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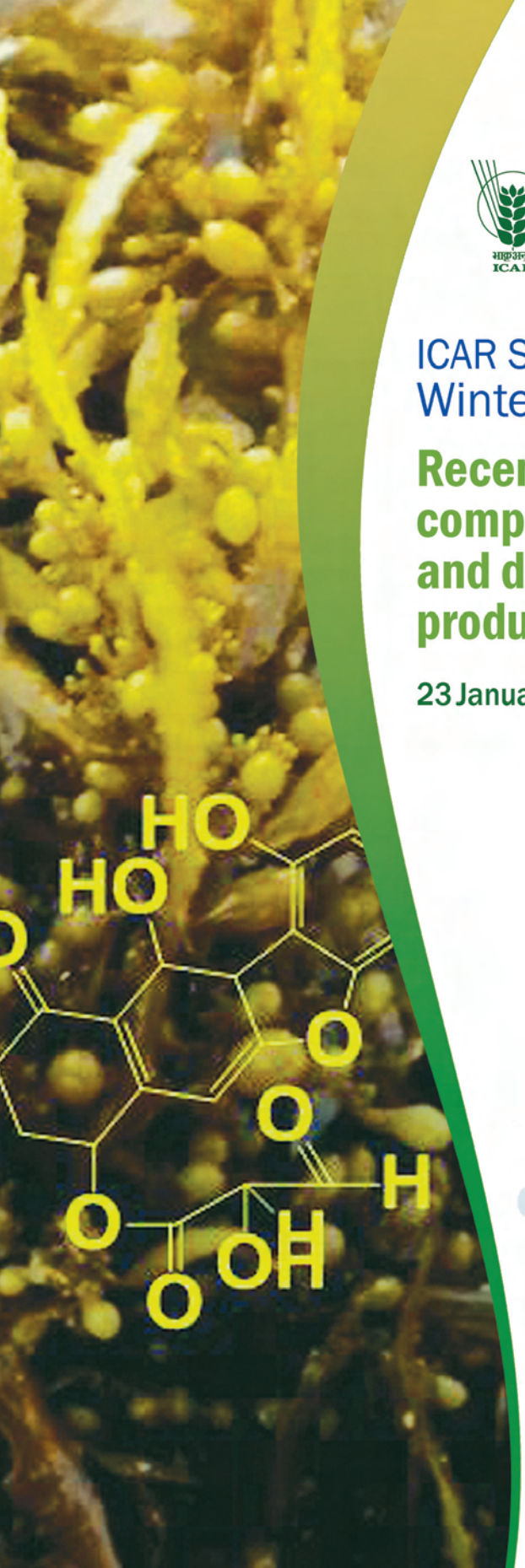
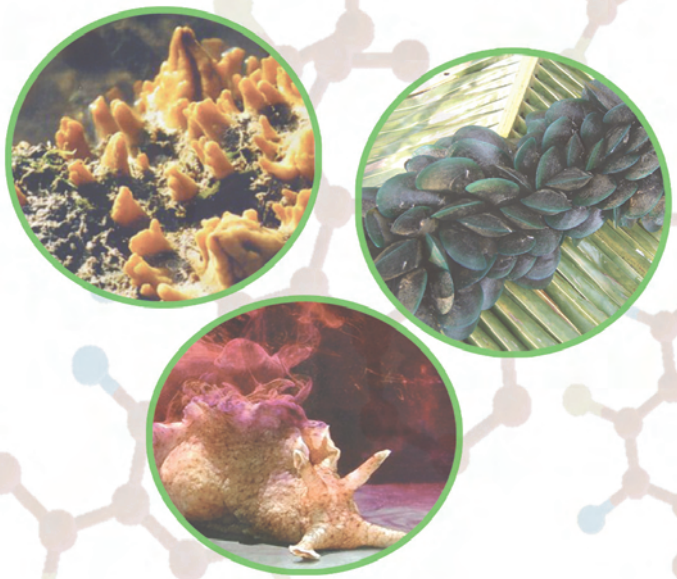


ICAR Sponsored Winter School on

Recent advances in bioactive compounds from marine organisms and development of high value products for health management

23 January to 12 February 2018



Marine Biotechnology Division
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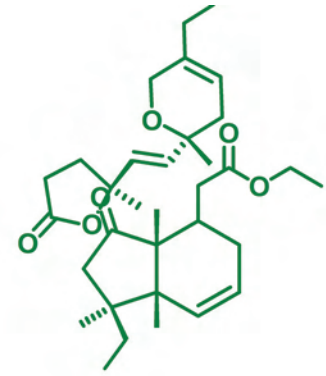

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Course Manual

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ICAR-Central Marine Fisheries Research Institute,
23 January - 12 February, 2018

Publisher :

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ICAR-Central Marine Fisheries Research Institute
Ernakulam North P. O., Kochi - 682 018, Kerala

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This manual has been prepared as a reference material for the ICAR funded Winter School on "Recent advances in bioactive compounds from marine organisms and development of high-value products for health management" held at Central Marine Fisheries Research Institute, Kochi during 23 January - 12 February, 2018

Edited by Foxit Reader

FOREWORD

There has been a growing interest in the marine derived bioactive compounds in the recent years, and the functional foods, enriched with natural ingredients have been proved to provide beneficial action for human health. Marine derived bioactive components and the functional food ingredients demonstrated to possess potential health benefits. High value secondary bioactive metabolites from the marine organisms are attracting attention because of the growing demand for new compounds of 'marine natural' origin, having potential applications in pharmaceutical fields, and concerns about the adverse effects by synthetic drugs and their derivatives. The pioneering R & D works at ICAR-Central Marine Fisheries Research Institute on marine bioprospecting envisaged a systematic approach involving chemical profiling of major species of marine organisms for bioactive pharmacophore leads for activity against various diseases, and a library of molecules with bioactive potential. The research work in this institute developed protocols to prepare various pharmaceutical leads, nutraceuticals/ functional food supplements enriched with lead molecules with different properties against various drug targets for use against various life-threatening diseases.

