Potential of marine algae (sea weeds) as source of medicinally important compounds

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Abstract

Scientific research has always been concerned with aspects of human health. There are several systems of medicines besides the globally accepted allopathy, which are based on compounds originating from natural products. Recent research has been centred around validation of the traditional knowledge on medicinal products. The traditional systems in India, China and forklore medicines in other parts of the world have indicated the potential of natural products consist of various chemical compounds that could be used as drugs. The search for drugs against five major dreadful diseases namely, cancer, AIDS, heart disease, diabetes and pulmonary disorders that attack the present day human from natural products has been in progress for some time. Microbes, plants and animals are the sources of natural products. In the past five decades, the research on bioactive chemicals from marine algae has been incited and several compounds with biological activity were isolated from algae. Generally, these are secondary metabolites produced for chemical defence against the biotic pressure of predators, consumers and epibionts. These potential drugs are now attracting considerable attention from the pharmaceutical industries due to the necessity of identifying substances that could be utilized for novel therapeutic purposes. Several compounds such as alginate, carrageenans, sulphated and halogenated polysachcharise and other derivatives have been shown to provide drugs that could be antiviral, anticancer and antimicrobial. The present account is on the potential of marine macro-algae for medicinally important products.

Keywords: algae, seaweed, bioactive chemical, microbes

Introduction

Algae belong to the primitive group of plants which evolved very early in the universe. Algae are both microscopic (microalgae) and macrophytic (macroalgae) occurring in freshwater as well as marine waters. In the marine ecosystem, the micro-algae are the major primary producers and the macro-algae are called as seaweeds, which flourish on surfaces of rocks, dead coral, stones, pebbles and any other suitable substrata are available for their attachment. Macro-algae are green algae (Chlorophyceae), brown algae (Phaeophyceae) and red algae (Rhodophyceae). Seaweeds are used as human food from 600 to 800 BC. In China, seaweeds were used from prehistoric time. In China and Japan, seaweeds are used as a stable diet item for a very long period. Fresh, dried and processed seaweeds are utilized for human consumption. Many types of seaweeds are used as food in Japan, China, Philippines and other countries of Indopacific regions. Seaweeds are one of the commercially important marine living and renewable resources of India. Commercial exploitation of marine algal species commenced in India since 1966 (Oza and Zaidi, 2001). One of the reports indicates that 1518 t of (dry weight) red algae and 2285 t of (dry weight) brown algae are utilized

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for manufacture of agar, alginate and liquid fertilizer (Kaliaperumal *et al.*, 2004). Seaweeds grow abundantly along the coastal waters of Tamilnadu, Gujarat, Andhra Pradesh, Orissa, West Bengal, Kerala, Maharastra, Lakshadeep and Andaman Nicobar Islands. There are also rich seaweed beds around Mumbai, Ratnagiri, Goa, Karwar, Vizhijzn, Pulicot and Chilka. Among the 20,000 species of seaweeds enumerated in the world, 271 genera and 1153 species are present in India with a total standing crop of 6, 77, 309–6, 82, 759 t fresh (Subba Rao and Mantri, 2006). According to Anantharaman *et al.* (2006), the total potential seaweed wealth is 8, 70,000 t fresh, present natural collection is 22,000 t fresh and through seaweed cultivation is 150 t dry. Natural habits of some of the prominent marine algae are presented in Fig. 1.

Medicinal potential of seaweeds

Seaweeds were considered to be of medicinal value in the orient as early as 3000 B.C. The Chinese and Japanese used them in the treatment of goitre and other glandular diseases. Romanians used the seaweeds for healing the wounds, burns and rashes. The British used Porphyra to prevent scurvy (vitamin C deficiency diseases) during long voyages. Seaweeds in general are used as verimifuge, for cough, stomach and chest ailments, bladder and kidney ailments (Schimmer and Schimmer, 1955, 1968; Hoppe, 1979; Stein and Borden, 1984; Smit, 2004; Anantharaman et al., 2006). Alginates from seaweeds are known to be used in the preparation of the moulds for denture (Fig. 2 (a)). A survey of literature on the potential of the products obtained from marine algae for medicinal use indicates the wide range of remedial compounds against several ailments. There is a very good potential in the seaweeds for obtaining novel compounds to be used as drugs against simple ailments and chronic diseases such as cancer, cardiac disorders, respiratory problems, diabetes, and virus attacks such as human immunodeficiency virus (HIV). The promise and potential appear enormous and the search has been on for over several years. The products so far encountered are antivirus, antibiotic, antitumour, antioxidant and vermifuges or antiparasitic. Table 1 gives the details of the algal species, the type of compounds obtained and their medicinal importance. However, only few products have found application in pharmaceutical preparations. Research work done for over four decades are presented below.

