Brief Overview of Bioactive Compounds in Seaweeds, Their Properties and Practical Applications in Functional Foods.

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Abstract - Seaweeds are a rich source of bioactive compounds as discovered by many research studies in recent history. Even though there are numerous methods to generate certain bioactive compounds from chemical modifications, advantages of extracting them from natural seaweeds have exceeded the artificial synthesis. However, practical applications of seaweeds are mainly observed to pharmaceutical industry, drug development and functional foods so far. This is due to the bioactive properties such as antiviral, antitumor, anticancer, anti-inflammatory and antilipidemic beneficial for such industries. Functional food market has also indicated a steady growth due to the health-conscious consumption pattern of the people creating even more demand on seaweeds. Most of the countries surrounded by coastal regions have indicated a growth of research on seaweeds in order to utilize them as biofuel. Idea behind this review is to provide a brief but a comprehensive understanding of metabolites, bioactive properties and applications of seaweeds.

Keywords: Anti-cancer, Anti-viral, Bioactive compounds, Functional food, Seaweeds

I. INTRODUCTION

Seaweeds are widely available source in the world. Even though seaweed is a broad term, it majorly signifies marine algae grown in bottom of the shallow depths of water. They are multicellular in nature and grow attached to rocks, dead corals, shells of the molluscs, pebbles, and other plant material that nourish them. Seaweeds propagate from very shallow depths to almost 0.2km in the shallow sea. But they are abundantly found in depths ranging from 35 – 40 in meters. Seaweeds have created consumer markets around the globe and countries such as Korea, China, Australia possess fast growing markets with variety of products specially under the food sector. As per common seaweed categorization, they are recognized as *Chlorophyceae* (green algae), *Rhodophyceae* (red algae) and *Pheophyceae* (brown algae) [1].

Therapeutic usage of the seaweed and research related to biologically active beneficial compounds began in the late 90's. Today it is applied in broad areas such as foods and beverages, medicine, polymers etc. As per growing carcinogenic substances in the environment, scientists have researched extensively to find a novel remedy with abundant resources. Seaweed was recognized as a source with anticarcinogenic chemical compounds [2]. Seaweeds consists with bioactive substance like lipids, polysaccharide, and polyphenols, with broad spectrum anti-fungal, anti-bacterial, and anti-viral properties [3] Currently, it is applied in variety of cancers. Seaweed extract is a new market for food consumers as extracts are nourished in so many vital micro and macro nutrients. These extracts traded directly as rich extracts of biostimulate [4].

Natural plant growth hormone and beneficial trace element are abundant in certain classes of seaweed. Hormones such as auxin, cytokines and gibberellins can be extracted for commercial use. Other phytochemical compounds extracted from seaweeds such as agar-agar, carrageenan and alginates being used as manure and animal fodder from decades. They are also used as additives in paper, dairy, textile and industries. Bioactive compounds in seaweed serve as additives in functional food. Seaweeds have certain physical aspects due to the manner they were built in molecular stage as they have both high molecular weight non-absorbing dietary fibres and low molecular weight easily absorbing compounds. [5] Brown seaweed variety, *Ascophyllum nodosum* is known to have the best extracts and they have indicated remarkable resistance to severe environmental stresses [6].

II. ACTIVE COMPOUNDS FOUND IN SEAWEEDS

A. Carotenoids

Carotenoids are natural pigments comprised with five isoprene rings. They are natural polymers with highly conjugated 40-carbon structures with almost 15 conjugated double bonds. Substitution of the oxo, hydroxy or epoxy groups at different position of the ring initiate formation of xanthophyll, yellow pigments in the carotenoid group [7]. Carotenoid pigments are abundant in higher plants, algae and photosynthetic bacteria absorbing wavelengths in the range of 400–550 in visible light. This cause the pigments to be in yellow, orange and red colours as they absorb violet to green

colour range in the visible spectrum. At least 600 different types of carotenoids play an important biological role in bacteria, algae, plants and animals [8]. Serving as an additional pigment of photosynthesis, stabilizing protein structures produced in photosynthesis, inhibiting photo and free radical oxidation are functions of carotenoids. Different seaweeds have different carotenoid pigments. Green seaweeds species consist of β-carotene, violaxanthin, zeaxanthine, neoxanthine and luetin. Brown seaweeds have β-carotene, fucoxanthine and violanxanthine while red seaweeds contain luetin, α and β carotene and zeaxanthin [9]. Several specific variations in the structure of carotenoids are found in algal carotenoids with respect to plant and bacterial carotenoids. Changes in the number of carbon atoms and the presence of unusual groups (allene groups, lactones) found in carotenoids such as peridinin and fucoxanthine [10].