ICAR-Central Marine Fisheries Research Institute is the pioneering marine research institute in India to work in the frontier area of bioactive molecule discovery from marine organisms as promising therapeutic agents against various diseases, aquatic food product technology, and development of high value products for health management. This prestigious research institute of Indian Council of Agricultural Research is working in the broad national interest of producing high value bioactive leads from the marine organisms, which would provide promising therapeutic agents against various diseases. This institute has developed and commercialized the nutraceutical products Cadalmin™ Green Algal extract (Cadalmin™ GAe) and Antidiabetic extract (Cadalmin™ ADe) as green alternatives to synthetic drugs to combat rheumatic arthritic pains and type-2 diabetes, respectively to a leading biopharmaceutical company in India. The anti-inflammatory nutraceutical Cadalmin™ Green Mussel extract (Cadalmin™ GMe) from Asian green mussel Perna viridis has been commercialized with Amalgam Group of Companies. Cadalmin™ Antihypercholesterolemic extract (Cadalmin™ ACe) has been developed from seaweeds to combat dyslipidemia leading to obesity, and the product was out-licensed to a leading Indian MNC in wellness and obesity management. Antimicrobial therapeutic product from marine bacteria as oral applicant has been developed and the product is in pipeline for commercialization. Seaweed-derived natural template inspired synthetic derivatives as potential pharmacophores were designed and developed. Several nutraceutical and cosmeceutical products from marine organisms are in pipeline, and are being commercialized.

The objective of the National level ICAR Winter School on "Recent advances in bioactive compounds from marine organisms and development of high-value products for health management" is to provide up-to-date information and acquaint the participants with the latest technologies on isolation and characterization of marine natural products of pharmaceutical importance from marine organisms, general and advanced methods of isolation procedures by chromatography, classification of organic compounds and their characterization by advanced spectroscopic experiments. This program further aims to give exposure to the chemical perspectives of marine organisms, primary and secondary bioactive metabolites from fish and marine organisms to develop bioactive compounds and high-value functional food products. Theory and practical classes will be conducted in these areas to provide the participants a hands-on experience.

This ICAR Winter School is organized with the full funding support from ICAR, New Delhi, and the twenty-five participants from various parts of India who are attending this programme were selected after scrutiny of their applications based on their bio-data. They are serving as academicians, such as Professors/Scientists, and in similar posts. The faculties include the knowledgeable scientists and professors from various parts of India and abroad. This training will enable the participants to efficiently carry out their academic programmes, and to plan research on bioactive molecule discovery in their respective laboratories and institutes so that they can formulate the strategies for research.

The Winter School on "Recent advances in bioactive compounds from marine organisms and development of high value products for health management" is very ideal for the current scenario of increasing lifestyle diseases and human health. Understanding the importance of natural products in the health care system of India, ICAR-Central Marine Fisheries Research Institute has reasonably contributed in the various aspects. The Manual released on this occasion covers all aspects of marine natural products prepared by the experts in their respective fields. I congratulate the Course Director of this programme, Dr. Kajal Chakraborty and Head of the Marine Biotechnology Division, Dr. P. Vijayagopal, along with other staff members of Marine Biotechnology Division and Central Marine Fisheries Research Institute for their sincere efforts in bringing out the manual in time, and to arrange the programme in a befitting manner.

A. Gopalakrishnan
Director, ICAR-Central Marine Fisheries Research Institute
Kochi, Kerala

PREFACE

Marine-derived bioactive components and the functional food ingredients with potential health benefits are an emerging area of research. The rich diversity of flora and fauna in the marine and coastal habitats of the Indian subcontinent represent an untapped reservoir of bioactive compounds with valuable pharmaceutical and biomedical use. Considering the underutilization of these groups of marine organisms, exploring bioactive compounds and development of any biologically useful products have benefits as health products. Comprehensive analyses demonstrated that during the last decade the average proportion of bioactive compounds among the new compounds is declining, though there are a large number of marine natural products yet to be explored. This may indicate that the research level of bioactivity is not keeping up with the discovery of new compounds. Thus, the research tools and methods for finding bioactivity need to be improved. The first improvement is about methods of spectral and bioactivity-guided separation and purification of marine-derived secondary metabolites, which combine the discovery of new compounds. These improvements in technology are dependent upon the automation in spectroscopy, which also allows the study of the functions of new compounds extracted from the target marine organisms. Second, for the discovery of new lead compounds and artificial intelligence for drug development evolved to a more mechanistic approach that targets specific molecular lesions. Combined with high-throughput screening through a large number of drug targets, bioactivity research against various life-threatening diseases will be effective in revealing the potentially useful biological properties of marine natural products. Furthermore, the discovery of new bioactive compounds from marine metabolites will form the basis for new drug leads. Thus, the new compounds will absolutely compose an abundant resource for future bioactivity research and drug development. Various medicinal and biomedical products from marine flora and fauna provide a myriad of benefits for human health and multiple life-threatening diseases, and therefore, are the attractive options for the food and pharmaceutical industry. The increasing interest in marine-based functional food ingredients and nutraceutical formulations in the last decade along with increased number of patents filed/granted have appropriately demonstrated the possibilities of bioactive from marine organisms to maintain and improve human health and well-being.

The present ICAR Winter School on "Recent advances in bioactive compounds from marine organisms and development of high-value products for health management" is designed to acquaint the participants with the advances in marine bioactive compounds with emphasis on the latest technologies on isolation and characterization of marine natural products of pharmaceutical importance. The course is planned in such a way that it covers both theoretical and practical aspect of recent advances in bioactive compounds from marine organisms. This programme will strengthen the knowledge of participants with regard to

the general and advanced methods of isolation procedures by chromatography, and their characterization by advanced spectroscopic experiments aspects.

