Development Of Functional Foods: Sea Weeds (Algae) Untouched Potential And Alternative Resource - A Review

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Abstract: "Let food be thy medicine and medicine be thy food" by Hippocrates was obscured with the advent of modern drug therapy and nutrition science until to twentieth century. The combination of consumer desires, advances in food technology, and new evidence-based correlation between nutrition to disease and disease prevention has created an unprecedented opportunity to concentrate on public health issues through diet and lifestyle. There is widespread interest these days to make a choice of functional foods from natural products that might promote health through specific bio-active compounds. Considering the diversity of biochemical's and capable of exerting functional bioactivities, a growing trend is developing across globe to use seaweeds in functional food development. Compounds isolated from seaweeds have various functional biological activities: antibacterial activity, antioxidant potential, anti-inflammatory properties, anti-e coagulant activity, anti-viral activity, and antifungal and apoptotic activity. Therefore, this review focuses on several bioactive chemicals in seaweeds and their biological activities for which they are responsible as a functional food ingredient.

Key words: Functional foods, Seaweeds, Bioactive compounds, Functional activity, chronic diseases

1. Introduction

"Let food be the medicine and medicine be the food" was embraced 2500 years ago by Hippocrates, the father of medicine [1],[2],[3],[4]. In the 19th century, this Philosophy was obscured with the advent of modern drug therapy [1], [3]and in the early twentieth century, nutrition science (preventing deficiencies and supporting body growth) was preoccupied. Today, this focus is shifting toward the concept of optimal nutrition [*5] , [6*] **i.e.** the role of diet in disease prevention and health promotion come to the fore front once again [1], [3]. It is noteworthy to comprehend that along with the ever-increasing consumer expectations toward convenience foods, the desire to maintain and improve health remains the key driver in the consumer goods market [*2], [6*]. Role of food as an agent for improving health and the advances in understanding the well-known correlation between nutrition and health, increased affluence and urbanization which are linked to a lifestyle where a daily routine requires less physical activity, the prevalence of chronic non-communicable diseases, characteristic of the modern age, such as obesity, osteoporosis, cancer, diabetes, allergies, and dental problems, demonstrates the great possibilities to maintain and develop a novel division of foods, called functional foods [7], [8], [9], [10] . Natural product (nutraceutical) interventions are currently being investigated on a large-scale basis as potential treatments to reduce risk of these diseases [11]**.** Functional food is a recent concept that originated in Japan (the birth place for the term functional food) but was further developed in the United States and in Europe. Functional foods cannot be a single, well-defined or well-characterized entity [*3], [4], [6], [12*], [*13], [14], [15],[16*]**.** A food can be regarded as functional food if it is satisfactorily affecting beneficially one or more target functions and health benefits in the body beyond the basic nutritional effects, in a way that is relevant to either improved state of health and well-being and/or reduction of risk of disease [*2] , [5] ,[9] , [17], [18*]. These substances provide essential nutrients often beyond quantities necessary for normal maintenance, growth and development, and/or other biologically active components that impart health benefits or desirable physiological effects [2]. A functional food must remain food and found naturally in foods or added to them as functional ingredients and it must demonstrate its effects in amounts that can normally be expected to be consumed in the diet: it is not a pill or a capsule, but part of the normal food pattern [*3*], [5], [*12*], [*13], [14], [15], [17], [19*] **.** The functional foods comprised in many forms: (i) conventional foods containing naturally occurring bioactive substances (e.g., dietary fiber), (ii) foods fortified, enriched or enhanced with bioactive substances (e.g., probiotics, antioxidants), and (iii) synthesized food ingredients introduced to traditional foods (e.g., prebiotics). Among the functional components, probiotics and prebiotics, soluble fiber, omega-3 – polyunsaturated fatty acids, conjugated linoleic acid, plant antioxidants, vitamins and minerals, some proteins, peptides and amino acids, as well as phospholipids are frequently mentioned. These active substances constitute a focus of contemporary science of human nutrition. A wide range of food products offer a variety of physiologically active compounds [*2], [18], [19], [20*], Seaweeds and seaweed-derived products are

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underexploited bio-resources and a source of such type natural ingredients for functional foods [21].

2. Emerging trends in the functional food industry

The marked trend and consumers growing interest in natural and healthy functional food products have forced researches and industry to develop novel products with functional ingredients [17], [22]. The market of functional food is indeed one of the fastest-growing within the global food industry [17]. Innovations introduced in the food industry in recent years mainly refer to new scientific and technical approaches in food processing and to introduce novel foods [*16*] . Innovation is today's business mantra and experts proclaim daily that the only hope for business survival is the ability to continue innovating [23**]** **.** Developing a new functional food requires detailed knowledge of the products and the customers, including quantitative and qualitative marketing studies and is an expensive process. In this context, the development of new functional food products and maintaining sustainable production, as it has to fulfill the consumer's expectancy for products and simultaneously delivering high quality food products with an added functionality to prevent life-style related diseases such as, cancer, obesity, diabetes, heart disease, stroke is one of the greatest challenges for food research facing in this century [12], [23]. In this regard , Functional foods represent one of the most interesting and main areas of research and innovation in the food industry [*16], [24*], due to their increasing demand derived from increasing cost of healthcare, the steady increase in life expectancy and the desire of older people for an improved quality of life in their later years [9], [16] **.**