Antiviral activity

Seaweeds contain certain compounds that possess antiviral activity. Sulphated polysachharides such as galactan sulphate was tested in the laboratory to be effective against HIV and Herpes simplex virus (HSV). Xylomannan sulphate is anti-HIV and respiratory syncytial virus (RSV). Carrageenn, Fucoidion, Chondrion and dollabellans show anti-HSV activity. Fucoidion is also against RSV and human cytomegalovirus. These studies have been carried out using human cell lines and in some cases animal sources. A sulphated polysaccharide from Schizymenia pacifica was first shown to possess anti-HIV reverse transcriptase in vitro (Nakashima et al., 1987a, b). Certain sulphated polysaccharides such as galactan sulphate from Aghardhiella tenera and xylomannan sulphate from Nothogenia fastigiata showed antiviral activities against HIV, HSV types 1 and 2 and RSV tested in the laboratory (Damonte et al., 1994, 2004; Witvrouw et al., 1994) and Kolender et al. (1995). These polysaccharides are shown to be active during the first stage of the RNA virus replication when the virus adsorbs onto the surface of the cell (De Clercq, 1996) and have very low cytotoxic activities towards mammalian cells. Carrageenans (Fig. 2(b)) from Gigartina skottsbergii have potent antiviral effects against different strains of HSV types 1 and 2 during the virus adsorption stage (Carlucci et al., 1997, 1999a, b). Carrageenans from cystocarpic and tetrasporophytic stages of Stenogramme interrupta had similar activity (C'aceres et al., 2000). High molecular weight galactan sulphate (Fig. 2(d)) from Gracilaria corticata (Mazumder et al., 2002) and Fucoidan (Fig. 2(c)) had potent antiviral properties towards viruses such as RSV (Malhotra et al., 2003). Malhotra et al. (2003) found that fractions containing an uncharacterised polysaccharide from Caulerpa sp., Corallina sp., Hypnea charoides, Padina arborescens and Sargassum patens have high antiviral activity against HSV types 1 and 2 and have low levels of cytotoxicity. Besides polysachchardes, antiviral activity by Chondriamide A (Fig. 2(e)) from Chondria atropurpurea against HSV type II (Palermo et al., 1992) and Kahalalide F (Fig. 2(f)) from Bryopsis for its anti-HIV qualities are reported (Haefner, 2003). Recently, methanolic extracts of three species of Sagassum were shown to possess anti-herpes property (Zhu et al., 2003) and hepatoprotective activity (Hiren et al., 2016). The red seaweed Solieria chordalis was abundant in coastal area of France. The extract of S. chordalis from the coast exhibited potential antiviral activity (Ann-Sophie et al., 2016). Structures of certain compounds obtained from marine algae are presented in Fig. 2

Antimicrobial activity

The methodology used for investigating the antimicrobial potential of the marine algae in the laboratory is the simple diffusion plate technique. The extracts of the selected seaweed obtained from water or organic solvents are tested against Gram-positive and Gram-negative pathogenic Potential of marine algae (sea weeds) as source of medicinally important compounds

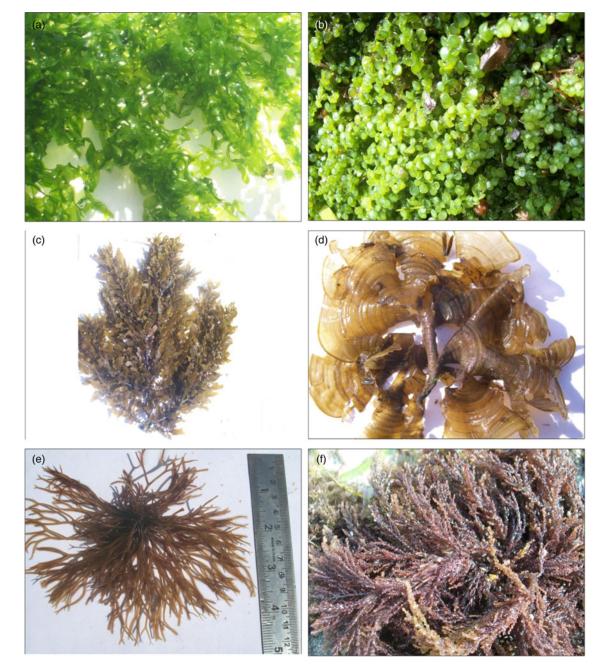
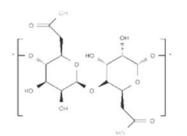
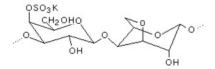


