CHAPTER 6

Review of Marine Algae as Source of Bioactive Metabolites: a Marine Biotechnology Approach

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1 Introduction

Marine algae are the primary food source of a vast ecosystem on our planet. The marine environments are totally dependent of this resource and so are we. It has been estimated that 80% of the oxygen from the atmosphere comes from phytoplankton. Phytoplankton is composed of a considerable variety of photosynthetic microorganisms. In the scientific community there is a concept, which is finding increasing acceptance, that cyanobacteria are not microalgae. Thus, we distinguish two groups: cyanobacteria or blue-green algae (Prokaryota) and microalgae (Eukaryota). According to this concept, we can consider marine microalgae as eukaryotic and photoautotrophic microorganisms.

There are three major groups of macroalgae, Chlorophyta (green algae), Rhodophyta (red algae) and Ochrophyta-Phaeophyceae (brown algae). Macroalgae (seaweed) are multicellular photoautotrophic organisms which besides being primary producers they play an important role in the structuring and maintenance of the marine ecosystems, introducing important nursery spots for a variety of marine species.

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The first industrial interest in studying algae started with the aquaculture industry for both microalgae and macroalgae (seaweed). The demand for seaweed as a direct food resource and the demand for fish production needed the application of aquaculture techniques. In the case of seaweed, this was the only choice for sustainable production. The production of microalgae was necessary for the feeding phase of fish larvae to ensure the survival of newly born juveniles and also for the feeding of zooplankton.

Microalgae production in fish tanks started to show some other advantages such as better water conditions and even more healthy fish production. Then the algae pigments, and their antioxidant capacity, were shown to be of considerable interest, not only for aquaculture but for the human food industry as well. β-carotene was a big production success from the marine microalgae *Dunnaliela salina* (Chlorophyta). This carotenoid is used as food additive, to give more orange to the food and to conserve it better as an antioxidant. This compound can also be found as a food supplement and there are many published studies that refer to β-carotene as a good antioxidant for human health among other carotenoids (Dufossé et al. 2005, Spolaore et al. 2006).

Besides the antioxidants, algae have other relevant compounds such as fatty acids, proteins, polysaccharides, vitamins and minerals. One of the reasons that make algae so suitable for biofuel production is their richness in fatty acids which can be converted into biodiesel, in the case of microalgae, and their richness in sugars which can be converted into bioethanol, in the case of seaweeds.

Polysaccharides and fatty acids derivatives, among other compounds, are the new potential resources for the pharmaceutical and cosmetic industry. Some of these products have shown antimicrobial, antiviral, antitumor and many other qualities. Algae extracts have considerable hydrating skills and cosmetic effects, leading to healthier treatments for human skin.

Another field where marine algae can be applied is in bioremediation. The problem of water pollution like industrial, urban or mining effluents and even crude oil spills, may have an answer in algae treatment. As referred before, the use of algae in aquaculture tanks results in an improvement in the quality of water and healthier growth of fish. This is accomplished with microalgae or seaweed and results in a new concept of integrated multi-trophic aquaculture (IMTA) (Fig. 1; Pinto and Abreu 2011). These characteristics along with some others, like metal accumulation, nutrients uptake or the capacity of crude oil metabolism, turns marine algae into a potential tool for remediation.

The aim of this chapter is to approach the potential that marine algae biotechnology has for different industrial interests and what can we expect of this science in the near future. For that reason, themes such as

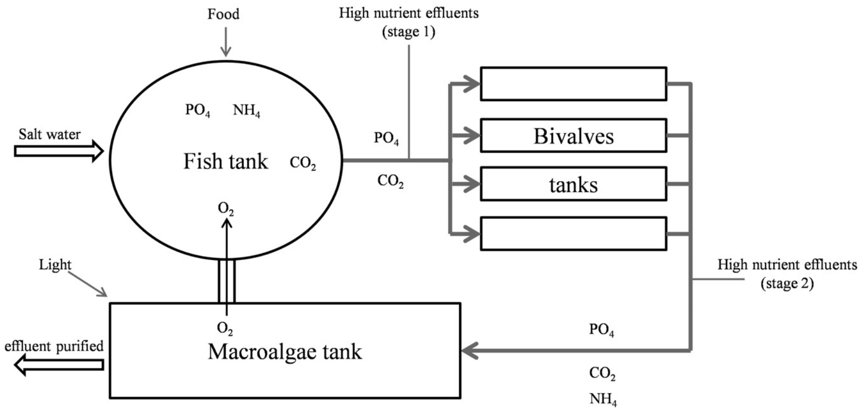

Figure 1. Illustration of an IMTA system. High nutrient effluents (stage 1): dissolved and suspended nutrients. High nutrient effluents (stage 2): dissolved nutrients.

pharmaceutical, food, cosmetics, bioremediation and industrial production will be discussed as potential fields for marine algae biotechnology application.

2 Bioactive Compounds of Marine Algae and their Potential Pharmaceutical Applications

The capacity that algae have in growth inhibition or toxicity against pathogenic microorganisms has been reported a long time ago. Take the example of Chlorellin, the metabolite isolated from *Chlorella vulgaris* (Chlorophyta) (Pratt et al. 1945). It is the presence of pathogenic agents and the need for defense against them that may contain the answer as to how it is possible for these organisms to produce so many interesting antimicrobial compounds.

Extensive work for the screening of antimicrobial effects as a way of research for the new antibiotics discovery, are very common and can usually reveal incredible work. Normally, for seaweeds, their antimicrobial capacity can change among groups of algae (green, red and brown), seasons of the year and area of the globe.

2.1 Antibacterial

Manivannan and collaborators (2011) made a screening for antibacterial effects. A series of bacteria, *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, *Enteroccoci* sp., *Proteus* sp., *Streptococcus* sp., *Pseudomonas aeruginosa*, *Vibrio parahaemolyticus*, *Salmonella* sp., *Shewanella* sp., *Vibrio fluvialis* and *V. splendidus*, *Enterococcus faecalis*, *Vibrio cholerae*, *Shigella flexneri*, *Staphylococcus epidermitis*, *Aeromonas liquefaciens* and *Bacillus subtilus*, were tested through *Turbinaria conoides*, *Padina gymnospora*, *Sargassum tenerrimum* (Phaeophyceae) extracts. All the tree algae could inhibit bacteria growth, some extracts better than others.

There is a good quantity of screening work for antimicrobial effects done all over the globe which has always revealed inhibition of bacteria growth (Osman et al. 2010, Rosaline et al. 2012).

The lipophilic phase, the result of an extraction from a *Skeletonema costatum* culture, showed significant antibacterial effect on *Listonella anguillarum* (Naviner et al. 1999). A study indicates that *Isochrysis galabana* (Prymnesiophyceae) extracts had growth inhibition effect on the multiple drug resistant (MDR) *Mycobacterium tuberculosis*. Further analyses suggested unsaturated fatty acids fractionated from those extracts may be the metabolites responsible for the growth inhibition (Prakash et al. 2010).

There is remarkable work on antibacterial effects from supernatant extracts obtained from *Nostoc caeruleum*, *Limnothrix redekei* (formerly *Oscillatoria redeckei*) (Cyanobacteria), *Thalassiosira profunda* (Bacillariophyceae) and *Leucocryptos marina* (Cryptophyta). The same work revealed antibacterial activity from the biomass extract of *Anabaena oscillatorioides* (formerly *Anabaena circinalis*), *Nostoc punctiforme*, *Pseudanabaena mucicola* (Cyanobacteria), *Monoraphidium contortum* (Chlorophyta), *Thalassiosira profunda* (Bacillariophyceae), *Leucocryptos marina* (Cryptophyta), *Amphidinium carterae* and *Gyrodinium estuariale* (Dinophyceae) (Scholz and Liebezeit 2012).

Phaeodactylum tricornutum (Bacillariophyceae) produces fatty acids with antibacterial capacity against multidrug resistant specimen of *Staphylococcus aureus* (Gram +) and marine pathogen *Listonella anguillarum* (Gram –) (Desbois et al. 2008).

