A REVIEW ON MARINE ALGAE AND ITS APPLICATIONS

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ABSTRACT

The ocean is the major essential source of structurally unique natural products that are mainly present in living organisms. The essential products extracted from marine microbes and marine algae are highly analyzed areas in instinctive product research. Marine algae are the novel food with potential nutritional values used for multiple purposes in industry and medicine. They show pharmacological activities which are helpful for the invention of bioactive compounds. Furthermore, marine algae have shown to provide an abundant source of natural bioactive compounds with antidiabetic, anti-inflammatory, antiviral, antifungal, hypolipidemic, antioxidant, anti-hypercholesterolemia, antibacterial, and antineoplastic properties. They produce new secondary metabolites that possess biological activities and have the potential to be developed as therapeutic agents. Marine algae provide a broad range of therapeutic beneficial both internally and externally. They are oxygen producers and also the food base for all aquatic life almost and economically main as a source of crude oil, food, and many pharmaceutical and industrial products for humans. The bioactive potential of different marine algae has been reviewed in the literature [3-6].

ALGAL CLASSIFICATION

There are three main classifications of algae – Chlorophyceae are green algae that contain the pigments chlorophyll a and b. (i.e., Chlamydomonas, Spirogyra, and Chlorella). Phaeophyceae are brown algae, they are mainly present in marine. They contain pigments such as chlorophyll A, C, carotenoids, and xanthophyll (i.e. Dicyotyl, Laminaria, and Sargassum). Rhodophyceae are red algae that contain the red pigment, r-phyceroerythrin (i.e., Porphyra, Gracilaria, and Gelidium). The fourth type of algae is blue-green algae (BGA) (Cyanobacteria) that are occasionally treated to be seaweed. This type of algae is often found in home aquariums where it will cover all surfaces in a short time and called as slime algae or smear algae [7].

ALGAL ULTRASTRUCTURE

The term algae (Latin – seaweeds) were first introduced by Linnaeus in 1753, meaning the Hepatica. They can be single celled or multicellular. Living things types of protocist also are known as cell-free protocist as they operate as total living organisms. They are common in all types of algae except Charophyceae, Phaeophyceae, and Rhodophyceae. The unicells may be motile or non-motile. The larger, multicellular algae have relatively complex tissues, which can be organized into organ-like structures that help certain functions [8].

Algae have chloroplasts for the process of photosynthesis and the algal cell wall is mostly cellulose. It also contains hemi-cellulose, mucilage, pectin, and other substances such as alginic acid, fucoidan, fucin, calcium carbonate, and silica. Chloroplasts are the most renowned feature of algal cells and they carry the photosynthetic pigments which are double membrane structures. Beating action of small filiform or thread-like protoplasmic appendages which is called as flagella helps for the movement [9].

ALGAL BIODIVERSITY

Indian coastline is longer about 5700 km including nine states on the mainland and about 7500 km including islands and union territories. Coasts with the broadest diversity of algae present in both temperate and tropical seas [10]. Algae are ubiquitous in marine, freshwater, and terrestrial habitats. The phylogenetic diversity of the algae is very broad and is reflected in an equally wide range of metabolisms and biochemical properties. A kind of brown algae develops the giant kelp forests near the California coast, while the other develops the floating kelp beds in the Sargasso Sea, a region of the North Atlantic Ocean. The golden brown algae (chrysophytes) are common microscopic organisms that provide food for zooplankton in freshwater. In general, it is found to be more than 6000 species of red algae. The typical red algae (Rhodophyta), a rose-colored multicellular organism is found globally. This alga can be found and live in deeper depth than brown and green algae because it takes in blue light. Another class of algae is Xanthophyta which are yellow-green algae that live in freshwater. Nearly 7000 species of green are spotted, according to the UC Museum of Paleontology. Freshwater green algae like Spirogyra in Charophyta phylum are highly related to plants. Green algae may present in marine or freshwater habitats, and some even grow in slightly wet soils. For example, sea lettuce (Ulva sp.) generally found in tidal pools and Codium sp., one species of which is commonly called ‘dead man’s fingers’ [7].

