Biotechnological applications of seaweeds

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Editor

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BIOTECHNOLOGY IN AGRICULTURE, INDUSTRY AND MEDICINE

BIOTECHNOLOGICAL APPLICATIONS OF SEAWEEDS

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BIOTECHNOLOGY IN AGRICULTURE, INDUSTRY AND MEDICINE

BIOTECHNOLOGICAL APPLICATIONS OF SEAWEEDS

ELHAFID NABTI
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FOREWORD

One of the key issues of our times, when big global challenges need to be solved for securing and improving the climate and a good future for mankind, is the sustainable use of abundant natural biological resources in a knowledge-based efficient manner. In addition to the optimization of agricultural practices with less applications of chemicals and the removal and avoidance of environmental pollution, the preservation of major ecosystems and balancing out ecological constraints and biotechnological developments are important tasks. The possibility to create new chances for income to people in especially rural areas is another important aspect and motivation to focus in on the better utilization of quite abundant natural resources. Since long, the seaweeds in coastal regions around the world are being used as fertilizer for agriculture. As can be learned in this book, the up-to-date knowledge about the potentials of seaweeds/macroalgae is enormous and a wide diversity of applications are available.

In the book "Biotechnological application of seaweeds", edited by Dr. Hafid Nabti, University of Béjaia, a wide scope of issues related to seaweed ecology, biodiversity and application is presented. The introductory chapter of S. Satheesh et al. on "Ecological significance of seaweeds in coastal ecosystems" presents an overview about the diversity of seaweeds and the diversity in each major group. Getting in on functional aspects, the occurrence and importance of seaweed-associated microbes for the morphology and nutrition of macro-algae is pointed out. In particular, the production of specific biologically active compounds, which protect the seaweed host, has for example led to the identification of biologic antifouling compounds. In coastal areas, seaweeds / macro-algae themselves are the living habitats for a huge diversity of invertebrates and thus for faunal life. In addition, the diversity and health of the macro-algal populations are valid bio-indicators for habitat quality. It is important to realize in time, that an extensive use of seaweeds for diverse important applications constitutes a serious threat to natural seaweed biodiversity. Therefore, there is urgent need for further developments to establish aquaculture systems for economically important seaweeds.

Due to the major life strategy of seaweeds/macro-algae to filter the seawater, macro-algae take up not only essential nutrients from the water body but also contaminants originating from agricultural run-off, like herbicides and pesticides but also nitrogen and phosphate fertilizers. This contributes to a large part to counteract eutrophication and contamination of coastal water. The important aspect of phyto-remediation of seaweeds is detailed in the chapter of Mourad Baghour. In addition to the removal of organic contaminants, the uptake of heavy metals is another important function of macro-algae to protect aquatic ecosystems. The use of macro-algae as bio-indicators for monitoring of environmental quality is also outlined in this chapter as well as different mechanisms of metal adsorption and accumulation and the degradation of organic pollutants.

A major aspect of the application of seaweeds is certainly to improve agriculture in several ways. In the chapter “Impact of seaweeds in agriculture” of D. Juvaraj and P. K. Gayathri, the reasons for many beneficial actions of seaweeds on plant development are outlined in detail. Seaweeds and seaweed-based products contain considerable amounts of macro- and micronutrients as well as plant hormones like auxins, gibberellines and cytokinins which support seed germination of plants but also growth and biomass development of crop plants. Due to their challenging life in salt water, macro-algae have developed an array for substances to prevent them from microbial attack as well as devastating grazing animals. Thus, macro-algae are themselves an effective and eco-friendly pesticide ready to be applied in different forms like seaweeds extracts, compost or mulch different commercial seaweed products. In addition, all seaweeds have developed excellent ways to cope with salt stress using so-called osmolytic substances like betaines or specific amino acids and sugars, which protect them from the inhibitory effect of high salt concentrations and a lack of available water in periods of dryness. Liquid seaweed concentrate is used as either soil conditioner due to their high content of polymeric carbon compounds or as foliar fertilizer. The different ways of plant growth promotion, like as soil conditioner, biofertilizer, growth stimulator or in pest and disease management are described in detail in the chapter of Juvaraj and Gayathri. The application of seaweeds to cope with salinity effects on crop plants is presented in the chapter of Cristina Cruz and

Ajit Varma. Experiments with the brown seaweed Ascophyllum nodosum are presented, which is used for centuries as biofertilizer and/or biostimulant to promote plant growth and improve its tolerance against biotic and abiotic stress, like increased salinity. The fertilization of salt stressed tomato plants with extracts of A. nodosum improves the salt tolerance, in particular the stabilization of Na+/K+ balance in leafs, and the uptake of Zn.

Last but not least a detailed overview about the manifold “Therapeutic and pharmaceutical applications of seaweeds” are contributed by Rai Abdelwahab. Due to their extremely high metabolic diversity, marine seaweeds have an outstanding position as source of pharmaceutical compounds which are used in medicine for treating e.g., diverse cancer forms, heart and lung diseases, asthma, eczema, arteriosclerosis, renal disorders, gall stones, stomach ailments, scabies, psoriasis and so on. Among the most important substance classes with pharmaceutic activity are alkaloids, terpenoids, sterols, phenolic compounds, but also halogenated alkans and alkens, hydroquinons, polysaccharides, glycoproteins and fatty acids. In addition, seaweed extracts provide a big reservoir of antibiotics against severely pathogenic Gram-negative and Gram-positive bacteria, different viruses and pathogenic fungi. Since oxidative stress is involved in various forms of pathophysiology, the wide range of antioxidant activity of an array of compounds of seaweeds have a broad scope of beneficial effects.

Thus, this book presents a timely compendium of major aspects of all aspects around seaweeds/macroalgae and presents much valid information about mechanistic aspects of the multiple beneficial aspects of seaweeds. The interested reader also gets the chance for further reading using the multiple lists of original publications in this highly relevant research field.

München/ Neuherberg, 27.11.2016

Anton Hartmann

Helmholtz Zentrum München,
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Chapter 1

AN INTRODUCTION TO THE ECOLOGICAL SIGNIFICANCE OF SEAWEEDS ON COASTAL ECOSYSTEMS

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ABSTRACT

Seaweeds (macroalgae) play a key role in coastal ecosystems by providing space for marine microorganisms and higher organisms, as a nursery ground for fishes and maintain the overall biodiversity structure. Seaweeds are also considered as major primary producers in the reef ecosystems and form an important part of trophic structure. For environmental monitoring programme, seaweeds are used as good bioindicators to assess the pollutant level in marine waters. Besides, many seaweed species have phytochemicals and attain economic significance. This chapter describes the ecological significance of seaweed communities in coastal ecosystems and discusses the need for conservation of seaweed beds.

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Keywords: seaweeds, ecosystem engineer, bioindicator, bioactive metabolites, coastal ecosystems

INTRODUCTION

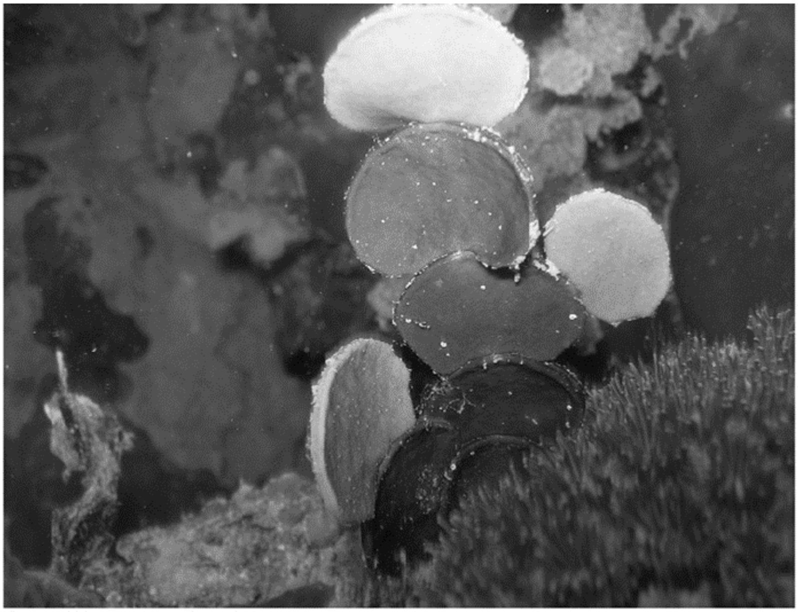
Seaweeds or macroalgae are the abundant space occupiers and primary producers in the marine ecosystems with great ecological and economic significance (Egan et al. 2013; Ba-akdah et al. 2005). Seaweeds grow abundantly along the coastline, particularly on rocky shore regions. Generally, they are abundant in the intertidal region due to the availability of the substratum (Figure 1).

Seaweeds are classified into three main groups based on the presence of photosynthetic pigments, storage of food products and fine structure of the cells (Dhargalkar and Kavlekar, 2004). The broad seaweed groups are Chlorophyceae (green algae), Phaeophyceae (brown algae) and Rhodophyceae (red algae). The green algae contain photosynthetic pigments such as chlorophyll *a, b* and carotenoids. In brown algae, the photosynthetic pigments include chlorophyll *a, c* and fucoxanthin. The carotenoid fucoxanthin and others give yellow to deep brown colour to the brown algae (Dhargalkar and Kavlekar, 2004). The red seaweeds have chlorophyll *a*, phycobilins and carotenoids as photosynthetic pigments. The colouration of red seaweeds is due to the presence of phycobilins which include red coloured phycoerythrin and blue coloured phycocyanin (Dhargalkar and Kavlekar, 2004).

There are considerable variations among the species which are classified under these three groups, particularly on ecological and physiological aspects (Toth and Pavia, 2007). For example, brown seaweeds are normally larger in size and some are commonly called as kelp (McHugh, 2003). Kelps (large seaweeds of the order Laminariales) are abundant throughout the temperate seas (Steneck et al. 2002) and provide an extensive ecosystem for many marine communities. Kelp forests usually support high primary productivity and enhanced secondary productivity in coastal ecosystems (Smale et al. 2013). Red and green macroalgae are small in size with the size ranging from a few centimeters to a meter (McHugh, 2003). Macroalgae lack specialized tissues such as root system and vascular structures which are present in plants (Graham and Wilcox, 1999). It has been estimated that about 200 species of seaweeds are exploited for valuable economically important products such as aging, agars, carrageenans and food products (Zemke-White and Ohno, 1999).

Seaweed production along the coastal regions of the world, particularly in Asian countries increases in the recent past due to the economic significance.

A



B

Figure 1. Distribution of seaweeds on coastal ecosystems. A) Growth of *Ulva* on a rocky shore B) *Halimeda* on a reef.

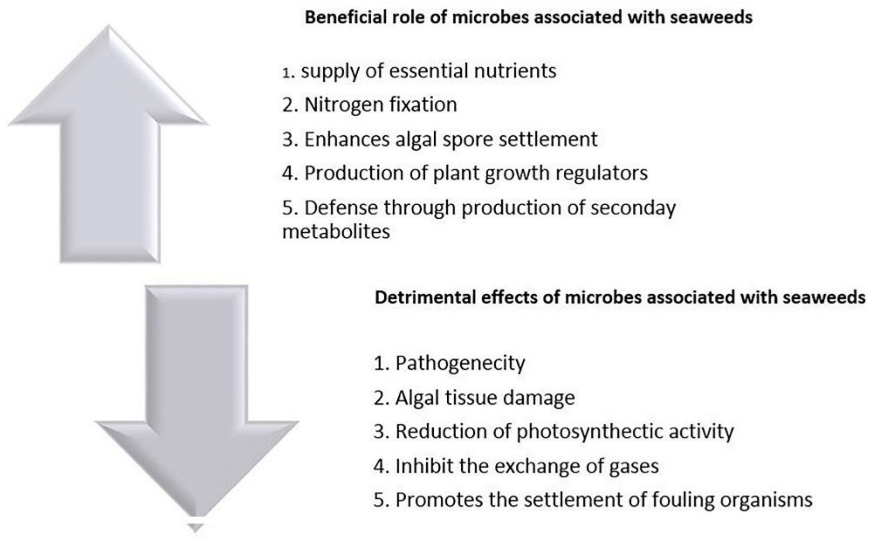


Figure 2. Possible advantages and disadvantages of microbes associated with seaweeds in coastal ecosystems.

Macroalgae-Microbe Association

All the living and non-living surfaces in the marine waters are colonized by the microbial population from the surrounding environment. The surface of marine invertebrates and macroalgae is also no exception as they are colonized by microorganisms (Egan et al. 2013; Satheesh et al. 2016). Seaweeds provide a microhabitat for many microorganisms with densities varied between 10^2 to 10^7 cells cm^{-2} depending on macroalgal species, sampling season and region (Armstrong et al. 2000; Bengtsson et al. 2010). The macroalga-microbe relationship is attributed for many purposes (Figure 2). The associated microorganisms, particularly the bacterial community provide protection and maintain the health of host alga (Egan et al. 2013). Many studies have indicated that bacterial communities associated with macroalgae are necessary for the normal morphological development of algal host (Matsuo et al. 2003; Singh et al. 2011). In addition, microbial communities also supply essential nutrients, mainly fixed nitrogen to the macroalgal host (Philips and Zeman, 1990). It has been noted that the nitrogen fixation activity of associated bacteria significantly influences the growth of seaweeds particularly red and green seaweeds (Chisholm et al. 1996; Singh et al. 2011; Singh and Reddy, 2014).

Research studies also indicated that bacterial communities associated with macroalgae enhance the settlement of zoospores in many algal species (Dillon et al. 1989; Joint et al. 2000; Shin, 2008). Another important role of microorganisms associated with the macroalgae is the production of plant growth regulators (Sing and Reddy, 2014). These plant growth regulators may affect the growth of the macroalgae as evidenced from previous studies (Spoerner et al. 2012). On the other hand, the microbial communities associated with seaweeds produce biologically active compounds (mainly for antifouling) and these compounds ensure the protection of the host (Goecke et al. 2010; Satheesh et al. 2016).However, some studies also revealed the negative aspect of microbes associated with macroalgae. For instance, the microbial films on macroalgae may reduce the incident light, inhibit the exchange of gases and hinder photosynthesis (Wahl, 1989; 2008). Also, the microbial communities associated with the algal surface may be a source of disease-causing pathogen to the host (Largo et al. 1995). While microbe-macroalga association provides an opportunity to explore some useful compounds, the functional role of this association in coastal ecosystem processes needs to be studied in detail.

SEAWEEDS AS A HABITAT FOR INVERTEBRATES

Seaweeds are reported to provide nutrition and shelter to diverse groups of invertebrates (Wikstrom and Kautsky, 2004; Cacabelos et al. 2010; Ba-akdah et al. 2015). Most importantly, the macroalgae increase the amount of space for attachment of sessile organisms; provide protection from environmental conditions such as wave action, desiccation and heat (Viejo, 1999). Studies from various coastal regions suggest that the invertebrates associated with the seaweeds are taxonomically and morphologically diverse, and exhibit a wide range of trophic habits. For example, these associated organisms may consist of filter feeders (Caine, 1977), detritus feeders (Zimmerman et al., 1979), predators which eat other epifauna (Roland, 1978) and herbivores which eat epiphytic algae or the host plant (Brawley and Fei1, 1987; Duffey, 1990; Viejo, 1999).

Marine invertebrates such as polychaetes, amphipods, isopods and gastropods are commonly observed on the surface of seaweeds and these organisms may form an important food source for juvenile fishes, which are also abundant in seaweed habitats (Bray and Ebeling, 1975; Jones, 1988). In general, by acting as refugia for marine invertebrates, seaweeds contribute largely to the maintenance of biodiversity and coastal ecosystem functioning. For example, diversity and abundance of organisms are high in those coastal habitats which possess vegetation than unvegetated regions (Steneck et al. 2002).

SEAWEEDS AS A BIOINDICATOR FOR ENVIRONMENTAL MONITORING

The coastal environments throughout the world are experiencing constant exposure to pollutants from anthropogenic sources. Many marine sessile organisms are considered as bioindicators for environmental quality assessment of the marine waters. A bioindicator is an organism which gives overall information on the presence or absence of a pollutant and the concentration. Seaweeds can be used as good indicators to monitor the environmental changes due to anthropogenic and natural stressors because of their sessile mode of life (attached to a substratum) and abundance in most of the rocky coastal regions of the world (Philips, 1980). Several previous investigations revealed the effectiveness of seaweeds as bioindicators of heavy metal pollution in the marine environment (Villares et al. 2001; Chaudhuri et al. 2007; Juanes et al. 2008) as they have the ability to accumulate the metals (Haroon et al. 1995).The thallus of the seaweeds absorbs the nutrients and other materials from the surrounding environment. Hence, the toxic elements present in the water will also get accumulated in seaweeds.

ROLE OF SEAWEEDS IN NUTRIENT RECYCLING IN COASTAL ECOSYSTEMS

The seaweeds are a source of nutrient recycling and act as a base for food chains in oligotrophic coastal waters (Blanche 1992). This is due to the fact that seaweeds have photosynthetic activities in which they absorb carbon dioxide and release oxygen. According to Ryther (1963), global benthic macroalgae production was estimated at about 10% of phytoplankton. Seaweeds support other biosystems such as reefs, seagrass meadows, and mangroves by exporting good amount of particulate organic matters carried out by currents and tides (Hurd et al. 2014). Further, seaweeds are reported to be involved in the biogeochemical cycling of nutrients, particularly, nitrogen and phosphorus (Atkinson and Smith, 1983; Lapointe et al. 1992). Seaweeds also play an important role in maintaining water quality by removing the nutrients and organic materials, particularly in the eutrophicated regions (Okuda, 2008).

MACROALGAL CHEMICAL DEFENSE AGAINST PREDATORS

The majority of the seaweeds produce secondary metabolites (Amsler 2008), also known as allelochemicals as a defense mechanism against herbivores. These compounds are toxic to microorganisms (Culioli et al. 2008) and invertebrates (Davis et al. 2005). The production of these biologically active compounds is due to the competition and predation (Hay 1996). Competition mainly occurs between macroalgal communities owing to the availability of limited space for growth and distribution. Macroalgae are constantly subjected to attack from various herbivores that feed on algae (Rothausler et al. 2005). Marine herbivores also play important roles in structuring and functioning of coastal ecosystems (McCarty and Sotka, 2013). For example, the distribution of macroalgal communities of coastal ecosystems mainly depends on the defense mechanism of the algae (Van Alstyne, 1989, Hay 1997).Many studies have demonstrated the ability of macroalgal compounds for preventing fouling and grazing by herbivores (Paul et al. 2001; Amsler and Fairhead, 2005; Pansch et al. 2009; Thabard et al. 2011). Macroalgae that exposed to higher herbivory and predation are reported to produce more biologically active compounds. This view is supported by the ability of the seaweeds to induce chemical defenses in response to the attack of herbivores (Flothe et al. 2014). The secondary metabolites produced by the seaweeds in response to competition and predation had biotechnological applications as they could be used as a potential lead for the development of biopharmaceuticals, nutraceuticals, and antifouling compounds.

