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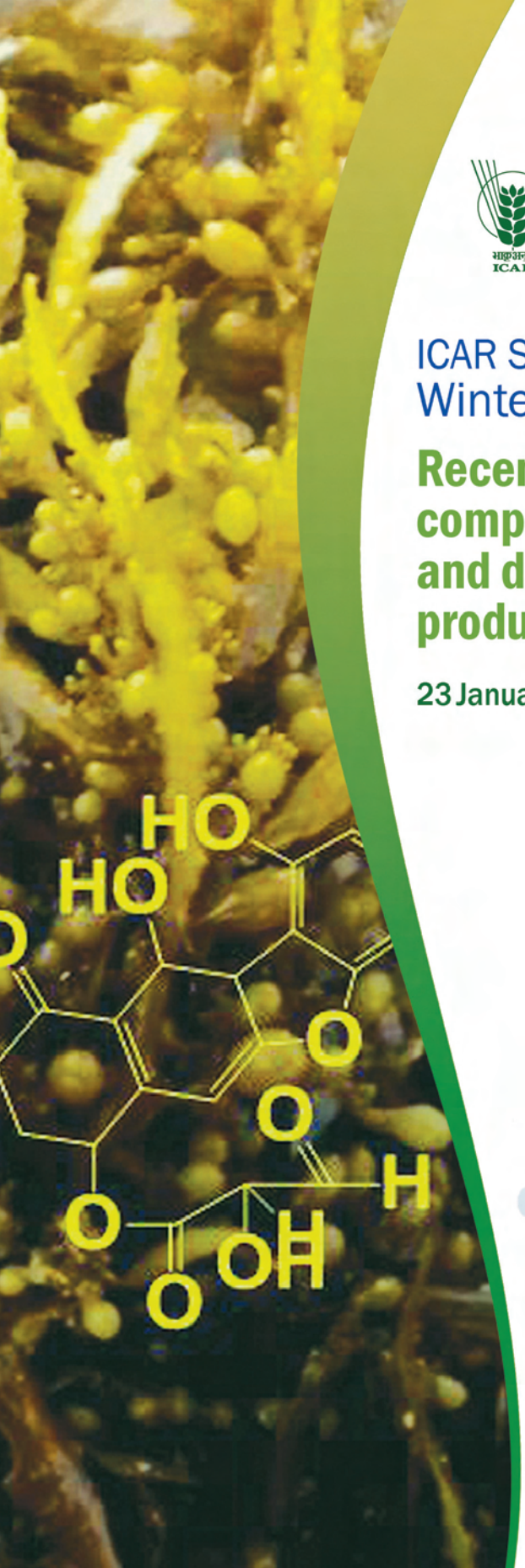
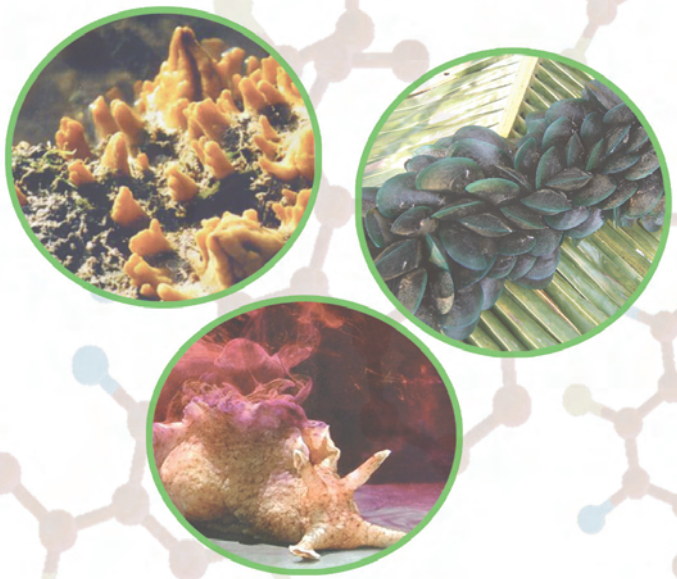


ICAR Sponsored Winter School on

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

23 January to 12 February 2018



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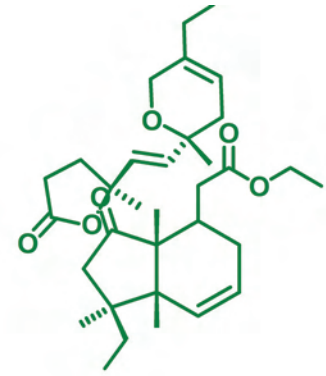

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Course Manual

ICAR-Winter School on

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

CMFRI Training Manual Series No. 13/2018
ICAR-Central Marine Fisheries Research Institute,
23 January - 12 February, 2018