Fig. 1. Some common medicinally important seaweeds. *fam.* Chlorophyceae: (a) *Ulva retivulata*, (b) *Caulerpa racemosa; fam.* Phaeophyceae: (c) *Sargassum tennerium* (d) *Padina gymnospora; fam.* Rhodophyceae: (e) *Gracillaria edulis*, (f) *Acanthophora spicifera.*

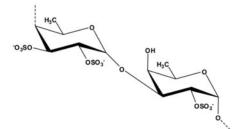
bacteria. The antagonistic compounds such as fatty acids, bromophenols, tannins, phloroglucinol and terpenoids are useful as antibiotics for killing of bacteria, fungi and viruses (Hashimoto, 1979). Such compounds are from Phaeophyceae (Glombitza, 1979) and halogenated compounds and laurinterol from several members of the Florideophyceae (Fenical, 1975) In a screening of 151 species of British marine algae, 54 were found to be antibacterial (Homsey and Hide, 1974) and in *Laminaria* saccharina (L.) Lamouroux (Phaeophyceae) maximum activity was in extracts from older parts of the thallus. *Bryopsis* sp. contained depsipeptides Kahalalide A and F, which were noted for their *in vitro* activity against *Mycobacterium tuberculosis* (El Sayed *et al.*, 2000). Halogenated furanone or fimbrolide (Fig. 2(g)) that belong to a class of lactones extracted from *Delisea pulchra* (a) Sodium alginate (after Fertah et al., 2014)



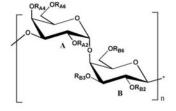
(b) Carageenans (after Jiao et al., 2011)



(c) Fucoidan (after Chevolot et al., 1999)



(d) Galactan sulphate (after Nishino et al., 1994)



(e) Chondriamide (after Palermo et al., 1992)



(j) B-1, 3 glucan (after Klarzynski et al., 2000)

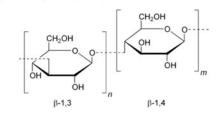


Fig. 2. Structure of compounds isolated and identified from marine algae. (a) Sodium alginate (after Fertah et al., 2014). (b) Carageenans (after Jiao et al., 2011). (c) Fucoidan (after Chevolot et al., 1999). (d) Galactan sulphate (after Nishino et al., 1994). (e) Chondriamide (after Palermo et al., 1992). (f) Kahalalide (after Hamann and Scheuer, 1993). (g) Halogenated Furanone or Fimbrolide (after de Nys et al., 1993). (h) Kainic acid (after Impellizzeri et al., 1975). (i) Phlorotannin (after Wang et al., 2008). (j) B-1, 3 glucan (after Klarzynski et al., 2000).

EMX-I

(f) kahalalide (after Hamann and Scheuer, 1993)

(g) Halogenated Furanone or Fimbrolide (after de Nys et al., 1993)

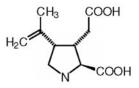
Halogenated Furanone Structures

MCA ring

MCAon

(h) Kainic acid (after Impellizzeri et al., 1975)

BEMX-3



(i) Phlorotannin (after Wang et al., 2008)

