Chaves FC, Rombaldi CV, Souza CR. Bioactive compounds and antioxidant activity of three biotypes of the sea asparagus *Sarcocornia ambigua* (Michx.) M.A.Alonso & M.B.Crespo: a halophytic crop for cultivation with shrimp farm effluent. S Afr J Bot 2018; 117: 95-100. [http://dx.doi.org/10.1016/j.sajb.2018.05.011]

[34] Gouda MS, Elsebaie EM, Alex J. Glasswort (*Salicornia* spp.) As a source of bioactive compounds and its health benefits: A review. J Food Sci Technol 2016; 13(1): 1-7.

[35] Sung JH, Park SH, Seo DH, Lee JH, Hong SW, Hong SS. Antioxidative and skin-whitening effect of an aqueous extract of *Salicornia herbacea*. Biosci Biotechnol Biochem 2009; 73(3): 552-6. [http://dx.doi.org/10.1271/bbb.80601] [PMID: 19270393]

[36] Kim S, Lee EY, Hillman PF, Ko J, Yang I, Nam SJ. Chemical structure and biological activities of secondary metabolites from *Salicornia europaea* L. Molecules 2021; 26(8): 2252. [http://dx.doi.org/10.3390/molecules26082252] [PMID: 33924656]

[37] Karan S, Turan C, Sanguni K, Eliuz EAE. Bioactive compounds and antimicrobial activity of glasswort *Salicornia europaea.* Indian J Pharm Sci 2021; 83: 229-37.

[38] Altay A, Celep GS, Yaprak AE, Baskose I, Bozoglu F. Glassworts as possible anticancer agents against human colorectal adenocarcinoma cells with their nutritive, antioxidant and phytochemical profiles. Chem Biodivers 2017; 14(3): e1600290. [http://dx.doi.org/10.1002/cbdv.201600290] [PMID: 27701810]

[39] Śanchez-Gavilań‌ I, Ramiŕez E, de la Fuente V, Baskose I, Bozoglu F. Bioactive compounds in *Salicornia patula* duval-jouve: A mediterranean edible euhalophyte. Foods 2021; 10(2): 410. [http://dx.doi.org/10.3390/foods10020410] [PMID: 33673201]

[40] Santhanam R, Ramesh S, Sunilson AJ. Biology and Ecology of Pharmaceutical Marine Sponges CRC Press. USA: Taylor & Francis 2018; p. 342.

[41] LaBarbera DV, Modzelewska K, Glazar AI, *et al.* The marine alkaloid naamidine A promotes caspase-dependent apoptosis in tumor cells. Anticancer Drugs 2009; 20(6): 425-36. [http://dx.doi.org/10.1097/CAD.0b013e32832ae55f] [PMID: 19369860]

[42] Anjum K, Abbas SQ, Shah SAA, Akhter N, Batool S, Hassan SS. Marine sponges as a drug treasure. Biomol Ther 2016; 24(4): 347-62. [http://dx.doi.org/10.4062/biomolther.2016.067] [PMID: 27350338]

[43] Karthikeyan A, Joseph A, Nair BG. Promising bioactive compounds from the marine environment and their potential effects on various diseases. J Genet Eng Biotechnol 2022; 20(1): 14. [http://dx.doi.org/10.1186/s43141-021-00290-4] [PMID: 35080679]

[44] Dayanidhi DL, Thomas BC, Osterberg JS. Exploring the diversity of the marine environment for new anti-cancer compounds. Front Mar Sci 2021; 7: 614766. [http://dx.doi.org/10.3389/fmars.2020.614766]

[45] Calcabrini C, Catanzaro E, Bishayee A, Turrini E, Fimognari C. Marine sponge natural products with anticancer potential: An updated review. Mar Drugs 2017; 15(10): 310. [http://dx.doi.org/10.3390/ md15100310] [PMID: 29027954]

[46] Choi K, Lim HK, Oh SR, Chung WH, Jung J. Anticancer effects of the marine sponge *Lipastrotethya* sp. Extract on Wild-Type and p53 Knockout HCT116 Cells. Evid Based Complement Alternat Med 2017; 2017: 1-6. [http://dx.doi.org/10.1155/2017/7174858] [PMID: 28127380]

[47] Morais SR, K C, Jeyabalan S, *et al.* Anticancer potential of *Spirastrella pachyspira* (marine sponge) against SK-BR-3 human breast cancer cell line and *in silico* analysis of its bioactive molecule sphingosine. Front Mar Sci 2022; 9: 950880. [http://dx.doi.org/10.3389/fmars.2022.950880]