Threats to Seaweed Biodiversity

Coastal ecosystems are considered as the most vulnerable environment to anthropogenic and climate change induced impacts. Mainly, human activities along the coastal region have increased in recent times that produced deleterious effects on the marine biota (McIntyre, 1977). Seaweed beds along with other coastal systems provide important services to the ecosystem and any change in these systems will affect the human societies (Harley et al. 2012). Seaweeds are under threat in developing countries, where they are being disturbed by a variety of human activities. Mainly, changes in the coastal regions due to reclamation or construction activities resulted in serious deleterious effects on seaweed habitats (Okuda, 2008). Also, changes in global temperature and ocean acidification process are causing major shifts in biological systems (Harley et al. 2012). Seaweed growth, recruitment, survival, and reproduction are influenced by different environmental parameters such as temperature, salinity and nutrient concentration (Luning and Neushul, 1978; Lobban and Harrison, 1997; Steen 2004). Increasing concern about the destruction of seaweed beds and changes to the habitats warrant observational and experimental studies on macroalgal communities for better management of natural marine systems.

Conclusion

Seaweeds are an important ecosystem engineer which provides space for many marine organisms and structuring the coastal biodiversity. The functional role of seaweeds in coastal ecosystems is multifold from nutrient recycling to harbour micro- and macro-organisms. While, seaweeds exploited for many commercial purposes, including biologically active materials, a holistic approach is needed for conservation of this precious coastal system. Aquaculture of economically important seaweeds is progressing mainly for the food market and biofuel production (Neori, 2009; Borines et al. 2011; Egan et al. 2013). In addition, secondary metabolites produced by the seaweeds could be utilized as a potential source for pharmacological compounds and antifouling compounds. The ecological and economic significance of seaweeds emphasize the need for adequate conservation and management strategies.

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Chapter 2

UTILIZATION OF SEAWEED IN SOIL FERTILIZATION-SALT TOLERANCE

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ABSTRACT

Salinity affects crop production worldwide. *Ascophyllum nodosum*, brown seaweed, has been used for centuries as a bio-fertilizer and/or bio-stimulant to promote plant growth and improve plant tolerance to biotic and abiotic stresses. However, the mechanisms of its bio-stimulatory activity are not well understood.

In this experiment, we investigated the effect of *A. nodosum* in alleviating the effects of salinity on tomato (*Solanum lycopersicum*) plants grown at 0-200 mM NaCl.

Results showed that *A. nodosum* promoted tomato plant growth under saline conditions due to the maintenance of the Na^+/K^+ balance. Its extract also interfered with Zn^+ leaf concentration.

Keywords: tomato, salinity, seaweed, stress tolerance, *Ascophyllum nodosum*

INTRODUCTION

For centuries, whole seaweeds and processed or purified concentrates of seaweeds have been used in agriculture to improve stress tolerance (Crouch et al. 1990) in plants and animals. *Ascophyllum nodosum*, *Laminaria*, *Fucus* and *Ecklonia*, are commonly used. Their growth-promoting effects are mediated by naturally occurring bio-stimulatory components, including essential micronutrients, traces of vitamins, and complex organic molecules, which may act in similar ways to phyto-hormones of terrestrial plants (Craigie 201; Stirk et al. 2003).

In some places, the practice was of great importance to agriculture and contributed to improvement of poor soils, which are now used to produce valuable vegetables. However, seaweed availability is seasonal, its use requires intensive labour, and the composition of the material collected varies over time (Rayorath et al. 2008). This contributes to price oscillation and unpredictable variations in crop productivity.

As a result of these problems, seaweed use in agriculture declined with the development of chemical fertilizers and their increased availability at low prices. However, interest in the potential of seaweeds in improving soil fertility has renewed in recent years as a consequence of the environmental problems associated with chemical fertilizer use. Part of the excess fertilizer that reaches coastal waters is incorporated into seaweeds, so their collection and application can return nutrients to the soil (Kuperin et al. 2013), thus contributing to a zero waste agriculture.

Traditionally, before application of seaweeds to soil, they had to be sun dried and then washed to remove excess salt, which could lead to soil salinization, affecting productivity of crops, particularly those which are more sensitive to salt stress such as legumes. Recently several liquid fertilizers based on processed seaweed, mainly from the genus *Fucus*, have emerged on the market. In organic farming, these products have been applied in foliar sprays as a source of nutrients, natural hormones and to stimulate the natural defences of cultivated plants against diseases (Ugarte et al. 2006).

We are now reaching a stage where we need to improve plant productivity, in order to increase food production without increasing the farming area. To achieve this, we are changing our concept of crop management. In order to maintain crop sustainability, it is necessary to consider the soil nutritional balance, and guarantee that suitable levels of nutrients are present in the soil and provided to crops. We are also understanding the importance of soil ecology and the microbial community (bacteria, archea, fungi, microfauna, algae) to the rhizosphere assemblage and plant productivity, defence and abiotic stress tolerance (Zodape et al. 2011). In this context, the use of seaweed in agriculture may regulate rhizospheric function and stimulate plant growth through interaction with nutrient acquisition and/or hormonal balance (Sponsel et al. 2010).

There is evidence that seaweed-based fertilizers promote plant hormone balance, influencing production and degradation of cytokines and auxins, nutrient use efficiency and photosynthetic activity, resulting in greater plant vigour and, consequently, improved plant growth. Seaweed extracts can also have a stimulating effect on plants, by promoting root formation, flowering and fertilization. Plant growth promotion due to the effect of seaweed is dependent on the plant species and growth conditions. There are reports of consistent increases in lettuce biomass, size of potato tubers, and carrot productivity (Sivasankari et al. 2006).

However, not much is known about the mechanisms by which seaweed extracts promote plant growth.

In this work, we show that fertilization with seaweed extracts promotes tomato tolerance to salinity, and that Zn is involved in the maintenance of the leaf N^+/K^+ balance.

MATERIAL AND METHODS

Plants were obtained from tomato (*Solanum lycopersicum*, cv money-maker) seeds. Three plants with two completely developed leaves were transplanted into 4 L blow-moulded pots filled with sandy soil and irrigated with Hewitt (1966) nutrient solution during 1 month under non-saline conditions. Sandy soil, pH 6.2, was collected from agricultural sites used for tomato cultivation in rotation with other crops. The seaweed used in this work was *Ascophyllum nodosum* obtained from a supplier to the biofertilizer industry. The algae were dried, powdered and 2.5 g were placed in vials containing 50 mL of distilled water. The vials were then autoclaved at 110°C for 30 min. After decantation, 10 mL of the supernatant were applied per pot at the time of sowing, and twice more at intervals of 30 days.

Plants were kept in a greenhouse with 25/20°C day/night temperatures, relative humidity 65-80%; and mid-day photon flux density 700-800 µmol m^{-2} s^{-1}. After this period, plants were submitted to salinity treatments (0, 50, and 100, 150 and 200 mM NaCl). In order to avoid osmotic shock, NaCl was added progressively in weekly steps of 50 mM day^{-1} (Hessini et al. 2012).

Plants were irrigated with nutrient solution (pH 6.0 ± 0.1) every 3 days, then harvested and separated into leaves and roots at the end of the vegetative stage (60 days after the beginning of salt treatment). There were 6 replicates per treatment in a total of 30 pots.

Plants were collected between 10:00 a.m. and 12:00 p.m. Plant dry weight (DW) was determined after oven drying samples to constant weight at 60°C. Na^+ and Zn^+ concentrations in dried plant leaves were determined by Inductively Coupled Plasma (Laboratório de Ionómica del CEBAS-CSIC, Murcia, Spain), with 6 replicates.

RESULTS AND DISCUSSION

Plants are sessile organisms that face a range of abiotic stresses, which are increasing on a global scale. High salinity is one of the major abiotic stress factors that significantly reduce crop yields and productivity. High NaCl conditions adversely affect plant growth through increased osmolarity, ion toxicity (i.e., Na^+, Cl^-, and SO_4^-), nutritional imbalance, and oxidative stress (Turkan and Demiral 2009). The main toxic effects of Na^+ include inhibition of enzyme activities and disruption of intracellular K^+/Na^+ homeostasis (Zhu 2002). To cope with high salinity, plants have developed a number of mechanisms (Jithesh and Wally 2012). Presently there is increasing interest in the use of naturally occurring ‘biostimulators’ for enhancing the growth of agricultural and horticultural crops. Bacteria, fungi and protozoa, as well as marine algae-based seaweed extracts, can produce or contain biostimulators (Kurepin et al. 2013) that improve plant tolerance to stress, including salinity (Figure 1). It is interesting that under control (no saline) or low salinity conditions there was no significant effect of the application of *A. nodosum* extracts. However, at 200 mM NaCl, *A. nodosum* treated plants were twice the size of untreated plants, and not much smaller than the controls. These results are in line with others showing that extracts of seaweeds, and in particular those of *A. nodosum*, can produce a stimulating effect on plant growth, promoting greater root formation, increased flowering and fertilization (Rayorath et al. 2008; Alam et al. 2014).

A. nodosum has been extensively used in agriculture as a plant biostimulant (Craige 2011). *A. nodosum* extract, when applied to plants, stimulates shoot growth and branching (Temple and Bomke 1989), increases lateral root development (Metting et al. 1990), and improves nutrient uptake (Yan 1993). It has also been reported to improve plants' tolerance to environmental stresses such as drought, salinity and frost (Nabati 1991; Nabati et al. 1994), and improve stress tolerance in sensitive crop plants. Studies on citrus, grapes, bermuda grass and Kentucky blue grass have demonstrated that *A. nodosum* extract improves abiotic stress tolerance (Zhang 1997; Zhang and Schmidt 1999; Fike et al. 2001). Several bioactive compounds, including betaines (such as -aminobutyric acid betaine, -aminovaleric acid betaine, laminine (N6, N6, N6-trimethyl lysine), and glycine-betaine have been detected in *A. nodosum* and in the commercial products of *A. nodosum* (Blunden et al. 1985). Therefore the mechanism by which *A. nodosum* extracts improves plant stress tolerance is complex and involves several parallel pathways.

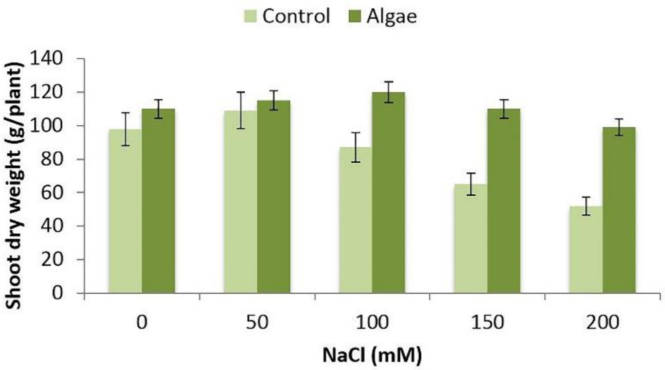

Figure 1. Biomass of plants (*Solanum lycopersicum*) not treated (Control) and treated with A. *nodosum* extracts (Algae) as a function of salinity. Bars represent mean values ± standard deviation (n = 6).

Taking into consideration the mineral composition of the leaves at the end of the experiment (Figures 2-4), it was evident that salinity was associated with a decrease in leaf K^+ concentration, accompanied by an increase in leaf Na^+ concentration. This Na^+/K^+ imbalance has been reported as a cause of salinity damage. Since Na^+ competes with K^+ for binding sites and hampers metabolism by inactivating enzymes responsible for essential cellular functions (Munns and Tester 2008; Kronzucker and Britto 2011; Shahbaz et al. 2012). Plants treated with *A. nodosum* extracts displayed neither decreased leaf

K^+ concentrations, nor increased leaf Na^+ concentrations in response to salinity (Figure 2 and 3). Even under the highest NaCl concentrations they maintained a Na^+/K^+ balance very similar to that of the control plants not exposed to salinity. The mechanism of entry of ions (including $K^+$and Na^+) into the root space, xylem loading and unloading, overall Na^+ distribution and its compartmentalization in the plant system are dependent on transport proteins for ionic fluxes, which are guided by the electrical gradient and membrane potential across the membranes (Zhang et al. 2009; Craig and Moller 2010; Hauser and Horie 2010; Kronzucker and Britto 2011; Hedrich 2012).

A high extracellular Na+ concentration increases the electrochemical gradient at the membrane, and thus favors passive transport. However, interpreting the effect of *A. nodosum* extracts is difficult, since there is currently little evidence of the direct involvement of a specific class of molecules in the regulation of ion selectivity in plants. Recent experiments with *A. nodosum* extracts suggest that their chemical components elicited endogenous biosynthesis of plant hormones (Rayorath et al. 2008; Wally et al. 2012). These hypotheses cannot be confirmed by our results, since hormonal analyses of the plants were not performed. However, based on the analysis of the leaf mineral components, one ion, Zn^+, did display a pattern across treatments which was in line with those of K^+ and Na^+ (Figure 4).

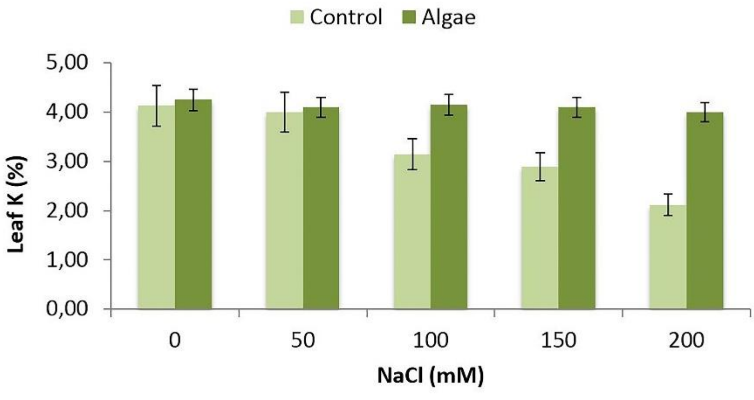

Figure 2. Potassium concentration in leaves of plants (*Solanum lycopersicum*) not treated (Control) and treated with *A. nodosum* extracts (Algae) as a function of salinity. Bars represent mean values ± standard deviation (n = 6).

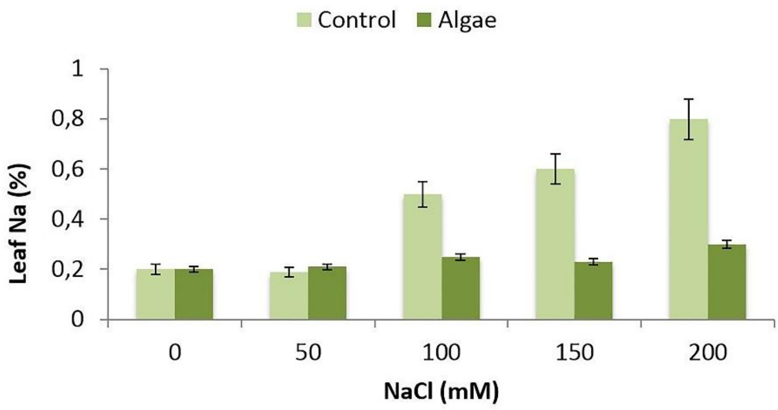

Figure 3. Sodium concentration in leaves of plants (*Solanum lycopersicum*) not treated (Control) and treated with *A. nodosum* extracts (Algae) as a function of salinity. Bars represent mean values ± standard deviation (n = 6).

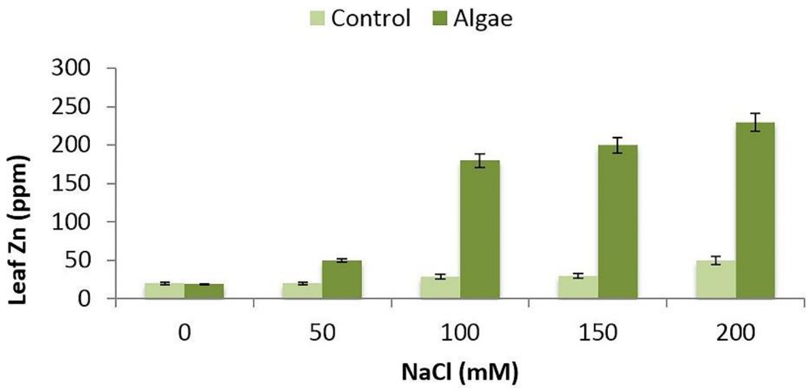

Figure 4. Zinc concentration in leaves of plants (*Solanum lycopersicum*) not treated (Control) and treated with *A. nodosum* extracts (Algae) as a function of salinity. Bars represent mean values ± standard deviation (n = 6).

This result makes sense considering the physiological functions of Zn^+. As a common consequence of many environmental stresses, enzymatic antioxidants' responses to oxidative damage are activated in order to protect cell structures. Zn^+ is a co-factor of many of the enzymes involved in the anti-oxidative stress, and it has even been suggested that Zn^+ may develop cells' protection against ROS-induced damage (Marschner 1995; Cakmak, 2000).

CONCLUSION

The main question that remains to be answered is how *A. nodosum* extracts interact with Zn^+ uptake and accumulation in leaves of tomato plants grown under saline conditions.

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Chapter 3

IMPACT OF SEAWEEDS IN AGRICULTURE

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ABSTRACT

Seaweeds contain a considerable amount of micronutrients and plant growth hormones like auxins, gibberellins, cytokinins, and betaines etc. which are supposed to help plant growth and also in seed germination. The extracts of seaweeds have proved itself as a highly effective and eco-friendly pesticide against various crop pests. This chapter provides an overview of the varieties of seaweeds, their ecology and their utilization worldwide. The main concept of this chapter delves into the possible utilization of selected seaweeds in agriculture. The various forms of seaweeds such as seaweed extract (SWE), compost, mulch etc. and their applications as bio-stimulators, growth promoters, crop protection, soil conditioner, and stabilizer are discussed.

Keywords: micronutrients, growth hormones, SWE, mulch, biopesticides

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INTRODUCTION

Seaweeds are a fascinating and diverse group of organisms living in the earth's oceans. They are found attached to rocks in the intertidal zone, washed up on the beach, as giant underwater forests and floating on the ocean's surface.

The seaweeds are either very tiny or quite large, growing up to 30 meters long. Although they have many plant-like features, the seaweeds are not true vascular plants; they are algae. They lack a specialized vascular system (an internal conducting system for fluids and nutrients), roots, stems, leaves, and enclosed reproductive structures like flowers and cones. Algae are a part of the Kingdom Protista, which means that they are neither plants nor animals.

All the parts of a seaweed are in contact with the water by which they are able to take up fluids, nutrients, and gases directly from the water, and do not need an internal conducting system. Like true plants, seaweeds are photosynthetic; they convert energy from sunlight into the materials needed for growth. Within their cells, seaweeds have the green pigment chlorophyll, which absorbs the sunlight they need for photosynthesis. Chlorophyll is also responsible for the green coloration of many types of seaweed. In addition to the chlorophyll, some seaweeds contain other light absorbing pigments. These pigments can be red, blue, brown or golden and are responsible for the beautiful coloration of red and brown algae. In addition, the pigments protect the seaweeds from UV radiation (Saranya 2013).

The Southern Coast of India bears luxuriant growth of seaweeds and more than 200 species of seaweeds have been found in this area. In the coastal waters, they grow almost like grass in large areas, extending over hundreds of kilometers. Indian seaweed industries depend on this coastline for the production of the phycocolloids agar, carrageenan, furcellaran, algin and many other commercially important products (Chapman 1980). The traditional uses of seaweed - as food, animal feed, and fertilizer supplements - remain important, but in most parts of the world, it is used as a raw material for certain chemical products that marine algae are now chiefly valued. The present chapter, whilst also considering the use of seaweeds in animal feedstuffs and fertilizers, deals principally with their positive impacts on agriculture.