The constant appearance and evolution of new antibiotic resistant organisms are the strong motivation for the continuation of this research. The revealing of all these potential compounds suggests that the next generation of antibiotics could have a significant origin in marine algae.

2.2 Antifungal

Some studies showed the capacity of certain algae to have antifungal capacity. It is more often encountered in microalgae, probably because of competition for the same resources.

Sometimes it is the strong toxicity of some compounds that make that capacity present, like stored polyketide, as the polycyclic ether macrolides, and the openchain polyketides (Cardozo 2006). The only problem is that they demonstrated such high toxicity that they cannot be applied in human therapy.

Amphidinolide B is a kind of compound that has antifungal capacity with high cytotoxic and antitumor capacity, too (Cardozo 2006).

Notable work was done with screening of the antifungal potential of seaweeds. The aim of the work was antimicrobial screening and while antibacterial effects from algae extracts are very common in other cited bibliography, antifungal properties are not that common although a variety of extracts from a group of algae were tested against a series of fungi and revealed positive results as antifungal reaction. The seaweeds *Turbinaria conoides*, *Padina gymnospora*, *Sargassum tenerrimum* (Phaeophyceae) revealed antifungal properties against all the fungal pathogens of the study, such as *Candida albicans*, *Penicillium* sp., *Aspergillus flavus*, *Aspergillus tetreus*, *Candida glabrata*, *Cryptococcus neoformans*. The exception was for *Aspergillus niger* (Manivannan 2011).

More screenings revealed the potential antifungal activity of some algae extracts of *Codium decorticatum*, *Caulerpa scalpelliformis* (Chlorophyta), *Turbinaria conoides*, *Sargassum wightii* (Phaeophyceae), and *Acanthophora spicifera* (Rhodophyta) (Lavanya and Veerappan 2012).

2.3 Antiviral

Fabregas and collaborators (1999) revealed endocellular extracts with virus inhibiting properties from microalgae *Porphyridium cruentum* (Rhodophyta), *Chlorella autotrophica* (Chlorophyta), *Isochrysis galbana* (Prymnesiophyceae) and *Dunaliella tertiolecta* (Chlorophyta) against rhabdovirus of viral haemorrhagic septicaemia (VHSV). The same extracts obtained from *P. cruentum* and *C. autotrophica* also inhibited African swine fever virus (ASFV). The exocellular extracts of all these microalgae had inhibitory properties too, except with the extracts of *I. galbana* against both VHSV and ASFV and *C. autotrophica* and *D. tertiolecta* against ASFV.

Assembled work revealed that seaweed are a potential tool for future application in antiviral research, with particular interest in HIV-1 infection due to some inhibition results; the same is the case for dengue (Mayer et al. 2010).

Phlorotannins, from *Ecklonia cava* and *Ishige okamurae* (Phaeophyceae), are phloroglucinol-based polyphenols responsible for anti-HIV activity. Lectins and polysaccharides of algae demonstrate some kind of effect against the infection capacity of the virus. Sulfated polysaccharides have been shown to inhibit the replication of enveloped viruses including members of the flavivirus, togavirus, arenavirus, rhabdovirus, orthopoxvirus, herpes virus families and HIV virus too. Sulfated polisaccharides of *Dictyota* *mertensii*, *Lobophora variegata*, *Spatoglossum schroederi*, *Fucus vesiculosus* (Phaeophyceae) and the genus of red algae *Grateloupia*, demonstrate some anti-HIV activity (Vo and Kim 2010).

Seaweed rich sulphated polysaccharides, such as fucans and alginates, produced from brown algae are good antiviral tools. Assembled works about these compounds consider *Undaria pinnatifida* (Phaeophyceae) fucans antiviral tools (Wijesinghea and Jeon 2012).

2.4 Antitumor

Herbivores have a persistent presence in the environment of marine algae. Among microalgae this behavior is mostly produced by the zooplankton, but adult fish and other adult organisms that feed by filtration play their role in this food chain too. Some microalgae develop silica structures that do not allow a predator to consume them because it just cannot swallow the algae. This way of defense is dominated by diatoms (Bacillariophyceae*)*, but the avoidance of being eaten by size and structural changes can be accomplished through the formation of colonial structures, too (Donk et al. 2010). So, as the colony grows bigger, with higher numbers of individuals, the more difficult it becomes for predators to swallow it, at least for small predators. Other algae develop ways of moving in the water column making them a more difficult target. Yet another way is the development of biochemical weapons.

These biochemical weapons can be toxins, repellents or compounds that can inhibit mitosis provoking some lower hatching rates or abnormal physical development in their predators or even compromising their egg development and metabolism (Donk et al. 2010).

Normally toxins are very harmful to organisms and some case studies have revealed that those produced by some marine microalgae have considerable consequences because of their strong interaction and toxicity.

Microalgae produce compounds that repel their predators. It is not yet known how the produced compounds react towards the predators to induce such behavior, but they work like an alert signal that induces other microalgae to produce mechanisms of predatory defense.

Antitumor compounds may be the ultimate and most enthusiastic discovery in microalgae. This type of compound is the most wanted because of the possibility of discovering a tool against cancer. Briefly, cancer is a direct result of abnormal cell division by mitosis, so, if microalgae produce compounds that act specifically inhibiting mitosis, they might be an answer for future cancer therapies. *Skeletonema costatum*, *Chaetoceros calcitrans*, *Guinardia delicatula*, *Guinardia striata*, *Odontella regia*, *Rhizosolenia setigera*, *Stephanopyxis turris*, *Thalassiosira pseudonana* (Bacillariophyceae), are some of the microalgae producing these metabolites (Donk et al. 2010).

It is reported that diatoms such as *Thalassiosira*, *Skeletonema*, *Odontella*, *Chaetoceros*, *Navicula*, *Nitzschia*, among others, together with some dinoflagellates (Dinophyceae) such as *Prorocentrum micans*, *Gymnodinium sanguineum*, and *Lingulodinium polyedra* (formerly *Gonyaulax polyedra*) induce low hatching and low fertilization success in copepods, even in high egg production. Those that could hatch were presented with some deformities, expressing marked morphological asymmetry which resulted in their death a few days after (Ianora and Poulet 1993, Ianora et al. 1999, Lee et al. 1999, Caldwell et al. 2002, Poulet et al. 2007). These morphological development alterations were proposed to be the result of compounds with some kind of mitosis inhibition effect that could accumulate in the reproductive organs of the copepods that were fed with a diatom or dinoflagellate rich diet and somehow were transferred to the eggs. Studies revealed that the strongly reduced hatching success of wild copepods feed on diatoms were due to the existence of short chain polyunsaturated aldehydes. These compounds are produced by cell disruption of the microalgae (Caldwell et al. 2002). Somehow, these compounds exist in the living cell at standard concentration, but the disruption of the cell leads to the liberation of these compounds to the surrounding medium which are recognized by other diatoms as a kind of signaling that might induce the overproduction of the compounds.

These events were already named as diatom-derived embryonic inhibition, and some of the agents were identified as two C_{10} short chain polyunsaturated aldehydes (PUAs) from *Thalassiosira rotula*, *Skeletonema costatum* and *Pseudo-nitzschia delicatissima* (Bacillariophyceae). Continuous research was carried out on this subject leading to the development of new methodologies for the study and detection of these compounds which gave us the idea of the existence of a range of PUAs: 2-trans,4-trans decadienal (DDE); 2-trans,4-trans,7-cis decatrienal and 2-trans,4-cis,7-cis decatrienal (Caldwell et al. 2002).

Some seaweed have demonstrated good effects against cancer cells and tumors. Compounds such as alginates, a type of polysaccharide produced in brown alga *Sargassum vulgare*, revealed antitumor effect by *in vivo* growth-inhibition (Sousa et al. 2006). Reviewed assembled work about different fucans of *Undaria pinnatifida*, *Ecklonia cava*, *Fucus evanescens*, *Saccharina gurjanovae* (formerly *Laminaria gurjanovae*), *Cladosiphon okamuranus* (Phaeophyceae), are considered as antitumor, anti-proliferation or anticancer candidates (Wijesinghea and Jeon 2011).