[48] Murniasih T, Putra MY, Bayu A, Wibowo JT. A Review on Diversity of Anticancer Compounds Derived from Indonesian Marine Sponges. 6th International Conference on Biotechnology Engineering (ICBioE 2021). IOP Publishing Ltd 2012; 1192. [http://dx.doi.org/10.1088/1757-899X/1192/1/012012]

[49] Elhady SS, El-Halawany AM, Alahdal AM, Hassanean HA, Ahmed SA. A new bioactive metabolite isolated from the red sea marine sponge *Hyrtios erectus*. Molecules 2016; 21(1): 82.

[50] Wilke DV, Jimenez PC, Branco PC, *et al.* Anticancer potential of compounds from the brazilian blue amazon. Planta Med 2021; 87(01/02): 49-70. [http://dx.doi.org/10.1055/a-1257-8402] [PMID: 33142347]

[51] Nguyen TND, Feizbakhsh O, Sfecci E, *et al.* Kinase-based screening of marine natural extracts leads to the identification of a cytotoxic high molecular weight metabolite from the mediterranean sponge *Crambe tailliezi.* Mar Drugs 2019; 17(10): 569. [http://dx.doi.org/10.3390/md17100569] [PMID: 31600933]

[52] Ortega V, Cortés J. Potential clinical applications of halichondrins in breast cancer and other neoplasms. Breast Cancer (Dove Med Press) 2012; 4: 9-19. [PMID: 24367189]

[53] Schwartsmann G, da Rocha AB, Berlinck RGS, Jimeno J. Marine organisms as a source of new anticancer agents. Lancet Oncol 2001; 2(4): 221-5. [http://dx.doi.org/10.1016/S1470-2045(00)00292-8] [PMID: 11905767]

[54] Warabi K, Matsunaga S, van Soest RWM, Fusetani N. Dictyodendrins A-E, the first telomerase-inhibitory marine natural products from the sponge *Dictyodendrilla verongiformis.* J Org Chem 2003; 68(7): 2765-70. [http://dx.doi.org/10.1021/jo0267910] [PMID: 12662050]

[55] del Sol Jiménez M, Garzón SP, Rodríguez AD. Plakortides M and N, bioactive polyketide endoperoxides from the Caribbean marine sponge *Plakortis halichondrioides.* J Nat Prod 2003; 66(5): 655-61. [http://dx.doi.org/10.1021/np030021h] [PMID: 12762801]

[56] Hamoda AM, Fayed B, Ashmawy NS, El-Shorbagi ANA, Hamdy R, Soliman SSM. Marine sponge is a promising natural source of Anti-SARS-CoV-2 scaffold. Front Pharmacol 2021; 12: 666664. [http://dx.doi.org/10.3389/fphar.2021.666664] [PMID: 34079462]

[57] Sagar S, Kaur M, Minneman KP. Antiviral lead compounds from marine sponges. Mar Drugs 2010; 8(10): 2619-38. [http://dx.doi.org/10.3390/md8102619] [PMID: 21116410]

[58] Appenzeller J. + 12. Agelasines J, K, and L from the Solomon Islands Marine Sponge *Agelas* cf. *mauritiana*. J Nat Prod 2008; 71 (8): 1451–54. Arch Toxicol 2017; 91(3): 1485-95. [PMID: 27473261]

[59] Lauritano C, Ianora A. Marine organisms with anti-diabetes properties. Mar Drugs 2016; 14(12): 220. [http://dx.doi.org/10.3390/md14120220] [PMID: 27916864]

[60] Deliorman Orhan D, Orhan N, Konuklugil B. Phenolic content, antioxidant and *in vitro* antidiabetic effects of thirteen marine organisms from mediterranean sea. Farmacia 2021; 69(1): 68-74. [http://dx.doi.org/10.31925/farmacia.2021.1.9]

[61] Kaur KK, Allahbadia G, Singh M. Development of protein tyrosine phosphatase 1B (PTPIB) Inhibitors from marine sources and other natural products-Future of Antidiabetic Therapy: A Systematic Review. Korean J Food Health Conv 2019; 5(3): 21-33.

