animal gelatin capsules in a niche market.

IV. FUTURE PROSPECTS

This work is expected to bring about a change in the scenario of seaweed based industries in India creating renewed employment opportunities in the country's coastal districts for the fisher folk who would participate in the large scale cultivation activities of value added seaweeds. We need to strive for materials security. We ought to look for new materials with new functions to contain the future demands of various dimensions. Seaweeds can play a significant role in this endeavor.

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REFERENCES

[1] D.J. de Vries, and P.M.Beart, "Fishing for drugs from the sea: status and strategies", Trends in Pharm. Sci., vol. 16, pp.275-279. 1995.

[2] www.fao.org.

[3] R.Meena, and A.K. Siddhanta, "Agar and Value Addition of Indian Agarophytes", in: A. Tewari (ed.), *Recent Advances on Applied Aspects of Indian Marine Algae with Reference to Global Scenario*, vol. 2, Bhavnagar, India; CSMCRI, 2006, pp.172-184.

[4] K. Subbaramaiah, "Resources, management and possible cultivation of some economic seaweeds in India", in:V.N. Rajarao (ed.), *Perspectives in Phycology* (Prof. M.O.P. Iyengar Centenary Celebration Volume), pp.337-339, 1990.

[5] A.K.Siddhanta, K.H. Mody, B.K.Ramavat, V.D.Chauhan, H.S.Garg, A.K.Goel, M. Jinandra Doss, M.N.Srivastava, G.K.Patnaik, and V.P.Kamboj, "Bioactivity of marine organisms: Part VIII - Screening of some marine flora of western coast of India", *Indian Journal of Experimental Biology*, vol.35, pp.638-643, 1997.

[6] A.K.Siddhanta, M.Shanmugam, K.H.Mody, A.M.Goswami, and B.K.Ramavat, "Sulphated polysaccharides of Codium dwarkense Boergs. from the west coast of India : Chemical composition and blood anticoagulant activity", *International J. Biological Macromolecules*, vol.26, pp.151-154, 1999.

[7] K. Eswaran, P.K.Ghosh, A.K. Siddhanta, J.S. Patolia, C.Periyasamy, A.S.Mehta, K.H.Mody, B.K.Ramavat, K.Prasad, M.R.Rajyaguru, S.Kulandaivel, C. R.K. Reddy, J.B. Pandya, A. Tewari, "Integrated method for production of carrageenan and liquid fertilizer from fresh seaweeds", *US Patent No.* 6,893,479.

[8] A.K.Siddhanta, R. Meena, K. Prasad, B. K.Ramavat, P. K. Ghosh, K. Eswaran, S.Thiruppathi, V.A.Mantri. "A cost-effective process for preparing agarose from Gracilaria spp", *US Patent Publication No.* US 2005/0267296 A1.

[9] R.Meena, A.K. Siddhanta, K.Prasad, B.K. Ramavat, K. Eswaran, S. Thiruppathi, M. Ganesan, Vaibhav A. Mantri and P.V. Subba Rao, "Preparation, characterization and benchmarking of agarose from Gracilaria dura of Indian waters", *Carbohydrate Polymers*, vol. 69, pp.179-188, 2007.

[10] S.D.Waldman, D.C. Kouto, M.D.Grynpas, R.M. Pilliar, and R A. Kandel, , "Multi-axial mechanical stimulation of tissue engineered cartilage: Review", *European Cells & Materials*, vol.13, pp.66-73, 2007.

[11] D.S.Bagal, A.Vijayan, R.C.Aiver, R. N. Karekar, and M. S. Karve, " Fabrication of sucrose biosensor based on single mode planar optical waveguide using co-immobilized plant invertase and GOD", *Biosensesors & Bioelectronics*, vol.22, pp.3072-3079, 2007.

[12] K. Zhang, M. E. Hawkins, B. Thomas, H.E. Brinkerhuff and H. Brinkerhuff, "Mineralized hydrogel, useful as implantable article e.g. in mineralized fillers, drug, growth factor and gene delivery, and in dental applications, comprises hydrogel and calcium phosphate mineral uniformly distributed within the hydrogel", *US Patemt No.* 2007098799-A1; *Japanese Patent No.* 2007117748-A; *European Patent No.* 1803442-A1.

[13] R.Meena, K.Prasad, and A.K.Siddhanta, "Preparation of genipin-fixed agarose hydrogel", *J Applied Polymer Science*, vol.104, pp.290-296, 2007.

[14] R.Meena, K.Prasad, and A.K.Siddhanta, "Properties of genipin-fixed kappa-carrageenan", *Inemational J. Biological Macromolecules*, vol.41, pp.94-101, 2007.