2.5 Biological Tools

Squalene is a polyunsaturated triterpene and is a natural biochemical precursor of cholesterol and other steroids. It is naturally produced by animals and plants. Known work was done with olive tree, sharks, cereals and other plants and animals (Reddy and Couvreur 2009, Grigoriadou et al. 2006, Nakazawa et al. 2011). Research on squalene is mostly applied in human health studies because of its great capacity for better delivery of vaccines, drugs and other substances through squalene emissions (Reddy and Couvreur 2009).

The stability related to some other individual capacities of this compound, such as antioxidant and even antitumor, make squalene an exceptional tool in medicine application as an adjuvant or other kind of tool. Binding this compound to drugs, or other compounds for therapy purposes, turns the therapy more successful than other emulsions. The reason is related to the protection of the drug due to squalene's stability and antioxidant aspect. This way, the therapeutic compound is protected from the surrounding metabolism influence which leads to its prolonged effect (Reddy and Couvreur 2009).

Because squalene is naturally produced in the human organism, found even in the skin, excreted as constitute of sebum, its use assures biocompatibility, thus making it less suitable for an immune reaction. This also is the key for the success of squalene emulsions for vaccination. Somehow, not only does it protect the drug or antigen but, due to its biocompatibility, the drug transportation and even recognition is higher than in traditional vaccine solutions (Reddy and Couvreur 2009).

There are microalgae that are known for high levels of squalene production which might be a better and more sustainable solution than liver oil from high depth sharks and better than other plant resources because of higher production rates (Yue and Jiang 2009, Kebelmann et al. 2012).

This compound is just an example of a biological tool with high commercial value that can be extracted from algae. Algae can reveal new biological tools that can be applied in research or other fields.

2.6 Toxins—Pharmacological Tools and Potential Drug Leads

It is rare to find eukaryotic microalgae that produce toxins because, in most aquatic environments, blue-green algae (Cyanobacteria) are responsible for toxins production by bloom formation (Table 1), although, there are some eukaryotic microalgae, such as some diatoms (Bacillariophyceae) and dinoflagellates (Dinophyceae), which originate harmful algal blooms (HAB) and produce some dangerous toxins that can affect the nervous system (Vasconcelos et al. 2010).

The subject of HAB is a very important area of research, especially if we consider the risk of human health safety at all water resources and touristic destinations such as beaches, estuaries, lakes and rivers. All this is to say that, the already known toxins produced by these organisms can provoke some serious problems, and depending on the toxins, even simple

Table 1. Marine algae biotoxins and their syndromes and mechanisms of action.

Microalgae	Toxins	Effects and/or syndromes	References
Anabaena spp.; *Oscillatoria* spp.	Anatoxins	Post-synaptic nicotinic agonist and acetylcholinesterase inhibitor	Cardozo et al. 2006
Pseudo-nitszchia spp.	Domoic Acid	Glutamate receptors; Amino acid Limited TNF-a and matrix metalloproteinase-9 release; amnestic shellfish poisoning (ASP)	Cardozo et al. 2006, Mayer and Hamann 2005
Gambierdiscus toxicus	Ciguatoxins	Voltage dependent sodium channel blockers; ciguatera fish poisoning (CFP)	Cardozo et al. 2006
Dinophysis spp., *Prorocentrum* spp.	Dinophysistoxins Okadaic acid	Ser/Thr protein phosphatases inhibitors; diarrhetic shellfish poisoning (DSP)	Cardozo et al. 2006
Nodularia spp.	Nodularins	Protein phosphatase types 1 and 2A inhibition; Liver failure and death by hipovolemic chock	Cardozo et al. 2006, Vasconcelos et al. 2010
Gymnodinium breve	Brevetoxins	Voltage-dependent sodium channel site 5; neurotoxic shellfish poisoning (NSP)	Cardozo et al. 2006
Alexandrium spp., *Gonyaulax* spp., *Gymnodinium* spp.	Saxitoxins	Voltage-dependent sodium channel site 1; paralytic shellfish poisoning (PSP)	Cardozo et al. 2006
Protoperidinium crassipes	Azaspiracid (AZA)	Diarrhetic shellfish poisoning (DSP)	Twiner et al. 2008
Dinophysis spp.	Pectenotoxin	Macrolidee Disruption of F-actin cytoskeletal; Induction of F-actin depolymerization	EFSA 2008, Mayer and Hamann 2005
Protoceratium reticulatum, *Lingulodinium polyedrum* and *Gonyaulax spinifera*	Yessotoxin	Lymphocyte [Ca2+]i homeostasis modulation; Inhibition of calcium channels	Paz et al. 2008, Mayer and Hamann 2005
Ostreopsis spp.	Palytoxin	General malaise and weakness, associated with myalgia, respiratory effects, impairment of the neuromuscular apparatus and abnormalities in cardiac function	Tubaro et al. 2011
Symbiodinium spp.	Zooxanthellatoxins	Vasoconstrictive	Gordon and Leggat 2010
Gambierdiscu sp., *Ostreopsis* sp.	Maitotoxin	Modulation of calcium and sodium influx	Mayer and Hamann 2005
Lyngbya majuscula	Antillatoxin	Potent neurotoxin; depolarization-evoked Na+ load, glutamate release, relief of Mg2+ block of NMDA receptors, and Ca_2 + influx	Li et al. 2001, Mayer and Hamann 2005

Microalgae: known species that produce toxins; toxins: known marine toxins produced by microalgae; effects and/or syndromes: known consequences or mechanism of action of the toxins.

skin contact or breathing during a swim could let to intoxication (Hinder et al. 2011).

In most environments, toxins bioaccumulate in the food chain and normally, high concentrations can be detected in the top food chain predator. In the aquatic/marine environment, seafood such as shellfish, which feed through a process of filtration, can accumulated high amounts of toxins because of their resistance to them.

The ingestion of contaminated shellfish can let to high intoxication leading to toxicological effects such as hepatotoxicity, dermal toxicity, cytotoxicity, neurotoxicity and, in some extreme cases, death (Hinder et al. 2011).

Marine biotoxins are classified in ten groups: azaspiracid (AZA), brevetoxin, cyclic imine, domoic acid (DA), okadaic acid (OA), pectenotoxin (PTX), saxitoxin (STX), yessotoxin (YTX), palytoxins (PlTX) and ciguatoxins (CTX) (EFSA 2008). Azaspiracid (AZA) is one example of a marine toxin that can be found in shellfish and one of the known microalga responsible for its presence is *Azadinium spinosum*, which allows the assumption that the entire group *Azadinium* spp. (Dinophyceae) might produce AZA.

The known toxicity of marine toxins and their common presence in food resources makes it necessary to study and develop methods of analysis, detection and clinical tests. The problem is the need for some quantities of the toxin for those tests. Once more, biotechnology enters to help beginning with the first step of culturing techniques, followed by extraction processes and purification of toxins (EFSA 2008, Jauffrais et al. 2012).

The most interesting part is the possibility of finding some other potential applications of the toxins in the study because of their known mechanisms of action in the organism (Table 1). For example, during some toxicological essays, the understanding of the toxin's action mechanism could lead to the discovery of unknown pharmacological tools (Mayer and Hamann 2005).

2.7 Other Pharmaceutical Capacities

Other capacities from algae that we can find are anticoagulant and antithrombotic activity from fucans of *Ecklonia cava*, *Fucus evanescens*, *Padina gymnospora*, *Ascophyllum nodosum*, *Sargassum fulvellum*, *Hizikia fusiformis*, *Saccharina cichorioides* (formerly *Laminaria cichorioides*) (Phaeophyceae).

There are anti-inflammatory compounds and tissue protection from the fucans of *A. nodosum*, *C. okamuranus*, *Saccharina japonica* (formerly *Laminaria japonica*); and immunomodulation from the fucan of *Fucus vesiculosus* (Wijesinghea and Jeon 2012, Xia et al. 2005). There are other capacities as the tissue protection, like the neuroprotective effect found in microalgae (Pangestuti and Kim 2011).