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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	Topic	Page
1	MARINE ORGANISMS: THE UNDEREXPLORED RESOURCES TO DEVELOP HIGH VALUE COMPOUNDS AND THERAPEUTIC PRODUCTS *A. Gopalakrishnan*	**1**
2	MARINE NATURAL PRODUCTS: A FUNCTIONAL FOOD PERSPECTIVE *P. Vijayagopal*	**14**
3	MARINE ORGANISMS-TREASURE HOUSE OF VALUABLE PRODUCTS AND THEIR CHEMICAL PERSPECTIVES *Kajal Chakraborty, Minju Joy, Soumya Salas, Soumya Krishnan*	**30**
4	CLASSIFICATION OF MARINE NATURAL PRODUCTS - CHEMISTRY AND BIOACTIVITY *Kajal Chakraborty, Soumya Salas, Minju Joy, Prima Francis, Subhajit Dhara*	**61**
5	INTRODUCTION TO NATURAL PRODUCTS *Dr. Meledath Govindan*	**82**
6	BIOACTIVE MARINE NATURAL PRODUCTS - A REVIEW *Dr. Meledath Govindan*	**94**
7	NATURAL PRODUCTS: ISOLATION, SEPARATION AND PURIFICATION *Dr. Meledath Govindan*	**108**
8	SPECTROSCOPIC METHODS TO CHARACTERIZE BIOACTIVE COMPOUNDS: NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY *Dr. Meledath Govindan*	**116**
9	INFRARED AND MASS SPECTROSCOPY *Dr. Meledath Govindan*	**128**
10	RECENT TRENDS IN MARINE NATURAL PRODUCTS DISCOVERY PROCESS: CHEMICAL BIOLOGY AND DEREPLICATION *Dr. Meledath Govindan*	**149**

Chapter	Topic	Page
11	SPECTROSCOPIC METHODS TO CHARACTERIZE BIOACTIVE COMPOUNDS: MASS SPECTROSCOPY *Dr. Meledath Govindan*	**160**
12	PHOTOSENSITIZERS AND PHOTODYNAMIC ANTIMICROBIAL CHEMOTHERAPY *Abdulaziz Anas*	**169**
13	NEW WEAPONS TO FIGHT BACTERIAL BIOFILMS IN HEALTH CARE *Rajendran N.*	**178**
14	MARINE MICROBES AS A SOURCE OF ANTIMICROBIAL COMPOUNDS *Kajal Chakraborty, Vinaya K.K., Tima Antony, Minju Joy, Sreemol C.K.*	**189**
15	X-RAY DIFFRACTION: ANALYSIS TECHNIQUES *Shibu M. Eappen*	**199**
16	SAFETY AND HAZARDS IN A CHEMICAL LABORATORY *Kajal Chakraborty, Minju Joy, Soumya Krishnan, Vinaya K. K.*	**204**
17	MARINE NANOPARTICLES AND ITS APPLICATIONS *Anu Gopinath*	**224**
18	RNA TARGETING BY ANTIBIOTIC MIMETICS *Franklin J.*	**230**
19	RECENT ADVANCES OF PREPARATIVE CHROMATOGRAPHY *Dr. Ajit Datar*	**233**
20	HYPHENATED TECHNIQUES: LC-MS *Dr. Ajit Datar*	**240**
21	FUNDAMENTALS OF SPECTROSCOPIC TECHNIQUES WITH REFERENCE TO FTIR *Anu Gopinath*	**259**
22	BIOACTIVE COMPOUNDS FROM MARINE ORGANISMS INCLUDING BACTERIA *Sarita G. Bhat, M. Chandrasekaran*	**268**
23	NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY (PROTON-NMR) *Anu Gopinath*	**274**

Chapter	Topic	Page
24	BIOACTIVE PROTEINS AND PEPTIDES FROM MARINE MICROORGANISMS *Manzur Ali P. P., Sapna K. K., Rakhamol K. R.*	**287**
25	SOLID PHASE SYNTHESIS OF PEPTIDES AS LIGANDS OF NANOPARTICLES FOR BRAIN DRUG DELIVERY *Jaya T. Varkey*	**292**
26	RECENT ADVANCES IN MARINE NATURAL PRODUCTS ISOLATION *T.P. Sajeevan*	**300**
27	CHIRAL MOLECULES FROM RENEWABLE RESOURCES AND THEIR APPLICATION *Grace Thomas*	**307**
28	THEORETICAL BACKGROUND OF COMPUTATIONAL CHEMISTRY *Abi T. G.*	**312**
29	NEW GENERATION ANTI CANCER DRUG UTILIZING MARINE BIOCOMPATIBLE RESOURCES *Jinu George*	**320**
30	CORALS AND SPONGES: IMPORTANT RESOURCE BASE OF BIOACTIVE COMPOUNDS *K. Vinod*	**323**
31	ADVANCES IN ALGAL BIOTECHNOLOGY AND BIOFUEL DEVELOPMENT *Valsamma Joseph*	**328**
32	MINING GENOMES FOR NOVEL BIOACTIVE COMPOUNDS *Toms C. Joseph and K. V. Lalitha*	**343**
33	CLINICAL TRIAL OF BIOACTIVE MOLECULES *K. Gopakumar*	**349**
34	ANIMAL MODELS FOR THE EVALUATION OF BIOACTIVE COMPOUNDS IN CANCER AND PRECEPTFOR THE ETHICAL USE OF ANIMALS IN CANCER RESEARCH *Bibu John Kariyil*	**358**
35	NATURAL PRODUCT INSPIRED SYNTHESIS OF BIOACTIVE COMPOUNDS *Krishnakumar K. S.*	**363**

Chapter	Topic	Page
36	BRYOZOA - TAXONOMY AND DIVERSITY: A POTENTIAL SOURCE OF MARINE BIOACTIVE MOLECULES *Nandini Menon N.*	**373**
37	BIOLOGICAL, TOXICOLOGICAL AND CLINICAL EVALUATION OF BIOACTIVE PHARMACEUTICAL LEADS WITH REFERENCE TO CANCER *Ramadasan Kuttan*	**380**
38	MARINE MICROALGAE: CULTURE AND THEIR INDUSTRIAL APPLICATIONS *K. Madhu, Rema Madhu, Suji Chandru, M. T. Vijayan and M. P. Mohandas*	**384**
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.*	**392**