I wish to thank the Education Division of Indian Council of Agricultural Research for giving us an opportunity to organize this ICAR Winter School. We are grateful to Dr. A. Gopalakrishnan, Director, ICAR-Central Marine Fisheries Research Institute, for his guidance, continuous interest in the course and providing all necessary facilities. I am highly obliged to Dr. P. Vijayagopal, Head, Marine Biotechnology Division for his guidance and support for the programme. All the scientists of Marine Biotechnology Division, technical staff, supporting staff and research scholars supported us in organizing the ICAR Winter School. I recall with gratitude the marvellous effort and help in preparing this manual by Minju Joy, Research Scholar of Marine Biotechnology Division. I take this opportunity to thank all the faculty members who have devoted their valuable time and contributed material for the preparation of the manual. I am confident that the Course Manual would aid the participants to enhance their knowledge and competence in the area of marine bioactive compounds and their applications for the development of high-value products for health management.

Kajal Chakraborty
Course Director

January, 2018

CONTENTS

CHAPTER

39

MARINE BIODIVERSITY: AN IMPORTANT RESOURCE BASE TO DEVELOP BIOACTIVE COMPOUNDS FOR HEALTH AND DISEASES

K. K. Joshi, Sethulakshmi M., Sheeba K. B., Thobias P. Antony and Varsha M. S.

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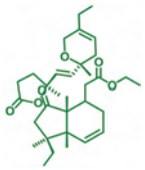
A bioactive compound means a substance which has a biological activity. The definition of bioactive compounds takes different dimensions like deriving from nature or synthetic, compounds usually occur in small quantity, adhere potential effect on human health. It is well known that many organism like sponge, jellyfish, fish, coral, mussels, bivalves, sea hare, seahorse, crustacean, marine plants and turtles yield bioactive compounds of great importance to human welfare.

The long coastline of 8129 Km^2 with an EEZ of 2.02 million Sq. km including the continental shelf of 0.5 million Sq. Km harbors extensively rich multitude of species. Vast regions of mangroves are found along the coast of West Bengal, Orissa, Andhra Pradesh, Tamilnadu, Maharashtra, Gujarat and Andaman Islands which extends up to about 682000 ha area. Coral reefs are found in the Gulf of Kutch, along the Maharashtra coast, Kerala coast, in the Gulf of Mannar, Palk Bay and the Wadge Bank along the Tamilnadu coast and around Andaman and Lakshadweep Islands. The variety of coastal ecosystems include brackish water lakes, lagoons, estuaries, back waters, salt marshes, rocky bottom, sandy bottom and muddy areas provides a home and shelter for the mega biodiversity of India. These regions support very rich fauna and flora and constitute rich biological diversity of marine ecosystems. This great mega diversity of abundant species along the Indian marine ecosystems provided immense opportunity for the exploration and utilization of the bioactive compounds.

FINFISH DIVERSITY

Indian fisheries have a long history, starting with Kautilya's *Arthasastra* describing fish as a source for consumption and provide evidence that fishery was a well-established industry in India and fish was relished as an article of diet as early as 300 B.C. The ancient Hindus possessed a considerable knowledge of the habit of fishes and the epic on the second pillar of Emperor Ashoka describing the prohibition of consumption of fish during a certain lunar period which can be interpreted as a conservation point of view. Modern scientific studies on Indian fishes could be traced to the initial works done by Linnaeus, Bloch and Schneider, Lacepède, Russell and Hamilton. The mid 1800s contributed much in the history of Indian fish taxonomy since the time of the expeditions was going through. Cuvier and Valenciennes (1828-1849) described 70 nominal species off Puducherry, Skyes (1839), Günther (1860, 1872, 1880) and *The Fishes of India* by Francis Day (1865-1877) and another book *Fauna of British India* Series in two volumes (1889) describing 1, 418 species are the two most



indispensable works on Indian fish taxonomy to date. Alcock (1889, 1890) described 162 species new to science from Indian waters.

Of the 33,059 total fish species of the world, India contributes of about 2492 marine fishes owing to 7.4% of the total marine fish resources. Of the total fish diversity known from India, the marine fishes constitute 75.6 percent, comprising of 2492 species belonging to 941 genera, under 240 families of 40 orders. Among the fish diversity-rich areas in the marine waters of India, the Andaman and Nicobar Archipelago, shows the highest number of species, 1431, followed by the east coast of India with 1121 species and the west coast with 1071. As many as 91 species of endemic marine fishes are known to occur in the coastal waters of India. As of today, about 50 marine fishes known from India fall into the Threatened category as per the IUCN Red List, and about 45 species are Near-Threatened and already on the path to vulnerability. However, only some species (10 elasmobranchs, 10 seahorses and one grouper) are listed in Schedule I of the Wildlife (Protection) Act, 1972 of the Government of India. The ecosystem goods and services provided by the fauna and flora and the interrelationship between the biodiversity and ecological processes are the fundamental issues in the sustainability and the equilibrium of the ecosystem.

BIOACTIVE COMPOUNDS AND USES

Bioactive compounds from fish plays an important role in providing immunity to several diseases like heart disease, asthma, mental illness, eye diseases, low birth weight, infertility, arthritis, immune-deficient diseases and nutrient deficiencies. Fish have a lot of noticeable dietary advantages more than the vegetables products, fruits other meat based non-vegetarian diets. Development of nutraceuticals from marine organisms is becoming one of the attractive options in the food manufacturing industry. There are a multitude of useful Nutraceuticals food ingredients available in the marine finfish resources. It is advisable to include fish in the daily menu diet to keep a healthy life (Table 1).