Algae are a source of new bioactive compounds against protozoan diseases (Felício et al. 2010). The genus *Symbiodinium*, belonging to the Zooxanthellae, accumulates some unique macrolides, an interesting toxin with a 62-membered macrolactone structure and potent vasoconstrictive activity (Cardozo et al. 2006). There is even interest in the antifouling property of algae (Maréchal et al. 2004).

Unfortunately in the pharmaceutical world, it is not enough to discover a new compound. Clinical research is done to study if the compound produces good results in its own function, with good success rates; biospecific behavior, with very low or no toxicity for human or animal treatment and some other subjects have to be considered. For the production to be suitable, some key processes are important, such as the biomass/compound ratio, the extraction and purification rate, the stability of the compound and finally if it is worth the trouble, or in other words, if it is commercially viable.

The problem here is that for every compound found, extraction and purification methods have to be studied. After finding the best method we have to be certain that the quantity of the compound produced by the algae is the highest; so, culturing studies are a necessary way to achieve the best compound/biomass ratio. Resuming, finding new marine drugs takes a lot of qualified research that can take a good many years.

3 Marine Algae and the Food Industry

As stated earlier, algae are the primary producers of most aquatic habitats. They are well known for their rich nutrient composition such as vitamins, lipids, proteins, carbohydrates and minerals. This makes these organisms a good and healthy source of food for those who realize these facts. Some of the most famous names of seaweed as direct source of food are *Ulva* (Chlorophyta), *Porphyra* (Rhodophyta), *Undaria*, *Laminaria*, *Himanthalia* and *Saccharina* (Phaeophyceae) (Pereira 2011). The high demand for this resource from some countries results in their increased production through aquaculture. Seaweed are gathered too but mostly as an unsustainable way. An ecological approach with sustainable gathering of seaweed for food is possible but it will never be enough for the total demand.

The same aspects are true for microalgae. They too are a primary food resource for human populations, but with less diversity of resources. The name *Spirulina* as a food source is not so recent. *Spirulina* spp. was used for many years as direct food supply in different regions of the globe for centuries, such as Central America and Africa. In the case of China, it was *Nostoc* (Milledge 2010). These genera of Cyanobacteria grow naturally with abundance in some salty or mineralized lakes or river channels. Local populations learned how to harvest, store and preserve these resources when nothing else was available to eat (Spolaore et al. 2006).

Besides their application as a human food resource by gathering, microalgae's first industrial production and applications were as feeding stocks for aquaculture. The advances in microalgae culturing techniques made possible their use as a source of food for all stages of some fish and bivalve mollusks or for larval stages of some crustaceans and fish. Thus, the aquaculture industry did not need to capture plankton and young fish from the oceans anymore.

There is a considerable variety of microalgae used for these means; those more often used, such as *Skeletonema* spp., *Thalassiosira* spp., *Chaetoceros* spp., *Phaeodactylum* spp. (Bacillariophyceae), *Isochrysis* spp. (Haptophyceae), *Tetraselmis* spp. (Prasinophyceae), *Chlamydomonas* spp. (Cryptophyceae), *Dunaliella* spp. (Chlorophyta) and *Spirulina* spp. (Cyanobacteria), are those whose nutrient composition is better known.

Today *Arthrospira platensis* (formerly *Spirulina platensis*) and *Spirulina maxima* are produced on a large scale for many different objectives from a food supplement perspective. They are easily found as capsules in natural products stores, as rations or supplement for aquaculture fish or ornamental fish and as rations for cattle and pets. Some farmers let this organism or other Cyanobacteria grow naturally in pounds which enrich the water for cattle (Cohen et al. 1991).

All this application of *Arthrospira* and *Spirulina* spp. is supported by the nutrient composition found, like the protein content of the biomass which is known to reach a high percentage of the total biomass content. This aspect together with the know-how of culturing techniques for *Spirulina* spp., makes this organism an alternative for feeding cattle rather than crops such as maize or soy. Even though we are talking of a fresh water resource, the marine species, *Spirulina subsalsa*, is also available and does not differ that much from the other fresh water genera.

The advantages of algae in diet due to their nutritional value, are well known, although in the future marine algae might be considered as functional food or nutraceutics (Gupta and Abu-Ghannam 2011, Mohamed et al. 2012).

There are products for quality and healthy feeding produced from diatoms and other microalgae for pet, cattle and other farmed animals (Milledge 2010). These are presented as ration foods, supplements and diatom sand, which is said to help and prevent against internal and external parasites (animal skin parasites).

There are many more interesting bioactive compounds that are of interest to the food industry (Pereira 2011, Gupta and Abu-Ghannam 2011), and some will be further discussed.

3.1 PUFAs

The lipid content of marine algae is well appreciated. Microalgae are those which produce such compounds in higher quantities than seaweed. What makes them so interesting are not only the saturated fatty acids, which are the primary reason for the burst of research on microalgae as a fuel resource. What really makes them a target is because they are excellent producers of unsaturated fatty acids and polyunsaturated fatty acids (PUFAs) (Cohen et al. 1991, Spolaore et al. 2006).

These metabolites are considered high value products because of their properties in general health when consumed. PUFAs can be found in fish biomass and are obtained by fish through an algae-rich diet in their environment. Initially, these PUFAs were industrially produced by the use of fish biomass; more properly, the fish waste produced from the fisheries. However, there was too much risk of getting undesired compounds in the final product such as toxins and other pollutants. Now, the best way of producing PUFAs for consumption is with microalgae production (Barclay et al. 1994).

There are studies that establish the importance of these metabolites in the early development of human fetus and during the development of the human baby. The presence of PUFAs in the organism ensures the good development of the nervous system and optic system and the general growth and well-being of the organism by means of homeostasis. The consumption of PUFAs works like we are giving the best tools for our organism to function resulting in an healthier status, for example, lowering the risk of heart diseases and, perhaps, giving better chances against some cancers, improving the immune system or protecting against inflammatory like diseases (Cardozo 2006, Milledge 2010).

That is why pregnant women and mothers who breast feed are advised to take PUFAs as supplements or to adopt a diet rich in PUFAs, in order to ensure the uptake of these supplements by the fetus or baby for its healthier development (Milledge 2010).

Another important role of these molecules, besides development regulation, is in regulatory physiology (Cardozo 2006).

Most marine microalgae produce PUFAs but the record holder in variety and quantity of these metabolites, compared with all biomass content, are the algae from Ochrophyta phylum, especially diatoms (Bacillariophyceae) (Milledge 2010). Work was done to find the most PUFA-rich algae among those that potentially might be used for aquaculture (Patil et al. 2006). The ω-3 kind of PUFA is the most common such as docosahexaenoic acid (DHA, 22:6ω3) and Eicosapentaenoic acid (EPA, 20:5ω3), produced, for example, by *Phaeodactylum tricornutum* (Desbois et al. 2008).

PUFA ω-6 is present in a wide variety of microalgae and is as much desired. Gamma-linolenic acid (GLA, 18:3ω6), which is industrially produced by *Spirulina* spp. for human consumption is also an example (Cyanobacteria). But there are marine algae used for producing the same compounds, though they are more applied for aquaculture feeding. Arachidonic acid (AA, 20:4ω6) can be found on *Porphyridium purpureum* (formerly *Porphyridium cruentum*) (Rhodophyta) (Bigognoa et al. 2002).

3.2 Phycocolloids (Polysaccharides)

Macroalgae are known for their high content in polysaccharides. In the algae group, seaweeds are the richest sources of sulphated polysaccharides. These compounds are very valuable resources for the food industry. They are used as additive agents because of gelling and thickening properties (e.g., alginates, agar and carrageenan) and can be found as the following European codes: alginic acid—E400, sodium alginate—E401, potassium alginate—E402, ammonium alginate—E403, calcium alginate—E404, propylene glycol alginate—E405, agar—E406, carrageenan—E407, semirefined carrageenan or "processed *Eucheuma* seaweed"—E407A (Pereira et al. 2013) (see also the Chapter 8).