[62] Barde SR, Sakhare RS, Kanthale SB, Chandak PG, Jamkhande PG. Marine bioactive agents: A short review on new marine antidiabetic compounds. Asian Pac J Trop Dis 2015; 5 (1): S209-13. [http://dx.doi.org/10.1016/S2222-1808(15)60891-X]

[63] Arai M, Han C, Yamano Y, Setiawan A, Kobayashi M. Aaptamines, marine spongean alkaloids, as anti-dormant mycobacterial substances. J Nat Med 2014; 68(2): 372-6.
[http://dx.doi.org/10.1007 / s11418-013-0811-y] [PMID: 24414399]

[64] Abdjul DB, Yamazaki H, Kanno S, *et al.* Haliclonadiamine derivatives and 6- *epi*-monanchorin from the marine sponge *Halichondria panicea* collected at iriomote island. J Nat Prod 2016; 79(4): 1149-54.
[http://dx.doi.org/10.1021/acs.jnatprod.6b00095] [PMID: 27035556]

[65] Acquah KS, Beukes DR, Seldon R, *et al.* Identification of antimycobacterial natural products from a library of marine invertebrate extracts. Medicines 2022; 9(2): 9.
[http://dx.doi.org/10.3390 / medicines9020009] [PMID: 35200753]

[66] Mostafa O, Al-Shehri M, Moustafa M. Promising antiparasitic agents from marine sponges. Saudi J Biol Sci 2022; 29(1): 217-27.
[http://dx.doi.org/10.1016/j.sjbs.2021.08.068] [PMID: 35002412]

[67] Han B, Hong L, Gu B, *et al.* Natural Products from sponges In: Li Z (Eds) Symbiotic Microbiomes of Coral Reefs Sponges and Corals Springer, Dordrecht 2019; 329-463.

[68] Rocha J, Peixe L, Gomes NCM, Calado R. Cnidarians as a source of new marine bioactive compounds--an overview of the last decade and future steps for bioprospecting. Mar Drugs 2011; 9(10): 1860-86.
[http://dx.doi.org/10.3390/md9101860] [PMID: 22073000]

[69] Santhanam R, Ramesh S, Shivakumar G. Biology and Ecology of Pharmaceutical Marine Cnidarians (Series: Biology and Ecology of Pharmaceutical Marine Life) CRC Press. USA: Taylor & Francis 2019; p. 598.
[http://dx.doi.org/10.1201/9780429200038]

[70] Hunt ME, Modi CK, Aglyamova GV, Ravikant DVS, Meyer E, Matz MV. Multi-domain GFP-like proteins from two species of marine hydrozoans. Photochem Photobiol Sci 2012; 11(4): 637-44.
[http://dx.doi.org/10.1039/c1pp05238a] [PMID: 22251928]

[71] Kawabata T, Lindsay DJ, Kitamura M, *et al.* Evaluation of the bioactivities of water-soluble extracts from twelve deep-sea jellyfish species. Fish Sci 2013; 79(3): 487-94.
[http://dx.doi.org/10.1007/s12562-013-0612-y]

[72] Rastogi A, Biswas S, Sarkar A, Chakrabarty D. Anticoagulant activity of Moon jellyfish *(Aurelia aurita)* tentacle extract. Toxicon 2012; 60(5): 719-23.
[http://dx.doi.org/10.1016/j.toxicon.2012.05.008] [PMID: 22652129]

[73] Stabili L, Rizzo L, Caprioli R, Leone A, Piraino S. Jellyfish bioprospecting in the mediterranean sea: antioxidant and lysozyme-like activities from *Aurelia coerulea* (cnidaria, scyphozoa) extracts. Mar Drugs 2021; 19(11): 619.
[http://dx.doi.org/10.3390/md19110619] [PMID: 34822490]

[74] Kim E, Lee S, Kim JS, *et al.* Cardiovascular effects of *Nemopilema nomurai* (Scyphozoa: Rhizostomeae) jellyfish venom in rats. Toxicol Lett 2006; 167(3): 205-11.
[http://dx.doi.org/10.1016/j.toxlet.2006.09.009] [PMID: 17069996]

[75] Kang C, Munawir A, Cha M, *et al.* Cytotoxicity and hemolytic activity of jellyfish *Nemopilema nomurai* (Scyphozoa: Rhizostomeae) venom. Comp Biochem Physiol C Toxicol Pharmacol 2009; 150(1): 85-90.
[http://dx.doi.org/10.1016/j.cbpc.2009.03.003] [PMID: 19303056]