CHAPTER

02

MARINE NATURAL PRODUCTS: A FUNCTIONAL FOOD PERSPECTIVE

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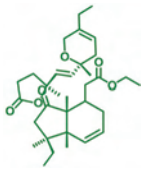
The twentieth century has seen significant changes in life styles of world population, essentially due to rise in purchasing power together with increased leisure and reduced physical activity. The life style changes had specific impact on food consumption pattern of general public. There was shift toward consumption of energy dense foods with high levels of sugar and saturated fats, which during the course of time showed detrimental effects on health, indicated by rapid global rise in chronic diseases such as obesity, coronary heart diseases, diabetes, hypertension and rheumatoid arthritis (WHO, 2004; Clydesdale, 2004). It has been calculated that, in 2001, these diseases contributed approximately 60% of the 56.5million total reported deaths in the world (WHO, 2003). As a consequence, public recognized the importance of both macro and micronutrients in food in maintenance of health, which also made them to return to natural foods and there has also been an increasing demand for functional foods and food supplements, especially from marine products.

MARINE PRODUCTS AS FUNCTIONAL FOODS AND NUTRACEUTICALS

Marine ecosystems have a high diversity of living organisms compared to terrestrial ecosystems providing numerous resources for human nutrition and health (Hill et al., 2010). Marine invertebrates are a diverse group with habitats in all ocean ecosystems, ranging from the intertidal zone to the deep sea environment. Organisms belonging to marine invertebrates are composed of different taxonomic groups, which can be classified into several major phyla, namely, Porifera (sponges), Cnidaria (corals, sea anemones, hydrozoans, jellyfish), Annelida (Polychaetes, marine worms), Bryozoa (moss animals or sea mats), Mollusca (oysters, abalone, clams, mussels, squid, cuttlefish, octopuses), Arthropoda (lobsters, crabs, shrimps, prawns, crayfish), and Echinodermata (sea stars, sea cucumbers, sea urchins) (Thorpe et al., 2000). This diverse group also includes macro algae, microalgae, bacteria, cyanobacteria, certain fish species and crustaceans that produce secondary metabolites as an adaptation to their hostile marine environment. Marine sources have received great attention recently; research on marine-derived molecules has discovered new bioactive compounds with important properties increasing their applicability as nutraceuticals in the food and supplement industries. Numerous molecules with biomedical functions are also supplied by marine ecosystems and are used as pharmaceuticals.

For a marine product to get acceptability, two important criteria need to be satisfied, namely, its sensory and nutritional properties. The functional value of any food, therefore,



should be viewed from the point of view of both nutritional functionality and sensory functionality. The definition of functionality, therefore, differs and from a nutritionist's point of view, the functional property is the presence of certain compounds in natural or processed food that can provide health benefits beyond basic nutrition. However, the food technologist views functional property as any property of food or food ingredient except its nutritional ones, which affects its use (Cherry, 1981)

NUTRACEUTICALS: DEFINITION

Nutraceuticals are health promising compounds or products that have been isolated or purified fromfood sources. The term "nutraceutical"is often used to refer to a food, dietary supplement, or biologically active compound that provides health benefits. A nutraceutical is defined as any substance that may be considered as food or part of food and provides medical or health benefits including the prevention and treatment of diseases. The term was coined in 1989 by the Foundation of Innovation of Medicine, New York. Nutraceutical may range from, isolated nutrients, dietary supplements, and diets to genetically engineered "designer" foods and herbal products.Examples are flavonoids isolated fromSoybean, fish oil capsules, herbal extracts, glucosamine, chondroitin sulfate, lutein- containing multivitamin tablets, and antihypertensive pills that contain fish protein derived peptides. These ingredients are not identified as essential nutrients, but are considered as bioactive substances with health benefit.Nutraceuticals are nonspecific biological therapies used to promote wellness, prevent malignant processes, and control symptoms. Phytochemicals and antioxidants are two specific types of nutraceuticals.There are multiple different types of products that come under nutraceuticals: Dietary supplements, Functional foods, Medical foods.

FUNCTIONAL FOOD: DEFINITION

The term "functional food" was coined in Japan in mid 1980s to describe processed foods that contain ingredients such as, oligosaccharides, minerals, polyunsaturated fatty acids, and fibers that address diseases such as hypertension, in addition to bring nutrition (Arai, 1996). A food can be regarded as functional if it is satisfactorily demonstrated to beneficially affect one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either improved health or well-being and to a reduction in the risk of disease. According to recent data, a functional food must remain food and it must demonstrate its effects in amounts that can normally be expected to be consumed in the diet.It is not a pill or a capsule, but part of the normal food pattern (Tsau, 2005). The U.S. Institute of Food Technologists Expert Panel defines functional food as food and food components that provide health benefit beyond basic nutrition. These foods provide essential nutrients often beyond qualities necessary for normal maintenance, growth, development, and the biologically active compounds that impart health benefit or desirable physiological

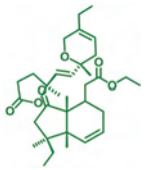
effects (Hasler, 1998.). The Institute of Medicine of U.S. National Academy of Science has defined functional foods as foods to which "one or more ingredients have been manipulated or modified to enhance their contribution to a healthful diet". From a European point of view, a food may be considered as functional if it contains a component with a selective effect of one or various biological functions, whose positive effects justify that it can be regarded as functional (physiological) or even healthy.