B. Carrageenan

Carrageenan is widely utilized food additive. It is used as an emulsifiers and stabilizer in dairy industry. Carrageenan the common name used for the family of naturally occurring water soluble sulphated galactan. These galactans have alternative backbone with α (1-4)-3, 6-anhydro-D-galactose and β (1-3)-D-galactose [11]. κ- and ι-carrageenan possess viscous and suspension qualities which makes it usable in many dairy products including chocolates, jells and concentrated milk. Carrageenan can also be used as a potential pharmaceutical as anti-tumour, anti-viral, anti-coagulant and immunomodulation activity [12] [13]. Also, carrageenan has the potential to treat STD, including HIV, herpes, gonorrhoea and genital warts [14]-[17]. Carrageenan is present under the commercial categories of λ, ι, κ, μ and ν-carrageenan due to their chemical differences at molecular levels. Due to the differences among compositions in seaweeds and the methods used in carrageenan extraction from seaweeds, there is about 20% weight to weight sulphate difference present among κ and λ Carrageenan. Due to the applicability in different fields and novel applications seaweeds are the only resource that can be used to supply the demand of carrageenan for future needs.

C. Alginate

Commercial production of the alginate began at early 20th century and it was discovered in 1880. Brown algae is the main source of alginate. Chemical structure of the alginate consists with a linear polysaccharide which has 1, 4 linked β-D-mannuronic and residues of α-L-guluronic acid [18]. Alginate is used in applications of food, pharmaceutical and textile industries. Alginate is a gelling agent as per its ability to form viscous solution and chelate ions. Alginate is available in two forms as acid and salt. Acid form of alginate is known as asalginic acid. Cell walls of the brown algae is rich in alginate salt and it is 45% dry weight of algal biomass [19] [20]. Alginate comprises of special type of dietary fiber unlike plants that has the functionality against excessive cholesterol, hypertension and toxic chemicals according to Murata and Nakazoe [21] [22] Also it has anti-cancer properties against the cancer-causing substances in intestine and stomach and hyperlipidemic properties [23]-[25].

D. Phycocolloids

Phycocolloids present in the cell walls of the seaweed. Three categories of phycocolloides are alginates, carrageenan and agar. phycocolloide is a polysaccharide of high molecular weight commonly used in cosmetic and food industry [26]-[28]. They are functionally active compound in detection mechanism between seaweeds and pathogens [29].

E. Polysaccharide

According to Holdt and Kraan, (2011) and Murata and Nakazoe (2001), Polysaccharides serve as major storage and structural components in marine algae. Large quantity of polysaccharides is available in the cell walls of algae. Polysaccharides are widely used to develop food additives such as stabilizers, emulsifiers and thickeners [30] [31]. They are also used as animal feed. According to Holdt, and Kraan (2011), Green algae species are known to have the highest amount of polysaccharide meanwhile *Ulva*, *Ascophyllum*, *Porphyra* and *Palmaria* contain higher quantity of polysaccharides with respect to other algae. Dietary fiber content in seaweed is quite high even though it cannot be digested by the human metabolism process. But they are beneficial in reducing the constipation and providing other medicinal remedies [32]. As seaweeds have higher polysaccharide content as 4 -76 % they have a very low amount of total fat and lipid comparatively. Hemicellulose amount in seaweed is ranging from 2 -10% of the dry weight. Each main algal species has inherent polysaccharide types. Red algae contain carrageenans and floridean starch. While green algae contain sulphated galactans, sulphuric acid polysaccharide. Holdt and Kraan, (2011) stated that brown algae carry laminarin, alginic acid and fucoidan.