Perhaps the longest established, most widespread and most proven use of seaweed is as a fertilizer. Wherever proximity to the coast has made access to the resource possible, seaweeds have been applied for many centuries to the land as direct and simple manure. Since 1950, the liquid seaweed products have enabled this practice to be extended, both geographically and in terms of specific uses (Blunden 1986).

Seaweeds contain reasonable quantities of nitrogen, phosphorous and potassium and they were extensively used, either directly or in the form of compost with cow dung as manure for vegetables in India. In seaweeds, the minerals and trace elements occur in water-soluble form and hence these could be easily taken up by plants (Booth 1966). The carbohydrates and other organic constituents of seaweeds are reported to increase the moisture holding capacity of soils. Seaweeds are a good source of potash and soda (Myklestad 1964).

The large brown algae, for example, *Macrocystis* and *Ascophyllum,* are the principal species used for manure. Their value as a fertilizer derives not so much from their nitrogen, phosphorus and potassium contents but rather from their unusual properties as a soil conditioner and growth promoter. The seaweed fertilizer has been demonstrated to produce positive effects additional to those to be expected from their content of N, K and P. For example, seaweeds and liquid seaweed manures appear to promote resistance to plant diseases and plant pests, induce the fruit setting and increase the germination rates (Crouch 1993).

SEAWEED ECOLOGY

Seaweeds are subjected to harsh environmental conditions as they occupy very dynamic strata of the oceanic ecosystem. Because seaweeds absorb gases and nutrients from the surrounding water, they rely on the continual movement of water past them to avoid nutrient depletion. The constant motion of ocean water also subjects seaweeds to mechanical stress. Seaweeds cope with mechanical stress by having a strong holdfast, a flexible stripe, and blades, and bending towards the substrate as waves move over them (Kaliaperumal 1987). Intertidal seaweeds are subjected to the stresses associated with exposure to air and weather conditions. To survive in the intertidal zone, seaweeds must be able to tolerate or minimize the effects of evaporative water loss and temperature and salinity changes. When exposed to air, the seaweeds lose water through evaporation. Some seaweed can dry out almost completely when the tide is out, then take up water and fully recover when the tide brings water back to them. Seaweeds living in tide pools are exposed to changes in water temperature and salinity caused by the weather conditions (Costa Pierce 2002).

When the tide is out mobile intertidal animals must also try to minimize water loss. One way they do this is by seeking out a moist hiding place under some seaweed. The intertidal seaweeds provide shelter for the invertebrates and also act as a food source for grazing animals (Dhargalkar 2005).

SEAWEED CLASSIFICATION

Seaweeds are classified into three major groups; the green algae (Chlorophyta), the brown algae (Phaeophyta), and the red algae (Rhodophyta) (Figure 1). The seaweeds are placed into one of these groups based on their pigments and coloration. The other features used to classify algae are; cell wall composition, reproductive characteristics, and the chemical nature of their photosynthetic products (oil and starch). Within each of the three major groups of algae, further classification is based on the characteristics such as plant structure, form, and shape (Dhargalkar 2004).

- Brown Algae (Phaeophyta)
- Green Algae (Chlorophyta)
- Red Algae (Rhodophyta)

Traditionally, the coastal communities worldwide have been using drift seaweed as soil amendment and fertilizer. This practice is, however, very limited among the farmers worldwide. Around 1.5 million metric tons of seaweeds are used as a nutritional supplement, fertilizer, and bio-stimulant (FAO 2006). Among the seaweeds classes listed above, brown seaweeds like *Fucus*, *Laminaria*, and *Sargassum* are mostly utilized in agriculture at coastline areas. Some of the commercial products available on the market are listed in Table 1.

Table 1. Commercial seaweed products

Type of seaweed	**Product**	**Manufacturer**
Ascophyllum nodosum	Maxicorp	Brandon products
Ecklonia maxima	Kelpak	Kelp Products International
Ascophyllum nodosum	Algea	Seagro
Durvillaea sp.	Seasol	Seasol International
Ascophyllum nodosum	Stimplex	Acadian SeaPlant
Ascophyllum nodosum	Seacrop	Atlantic laboratories
Ascophyllum nodosum	Biovita	PI Industries Ltd.

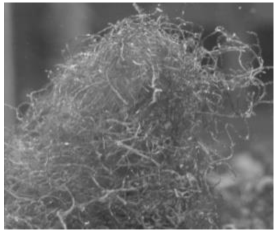
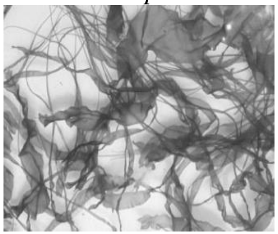
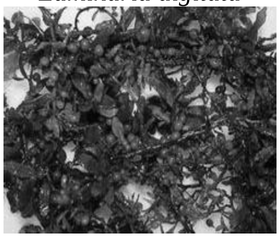
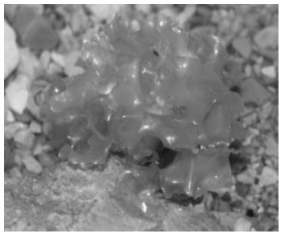
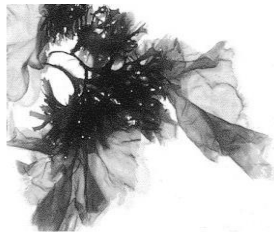
Brown Algae (Phaeophyta)	**Green Algae (Chlorophyta)**	**Red Algae (Rhodophyta)**
 *Fucus vesiculosus*	 *Chaetomorpha linum*	 *Gracilaria edulis*
 *Laminaria digitata*	 *Ulva intestinalis*	 *Gelidiella acerosa*
 *Sargassum wightii*	 *Ulva lactuca*	 *Porphyra sp.*

Figure 1. Varieties of seaweeds.

UTILIZATION IN AGRICULTURE

Seaweeds have been used in agriculture in various forms owing to the advantages it holds in nature. Some of them are listed below:

1. Enhance soil fertility

Seaweeds are rich in beneficial trace minerals and essential nutrients required for the plant growth. In addition to these, the seaweeds have hormones that stimulate plant growth. When mixed with the soil, the nutrients enrich the fertility of the soil and improve the nature of the soil (Stephenson 1968).

2. Improves root and shoot growth and development

Seaweed fertilizer contains lots of ready to use micro-nutrients which can be readily absorbed by the plants without any further chemical decomposition. This enhances the root and shoots development in plants at a faster pace (Gayathri et al. 2013).

3. Promotes the growth of symbiotic soil microbes

The seaweeds serve as a suitable growth medium for beneficial microbes that in turn play an important role in nutrient recycle (Verkleij 1992).

4. Increases nutrient uptake

Seaweeds have the necessary micro-elements and nutrients which on absorption increases the nourishment of the plants (Pramanick 2013).

5. Defensive against pests and diseases by crystal formation

The pests are immediately repelled by two things – salt and sharp-edged materials. Seaweed has a natural salt content, which repels unwanted organisms, and within a few days of application, it dries and becomes quite crispy. Pests do not like “crispy” surfaces, as the sharp salty edges cut into the soft body tissue (Jayaraj2015).

6. Triggers flowering and fruit yield

Seaweeds are reported to contain the growth-promoting hormones like auxins and gibberellins, which triggers root and shoot formation.

*Better moisture retention

*Induces seedling germination

Seaweeds act as a source of bio-stimulants and organic matter, which led to their extensive use in agriculture (Sridhar 2011).

BIOFERTILIZER

Seaweeds have been utilized as a bio-fertilizer over many years to enhance the fertility of the soil and improve the productivity of seasonal crops. Several approaches were followed to use the seaweeds as bio-fertilizers.

SEAWEED EXTRACTS (SWE)

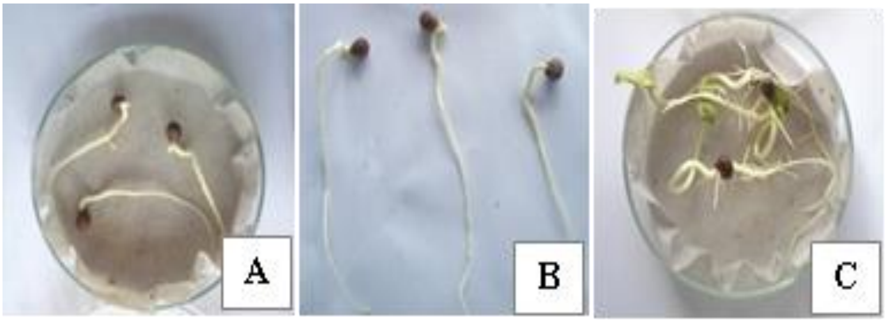


Figure 2. Germination of Okra seeds by three SWE.

(A) *Chaetomorpha linum.* (B)*Enteromorpha intestinalis.* (C) *Gracilaria edulis.*

The liquid extracts were widely used since 1950 and many commercial products are used worldwide currently. These liquid extracts were reported to improve the soil aeration and structure thereby makes the mineral nutrients available for the plants to a large extent (Zodape 2008). This may act as a stimulant, which increases the seed germination rate (Fig 2) and thereby supports shoot and root development. Seaweeds may improve the yield of flowers and fruits production by behaving like a chelator. Seaweed extracts were observed to be composed of many micro and macronutrients, which are essential for the growth of plants (Anantharaj 2001). Commonly used seaweed extracts were made from *Fucus sp., Ascophyllum nodosum, Laminaria, Turbinaria, and Sargassum spp* (Zodape 2001).

Various methods are available to prepare the seaweed extracts and widely categorized as physical and chemical methods. Physical methods include disruption using high pressure or milling whereas the chemical methods include heating seaweeds with various solvents to produce a 100% extract (Anantharaj and Venkatesalu 2001). The nutritive value of extracts may be enhanced by micronutrients addition, because the quality of extract may vary according to the place/season of collection and the process of extraction used.

Treatment with the SWE was observed to increase the photosynthetic pigments, protein, soluble sugars, starch, phenols, vitamin C, free amino acids, and the lipid content in crop plants like tomato, lady finger, fenugreek, mustard, maize, green gram and cluster bean (Mohanty et al. 2016). The presence of minerals, hydrophilic potash and other trace elements in SWE are readily absorbed by plants and regulate the deficiency of nutrients in plants. The non-toxic, non-polluting and biodegradable nature of the SWE makes it a desirable candidate for the agricultural application.

Seaweed Mulch/Compost

There are certain drawbacks in the application of foliar spray viz. rain wash out, recurrent applications, low absorption rates by leaves etc. In this case, seaweeds are used in the form of compost in combination with cow dung or any organic matter in India (Kalimuthu et al. 1987). On applying to the soil as compost, the carbohydrates (e.g., laminarin, fucoidan, alginate etc.) and the other organic constituents of the seaweeds tend to increase the moisture-holding capacity of the soil. It was reported that 0.1 g of sodium alginate, when added to 100 g of soil, increased the water holding capacity by 11% (Stephenson 1968). Similarly, the decomposed brown seaweeds provide polyuronides such as alginates and fucoidans to the soil bacteria that dwell in the rhizosphere. These are hydrophilic polysaccharides, which absorb soil moisture, swell into a gel and provide better aeration to the soil (Myklestad 1964). The aeration improves the growth and activity of symbiotic soil bacteria, which can fix atmospheric nitrogen to the plants. The compost may serve as a soil conditioner by enhancing the capillary activity of the soil pores and sustained release fertilizer improving aggregation of the soil. The properties of the compost, which are responsible for improving the soil fertility, are biochemical composition, the pattern of mineralization and synchronization of minerals and nutrients with the demand for the crops.

Growth Stimulator

Bio-stimulant (metabolic enhancer) is defined as a constituent other than the fertilizer that shall promote plant growth when applied in diluted proportion. The fertilizers supply the nutrients whereas the bio-stimulants induces root and shoot elongation, initiation of metabolic functions and alter cell division. The seaweed extract has to be diluted in the ratio of at least 1:1000 before applying as a foliar spray since the extract shall act as a bio-stimulant only at low concentration (Hattori 1999). A high concentration of the metabolic enhancers may be phytotoxic and may cause severe damage to plants.

Several researchers reported that the seaweeds contain plant hormones like auxin, cytokinin, gibberellic acid, betaines and sterols among which cytokinins are present in larger proportion when compared to other phytohormones. Cytokinins help in drawing the mineral and nutrients from the surrounding environment into the plant tissues and stimulate the plant growth (Mooney and Staden 1986). The cytokinins improve cell division and cell wall formation which are the prime factors to initiate growth in a plant. Cytokinins are important in seed germination by stimulating cell enlargement in cotyledons and initiate radical growth (Letham 1994). It influences the unloading of phloem into the cytoplasm, reduces leaf senescence and accelerates differentiation of the chloroplasts (Aldworth 1987). In plants, cytokinins are naturally secreted in the root and signal the plant to produce larger foliage. When given as a growth stimulant, the ratio of cytokinin to auxin should be balanced well. An increased level of cytokinins promotes the growth above the ground level only leaving the roots in an underdeveloped state.

Auxins are the second highest growth hormones present in the seaweed and are believed to kindle the root growth in various plants. Based on the quality and mass of the root, the nutrient uptake by the plant shall be determined. A denser root is articulated towards better absorption of nutrients as well as better support for the plant (Zhao 2010).

Sodium salts were believed to enhance the metabolism and synthesis of chlorophylls in plants (Khan 2009). The plants treated with seaweeds were observed to retain the chlorophyll content for a longer period of time when compared with the control crops. Certain seaweed extracts have betaines which greatly decreases the chlorophyll degradation and show longer photosynthetic retention. In few studies, the dry weight of root and shoot developed in seaweed treated plant measured greater than the untreated plants.

Table 2. List of various types of pest attacking important agricultural crops

Agricultural crops	Crop plant	Pests
Cereals and millets	Paddy	*Scirpophaga incertulas, Orseolia oryzae, Spodoptera mauritia, Pelopidas mathias, Cnaphalocrocis mainsails, Melanitis ismene, Psalis pennatula, Hieroglyphus banian, Dicladispa armigera, Hydrellias asakii*
	Sorghum	*Atherigona varia soccata, Chilo partellus, Sesamia inferens, Helicoverpa armigera, Peregrinus maidis, Contarinia sorghicola,*
	Maize	*Atherigona orientalis, Cryptoblabes gnidiella, Myllocerus sp., Chilo partellus, Sesamia inferens, Pyrilla perpusilla, Helicoverpa armigera, Rhopalosiphum maidis, Calocoris angustatus, Peregrinus maidis*
	Pennisetum glaucum	*Atherigona approximate, Geromyia penniseti, Chilo partellus, Sesamia inferens, Nezara viridula*
	Finger millet	*Sesamia inferens, Calocoris angustatus, Rhopalosiphum maidis, Tetraneuranigri abdominalis,* ***Spodoptera exigua,****Chrotogonus trachypterus, Nephrosclerosis medinalis*
Pulses	*Cajanus cajan*	*Helicoverpa armigera,Lampides boeticus, Euchrysops cnejus, Exelastis atomosa, Maruca testulalis, Etiella zinckenella, Adisura atkinsoni, Melanagromyza obtuse, Aceria cajani*
	*Vigna mungo***,** *Vigna radiate*	*Helicoverpa armigera, Empoasca kerri, Marucat estulalis, Riptortus pedestris, Etiellazincke nella, Coptosoma cribraria, Lampides boeticus, Bemisia tabaci, Euchrysops cnejus, Mylabris phalerata, Aphis craccivora*
	Vigna unguiculata	*Helicoverpa armigera, Empoasca kerri, Maruca vitrata, Riptortus pedestris, Etiella zinckenella, Lampides boeticus, Euchrysops cnejus, Aphis craccivora, Mylabris phalerata, Bemisia tabaci, Coptosoma cribraria*
	Soybean	*Spilosoma oblique, Aphis spp., Helicoverpa armigera, Apheliona maculosa, Spodoptera litura, Oberea (Obereopsis) brevis, Thrips tabaci, Melanagromyza sojae, Bemisia tabaci*
Oil seeds and cash crops	**Sun flower**	*Helicoverpa armigera, Spilosoma obliqua***,** *Amrasca biguttula, Psittacula krameri, Spodoptera litura*
	Groundnut/Peanut	*Amsacta albistriga, Empoasca kerri, Aproaerema modicella, Scirtothrips dorsalis, Spilosoma (Diacrisia) oblique, Sphenoptera indica***,** *Spodopteralitura, Helicoverpa armigera,Aphis craccivora*
	Cotton	*Helicoverpa armigera, Pectinophora gossypiella, Earias vittella, Pempherulus affinis, Sphennoptera gossypii, Spodoptera litura, Mylloecerus undecimpustulatus, Amrasca biguttula, Aphis gossypii*
	Sugar cane	*Chilo infuscatellus snellen, Chilo sacchariphagu sindicus, Scirpophaga excerptalis, Aleurolobus barodensis, Ceratovacuna lanigera, Saccharicoccus sacchari*

Courtesy: http://agritech.tnau.ac.in/

PEST MANAGEMENT

Almost 40% of crop production is destroyed by insects and pests throughout the world. More than 70,000 varieties of pests are available throughout the world and some of the pests which make damages to the prime crop plant around the globe are listed in Table 2. These pests are controlled by use of chemical pesticides (nearly 3 million tons/year) along with crop rotation and other biological methods (Pemsl 2006). The pest outbreaks may be due to change in the environmental condition which includes weak soil bases, change in the ecosystem and also due to native pests and pathogens. The use of chemical pesticides may destroy the beneficial organisms present in the agricultural land and on continual usage may develop resistant to the native pest. The pesticides or insecticides may also alter the physiology of the crop plants which in turn make the crop more susceptible to new pest varieties. When we observe the crop production, approx. 90% crops are newly introduced as hybrid variety in the agricultural land and these varieties do not have the natural resistance to the native pests which makes them a potent parasite (Patricia 1998).

Pests dwell in the soil where there is a high concentration of organic compounds. They tend to feed on the shoots and roots from the fresh seedling thereby disturbing the normal growth and development of a plant. Seedlings are least resistant towards pest attack and can cause enormous economic damage. The soil-borne pests can be controlled by prior treatment of seeds with pesticides and then planted. While using seaweed extracts, the seeds are soaked in the extract for a stipulated period of time and shade-dried before plantation. Seaweeds contain natural salt like sodium, chloride, and potassium which when applied on the seed get dried by the atmosphere. The dried salt gets converted into sharp crystals and prevents the slugs/pests from holding onto the plants. The reason is that the crystals tear away the soft tissues of the pests and makes significant damage. The extracts do not allow the pests to lay their eggs and hence reduces the chance of pest population explosion. It also restricts the movement of the pest in and around the area of application.

STRESS MANAGEMENT

Drought, salinity, and temperature are some of the abiotic stresses, which tend to decrease the crop yield. The rhizosphere is an area around the root mass of plants which holds symbiotic bacteria and provides nutrient to the plant in drought condition. As discussed earlier, the plant growth hormones present in the seaweed compost develops a better environment for the soil microbes and increases the drought tolerance in many plants. The stronger root structure also supports the plant to resist against a certain type of epidemic diseases which outburst in stress conditions. The stress due to drought declines the chlorophyll content and nitrate reductase activity. The photosynthetic pigments are enhanced and few reports suggested about the faster recovery of crop plants like maize, ragi etc. by the application of SWE. SWE were found to induce the defensive enzymes (e.g., chitinase, flucanase, lipoxynase, peroxidase etc.) of plants, which reduces disease during stress conditions.