WHAT ARE NUTRACEUTICALS AND HOW THEY ARE DIFFERENT FROM DRUGS?

The term "nutraceutical" was coined by Dr. Stephen DeFelice, founder and chairman of the Foundation for Innovation in Medicine. He defined nutraceutical as "...any substance that is a food or a part of a food and provides medical or health benefits, including the prevention and treatment of disease". Nutraceutical has been defined as "concentrated, isolated, or purified" pharmacologically bioactive molecules. Nutraceuticals are clearly not drugs, and unlike synthetic drugs, the potential pharmacologically active substances are derived from natural sources, and are concentrated by using green extraction/purification techniques. The purification process eliminates the unnecessary components in the product, and increases the quantities of the intended pharmacophor(s), which are specifically active against a particular disease. This apparently leads to greater pharmacological activities of the nutraceutical products, while maintaining the mean lethal dose (LD_{50}) greater than the threshold limits that indicate the safety of the products. The LD_{50} of the nutraceutical products developed by ICAR-Central Marine Fisheries Research Institute were found to be greater than 4000 mg/kg body weight of the mammalian subjects that indicate safety of products. Since early 2000s, world has viewed the extensive growth of the billion dollar nutraceutical industry, and nutraceuticals are the preferred product portfolio of the leading pharmaceutical companies in India and abroad. The nutraceuticals portray a distinctive intersection of pharmaceutical and food products, and will continue to have great attraction because they are naturally derived concentrated pharmacologically active compound(s), and therefore are intended to function as "Natural Drug". The greatest challenge remains to formulate regulatory guidelines to enable physicians to prescribe this group of specialized medicines, and will encourage research and development of this group of products.

SOURCES OF MARINE FUNCTIONAL FOOD INGREDIENTS

Marine resources are a source of high value-added compounds with nutraceutical value to be used as functional ingredients: omega-3 oils, chitin, chitosan, ûsh protein hydrolysates, algal constituents, carotenoids, collagen, taurine and other bioactive compounds (Kadam and Prabhasankar, 2010). Chitin and chitosan are polysaccharides, which are gaining much attention. Fish protein hydrolyzates are enzyme hydrolysis products of ûsh proteins. Algae and seaweed have been found to be good source of dietary ûbre and antioxidants and



carotenoids on other hand ûsh bone and shark cartilage are extensively used as source of calcium. As people become increasingly aware of the relation between diet and good health, the consumption of ûshery products will most likely increase. They are perceived as an excellent source of high quality protein, containing lipids with high levels of unsaturated fatty acids, and perhaps contributing to the enhancement of human health by reducing the risk of cardiovascular disease. Likewise, seafood is characteristically tender, easily digested, and a good source of many important minerals. Marine food sources have found enormous compounds, which are good for health and are having neutraceutical value.

ALGAE

Algae, in particular, edible algae sometimes referred as seaweeds, are a very interesting natural source of compounds with biological activity, that may be used as functional ingredients, and considering their great taxonomic diversity, research on identiûcation of biologically active compounds from algae can be seen as an almost unlimited source. Moreover, such extracts are virtually fat and calorie-free, making them increasingly sought for commercial purposes. Macroalgae, i.e. Sargassum species, have been found to be good sources of dietary ûber and carotenoids with antioxidant activity and play important roles in the prevention of neurodegenerative diseases (Chandini et al., 2008; Je et al., 2009; Kadam and Prabhasankar, 2010). Food reserves of brown algae are typically complex polysaccharides and higher alcohols; many bioactive metabolites have been isolated from the sea-algae with different pharmacological activities such as cytotoxic, antitumor, nematocidal, antifungal, anti-inûammatory and antioxidant (Gamal, 2010; Je et al., 2009). Algins, carrageenans and agar are examples of polysaccharides derived from algae that are widely used as thickeners and stabilizers in foods as well as for gels (Rasmussen and Morrissey, 2007). Sulphatedfucans, such as fucoidans from brown algae, carrageenans from red algae and ulvans from green algae, have been known to act as modulators of coagulation as well as reveal antithrombotic, anti-inûammatory, antioxidant, anticancer and antidiabetic activities, among others (Pomin, 2009).

MICROALGAE

Microalgae are considered important producers of some highly bioactive compounds found in marine resources; they can be used to improve food nutritional proûle due to their richness in PUFAs and pigments such as carotenoids and chlorophylls (Gamal, 2010).Microalgae can be used to enhance the nutritional value of food and animal feed, they play a crucial role in aquaculture and they can be incorporated into cosmetics (Spolaore et al., 2006). Microalgae are also rich in pigmentslike chlorophyll (0.5% to 1% of dry weight), carotenoids (0.1% to 0.2% of dryweight on average and up to 14% of dry weight for â-caroteneofDunaliella) and phycobiliproteins.