[76] Avila C, Angulo-Preckler C. A minireview on biodiscovery in antarctic marine benthic invertebrates. Front Mar Sci 2021; 8.
[http://dx.doi.org/10.3389/fmars.2021.686477]

[77] Singh H, Parida A, Debbarma K, Ray DP, Banerjee P. Common marine organisms: A novel source of medicinal compounds. Inter J Bio Sci 2020; 7(2): 39-49.
[http://dx.doi.org/10.30954/2347-9655.02.2020.1]

[78] Fattorusso E, Romano A, Taglialatela-Scafati O, Achmad MJ, Bavestrello G, Cerrano C. Xenimanadins A–D, a family of xenicane diterpenoids from the Indonesian soft coral *Xenia* sp. Tetrahedron 2008; 64(14): 3141-6.
[http://dx.doi.org/10.1016/j.tet.2008.01.120]

[79] Figuerola B, Avila C. The phylum bryozoa as a promising source of anticancer drugs. Mar Drugs 2019; 17(8): 477.
[http://dx.doi.org/10.3390/md17080477] [PMID: 31426556]

[80] Ciavatta ML, Lefranc F, Vieira LM, *et al.* The phylum bryozoa: From biology to biomedical potential. Mar Drugs 2020; 18(4): 200.
[http://dx.doi.org/10.3390/md18040200] [PMID: 32283669]

[81] Tian XR, Tang HF, Tian XL, Hu JJ, Huang LL, Gustafson KR. Review of bioactive secondary metabolites from marine bryozoans in the progress of new drugs discovery. Future Med Chem 2018; 10(12): 1497-514.
[http://dx.doi.org/10.4155/fmc-2018-0012] [PMID: 29788787]

[82] Kim S, Ravichandran YD, Kim M, Kung W. Bioactive marine natural products in drug development. J Mar Biosci Biotech 2007; 2(4): 209-23.

[83] Göransson U, Jacobsson E, Strand M, Andersson H. The toxins of nemertean worms. Toxins 2019; 11(2): 120.
[http://dx.doi.org/10.3390/toxins11020120] [PMID: 30781381]

[84] Qi Y, Zhou J, Shen X, *et al.* Bioactive properties of peptides and polysaccharides derived from peanut worms: A review. Mar Drugs 2021; 20(1): 10.
[http://dx.doi.org/10.3390/md20010010] [PMID: 35049866]

[85] Righi S, Forti L, Simonini R, Ferrari V, Prevedelli D, Mucci A. Novel natural compounds and their anatomical distribution in the stinging fireworm *Hermodice carunculata* (Annelida). Mar Drugs 2022; 20(9): 585.
[http://dx.doi.org/10.3390/md20090585] [PMID: 36135774]

[86] Harnedy PA, FitzGerald RJ. Bioactive peptides from marine processing waste and shellfish: A review. J Funct Foods 2012; 4(1): 6-24.
[http://dx.doi.org/10.1016/j.jff.2011.09.001]

[87] Šimat V, Rathod NB, Čagalj M, Hamed I, Generalić Mekinić I. Astaxanthin from crustaceans and their byproducts: A bioactive metabolite candidate for therapeutic application. Mar Drugs 2022; 20(3): 206.
[http://dx.doi.org/10.3390/md20030206] [PMID: 35323505]

[88] Available From: https://www.apollopharmacy.in/salt/ASTAXANTHIN

[89] Derby C. Cephalopod ink: Production, chemistry, functions and applications. Mar Drugs 2014; 12(5): 2700-30.
[http://dx.doi.org/10.3390/md12052700] [PMID: 24824020]

[90] Santhanam R, Gobinath M, Ramesh S. Biology and Ecology of Pharmaceutical Marine Molluscs (Series: Biology and Ecology of Pharmaceutical Marine Life) CRC Press. USA: Taylor & Francis 2019; p. 218.

[91] Pati P, Sahu BK, Panigrahy RC. Marine molluscs as a potential drug cabinet: An overview. Indian J Geo-Mar Sci 2015; 44(7): 961-70.