Table 1. Therapeutic use of marine natural products derived from fish

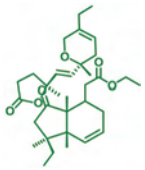
Compound Name (Trademark)	Original NP/ Source Organism	Therapeutic Area
Omega-3-fatty acids/ (Lovaza®)	Fish	Hypertriglyceridemia
Omega-3-fatty acids/ (Lovaza®)	Fish	Hypertriglyceridemia
Chrysophsins	*Chrysophrys (pagrus) major*	Antimicrobial
Parasin I, Pelteobagrin	*Parasilurus asotus, Pelteobagrus fulvidraco*	Antihypertensive Antimicrobial
Peptides	Bonito	ACE inhibitor
FPH	Tuna, Sardine, Salmon	ACE inhibitor, Antioxidant
Omega-3 PUFA (DHA and EPA)	Salmon, Sardines, Tuna, Mackerel, Bonito	Anticardiovascular, Anti-obesity
Omega-3 PUFA (DHA and EPA)	Cod	Anticardiovascular, Anti-inflammatory
Vitamin D	Fish oil	Antiricks, Anti-osteomalacia

FISH USED AS TRADITIONAL MEDICINE

Consumption of fish started from time immemorial as human started hunting of animals and organism. Initially, it was taken as food and later started developing it as food supplement and in traditional medicines. The time tested such treatments are still prevalent in some of the traditional communities around the world. The fishes were used as the traditional medicines for the treatment of Asthma, Antibiotic and used as Pain killer (Table 2).

Table 2. Fish used as Traditional Medicines

Common Name	Species	Uses
Atlantic Tarpon	*Tarpon atlanticus*	Burned scale breathe the smoke to heal headache and asthma. Scale used to make tea to treat asthma
Cascarudo	*Callichthys cf. callichthys*	To treat asthma.
Coco Sea Catfish	*Bagre bagre*	Eye is used for alleviate pain
Cod	*Gadus cf. marhua*	Put the hide (skin) on furuncles.
Croak	*Micropogonias fumieri*	Otolith is used to make a tea
Curimata	*Prochilodus sp.*	The fat and make a plaster to treat boils.
Grunt	*Haemulon sp.*	Rub the fat of the liver over swollen areas.
Long-Snout Seahorse	*Hippocampus reidi*	Sun-dried and toast grinded seahorse is used to treat asthma.
Marine Catfish	*Sciadeichthysluniscutis*	Globe of the eye is used for alleviate pain.
Pufferfish	*Colomesus sp.*	Liver ("fel") in the tooth to alleviate toothache; Get the hide (skin) and cover the wounds with it.
Remora	*Echeneis naucrates*	Sucking disk used to make to treat bronchitis and asthma.
Sheepshead Porgy	*Calamus pena*	Pena (fin) tea used for asthma
Snook	*Centropomus undecimalis*	Fat is used to cure swollen legs.
Swamp eel	*Synbranchus marmoratus*	Rub a live fish over an infant child's legs to make him/her walk sooner.
Toadfish	*Thalassophryne nattereri*	Globe of the eye is used for its own injury.



ELASMOBRANCHS

The elasmobranchs consists of sharks, sawfishes, rays, skates and guitar fishes. They are fished using different types of gears and in recent years have assumed great significance in the export market. They are exploited by a variety of fishing gears like gill nets, long lines and trawls along the Indian coast by both traditional and mechanized sector. Though there is no directed fishing for elasmobranchs in certain places of Tamilnadu, large meshed bottom set gill nets called as 'thirukkuvalai' are operated for fishing the rays. They are all predatory feeding on a wide range of zooplankton to benthic invertebrates, bony fishes, other sharks, turtles, seabirds and marine mammals. Elasmobranchs have been used as traditional medicines from time immemorial for different disease occurring in human beings. Shark derivatives like fins and bones are utilized in the traditional Chinese medicines (Table 3).

Table 3. Elasmobranchs used as Traditional Medicines

Common Name	Species	Uses
Electric ray	*Narcine brasiliensis*	Put the fat on the tooth to treat toothache.
Scalloped Hammerhead	*Sphyrna lewini*	Liver fat used for treat asthma, rhematic parts and wounds.
Sharpnose Shark	*Rhizopriododon sp.*	Liver fat used for treat asthma, rhematic parts and wounds.
Smalltail Shark	*Carcharhinus porosos*	Liver fat used for treat asthma, rhematic parts and wounds.
Stingray	*Myliobates sp.*	Toasted spur tea is used for curing asthma and spur powder used for alleviate pain in tooth. Fat used over wounds.

BIOLOGY AND CONSERVATION

The Whale shark is huge, sluggish, pelagic filter-feeder, often seen swimming on the surface. Viviparous and gravid female have 300 young ones of several stages of development. The protected elasmobranchs as per the Wildlife (Protection) Act, 1972, Schedule I are *Rhincodon typus* (Whale shark), *Anoxyprisits cuspidatus* (Pointed saw fish), *Prisits microdon* (Largetooth sawfish), *Prisitis zijsron* (Longcomb sawfish), *Carcharhinus hemiodon* (Pondicherry shark), *Glyphis gangeticus* (Ganges shark), *Glyphis glyphis* (Speertooth shark), *Himantura fluviatilis* (Gangetic sting ray), *Rhyncobatus djiddensis* (Giant guitarfish) and *Urogymnus asperimus* (Thorny ray).

Among elasmobranchs sharks have an unusual combination of biological characteristics like slow growth, delayed maturation, long reproductive cycles, low fecundity and long life spans. Generally elasmobranchs have been considered slow growing animals, but as in the other fishes, the rate of growth (cm/yr) decreases continually as the individual ages. Amount of growth occurring in a shark population, averaged over the individuals in the population, then the growth may be considered quite slow. Shark produces young that hatch or are

born with a fully developed which are relatively large at birth. The energy needed to produce large, fully developed young results in great energy demands on the females to have long reproductive cycles and gestation periods of one or two years in most species. The number of young or "pups" per brood usually ranges from two to a dozen. Many species of sharks are known to be long-lived. The *Squalus acanthias* have 65-70 years, and *Carcharhinus leucas* 27 years. Majority of the large sharks is slow to mature. The shallow coastal waters are known as 'nurseries' to give birth to their young and young spend their first months or years. Most of the commercially important species that are *Carcharhinus, Sphyrna, Rhizoprionodon and Negaprion* have shallow water nurseries. These sharks are very vulnerable to modern fishing operations and are easily overfished.