MARINE FISH

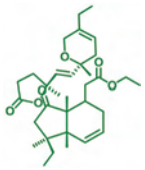
Fish and ûsh wastes are known sources of bioactive ingredients: i) calcium from ûsh bones; ii) ûsh oils rich in PUFAs from ûsh livers; iii) protein hydrolysates of high biological value, peptides with antihypertensive activity and aminoacids, such as taurine, which have antioxidant activity and positive effects on cardiovascular system, from ûsh proteins; iv) vitamins, antioxidants and minerals (Guerard et al., 2010; Kadam and Prabhasankar, 2010). Fish occupy the highest position in marine animal consumption and are important to the world economy. In 2012 fish provided approximately 16% of the world's protein requirements with herring, salmon, cod, flounder, tuna, mullet and anchovy being the most common species of fish used for food (Kim et al., 2012). One of the largest commercially canned fishery products in the world is tuna. According toFAO of United Nations (2010), the total catch of the commercial tuna species increased from 162,980 metric tons in 1950 to more than 4.2 million metric tons in 2007 (Herpandi et al.,2011). The nutritional benefits of fish consumption are due to the presence of proteins, unsaturated essential fatty acids, minerals (for example, calcium, iron, selenium and zinc), and vitamins, namely Vitamin A, B3, B6, B12, E and D. Research has also shown that peptides derived from fermented fish following enzymatic treatment may be useful therapeutics for the treatment of many common acute and chronic diseases such as viral infections, cancer and Alzheimer's disease (Vo et al., 2010 ; Wijesekara et al., 2010).

MARINE INVERTEBRATES

Marine invertebrates, like sponges, molluscs, echinoderms and crustaceans, are sources of bioactive peptides, steroids, terpenoids, strigolactones, alkaloids, ether and phenols (Hu et al., 2011). Extracts or compounds isolated from marine invertebrates are known to include antibacterial, antiviral, anthelmintic, antifungal, antihypertensive, and anticancer and have immune modulatory properties. A great deal of research has been conducted on these molecules particularly for the development of many new therapeutic agents (Mayeret al., 2009).

SPONGES

Sponges are sessile metazoans that consist of a gelatinous material, mesophyl, and are simplest form of multicellular animals. Their hollow pitcher-like body is reinforced by spicules (a needle-like silica/calcium structure) and spongia (collagen fibers) (Uriz et al., 2003). Chemically-diverse compounds like alkaloids, terpenoids, polyketides, macrolides, polyphenolic compounds, peptides and sterols are isolated from sponges with potential to cure various ailments (Thoms et al., 2007).



MOLLUSCS, ECHINODERMS AND CRUSTACEANS

Molluscs, together with echinoderms, have been widely consumed as marine foods and are considered natural functional foods. Extensive research has been performed on bioactive molecules from these sources revealing many significant findings. Bioactive peptides obtained from the fermented blue mussel and oyster sauces significantly decrease hypertension (Wijesekara et al., 2010) whilst ground abalone and its shells are used for treating eye diseases (Kim et al., 2012). Many Asian populations consume cuttlefish, squid, octopus and nautiloids due to their therapeutic effects, for example rickets are cured with the bones of cuttlefish, as well as gastrointestinal disorders and ear inflammation (Kim et al., 2012). Crustaceans are the biggest and most economically important class of marine arthropods in the global fisheries markets; they also have significant roles in nutraceutical industries (Kim et al., 2010). In particular, crabs, prawns and shrimps have gained great attention due to their effective utilization and health benefits (Smith et al., 2010). Nutrient composition of marine crustaceans like shrimp and krill was analyzed and found to decrease the total blood lipids in humans, and improve Vitamin A levels, specific proteins, and eicosapentaenoic acid, omega-3 fatty acids.

MARINE BACTERIA AND FUNGI

Marine bacteria and fungi are being considered as new sources for marine natural products (Duarte et al.,2012;Imhoffet al.,2011).Marine fungi (yeasts) with high concentration of ã-amino-butyric acid (GABA), a promising functional and healthy food ingredient, has been reported by Masuda et al., (2008).Marine extremeophylic bacteria are also of particular interest since they have metabolic pathways adapted to various extreme marine environments; the extremophiles are still a huge source of unknown and uncultivated bacteria; many microbial exopolysaccharides and enzymes from extremophiles have potential and unique properties (Laurienzo, 2010). Diatoms are also particular organisms that besides being photosynthetically robust organisms with a high degree of ûexibility to adapt to different environments (from the Equator to the Ice sea), which is of interest for biotechnological applications, they are able to produce substances for functional foods (Bozarthetal., 2009); the most relevant functional ingredients are PUFAs such as EPA, ARA, DHA and other omega-3 fatty acids.

MARINE FUNCTIONAL FOOD INGREDIENTS

Marine ecosystems provide a diverse range of bioactive molecules with extensive applications as nutraceuticals in the food and supplement industries. These bioactive molecules can be proteins, peptides, polysaccharides, fatty acids, polyphenols, probiotics, enzymes, vitamins and minerals. The remaining sections of this review discuss the physical and chemical properties of these different molecules and how they contribute bioactivity in the context of nutraceutical applications.

PROTEINS

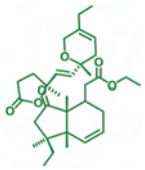
Proteins from marine sources including fish (cod, tuna, herring, rout, hake, and haddock), crustaceans, molluscs, extremophiles like Dunaliella, and seaweeds have unique properties such as gel-formation, film and foaming capacity, antioxidant, anticoagulant and antimicrobial activity. For example, collagen, gelatin and albumin are common marine proteins used in foods and are enzymatically hydrolyzed for the production of bioactive peptides which may have the potential to be used as nutraceuticals. The marine protein protamine is also used as a natural antibacterial preservative in the food industry.