[92] Tortorella E, Giugliano R, De Troch M, Vlaeminck B, de Viçose GC, de Pascale D. The ethyl acetate extract of the marine edible gastropod *Haliotis tuberculata coccinea*: A potential source of bioactive compounds. Mar Biotechnol 2021; 23(6): 892-903.
[http://dx.doi.org/10.1007/s10126-021-10073-0] [PMID: 34714443]

[93] Esparza-Espinoza DM, Santacruz-Ortega HC, Chan-Higuera JE, *et al.* Chemical structure and antioxidant activity of cephalopod skin ommochrome pigment extracts. Food Sci Technol 2022; 42:

e56520.
[http://dx.doi.org/10.1590/fst.56520]

[94] Chakraborty K, Krishnan S, Joy M. Antioxidative oxygenated terpenoids with bioactivities against pro-inflammatory inducible enzymes from Indian squid, *Uroteuthis (Photololigo) duvaucelii*. Nat Prod Res 2021; 35(6): 909-20.
[http://dx.doi.org/10.1080/14786419.2019.1610957] [PMID: 31135235]

[95] Jeyasanta I, Patterson J. Bioactive properties of ink gland extract from squid *Loligo duvauceli.* Ecología 2019; 10(1): 9-19.
[http://dx.doi.org/10.3923/ecologia.2020.9.19]

[96] Nadarajah S, Vijayaraj R, Mani J. Therapeutic significance of *Loligo vulgaris* (Lamarck, 1798) ink extract: A biomedical approach. Pharmacognosy Res 2017; 9(5) (1): 105.
[http://dx.doi.org/10.4103/pr.pr_81_17] [PMID: 29333051]

[97] Hernández-Zazueta MS, Luzardo-Ocampo I, García-Romo JS, *et al.* Bioactive compounds from *Octopus vulgaris* ink extracts exerted anti-proliferative and anti-inflammatory effects *in vitro*. Food Chem Toxicol 2021; 151: 112119.
[http://dx.doi.org/10.1016/j.fct.2021.112119] [PMID: 33722603]

[98] Santhanam R, Ramesh S, David SR. Biology and Ecology of Pharmaceutical Marine Life: Echinoderms (Series: Biology and Ecology of Pharmaceutical Marine Life) CRC Press. USA: Taylor & Francis 2019; p. 435.
[http://dx.doi.org/10.1201/9780429060236]

[99] Ghelani H, Khursheed M, Adrian TE, Jan RK. Anti-inflammatory effects of compounds from echinoderms. Mar Drugs 2022; 20(11): 693.
[http://dx.doi.org/10.3390/md20110693] [PMID: 36355016]

[100] Cirino P, Brunet C, Ciaravolo M, *et al.* The sea urchin *Arbacia lixula*: A novel natural source of astaxanthin. Mar Drugs 2017; 15(6): 187.
[http://dx.doi.org/10.3390/md15060187] [PMID: 28635649]

[101] Khalil EA, Swelim H, El-Tantawi H, Bakr AF, Abdellatif A. Characterization, cytotoxicity and antioxidant activity of sea urchins (*Diadema savignyi*) and jellyfish (*Aurelia aurita*) extracts. Egypt J Aquat Res 2022; 48(4): 343-8.
[http://dx.doi.org/10.1016/j.ejar.2022.05.005]

[102] Soleimani S, Pirmoradloo E, Farmani F, Moein S, Yousefzadi M. Antidiabetic and antioxidant properties of sea urchin *Echinometra mathaei* from the persian gulf. J Kerman Univ Med Sci 2021; 28(1): 104-15.

[103] Vasileva EA, Mishchenko NP. Cytotoxicity of quinonoid pigments from sea urchins. Proc 2nd International Conference and Exhibition on Marine Drugs and Natural Products 2017.

[104] Milito A, Cocurullo M, Columbro A, *et al.* Ovothiol ensures the correct developmental programme of the sea urchin *Paracentrotus lividus* embryo. Open Biol 2022; 12(1): 210262.
[http://dx.doi.org/10.1098/rsob.210262] [PMID: 35042403]

[105] Vasconcelos A, Sucupira I, Guedes A, *et al.* Anticoagulant and antithrombotic properties of three structurally correlated sea urchin sulfated glycans and their low-molecular-weight derivatives. Mar Drugs 2018; 16(9): 304.
[http://dx.doi.org/10.3390/md16090304] [PMID: 30200211]

[106] Xie X, Ma L, Zhou Y, *et al.* Polysaccharide enhanced NK cell cytotoxicity against pancreatic cancer *via* TLR4/MAPKs/NF-κB pathway *in vitro/vivo*. Carbohydr Polym 2019; 225: 115223.
[http://dx.doi.org/10.1016/j.carbpol.2019.115223] [PMID: 31521276]