EDIBLE AND POISONOUS ALGAE

Edible seaweed which comes under the type of brown algae is a vegetable of the sea, a food source for ocean life and humans who
consume it in its many forms. Low-calorie and nutrient-dense, edible seaweed has long been harvested and consumed in Asian cuisines, particularly those of Japan and Korea. Six common types of seaweed are in the list of Japanese human diet and they are commonly called Nori, Kombu, Wakame, Ogonori, Umibudo, and Hijiki [11]. One of the edible green seaweed called sea lettuce grows in the coasts of the world’s oceans. It is one of the important food for sea animals such as sea slugs and manatees and humans also eat it for centuries. Marine algae Spirulina have an exceptionally high protein content of which 90% is digestible. Spirulina is a microalgae which might be a promising source of protein for human nutrition in protein deficiency or malnutrition [12]. On the other hand, some algae can be harmful to humans. For example, a disease of the humans called ciguatera caused by the consumption of tropical fish which feed on the alga such as Gambierdiscus or Ostreopsis can be disastrous. Other algae called Heterosigma (class Raphidophyceae) and Dictyocha (class Dictyochophyceae) are suspected fish killers. Some seaweeds have high concentrations of arsenic when eaten and may cause arsenic poisoning. Hizikia is brown algae that contain adequate amount of arsenic to be used as a rat poison [13].

**ANTIOXIDANT ACTIVITIES**

Antioxidant activities were identified in different types of marine algae such as red, green, and brown algae species [14]. Out of the total 5000 fresh water habitat reported, approximately 3% is Rhodophyta, the red algae [15]. Ethanol extracts of the Callithyris japonica [16] and Gracilaria tenussipitata [17] species of red algae have antioxidant effects. Ethanol extracts of C. japonica suppressed cellular apoptosis and active antioxidant enzymes [16]. Studies were examined with the HT-29 cell line which showed that treatment with an aqueous extract of G. tenussipitata enhanced the recovery of these cells from H2O2 induced DNA damage, counteracts cellular proliferation, and induced G2/M arrest [17]. Green algae – these algae are found in lakes, oceans, and fresh water bodies. Some even grow in soils and live in tree trunks. The overall population of green algae is estimated to be more than 500 genera and 8500 species [18]. Free radical scavenging tests revealed the antioxidant activity of Ulva fasciata Delile due to the presence of sesquiterpenoids [19]. Flavonoids are rich in Ulva lactuca and having great antioxidant properties [20]. Extraction of Ulva reticulata using hot water reduced hepatic oxidative stress [21]. Seaweed U. reticulata occurs on the Kanyakumari coast of India. BGA or Cyanobacteria belong to the photosynthetic prokaryotes existing in the aquatic ecosystems. Few BGA species such as Aphanizomenon flos-aquae, Spirulina platensis, Spirulina maxima, Spirulina fusiformis, and Nostoc commune var. sphaeroides Kutzing (NO) are consumed by major population of humans for centuries [22-26]. They are generally prevalent in tidal pools. The antioxidant effects of Anabaena species methanol extract were revealed by DPPH radical scavenging activity [27]. The antioxidant effect of phycobiliprotein phycoerythrin in S. platensis was analyzed by ascorbate/iron/H2O2 assays [28].

**ANTICANCER EFFECTS OF MARINE ALGAE**

Cell proliferation of human leukemic cell lines was inhibited using the aqueous extracts of Gracilaria corticata [29] and Sargassum oligocystum [30]. Similarly, ethanol [31] and methanol [32] extracts of G. tenussipitata were reported to have antiproliferative activity on C49-22 oral cancer cells and also responsible for cellular apoptosis, oxidative stress, and DNA damage. Methanolic extract of Plocamium tefarius-induced caspase-dependent apoptosis in HT-29 colon cancer cells [33]. Glycoproteins from Laminaria japonica [34] and fucoids from Sargassum hornery, Ecklonia cava, and Costaria costata [35] exhibited anticancer effects on human colon cancer cells. Hetero fucans extracted from Sargassum filipendula showed antiproliferative property on cervical, prostate, and liver cancer cells [36]. BGA also confirmed the anticancer effects of Spirulinae extracted [37] recombinant glycoproteins, in specific Microcystis viridis lectin [38], and cryptophycin [39,40]. The red algae Laurencia viridis are an essential source of squalene- derived secondary metabolites. Three squalene-derived brominated triterpenes dehydrothysiferol [41], isodehydrothysiferol [42], and 10-epidehydrothysiferol [43] were isolated from L. viridis, exhibited potent cytotoxic activity besides a number of cancer cell lines.