PEPTIDES

Bioactive peptides are protein fragments ranging in size from 2-20 amino acid residues that may be generated from parent proteins during digestion or processing (Di-Bernardini et al., 2011). Two factors can influence the type of bioactive peptides produced: (1) the primary sequence of the protein substrate; and (2) the specificity of the enzyme(s) used to generate such peptides. Furthermore, bioactive peptides can be generated from proteins using hydrolysis (acid or alkaline), cooking or fermentation. These peptides have a range of bioactivities including antimicrobial, immunomodulatory, antithrombotic, and antihypertensive activity (Murrayet al., 2007). They are considered highly significant compounds. Research is being performed to understand peptide structure, composition and sequences. Bioactive peptides have various regulatory functions on specific cellular target formulations (Agyei et al., 2011). Many researchers have focused on the development of pharmaceutical compounds from marine-derived peptides particularly for ACE inhibition and antihypertensive function (Byun, et al., 2001). Marine proteins from fish, molluscs and crustaceans are amongst the richest sources of bioactive molecules (Rajapakse, 2005). Collagen is a valuable part of bovine and porcine meat and is used in different industries like cosmetics, pharmaceutics, food and biomedicine.Meat collagen is an excellent source of bioactive peptides that function as antihypertensives and antithrombotics as well as inhibitors of brush border enzymes like dipeptidyl peptidase-IV (Minkiewicz, et al., 2011).

FATTY ACID

Marine fish species and algae have been identified as sources of polyunsaturated fatty acids which are rich in ù-3 or ù-6 fatty acids. The presence of these unsaturated fatty acids in marine-derived foods increases their applicability as nutraceuticals in the food industry (Harris et al., 2010). Marine-based nutraceuticals have many unique features not found in nutraceuticals obtained from terrestrial resources, and this is one of the reasons why they are gaining more attention. The most common sources of marine oils are fungi (Phycomycetes), fish (salmon, tuna, sardines, and herring), microalgae, extremophiles, macroalgae (Bryophyta, Rhodophyta) and krill. Consumption of marine oils provides



numerous health benefits like visual and neurodevelopment, amelioration of diseases such as hypertension and arthritis and a reduced risk of cardiovascular problems (Sijtsma, 2004).

PHENOLIC COMPOUNDS AND PREBIOTICS

Phenolic compounds found in marine algae are known mainly as a mechanism of adaptation for oxidative stress (Shibata et al., 2008). Usually phlorotannins are the most abundant polyphenols found in the marine brown algae whereas flavonoids contribute most to the total phenolic content in green algae. The brown algal phlorotannin profile mainly consists of phloroglucinol, eckol, and dieckol(Shibata et al., 2008). Antioxidant activity has also been reported from phlorotannins enabling these phenolic compounds to be used as active ingredients in nutraceuticals(Arct et al., 2008). Similar to polyphenols, carotenoids, synthesized in certain marine bacteria and algal species, also have antioxidant properties which increase their applicability as nutraceuticals. Carotenoids are lipid-soluble, natural pigments with 40-carbon structures(Lee et al., 2007). Different carotenoids are synthesized within the marine organisms, for example, â-carotene, astaxanthin and fucoxanthin are known to have a high antioxidant capacity. Antioxidants have protective roles against excess reactive oxygen species, and also act against oxidative rancidity and peroxidation products like superoxide anions, hydroxyl radicals and hydrogen peroxide that cause deterioration of foods. Currently, commercial preparation of â-carotene and astaxanthin is available using Dunaliella species and Haematococcus species, respectively (Vidanarachchi et al., 2011.) Prebiotics are non-digestible, selectively-fermented compounds that stimulate the growth and activity of beneficial gut microbiota which, in turn, confer a health benefit to the host. Usually, prebiotics are oligosaccharides such as chitosan oligosaccharides, while certain other algal polysaccharides have prebiotic activity(Sullivan et al., 2010). Bifidogenic benefits have been reported from exopolysaccharides produced by marine lactic acid bacteria (Honypattarakere, et al., 2012). Further, the cyanobacterial biomass of Spirulinaplatensis is able to stimulate both Lactobacillus and Bifidobacterium, promoting their prebiotic effect. Photosynthetic pigments are obtained from red and blue-green algae, aquatic plants, microalgae and seaweed. These pigments provide nutraceuticals, natural food coloring, anti-inflammatory, anticarcinogenic, antioxidant compounds (Ramirez et al., 2003).

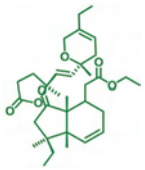
ENZYMES, VITAMINS AND MINERALS

Enzymes have the ability to change other molecules into valuable biotechnological tools that can be used in food and nutraceutical industries. As food ingredients, enzymes can influence factors such as spoilage, storage, processing and safety. Enzymes derived from marine sources are lipase, chitinolytic enzymes, polyphenol oxidase (Catecholase, tyrosinase, cresolase, polyphenolase, catechol oxidase, phendase), and transglutamase, and red algal enzymes involved in a starch degradation pathway (for eg. á-1,4-glucanase). They have excellent chemical, physical and/or catalytic properties compared with their terrestrial

counterparts. They also have the ability to be inactivated at moderate temperatures and show high catalytic activity when the temperature is low (Diaz-Lopez et al., 2000). Additionally these enzymes are used as food ingredients. They are used in food processing due to their salt tolerance, specificity, diverse properties and high activity at mild pH (Okada et al., 2007). Biomolecules such as enzymes isolated from extremophiles can be highly useful in the food industry due to their unique activities under abnormal conditions, and it has been widely accepted that extremophiles have strong potential to be valuable resources for use in biotechnology (Fujiwara et al., 2002). Vitamins and minerals perform many essential functions in the body, for example, they provide transport inside cells and also serve as cofactors during metabolic processes. Seaweeds are rich sources of vitamins and minerals including iron, iodine, manganese and zinc (Parr et al., 2006). Some types of seaweed could be used as natural sources of iodine (Pena-Rodriguez et al., 2011).Marine ûsh oils are rich sources of vitamins A, D, and E. Vitamin A is concentrated mostly in ûsh liver oils. Halibut and cod liver oils are rich sources of vitamins A and D. Sardine ûsh contains up to 4500 IU of vitamin A and up to 500 IU of vitamin D per 100 g of meat, with an average of 125 ìg/g of oil.