BIOACTIVE COMPOUNDS AND USES

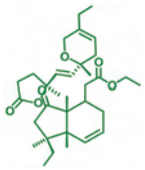
Shark-fins are one of the most luxurious fish products in the world that get higher prices in the export market. The white fins gave a superior yield than the black fins. The lower lobe of tail from *Carcharhinus falciformis* gave the superior quality fin needles. Fin needles have very high nitrogen content, very low ash and no oil content and no non-protein nitrogen as compared to flesh. The pigeye (*Carcharhinus amboinensis*), the black-tip (*Carcharhinus limbatus*), the sandbar (*Carcharhinus plumbeus*), and the hammerhead sharks are providing best quality and big fin. All the internal organs like heart, liver, kidney, pancreas, spleen, intestine, stomach and cartilage of the shark species: Portuguese dogfish, black dogfish, and leaf scale gulper shark showed antimicrobial activity against the bacteria and yeast. Cartilage of shark (*Prionace glauca*) contains glucosamine and chondroitin sulphate which can be utilized as anti-aging supplement (Table 4).

Table 4. Therapeutic use of marine natural products derived from Sharks

Compound Name (Trademark)	Original NP/ Source Organism	Therapeutic Area
Squalamine	*Squalus acanthias*	Cancer
Shark cartilage/ (Neovastat®)	Shark	Cancer
Calcium-binding protein	Shark	Cancer
FPH	Shark meat, Loach, Pacific hake	ACE inhibitor, Antimicrobial

MARINE MOLLUSCS

A total of 3271 species of molluscs distributed among 220 families and 591 genera, of which 1900 are gastropods, 1100 bivalves, 210 cephalopods, 41 polyplacophores and 20 scaphopods. Among these 8 species of oysters, 2 species of mussels, 17 species of clams, 3 species of pearl oysters, 3 species of giant clams, 1 species of windo-pane oyster and gastropods such as Sacred Chank, Trochus, Turbo and 15 species of Cephalopods are exploited from the Marine sector of India. Scaphopoda are commonly known as the tusk shells and diversity includes about 10 species. Polyplacophora include about extant species



are entirely marine, and inhabit hard bottoms and rocky coasts. A total of 40 species of polyplacophora have been reported from India.

Gastropoda includes Prosobranchia (Sea snails), Opisthobranchia (Gastropods) and Pulmonata (Snails, slugs). The diversity of prosobranchian species was 2550 species, 400 species of gastropods. *Prosobranchia* (Sea snails). *Prosobranchia* includes sea snails, land snails and freshwater snails. Prosobranch means *gills in front* (of the heart). In contrast *Opisthobranch* means *gills behind* (and to the right of the heart). Prosobranchs have their gills, mantle cavity and anus situated in front of their heart. Most prosobranchs have separate sexes. The diversity of prosobranchian species was at the tune of 2550 species and 20 species of pulmonates was recorded from India. Bivalvia (Clams, oysters) are mollusks with laterally compressed body in a shell in two hinged parts with diversity include about 667 species in India. List of protected marine molluscs as per the Wildlife (Protection) Act, 1972 Schedule-I are *Cassis cornuta*, *Charonia tritonis, Conusmalne edwardsi, Cypreacasis rufa, Nautilus pompilus, Hippopus hippopus, Tridacna maxima, Tridacna squamosal* and *Tudicla spiralis*.

BIOACTIVE COMPOUNDS FROM MUSSELS

Mollusc species incorporated into a broad range of traditional natural medicines, as the active ingredients. Defence systems in molluscan species against viruses, including many that are human pathogens were extracted from abalone, oyster, mussels and other molluscs. Mussels forms as an important source for the development of useful foods, food ingredients and pharmaceuticals (Table 5).

Table 5. Biological activity of Biomaterials derived from Mussels

Origin/ product	Mussel species	Biological activity - name of bioactive protein/ peptide
Fermented sauce	*Mytilus edulis*	Antioxidant
Blood	*Mytilus edulis*	Antimicrobial, Mytilusdefensin A, Mytilusdefensin B
Hemocytes	*Mytilus galloprovincialis*	MGD-1, MGD-2
Hemocytes	*Mytilus edulis, Mytilus galloprovincialis*	Mytilin A, Mytilin B
Hemocytes	*Mytilus galloprovincialis*	Mytilin C, Mytilin D, Mytilin G1,
Hemocytes	*Mytilus galloprovincialis*	Myticin A , Myticin B, Myticin C
Proteic extract	*Mytilus galloprovincialis*	Anti-inflammatory
Fermented sauce	*Mytilus edulis*	Antihypertensive
Blood	*Mytilus edulis*	Antifungal, Mytimycin
Edible part	*Mytilus edulis*	Anticoagulant
Cell-free haemolymph	*Perna canaliculus*	Anti-thrombin
Byssus	*Mytilus edulis*	Adhesive for surgical applications

BIOACTIVE COMPOUNDS FROM GASTROPODS

Gastropods are asymmetrical mollusc with a coiled shell. Body of gastropods was divided into 4 regions: head, foot, visceral mass and mantle. The asymmetry of the internal anatomy of gastropods results from a twist of 180^{o} called torsion during larval development. Gastropods are divided into four subclasses namely Prosobranchai, Opisthobranchia, Pulmonata, and Gymnomorpha. Although there are about 1900 species of gastropods available along the Indian coast 15 species are edible. The shells of these gastropods are used as raw material for many calcium carbonate industries (Table 6).