**AGRICULTURAL PRODUCTS FROM ALGAE**

Algal extracts have several applications in the field of agriculture such as fertilizers, plant biostimulants, or bioregulators of plant growth. Plant growth regulators are different from fertilizers because they alter cell division, root and shoot elongation, flowering, and other metabolic functions, whereas fertilizers only provide nutrients essential for the growth of plants [44]. Cytokinin is the most important plant growth regulator in seaweed. However, trace minerals extracted from seaweed play a major role in nutrition and physiology, acting as enzyme activators [45].

**ANIMAL PRODUCTS FROM ALGAE**

Seaweed extracts can be potentially exploited as feed additives [46] due to their performance in growth and reduction of pathogenic bacteria [47]. Algae and their extracts have many beneficial effects as food additives. Humans lag behind in algae diets and are currently formulated as commercially potent species in aquaculture and agriculture. Many algal species exhibit beneficial effects in poultry, mammals (nematodes, shrimp, and abalone), finfish (sea bream to salmon), and sheep (both ruminants and monogastric species) [48]. The antioxidant properties of astaxanthin (red-colored carotenoids) are extracted from green algae Haematococcus pluvialis. It was shown that the supplementation of astaxanthin-rich extract to the diet of mice improved cholesterol and lipid metabolism as well as antioxidant defense mechanisms [49]. This action was helpful in mitigating the progression of atherosclerosis [50].

**COSMETIC PRODUCTS FROM ALGAE**

Algae are the potential organisms playing a key role in the current research and development, producing new biochemically active compounds [51]. Algal extracts are used mostly in the face and skin care products, anti-aging cream, regenerating skin cream, emollient products, anti-irritant products, sun protection cream, and hair care products [52]. Algal extracts have been already used as sources of cosmeceuticals. Extractions of carotenoids and astaxanthin from marine algal species have received more attention for cosmeceutical purposes. Carotenoids and astaxanthin extracted from marine algae were explored for cosmeceutical purposes [53]. Extract of brown seaweeds (containing fucoidan fractions) are applicable in cosmetology as fibroblast proliferation activators in treatments aimed at aesthetics, for example, in anti-wrinkle treatments or in the prevention of skin aging without patent infringement [54]. The methanolic extract of Gordinia pilulifera exhibited strong antioxidant activity and displayed a protective effect on ultraviolet A-induced oxidative stress of the human dermal fibroblast cell. The obtained results suggested that macroalgal extract may be a potential source of natural anti-photaging compounds [55].

**BACTERICIDAL ACTIVITY**

The phlorotannins present in brown algae are effective against certain pathogenic foodborne bacteria. The growth of Campylobacter jejuni and Vibrio paraheamolyticus has been suppressed by dieckol and 8,8-bieckol, phlorotannins isolated from Ecklonia karoae [56]. Campylobacter spp. was reported to be most susceptible to phlorotannins and the growth of Staphylococcus aureus was effectively reduced by phlorotannins present in the hexane fraction of Ecklonia stolonifera [57]. Their antibacterial activity is based on their molecular weight. Another compound, phlorotannin containing extract of brown seaweed Ascosphyllum nodosum has been shown to reduce the prevalence of Escherichia coli O157:H7 in bovine feces [58].

**PHARMACEUTICAL INDUSTRY**

Marine algae, an important source of bioactive metabolites has a key role in drug development area inside pharmaceutical industry. Vast studies have been conducted on algae-based bioactive compounds from Arthrospira (Spirulina), Dunaliella salina, Botryococcus braunii,
Chlorella vulgaris, Nostoc, and H. pluvialis and with high antimicrobial, anticoagulant, antiviral, antifungal, anti-inflammatory, antioxidant, and antitumor activity [59-63]. Protocists have a good ability to fold proteins into advanced three-dimensional structures. In San Diego, algae produced human antibodies and human therapeutic drugs such as human vascular endothelial growth factors for treating patients affected by pulmonary emphysema [64]. Chlamydomonas reinhardtii, the green algae model produces many therapeutic proteins for human and animals including full-length human antibodies [65].