OMEGA-3 FATTY ACIDS

Omega-3 oils are incorporated in bakery products, pastas, dairy products such as milk, yogurt and juice as well as nutrition bars. Novel microencapsulated oil prepared by Ocean Nutrition Canada, known as MEG 3 remains protected from environment until it reaches the gastro intestinal tract (Young and Conquer,2008).A study by Conquer and Holub (1998) showed that DHA supplementation in humans increased serum DHA as non-esteriûed fatty acid at levels that were potentially antithrombotic. Liu, Wallin, and Saldeen (2001) found a signiûcant increase in plasma omega-3 fatty acids and in HDL-cholesterol in 36 hyper lipidemic patients fed with bread containing ûsh oil. Park, Choi, and Kim (2000) reported that ûsh oil had a protective effect against cardiovascular disease by inhibiting hepatic HMGCo- A reductase activity and increasing hepatic microsomal ûuidity, leading to a reduction in plasma lipids. The ability of ù-3 polyunsaturated fatty acids to modulate tumor-cell growth was demonstrated for EPA by Chiuand Wan (1999). They showed EPA arrested cell-cycle progression at G0/G1 phase, inducing necrosis in human leukemic HL-60 and K-562 cells in vitro. EPA, however, only induced apoptosis in HL-60 cells by down regulation of Bcl-2. Consequently, PUFAs and their derivatives and analogues are important neutraceutical and pharmaceutical targets (Ward and Singh, 2005). Omega fatty acids have potential application in health promotion; prevention from atherosclerosis, protection against arrhythmias, reduce blood pressure, beneûcial for diabetic patients, ûght against manic-depressive illness, reduce symptoms in asthma patients, protection against chronic obstructive pulmonary diseases, alleviation of symptoms of cystic ûbrosis, prevent various cancers, provide bone health, and improve brain functions in children.



CHITIN

Chitin, second most abundant natural polymer, is extractable from crustaceans (Honorkarand Barikani, 2009). Chitosan, a chitin derivative resulting from processing shells and bones from crab, shrimp, cuttleûsh, etc., is a biodegradable and biocompatible polymer with antibacterial activity which can be used as a food preservative. Biological activities of chitosan and chito-oligosac charides (hypocholesterolemic, antimicrobial, immunity enhancing, antitumor, anticancer, antioxidant, etc.) and the potential application in food, among other applications are reviewed by Xia et al., (2011). Chitin and chitosan polymers have unique structures properties, highly sophisticated functions and wide ranging applications in variety of ûelds such as agricultural, chemistry, medicine, biotechnology, the pulp and paper industry, cosmetics, water treatment and foods (Chandy and Sharma,1990).Chitosan is approved for use as a food additive or dietary supplement in countries such as Japan, England, USA, Italy, Portugal, and Finland. In 1992, chitosan was accepted as a functional food ingredient by Japan's health department. The main producers of chitosan are Japan and the United states with smaller operations in India, Italy and Poland (Chen andSubirade, 2005). Chitin and chitosan have a variety of nutraceutical applications, including immune-enhancement, disease recovery, and use as dietary ûbre. Their ability to be usefulinthesareasislargelydependentonfactors such as molecular weight and degree of N-acetylation, which can greatly inûuence solubility and interactions with other biomolecules.

CHLOROPHYLL

Chlorophyll a, phycocyanins, and phycoerythrin are pigments of interest found in cyanobacteria which are also named as blue-green algae. These microorganisms present a secondary metabolism that produces several compounds: some are problematic for public health since they are strong hepatotoxins or neurotoxins whereas others reveal potential biological activities such as anticancer, antibacterial, antifungal, and immunosuppressive properties; these have all been reviewed by Gamal(2010).Owing to their rich chemical composition, which depends on microalgae species, they can be used as a nutritional supplement or represent a source of food natural colorants as soon as their safety is assured (Mata et al., 2010; Spolaore et al., 2006).

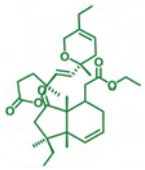
POLYSACCHARIDES

Algae have mainly been used in western countries as raw material to extract alginates (from brown algae) and carragenates (from red algae). Algae also contain multitude of bioactive compounds that might have antioxidant, antibacterial, antiviral and anti-carcinogenic properties. Consumption of dietary ûbre has a positive inûuence on several aspects related to health such as reducing the risk of suffering from colon cancer, constipation, hypercholesterolemia, obesity and diabetes. Besides, many constituents of dietary ûbre