F. Agar

Agar is a formulation of agarose, agro-pectin and several other polysaccharides and it is the common name for of seaweeds galactans consists with α (1-4)-3, 6-anhydro-L-galactose and β 9(1-3)-D-galactose residues with considerably low amount of sulphate esterified. As it is a mixture of suphated polysaccharides, brown algae serve as the main source of extraction apart from several red algae [33]-[35]. This viscous gelling agent possesses similar properties to carrageenan and also utilized for similar purposes. Depending on the quality of the agar, it is used for different purposes. The agar quality mainly depends upon the physiochemical property and additionally related to environmental factors, growth and reproductive cycle. Low quality agar is used in food production and for its additives. Also used in paper, textile and adhesive industries. Medium quality ones are used for biological culture production, and in pharmaceutical industry as bulking agents, anticoagulant agents. High quality ones are used for sensitive separation techniques of intermolecular biology such as electrophoresis. According to Murata and Nakazoe (2001) agar absorb ultraviolet light, most of the electrophoresis systems arrive with inbuilt UV light. Agar-agar can decrease blood glucose levels and it can serve as an anti-aggregation agent for red blood cells. Agar derivatives such as oligosaccharides has anti-inflammatory properties and also suppresses the enzyme

associated with production of nitric oxide [36]. Agar derivatives has indicated anti-cancer properties, antioxidant properties [37] [38].

G. Dietary Fibers

Dietary fiber content found in seaweed is quite higher than plants [39] [40]. These fiber content range from 33 - 62% in their dry weight. Seaweed fibers consist of both water-soluble fibers as cellulose, mannans and water insoluble fibers as agars, alginic acid, laminarin, furonan and porphyrin. As mentioned under polysaccharides, these fibers have numerous health benefits as anticancer, anticoagulant, anticholesteremic, antiherpetitic and antiviral activity. They can also assist in reducing the obesity via high fiber diets as they modify the digestibility protein and add bulk to the food content getting digested. [41]-[45]. The seaweeds dietary fibers contain some valuable nutrients that make them ideal as functional foods and nutraceutical for human consumption [46]

H. Fatty Acids and sterols

Fatty acids are now commonly used in biomedical and nutraceutical due their unique chemical compositions. Other than curing cardiovascular diseases, one of the common application of fatty acids is reduction of obesity [47] [48]. EPA (Eicosapentaenoic) a precursor of hormones in higher plants and animals, has been found in wide variety of marine algae class but only some of them have the feasibility to meet the industrial production, limitations are caused mainly as per the fact that majority of marine algae have low specific growth rates and low cell densities when grow in autotrophic condition [49]. Seaweeds are not a good source for commercial fatty acid extraction like fish due to above reasons and additional reasons such as lower lipid content in algae.

Sterols are the major nutritional component found in seaweed as they comprise of many cells that utilize cholesterol as a structural sterol in cell wall. Despite of the criticism received worldwide, cholesterol is an essential nutrient to human body as they act as hormones and secondary messengers in signal transferring process. Certain sterols such as β-sitosterol and fucosterol leads to the decrease the concentration of cholesterol in the blood serum [50]. Number of sterols present inside each type of species varies due to many factors. Green seaweeds comprised of 28 isofucocholesterol types, 24 methylene cholesterols, cholesterol and β-sitosterol while brown seaweeds contain fucosterol, cholesterol and brassicasterol. Brown seaweeds contain fucosterol meanwhile Red seaweeds contain sterols such as desmosterol, sitosterol, fucosterol, cholesterol and chalinasterol [51].