These additives can be found in aqueous based jellifying deserts, low calorie jelly, flans, puddings, chocolate milk, milk derivatives, ice-creams, soy milk, cheeses, processed and canned meat, beer, gravy, sauce, jam and other processed foods.

Members of the red algae (Rhodophyta) produce galactans (e.g., carrageenans and agars).

Brown algae (Ochrophyta, Phaeophyceae) produce uronates (alginates) and other sulphated polysaccharides (e.g., fucoidan and laminaran).

3.2.1 Agar

Agar is well known as an inert support medium for microbial culture but it also has applications as a gelling agent for food.

Although agar was found in a variety of red algae, those industrially more important are the genera *Gelidium*, *Pterocladiella*, *Gelidiella*, and *Gracilaria* (Pereira et al. 2003, Pereira 2011, Pereira et al. 2013).

3.2.2 Carrageenan

There are three commercial carrageenans, kappa-, iota-, and lambda-carrageenans but in nature, there is a variety of carrageenan hybrids due to the existence of different precursors and their concentrations in the algae content. Each type of carrageenan has a property, the kappa type forms hard, strong, and brittle gels, iota-carrageenan forms soft and weak gels and lambda-carrageenan acts as a thickening agent.

This compound is industrially obtained by *Kappaphycus alvarezii*, for kappa-carrageenan, *Eucheuma denticulatum*, for iota-carrageenan, and genera *Gigartina* and *Chondrus*, for lambda-carrageenan (Pereira et al. 2009a,b, Pereira 2011, Pereira et al. 2013).

3.2.3 Alginic acid and derivates

Alginic acid is extracted from brown algae (Ochrophyta, Phaeophyceae) as a mixed salt of sodium and/or potassium, calcium and magnesium and its composition varies in each algae.

Alginic acid is the precursor of its derivatives such as the famous alginate. The commercial species selected by industry for the extraction of this compound are *Macrocystis pyrifera* and *Ascophyllum nodosum* but an extended range of other raw material such as *Laminaria*, *Lessonia*, *Alaria*, *Ecklonia*, *Eisenia*, *Nereocystis*, *Sargassum*, *Cystoseira* and *Fucus* are also used (Pereira 2011, Pereira et al. 2013).

This type of polysaccharide not only shows appropriate use in the food industry, but there are studies revealing some antitumor and other types of pharmaceutical applications (Sousa et al. 2006).

3.2.4 Fucans

Fucans are an example of sulphated polysaccharides extracted from brown algae (Ochrophyta, Phaeophyceae). The most studied is fucoidan and it is already commercially produced using *Fucus vesiculosus* as raw material (Pereira et al. 2013).

It is not a candidate for the food industry as an additive, but it shows great prospects for the pharmaceutical field. Now, the most appropriate use for this compound is its application as a food resource, or better, as a nutraceutical.

Functional food as a health improver is more and more common today. It is easier to put a functional food in the market than a new pharmaceutical drug because of the long processes needed to assure the safety procedures of use for that drug. If in a short term we want to put a functional derivative from seaweed in the market, the best way is to select one from an already considered edible seaweed. This way the safety of the product is already secure, although, we still have to prove the beneficial use of our product and how there is more advantage in the use of this pure derivative product from a seaweed instead of the all seaweed.

3.2.5 Laminaran

Laminaran and its derivatives are other sulphated polysaccharides that could become functional food. Extracted from some brown seaweed (Laminariales), they have a lot of potential in the area of health, for example, it has known antitumor effects (Ibrahim et al. 2005).

3.3 Pigments

3.3.1 Carotenoids

Carotenoids are widely explored compounds by the food industry because of their color and, in the case of β-carotene, astanxantin and fucoxanthin, their known antioxidant capacity (radical scavenging activity). Recent studies reveal a range of properties that some pigments have, such as antitumor effects, apoptosis induction on cancer cells and anti-inflammatory effects (Dufossé et al. 2005, D'Orazio et al. 2012).

3.3.2 β-carotene

Although most of the time, the β-carotene used is the synthetic one, producers and consumers are increasingly demanding the use of the naturally produced one by *Dunaliella salina* (Chlorophyta) (Spolaore et al. 2006, Milledge 2010). Chicken eggs enriched with β-carotene or lutein can be found in the supermarkets, although there is no reference or publicity of these supplements in the eggs sold, they are widely used to enhance the appearance of egg yolks to a deeper shade of orange. To achieve this result the carotenoids are given through the food consumed by chickens which will later be part of the egg yolk.

This kind of strategy is not so recent; moreover, for human health purposes, the efforts are focused on the production of functional foods (nutraceuticals) (Spolaore et al. 2006, Milledge 2010, Gupta and Abu-Ghannam 2011, Mohamed et al. 2012). Although some communities who know the nutritional advantages of an algae rich diet consume it traditionally, it may not be available to all, and neither does it appeal to everyone. However, people who may never have eaten algae in their life might reconsider its inclusion in their diet if studies show that it confers significant health benefits.

The use of algae pigments as an objective for food application might have started with fish aquaculture. Aquaculture industry is the industry with the most focus on this matter (Dufossé et al. 2005). As said before, the food resources for aquaculture fish were and still are, mostly rations obtained and developed from fisheries industries that use fish waste (body parts of fish considered unfit for human consumption). In aquaculture, these rations are suited to carnivorous fish. They have high levels of proteins and oils and are enriched with vitamins and minerals if needed. The problem arose when consumers did not want to buy full grown salmon reared for commercial purposes, because it did not have the typical "salmon color".

Research was done to resolve this problem and it was discovered that the color of the wild salmon, originates from its diet that is rich in krill, an orange/pink crustacean. This crustacean is rich in carotenes and β-carotene. But krill does not produce these pigment, it gets them through its microalgae rich diet. The problem was solved by enrichment of the fish rations with a good percentage of microalgae or directly with the pigments. The salmon started to gain its true color and got more acceptance from consumers.

Carotenoids have proved to be of interest to human health. They have provitamin A activity, and can still remain active where the normal vitamin C cannot in low oxygen rates. These pigments, such as β-carotene, modulate UVA induced gene expression, protect the skin and eyes from photo-oxidation against UV light, and prevent human eye disease such as cataract (Dufossé et al. 2005).

3.3.3 Astaxanthin

Astaxanthin can play a diversity of roles, such as prevention of some human pathology, like skin UV-mediated photo-oxidation, inflammatory processes and even cancer (Spolaore et al. 2006).

When natural astaxanthin started to be industrially produced, some salmon aquacultures preferred the use of this pigment or added it to the salmon diet. This pigment, as with β-carotene, is a large scale production compound extracted from the freshwater microalgae *Haematococcus pluvialis* (Chlorophyta) (Dufossé et al. 2005, Spolaore et al. 2006). It is not only the living red color of this compound that the food industry contemplates, but its antioxidant capacity, higher than β-carotene that considerably increases the value of this product. While it is the "know-how" of *H. pluvialis* culturing techniques that makes this organism the target for astaxanthin, this metabolite is present in a large variety of marine microalgae.

3.3.4 Fucoxanthin

Fucoxanthin is a xanthophyll present in Ochrophyta phylum of algae that, with the presence of the other pigments, gives a brown-yellow or olive-green appearance. As with all carotenoids, the antioxidant effect is remarkable, but in this case, antitumor effects, apoptosis induction on cancer cells, anti-inflammatory effects and radical scavenging activity were reported. Ultimately, we have to focus on the most probable application of this compound. The most promising one is in the food industry or, more precisely, in functional food (nutraceutical). It is a shorter way to reach the consumer and the health benefits are strongly supported in the bibliography which, recently, has been focused on the capacity that fucoxanthin has to modulate the expression of specific genes responsible for cell metabolism (D'Orazio et al. 2012).

The results of those studies are those which can affirm the activities recently mentioned for fucoxanthin, such as apoptotic cell death in primary effusion lymphoma (antitumor effect), through the functional inhibition of Hsp90 chaperon, abdominal white adipose tissue burner as mRNA, protein inducer through modulation of the UCP1 gene, and other good consequences that might be called positive secondary effects of the uptake of this remarkable compound (D'Orazio et al. 2012).