Production of bioactive compounds by green algae is a fortunate thing to pharmaceutical research [66-70]. The biomass of Nostoc is being used as a dietary supplement composing rich protein, lipids, and fatty acid content. The clinical value has been established for these microalgae due to its application in curing fistula and also certain type of cancer [71].

PAINT, PRINTING, AND DYING INDUSTRY

Green algae are applied as natural anti-fouling agent in the recently developed paints. Macr algae produce an array of natural compounds to protect itself from natural enemies [72]. Asparagopsis, Laurencia (red alga), and Sargassum (brown algae) act as an important source of antifouling compounds. At present, one omeaazeline and four polyether triterpenoids are reported with anti-macroloung activity from Laurencia sp. and L. viridis, respectively [73]. Dai Nippon Ink and Chemical Company from Japan extracted a blue phycocyanin from S. platensis and sold to the market as a natural blue pigment called "tina blue" which is commercially used in food preparation and cosmetic products. Other applications are confectionaries, candied ices, and sherbets [74].

ANTI-INFLAMMATORY SUBSTANCES

Microalgal biomass is capable to produce several anti-inflammatory compounds. Due to their anti-inflammatory properties, they are considered for applications in tissue engineering for the development of scaffolds and also for reconstitution of organs and tissues [75,76]. β-1,3-glucan, an important bioactive compound extracted from Chlorella acts as an active immune stimulator for free radical and blood cholesterol reduction. The effect of this compound in curing gastric ulcers, sores, and constipation has been studied. It is also demonstrated to prevent the occurrence of diseases such as atherosclerosis and hypercholesterolemia and proved to have some antitumor activity [52].

Sulfated polysaccharides (SPs) having anti-inflammatory activity are used for skin treatments by inhibiting the mobility and adhesion of polymorphonuclear leukocytes [77].

ANTIMICROBIAL ACTIVITY

Another study conducted by M. Kuniyoshi proved that the algae Cladophora have antimicrobial activity against certain microorganisms. The green algal extract of Cladophora fasicularis was separated using different chromatographic techniques to collect 2-[(20,4-dihydroxyphenoxyl)-4,6-dihydroxanisole [78]. It also actively inhibited the growth of E. coli, Bacillus subtilis, and S. aureus [78].

ANTIFUNGAL ACTIVITY

Capisterones, a triterpene sulfate esters present in green algae Penicillus capitatus have high antifungal property against algal pathogen Linda thalassiae [79]. Crude extracts from certain red algae species were examined for the presence of antibiotic activity against few pathogenic fungi [80]. The eminent fungical activity was found in marine macroalgae to recover patients from chronic asthmatic states. In particular, L. paniculata was studied to have excellent antifungal activity and so it is recommended as a promising candidate to attain a novel antifungal agent [81].

ANTI-COAGULANT ACTIVITY

More than 50 years, heparin is widely used commercially for the prevention of venous thromboembolic disorders. However, heparin is reported to have many side effects such as development of thrombocytopenia, acquired antithrombin deficiencies, and congenital ineffectiveness in inhibiting thrombin bound to fibrin [82]. Investigations on blood anticoagulant properties from marine brown algae [83] report that SPs act as an alternative source for novel anticoagulant drugs [84-86]. Anticoagulant activity is one of the most widely considered properties of SPs [87,88]. Many other anticoagulants with SPs are isolated and characterized. Sulfated galactans (carrageenan) and sulfated fucoids from marine red algae [89-91] and brown algae, respectively, are the two types of SPs identified with significant level of anticoagulant activity [92-94].