Table 6. Biological activity of Biomaterials derived from Gastropods

Origin/ product	Species	Biological activity - name of bioactive protein/ peptide
Lipophilic extract from the digestive gland	Abalone *Haliotis laevigata* and *H. rubra*	Antiviral activity occurs postentry
Hemolymph plasma		Prevent viral attachment and entry into cells
Aqueous extract from canned abalone	Abalone *H. rufescens*	Unknown
Peptide extract from whole organism	Periwinkle *Littorina littorea*	Unknown
Kelletinin A	Snail *Buccinulum corneum*	Inhibit viral transcription and DNA RNA synthesis
Glycosylated functional unit of hemocyanin/RtH2	Veined rapa whelk *Rapana venosa*	Prevent viral attachment to cells by interacting
Hemocyanin extract	Snail *Helix lucorum*	Inhibition of viral DNA replication
Solid phase extraction (SPE)	Whelk *Buccinumun datum*	Unknown

BIOACTIVE COMPOUNDS FROM BIVALVES

Bivalves are aquatic molluscs showing bilateral symmetry. Their shell composed of two calcareous valves. Both valves are convex and show an alteration of bilateral symmetry. They got two adductor muscles. Bivalves along the Indian coastline form an important source of food, raw material for industries, indigenous medicine and it is widely used as cheap source of food. Bivalves contain about 28% calories of fat, protein with essential amino acids for the human nutrition. The polyunsaturated fatty acids have been extracted from bivalve flesh (Table 7).

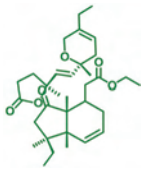


Table 7. Biological activity of Biomaterials derived from Bivalves

Origin/ product	Species	Biological activity - name of bioactive protein/ peptide
Water and ammonium sulfate	Clam *Mya arenaria*	Inhibit viral infection (LT-1
Partially purified ammonium sulphate	Clam *Mercenaria mercenaria*	Unknown
80% SPE-fraction	Clam *Ruditapes philippinarum*	Unknown
80% SPE-fraction	Cockle *Cerastoderma edule*	Unknown
Mytilin	*Mytilus galloprovincialis*	Inhibit viral transcription
Defensin		Unknown
Lectin	*Crenomytilus grayanus*	block viral entry
Acetic acid extract/paolin 2	Oyster *Crassostrea virginica*	Unknown
Hemolymph plasma	Oyster *C. gigas*	Inhibit viral attachment
Hemolymph plasma	Oyster *C.rhizophorae*	Inhibit viral attachment
80% SPE-fraction	Oyster *Ostrea edulis*	Unknown
Spisulosine (ES-285)	*Spisula polynyma*	Cancer

SEA HARE

Sea hare belongs to the Phylum Mollusca. It is a Sea Hare, which is a special group of sea slugs belonging to the Order Anaspidea, and it is in the Family Aplysiidae. They are herbivorous and found in seagrass beds in shallow areas. Sea hares are shell less mollusks and the exposed soft body triggers to produce effective chemical defence system. The genus *Aplysia* was the most studied for the bioactive compounds and around 58 new natural products being produced so far. *Aplysia* sea hares are herbivorous mollusks, which have been confirmed to be a rich source of secondary metabolites, generally of dietary source. Bioactive compound dolastatin 10 was first obtained from the Sea hare *Dolabella auricularia* and antibody-dolastatin 10 conjugate, was approved by the FDA for the treatment of Hodgkin's lymphoma (Table 8).

Table 8. Marine natural products derived from Sea hare

Original NP/Compound Name (Trademark)	Source Organism	Therapeutic Area
Dolastatin/ (Adcetris®)	Sea hare *Dolabella auricularia*	Cancer
Dolastatin 10/CDX-011 Dolastatin 10/SGN-75	*Dolabella auricularia*	Cancer
Dolastatin 10/ASG-5ME	*Dolabella auricularia*	Cancer
Dolastatin 10/Soblidotin	*Dolabella auricularia*	Cancer
Dolastatin 15/Synthadotin	*Dolabella auricularia*	Cancer
Dolastatin 15/Tasidotin (ILX-651)	*Dolabella auricularia*	Cancer

MARINE INVERTEBRATES

Marine invertebrates have been a rich source of potent bioactive compounds, chemical compounds which leads to the production of antiviral, antifungal and anticancer drugs. Venomous organisms like corals, cone shells, octopuses, sea urchins are rich source of toxins which can be utilized for treatment of cancer and cardiovascular disorders Marine sponges, Ascidians, bryozoans, are the major source of bioactive compounds (Table 9).

Table 9 .Marine natural products and their use in health benefits

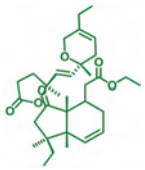
Compound name	Source	Disease area
Protein kinase inhibitors/ Bryostatin-1	Bryozoan	Cancer
Bryostatin I	Bryozoan *Bugula neritina*	Cancer, Alzheimer's
GTS21	Nemertine worm	Alzheimer's disease, Schizophrenia
OAS1000	Soft coral	Wound healing, inflammation
Trabectedin (Yondelis®)	*Ecteinascidia turbinata*	Cancer
DMXBA (GTS-21)	Anabeseine/ worm *Paranemertes peregrina*	Alzhemier's
Lurbinectedin (PM01183)	Ecteinascidins/ tunicate *Ecteinascidia turbinata*	Cancer
Marizomib	Salinosporamide A/ Marine actinomycete *Salinispora tropica*	Cancer
Plinabulin (NPI-2358)	Halimide (NPI-2350)/marine fungus *Aspergillus sp.*	Cancer
Chitin and chitosan	Crustaceans (shrimp, crab, crayfish)	Antimicrobial, Anticancer, Anti-inflammatory, Hypocholesterolemic
Plidítepsin (Aplidin®)	Ascidian *Aplidium albicans*	Cancer
Omega-3 PUFA (DHA and EPA)	Ascidian	Anticancer

BRYOZOA (MOSS ANIMALS)

They are known as Polyzoa, Ectoprocta or moss animals are aquatic invertebrate animals. Size range from 0.5 millimeters long, and are filter feeders. Most marine species live in tropical waters, but a few occur in oceanic trenches, and others are found in polar waters and few prefer brackish water. Over 4,000 living species are known. One genus is solitary and the rest colonial.

PELAGIC TUNICATES

Thaliaceans are free-floating for their entire lifespan. They include both solitary and colonial species. Thaliaceans have 30% carbon by mass. Therefore, their dense bodies sink to the bottom of the oceans when they die and this may be a major part of the worldwide carbon cycle. A total of 40 species was reported from India.