3.3.5 Chlorophylls

Chlorophylls are other metabolites well appreciated by the food industry. Although chlorophyll is easily found in every plant, they are in all algae too. There is no algae production for exclusive extraction of chlorophylls, but its obtention as a secondary product of an algae production is more likely to happen. It would be a loss of value if in the process of producing a determinant product we could not separate the chlorophylls and isolate them. The reason is because these pigments are largely used in food industry and mixed with other pigments to obtain a large variety of colors. Above all of these advantages, it is important to refer that these compounds are increasing in use to put an end to the use of synthetic pigments for the food industry.

3.3.6 Phycobiliproteins

Phycobiliproteins are the pigments that give most organisms of the Cyanobacteria group their blue-green color and Rhodophyta group their red color, from such algae like blue-green algae *Arthrospira* and the red algae *Porphyridium* respectively (Spolaore et al. 2006). Again, these colors offer natural pigments for food processing (Milledge 2010), substituting for synthetic colorants. For the same reasons, cosmetic and pharmaceutical industries too use these pigments for their products as colorants. Beyond these applications, phycobiliproteins possess some other interesting characteristics that make them excellent tools in research. Because of their capacity of fluorescence in known wavelength, studies in immunology are using these pigments as markers in assays for those research studies (Spolaore et al. 2006).

4 Marine Algae as Tools for Bioremediation

Algae are very profitable tools for bioremediation. For instance, high levels of nutrients in water are always the promoters of algae blooms, not only microalgae but seaweeds too, and it normally leads to eutrophication of the water systems. In this situation, algae might look to be the problem, although they are only responding to environmental changes. The most important to retain of this algae behavior is that it can be a helpful tool for eutrophication problems. The strategy is to treat these high nutrient effluents before they reach the water environment. Not all waste water treatment stations (WWTS) have the tertiary treatment required for high nutrient water effluents, and when they do, it is a chemical treatment that is usually adopted. Nowadays the possibility of using microalgae instead of chemical treatment for high nutrients effluents is a well known matter.

Microalgae are the most suitable for this kind of job—they grow fast, are in suspension and there is the potential for biomass recovery for industrial production, such as biofuel and cattle feed depending on their quality. What made this possible is the knowledge of some algae with good growth rates and high lipid production that can really be a solution for the future of pollution issues (Rawat et al. 2010).

Macroalgae are not mentioned because most of the industry and even WWTS's are located near fresh water sources where effluents are more likely to be discharged. There are no known fresh water macroalgae suitable for these kinds of treatments but there are a lot of industries with near-shore activity that could use macroalgae as a bioremediation tool for high nutrient problems.

We can take the example of the fish aquaculture industry. Fish production in aquaculture is a polluting activity because of the big population of fish that needs to be fed and that produces high quantities of excrement in a limited area. Not all the food is consumed which, together with the excrement, produces effluents of high nutrient concentrations. Those effluents could be used by algae before getting to the seawater. This would solve the fish production problem and at the same time there would be profit with the algae biomass recovery.

The other benefits from introducing a controlled algae culture is the reduction of CO_2 and production of O_2. This simple task performed by algae result in a healthier environment for fish, reducing the risk of anoxia and establishing some balance within the bacteria population. If the environment is rich in O_2, only aerobic bacteria can develop, normally, those less problematic. This way we might reduce infections, not only with O_2 but with healthy competition for nutrients between algae and bacteria.

Nitzschia sp., a benthic microalga, is a good example of how algae can serve as a tool. Studies have revealed that biofilm development of this alga in organic enriched sediments led to the recovery of those sediments, not only by direct action of the algae but because of the production of O_2 that promoted aerobic biodegradation among bacteria (Yamamoto et al. 2008).

Bioremediation in the algae world is more related to the microalgae domain. Studies about heavy metal uptake, like cadmium uptake by *Chlorella* sp. and other Chlorophyta and Cyanobacteria are common in the published bibliography for other heavy metals such as iron and aluminium (Matsunaga et al. 1999, Harun et al. 2010, Richards and Mullins 2012). In this case we are talking about the incorporation of the metal into the algae body which makes possible to recover the pollutant source with the biomass harvesting.

Seaweed might seem a difficult tool to apply because of a slower growth rate and the need for substrate fixation. Would that problem be solved with the use of extracts? Research with *Ascophyllum nodosum* demonstrates it as a good tool for heavy metal absorption, as is *Fucus vesiculosus* (Phaeophyceae). This capacity happens to be related with the biochemical composition of the cell wall (polysaccharides) (Harun et al. 2010).

There is record of the capacity that algae have on the degradation of lindane, an organochlorine. An experiment with microalgae, regarding their quick capacity to adapt when environment conditions change reported that *Desmodesmus intermedius* (formerly *Scenedesmus intermedius*) (Chlorophyta) was able to adapt and grow with a high concentration of this contaminant among other species that could not. This involved not only proof of a quick adaptation capacity but also the capability to metabolize organochlorines (González et al. 2012). *Navicula* sp., *Phaeodactylum tricornutum*, *Nitzschia* sp. and *Synedra* sp. (Bacillariophyceae) are examples of algae that can degrade phloroglucinol and naphthalene; other freshwater algae can degrade herbicides including the marine diatom *Skeletonema costatum* (Yang et al. 2012). This makes way for new research about finding microalgae that can solve the problem of degrading other toxic compounds.

Oil spills are some of the most complicated situations. In places with such problems, the toxicity is so high that biodiversity is drastically diminished and it takes years before the local ecosystem gets restored. The petroleum compounds have a strong negative effect on the primary producers, such as algae although, the same organisms are, possibly, an advantage for crude polluted environments. The study of some microalgae has shown their capacity for physiological adaptation and was supposed to result in genetic adaptation too (Romero-Lopez et al. 2012). If that is true, microalgae genetic mutations due to petroleum contaminants exposure could result in the creation of new natural tools for these kinds of bioremediation.

Algae can really surprise us with their versatile and complex behavior. Overall there is enough knowledge for the application of algae in bioremediation, at least in the near future in high nutrients effluents.

5 Cosmetic Potential of the Marine Algae

Algae are used for their therapeutic capacity in cosmetic application or in areas of health and body care, like spa treatments. Thalassotherapy is the use of the therapeutic benefits from the sea. Normally, it is the application of seawater bath treatments with the help of some mixes of salts, sand and seaweed infusions. We might even say that this therapy makes good use of natural and biological tools to help the skin and body of a person through the combination of ingredients from the sea (Pereira 2010).

The sea ingredients all together with some relaxing approaches and techniques are why thalassotherapy is so appealing by those whom had the opportunity to experiment it.

Although, there is particular interest to fully understand what are the agents responsible for such therapeutic effects. Separate these sea ingredients and study them individually seems to be a smart strategy to the development of new products for the cosmetic industry. For example, some sunscreen contain algae extracts or more purified compounds that protect the skin from solar radiation. Some seaweed (Ochrophyta, Phaeophyceae) and microalgae are widely used for sunscreen production.

If we still think about the possibility to use only one compound from algae, and that it is more reliable to isolate only that compound from the algae to achieve our case-study goal we are looking away from a problem. Sometimes research of new natural compounds for health and care applications reveals that it is not the isolated compound that makes the difference, but the synergy from the interaction of a group of compounds which results in therapeutic solution.

Is the thalassotherapy pure result from the algae used in it? Maybe. But why does it results better with seawater and salt? Perhaps because of the behavior and reaction of the algae compounds together with other compounds present in the seawater and salt.

Today it is very common to encounter the words "algae extract" and/or "seaweed extract" on the labels of many products. It might be because the product genuinely contains an extract although, when the industry uses a specific extract or compound from the algae for the formulation, it is very common to use the strategy of only revealing in the label that there is an extract instead of revealing the name of the compound. Nevertheless, what cannot be forgotten is that the product's utility might be due to a complex group of compounds instead of just one.

With that said, it is in our interest to analyze which algae and compounds are used in the cosmetic and body-care industry.