ANTIVIRAL ACTIVITY

The antiviral efficacy of marine algal polysaccharides was first revealed by Gerber et al. [95] who studied the effect of polysaccharides extracted from Gledium cartilagineum (Rhodophyceae) in protecting the embryonic eggs from influenza B or mumps virus. These polysaccharides that are possessing antiviral activity are found to be highly sulfated [96]. The replication of enveloped viruses such as Orthopoxovirus, flavivirus, herpes virus, togavirus, rhadovirus, and Arenavirus families is inhibited by many species of marine algae having significant complex structural SPs [97]. Polysaccharides have envisaged much consideration as antiviral compounds due to their inhibition of algal polysaccharides against mumps and influenza virus [98]. Several fucans from the seaweed species Dictyota nertensis, Lobophora variegata, Spotossilus Schroederi, and Fucus vesiculosus were reported to successfully inhibit the activity of HIV reverse transcriptase [99]. Griffithsia sp. (red algae) are the source for a novel lectin, identified as Griffiths in having molecular weight of 12.7 kDa. This protein made of 121 amino acids is reported to demonstrate promising anti-HIV activity [100].

HYPOGLYCEMIC EFFECT

Diabetes mellitus belongs to the group of diseases that occur due to excess sugar in the blood (high blood glucose). It happens to be the most important metabolic disease with fast increasing prevalence, which is a major public health concern worldwide. The brown macroalgae, S. oligocystum, improve the diabetic by reducing insulin resistance, decreasing glucose concentration and regeneration of pancreatic damaged β-cell [101]. Fucosterol, isolated from Pelvetia silicosa, was shown to decrease serum glucose levels and to inhibit glycolgen degradation in streptozotocin-induced diabetic rats [102]. High α-glucosidase inhibitory activity is found in Pelvetia babingtonii (Harr.) De Toni (Fucaceae) extract which also suppresses postprandial hyperglycemia [103]. A. nodosum (L.), L. Lolis, brown algae predominant in dominant rocky intertidal grow profusely on the northeastern coast of North America and the northwestern coast of Europe [104]. Water extracts of the algae have strong inhibition for α-glucosidase and its phenolic compounds which indirectly lower the blood glucose levels [105]. Eisenia bicyclis (Kjellman) Setchell (Lessoniaceae), an enduring and day-to-day consumed edible brown alga lives in the middle of Pacific seashores of Korea and Japan. Derived of phlegrolucinol, isolated from E. bicyclis, shows high potential for the elective therapy for diabetic complicated patients by inhibition of advanced glycation end products formation and α-amylase activity [106]. Fucoxanthin is a marine carotenoid extracted from edible brown macroalgae, namely, E. bicyclis (Arame) and Undaria pinnatifida (Wakame), is found to cure insulin resistance and also to ameliorate blood glucose levels [107]. Polysaccharides isolated from U. lactuca could significantly decrease the blood glucose by their potential inhibitory effect on key enzymes closely related to starch digestion and absorption in both plasma and small intestine [108]. In another study, the ethanolic extract of Ulva rigida was reported to decrease the blood glucose concentrations and occurrence of micronuclei in diabetic rats [109,110].

NUTRITIONAL APPLICATIONS

Global demand for nutritional food apart from traditional and nutritional values is to use the food for functional values too. Seaweeds contribute as a balanced diet, on providing fiber, protein, minerals, vitamins, and low-fat carbohydrate content [111]. The prominent trait of Chlorella is the presence of rich protein and vitamin (single-cell protein). It contains Vitamins C, pro-Vitamin A, thiamine,
rhodovulphin, pyridoxine, niacin, pantethenic acid, folic acid, inositol, and p-aminobenzoic acid. It possesses all the essential amino acids well suited for both human beings and animals [112]. One such food is BGA, Spirulina, which has been a part of the human diet for thousands of years as per archeological evidence. The potential health benefits of Spirulina must be adequately recognized and implemented thus making full use of this nature's gift. The global availability across all the regions of the world makes algae easily offered at economical prices for access to all classes of the population [113]. Seaweeds are eaten as whole foods by a relatively small percentage of the world population, in a relatively limited geography. Scientists in the Asian countries have reported that the Japanese are the largest consumers of marine algae reporting an annual consumption per individual as 1.6 kg dry weight, which contributes immense health benefits [114,115].