The SWE showed the presence of many bioactive substances which pertain to the antioxidant activity imparted by them. Under environmental stress condition, reactive oxygen species (ROS) are produced in the plants which should be neutralized by the antioxidants secreted within the plants. But this balance between ROS production and the quenching mechanism will be disturbed if the plant is under stress for a very long period of time. The plant hormones are also secreted in various environmental conditions and are seasonal dependent. The phytohormones mobilize from production site to action site and act as messengers that control various metabolic functions. The bioactive compounds and the phytohormones, which are available in the seaweeds, shall help the plant to recover from the environmental stress condition and enhance the stress tolerance capability (Gayathri et al. 2016).

DISEASE MANAGEMENT

Many bacterial species, fungi, mycoplasma, and virus are known to produce severe diseases in the plants. Some of the major diseases caused by these microorganisms to crop plants are shown in Table 3. Reports say that SWE can increase the resistant towards diseases in plants (Pardee et al. 2004). Continuous applications of SWE to the plants may decrease the level of nematode attack. The secondary metabolites present in seaweeds shall be responsible for enhancing the defense mechanism of the host plants, controls the population of the parasites, and thus improves disease resistance. Certain seaweeds have also been reported to have antimicrobial activity against Gram positive and Gram negative organisms which may be attributed to the presence of acrylic acid like 1-aminocyclopropane-1-carboxylic acid.

Table 3. Pictorial representation of various plant diseases and the responsible pathogens

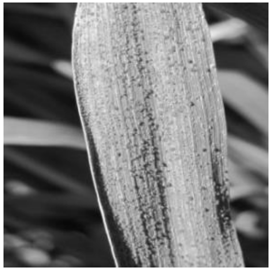
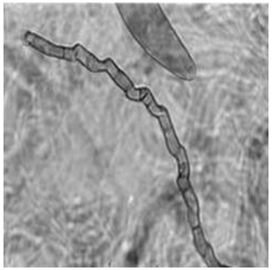
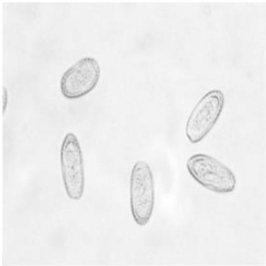
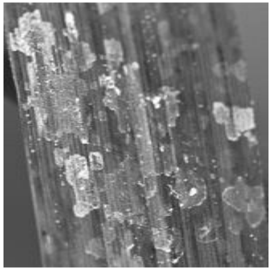
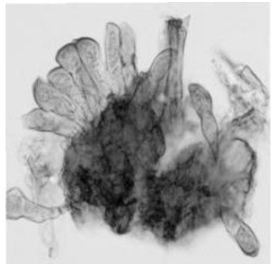
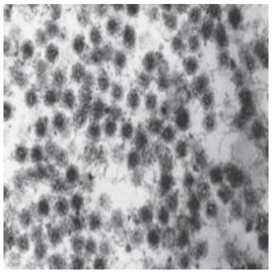
Disease	**Organism**	**Disease**	**Organism**
Blast 	*Pyricularia oryzae* 	*Leaf rust* 	*Puccinia recondita* 
Brown spot 	*H. oryzae* 	*Stem Rust* 	*Puccinia graminis* 

Table 3. (Continued)

Disease	Organism	Disease	Organism
Leaf blight 	*Xanthomonas oryzae* 	*Yellow rust* 	*Puccinia striiformis* 
Ragged stunt virus 	*Rice ragged stunt virus* 	*Mildew* 	*Erysiphe graminis* 

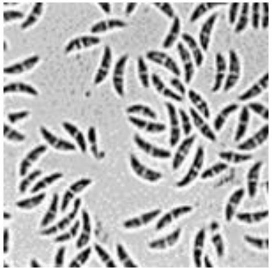
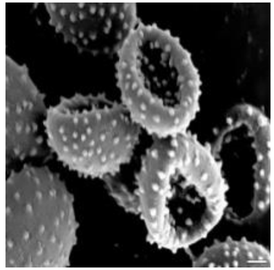
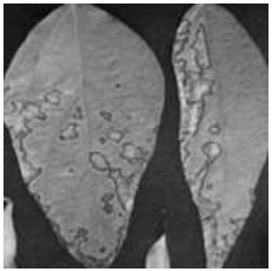
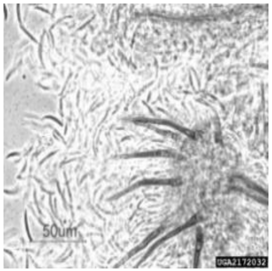
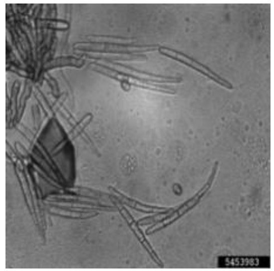
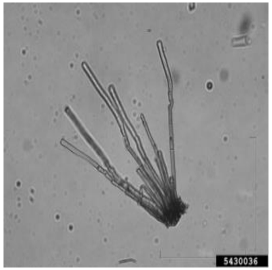
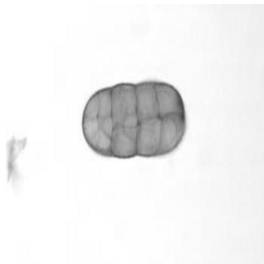
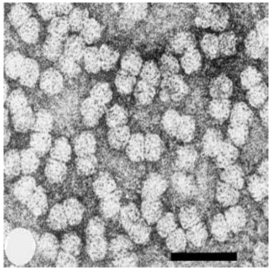
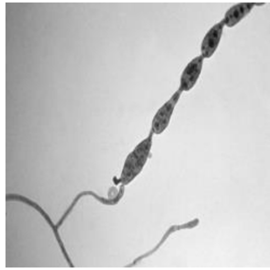
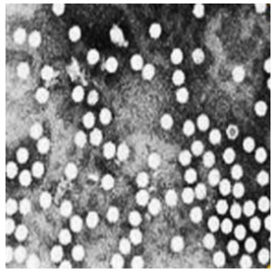
Disease	**Organism**	**Disease**	**Organism**
Leaf scald 	*Microdochium oryzae* 	**Loose Smut** 	*Ustilago tritici* 
Anthracnose/pod blight 	*Colletotrichum truncatum* 	**Early leaf spot** 	*Cercospora arachidicola* 

Table 3. (Continued)

Disease	Organism	Disease	Organism
Purple seed stain 	*Cercosporaki kuchii* 	*Stem rot* 	*Sclerotium rolfsii* 
Charcoal rot 	*Macrophomin aphaseolina* 	*Late leaf rot* 	*Phaeoisariopsispersonatum* 

Disease	**Organism**	**Disease**	**Organism**
Yellow mosaic 	MBYMV 	**Alternaria leaf disease** 	*Alternaria arachidis* 
Banana Bract 	Potyvirus 	**Bunchy Top** 	*Bunchy top virus* 

Courtesy: http://agritech.tnau.ac.in/

The *A. nodosum* extract was reported to improve the disease resistant in capsicum plant due to the increased peroxidase activity and phytoalexin level. Cabbage seedlings treated with 1% SWE before inoculation decreased the incidence of a disease caused by *Phythium ultimum* (Walsh 2006). The extract of *Ascophyllum* species reduced the dollar spot disease caused by *Sclerotinia*, bacterial leaf spot caused by *Xanthomonas* and infection of *M. phaseolina* in the creeping bent grass, tomato and okra respectively (Jayaraj 2015).

The general mechanisms with which seaweeds impart disease resistance in plants are listed below:

- Improved vigor of the plant contributed by the robustness, increased photosynthesis, enhanced mobilization of the nutrients, improved regeneration and augmentation.
- Increased the presence of secondary metabolites like flavonoids, terpenoids, tannins, phenols, antioxidants and pigments.
- The signaling molecules may induce the systemic resistance in plants.
- Inhibition of microbial growth or killing of pathogen due to the antimicrobial agents present in the extract.
- Enhanced production of disease resistant enzymes and inducing the transcription of defense genes by the sugars and betaines in SWE.

CONCLUSION

Seaweeds, unlike plants growing in soil, take up the majority of their nutrients from the medium they live in: the seawater. They absorb nutrients directly into their tissues. The ‘roots’ on seaweeds have the main function of anchoring the plant. There are over 79 minerals and trace elements in seaweed, and using seaweed is a superior way of bringing in copper, manganese, potassium, phosphorus, iron and zinc to the soil, plants, and animals in a plant-available form.

Liquid seaweed concentrate is used either as a soil conditioner or as a foliar fertilizer. It could be applied in a concentrated form or much diluted and can be easily mixed with other sprays. The use of liquid concentrate for soil conditioning gives quick results, but not necessarily long lasting. For barren soils, a seaweed meal might be more beneficial in the longer term. The cost of seaweed meal applications is considerably higher than for concentrate applications, and this is a point that must be considered for larger acreages.

This chapter dealt with all the beneficial applications of seaweeds for various agricultural practices.

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Chapter 4

EFFECT OF SEAWEEDS IN PHYTO-REMEDIATION

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ABSTRACT

Heavy metals and organic pollutants are introduced into the aquatic ecosystems as a result of human activities involving agricultural uses, industrial discharges, domestic effluents and agricultural runoff. These contaminants such as herbicides, pesticides, nitrogen and phosphate fertilizers, heavy metals... etc., have negative impacts on both the stability of the natural aquatic environment (intensification of eutrophication, contamination and disappearance of certain animal and plant species...) and can cause adverse effects on human health. Recently there has been an increasing interest in using seaweeds for water quality assessment and for removal of heavy metals and organic pollutants. In this review, we will discuss the use of macroalgae as bioindicators for monitoring and protecting aquatic environments and different mechanisms used by these seaweeds for metal accumulation and detoxification.

Keywords: biosorption, bioaccumulation, phytoremediation, seaweeds

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1. INTRODUCTION

The accumulation of organic pollutants (pesticides, PCBs, DDT…) and heavy metals (Cd, Pb, Se, As…) in the aquatic systems can cause serious problems on environment and organisms affecting negatively the stability of many aquatic ecosystems and can also cause difficulties for animals and human health [1]. Although some metals are necessary for biological processes, all of them are toxic at high concentrations. This is due to their oxidative capacity to form free radicals and their ability to replace essential metals in enzymes, interrupting their normal activity [2]. Other metals are not essential and accumulate in different organisms and because of this they are toxic even at low concentrations. Mercury, chromium, lead, arsenic, copper, cadmium, cobalt, zinc, nickel, beryllium, manganese and tin are the most toxic heavy metals according to the United States Environmental Protection Agency (EPA) [3]. Many aquatic ecosystems have been subjected to industrial waste discharge. Domestic and agricultural pollution generating both organic and inorganic contamination, such as pesticides and heavy metals, are leading to widespread contamination of both surface and groundwater by runoff. Metals are introduced into the aquatic ecosystems as a result of weathering of soil and rocks, from volcanic eruptions and from a variety of human activities involving mining, processing and use of metals and/or substances containing metal contaminants [4]. These heavy metals may also be derived from remobilization from natural soils due to the changes in local redox conditions and the corrosion of subsurface engineering structures due to prolonged submergence under acidic groundwater [5]. Studying the bioavailability and origin of heavy metals from the Nador lagoon sediments, González et al. [6] found that the most important trace-element anomalies (As, Cd, Co, Cu, Mn, Pb, Zn) were found, mainly around industry and old mining activities. Industrial activity has led to very high heavy metal concentrations on the environment, which are in general 100–1000 fold higher than those in the Earth's crust, and locally, living organisms can be exposed to even higher levels [7]. In a river polluted by base-metal mining, cadmium was the most mobile and potentially bioavailable metal and was primarily scavenged by non-detrital carbonate minerals, organic matter, and iron-manganese oxide minerals [8]. Although mercury is a naturally occurring element and it was always present in the environment, global human activity has led to a significant increase of mercury released into the atmosphere, aquatic environment and land [9]. Wang et al. [10] suggested that the most important anthropogenic sources of mercury pollution in aquatic environment are atmospheric deposition, urban discharges, agricultural material runoff, mining, fossil fuel use and industrial discharges, burning of coal, and pharmaceutical production [10]. In order to control heavy metal levels before they are released into the environment, the treatment of the contaminated wastewaters is of great importance since heavy metal ions accumulate in living species with a permanent toxic and carcinogenic effect [11, 12]. The most common treatment processes used include chemical precipitation, oxidation/reduction, ion exchange, membrane technologies, especially reverse osmosis, and solvent extraction. Each process presents advantages, disadvantages and ranges of applications depending on the metal ion, initial concentration, flow rate or raw water quality [13]. Martínez-Jerónimo et al. [14] suggested that chemical contaminants present in the aquatic ecosystem may be immobilized and accumulated in sediments or may be subject to transformation and activation processes [14]. Depending on biogeochemical processes, many organic pollutants like hydrocarbons are involved in adsorption, desorption and transformation processes and can be made available to benthic organisms as well as organisms in the water column through the sediment–water interface [15].

Physicochemical processes, conventionally used for metal removal, often have high operating costs, generate large amounts of sludge which require a proper disposal, or are ineffective when aim is to achieve very low residual levels [3, 16].

Relatively recently, there has been increasing interest on the use of bioremediation as the most desirable technology which uses seaweeds and other organisms for removal of environmental pollutants or detoxification to make them harmless [1, 17, 18]. Seaweeds can eliminate heavy metals by two processes: bioaccumulation and biosorption. Biosorption is a term that describes the removal of heavy metals by the passive binding to non-living biomass from an aqueous solution; however, the bioaccumulation describes an active process whereby removal of metals requires the metabolic activity of a living [19]. Investigation on organic xenobiotics bioaccumulation/ biodegradation in green algae is of great importance from environmental point of view because widespread distribution of these compounds in agricultural areas has become one of the major problems in aquatic ecosystem [20]. Some algae and microorganisms have developed various strategies for their survival in heavy metal-polluted habitats, these organisms are known to develop and adopt different detoxifying mechanisms such as biosorption, bioaccumulation, biotransformation and biomineralization, which can be exploited for bioremediation either *ex situ* or *in situ* [21-24]. Biosorption may be simply defined as the removal of substances from solution by biological material. Such substances can be organic and inorganic, and in soluble or insoluble forms [25]. Biosorption is a physico-chemical process and includes such mechanisms as absorption, adsorption, ion exchange, surface complexation and precipitation.

This chapter will highlight our current understanding on the involvement of seaweed in bioremediation of heavy metals and different strategies used by these species for metal accumulation and detoxification.

2. Mechanisms of Metal Accumulation and Detoxification

2.1. Cell Wall Adsorption

There are several chemical groups that could contribute to the metals acquisition by biomass: acetamido groups of chitin, structural polysaccharides of fungi, amino and phosphate groups in nucleic acids, amino, amido, sulfhydryl, and carboxyl groups in proteins, hydroxyls in polysaccharides, and mainly carboxyls and sulfates in the polysaccharides of marine algae that belong to divisions Phaeophyta, Rhodophyta, and Chlorophyta [26].

Algae have been used extensively as biosorbent material more than other kinds of biomass [27, 28]. Their ability focused on the composition of cell wall which includes molecules such as chitin, polysaccharides, proteins and lipids. These molecules have different groups such as phenolic, hydroxyl and carboxyl, which can form complexes with heavy metals. Previously, Wang et al. [29] suggested that polysaccharides such as cellulose, chitin, and alginates that are constituents of cell walls of fungi and algae participate in capturing metals. Stary and Kratzer [30] reported that the algae cell wall behaves like a weak acidic cation exchanger containing various cell wall ligands with different exchange capacities.

The cell walls of seaweeds (Phaeophyta, Rhodophyta and many Chlorophyta) are composed of at least two different layers (Figure 1). The innermost layer consists of a microfibrillar skeleton that imparts rigidity to the wall [19]. The outer layer is an amorphous embedding matrix [32, 33]. Takeda and Hirokawa [34] demonstrated that the cell wall of the green algae *Chlorella ellipsoidea* was composed of two major constituents: alkali-soluble hemicellulose and alkali insoluble rigid wall. The former was composed of neutral sugars, rhanmose, xylose, arabinose, mannose and glucose, and the letter had glucosamine as a main constituent.

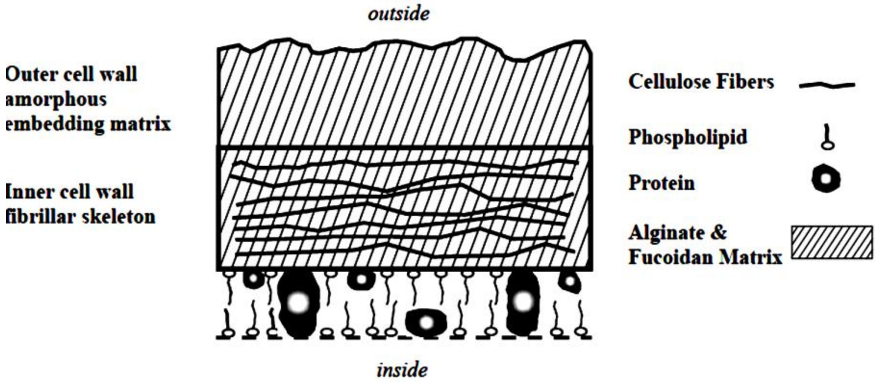

Figure 1. Cell wall structure in the brown algae [31].

The most common fibrillar skeleton material is cellulose which imparts rigidity to the cell wall [35]. It can be replaced by xylan in the Chlorophyta and Rhodophyta in addition to the mannan in the chlorophyta [19]. Besides cellulose, red and green algae contain, respectively, agar and carragenates, rich in sulfated polysaccharides, and glycoproteins, which comprise amino, carboxyl, sulfate and hydroxyl groups [36].

Lahaye and Robic [37] reported that among the polymers synthesized by the green seaweed *Ulva* and *Enteromorpha* cell wall polysaccharides represent around 38-54% of the dry algal matter. These include four polysaccharide families in *Ulva* sp.: two major ones, the water-soluble ulvan and insoluble cellulose, and two minor ones, a peculiar alkali-soluble linear xyloglucan and a glucuronan (Figure 2). The carboxylic and sulphate groups of these polysaccharids have been identified as the main metals equestering functional ionic groups in marine algal cell wall [38].

Davis et al. [19] suggested that the phaeophyta algal embedding matrix is predominately alginic acid, with smaller amounts of the sulphated polysaccharide fucoidan, while the Rhodophyta contain a number of sulphated galactan (e.g., agar, carrageenan, porphyran, etc.). Both the Pheaophyta and Rhodophyta contain the largest amount of amorphous embedding matrix polysaccharides making them potentially excellent materials for heavy metal binding.