Algae applications are focused on the skin and body treatment market through skin care products. Today we have several products that indicate the inclusion of algae extracts in the composition of anti-aging, regenerating, anti-irritant, slimming and exfoliating creams.

Algae have antioxidants, gene expression inducers, antimicrobials, vitamins, and a diversity of minerals and hydrating compounds such as some proteins, lipids and polysaccharides. If we collate this information and extrapolate it to the skin care and treatment area of research, we could get some interesting results. The simple coloration of the pigments is of interest to the cosmetic industry.

Such work has been done by some cosmetic companies and it has resulted in skin care products like tissue regeneration, wrinkle reduction, prevention of striae formation, cell proliferation, regulation of skin metabolism, etc., with the use of *Chlorella vulgaris* (Chlorophyta) and *Spirulina* sp. (*Arthrospira*) (Cyanophyceae) (Spolaore et al. 2006).

Some sunscreens include microalgae compounds rather than the usual macroalgae compounds for skin and hair. Reference to *Nannochloropsis* sp. (Eustigmatophyceae) as having anti-wrinkling properties and *Dunaliela salina* (Chlorophyta) as having cellular proliferation stimulation with positive effect on skin metabolism are examples. There are anti-aging creams, refreshing, regenerative care products, and emollients as an anti-irritant (Spolaore et al. 2006).

Squalene was already subject for the pharmaceutical field, even though, it finds its application in the cosmetic field too. Substance protection, metabolism precursor, and biocompatibility are among some of the remarkable known functions of this compound (Mayer 2005, Xia et al. 2005, Spolaore 2006, Cardozo 2006, Reddy 2009, Pangestuti 2011, Wijesingher and You-Jin 2011, Mohamed 2012, Scholz 2012, Pereira 2013).

For skin care applications, it not only helps in stabilizing emulsions and protecting the skin tissue through its capacities, but brings more quality for a product because it is a natural alternative among other synthetic compounds used in the cosmetic industry. Thanks to its biocompatibility, squalene helps the product to be better absorbed by the skin tissue, resulting in superior effects.

The high demand for squalene not only for the pharmaceutical industry but for the cosmetic industry too, results in work related with the discovery of algae as a new source for it (Grigoriadou et al. 2006, Cai-Jun and Jiang 2009, Nakazawa et al. 2011, Kebelmann et al. 2012).

6 Marine Algae Biotechnology: Some Industrial Principles

Now with all the information mentioned before we can declare that marine algae are a research field of interest with economic potential.

If we want to start in this field we have to consider all the steps, since algae growth until compound extraction and final product production. This way, the first step would be to choose between macroalgae or microalgae.

6.1 Macroalgae Biotechnology

The advantage in the use of macroalgae is, for sure, the naturally available biomass and the simple method of handling this resource. Seaweed grows naturally in the environment and is easily collected for further application. Today we feel more responsible for the ecosystems and the environment. We know that actions have consequences and that if we develop an industrial project based on the wild harvesting of seaweed for industrial production, we are not making a sustainable choice. Not only for the future of the selected seaweed and the ecosystem where it was taken from, but for the company as well because as soon as the seaweed was gone the company could not continue its activity.

The natural biomass production of seaweed takes time and can be seasonal depending on its location in the globe. With a production through gather, there is the risk of a local decimation of the entire selected specie of algae.

Unless the location, where the seaweed gather takes place, is well handled with sustainable management and coordination, with instructed personnel that respect the seasonal growth of the seaweed, the next generation of biomass growth will not be secured and would result in drastic consequences for the industrial activity.

This is why large scale seaweed production around the globe is done through aquaculture techniques. Off-shore and in-shore, the long-line strategy of growing seaweed is a very effective method. Sometimes it can be more difficult, with the need of a previous embryo production and seeding (Morrondo 2011). Sometimes, we just need to get an adult specimen, fix it in a line and collect only part of the algae body so that vegetative reproduction for the next gathering season is assured.

This might seem fairly simple to replicate, but in fact, it is not so. Not every country has a stable shore, such as in some of the equatorial and tropical regions of the globe, for off-shore production. The alternative could be in-shore production, although, once more, not all shores have such calm waters that guarantee the safety of investing in a long-line strategy. That is why the installation of such aquaculture production is typically made in estuaries, lagoons and other brackish-water environments.

In brief, to grow seaweed, we need water, nutrients and light (Figs. 1 and 2), all available in the environments referred to earlier. Sometimes, nutrient availability is more critical in biomass production; normally, higher levels of nutrients than those found in the natural environment are always more suitable for biomass production.

If the seaweed production is in a closed system, we can control the amount of nutrients available in the water column and if needed add more to it. There are different solutions that may be considered. For example, estuarine waters naturally contain more organic nutrients, not only because of the normal input from river waters but more because of excess fertilizers from agriculture fields that enter the water courses of the rivers. The use of these waters may be an alternative to the use of fertilizers. We can even say that we are practicing bioremediation through biological uptake of excessive nutrients. Even though, the freshwater from river will still be a problem for

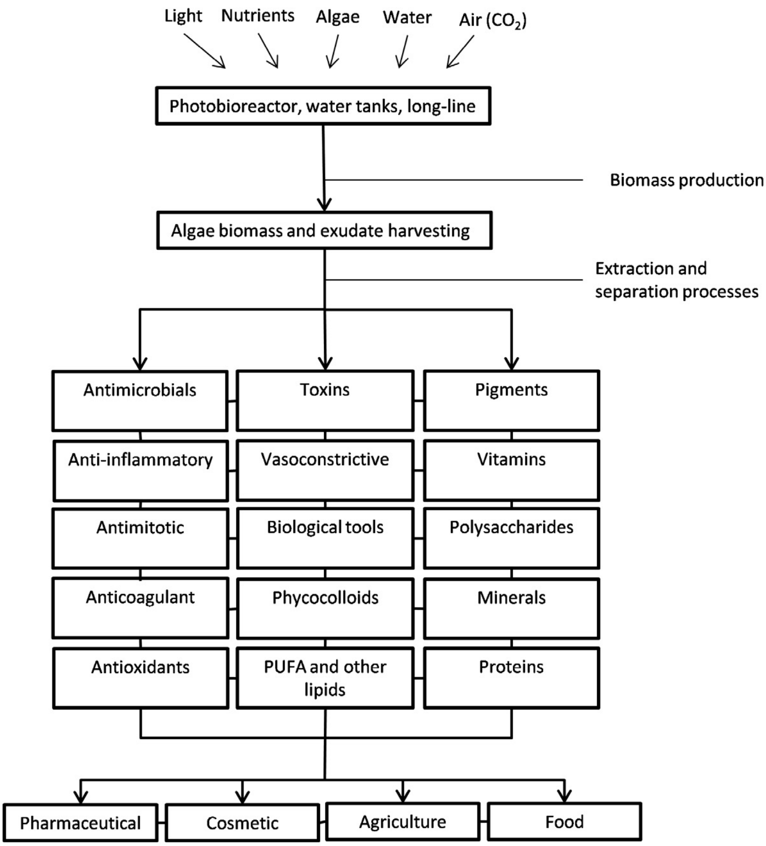

Figure 2. Schematic of the steps of an algae biotechnology production.

the aquaculture due to low salt concentration during raining periods. Once more, a closed aquaculture system may do the work, but the best way of solving this problem is through the algae itself. If our seaweed is already familiar to all these salinity changes, even the stress of low salinity might affect the biomass production, the seaweed will still survive and carry on.

One of the most suitable strategies is the integrated multi-trophic aquaculture system (IMTA) (Fig. 1). This situation resolves the nutrient issue in more than one way. As mentioned before, fish aquaculture causes the problem of high nutrient production due to fish or shellfish feeding and excrement. If these waters get to a seaweed production tank before reaching the environment again, the nutrient uptake by seaweed will solve the high nutrient pollution and stimulate the biomass production of algae (Pinto and Abreu 2011, Abreu et al. 2011).