3. Potential of Seaweeds for Development of Functional Foods

Seaweeds are also called macro-algae, and can be classified into three broad groups based on pigmentation: brown (Phaeophyceae), red (Rhodophyceae) and green (Chlorophyceae) **[**25], [26], [27], [28]**.** Naturally growing seaweeds are often called wild seaweeds, in contrast to seaweeds that are cultivated or farmed [29]. There has been a combined effort among scientists to explore and utilize varying food sources to develop functional foods to cater the ever-increasing demand from the consumers, who seek health-promoting roles of dietary compounds [2]. Due to the environment where they grow seaweeds are a potential candidate as the source of unique and interesting biologically active substances and essential nutrients for human nutrition [30] .

3.1 Global Production of seaweeds

Seaweed has found a place in human cuisine going back to the fourth century in Japan and the sixth century in China, the main centres of world seaweed activity [29], [30]. To date more than 14.7 million tons of seaweeds are commercially produced worldwide, 6% collected from wild stock, the rest 94% is farmed or cultivated [30], [31] , 99.95 % of the global farmed volume are all situated within Asia: Most productive is China with 54 % followed by Indonesia with 20 % and the Philippines with 12 %. Chile is most producing country outside Asia having 88,147 tons in 2009. Next ranking according to production volume are countries mostly from Africa (e.g., Tanzania, Madagascar, South Africa, and Namibia) with 108,400 t in 2009 and Western Europe (e.g., Spain, France, Italy, and the Russian Federation), which are responsible for the remaining biomass production volumes. Finally, the Pacific Ocean Islands grow just a small amount of seaweed and produced 2,377 tons in 2009 (Fiji, Kiribati, and Solomon Islands) [31]. Nowadays seaweeds are used not just for human food, but in a variety of advanced applications [30], [32].

3.2 Functional food ingredients in seaweeds

One of the ways most often employed by food manufacturers in the production of novel functional foods is the addition of one or more interesting bioactive compounds , referred to as functional ingredients, responsible for the functional bioactivities that the new product might present to a traditional food [40], [41] . Considering the diversity of biochemicals such as proteins, peptides, amino acids, polysaccharides, phenolics, lipids, polyunsaturated fatty acids, vitamins and minerals and their functional properties in seaweeds that are capable of exerting bioactivities, a growing trend is developing across globe to employ seaweeds in functional food development. However, several factors need to be taken into consideration in designing seaweed-based functional foods to obtain the market success [2], [26], [42], [43], [44], [45] , [46] . Compounds isolated from marine macro algae have demonstrated various biological activities, such as antibacterial activity, antioxidant potential, anti-inflammatory properties, anti-coagulant activity, anti-viral activity, antifungal and apoptotic activity [27] ,[38] .

3.3 Compositions of sea weeds

Seaweeds have been increasingly viewed as potential sources of bioactive compounds with immense pharmaceutical, biomedical and nutraceutical importance [33], [34] . The chemical composition of seaweeds is not well- known as the terrestrial plants but it is known to be rich in nutritional elements such as carbohydrates, protein, vitamins and minerals as well as bioactive compounds such as polyphenols, terpenoids, carotenoids and tocopherols [28], [33], [34], [35], [36], [37] though, the content of these elements varies depending on season , age , area of production and environment *36*, *37* . Seaweeds are low in calories from a nutritional perspective. The lipids, which are present in very small amounts, are unsaturated and afford protection against cardiovascular pathogens [38] and even though the carbohydrate content is high, most of this is dietary fibres and not taken up by the human body. However, dietary fibres are good for human health as they make an excellent intestinal environment [28] , [39] .

3.3.1 Proteins

The protein content of seaweeds (algae) varies greatly with species and seasons [47] . Very important bioactive proteins that can be extracted from macro algae are phycobiliproteins and lectins. Lecins (low molecular weight, thermostable proteins) can recognise and bind to specific carbohydrate structures and take part in many biological processes like intercellular communication and those isolated to date have highly novel amino acid sequences. According to the reports of [*43*], [*46*] they have also antibacterial, antiviral or anti-inflammatory activities . The

protein digestibility is limited by the non- protein fraction, which accounts for 10–20% of the nitrogen content .The isolation of protein from algae is difficult due to viscous polysaccharides; the use of buffers and detergents for effective cell lysis and removal of polysaccharide was proposed [*42*]. Algal proteins are relatively untapped resource which has been less intensely investigated with regard to composition, structure and bioactive potential than other algal constituents. Their potential is exhibited by the fact that in several cases extracts from a single species have been reported to have multiple bio- activities e.g. pepsin digests from Porphyra yezoensis have been reported to have ACE-inhibitory, anti-mutagenic, blood sugar reducing, calcium precipitation inhibition, cholesterol lowering, antioxidant, and improved hepatic function activities [46].