SEA SQUIRTS

Ascidians are found all over the world, usually in shallow water with salinities over 2.5% the members of the Thaliacea and Larvacea swim freely like plankton, sea squirts are sessile animals. A total of 50 species belonging 21 genera have been reported from India against 2000 species of Asidian in the world.

TURTLES

Five species of sea turtles were reported In India, which include, Olive Ridley (*Lepidochelys olivacea*) Green Turtle (*Chelonia mydas*), Leather back (*Dermocheylus olivacea*), Hawksbill (*Eretmocheylus imbricate*) and Logger head (*Caretta caretta*). CMFRI has developed a national research programme and surveyed the nesting grounds along the Indian coast, monitored their incidental catch and strengthened the National Resource Data of turtles. All the five species were included in the list of protected animals as per the Wildlife (Protection) Act, 1972 Schedule I.

MARINE MAMMALS

Marine mammals come under the class Mammalia; globally 130 species were so far recorded. All marine mammals belonging to the whales, dolphins, porpoises and dugong are rare and endangered, and are listed under CITES. They included in three orders, namely Cetacea (whales, dolphins, and porpoises), Sirenia (manatees and dugong), Carnivora (sea otters, polar bears and pinnipeds like seals and walrus). In India, 31 species of marine mammals (30 species of Cetacea and one species of Sirenia) are documented accounting to one fourths of the world's marine mammalian fauna and almost 8% of the total Indian mammalian fauna.

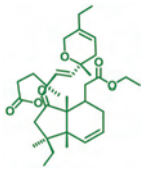
The species diversity of dolphins in India is one among the richest in the world. A total of five species, dolphins was recorded from our seas. They are *Stenella longirostris* (Spinner dolphin), *Sousa chinensis* (Humpback dolphin), *Delphinus delphis* (Common dolphin), *Tursiops truncates* (Bottle nose dolphin) and Rissos dolphin. Whales constitute the most dominant groups of marine mammals. They usually occupy in the temperate and polar oceanic waters, they migrate to tropical waters for breeding and avoid extreme climatic conditions during certain seasons. Body of whale protects them from thermal changes, store of energy for migration and helps in maintaining the buoyancy. Whales are classified into Odontoceti (toothed whales) and mysticeti (baleen whales). All the Cetaceans are included in the list of protected animals. They are *Indopacetus pacificus* (Longmans beaked whale), *Balaenoptera borealis, B. musculus*, *B. acutorostrata*, *Pseudocra crassidens*, *Pysester macrocephalus, P. catodon, Ziphius carvirostris* and *Balaenoptera sp.*

MARINE PLANTS

Mangroves trees up to medium size and shrubs that grow in saline coastal sediment habitats in the tropics and subtropics. Sea grasses are flowering plants from one of four plant families (Posidoniaceae, Zosteraceae, Hydrocharitaceae, Cymodoceaceae), all in the order Alismatales grow in marine, fully saline environments. A total of 14 species of sea grasses in six genera are reported from the Indian seas. Macro algae (Sea weeds): Macro algae are large multicellular plants that resemble vascular plants, but lack the complex array of tissues used for reproduction and water transport. They are found in red (Rhodophyta), green (Chlorophyta) and brown (Phaeophyta) divisions. The colours of macro algae are due to different pigments that the algae use to convert the sunlight into chemical energy via photosynthesis. A total of 1010 species of macro algae has been reported from India. A large number of seaweed species known from the Indian seas are edible and serve various industrial purposes. The edible seaweeds from 70% of the standing stock of 100,000 t, followed by algin (16%), Carrageenan (8%) and agar (6%) yielding seaweeds. The edible seaweeds are known to be rich in protein (20 to 25%) Carbohydrates (16 to 24%), lipids (6 to 11%) vitamins and amino acids (Table 10).

Table 10. Bioactive compounds derived from plants and their application

Compound Name	Source	Disease area
Porphyran	Nori	Antioxidant
Spirulan	*Arthrospira platensis*	Antiviral, Anticoagulant
Fucoidan	*Laminaria japonica*	Anticoagulant, Antioxidant
Galactan	*Codium fragile*	Antiviral, Immunostimulating
Mannans	*Nemalion helminthoides*	Antiviral, Immunostimulating
Ca	*Ulva pertusa, Scytosiphon lomentaria*	Strengthening of teeth and bone, Anti-osteoporosis
I	*Ascophyllum nodosum*	Antigoiter, Reduce risk of abortion, stillbirth
Mg	*Ascophyllum nodosum*	Neuroprotective, Antidepressant, Antiasmatic
Zn	*Eisenia bicyclis, Hizikia fusiforme*	Antidepressant, Reproductive health
Vitamin B $_{12}$	*Porphyra tenera, Sargassum fulvellum*	Anti-aging, Antianemia
Vitamin C	*Gelidiella acerosa, Padina pavonica*	Antioxidant, Strengthening of the immune system
Vitamin E	*Ascophyllum nodosum*	Antioxidant, Prevention of CVD
Carotenoids: â-carotene	*Dunaliella salina, Haematococcus pluvialis*	Skin health benefits, Antioxidant, Anticancer
Chlorophylls	All classes of algae and cyanobacteria	Anticancer
Phycobilins, phycoerythrin	Cyanobacteria, Red Algae	Antioxidant, Anticancer



MARINE MICROBES

Marine microbes include microalgae, Bacteria, protozoa, fungi and viruses. Interestingly microbes forms 98% of the biomass of the world oceans and supply more than half of the oxygen essential for the ecosystem functions. Microbes controls the biogeochemical cycles of important elements like carbon, hydrogen, oxygen, nitrogen, phosphorous, sulfur, sodium, potassium, magnesium and calcium. The marine microbes help in degradation and regeneration of organic matter in the ocean ecosystem for ecosystem balance. In marine environment all primary production is coming from micro algae and cyanobacteria. The microorganisms act on the biowaste and undergo degradation which results in less toxic biological products. This is called bioremediation and it is considered to be the best method for the contaminated areas. Identification of suitable microorganisms for bioremediation process helps in reduction in the contaminated products (Table 11).