On seaweeds, a renewable bioresource - Bioactive compounds and biomaterials derived therefrom

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Abstract

There exist an estimated 3 million to 500 million different species in the marine biosphere representing approximately a half of total global biodiversity and 7000 species of which are marine algae. Algae are one of the oldest living organisms on the earth. They have been found as fossils from the Precambrian period and are estimated to be 1 to 3 million years old. Marine macro algae or seaweeds are distributed widely in all oceans of the world. These plants present a number of challenges to chemists, biochemists and ecologists alike, obviously for the reason that these organisms have survived the global changes that have been happening in the intervening millions of years of evolution. It would be reasonable to assume that this survival mechanism was directly related to the metabolites which imparted a unique strength of adaptability on these plants. What else could be more attractive a renewable bioresource than seaweeds to work on? Seaweeds have been reported to be bioactive of different kinds e.g. neurotoxic, hypotensive, cytotoxic, AIDS antiviral, antithrombic, immunomodulatory and anticancer. There is a possibility that these can be developed into drug or drug intermediates. Seaweed polysaccharides e.g. agar, agarose, carrageenans and alginate have been well known to be used as gelling and thickening agents in food and other industrial uses. Recent applications include its use as biomaterials which can be used in pharmaceutical and health care industries. These being renewable resource-based materials hold promise for potentially new and sustainable applications. In this article these aspects will be described with a focus on Indian scenario. India has been identified as one of the 12 mega-diversity countries. The work that has been done in the area of seaweeds research including large scale cultivation and value addition, pushing seaweeds up the value chain particularly the species of Indian waters, which were little known for their utility, will be described.

Key words: Seaweeds; polysaccharides; bioactive compounds; biomaterials

I. INTRODUCTION

There exist an estimated 3 million to 500 million different species in the marine biosphere representing approximately a half of total global biodiversity and 7000 species of which are marine algae [1]. Algae are one of the oldest living organisms on the earth. They have been found as fossils from the Precambrian period and are estimated to be 1 to 3 million years old. Marine macro algae or seaweeds are distributed widely in all oceans of the world. These plants present a number of challenges to chemists, biochemists and ecologists alike, obviously for the reason that these organisms have survived the global changes that have been happening in the intervening millions of years of evolution. It would be reasonable to assume that this survival mechanism was directly related to the metabolites which imparted a unique strength of adaptability on these plants.

II. SEAWEED RESOURCES

Bioresources are natural wealth that are obtained from the biological systems. It is generally renewable, so its supply can be sustained by continually generating the resources employing appropriate technologies. This is an age-old strategy being practiced by humans since the dawn of civilization, revitalizing the ecosystem in a continuous process. This is nothing but replication of natural processes in a planned manner rendering the living systems renewable.

Seaweeds belong to the marine plant resources and are found all over the seas of the world. The uses of seaweeds are in the domain of food, feed, pharmaceuticals and certain other value added products, which are basically compounds isolated from these resources or formulation based. Chemically, the compounds belong to all classes e.g. lipid and water solubles. Seaweeds are collected from the intertidal region of the sea during low tides as well as from the depth of the sea up to 20 metres. For these purposes hand picking and SCUBA diving techniques are employed.

A. Seaweed Resources: Business opportunities

The seaweed industry is worth US$ 1 billion. While agarophytes are in good demand with values increasing, carrageenophytes and alginate-bearing seaweeds have a tendency towards oversupply. World seaweed demand has grown at about 10% annually. The Asia-Pacific produced 80% of this total and exported an estimated US$ 250 million in seaweeds and seaweed products. Contrary to seaweed production, 90% of the seaweed colloid industry is concentrated in the developed West followed by Japan and the Republic of Korea. Demand for phycocolloids has grown between 1030% per year. Some 400 000 MT (product weight) of edible seaweeds including, *Porphyra*, *Laminaria*, *Hizikia* and *Undaria* are mainly produced, consumed and traded amongst Japan, Korea and China. An emerging market is the USA.

World production of seaweed was approximately 400000 MT in 1988, with production levels similar for the last 5 years. The Asia-Pacific produced 80% of this total and exported an estimated US$ 250 million in seaweeds and seaweed products. Seaweeds and aquatic plants are broadly classified into brown, red, green seaweeds and miscellaneous plants. Of these red and brown seaweed are the most important commercially. The main groups were produced in the following order: brown seaweeds (2.5 million MT, 66.5%), red seaweeds (1.25 million MT, 33%) and green seaweeds (15 000 MT, 0.4%). The overall world consumption (MT/dry weight) are as follows: Food for direct consumption- 400 000 MT; Seaweed colloids - 50 000 MT

While traditionally seaweeds were collected from the wild, virtually all brown seaweed, 63% of red seaweed and 68% of green seaweed are now maricultured. The main species maricultured are *Laminaria japonicus*, (Phaeophyceae), *Undaria pinnatifida*, (brown seaweeds), *Kappaphycus* spp., *Gracilaria* spp, *Porphyra tenera*, (red seaweeds) and *Monostroma nitidum* (green seaweed). In India *Kappaphycus* is being cultivated in the large scale in the sea by M/s Pepsico India Holdings Ltd. at the southeast coast [2].