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Table 1. Medicinally important	compounds from marine algae
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Medicinal potential	Algal species	Isolated compounds	Biological activity	References
Antiviral	Schizymenia pacifica	Sulphated polysaccharides	Anti-HIV reverse transcriptase	Nakashima <i>et al.</i> (1987a, b)
	Aghardhiella tenera Nothogenia fastigata	Galactan sulphate Xylomannan sulphate	Antiviral activity against HIV, HSV 1 & HSV 2, RSV	Witvrouw <i>et al.</i> (1994), Damonte <i>et al.</i> (1994) Kolender <i>et al.</i> (1995)
	Gigartina skottsbergii	Carrageenans	Antiviral activity against HSV 1 & HSV 2	Carlucci <i>et al</i> . (1997, 1999a, b)
	Stenogramme interrupta	Carrageenans	Antiviral activity against HSV 1 & HSV 2	C´aceres et al. (2000)
	Gracilaria corticata	High molecular weight galactan sulphate, Fucoidan	Antiviral activity against RSV	Mazumder <i>et al</i> . (2002) Malhotra <i>et al</i> . (2003)
	Chondria atropurpurea	Chondriamide A	Antiviral activity against HSV type II	Palermo <i>et al</i> . (1992)
	Bryopsis sp.,	Kahalalide F	Anti-HIV	Haefner (2003)
	Sargassum chordalis	Extract	Antiviral	Ann-Sophie et al. (2016
Antimicrobial	Laminaria saccharina	Crude extracts	Antibacterial	Homsey and Hide (1974)
	<i>Bryopsis</i> sp.,	Depsipeptides Kahalalide A and F	Against Mycobacterium tuberculosis	El Sayed <i>et al</i> . (2000)
	Delisea pulchra	Halogenated furanone or fimbrolide	Inhibition of <i>Pseudomonas</i> <i>aeroginasa</i> infection and formation of biofilm in the lungs of cystic fibrosis sufferers	Kjelleberg and Steinberg (2001)
	Gracilaria cornea, Laurencia intricate, L. papillosa	Crude extracts	Antibacterial	
	Liagora farinose, Dasycladus vermicularis, Lobophora variegate			Anantharaman <i>et al.</i> (2006)
	Padina pavonica			Ali et al. (2010)
	Sargassum subrepindum			Abu-El-Wafa <i>et al.</i> (2011)
	Himanthalia elongata			Rajauria <i>et al</i> . (<mark>2012</mark>)
Vermifuge activity	<i>Digenea</i> sp.,	Kainic acid	Antihelmintics against ascaris	Nisiwaza (1979)
	Corallina officinalis, Durvillaea sp., Sargassum sp.,	Kainic acid	Active against tape worm	Hashimoto (1979)
Anti-oxidant activity	Porphyra yezoensis	Polysaccharide	Superoxide radical scavenging activity	Xue <i>et al</i> . (1998)
	Sargassum pallidum	Polysaccharide	Superoxide radical scavenging activity	Ye et al. (2008)
	Caulerpa lentifera, C. racemosa, Sargassum polycystum	Phenol	Radical scavenging activity	Matanjum (2016)
	Saccharina Latissima	Extract	Seasonal variation in antioxidant activity	Ann-Dorit <i>et al</i> . (2016)

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Table 1. (Cont.)

Medicinal potential	Algal species	Isolated compounds	Biological activity	References
Antitumour and anticoagulant activity	Kappaphycus strictum	Aqueous and methanolic extract	Antiproliferative activity of HeLa cancer cell	Lau <i>et al</i> . (2009)
	Kappaphycus strictum	Kappa Carrageenan oligosaccharides	Inhibition of formation of sarcoma	Yuan <i>et al</i> . (2006)
	Eucheuma cottonii	Polyphenol rich extract	Suppress breast tumour	Nanovar et al. (2012)
	Sargassum vulgare, Soleria chordelia, Laminaria digitalis, Padina pavonica, Hydroclathrus clathratus and Enteromorpha sp.,	Polysaccharides such as Alginates, Carrageenan, Beta-1,3 glucan and other polysaccharides	Antiproliferative	de Souse <i>et al.</i> (2007), Stephan <i>et al.</i> (2010), Vetrika and Yuin (2004), Awad <i>et al.</i> (2009), Jiao <i>et al.</i> (2009)
	Caulerpa racemosa, Gracilaria caudata, Halymenia floresia and Padina gymnospora	Sulphated polysaccharides	Anticoagulant and antithrombic activity	Rodrigues <i>et al.</i> (2011)

(Kjelleberg and Steinberg, 2001). These are active against chronic Pseudomonas aeruginosa infection and formation of a 'biofilm' in the lungs of cystic fibrosis sufferers (Høiby, 2002). Antibacterial activity was studied in several seaweeds and positive results are obtained in Gracilaria cornea, Laurencia intricata, Laurencia obtusa and Laurencia papillosa. The extracts of Liagora farinose, Dasycladus vermicularis and Lobophora variegate have the highest inhibition zones and a wide spectrum of antibacterial activity (Anantharaman et al., 2006). Ali et al. (2010) found a seasonal variation in the production of compounds of antibacterial activity in Padina pavonica (L.) Thivy from Tunisian coasts. The extracts from algae during the warmer months showed best activities against Gram-positive and Gram-negative strains of several bacteria. Sargassum subrepindum (Abu-El-Wafa et al., 2011) from Egypt and Himanthalia elongata from West Coast of Ireland (Rajauria et al., 2012) are the recent reports of antibiotic potential of brown algae. Extracts of several marine algae from various localities have been shown to possess antimicrobial characteristics (Shanmughapriya et al., 2008; Alang et al., 2009; Demirel et al., 2009; Cox et al., 2010; Manivannan et al., 2011; Ferreres et al., 2012; Kayalvizhi et al., 2012; Arunkumar et al., 2013; Elnabris et al., 2013; Al-Saif et al., 2014).