[107] Wu L, Yang X, Duan X, Cui L, Li G. Exogenous expression of marine lectins DlFBL and SpRBL induces cancer cell apoptosis possibly through PRMT5-E2F-1 pathway. Sci Rep 2014; 4(1): 4505.
[http://dx.doi.org/10.1038/srep04505] [PMID: 24675921]

[108] Hou Y, Vasileva EA, Carne A, McConnell M, El-Din A Bekhit A, Mishchenko NP. Naphthoquinones of the spinochrome class: Occurrence, isolation, biosynthesis and biomedical applications. RSC Advances 2018; 8(57): 32637-50.
[http://dx.doi.org/10.1039/C8RA04777D] [PMID: 35547692]

[109] Chen YC, Hwang DF. Evaluation of antioxidant properties and biofunctions of polar, nonpolar, and water-soluble fractions extracted from gonad and body wall of the sea urchin *Tripneustes gratilla*. Fish Sci 2014; 80(6): 1311-21.
[http://dx.doi.org/10.1007/s12562-014-0808-9]

[110] Lum K, Carroll A, Ekins M, *et al.* Capillasterin A, a Novel Pyrano[2,3-f]chromene from the Australian Crinoid *Capillaster multiradiatus*. Mar Drugs 2019; 17(1): 26.
[http://dx.doi.org/10.3390/md17010026] [PMID: 30621172]

[111] Dai J, Liu Y, Jia H, Zhou YD, Nagle DG. Benzochromenones from the marine crinoid *Comantheria rotula* inhibit hypoxia-inducible factor-1 (HIF-1) in cell-based reporter assays and differentially suppress the growth of certain tumor cell lines. J Nat Prod 2007; 70(9): 1462-6.
[http://dx.doi.org/10.1021/np070224w] [PMID: 17844994]

[112] Ke ZY, Chen J-W, Wu B-Y, *et al.* A new angular naphthopyrone from feather star *Comanthus parvicirrus* (Müller, 1841). J Mol Struct 2022; 1253: 132261.
[http://dx.doi.org/10.1016/j.molstruc.2021.132261]

[113] Wätjen W, Ebada SS, Bergermann A, *et al.* Cytotoxic effects of the anthraquinone derivatives 1′-deoxyrhodoptilometrin and (S)-(−)-rhodoptilometrin isolated from the marine echinoderm *Comanthus* sp. Arch Toxicol 2017; 91(3): 1485-95.
[http://dx.doi.org/10.1007/s00204-016-1787-7] [PMID: 27473261]

[114] Lum KY. Chemical and Biological Investigations of Australian Crinoids Thesis: School of Environment and Sc . Griffith University: Lum, PhD Thesis 2020.
[http://dx.doi.org/10.25904/1912/1921]

[115] Liang Q, Ahmed F, Zhang M, *et al. In vivo* and clinical studies of sea cucumber-derived bioactives for human health and nutrition from 2012-2021. Front Mar Sci 2022.
[http://dx.doi.org/10.3389/fmars.2022.917857]

[116] Santhanam R, Ramesh S. Biology and Ecology of Pharmaceutical Marine Tunicates (Series: Biology and Ecology of Pharmaceutical Marine Life) CRC Press. USA: Taylor & Francis 2019; p. 188.
[http://dx.doi.org/10.1201/9780429321788]

[117] Ramesh C, Tulasi BR, Raju M, Thakur N, Dufossé L. Marine natural products from tunicates and their associated microbes. Mar Drugs 2021; 19(6): 308.
[http://dx.doi.org/10.3390/md19060308] [PMID: 34073515]

[118] Vervoort H, Fenical W, Epifanio RA. Tamandarins A and B: New cytotoxic depsipeptides from a Brazilian ascidian of the family Didemnidae. J Org Chem 2000; 65(3): 782-92.
[http://dx.doi.org/10.1021/jo991425a] [PMID: 10814011]

[119] Badre A, Boulanger A, Abou-Mansour E, *et al.* New alkaloids from the carribean ascidian *Lissoclinum fragile*. J Nat Prod 1994; 57(4): 528-33.
[http://dx.doi.org/10.1021/np50106a016] [PMID: 8021654]

[120] Ullah S, Ahmad T. Nutritional and medical importance of fish: A mini review. Reviews Of Progress 2014; 2: 1-5.