B. World market of agar

Major agar producing countries: Japan, Spain, Chile, Mexico, China, and Korea. World production per annum : 110,000 dry tons, a total of USD 100-200 million. Agar producing seaweeds : *Ahnfeltia, Gelidium, Gelidiella, Gracilaria, Pterocladia species*. Agar is produced mainly from *Gelidium* and *Pterocladia*. *Gelidium* occurs in Indian waters sparsely, with no report of Pterocladia occurring. *Gelidiella* and *Gracilaria* spp. occur in Indian waters abundantly. The major applications of agar include - bacteriological and microbiological (ca.5% of the total sales) and the remaining find use in food industry as standard thickener. The cheapest food grade agar is ca.USD 50.00 per kg. The bacteriological variety is the most expensive costing up to USD 25,000 per kg. The market of agar has an estimated growth of 5-10% per annum. New potential applications have been reported in the areas of microfluidic devices and biomaterials [3].

C. World Production of Seaweeds

Seaweeds and aquatic plants are broadly classified into brown, red, green seaweeds and miscellaneous plants. Of these red and brown seaweed are the most important commercially. In 1988, the total seaweed production was about 4 million MT (wet weight) (FAO, 1990). The main groups were produced in the following order: brown seaweeds (2.5 million MT, 66.5%), red seaweeds (1.25 million MT, 33%) and green seaweeds (15 000 MT, 0.4%).

While traditionally seaweed was collected from the wild, virtually all brown seaweed, 63% of red seaweed and 68% of green seaweed are now maricultured (Table 4). The main species maricultured are Laminaria japonicus, (Phaeophyceae), Undaria pinnatifida, (brown seaweeds), Eucheuma spp, Gracilaria spp, Porphyra tenera, (red seaweeds) and Monostroma nitidum (green seaweed).

Leading producers of seaweed in 1988 were China, Japan, Republic of Korea followed by the Philippines, USSR, Norway and Chile. The Asia-Pacific region, accounts for the production of some 3 million MT (80%) of the world's total production mainly for the colloid industry while seaweed for human consumption is mainly produced in the 3 major consuming countries - China, Japan, Republic of Korea and Taiwan [2].

D. Standing seaweed biomass of India

Agarophytes comprising mainly of *Gelidiella acerosa* and *Gracilaria edulis* (5000 MT/y, wet weight). Alginophytes are *Sargassum* spp. *Turbinaria* spp. (50000 MT/y, wet weight). Carrageenophytes include *Hypnea musciformis* (3500 MT/y, wet weight). *Kappaphycus* were almost non-existent in the Indian waters barring one isolated report of its sighting. Currently it is being maricultured by M/s Pepsico India Holdings Ltd. at the southeast coastal waters of India. Others seaweed species of non-specific utilities have been estimated to be ca. 17000 MT/y, wet weight [4]. Therefore, mariculture of value added seaweeds species is a must for ensuring regular supply of raw material.

E. Marine Bioactives

The marine biosphere houses an estimated 3 to 500 million species of organisms. The opportunity to discover new species and therefore, new chemical diversity has increased through the application of new tools to explore the marine environment. This new chemical diversity combined with our current understanding of disease processes improves the ability to discover compounds of therapeutic utility [1].

F. Seaweeds in Health care

Ancient Roman literature (Virgil and Horace, 70 -19 BC; Pliny the Elder, 23-79 AD), early Chinese Materia Medica (Shen Nung Ben Cao Jing, 200 BC and Ben Cao Gang Mu, 1518-1593) as well as Indian Ayurvedic literature (Bhavaprakasa, 16th Century AD) have recorded various bioactivities of seaweeds envisaging toxicity to cooling and soothing agent healing maladies in humans. The late nineteenth century onwards history is replete with discoveries and inventions in all areas of science and technology affording new medicines and related compounds empowering man to manage health care job efficiently and meaningfully. Seaweeds have been reported to be the source of many bioactive and nutritionally important compounds e.g. antibacterial, antiviral, immunomodulator, cytotoxicity, anticancer, blood anticoagulant, antifertility, vitamins, proteins and minerals.