Now, for the industrial part, the best way to profit from seaweed is to use all its content, or at least attempt to do so. Normally, a company focuses on a single compound of interest; however, it would be wrong to not take into consideration, the remaining contents of the seaweed. We know, for instance, that some seaweed are used as food, that they have potential health and body-care properties, that they are rich in sugars, vitamins, minerals, proteins—in other words, they are a powerful and versatile resource (Fig. 2).

Thus, it is in a company's best interests to consider not only the compound selected for its high market value, but all the other compounds as well. Algae are a very good resource as fertilizers for agriculture, and vegetal solution for animal feeding such as pet and cattle. They originate extracts and/or other isolated compounds for the cosmetic, food and pharmaceutical industries. Their notable sugar content is a profitable way to produce bioethanol through the seaweed biomass residues produced from another industry.

Sometimes the aggressive methods used in the industry do not allow the efficient use of the total content of the biomass, but with a carefully designed method we can improve the efficiency and obtain more than just one compound/product.

6.2 Microalgae Biotechnology

An industry sector for microalgae production is already in existence. It would appear that it all started with freshwater species because freshwater is easier to get then seawater. The truth, however, is that the history of microalgae culture, from an industrial perspective, started with the fish aquaculture industry. The need of these organisms for the purpose of fish feed led to research in culturing techniques for quality biomass production. A diverse group of algae were cultivated for several years which resulted in a considerable update of the knowledge in culturing techniques. Over the years, continued studies of these algae revealed some compounds of interest like vitamins, PUFA, carotenoids, etc. It seems that it is only a matter of adjusting the already known culturing technique for the algae to produce our desired compound.

This made some names of algae famous such as *Chlorella* sp., *Dunaliella* sp., *Spirulina* sp., *Haematococcus pluvialis*, *Phaeodactylum tricornutum*, *Skeletonema costatum*, *Isochysis galabana*, *Oscillatoria* sp., *Thalassiosira* sp., *Nostoc* sp.

Although it might appear easy to buy some of these strains from culture collections of algae and start an industrial production, there is hard work that needs to be carried out which together with the time needed to achieve satisfying results for industrial purposes, may be the reason for poor investment in this field comparing to other industrial fields.

Fortunately, the times are changing. Research on microalgae continues and is waiting to be applied. Today the word "microalgae" is more recognized along with photobioreactors production, industrial scale photobioreactor production.

The development of photobioreactors technology was and still is critical. There are always new developments that determine new advantages in microalgae biomass production. One reason for that constant dynamic in this technology is because we have to consider the demands of our selected microalga and build an adequate reactor for it.

Nowadays, if we want to start a business in the field of microalgae we could produce already existing commercial microalgae because there is high demand for f microalgae biomass. Fish, together with other organisms of aquaculture industry, are an example of consumers for those microalgae because it seems that there is not enough biomass availability to meet the demands of the aquaculture industry.

Does this situation look like a good opportunity? Perhaps it is for plans in the near future. However, it is still is a replication of what has already been done.

Every country and every region has a specific kind of microalgae flora, adapted to the local weather conditions all through the year. This is a powerful tool that is not often exploited. Industrial production of algae will always be dependent on local environmental conditions. We are talking about weather conditions throughout a year, like temperature and light radiation oscillations. For open pounds or open reactors we have also to consider the surrounding biota that can influence microalgae culture.

A very good strategy to take in consideration is the study of local microalgae flora. First, we should carry out the observation of samples, identification of most of the species and the identification of those which are dominant in local weather conditions and those that are easy to culture.

Then, the next step is to access the value of those algae by studying their potential and compounds through quality analyses (Fig. 2).

There will always be compounds of interest in algae for the industrial domain (Fig. 2). The only doubt that remains is if industrial production of the selected algae will be a commercially viable proposition. This not only depends on algae itself and the culture technique used but also on the biorefinery sector and its extraction and separation techniques.

Industrial production of microalgae results in a biomass production that is much more like a microalgae paste obtained from the culture. The remaining culture medium also has compounds, exudates of algae that have commercial interests too.

It is not possible to defragment and isolate all the algae compounds at the same time because there are different techniques for each type or group of compounds that influence the possibility of later isolating other compounds. But there is the possibility of separation, isolation and extraction of some compounds that assures that the rest of the biomass can be used. All will depend on the priority of the company, in what it selects as the final compound.

For example, lipids and living algae can be separated from the aqueous mixture. This leads to three fronts on which we can work: living microalgae, lipids, aqueous mixture. The most complex work is with the living algae because of the abundance of compounds in it. The right strategy might be in developing the best methods of extraction to get the most compounds and use the remaining biomass as valuable extracts for cosmetic, agriculture or other industries.

There are always ways to maximize profit of algae, it all depends on the industrial design of the production unit of the company. Above all, it depends on the time expended in laboratory research before scaling up production levels.

7 Conclusion

Marine algae are important resources in human society. Their use comes far from the past and still reveals extreme importance today, proven by their industrial application and continuous research that reveal new discoveries. Algae can lead to new drug therapeutics against pathogens with antibacterial, antifungal, antiviral and antiprotozoal activity. This research field is so important because not only there is a lack of antiviral and antiprotozoal medicines, but the continuous rise of antibiotic resistant strains of fungi and bacteria demands new antibiotic resources.

Besides, the effective antiviral activity of algae against HIV is a motivation against a disease that is very difficult to treat and affects a considerable number of the human population. Cancer too is a motivation to research tools and mechanisms that will guarantee some effective therapies in the future. Cancer is a very complex pathology and its characteristics differ from one patient to another. Some new discoveries among marine algae could let to the next generation of cancer treatments.

Algae toxins are of major concern because of their presence in food or bathing waters. Continuous work for monitoring and discovery of new biotoxins from these organisms are of high relevance, though, we must always consider the possibility of their having potential applications that need to be studied, especially in the pharmaceutical field.

There are plenty of other fields of research—anticoagulants, antithrombotics, anti-inflammatory, tissues protectors (neuroprotectors), immunomodulators, and vasoconstrictors—where marine algae can be part of future work.

The food industry is a field where algae are widely used. Possibly, the lack of acceptance in western society might change in the coming years thanks to the consistent work and propaganda by the scientific community related to the nutritional value and health benefits of algae consumption. However, nothing should obstruct studies and intention of production for their application as functional food. Studying algae as a known food resource but for pharmaceutical properties only encourages more algae production with a commercial objective, not only for unprocessed algae, but for the production of extracts too.

As pharmaceutical properties are studied among algae, new products for cosmetic application can be produced from new compounds. As long as the algae source of such compounds are reported from those which are used as food and have no toxic effect, their cosmetic application can be considered as biological, natural, and biocompatible, with no harmful effects. Or, perhaps, algae can become the source of already known compounds that were more difficult to obtain or whose acquisition was not ecologically acceptable and sustainable (e.g., squalene).

An interesting field of intervention for marine algae is in the bioremediation department. There is enough work that could lead to *in situ* application specifically in high nutrients concentration effluents that dramatically affect some natural ecosystems. It has been proved possible and even profitable. The biomass produced through this mechanism can be used for a variety of purposes. Using algae in heavy metals remediation is a different matter. Algae have the tendency to incorporate and accumulate such pollutants. This makes the algae unsuitable for use as food; however, there must be other applications for the heavy metal contaminated biomass. There is the possibility of using such biomass as biofuel and particular extracts production.

The culturing technology of algae is a dynamic sphere with continuous updates. There is always the possibility to improve and there is always new developments in technology that can help to make the difference. What may be important to know is that a good strategy is the use of local algae resources and the association of culturing methods together with other trophic groups of aquaculture. This way there is innovation and competition between other producers. The problem is that to start such activity some scientific research as to get done and it takes a lot of time and resources. But, in the end, it could originate new strategies with high value compounds from other algae than the commercial ones.

To use the available know-how of to initiate an industrial activity with a commercial specie sounds tempting. The problem is that this strategy might not be the most adequate because the algae is not indicated for the climate of our region of activity. Besides that, we would steel not be different from other industrial algae producing companies which would make it very hard to get into the market.

In conclusion, marine algae are a source of new bioactive compounds and are tools for biotechnological application with wide industrial uses, not only for commercial interest but as a versatile ecological and sustainable resource.

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