III. BIO-ACTIVITY OF SEAWEED

A. Antiviral Activity

Rhodophyta such as *Aghardhiella tenera* and *Nothogenia fastigiate* comprise of certain sulphated polysaccharide that demonstrate antiviral activity against the viruses that are directly affecting human health [52]-[54]. Surprisingly they have indicated positive results towards HIV, HPV 1., HPV 2 viruses. The mode of activity of the polysaccharide is the key to prevent such viral infections at the first stage of the RNA replication on above viruses [55] [56]. One of the important requirements that a polysaccharide with above conditions must suffice is their lower cytotoxicity towards mammalian cells. Most of the seaweed extracts meet the need of lesser cytotoxins. Carrageenan also indicate antiviral activities against HIV and strains of HPV virus. Scientists have researched to develop a commercially available product which act as a barrier to prevent the transmission of HIV. As a result, Carragaurd was developed and it is a carrageenan-based microbicide to prevent HIV and other sexually transmitted diseases. Even though most of the polysaccharide from HIV capable of inhibiting RNA at the initial stage of the HIV RNA replication, a sulphated polysaccharide from *Schizymenia pacifica* can inhibit HIV at later stage in HIV replication [57] [58]. Fucoidan show another mode of antiviral activity by inhibiting the binding of viral particle to host cell [59]. Additionally, galactan sulphate in *Gracilaria corticate* can inhibit HSV 1 and 2 and Fucoidan mentioned above is antiviral against HIV, HSV 1, HSV 2 and human cytomegalovirus [60]-[63].

B. Antibiotic Activity

Several organic compounds present in macroalgae species indicate broad-spectrum antibiotic activity. Alkenes, alcohol, aldehyde, ketone, halogenated alkanes, sterol, phenol, haloforms and hydroquinone are instances for such compounds present. It's a known fact that the alcohol and phenols are used for household and laboratory cleansing purposes as they possess antiseptic qualities. But one of the limitations about such compounds is that they can only impose lethal effects on microbes at toxic concentrations inside the body. As reported the antibacterial activity of such compounds have a mode of action to disrupt the intra and inter cell communication among bacterial cells [64]. They inhibit the furanone compounds on the quorum sensing mechanism in gram negative bacteria by imitating as intracellular signal antagonist. As an antibiotic agent, fimbrolide, lactones from *Delisea pulchara*, used effectively against bacterial anti-fouling [65] and against chronic Pseudomonas aeruginosa infection.

C. Anti-Inflammatory Activity

Red seaweeds are plentiful in polyunsaturated fatty acids such as eicosapentaenoic and docosahexanoic. They are also known as poly unsaturated fatty acids [66] [67]. Among them, eicosanoid and its derivatives are received much more attention in research because of its anti-inflammatory properties [68]. Eicasanoids types such as leukotriens and hydroxyleicotetraenoic acid indicate biological activeness like chemo attraction of netrophills or smooth muscle cell. The combined effect of both prostaglandins and expansion of Laminaria stipes produced from brown seaweeds are well known as cervical dilators in obstetrics and gynecology [69]-[71].

D. Anti-Thrombic and Anti-Coagulant Activity

Anti thrombic and anti-coagulant activity is present in fucoidan polysaccharide and their activity serves under both invivo and invitro conditions. Their activity is conducted via heparin cofactor II or anti-thrombin III which are blood coagulation inhibitors [72] [73]. Fucan and thrombin interaction result in anti-coagulant activity intensiveness of the activity increase with the amount sulphation [74]-[76]. *Fucus vesiculosus* and *Ascophyllum nodosum* are two reliable sources of anti-coagulant, sulphated fucan. It is also used as a substitute for heparin from cattle which has a disadvantage of transmitting bovine spongiform encephalitis [77]. Additionally, inhibition of thrombin from platelets and thrombin induced platelet accumulation is mediated according to the concentration of Fucan unlike heparin. Fucan indicates a dosage dependency in inhibition of thrombin induced thrombosis and also it lacks the hypotensive effect found in thrombin [78].

E. Antilipemic, Hypocholesterolaemic Activity

Cardiovascular diseases are on rise due to the eating patterns and busy lifestyles of the people. Causative factors behind cardiovascular diseases are high plasma cholesterol level and high blood pressure. Macro alga such as, *funoran, fucoidan, porphyrin, laminaran, ulvan* and alginate have been noted to produce bioactive materials that respond to reduced cholesterol absorption in gut. Those bioactive substances are known as hypolidemic and hypocholesterolemic compounds according to Panlasigui et al. (2003). Hypocholesterolemic response is generated by increasing fecal cholesterol content and a hypoglycemic response [79] [80]. Hypolidemic response is caused by lowering of systolic blood pressure and reduction of the total cholesterol, freely available cholesterol, phospholipids, and triglyceride in the liver. Ethanolic extracts of *Colpomenia sinuosa, Iyengaria stellata, Solieria robusta, Spatoglossum asperum* and *Caulerpa racemosa* demonstrate hypolipidemic activities [81]. Other than mediating the lipids, methanolic extract from *Pelvetia babingtonii* indicates positive results towards postprandial hyperglycemia and controlling glycaemic index [82]. These bioactive compounds have contributed to the nutraceutical industry.