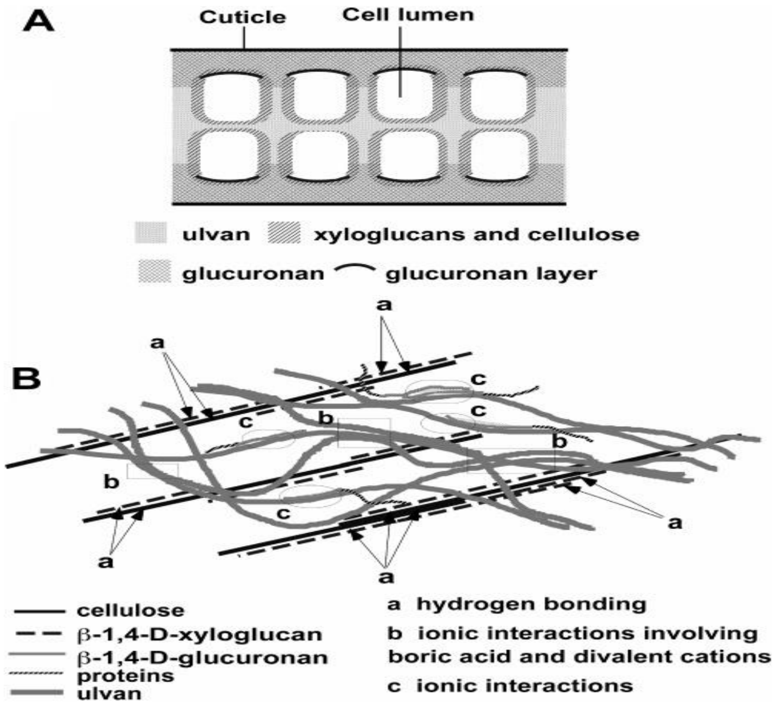

Figure 2. Distribution of the different *Ulva* sp. cell wall polysaccharides in a schematic cross section of a thallus (A) and proposed associations between the different cell wall polysaccharides (B) [37].

Poly-anionic polysaccharides of the red seaweed, associated with the cell walls and intercellular spaces, sequester cations through an ion exchange mechanism, thus partially preventing entry of metal ions into cells [39-41]. The brown algae have proven to be the most effective and promising substrates for the adsorption of heavy metals. The properties of cell wall constituents, such as alginate and fucoidan, are chiefly responsible for heavy metal chelation [19]. Carboxyl and sulfate are the predominant functional groups in brown algae cell walls, which are mainly composed by cellulose, alginic acid and sulfated polysaccharides [36].

2.2. Vacuolar Compartmentation

The vacuole is a suitable storage reservoir for excessively accumulated heavy metals [42]. Recently, Seth et al. [43] reported that translocation and storage of metals into vacuoles are an important phenomenon found in non-accumulators where it is an efficient defence strategy against elevated metal concentrations.

Suresh and Ravishankar [44] reported that algae have the ability to hyperaccumulate various heavy metals by the action of phytochelatins and metallothioneins forming complexes with heavy metals and translocate them into vacuoles. Hall [45] suggested that the efflux of ions at the plasma membrane or transport into the vacuole by tonoplast-located transporters are the two ways of reducing levels of toxic metals in the cytosol and so are potentially important mechanisms for heavy metal tolerance. The objective of this compartmentation is to remove the metals from the cytosol or other cellular compartments where sensitive metabolic activity takes place [46-48]. Therefore, the central vacuole seems to be a suitable storage reservoir for excessively accumulated heavy metals [42]. Volland et al. [49] reported that Al2(SO4)3 treatment resulted in an increase of the number of vacuoles as a mechanism for the accumulation and retention of heavy metals.

Cobbett and Goldsbrough [50] showed that the potential toxicity of accumulated metals can be decreased as a result of the formation and subsequent sequestration of "metal-phytochelatin complexes" in vacuoles *via* transport across the tonoplast. Similarly, Heuillet et al. [51] suggested that the metal–metallothionein complex ends up in the vacuole of the cell. This was observed in the microalga *Dunaliella bioculata*. The compartmentalization of Zn in vacuoles seems to be a general crucial detoxification mechanism for cells [52, 53]. In *Cardaminopsis halleri,* a heavy-metal-tolerant plant, the vacuole is the main depot for Zn, where it is stored as zinc silicate [54]. Increased uptake of metals has been achieved in several examples using transporters located in the tonoplast that sequester metals into the vacuole [55-57].

Kakinuma et al. [58] reported that the accumulation of most of the metal ions is driven by the electrochemical potential by electrogenic proton influxes via the vacuolar H^+-ATPase. Cd is transported across the tonoplast by a Cd^{2+}/H^+ antiport mechanism [59]. Rahman and Hassler [60] showed that the Phytochelatins build a complex with arsenite (As(III)–PC) and are sequestered into vacuoles through the activity of ATP binding cassette (ABC) transporters, being finally excreted from the cells. Song et al. [61] suggested that essential metal ions, such as Zn(II), Cu(II), and Mn(II), can be transported into vacuoles as forms of "PC2-metal complexes" through the putative ABC transporter(s).

2.3. Intracellular Sequestration

To maintain low concentrations of free metals in cytoplasm, plants have developed the competitive mechanism for chelation between heavy metals and low-molecular-weight (LMW) compounds [43]. LMW molecules are either thiol-containing compounds (metallothioneins: MTs, GSH, PCs) or not (e.g., histidine, nicotianamine, etc.).

Heavy metals are intracellularly chelated through the synthesis of amino acids, organic acids, glutathione (GSH), or heavy metal-binding ligands such as metallothioneins (MTs), phytochelatins (PCs) [42].

2.3.1. Chelation by Glutathione

Recent research studies provided experimental evidence that a strong antioxidant system, including high glutathione (GSH) levels, is present in different hyper-accumulators and that it is either needed or at least a beneficial trait in metal tolerance [62]. Glutathione (GSH), a nonenzymatic antioxidant, is a low molecular weight thiol implicated in a wide range of metabolic processes and constitutes an important plant defense system against environmental stresses, including HMs [42, 63]. Seth et al. [43] reported that GSH plays a crucial role, as it is not only important in metal chelation, but also in antioxidative defence and redox signalling, as well as in plant growth and development. Glutathione is a precursor for PCs synthesis, is also involved in the detoxification of toxic oxygen species [64], and is generated in response to pesticides [65]. GSH removes metals directly through chelation which processis catalyzed by the glutathione S-transferase [66]. Hossain et al. [42] suggested that GSH protects proteins against denaturation caused by the oxidation of protein thiol groups under stress and plays an indirect role in protecting membranes by maintaining α-tocopherol and zeaxanthin in the reduced state. Ahner et al. [67] reported that GSH has other functions, including the formation of phytochelatins, which have an affinity for heavy metals and are transported as complexes into the vacuole, thus allowing plants to have some level of resistance to heavy metals. Transgenic plants expressing glutathione (GSH) offer great promise for enhancing the efficiency of Cd phytoextraction from polluted soils and wastewater. These plants may also show increased tolerance to, and accumulation of, other heavy metals, because PCs are thought to play a role in tolerance of a range of heavy metals, especially nonessential heavy metals such as mercury and lead [1].

Torricelli et al. [68] analysed the GSH levels in wild type and chromium-tolerant strains of *Scenedesmus acutus*. The authors found that tolerant strain showed higher levels of reduced glutathione when the cells were exposed to Cd^{2+}.

In the green seaweeds there was an increase in the concentration of GSH with time of exposure to Cd (approximately two-fold higher in *Ulva lactuca* than in *Codium fragile*) when compared to controls [69]. *However, in the red seaweed Gracilaria gracilis* the concentration of GSH did not change. This is probably a consequence of lower intracellular accumulation of Cd by red than brown seaweeds, as previously reported for *Gracilaria tenuistipitata* and *Sargassum thunbergii* [70]. A reduction in the concentration of GSH with increased production of PCs was also evident when *Fucus serratus* was exposed to Zn, but the decrease was apparent after only 4 days [69].

Agrawal et al. [71] analysed the effect of different Hg treatments on glutathione content in a green algae *Chlorogonium eleongatum* (Dang) and they found that Mercury treatments increased the concentration of total glutathione, including both oxidized (GSSG) and reduced (GSH) Glutathione. The two brown seaweeds *Fucus serratus* and *Fucus vesculosus*, living in an environment with high concentrations of metals, maintained high concentrations of GSH despite synthesis of PCs, although the proportions of GSH to PCs differed between the two species; *Fucus vesiculosus* had a higher proportion of GSH [69]. Wu and Lee [72] showed that total GSH level did not change in *Ulva fasciata* exposed to increasing concentrations of copper, but GSH level increased in *Ulva lactuca* exposed to cadmium excess [73]. Thus, ulvophytes showed different antioxidant responses to heavy metals and, until now, *Ulva compressa* is the only ulvophyte showing GSH synthesis in response to copper excess [74].

2.3.2. Chelation by Phyochelatins

Phytochelatins (PCs), small sulphur-rich oligopeptides of the general structure (Glu-Cys)*n*-Gly, n = 2–11 and synthesized from reduced glutathione (GSH), are involved in homeostasis and detoxification of metals in the cells of higher plants, eukaryotic microalgae, some fungi. PCs are synthesized from GSH; the metal binds to the constitutively expressed enzyme γ -glutamylcysteinyl dipeptidyl transpeptidase (PC synthase), thereby activating it to catalyze the conversion of GSH to phytochelatin [75].

Algal species can respond to heavy metal exposure by synthesizing metal binding proteins known as phytochelatins [76]. Gekeler et al. [77] demonstrated that algae sequester heavy metals by an identical mechanism as higher plants, namely via complexation to phytochelatins. The two standard characteristics attributed to the PCs are that (1) PC synthesis can be stimulated in cells exposed to various metal ions such as Cd, Cu, Hg, Ni, Zn, Pb and Ag and (2) the formed PCs are capable of binding to multiple types of metals and metalloids [78, 79]. After the activation of PC synthase by the HM ions and HM chelation by the PCs synthesized, the HM ion complex is transported to the vacuole and stabilized there by forming a complex with sulfides or organic acid [80].

Some seaweeds show a high capacity for accumulation of heavy metals as results of tolerance mechanisms and many algae synthesize phytochelatins (PCs) that can form complexes with heavy metals and translocate them into vacuoles [44]. Pawlik-Skowrońska et al. [69] showed that seaweeds differ in their capacity to produce PCs, even when growing under the same environmental conditions and levels of pollution and the production of PC depends on factors such as morphology, biochemical composition (e.g., polysaccharides), intracellular metal accumulation and the status of the precursor for PC production.

Mellado et al. [74] reported that copper induced the synthesis of ascorbate, glutathione and PCs in *Ulva compressa* suggesting that these compounds are involved in copper tolerance. The total concentration of PCs measured in *Fucus* spp. and *S. chordalis* were positively correlated with the levels of metal contamination at the sites sampled and with the total concentrations of metals in the seaweeds [69]. Yadav [81] reported that PCs are synthesized inductively by exposure to not only Cd, but also by other heavy metals such as Hg, Cu, Zn, Pb and Ni. During the exposure of plants to such metals, PCs are synthesized from GSH by phytochelatin synthase (PCS) activity. Thus, marine macroalgae differ in their abilities to synthesize PCs in response to heavy metals and, in particular, *Ulva compressa* is the only ulvophyte showing synthesis of PCs in response to copper excess.

PCs ensure the homeostasis of Cu and Zn by transferring them to the apoenzymes in the necessary amount. The remaining amount of these metals are transferred to the vacuoles [75]. Recently, Roncarati et al. [82] studied the intra-specific responses to Cu-stress in two strains of the brown alga *Ectocarpus siliculosus* (Es524 and LIA), and they found that the higher intra-cellular concentrations of Cu, lower production of PCs, and lower expression of enzymes involved in GSH-PCs synthesis may be contributing to an induced oxidative stress condition in LIA, which explains, at least in part, the observed sensitivity of LIA to Cu. In Es524, there was an increase in the transcripts of γ-GCS, GS and PCS, particularly under high Cu exposure. Ahner et al. [67] reported that the two marine algae, *Thalassiosira weissflogii* and *Thalassiosira pseudonana*, produce phytochelatins in great amounts due to the higher activity of phytochelatin synthase, which has greater affinity for the glutathione substrate or metal ions. Increased production of PCs was also evident in the red seaweed, *G. gracilis*, upon exposure to Cd. Given that concentrations of PCs vary with intracellular concentrations of metals [83, 84], the data from the field and experimental studies suggest that the concentrations of PCs in seaweeds are mechanistically linked to uptake of metals and that they reflect the bioavailability of metals.

2.3.3. Chelation by Metallothioneins

Metallothioneins (MTs) are low molecular mass cysteine-rich proteins that can bind heavy metals such as Cd, Zn and Cu in thiol groups [85, 86] and can participate in the homeostasis of intracellular metal ions [87]. Since their discovery as Cd-binding proteins present in horse kidney, MT proteins and genes have been found throughout the animal and plant kingdoms as well as in the prokaryote *Synechococcus* and seaweeds [50, 88]. Ahn et al. [89] reported that plant MTs are thought to be primarily involved in cellular ion homeostasis. While it is likely that plant PCs and MTs both participate in heavy metal detoxification, their distinctive roles have not been clearly demonstrated. In the absence of MTs, or another ligand, free copper ions would precipitate a cascade of oxidative damage and disrupt the controlled senescence program [50]. Metal coordination takes place through the large number of cysteine sulfurs present in the protein forming two metal-binding domains in mammalian, crustacean, plant, and algal MTs [88-92]. Castiglione et al. [93] reported that besides detoxification, MTs may also take part in the regulation of gene expression and cell metabolism, by donating/accepting metal ions (e.g., Zn) to/from metal-dependent DNA-binding proteins or metalloenzymes [93]. The peptide is synthesized by some seaweed, which chelates metals and stores them in compartments within cell or segregates them from surrounding environment, hence preventing free heavy metal circulation inside the cytosol [94]. Since other stresses, like heat shock and aluminium, also induce this type of expression, it was suggested that these MTs might express as part of a general stress response [50]. There is, however, some evidence to suggest that MTs are involved in copper homeostasis and detoxification [95]. The biosynthesis of MTs is regulated at the transcriptional level and is induced by several factors, including hormones, cytotoxic agents, and HMs, such as Cd, Zn, Hg, Cu, Au, Ag, Co, Ni, and Bi [96, 97].

Morris et al. [88] identified and characterized the gene for metallothionein in brown seaweed *Fucus vesiculosus*. Recombinant metallothionein from brown seaweed *Fucus vesiculosus* (rfMT)1 has been reported to remediate arsenic [98].

2.3.4. Chelation by Amino Acids, phytate and Organic Acids

Besides the thiol-containing compounds (metallothioneins: MTs, GSH, PCs), other classes of metal-chelating agent have also been used for metal homeostasis, detoxification and tolerance (e.g., citrate, proline, malate, oxalate, nicotianamine (NA), histidine (His), phytate etc.) [99]. Kim et al. [100] found that transgenic *Arabidopsis* and tobacco plants that constitutively overexpress the barley nicotianamine synthase gen increased nicotianamine biosynthesis and conferred enhanced tolerance of high levels of metals particularly nickel. However, Hanikenne et al. [101] reported that phytosiderophore or his precursor nicotianamine are not found in algae and this function may thus have appeared after the emergence of land plants.

Amino acids and their derivatives, such as histidines, glycine, beetaine, proline, arginine, glutamate and cysteines, in isolation and/or in coordination with thiol compounds contribute to metal chelation in plants [45, 62, 102]. Sharma and Dietz [62] reported that upon exposure to metals, plants often synthesize a set of diverse metabolites that accumulate to concentrations in the millimolar range, particularly specific amino acids, such as proline and histidine, peptides such as glutathione and the amines spermine, spermidine, putrescine, nicotianamine, and mugineic acids [62]. Various peptides consisting of metal-binding amino acids (mainly histidine and cysteine residues) have been studied for enhanced heavy metal accumulation by bacteria [103, 104]. Histidine (His) has a high capacity to chelate heavy metals. The histidyl dipeptide *carnosine* (b-alanyl-l-*histidine*) with antioxidant activity thought to be associated with its ability to chelate transition metals was also characterized in red seaweed *Ancanthophora delilei* [105].

Organic acids such as malate, oxalate, aconitate, malonate, tartrate and citrate have been evidenced to contribute to metal chelation [45, 62, 102, 106]. Wuana et al. [107] suggested that citrate appeared to offer greater potentials as chelating agents for heavy metals. Citric acid has been considered a major ligand at low Cd concentrations [108]. Jauregui-Zuniga et al. [109] showed that calcium oxalate could play an important role in heavy metal detoxification. Previously Mathys [110] proposed that malate chelated Zn in the cytosol and the complex was moved into the vacuole, where the uniformly abundant oxalate chelated the Zn, to free malate for return to the cytosol. Another ligands that can bind metals such as Zn and Alare phytates [111].

Phytate are potential ligands for heavy metals and are found to play a role in tolerance and detoxification [42].

3. Role of Seaweed in Biomonitoring of Water Pollution

Biomonitoring (Biological monitoring) is the specific application of biological response for the evaluation of environmental change for using this information in quality control program. Recently, there has been a growing interest in using algae for biomonitoring eutrophication, organic and inorganic pollutants, despite some problems associated with seasonal variations, temperature and salinity conditions and intrinsic factors such as age and growth rate [112-117]. Algae are an ecologically important group in most aquatic ecosystems and have been an important component of biological monitoring programs [118].

Chaudhuri et al. [119] reported that macroalgal species could be good biomonitors of contaminants that tend to reside in the dissolved phases (like heavy metals) compared to those contaminants that are lipophilic (like oraganochlorines). These lipophilic contaminants will not be readily taken up by macroalgal species, due to their low lipid content.

As an alternative to the direct determination of heavy metals in seawater, these can be assayed in a suitable biomonitor, namely a marine macroalgae, and knowing the corresponding concentration factors, the mean metal contents in seawater can be estimated [112]. Seaweeds are used as bioindicators because of their distribution, size, longevity, presence at pollution sites, ability to accumulate metals to a satisfactory degree and ease of identification [120-122]. Wan Maznah [118] suggested that algae are ideally suited for water quality assessment because they have rapid reproduction rates and very short life cycles, making them valuable indicators of short-term impacts.

The seaweeds species can directly reflect the water quality assessment because they are sensitive to some pollutants, and algal metabolism is sensitive to the variation of environmental and natural disturbances [118]. The seaweeds are used in biomonitoring because they are easily cultured in the laboratory and sampling is easy, inexpensive and creates minimal impact on resident biota; relatively standard methods exist for the evaluation of functional and non-taxonomic structural characteristics of algal communities [123-127].

The brown algae *Cystoseira* sp., and the green algae *Ulva* sp. and *Enteromorpha* sp. have high potential as cosmopolitan biomonitors for trace metals in the Aegean Sea [128]. Previously, Leal et al. [112] suggested that the marine benthic macroalgae *Enteromorpha* spp. and *Porphyra* spp. can be used as biomonitors of the seawater contents of Cd, Cu, Hg and Pb. In recent years, several species of the green algae *Enteromorpha* and/or *Cladophora* have been utilized to measure heavy metal levels in many parts of the world [129]. The high uptake of metals in green algae (*Ulva lactuca* and *Enteromorpha intestinalis*) and brown algae (*Padina gymnospora* and *Dictyota bartayresiana*) suggested that these algae may be used as potential biomonitors for heavy metal pollution [130]. Wong et al. [131] used *Enteromorpha crinita* as a biomonitor in the Hong Kong waters, and Say et al. [132] advocated the use of Enteromorpha species as biomonitors in temperate coastal waters.

4. Bioremediation by Seaweeds

Bioremediation is the use of seaweeds or other organisms to reduce the concentrations or toxic effects of contaminants in the aquatic ecosystems. Phytoremediation is defined as a process of decontaminating soil and aquatic systems by using plants, fungi or algae to remove or degrade organic and inorganic pollutants [1]. Zhou et al. [133] defined the bioremediation as a scientific technique for assessing environment including human exposures to natural and synthetic chemicals, based on sampling and analysis of an individual organism’s tissues and fluids. This technique takes advantage of the knowledge that chemicals that have entered the organisms leave markers reflecting this exposure.