Vermifuge activity

Marine algae were largely used in Asian marine regions for remedies and preventives since the people of the area were involved in maritime activities. Extracts of the red alga *Digenea* (Ceramiales) and other marine algae have been used as vermifuges or anthelmintics (killing intestinal worms, such as *Ascaris*) for over a thousand years as a most efficient vermifuge (Nisiwaza, 1979). The active component is kainic acid (Fig. 2(h)), which kills the tape worm. The red alga *Corallina officinalis* L., species of the brown algae *Durvillaea* and *Sargassum* and the green alga *Viva* spp. are also sources of vermifuges (Hashimoto, 1979).

Antioxidant activity

Seaweeds are known to contain compounds such as glutathione peroxidase, catalase, superoxidedismutase and polyphenols with antioxidant or free radical scavenging properties. Specific techniques were used for the antioxidant or radical scavenging assays such as ABTS radical decolourization (beta-carotene bleaching) assay, DPPH radical scavenging assay and Ferric Reducing Antioxidant Assay (FRAP assay). Antioxidant properties of polysaccharides in scavenging superoxide radicals in Porphyra yezoensis was reported by Xue et al. (1998), Sargassum pallidum in Yellow sea, China (Ye et al., 2008) and certain brown algae by Liu et al. (2007). Matanjum (2016) analysed the antioxidant activities and phenolic contents and found Caulerpa lentifera, C. racemosa and Sargassum polycystum possessed very good radical scavenging activity. Brognioutella sp., had best antioxidant activity among 24 red algal species tested from Brittany Coast, France (Zubia et al., 2009). In Porphyra sp., activity of the endogenous enzymes was increased by sulphated galactans (Mohamed et al., 2012). Seaweeds occurring in South Indian coasts were screened for antioxidant activities (Vadiapudi and Chandrasekhara Naidu, 2010; Karthika Devi et al., 2011; Vijayabaskar and Shyamala, 2012; Indu and Srinivasan, 2013). Gracilaria changii has very good free radical scavenging property (Chan *et al.*, 2014). Natural antioxidants derived from marine algae have the potential for improving oxidative stability of lipids in food systems. The phlorotannin compounds (Fig. 2(i)) with better antioxidant activity were identified through HPLC–DAD–ECD–QTOFMSn (Ditte *et al.*, 2016). The seasonal variation in the antioxidant activity of sugar Kelp (*Saccharina latissima*) in different cultivation sites were recently reported (Ann-Dorit *et al.*, 2016).

Antitumour activity/anticoagulant activity

Marine algae have been a good source of compounds that could be used for antitumour treatments. Kashiwagi et al. (1980) showed antitumour activity against lymphocytic leukaemia and Ehrlich ascites tumour in mice in extracts obtained from marine algae from Pacific islands. Chinese have used decoctions of Sargassum spp., Laminaria spp. as herbal medicines to treat cancer and a preliminary study reveals inhibition of leukaemia tumours (Yamamoto et al., 1974). Cho et al. (1997) found that several red and brown algae had compounds that inhibited colon cancer cell growth. Iodine rich kelps, Laminaria (Funahashi et al., 2001), Champia feldmanni, Undaria pinnatifida (Maruyama et al., 2003), Dictyopteris divaricata and Sargassum thumbergia (Kim et al., 2009) were all found to be good sources of antiproliferative and antitumourproducing compounds. Lau et al. (2009) have shown that both aqueous and methanolic extracts from Kappaphycus strictum had higher antiproloferative activity of HeLa cancer cells compared with K. alverezii. The role of k-carrageenan oligosaccharides from K. strictum in the inhibition of the formation of sarcoma was reported by Yuan et al. (2006). Polyphenol-rich extracts of Eucheuma cottonii suppressed breast tumour via hormone modulation and apoptosis induction (Nanovar et al., 2012). Alginates from Sargassum vulgare, carrageenan from Soleria chordelia, B-1,3 glucan (Fig. 2(j)) from Laminaria digitalis, unknown polysaccharides from Padina pavonica and Hydroclathrus clathratus and Enteromorpha intermedia were shown to be antiproliferative (Vetrika and Yuin, 2004; de Souse et al., 2007; Awad et al., 2009; Jiao et al., 2009; Stephan et al., 2010). Fucoidan is found to be effective against bile duct cancer and breast cancer. Examples of algal extracts inhibiting various steps of cancerous tumour development or cell proliferation are outlined in detail by Mohamed et al. (2012). Several green, brown and red seaweeds are reported to contain sulphated polysaccharides (in the aqueous extract) which has anticoagulating and antithrombic activity. Caulerpa racemosa, Gracilaria caudata, Halymenia floresia and Padina gymnospora are reported in studies from Brazilian coast to be the source of anticoagulating substances (Rodrigues *et al.*, 2011).