**ECONOMICAL IMPORTANCE OF ALGAE**

Algae are cost effectively vital due to its broad spectrum of applications as food, fodder, pisciculture, fertilizer, etc. They are a healthy source of carbohydrates, fats, proteins, and Vitamins A, B, C, and E, as well as minerals such as iron, potassium, magnesium, calcium, manganese, and zinc. People of countries such as Ireland, Scotland, Sweden, Norway, North and South America, France, Germany, Japan, and China use it as food ingredients for centuries. Protocist is used because the fodder to feed placental mammal-like bovine and chickens. In aquaculture, algae are predominant in the production practice. Plankton and zooplankton are the food consumed by fishes. It helps to balance a healthy marine ecosystem, as algae act as natural CO$_2$ sequester and O$_2$ provider [116]. Heavy metal pollution from various industries and other domestic sources is a serious threat to the aquatic ecosystem, ultimately leading to loss of biological diversity and biomagnifications of toxic metals into the food chain. Algae are the major organisms that absorb and store heavy metals. Since algae are present at the base of the aquatic food chain, they are a very important vector for bringing up pollution to the top levels of the tropical food chain in aquatic environments [117]. Some common forms of Cyanophyceae help in fixing atmospheric nitrogen and also to enrich the soil [118].

**ALGAE PRODUCTION IN GLOBAL MARKET**

The global algae production is segregated on the basis of type, source, form, application, and region. Based on the type, the algal market is labeled as Spirulina, Chlorella, Astaxanthin, beta-carotene, and hydrocolloids. Based on source, the global algal produce is categorized into brown algae, BGA, red algae, and green algae. Based on region, it is classified across the globe in North America, Europe, Asia-Pacific, and LAMEA [119]. The overall space used for the cultivation of Porphyra throughout Japan is estimated around 155 acres. Approximately every year 4000-5000 metric tons of algae (dry weight) are being produced and it creates a hike in revenue compared to other marine products including fish and whales. Laminaria cultivated excessively in Japan and China. The cultivation of algae resembles more of a crop plant, resulting in the evolution of a strong economic crop. In many countries, factories are established for processing of seaweed into appropriate cattle feed [112]. Consumption of healthy edible produce and dietary supplements, due to changes in the lifestyle of the people, has changed the perspective of this market. Fig. 1 shows the ultrastructure of the algae. The annual growth rate of algal product market is estimated to increase by 4.2% between 2018 and 2025 due to the high demand for natural products. The market players put forward proactive efforts to formulate algae-based edible products to meet the required quality, texture, and nutritional demand of consumers [119].

**INDIAN SCENARIO OF ALGAL MARKET**

A new series of drug and nutrition-based products are recently being developed from algae. Spirulina, one of the important pharmaceutical products is having high market demand in India [120]. Over the past 15 years, India stands as one of the major producers of algal biomass [121]. Herbal hills: Herbal hills cultivate manufactures and export various ayurvedic herbal products and various algae products as Spirulina tablets in India. In India, Shilin Chlorella is the foremost company in the commercial production as a nutritional supplement from July 2015. Parry Nutraceuticals: The corporate is one the simplest providing microalgae health supplements, with headquarters in city, and a division of E.I.D. Parry (I) Ltd. In India, algae company is the pioneer company focusing on algae as nutraceuticals. The main products of the company are Chlorella factor that provides a potential food candidate due to its high quality, texture, and nutritional demand of consumers [119].

**AVAILABLE FORMS OF ALGAE**

Global demand is high for macroalgal and microalgal foods because algae have many functional benefits compared to traditional aspects
of nutrition and health care [123]. For centuries, marine algae are predominant in the field of food and drugs. Algal species have the applications in food dairy pharmaceuticals, industry, and cosmetics. Biodiesel, hydrogen gases, biobutanol, and bioethanol can be prepared by algae [124]. The available form of algae is oil, soft starch capsules, tablets, and powders. Algae can be consumed in the form of capsules, tablets, or powders. Since 2003, the oil that is rich in omega-3 fatty acids obtained from the microalgae Schizochytrium sp. and containing docosahexaenoic acid and some eicosapentaenoic acid has been approved in Europe as a novel food [125].

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