However, phycoremediation is defined as a process of decontaminating soil or aquatic systems by using microalgae or seaweeds. Such a process has been used to clean up heavy metals, toxic aromatic pollutants, acid mine drainage, pesticides and xenobiotics and organic compounds [134].

Recently, the use of aquatic plants especially micro and macro algae has received much attention due to their ability to absorption of metals and taking up toxic elements from the environment or rendering them less harmful [135]. Sivakumar et al. [136] suggested that microalgae are capable of producing lipids and hydrocarbons quickly and their photosynthetic abilities make them a promising candidate for wastewater treatment (bioremediation) and can be used as an alternative energy source (Biodiesel). Worldwide, trees, grasses, herbs, and associated fungi and microorganisms are being used increasingly for cleaning polluted sites. Phytoremediation is "on the brink of commercialization" [137], and is given a rapidly increasing market potential [138]. The phytoremediation market is still emerging in Europe, while in the US revenues are likely to exceed $300 million in 2007 [139]. Mudgal et al. [134] suggested that the plant used in the phytoremediation technique must have a considerable capacity of metal absorption, its accumulation and strength to decrease the treatment time. Besides cost-effectiveness, bioremediation is a permanent solution, which may lead to complete mineralization of the pollutant. Furthermore, it is a non-invasive technique, leaving the ecosystem intact. Bioremediation can deal with lower concentration of contaminants where the cleanup by physical or chemical methods would not be feasible [15]. Many green (Table 1), red (Table 2) and brown seaweeds (Table 3) are known to be a good heavy metal hyperaccumulators and can be used in bioremediation of polluted ecosystems.

The seaweeds can eliminate heavy metals by two processes: bioaccumulation and biosorption.

4.1. Bioaccumulation

Bioaccumulation is a process that allows for binding toxic metals or organic substances inside a cell structure [140]. Bioaccumulation is an active metabolic process driven by energy from a living organism and requires respiration [3, 141]. It has been reported that stronger ligands, as they have been shown to complex metals in non-hyperaccumulators, are in hyperaccumulators used for transient binding during transport to the storage sites [142]. This confirmed that enhanced active metal transport, and not metal complexation, is the key mechanism of hyperaccumulation. The hyperaccumulating plants store metals in the vacuoles because in this organelle only enzymes like phosphatases, lipases, and proteinases [143, 144] are present, which have not been found to be a target of heavy metal toxicity. Suresh and Ravishankar [44], reported that seaweeds proved to be effective in hyperaccumulation of heavy metals as well as degradation of xenobiotics. Many seaweeds are able to accumulate high levels of trace metals (Tables 1, 2, 3), which are sometimes larger than those found in water samples from the same site [41, 145]. Seaweeds are able to accumulate trace metals, reaching concentration values that are thousands of times higher than the corresponding concentrations in sea water [146-148]. Henriques et al. [149] showed that bioaccumulation as a full remediation process brings great advantages but only if the contaminated water fulfils the criteria of minimal growth medium and exerts no critical toxic effect to cells. Gosavi et al. [150] demonstrated that four genera of macroalgae (*Ulva*sp.,*Enteromorpha*sp.,*Chaetomorpha* sp. and *Cladophora* sp.) accumulated significant amounts of Fe, Al, Zn, Cd, Cu, As and Pb, noting that cadmium was absorbed better by *Cladophora*sp., while *Chaetomorpha* sp. and *Enteromorpha* sp. absorbed lead better. Previously, Tukai et al. [151] demonstrated that higher concentrations of as were found in brown seaweeds when compared with the red and green species. To study the removal of Hg from water by the living algae, Henriques et al. [149] assessed and explored the bioaccumulation capabilities of three different macroalgae species, *Ulva lactuca* (green), *Gracilaria gracilis* (red) and *Fucus vesiculosus* (brown) and they found that all seaweeds showed huge accumulation capabilities, reaching up 209 μg of Hg per gram of macroalgae (dry weight), which corresponds to 99% of Hg removed from the contaminated seawater. *Ulva lactuca* was the fastest to accumulate Hg. Leitenmaier and Küpper [142] reported that hyperaccumulators have been found for many heavy elements and within many groups of plants and algae, including at least the following: Al, As, Cd, Cu, I, Mn, Ni, Se, Zn [142]. Tonon et al. [152] evaluated the absorption of metals by three species of *Gracilaria*: *Gracilaria tenuistipitata, Gracilaria domingensis* and *Gracilaria Birdiae*. The differences between the three species in the concentrations of the various elements, probably is due to physiological, biochemical or genetic differences between the seaweeds or to different acclimatization events that occurred in their environments or microenvironments. These results suggest that some red seaweed is metal bio-bioaccumulating organisms. Pawlik-*Skowrońska et al.* [69] *reported that the two Fucus spp., Fucus serratus* and *Fucus vesculosus*, accumulated higher total concentrations of metals than either *Ulva intestinalis* or *Solieria chordalis* independently of the level of contamination. This high capacity for accumulation of metals by these seaweeds, and especially *Fucus* spp., when exposed to complex metal mixtures in their natural habitats indicates that they must have effective mechanisms for metal homeostasis and detoxification.

4.2. Biosorption

Biosorption is a physiochemical process that occurs naturally in certain biomass which allows it to passively concentrate and bind contaminants onto its cellular structure [153]. Velásquez and Dussan [3] reported that biosorption is a metabolically passive process, meaning it does not require energy, and the amount of contaminants a sorbent can remove is dependent on kinetic equilibrium and the composition of the sorbents cellular surface.

Biomass from many organisms including fungi and algae has been extensively studied as an alternative adsorbent in removal of heavy metal ions [154, 155]. The mechanism of biosorption is based on a number of metal-binding processes taking place with components of the cell wall [38].

Furthermore, there are other factors affecting the biosorption of metals by seaweed biomass that should be considered, such as cell size and morphology, pH of the external media, cation and anion concentration in the external media, metal speciation, temperature and physiology of the biomass used for the metal [156]. It has been established that metal sequestration is achieved through the following processes: physical sorption, ion exchange, chelation; and ion fixation in inter- and intrafibrillar capillaries and spaces of the structural polysaccharide matrix as a result of the concentration gradient and diffusion through cell walls [157-159]. Previously, Tsezos and Volesky [160] reported that alginates of marine algae usually occur as natural salts of K^+, Na^+, Ca^{2+} and/or Mg^{2+}. These metallic ions can exchange with the counter ions such as Co^{2+}, Cu^{2+}, Cd^{2+} and Zn^{2+}, resulting in the biosorptive uptake of the metals.

It was shown that the brown seaweeds contained the greatest number of acidic functionalities (both total and weak) on the seaweed surface. Since it is thought that carboxyl groups (weak) are primarily responsible for metal sorption, especially in brown seaweeds (Tables 1, 2, 3), it was expected that the brown species would exhibit superior biosorption performance over the other seaweeds [161]. Vijayaraghavan et al. [162] showed that the marine green alga *Ulva reticulate* was found to be an effective biosorbent for the removal of copper, cobalt and nickel from aqueous solutions. Therefore, cell wall composition of green algae provides binding sites such as carboxyl hydroxyl amino and sulphate for metal ions [163-166] and (4) its collection from coastal regions can solve possible eutrophication problem. One of the most common macroalgae used in past studies of heavy metal biosorption from the environment, as well as for the removal of nitrogen and ammonia in fish aquaculture is the green alga *Ulva* [166, 167].

Using green seaweed, Zeroual et al. [168] found that *Ulva lactuca* can successfully used for mercury biosorption. Previously, Kuyucak and Volesky [169] observed that a green alga *Halimeda opuntia* performed equally well in cobalt biosorption along with one of the best-performed brown seaweed *Ascophyllum nodosum* at higher pH conditions.

Murphy et al. [161] studied the biosorption performance of Cu(II) by the dried biomass of the two red seaweeds *Palmaria palmata* and *Polysiphonia lanosa*, and they found that carboxyl and sulphonate functionalities involved in binding Cu(II) in both species. However amino and hydroxyl groups took part in Cu(II) binding in *P. lanosa*.

Alkhalifa et al. [170] suggested that the main mechanisms of heavy metals biosorption by brown algae include some key functional groups such as carboxylic groups, which are generally the most abundant acidic functional group in the brown algae. They constitute the highest percentage of titratable sites (typically greater than 70%) in dried brown algal biomass. The adsorption capacity of the algae is directly related to the presence of these sites on the alginate polymer, which itself comprises a significant component (up to 40% of the dry weight) [170].

Table 1. Uptake and accumulation of metals by some green seaweeds

Metal	Species	References
As	*Codium cuneatum* *Maugeotia genuflexa* *Rhizoclonium tortuosum* *Ulothrix cylindricum*	[171] [172] [69] [173]
B	*Caulerpa racemosa*	[174]
Ba	*Codium cuneatum*	[171]
Cd	*Enteromorpha sp.* *Cladophora fasicularis* *Codium tomentosum*	[128] [175] [176]
Co	*Enteromorpha intestinalis* *Ulva lactuca*	[176] [176]
Cr	*Enteromorpha sp.* *Ulva sp.*	[128] [177]
Cu	*Codium tomentosum* *Enteromorpha sp.* *Rhizoclonium tortuosum* *Ulva lactuca* *Ulva sp.*	[176] [112] [69] [121] [128, 130]
Fe	*Codium cuneatum* *Enteromorpha sp.* *Ulva lactuca*	[171] [128] [130, 178]
Hg	*Enteromorpha sp.* *Ulva lactuca*	[112, 128] [149]
Mn	*Ulva lactuca*	[176]

Table 1. (Continued)

Metal	*Species*	References
Ni	*Ulva lactuca*	[176]
	Enteromorpha intestinalis	[176]
Pb	*Cladophora fasicularis*	[175]
	Enteromorpha sp.	[128, 130]
	Rhizoclonium tortuosum	[69]
Sr	*Codium cuneatum*	[171]
Zn	*Enteromorpha sp.*	[128]
	Rhizoclonium tortuosum	[69]
	Ulva lacuca	[121, 130]
	Ulva reticulata,	[179]

Table 2. Uptake and accumulation of metals by some red seaweeds

Metal	Species	References
Cd	*Gelidium floridanum*	[180]
	Gracillaria compressa	[176]
	Kappaphycus alvarezii	[181]
	Porphyra spp.	[112]
	Pterocladia capillacea	[176]
Co	*Gracillaria compressa*	[176]
	Jania rubens	[176]
	Kappaphycus alvarezii	[181]
	Pachymeniopsis sp	[182]
	Polysiphonia lanosa	[183]
Cu	*Gracillaria compressa*	[176]
	Porphyra spp.	[176]
	Solieria chordalis	[69]
Fe	*Gracilaria pachidermatica*	[171]
	Laurencia papilosa	[171]
	Pterocladia capillacea	[176]
Hg	*Gracilaria gracilis*	[149]
	Porphyra spp	[112]
Ni	*Gracillaria compressa*	[176]
	Gracillaria verrucosa	[176]
Pb	*Gracilaria pachidermatica*	[171]
	Gelidium floridanum	[180]
	Porphyra spp	[112]
Se	*Gracilaria edulis*	[183]
Sr	*Laurencia papilosa*	[171]
Zn	*Pterocladia capillacea*	[176]

Table 3. Uptake and accumulation of metals by some brown seaweeds

Metal	Species	Reference
As	*Fucus serratus*	[69]
Au	*Ascophyllum nodosum*	[185]
	Chondrus crispus	[185]
	Palmaria palmata	[185]
	Palmaria tevera	[185]
	Rhodymenia palmata	[186]
	Sargassum natans	[185]
Ba	*Padina durvillaei*	[171]
	Sargassum sinicola	[171]
Cd	*Ascophyllum nodosum*	[187]
	Cystoseira sp.	[128]
	Fucus vesiculosus	[187]
	Padina gymnospora	[130]
	Sargassum natans	[187]
	Turbinaria conoides	[141]
Co	*Ascophyllum nodosum*	[169]
Cr	*Cystoseira sp.*	[128]
	Dictyota bartayresiana	[130]
	Fucus vesiculosus	[183, 188]
	Sargassum sp.	[141]
	Turbinaria conoides	[141]
Cu	*Fucus serratus*	[189]
	Padina pavonica	[121]
	Rhizoclonium tortuosum	[69]
	Sargassum boveanum	[170]
	Sargassum filipendula	[190]
	Sargassum fluitans	[190]
	Turbinaria conoides	[141]
Fe	*Fucus vesiculosus*	[188]
	Cystoseira sp.	[128]
	Padina durvillaei	[171]
	Sargassum fluitans	[191]
	Sargassum sinicola	[171]
Hg	*Cystoseira sp.*	[128]
	Fucus vesiculosus	[149]
Mn	*Padina gymnospora*	[130]
Ni	*Ascophyllum nodosum*	[192]
	Fucus vesiculosus	[188, 192]
	Padina gymnospora	[130]
	Sargassum fluitans	[192]
	Sargassum natans	[192]

Table 3. (Continued)

Metal	Species	References
Pb	*Ascophyllum nodosum*	[192]
	Cystoseira sp.	[128]
	Fucus vesiculosus	[192]
	Sargassum natans	[192]
	Sargassum vulgare	[192]
	Turbinaria conoides	[141]
Sb	*Turbinaria conoides*	[193]
	Sargassum sp	[193]
Sr	*Padina durvillaei*	[171]
	Sargassum sinicola	[171]
Zn	*Cystoseira sp.*	[128]
	Fucus vesiculosus	[194]
	Laminaria japonica	[194]
	Padina pavonica	[121]
	Sargassum angustifolium	[170]
	Sargassum fluitans	[194]
	Sargassum latifolium	[170]

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Chapter 5

THERAPEUTIC AND PHARMACEUTICAL APPLICATION OF SEAWEEDS

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ABSTRACT

Our planet is supposed to host 11.213 billion people by the end of the year 2100. Such demographic explosion poses serious problems for human life quality and security. Generally, the term "seaweed" is conventionally used to designate multicellular marine algae. In the last three decades, and due to the high diversity of their metabolites, seaweeds are used in medicine to treat gall stones, stomach ailments, eczema, cancer, renal disorders, scabies, psoriasis, asthma, arteriosclerosis, heart disease, lung diseases, ulcers, etc. Compounds like carotenoid, polysaccharides, fatty acids, glycoproteins, haloforms, halogenated alkanes, alkenes, alcohols, aldehydes, hydroquinones, ketones, phlorotannins, pigments, lectins, alkaloids, terpenoids, sterols and some heterocyclic and phenolic compounds are among the most important seaweed substances that receive attention from pharmaceutical companies for use in drug development, or from scientists in the field of medical

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research. The potential pharmaceutical, medicinal and investigatory applications of these compounds in antibiotic, antiviral, anticancer, antioxidants, anti-inflammatory, anticoagulants, and antidiabetic production are discussed in this chapter.

Keywords: seaweeds, antibiotic, antiviral, anticancer, anticoagulants, antidiabetic, analgesic.

INTRODUCTION

The term "seaweed" is conventionally used to designate multicellular marine algae (red, green and brown algae). However, the unicellular (spores or zygotes) stage seems to be an obligatory present stage in the life cycle of all described seaweeds (Lobban and Harrison 1997). Seaweeds are photosynthetic organisms, able to fix carbon dioxide to form complex organic compounds and release high amounts of oxygen in the atmosphere. Thus, suggesting that algae are the true lungs of earth (Pereira 2016). Based on pigmentation, seaweeds were classified to: 1) Green algae (Chlorophyta), characterized by their photosynthetic pigments such as Chlorophyll a and b, contained in special structures known as chromatophores. 2) Brown algae (Phaeophyta), that varies in color from olive-yellow to deep brown. These colorations are due to fucoxanthine and carotenoid pigments. 3) Red algae (Rhodophyta), characterized by their water-soluble phycoerythrin and phycocyanin pigments, in addition to carotene and chlorophyll (Verlecar and Rathod 2004). The differences between these groups are more important than those indicated by this simple designation; ultra-structural and metabolic characteristics such as photosynthetic pigments, storage compounds, fine structure of chloroplasts and their cell wall composition, are variable from one group to another and even from one species to another in the same group (Rindi et al. 2012).

The world's population is supposed to surpass 9.725 and 11.213 billion habitants by the end of the years 2050 and 2100; respectively. This demographic explosion poses serious problems for human life quality and security (UN 2004, Ashraf et al. 2012, UN 2015). Recently, seaweeds figure prominently among the proposed solutions for sustainability challenges, aiming to unlock seas and oceans potential as primordial sources of food and feed production worldwide. In addition to their use as fertilizers, fungicides, herbicides, condiments, dietary supplements and as resources of phycocolloids such as agar, seaweeds can be a substantial feedstock for biomass, biofuel production, and for animal feeds. Impressively, and due to the high diversity of their chemistry, seaweeds are used in medicine to treat gall stones, stomach ailments, eczema, cancer, renal disorders, scabies, psoriasis, asthma, arteriosclerosis, heart disease, lung diseases, ulcers, etc.(Smit 2004, Ye et al. 2008, Peng et al. 2015, Tiwari and Troy 2015). Away from medicine, my story with seaweeds started with Pr. Nabti Elhafid in 2013, when we carried interesting works about the role of natural compatible solutes from tow marine chlorophytes “*Ulva lactuca* and *Enteromorpha intestinalis*” in improving both rhizobacterial and plant growth under salt stress. In this chapter, we tried to summarize the most important aspects of therapeutic and pharmaceutical application as well as the principal bioactive molecules of seaweeds used in pharmaceutical area, lightening with examples the major species used in antimicrobial, antitumor, antiviral, antioxidant, anticoagulant and other fabrications worldwide.

Seaweeds, a Big Tank of Antibiotics

The famous works of Pasteur and Koch have opened a large window in science, establishing that microorganisms are the causative agents of infectious diseases. In parallel, through the works of Paul Ehrlich on a “magic bullet” that selectively targets microbes but not hosts and his development of anti-syphilis drugs (1904-1909), together with the amazing discovery of Penicillin by Alexander Fleming (1929), it becomes well established the existence of molecules able to attack specifically disease-causing microorganisms in the host. Since that, scientists are continually developing different protocols to synthetize chemicals and purify bioactive molecules from different sources that have inhibitory effects against pathogenic microorganisms (Franklin et al. 2005, Aminov 2010). It is well admitted that chemical composition of seaweeds contains a wide range of molecules having antibiotic activities, especially halogenated molecules such as haloforms, halogenated alkanes and alkenes, alcohols, aldehydes, hydroquinones, ketones, polysaccharides, fatty acids, phlorotannins, pigments, lectins, alkaloids, terpenoids, sterols and some heterocyclic and phenolic compounds (Lincoln et al. 1991, Smit et al. 2004, Pérez 2016).