F. Enzyme Inhibitors and Stimulants

There are several occasions where seaweed extracts act as enzymatic inhibitors. Also, their mode of action and mechanism differ according to molecular structure. In human, the phospholipase A2 enzyme involves in variety of inflammatory diseases by producing archidonic acid [83]. The Phospholipase A2 enzyme therefore used to act as target for certain anti-inflammatory drugs. There are many active compounds that act against phospholipase A2 extracted from seaweed. Few of them are cyclocymopol, cymopol and prenylated bromohydroquinones from *Cympolia barbata*; rhiphocephalin from *Rhipocephalus phoenix*; caulerpenynesesquiterpene from *Caulerpa prolifera*; A fatty acid derivative from *Liagora farinose*; an orthoquinine from *Stypopodium zonale*, a macrocyclic enol-ether from *Phacelocarpus labillardieri* [84]. Additionally, *Caulerpa taxifolia* are used as inhibitors of pancreatic lipase [85]. Fucoidan has the ability to supress snake venom as it inhibits cytotoxic and myotoxic activities of PLA2 myotoxins which can result in muscle necrosis via snake bites [86].

IV. APPLICATIONS ON FUNCTIONAL FOOD

In general, foods that promote health conditions has resulted in the use of the term “functional foods”. They can provide health benefits by reducing the occurrence of chronic diseases and enhancing the ability to manage chronic diseases which improves the quality of life. Food science has moved from identifying nutritional deficiencies to convert into a developed food product that improve optimal health of the people. When developing functional foods, it is important to minimize losses in the nutraceutical properties, particularly during processing, in order to ensure retention of high levels of bioactivity in the final product. In addition, functional foods should have an acceptable sensory profile and consumer appeal, as in some cases the incorporation of bioactive components can influence the product flavour, aroma, or texture. A research study was conducted to study the results of incorporating *H. elongata* into pork sausages to replace animal fat and studied the effects on meat batter gelation [87]. Beef patties were developed in another study by adding *U. pinnatifida* in the sense of reducing salt and fat levels [88]. *U. pinnatifida* and *Sargassum marginatum* were added to pasta to increase antioxidant levels [89] [90]. The green seaweed *Monostroma nitidum* was incorporated into noodles to develop a new product; the resulting cooking yields were improved by up to one-third [91]. Another study incorporated the brown seaweed *Laminaria japonica* into pork patties in order to reduce fat content and increase DF levels; the resulting product had better sensory scores on overall acceptability when compared to the control [92]. It is also reported that *H. elongata* added to restructured poultry was found acceptable by sensory panels [93].

V. CONCLUSION AND SUGGESTIONS

It can be concluded that seaweeds are abundant source with a huge potential in pharmaceutical and food industries and they are vital components of sustainability in all ecosystems. Many researches have been conducted to reveal the capabilities and productive aspects of seaweeds since late 90’s. Chemical substances of the seaweed extracts vary in the purpose of utilization. They can be used as treatments to severe disease conditions as well as to develop new technologies. Natural anti-foulants, and UV-sunscreens are some instances. Yet most of the treatments are in development stage but indicate promising results. There are many bioactive compounds in seaweeds which are not exploited for the betterment of the mankind. It is predicted that will be used as a source of minerals such as iron and other minerals which are important for our normal body function. Also, they will be used against viral infections such as HIV, HPV and against more bacterial strains as an antibiotic. Treatment methods for cancers and tumours will also be implemented upon them. Functional food

market will grow with the novel influence towards healthy food consumption among people.

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