Table 11. Biomaterials from Microbes

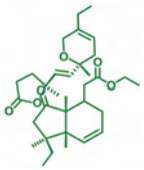
Compound Name	Source	Disease Area
Dolastatin 15	Cyanobacteria	Antimicrotubule, antitumor
Curacin A	Cyanobacteria	Antimicrotubule
Toyocamycin	Cyanobacteria	Antifungal
Resistoflavine	Actinomycetes	Anticancerous, antibacterial
Marinomycin A	Actinomycetes	Antitumor, antibiotic
Daryamide C	Actinomycetes	Antitumor
Violacein	Actinomycetes	Antiprotozoal
Macrolactin S, Pyrone I and II	Bacteria	Antibacterial
MC21-B	Bacteria	Antibacterial
Meleagrin, Oxaline	Fungi	Antitumor
Alternaramide	Fungi	Antibacterial
Norharman	Algae	Enzyme inhibitor
Calothrixin-A	Algae	Antimalarial, anticancerous
Eicosapentanoic acid (EPA)	Algae	Treats heart disease
Macrolactin V	Symbiotic microbes	Antibacterial, antilarval
DAPG	Symbiotic microbes	Antibacterial
BE-43472B	Symbiotic microbes	Antibacterial

ANTIDIABETIC DRUGS

Diabetes causes high morbidity and mortality in human beings due to the complications arising from the disease. In recent years lot of research has been undergone to find a new bioactive compound for the treatment of diabetes. In these perspective aquatic organisms such as bacteria, marine plants, sponges, marine invertebrates and fishes forms highly potential candidates for discovery of novel drugs for diabetes. So far several bioactive compounds have been isolated and screened for developing anti diabetic drugs from marine organisms (Table 12). Hopefully in near future, we will get an antihyper glycemic and antidiabetic natural drug from marine organisms which may reduce the side effects of the present drugs.

Table 12. Antidiabetic drugs and their application

Species	Compounds	Activity
Streptomyces sp.	Pyrostatins A and B	N-acetyl-glucosaminidase inhibition
Fungus *Cosmospora sp*.	Aquastatin A	PTP1B Inhibition
Chlorella zofingiensis	Astaxanthin	AGE formation inhibition
Chlorella protothecoides,	Astaxanthin, lutein and eicosapentaenoic acid	AGE formation inhibition
Isochrysis galbana, Nannochloropsis oculata	Docosahexaenoic and Eicosapentaenoic acids	Clinical values and intestinal inflammation
Grateloupia elliptica	2,4,6-tribromophenol	α-glucosidase
Symphyocladia latiuscula	Bromophenols	Aldose reductase inhibition
Palmaria sp.	Phenolic extracts	α-amylase inhibition
Ecklonia cava	Methanolic extracts	Reduce plasma glucose levels
Pelvetica siliquosa	Raw extracts	Reduce plasma glucose levels increase insulin concentration
Alaria sp.	Phenolic extracts	α-amylase inhibition
Ecklonia stolonifera	Phlorofucofuroeckol-A	AGEs inhibition
Ecklonia stolonifera	Methanolic extracts	Reduce plasma glucose
Ecklonia cava	Polyphenol-rich extracts	Reduce plasma glucose levels
Eisenia bicyclis	Dieckol. Eckol	α-amylase inhibition
Ishigeo kamurae	Diphlorethohydroxycarmalol	α-amylase andá-glucosidase
Ulva rigida	Raw extracts	Reduce plasma glucose levels
Posidonia oceanica	Raw extracts	Reduce plasma glucose levels
Cladophora rupestris	Raw extracts	α-amylase and á-glucosidase
Agelas mauritianus	á-GalCer	Protection beta pancreatic cells
Dysidea villosa	Dysidine	PTP1B inhibition
Sinularia firma	Methanolic extracts	Reduce plasma glucose levels
Fish oil	$_{n-}$3 PUFAs	Restoration insulin receptor and its substrate phosphorylation



CONCLUSION

About 79% of the earth surface is covered with water and which is occupied by high density of aquatic organisms, which are relatively unexplored and represents vast scope for discovery of new bioactive compounds to combat major Life threatening diseases such as Cancer, AIDS and Malaria. Research in these lines focuses on marine organisms like sponges, marine invertebrates, molluscs, fish protein hydrolysate, antimicrobial peptides, cancer inhibiting agents and immunostimulant bioactive compounds. Research development in bioactive compounds from marine organisms will aid in sustainable utilization of biodiversity resources which will eventually pave way to biodiversity conservation.

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Inauguration of winter school 2018 by Padma Bhushan Dr. Manju Sharma

Photo with Dr. K. Gopakumar, Formerly DDG ICAR (Fy)

Field visit to India Sea Foods

Field visit to BOS Naturals

Field visit to Accelerated Freeze Drying Co. Ltd

Photo with Dr. Meledath Govindan

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WELCOME
Sitting (L to R) Minimol K.C., Grace Thomas, Kajal Chakraborty (Course Director), P. Vijayagopal (Head, Marine Biotechnology Division), A. Gopalakrishnan (Director), Paulson Mathew, Sathu T., Radhakrishnan E.K.
Standing (L to R) Aswathy Elizabeth Mani, Sreemol C.K., Prima Francis, Soumya Krishnan, Minju Joy, V. Rani, Seeja Thomachan Panjikkaran, Sheneya Festus, Drishya K., Anie Y., Suja Rani S., Sindhu Issac, Teena P. Varghese, Magna Thomas, Santwana Palai, Norma Xavier Chelat, Naheef K., Satya Narayan Sahoo, Jaimin Hareshbhai Bhatt, Ajoy Saha, Senthil Kuppusamy, Kedar Shashikant Damle, Shubhajit Dhara, Midhun Dominic C.D., Manukuttan K.S., Suji Chandru, Tima Antony, Soumya Salas

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ISBN-978-93-82263-21-0
9 78-93-82263-21-0