Pharmaceutical importance of seaweeds

Seaweeds have already found application as household medicine and pharmaceutical formulations in Southeast Asia and other parts of the world. Some of the instances are cited below.

- (i) Obesity and diabetes: Extracts of Pelvetia babingtonii and Ascophyllum nodosum had potent alphaglucosidase activity to support post parandial hyperglycaemia (Kim et al., 2008). Extracts of pacific edible brown alga contain antidiabetic insulin-like and insulin-secreting activity (Kang et al., 2008). The brown seaweeds contain high-dietery fibres and Fucoxanthin the main carotenoid showed antiobesity effects and reduced blood glucose (Abidov et al., 2010). A recent Korean National Health survey revealed that seaweed consumption decreased diabetic risk in men (Lee et al., 2010). The effects of seaweed extracts in preventing antiobesity and peroxidation in rats were studied via assessing the plasma lipids and plasma and organs malondialdehyde concentrations. These findings showed positive effects in inhibiting weight gain and have promising value in preventing obesity (Matanjum et al., 2016).
- (ii) Obstetrical uses: The dried stipes of *Laminaria* spp. have been used in obstetrical and gynaecological practices as a natural dilator of the cervix, thus making gynaecological treatment easier (Strauss *et al.*, 1979; Ye *et al.*, 1982). *Laminaria* was found to be particularly effective in intrauterine devices (IUD) for birth control (Manabe *et al.*, 1982).
- (iii) Goitre treatment: Goitres are due to low iodine content in food. Marine algae are excellent sources of iodine and 'goitre sticks' made of *Phyllogigas*. Dried *Ulva* and *Porphyra* are used in the Peruvian Andes. The Chinese have used *Sargassum* as a remedy since 2700 BC. Vitamin A deficiency occurring in restricted areas of Burma can also be overcome by use of seaweed supplements in the diet (Michanek, 1979).
- (iv) Hypertension: Seaweed hydrolyzates have antihypertensive properties and the examples are peptides from *Undaria pinnatifida* (Sato *et al.*, 1996) and phlorotanins from *Eklonia stolonifera* (Jung *et al.*, 2006). Carrageenans from red algae have dislepidaemic and lipids and bring down levels of cholesterol.
- (v) Wound healing: Carbohydrate polymers like alginic acid are used in wound management. Alginates are highly viscous bio-absorbable guluronic and mannuronic acid polysaccharides. Hydrophilic sponges

produced from calcium alginate have good absorption property of both blood and wound exudates as well as pain-stimulating compounds (Lloyd *et al.*, 1998; Matou *et al.*, 2002).

(vi) Pharmaceutical formulations: The pharmaceutical uses of algae involve the phycocolloids isolated from the selected members of brown and red algae. Carrageenan can be used in cough syrup emulsions (Chapman, 1979). Carrageenan and the other phycocolloids, such as fucoidan are used as binding agents for medical tablets. The bioactive ultra-high viscosity gels from alginates obtained from Lessonia trabeculata and Lessonia nigrescens are promising biomaterial approach for tissue engineering has been reported (Michel et al., 2016). Sulphated polysaccharides from marine algae show very good anticoagulant activity. Alginates are a family of polysaccharides from brown seaweeds namely Laminaria hyperborean in Norway. The characterized alginate gels with chitooligosaccharides of varying composition as cross linkers for tissue engineering, cell immobilization and drug release has been established in Norway (Yiming et al., 2016)

Conclusion

The potential of the marine algae as source of compounds of medicinal importance is enormous. The general consensus of scientists is that the marine algae are less exploited and new formulations with novel compounds obtained from them could yield more useful and effective drugs. The search for remedies of human maladies appears to be a continuous process. It is our wish and hope that the marine algae will play a major role in the protection of human health.

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