show antioxidant activity as well as immunological activity (Suzuki et al., 2004). In this sense, *U. pinnatiûda* showed some positive effect on cardiovascular diseases (hypertension and hypercholesterolemia) (Ikeda et al., 2003); this alga contains basically dietetic ûbre, being its principal component alginate. This alginic acid has demonstrated to reduce hypertension in hypertensive rates (Ikeda et al., 2003). There are numerous commercial applications of marine polysaccharides in food, beverages and supplements. Marine polysaccharides, extracted from algae, crustaceans and other marine organisms include fucans/fucanoids, carrageenans, hydrocolloids and glycosaminoglycans. These molecules have many biological functions including antiviral, anticoagulant, antiproliferative, antithrombotic and anti-inflammatory activity (Berteau et al., 2003). Carrageenans and alginates are linear biopolymers that have been identified as the most abundant polysaccharides found in red and brown algae, respectively (Kim, et al., 2008). Apart from alginate, brown algae also contain highly complex, sulfated matrix polysaccharides called fucoidans. The complex structure of the fucoidans extracted from different marine species varies in saccharide composition, sulfate content, and positions of sulfate groups, molecular weight, linkage mode, and sequence of saccharide residues (Li et al., 2008). Structural sulfate groups improve the biological properties of fucoidans which enables their application as nutraceuticals in the dairy industry (Vidanarachchi et al., 2011).

CAROTENOIDS

The carotenoids, found in nature, can be classiûed into two: hydrocarbons, such as â-carotene, xanthophylls, and the oxygenated derivatives of carotenes such as astacene, astaxanthin,canthaxanthin, cryptoxanthin, echionine, lutein, neoxanthin, violaxanthin, and zeaxanthin. Originally of interest for their use as a food colouring agent, and still used as such, these compounds give some ûsh and shellûsh their reddish pink colour. The two main carotenoids, astaxanthin and canthaxanthin are extracted from crab and shrimp processing. Newer uses for both these compounds have been identiûed. Their highly antioxidative properties make them candidatesasfunctionalfoodingredients.Astaxanthinmayhaveauseasan anti-aging compound, whilst canthaxanthin could contribute to treatments for Alzheimer's and Parkinson's disease, high cholesterol, strokes and cancer (Miyashita and Hosokawa, 2008). Crabs are important crustaceans, in which carotenoids occur. Astaxanthin and its esters were found to be the major carotenoids in red kelp crab, *Taliepesnuttalli*, snow crab *Chinocetesopilio*, hermit crab, *Paralithodesbrevipes*, and blue crab (Sachindra et al., 2005). Astaxanthin is a very potent antioxidant. Several studies have shown that its activity can be several folds higher than that of other antioxidants, for example B-carotene and Vitamin E. The powerful antioxidant activity also can play a role in astaxanthin'senhancement of immune responses, liver function and eye, joint, prostate, and heart health. It can also be used incardiovascular health, neurodegenerative diseases and anticancer activity (Olaizola, 2008).



Wakame (*Undariapinnatiûda*) is one of the most popular edible seaweed in Japan and has been found to contain 5-10% fucoxanthin apart from containing polar lipids such as glycolipids. Health beneûts of fucoxanthin are anticancer effect - it is evaluated that neoxanthin and fucoxanthin were reported to cause a remarkable reduction in growth of prostate cancer cells, and also demonstrated antiobesity activity and anti-inûammatory activity (Miyashita and Hosokawa, 2008). Fucoxanthin is other major biofunctional pigment of brown seaweeds and the content in various edible seaweeds including *U. pinnatiûda* has been reviewed by Hosakawa et al., (2006).

CALCIUM AND FISH BONE

Fish bone is considered as a potential source of calcium. Fish bone material derived from processing of large ûsh is a useful calcium source. To use ûsh bone as a calcium fortiûcant, the bone should be converted into an edible form by softening its structure. Fish bone powder is a potential value-added by-product of the tuna processing industry.The calcium containing powder from ûsh bone could be used for the fortiûcation of ûsh products such as surimi (Shungan, 1996).

CONCLUSIONS

Marine products, due to its phenomenal biodiversity, are treasure house of many novel healthy food ingredients and biologically active compounds such as ûsh oils, ûsh proteins, and seaweeds. Marine functional ingredients such as ûsh oils, seaweeds and ûsh proteins have found application productindustry. These are added in the form of fortiûcants and nutritional enrichments in food. These products have shown considerable improvement in EPA and DHA contents of breads and other bakery products leading to reduction of cardiovascular diseases which is major health concern of 21st century.Marine nutraceuticals are both a coherent and attractive option for the food industry as there are a multitude of functional food ingredients that can be derived from marine sources. It is also believed that, as people become increasingly aware of the association between diet and good health, the consumption of fishery products will most likely increase. Moreover, in relation to marine algae, their content in proteins, carbohydrates, lipids, fibre, metabolites, etc. can be influenced by their growing parameters (water temperature, salinity, light and nutrients). This means that, from a biotechnological perspective, algae can be considered as natural bioreactors, able to provide different types of compounds at different quantities-an appealing attribute to the functional food industry. Despite the vast possibilities for use of marine bioactives in food, more multidisciplinary research is needed. Consequently, ongoing efforts should be made into the research and development of marine functional foods with prospect that, in the future, their consumption could lead to a reduction in the prevalence and severity of chronic diseases. Thus, constant efforts in research and development in the ûeld of marine

functional food ingredients is needed for the future diet which will help in reducing all health problems of human beings

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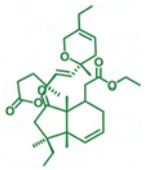

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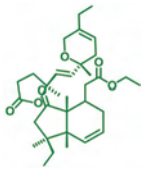

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Inauguration of winter school 2018 by Padma Bhushan Dr. Manju Sharma

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

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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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