Crude extracts from brown, red and green seaweeds have been used all over the world for their antibiotic activities. For example, Varier at al. (2013) tested the effect crude extracts from the Indian red seaweeds *Gelidiella acerosa*, *Gracilaria verrucosa* and *Hypnea musciformis* against *Salmonella* *paratyphi*, *Enterococcus aerogenes*, *Staphylococcus epidermidis*, *Salmonella typhi* and *Shigella flexneri*. The results showed different activities from extract to another, from bacteria to another and from extraction solvent to another. Another study realized by Moorthi and Balasubramanian (2015) revealed the antibacterial activity of acetone and chloroform extracts from the seaweed *Sargassum muticum* against human pathogens such as *Micrococcus* sp., *Salmonella paratyphi* and *Shigella flexneri*. In addition, Acetone, Methanol, Chloroform, Diethyl ether, Ethyl acetate, Ethanol and Petroleum ether extracts from the green algae *Codium adherens, Ulva reticulata* and *Halimeda tuna* were tested for their antibacterial activities. The results showed that ethanol extract gave better activity against *Staphylococcus* sp., while the tested seaweed showed different inhibitory effects against *Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus, Enterococci* sp., *Proteus* sp., *Streptococcus* sp., *Pseudomonas aeruginosa, Vibrio parahaemolyticus*, *Salmonella* sp., *Shewanella* sp., *Vibrio flurialis, and Vibrio splendidus.* Extracts efficiency was variable from one solvent to another and from one species to another (Karthikaidevi et al. 2009). Saidani et al. (2012) screened the antifungal activity of four Algerian marine algae *Rhodomella confervoides* (Rodophyceae), *Ulva lactuca* (Chlorophyceae), *Cystoseira tamaricifolia* and *Padina pavonica* (Phaeophyceae) against *Aspergillus niger* (939N), *Candidaalbicans* (ATCC 1024) and *Mucor ramaniannus* (NRRL 1829). Their results suggest that marine algae harvested from Algerian coast present high antifungal activities, making of them interesting sources of natural antibiotic compounds. In addition, antiprotozoal activity of seaweeds also attracts scientific attention, looking for new bioactive molecules against parasites. Thereby, ten Turkish marine algae (*Caulerpa rasemosa*, *Codium bursa*, *Cystoseira barbata*, *Cystoseira crinata*, *Corallina granifera*, *Jania rubens*, *Ceramium rubrum*, *Gracilaria verrucosa*, *Dasya pedicellata* and *Gelidium crinale*) were tested for their antiprotozoal activities against four parasites *Plasmodium falciparum*, *Trypanosoma brucei rhodesiense*, *T. cruzi* and *Leishmania donovani*. The results showed that all seaweed extracts were active against *T. brucei rhodesiense* and *Leishmania donovani*, while the majority of extracts showed antiplasmodial activity, revealing that seaweeds could constitute a potential source of antiprotozoal compounds (Süzgeç-Selçuk et al. 2011). Many other works highlighted the efficiency of crude extracts from seaweeds in inhibiting bacterial, fungal and protozoal growth and the possibility of exploiting them as new sources for antibiotics worldwide (Manivannan et al. 2011, Pandian et al. 2011, Vonthron-Sénécheau et al. 2011, Oumaskour et al. 2012, Peres et al. 2012, Moorthi and Balasubramanian 2015, Pérez et al. 2016).

Away from crude extracts, researchers are more to more focusing on extraction, isolation and purification of new molecules with antibiotic activities from seaweeds. Fucoidan from the marine macro-algae *Sargassum wightii* revealed interesting antibacterial activity against human pathogens such as *Escherichia coli*, *Klebsiella pneumonia*, *Vibrio cholera*, *Proteus sp.*, *Pseudomonas aeruginosa* and others (Marudhupandi and Kumar 2013). Kantachumpoo and chirapart (2010) found that polysaccharides from the two marine algae *Colpomenia sinuosa* and *Sargassum polycystum*, collected from the province Chon Buri-Thailand, present an inhibitory activity against *Candida albicans*. Furthermore, Alghazeer et al. (2013) found that Alkaloids from the brown marine algae *Cystoseira barbata* could inhibit the growth of the human pathogen Klebsiella spp.They also discussed the inhibitory effect of alkaloid extract from the red seaweed *Dictyopteris membranacea*, showing itsantibacterial activity against *Salmonella typhi*. Concerning phlorotannins, Eom et al. (2012) summarized the antimicrobial activities of compounds such as Eckol, dieckol, dioxinodehydroeckol, fucofuroeckol-A, 7-phloroeckol, Phlorofucofuroeckol-A, 8,8'-Bieckol and phloroglucinol against bacteria and fungi like methicillin-resistant *Staphylococcus aureus* (MRSA), *Trichophyton rubrum, bacillus cereus, Salmonella thyphimurium, Klebsiella pneumonia* and others. Lee et al. (2014) reported the antibacterial activity of a fucofuroeckol-A purified from the brown seaweed *Eisenia bicyclis* against acne-related bacterium *Propionibacterium acnes*. In addition, the antifungal activities of dieckol from the brown alga *Ecklonia cava* against *Trichophyton rubrum*, the most common causative agent of dermatophytic nail infections in humans, was described in the work of Lee et al. (2010). The results obtained with microscopic observation indicated that dieckol exhibited fungicidal activity against *T. rubrum* due to loss of its membrane integrity. Nagayama et al. (2002) studied the bactericidal activity of five phlorotannins (phloroglucinol, eckol, Phlorofucofuroeckol-A, dieckol and 8,8′-bieckol) purified from the brown alga *Ecklonia kurome* against *Staphylococcus aureus* ATCC 25923 (MRSA), *Bacillus cereus* ATCC 19637, *Campylobacter jejuni* CIP 702, *Escherichia coli* ATCC 25922, *Salmonella enteritidis* S-48, *Salmonella typhimurium* ATCC 14028 and *Vibrio parahaemolyticus* KR1151. No toxicity was obtained on mice treated with the same bactericidal concentrations of algal phlorotannins.

Among thirty-eight seaweeds samples, crude extract from the rhodophyta *Laurencia papillosa* showed the highest antibacterial activity against

Staphylococcus aureus ATCC 25923, *Bacillus subtilis* ATCC 6051, *Escherichia coli* ATCC 8739 and *Pseudomonas aerugenosa* ATCC 9027. The active fraction was identified as a cholesterol derivative (24-propylidene cholest-5-en-3β-ol) using gas chromatography mass spectrometry (GC–MS). The purified compound had a minimum inhibitory concentration that ranged from 1.2 to 1.7 µg/ml against the four clinical isolates *Escherichia coli*, *Pseudomonas aerugenosa*, *Klebsiella pneumoniae* and *Shigella flexneri*. These results suggest the usefulness of the purified sterol as potential lead molecule for broad-spectrum drug development, and confirm the potential of seaweeds as an important natural source of antimicrobial compounds for pharmaceutical industries (Kavita et al. 2014). Similarly, Rajauria et al. (2013) succeeded to isolate and partially identify a bioactive fucoxanthin from the Brown Seaweed *Himanthalia elongata*. The isolated fucoxanthin revealed strong antibacterial activity against the human pathogen *Listeria monocytogenes* (inhibition zone: 10.27 mm, 25μg compound/disc). It is also important to mention the interesting work of Kasanah et al. (2015) that constitute an excellent synthesis of the most important molecules used as antibacterial compounds from red seaweeds, particularly those belonging to bromophycolides and neurymenolides classes.

ANTIVIRAL COMPOUNDS IN SEAWEEDS

Viral infections are in the first line of mortality causes worldwide. For example, hepatitis A virus touch more than 80% of the population in some developing countries, while hepatitis B and C viruses affect about 360 and 123 million persons on the planet respectively and 30 million are attained by HIV. Under pressure of their high mortality, together with the permanent threat of emerging virulent strains, an important number of drugs have been developed face to viral threats. Their effectiveness is limited by viral resistance and drug safety (Dwivedi et al. 2013, Sousa et al. 2016).

Marine macro-algae could be cultured in high volumes without demanding a lot of care. Among a wide range of therapeutic compounds produced by seaweeds, some of them are characterized by antiviral activities (Pinto et al. 2012, Peng et al. 2013, Anbuchezhian et al. 2015, Pérez et al. 2016). Yasuhara-Bell and Lu (2010) summarized the antiviral activities of marine compounds, including those produced by seaweeds, toward a wide range of viruses such as: herpes viruses (HSV-1, HSV-2, HCMV), togaviruses, paramyxoviruses (RSV), rhabdoviruses (VSV), human immune deficiency viruses (HIV), mumps virus and influenza B virus etc. Hudson et al. (1999) studied the antiviral activity of 13 Korean seaweed against the herpes simplex (HSV), Sindbis virus (SINV) and poliovirus. The *Codium fragile*-extract showed high activity against the three viruses, while *Enteromorpha linza*, *Colpomenia bullosa*, *Scytosiphonlo mentaria*, and *Undaria pinnatifida*-extract were active only against HSV and SINV. The other algae (*Ulvapertusa*, *Ishige okamurai*, *Sargassum sagamianum*, *Carpopeltis affinis*, *Corallina pilulifera*, *Grateloupia turuturu*, *Symphyocladia latiuscula* and *Symphyocladia marchantioides*) were selective against either HSV or SINV. The antiviral activity of aqueous, methanolic, chloroform-methanolic and dichloromethanolic extracts from 16 Moroccan red seaweed was tested against Herpes simplex virus type-1 (HSV-1) using cell viability method. Algal extracts from *Asparagopsis armata*, *Ceramium rubrum*, *Gelidium pulchellum*, *Gelidium spinulosum*, *Halopitys incurvus*, *Hypnea musciformis*, *Plocamium cartilagineum*, *Boergeseniella thuyoides*, *Pterosiphonia complanata* and *Sphaerococcus coronopifolius* inhibited the *in vitro* replication of the virus at an effective concentration (Rhimou et al.2010). Furthermore, Wang et al. (2008) and Koishi et al. (2012) described the antiviral activity of crude extracts from seaweeds such as *Canistrocarpus cervicornis*, *Padina gymnospora*, *Palisada perforate*, *Caulerpa racemose*, *Hydroclathrus clathratus* and *Lobophora variegate* against dengue virus (DENV), HSV-1 and HSV-2.

Polysaccharides (sulfated polysaccharides in particular), poliketides, terpenoids, peptides and glycolipids such as monogalactosyl diacylglycerides (MGDG), digalactosyl diacylglycerides (DGDG), and sulfoquinovosyl diacylglycerides (SQDG), constitute the major part of antiviral compounds that have been purified and identified from seaweeds (Adhikari et al. 2006, Bandyopadhyay et al. 2011, Cardozo et al. 2011, de Souza et al. 2012, Kind et al. 2012, Saha et al. 2012). In 2013, Plouguerné et al. isolated and identified the detailed chemical structure of an anti-herpes compound from the Brazilian brown seaweed *Sargassum vulgare*. This active compound was purified from the lipid fraction of the crude extract and identified as sulfoquinovosyl diacylglycerols (SQDGs). SQDGs showed high antiviral activity against herpes simplex virus (HSV-1 and HSV-2). Wang et al. (2007) isolated and purified a SQDG with high antiviral activity against both HSV-1, HSV-2 and Coxackie virus B3 (Cox B3) from an n-butanol fraction of an aqueous extract of the green algae *Caulerpa racemosa* collected from the south China sea. In addition, Mandal et al. (2007) analyzed a sulphated-fucan-containing fraction isolated from the brown seaweed *Cystoseira indica*. The main fraction (CiF3) obtained by anion exchange chromatography of the crude aqueous extract had strong antiviral activity against the two viruses HSV-1 and HSV-2. The major polysaccharide in the fraction (CiF3) was identified as a sulfated fucan with a molecular mass of 35 kDa. It contains a backbone of α-(1→3)-linked fucopyranosyl residues substituted at C-2 with fucopyranosyl and xylopyranosyl residues. In the last few years, many other sulfated polysaccharides have been isolated from seaweeds like *Adenocystis utricularis*, *Sphaerococcus coronopifolius*, *Boergeseniella thuyoides* and *Cladosiphon okamuranus*. Such compounds were identified as antiviral molecules against a wide range of viruses such as Newcastle Disease Virus (NDV), Herpes simplex virus (HSV-1, HSV-2) and Human immunodeficiency virus (HIV) etc.(Ponce et al. 2003, Trinchero et al. 2009, Bouhlal et al. 2011, Elizondo-Gonzalez et al. 2012). Furthermore, Soares et al. (2007) showed that extract from the Brazilian seaweed *Stypopodium zonale* contains compounds such as merediterpenoids aromatic acid, epitaondiol and peroxylactone with high antiviral activity against the herpes simplex virus (HSV-1).

PLACE OF SEAWEEDS IN THE FIGHT AGAINST CANCER

Historically, seaweeds were used for a long time in both traditional Chinese and Folk Japanese medicine to treat tumors. In such populations, where seaweeds constitute a regular part of their diet, the rates of tumors development are dramatically lower (Teas et al. 2013). In Europe, the first reported use of seaweed was in 1970, when an English physician used ash from kelp to treat goiter (Hayes 2015). An interesting study realized by Yang et al. (2010) on the relation between two seaweed consumption (*Porphyra* sp. and *Undaria pinnatifida*) and breast cancer. In this study, 362 Korean women aged between 30 and 65 years old, were histologically confirmed to have breast cancer and compared to control cases visiting the same hospital. Among other characters, controls were matched to cases based on their diet, estimated by the quantitative FFQ with 121 items, including the two studied seaweeds. The results showed high inverse correlation between *Porphyra* sp. intake and the risk of breast cancer. Namvar et al. (2013) highlighted several *in vivo* and *in vitro* pharmacological studies describing Seaweed anticancer effects and underlined the possibility that these therapeutic properties may be attributed to the biologically active metabolites produced by seaweeds. In 1989, Fernandez et al. isolated and characterized an antitumor active agar-type polysaccharide from the red macro-algae *Gracilaria dominguensis* using a cold-water extraction followed by cetyltrimethylammonium bromide fractionation. The obtained sulfated galactan (CT-1) presented high inhibition of the Ehrlich ascites carcinoma transplantation in mice. Ye et al. (2008) succeeded to obtain two polysaccharide fractions SP-3-1 and SP-3-2 from the brown seaweed *Sargassum pallidum*. These fractions showed high antitumor activity against the human hepatoma cell line "HepG2 cells," human lung cancer cell line "A549 cells," and human gastric cancer cell line "MGC-803 cells." The authors attributed this antitumor activity to the molecular weight of the fractions and their high sulfate content. Mhadhebi et al. (2014) tested the antioxidant, anti-inflammatory and antiproliferative effects of aqueous extracts of three Mediterranean brown seaweeds of the genus *Cystoseira*. Aqueous extracts from the algae *Cystoseira crinita*, *C. sedoides* and *C. compressa* showed a significant antiproliferative effect against Human tumor cell lines HCT15 and MCF7. This pharmacological property was positively correlated with the total phenol content and the antioxidant activity of the extracts. Other works suggested the implication of compounds such as phlorotanins, fucoidans and terpenes (diterpene mediterraneol, usneoidone E and Z etc.)in the antitumoral, antiproliferative and anticancer activities that characterize algal extracts (Francisco et al. 1985, Urones et al. 1988, Fisch et al. 2003, Huicheng 2010, Lowenthal and Fitton 2015). In addition, Boominathan and Mahesh (2015) underlined the important role of carotenoid compounds such as β-carotene, astaxanthin and fucoxanthin in suppressing carcinogenesis. Being highly effective as antioxidant (oxidative stress is putatively involved in cancer development), carotenoids such β-carotene, α-carroten, fucoxanthin, astaxanthin, canthaxanthin, zeaxanthin and lutein could constitute important additive or drugs for cancer prevention (Kotake-Nara et al. 2005, Boominathan and Mahesh 2015). Otherwise, seaweeds belonging to the genera *Bryopsis*, *Sargassum* and *Kappaphycus* are able to produce compounds like kahalalide F, alginate and kappa-carrageenan, known for their impressive anticancer activities (Pereira and Costa-Lotufo 2012). Kim et al. (2014) investigated the cytotoxic and apoptotic effects of an ethanol extract derived from the marine brown alga *Dictyopteris undulata* against human colon adenocarcinoma cells. The obtained result showed that this algal extract induced apoptotic cell death in three colon-cancer cell lines SW480, SNU407 and HT29, and proved its usefulness as a therapeutic agent for colon cancer attenuation.

ANTIOXIDANTS FROM SEAWEEDS

Recently, due to knowledge accumulation about production and metabolism of reactive oxygen and nitrogen species (ROS and RNS), and understanding damages related to free radicals and their derivatives, oxidative stress has become one of the most alarming topics between researchers. The imbalanced generation of ROS and RNS (pro-oxidants) in a system, exceeding its ability to neutralize and eliminate them, produces oxidative stress (Rahman et al. 2012, Rahal et al. 2014). For more than four decades, oxidative stress remained known to be implicated in various forms of pathophysiology of inflammation, neurodegenerative disorders, diabetes mellitus, atherosclerosis, fibrosis, cancer, and reperfusion injury (Hybertson et al. 2011, Vadlapudi et al. 2012). In response to oxidative stress, the body synthesize and/or accumulate antioxidants such as superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase, minerals like Se, Mn, Cu and Zn, and vitamins like vitamin A, C and E (Irshad and Chaudhuri 2002).Antioxidant compounds from seaweeds constitute a potential source of antioxidant compounds in nature such as ascorbate, glutathione, carotenoids, mycosporine-like amino acids, catechins, gallate, phlorotannins, eckol, ascorbic acid, tocopherols etc. (Mariya and Ravindran 2013, Farasat et al. 2014).

Ismail and Hong (2002) studied the antioxidant potential of crude extracts from the marine algae *Porphyra* sp. *Laminaria* sp. *Undaria* sp. and *Hijikia* sp. Water extract from *Porphyra* sp. *Laminaria* sp. and *Hijikia* sp. exhibited higher radical scavenging activity than *Undaria* sp. this last exhibited the highest antioxidant and free radical scavenging activities when extracted with ethanol. Likewise, aqueous and ethanolic extracts from the Thailand Gulf seaweeds *Sargassum binderi* Sonder, *Amphiroa* sp., *Turbinaria conoides* (J. Agardh) Küzting and *Halimeda macroloba* showed high antioxidant and scavenging activity of both ABTS [2, 2’-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)] and DPPH (2, 2- diphenyl-1-picrylhydrazyl) radicals (Boonchum et al. 2011). Other studies discussed the total antioxidant activity of crude extracts from seaweeds such as *Dictyota dichotoma*, *Dictyota indica*, *Iyengaria stellata*, *Padina pavonica*, *Sargassum swartzii*, *Sargassum variegatum*, *Stoechospermum marginatum*, *Stokeyia indica*, *Jolyna laminarioides*, *Caulerpa taxifolia*, *Halimeda tuna*, *Ulva* sp., *Solieria robusta*, *Melanothamnus afaqhusainii*, *Eucheuma cottonii*, *Padina* sp., *Chaetomorpha linum*, *Grateloupia lithophila*, *Sargassum wightii*, *Jania rubens* and *Pterocladia capillacea*. For this, different protocols were used like total antioxidant assays, reducing power, DPPH radical scavenging activity, ABTS radical scavenging activity, Deoxyribose scavenging activity, H2O2 radical scavenging assay, Lipoxygenase activity and Nitric oxide radical inhibition assay (Farasat et al. 2013, Foon et al. 2013, Indu and Seenivasan 2013, Khairy and El-Sheikh 2015, Tariq et al. 2015).