In India, a national project on Drugs from the Sea is under way involving university laboratories, national labs, and research institutes for more than 15 years under the funding support from Minsitry of Earth Sciences (erstwhile Department of Ocean Development), Government of India. Central Salt and Marine Chemicals Research Insitute (CSMCRI) at Bhavnagar (Gujarat), is one of the participants in this project, entrusted with the investigation on bioactivities of seaweeds of Indian waters. In a continuing process, many seaweeds the are occurring in the Indian coasts are being investigated through bioassay followed by chemical studies to identify bioactive molecules which could be developed into drug or drug intermediates [5]; during this investigation we have found blood anticoagulant seaweed polysaccharides [6].

G. Toxicity concerns

Almost all macroalgae are safe to eat with the exception of *Acanthophora specifera*, *Gracilaria edulis*, and *Gracilaria coronopifolia*, which were intermittently reported to be toxic caused by the presence of aplysiatoxin and debromoaplysiatoxin, which have previously been obtained from the sea hare and from blue-green algae.

H. Direct value addition of seaweeds

India has been identified as one of the 12 mega-diversity countries. More than 7000 km long coastline of India is endowed with in excess of 600 species of seaweeds, most of which have remained chemically uninvestigated. In an ongoing program of CSMCRI value addition of seaweeds have been done preparing various useful products from seaweeds. The important developments that have taken place in CSMCRI during is in the area of seaweeds research including large scale cultivation and value addition, pushing seaweeds up the value chain particularly the species of Indian waters, which were little known for their utility. From fresh *Kappaphycus alvarezii* two products have been isolated the sap being used as foliar spary and carrageenan [7] In field trials, the sap has been demonstrated to enhance growth of many crops e.g. corn, Basmati paddy, sugar cane, brinjal, wheat, potato, chilli and soyabean. The sap has promoted growth enhancement, when used as foliar spary, from 10% to 40%, the latter being with sugar cane (data courtesy M/s Pepsico India Holdings Ltd.).

A novel method has been developed in our laboratory for the preparation of a superior quality agarose from Indian agarophyte. This process is eco-friendly and considered "green process". Agarose has been prepared from red seaweed species *Gracilaria dura*, occurring on the Gujarat coast. This seaweed has been little known for its utility. The agarose that is prepared is comparable in performance to that of a Sigma product (A9539). The process is patented [8,9].

III. BIOMATERIALS

Biomaterials encompass biocompatible materials that are used to construct artificial organs, rehabilitation devices, forms drug delivery system or prostheses and replace natural body tissues. These are based on protein, polysaccharides, ceramics, metals. Seaweeds are the only natural source of industrially important phycocolloids e.g. agar, agarose, carrageenan and alginate, except the latter which is also produced by certain bacteria. These phycocolloids or polysaccharides are very important biopolymers presumably because of their hydrophilic nature facilitating important functions in the living organisms, and these have inspired researchers for developing important materials based on these polysaccharides through their physical and chemical modifications. Indeed, an apparently simple gelling material agar widely used in food and microbiology applications, has now acquired a prominent position in biomaterials research. Superior quality agarose gels are traditionally used in DNA electrophoresis and other molecular biology applications [3]. Agar/agarose has been used as the hydrogel, which has a function to promote chondrogenesis (cartilage formation), was employed to act as analogues of native extracellular matrix (ECM) for effectively entrapping chondrocytes [10]. Agarose has been used in fabricating glucose biosensor [11], and mineralized hydrogel [12]. Acid sensitive galactan polymers such as agar and carrageenan have been converted to materials in our laboratory, which are rock stable in acid. These being renewable resource-based materials hold promise for potentially new and sustainable applications [13,14]. Modified seaweed polysaccharides have been prepared; the products showed improved swelling capacities unlike their precursors. Their overall stability in various pH media and improved swelling properties set them out for new applications in the domain of pharmaceutiecals and personal care industries [13-16]. We have also prepared prepared soft capsule shells based on kappa-carrageenan, the process of which is patented [17]. These capsule shells would replace the

[15] K. Prasad, G. Mehta, R. Meena, and A.K. Siddhanta, "Hydrogel forming agar graft-PVP and -carrageenan-graft-PVP blends: Rapid synthesis and characterization", *J. Applied PolymerScience*, vol.102, pp.3654-3663, 2006.

[16] K. Prasad, R. Meena and A.K. Siddhanta, "Microwave induced rapid one-pot synthesis of -carrageenan-g-PMMA copolymer by potassium persulphate initiating system", *J. Applied Polymer Science*, vol.101, pp.161-166, 2006.

[17] P. K. Ghosh, A.K.Siddhanta, K.Prasad, R.Meena, A.Bhattacharya, "Process of preparation of biodegradable films from semi refined kappa carrageenan", *US Patent No.* 7067568.