[121] Santhanam R, Ramesh S, Nivedhitha S, Balasundari S. Pharmaceuticals and Nutraceuticals from Fish and Fish Wastes Apple Academic Press; New York 2022; 302.
[http://dx.doi.org/10.1201/ 9781003180548]

[122] WHO. Naming the coronavirus disease (COVID-19) and the virus that causes it. Available From: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it

[123] Meštrović T. Marine resources could be promising drug candidates against SARS-CoV-2 Omicron 2022. Available From: https://www.news-medical.net/news/20220424/Marine-resources-coul--be-promising-drug-candidates-against-SARS-CoV-2-Omicron.aspx

[124] Zaporozhets TS, Besednova NN. Biologically active compounds from marine organisms in the strategies for combating coronaviruses. AIMS Microbiol 2020; 6(4): 470-94. [http://dx.doi.org/10.3934/microbiol.2020028] [PMID: 33364539]

[125] Available From: https://www.medchemexpress.com/gallinamide-a.html

[126] Cappello E, Nieri P. From Life in the Sea to the Clinic: The marine drugs approved and under clinical trial. Life 2021; 11(12): 1390. [http://dx.doi.org/10.3390/life11121390] [PMID: 34947921]

[127] Wu AC, Jelielek KK, Le HQ, *et al.* The 2021 marine pharmacology and pharmaceuticals pipeline. FASEB J 2022; 36: S1. [http://dx.doi.org/10.1096/fasebj.2022.36.S1.L7586]

[128] Murugesan S. + 12. screening and druggability analysis of marine active metabolites against SARS-CoV-2: An integrative computational approach. Int J Transl Med 2023; 3(1): 27-41.

[129] Rader RA. (Re)defining biopharmaceutical. Nat Biotechnol 2008; 26(7): 743-51. [http://dx.doi.org/10.1038/nbt0708-743] [PMID: 18612293]

[130] Available from: https: //www. bachelorsportal .com/ studies/313297/ marine-pharmaceutical -science. html

SUBJECT INDEX

A

Santhanam Ramesh, Ramasamy Santhanam & Veintramuthu Sankar

B

C

D

E

F

G

H

I

K

L

M

N

O

P

R

S

T

V

W

Santhanam Ramesh

Santhanam Ramesh, Ph.D. is presently serving as vice-principal, Karuna College of Pharmacy Kerala University of Health Sciences, Palakkad Kerala, India. He has 12 years of teaching and research experience. He was a visiting professor at the Medical Institute of the North-Caucasian State Humanitarian and Technological Academy (The state university), Cherkessk, Karachay-Cherkessia, Russia. He is an associate member of the Academic Pharmacy Group of Royal Pharmaceutical Society, London; member of the International Society for Pharmacoeconomics and Outcome Research (ISPOR), USA; and member of the British Society for Nanomedicine, U.K. Prof. Ramesh has 11 books and 20 research papers to his credit.

Ramasamy Santhanam

Ramasamy Santhanam, Ph.D. is the former dean of the Fisheries College and Research Institute (FC & RI), Tamil Nadu Dr. J. Jayalalithaa Fisheries University, India. He has about 40 years of teaching and research experience in marine/ fisheries sciences. Prof. Santhanam has so far published 40 books on various aspects of marine life, fisheries environment, fisheries biology, and aquaculture. He was a member of the American Fisheries Society, USA; World Aquaculture Society, USA; Global Fisheries Ecosystem Management Network (GFEMN), USA; and the IUCN's Commission on Ecosystem Management, Switzerland

Veintramuthu Sankar

Veintramuthu Sankar, Ph.D. is vice principal & professor and head of the Dept. of Pharmaceutics, P.S.G College of Pharmacy, Coimbatore (Tamil Nadu, India). He is an international expert in biopharmaceutics and pharmacokinetics. He is the recipient of best pharmacy teacher from The Tamil Nadu Dr. MGR Medical University, Chennai; PSG Son's and Charities Coimbatore; and Indian Pharmacy Graduates Association, Chennai. He has participated in 4 international and 12 national conferences and has presented papers. He is the editor for "International Journal of Pharma Research"; and reviewer for the "Informa World Journal (UK)" and "Biosciences Asia (Thailand)". He is an active member of pharmacy bodies viz. IPA, APTI, IPGA and IHPA. Prof. Sankar has one patent and two textbooks entitled: "Novel Drug Delivery Systems" and "Basic Protocols in Regulatory Affairs"; and about 100 research papers in national and internationally reputed journals.