The efficiency of polysaccharides, especially sulfated polysaccharides, from marine algae such as *Dictyopteris Justii*, *Sargassum graminifolium*, *Padina gymnospora*, *Gracilaria birdiae*, *Gigartina skottsbergii*, *Schizymenia binderi*, *Lessonia vadosa* and *Fucus vesiculosus*, was largely studied in the last few years (Rupérez et al. 2002, Barahona et al. 2011, de Souza et al. 2007, Souza et al. 2012).Melo et al. (2013) extracted and purified four sulfated polysaccharides [fucoglucoxyloglucuronan (DJ-0.3v), heterofucan (DJ-0.4v), and two glucans (DJ-0.5v and DJ-1.2v)]from the brown seaweed *Dictyopteris Justii*. The polysaccharides DJ-0.4v and DJ-0.5v showed high antioxidant activity in some in vitro tests (determination of total antioxidant capacity, reducing power, and hydroxyl radical scavenging activity, superoxide radical scavenging activity, ferrous and copper chelation assays). The antioxidant activities of polysaccharides from the brown seaweed *Sargassum graminifolium* were assayed by determining their reducing power, their ability to scavenge superoxide radicals, and their activity in the DPPH assay. The ability of these polysaccharides to inhibit calcium oxalate crystallization, together with their antioxidant activities suggest their usefulness in treating urinary stones (Zhang et al. 2012).

Phlorotannins are phenolic compounds restricted to polymers of phloroglucinol. Among other characters, phlorotannins from marine algae have an important antioxidant activity. Sathya et al. (2013) isolated a dichloromethane fraction with high antioxidant activity from the crud extract of the brown seaweed *Cystoseira trinodis*. It was further fractionated using column chromatography. The column-purified fractions were subjected to thin-layer chromatography to obtain seven sub-fractions. Most of the fraction, analyzed and identified as phlorotannins, had antioxidant activity. Furthermore, Kim et al. (2011) tested the hepatoprotective effect of phlorotannins from the seaweed *Eisenia bicyclis* against oxidative stress induced by *tert*-Butyl Hyperoxide (*t*-BHP). For this, crude ethanol extract and its serial solvent fractions were screened. Five phlorotannin compounds (eckol, 6,6’-bieckol, 8,8’-bieckol, dieckol and phlorofucofuroeckol A), purified from the ethyl acetate fraction, and showed high hepatoprotective effect against *t*-BHP-induced cell death in HepG2 cells, suggesting their possible development as potential candidates for natural hepatoprotective agents. Antioxidant activity of phlorotannins from seaweeds like *Eisenia* *bicyclis*, *Ecklonia cava*, *Ecklonia kurome*, *Fucus vesiculosus*, *F. spiralis*, *Cystoseira nodicaulis*, *C. tamariscifolia* and *C. usneoides*, was also discussed by researchers such as Ahn et al. (2007), Shibata et al. (2008), Ferreres et al. (2012), Wang et al. (2012), and others. Elsewhere, fucoxanthin from the seaweed *Hijikia fusiformis* was its richest carotenoid compound. This fucoxanthin also revealed high radical scavenging efficiency (Yan et al. 1999). Airanthi et al. (2011) assayed antioxidant activities of some edible seaweed in Japan (*Eisenia bicyclis*, *Kjellmaniella crassifolia*, *Alaria crassifolia*, *Sargassum horneri* and *Cystoseira hakodatensis*). Their results suggest that the antioxidant activity of the seaweed *C. hakodatensis* is mainly due to its fucoxanthin and phenolics compounds with high radical scavenging activities.

ANTI-INFLAMMATORY, IMMUNOMODULATORY AND ANALGESIC COMPOUNDS

Oxidative stress is implicated in various forms of pathophysiology of inflammation. A wide range of brow, red and green seaweed are known to contain antioxidants with anti-inflammatory activity. Studies of anti-inflammatory compounds in seaweeds range from the revelation of seaweed crude extracts to the study of certain isolated, purified, and characterized molecules (polysaccharides, carotenoids, phlorotannins, polyunsaturated fatty acids etc.) (Lee et al. 2013). Vázquez et al. (2011) studied Anti-inflammatory and analgesic activities of the red seaweed *Dichotomaria obtusata*. In the classical tests used on mice (ear edema induced by TPA and writhing induced by acetic acid), aqueous extract of the algae inhibited ear edema in a dose-dependent manner and reduced abdominal writhes in mice, suggesting that this algal extract possesses therapeutic potential in the treatment of peripheral painful or/and inflammatory symptoms. Several studies have focused on anti-inflammatory activities of complete fractions or crude extracts from red, green and brown marine macroalgae (*Capsosiphon fulvescens*, *Codium fragile*, *Colpomenia sinuosa*, *Ishige okamurae*, *Chondrus ocellatus*, *Carpopeltis cornea*, *Cystoseira sedoides*, *Padina tertastomatica*, *Sargassum wightii*, *Spatoglossum schroederi*, *Dichotomaria obtusata* etc.) (Khan et al. 2008, Mhadhebi et al. 2011, Delgado et al. 2013, Radhika et al. 2013, Júnior et al. 2014).

The Algal sulfated polysaccharide from the seaweed *Eckloniacava* significantly inhibited nitric oxide production, prostaglandin-E2 (PGE2) production and suppressed inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) expression when tested in LPS-stimulated RAW 264.7 macrophages. Suggesting that this polysaccharide could be used as an effective immunomodulatory mediator with a variety of beneficial effects, implicated in anti-inflammatory agents-modulation (Kang et al. 2011). Sulfated polysaccharides from the red algae *Gracilaria cornea* (Gc-TSP) showed significant analgesic and anti-inflammatory effects when tested in mice model. Thus, weak doses of Gc-TSP (3 and 9 mg ⁄ kg) significantly inhibited paw edema induced by carrageenan, especially at 3 hour after treatment. In addition, Gc-TSP significantly reduced nociceptive responses, as measured by the number of writhes, at all tested doses, indicating that Gc-TSP possesses important analgesic and anti-inflammatory activities (Coura et al. 2012). Fucans fraction from the brown seaweed *Ascophyllum nodosum* was termed (BS8) and tested for its ability to modulate complement activation. BS8 inhibited the formation of classical pathway C3 convertase by inhibiting C1 activation, C4 cleavage, suppressing the binding B-C3b and by interfering with the stabilizing function of Properdin. BS8 was more efficient than heparin in inhabiting complement activation and exhibiting lesser anticoagulant activity. These results suggest that sulfated polysaccharides from *Ascophyllum nodosum* could play an important role as immunomodulatory compounds (Blondin et al. 1994). De Araújo et al. (2011) studied the role of a sulfated polysaccharide (SP-Sf), isolated from the red seaweed *Solieria filiformis,* as analgesic and anti-inflammatory compound. For this, they treated mal Swiss mice with the polysaccharide 30 minutes before the injection of 0.8% acetic acid, 1% formalin or 30 min prior to a thermal stimulus. 1, 3 or 9 mg/kg of SP-Sf significantly reduced the number of writhes and the second phase of the formalin test. In addition, SP-Sf did not cause a significant antinociceptive effect in the hot plate test, suggesting that its antinociceptive action occurs through a peripheral mechanism, suggesting that this sulfated polysaccharide may be a key tool for studying inflammatory processes associated with nociception.

In an interesting study, a blend of three extracts from different species of brown seaweeds (*Fucus vesiculosis*, *Macrocystis pyrifera* and *Laminaria japonica*) was administrated, together with some nutritional additives, to 10 randomized participants that receive either a 100 mg (n = 5) or 1000 mg (n = 5) dose over 4 weeks. The objective was to investigate the changes in lymphocyte subsets (primary outcome measures), and to follow the changes in T-lymphocyte (CD4 and CD8) activation, phagocytosis of granulocytes and monocytes, T helper 1/T helper 2 cytokines, and serum oxygen radical absorbance capacity (secondary outcome measures). The mixture used in this experiment was safe for administration during four week and was demonstrated to have significant potential as an immune modulator of the studied parameters (Myers et al. 2011). Kim and Joo, (2008) highlighted the Immunostimulatory effects of fucoidan from the brown seaweed *Fucus vesiculosus* on bone marrow-derived dendritic cells. This polysaccharide significantly increased the viability of DCs, the production of interleukin-12 and tumor necrosis factor-α, and the expression of major histocompatibility complex class I, class II, CD54, and CD86 molecules. In fucoidan treated dendritic cells, p65 molecules of nuclear factor-κB translocated from the cytosol to the nucleus, suggesting that Immunostimulatory and maturing effects of this fucoidan on dendritic cells, via a pathway involving at least the nuclear factor-κB. Furthermore, the important role of sulfated polysaccharides from seaweed (*Cauler pamexicana*, *Cauler pacupressoides*, *Nemalion helminthoides* etc.) as anti-inflammatory, analgesic and as immune-reactions modulators was widely studied (Patel 2012, Rodrigues et al. 2012, Carneiro et al. 2014, Pérez-Recalde et al. 2014, Raposo et al. 2015).

The*ω*-3 polyunsaturated fatty acid (PUFA) of stearidonic acid (SA), *ω*-3 PUFA of eicosapentaenoic acid (EPA) and *ω*-6 PUFA of arachidonic acid (AA) were extracted and purified from the Brown seaweed *Undaria pinnatifida*, then tested for their anti-inflammatory activity using BALB/c mice. The effect of these compounds was revealed by comparing ear edema and erythema after application of Phorbol 12-myristate 13-acétate (PAM). Indomethacin was used as positive control. The three molecules showed significant anti-inflammatory activities and were active against edema, erythema, and blood flow in mice (Khan et al. 2007). Moreover, Heo et al. (2010) evaluated the anti-inflammatory effect extract from the brown algae *Myagropsis myagroides*, using lipopolysaccharide-stimulated RAW 264.7 macrophages. The extract possesses high ability to inhibit nitric (NO) oxide production. The active compound was later identified as fucoxanthin. Therefore, it inhibited NO production, reduced inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) protein expressions, and slightly reduced the prostaglandin E2 (PGE2) production. Their results suggest that the studied fucoxanthin may be useful in therapeutic approach for inflammatory diseases. Jaswir and Monsur (2011) also reviewed the diversity of anti-inflammatory compounds of macro-algae origin (*Sargassum swartzii*, *Ulva reticulate*, *Dichotomaria obtusata*, *Turbinaria conoides*, *Sargassum micracanthum*, *Galaxaura marginata* etc.).

ANTICOAGULANTS AND ANTI-THROMBIC ACTIVITIES

Anticoagulants are a class of drugs that work to prevent blood coagulation (clotting). They are used to treat and prevent blood clots that may occur in your blood vessels (Thrombosis) (Ekanayake et al. 2008). Seaweeds are known to be an exploitable source of anticoagulant compounds. Sulfated polysaccharides, particularly fucose containing polysaccharides, are the main source of such activity in seaweeds (Millet et al. 1999, Smit 2004, Yende et al. 2014). During the nineties, Takashi Nishino and his colleagues published a series of works on molecules with anticoagulant activity, including sulfated polysaccharides, and having as source the brown seaweed *Ecklonia kurome*. In 1989, his work "isolation, purification and characterization of fucose-containing sulfated polysaccharides from the brown seaweed *Ecklonia kurome* and their blood anticoagulant activities" opened. Compared to heparin (a standard anticoagulant), the four purified polysaccharides (B-I, B-II, C-I, C-II) showed a blood anticoagulant activity between 24 and 85%, with respect to APTT (activated partial thromboplastin time) (Nishino et al. 1989). Later, they published another work discussing the composition the anticoagulant C-II, previously isolated from the same marine algae *Ecklonia kurome.* Their analysis results suggested a structure of a highly branched, new type of fucan sulfate containing a backbone of (1+3)-linked L-fucosyl residues having sulfate groups mainly attached to c-4 (Nishino et al. 1991). At the same year, they discussed the influence of sulfate content in the same polysaccharide (C-II) on its anticoagulant activity. For this, they prepared fucans having different sulfate content by solvolytic desulfation of C-II and compared chemical, physical and anticoagulant activities of the product. Their results suggest that the sulfate content strongly affect anticoagulant activity of the fucan, and that fucans having a ration "sulfate/total sugar" < 0.3 had no anticoagulant activity (Nishino and Nagumo 1991). In 1999, they analyzed the effect of the molecule C-II on generating inhibitory effect of thrombin and factor Xa by measuring the amidolytic activities using the respective specific chromogenic substrates in both plasma and purified systems. C-II significantly inhibited the factor Xa generation, blocked prothrombinase formation and preventing intrinsic factor Xa generation. Moreover, C-II was more efficient in inhibiting thrombin generation than in inhibiting its activity (Nishino et al. 1999). Li et al. (2015) characterized a sulfated polysaccharide from the green algae *Codium divaricatum*. This polysaccharide, designated CP2-1, revealed to be a galactan, which is highly sulfated and substituted with pyruvic acid ketals. Its backbone was mainly composed of (1→3)-β-D-galactopyranose residues, branched by single (1→)-β-D-galactopyranose units attached to the main chain at C-4 positions. The APTT assay demonstrated that the pyruvated galactan sulfate CP2-1 is very efficient as anticoagulant may be a potential source of anticoagulant polysaccharide with novel structure. Other studies showed the possibility of extracting and purifying sulfated polysaccharides with anticoagulant activities from seaweeds such as *Sargassum fulvellum* and *Pachymeniopsis elliptica* used as substrate for fermentation (Ekanayake et al. 2008, Zoysa et al. 2008). Seaweeds like *Turbinaria ornata*, *Dictyo pterisdelicatula*, *Codium divaricatum*, *C. adhaerence*, *C. latum*, *C. fragile* and *Padina gymnospora* have also been screened for their polysaccharides having anticoagulant activities (Silva et al. 2005; Ciancia et al. 2010; Arivuselvan et al. 2011; Magalhaes et al. 2011).

ANTIDIABETIC COMPOUNDS IN SEAWEED

Diabetes is a significant cause of continued bad health and premature mortality. It claims more lives per year than HIV with almost one death every ten seconds. The glucose levels regulation in blood is principally based on a negative feedback loop that acts through insulin and glucagon release by both β and α cells of the pancreas, respectively. Thus, diabetes reduces the individual ability to regulate glucose levels in the blood stream, producing various major and minor complications (Kaul et al. 2013).

As time goes on, seaweeds showed significant performance in decreasing or attenuating diabetes complications as important sources of antidiabetic compounds. Thennarasan et al. (2015) studied the hyperglycemic activity of methanolic extracts from the seaweeds *Ulva lactuca*, *Grateloupia lithophila* and *Stoechospermum marginatum*, using an *in vitro* enzymatic assay (α-glucosidase inhibition). Compared to the positive control Acarbose, the two seaweeds *G. lithophila* and *U. lactuca* were more efficient in inhibiting α-glucosidase, with IC_{50} = 427 μg/mL and highest IC_{50} = 760 μg/mL, respectively. The effect of extracts from the brown seaweed *Sargassum polycystum* on Type 2 diabetic rat model (T2DM), compared to that induced by the medicament metformin, was screened by Motshakeri et al. (2014). After 22 days of treatment, the pathological lesions of the livers and kidneys in the diabetic rats were alleviated by both algal extracts (150mg/kg body weight) and by metformin. Oral administration of algal crude extract (300mg/kg body weight) and metformin revealed pancreas protective or restorative effects. Lamela et al. (1989) assayed the hypoglycemic resulting in oral administration of ethanolic extract from the algae *Laminaria ochroleuca*, *Saccorhiza polyschides* and *Fucusvesiculosus,*as well as the intravenous administration of crude polysaccharides and protein solutions from *Himanthaliu elongata* and *Codium tomentosum*, using normal alloxan-diabetic male New Zealand rabbits, respectively. Oral administration of 10 g/kg of F. vesiculosus extract caused significant reduction of blood glucose. *S. polyschides* extracts increased serum triglyceride levels by 36%, 6 h after administration of a 20 g/kg dose. Crude polysaccharides and protein solutions from *H. elongata* showed significant drop in the glycemia of normal animals.

Hardoko et al. (2014) performed an investigation of laminaran ability, fucoidan and alginic fractions from the two brown seaweeds *Sargassum duplicatum* and *Turbinaria decurens* brown seaweed as an antidiabetic agent using the α-glucosidase inhibition-assay. Alginic fraction showed no inhibition activity, while laminaran fractions were more active against α-glucosidase than fucoidans. Laminaran fraction from *Sargassum duplicatum* was the most active (IC50 = 36.13 ppm), followed by laminaran of Turbinaria (IC50 = 44.48 ppm), fucoidan of Turbinaria (IC50 = 63.39 ppm) and fucoidan of Sargassum (IC50 = 75.10 ppm), respectively. Rafiquzzaman et al. (2014) succeeded to purify a hypoglycemic glycoprotein from the edible brown seaweed *Undaria pinnatifida*, through monitoring α-glucosidase inhibition and glucose transport across yeast cell. Their results suggest that this glycoprotein may be used as bioaccessible food additives for controlling postprandial hyperglycemia. After screening α-glucosidase inhibition and glucose uptake stimulatory activities in several species of marine algae from Atlantic Canada, Zhang et al. (2007) highlighted the antidiabetic activity of polysaccharides- and polyphenolic-enriched fractions from the brown seaweed *Ascophyllum nodosum*. Crude polyphenol extract, enriched polyphenolic fraction and polysaccharide extract were prepared from *A. nodosum* powder and administrated to streptozotocin-diabetic mice for up to 4 weeks (200 mg/kg body mass). Crude polyphenol extract and enriched polyphenolic fraction improved abstaining serum glucose level in diabetic mice. Crude polyphenol extract also normalized the reduction in liver glycogen level in diabetic mice. The three fractions enhanced antioxidant capacity in animal's blood. Crude extracts from different seaweeds such as *Padina boergesenii, Halimeda macroloba, Padina sulcata, Sargassum binderi, Turbinaria conoides, Ulva lactuca, Grateloupia lithophila, Stoechospermum marginatum Symphylocladia latiuscula, Laminaria japonica, Sargassum binderi, Padina sulcata, Turbinaria conoides* etc., and different compounds such as poly-, monounsaturated fatty acids and polysaccharides were tested for their antidiabetic activities. These studies are mostly based on extracts or fractions ability to reduce glucose levels via inhibition of α-glucosidase and α-amylase activities or via miscellaneous mechanisms (AGE formation inhibition, Aldose reductase inhibition, Stimulation of GIP and GLP-1 secretion, increasing glucokinase activity etc.). Some seaweed compounds are indirectly implicated in antidiabetic activity due to anti-obesity and anti-inflammatory properties (Chin et al. 2014, Senthilkumar et al. 2014, Murugesan et al. 2015, and Sharifuddin et al. 2015).

CONCLUSION

Human life on earth is facing several problems such as global warming, resource depletion and uncontrollable industrial practices. To meet its increasingly growing requirements, humanity was found obliged to exploit new resources on the globe, seeking for renewable and ecofriendly alternatives to avoid environment degradation. In marine environments, seaweeds are the most important biomass producers that represent potential source of new diverse and unique compounds. For long-time, and especially in the last few years, marine algae were used in several areas such as food, chemical, medical and pharmaceutical industry. Therefore, the compounds cited in this chapter do not cover all the existing neither the discovered algal compounds that could be used in pharmaceutical application, but they do cover the most frequently encountered part of them. In addition, a large portion of these same molecules is used in other domains such as ecofriendly pesticides production, agrochemical compounds, drugs and tools for use in chemical, biochemical and medical research etc. However, (1) improving extraction methods, (2) standardizing analytical protocols for fractionation and safety-evaluation of the purified compounds, (3) identifying active molecules from the already studied crude extracts, (4) seeking for new compounds from new algal material and (5) paying more attention to develop innovative projects constitute essential practices to ensure better use of marine algae in pharmaceutical industry.

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