3.3.2. Peptides

Bioactive peptides are food-derived peptides that exert a physiological, 'hormone-like', beneficial health effect [48], [49] . Proteins and peptides from food sources such as dairy, eggs, meat and fish are well documented as agents capable of reducing high blood pressure and are thought to be able to prevent cardiovascular disease (CVD) [49] that may act as inhibitors of important enzymes such as Angiotensin I converting enzyme (ACE-I) and rennin [46], [50], [51], [52] . Angiotensin-I-converting enzyme (EC 3.4.15.1; ACE) plays an important physiological role in the regulation of blood pressure by converting angiotensin I to angiotensin II, a potent vasoconstrictor. Therefore, the inhibition of ACE activity is a major target in the prevention of hypertension [*53*], [*54*] . The researchers found a renin-inhibitory peptide in the seaweed Palmaria palmata. This is significant as renin-inhibitory peptides have not been identified from seaweed species before [*18], [49*] , [*55*],[*56*] **.** Bioactive peptides are inactive within the sequence of their parent protein, enzymatic hydrolysis of proteins releases specific small bioactive peptides or free amino acids either during gastrointestinal digestion or during food processing and therefore, may contribute to increase the nutritional value of food proteins. They usually contain 2–20 amino acid residues per molecule, but in some cases may consist of more than 20 amino acids [*18*], [*23*], [*47*], [*57*] , [*58*].

3.3.3. Amino acids

Most seaweed species contain all the essential amino acids and are a rich source of the acidic amino acids, aspartic acid and glutamic acid. Whilst threonine, lysine, tryptophan, sulphur amino acids (cysteine and methionine) and histidine have been perceived as limiting amino acids in algal proteins, their general levels in algal proteins are higher than those found in terrestrial plants [36], [42] .

3.3.4. Polysaccharides

Polysaccharides from natural sources are found to be effective, non-toxic substances with a wide variety of activities. Although this evidence seems to be of value, detail researches on polysaccharides derived from seaweeds are wanted [*44], [59*] Significant amounts of seaweed derived polysacchariused have many applications like they are used in food, beverages, pharmaceuticals stabilizers, emulsifiers, thickeners, feed etc, and other products for human consumption [60], [61]. Polysaccharides can act as prebiotics (substances that stimulate the growth of beneficial bacteria in the digestive track) and exert growth-promoting and health- improving effects [43], [62] . Many of them are soluble dietary fibers which have positive effect on the digestive track of animals (i.e. alginic acid), are effective and non-toxic antioxidants. The contents of polysaccharides show seasonal variations. The total level of these compounds in seaweeds is up to 76% of dry weight. Among many different algal polysaccharides, the most important are galactans, fucoidan, laminarin and alginates [*42], [43*], [*44*], [*61*] . Sulfated galactans are found both in the intercellular matrix and in the cell wall. Galactan is a macromolecule containing disaccharide-based repeating units: [→3)-β-D- Gal*p*-1→] and either [→4)-α-Gal*p*-(1→] or 3, 6-anhydro-α-Gal*p* (1). Depending on the optical configuration of the second unit, agarans (D) and carrageenans (L) are distinguished. The substituents of the main chain of galactans are sulfate groups, methoxyl groups, pyruvic acid acetals and glucosyl side chains. These groups can be irregularly distributed through the macromolecule. Galactans have anti-tumor and antiviral properties [43]. Furthermore, sulfated polysaccharides isolated from marine alga also have been shown to exert radical scavenging activities in vitro and in vivo [44], [60], [63]. Fucoidan is a sulfated polysaccharide found in brown seaweeds. The macromolecule contains α-1, 3-linked sulphated L-fucose as main sugar unit and sulfate ester groups. The chemical composition depends on the algal source and harvesting time. The amount of fucoidan in algae is about 10% of dry mass. The absorption and bioavailability of fucoidan depends on its molecular weight. Compared to high molecular fucoidan (HMF), low molecular fucoidan (LMF) is bioavailable in the highest degree. It has anti-inflammatory, antiviral, anti-tumor and antioxidative activities. Antiviral properties of fucoidan participate in inhibition of viral-induced syncytium formation [7], [43], [44], [60]. Laminarin is one of the major polysaccharides found in brown algae. It has a chemical structure consisting of β-(1→3)-linked glucose in the main chain and random β-(1→6)-linked side-chains. The content of laminarin in seaweeds is about 10% of dry weight, but seasonally it can reach up to 32%. Laminarin is a dietary fibre, can act as a prebiotic, has antiviral and antibacterial properties. Antioxidative acitivity of laminarin depends on its molecular weight and chemical structure [43], [44]. Laminarin, composed of (1, 3)-b-D-glucopyranose residues, has a relatively low molecular weight and its structural features are species dependent. Laminarin is a modulator of intestinal metabolism, an activator of immune function but a less potent antioxidant than other components [42]. Alginates are absent in terrestrial plants. They can be extracted from brown seaweeds, in which they constitute up to 47% of dry biomass. Alginates can be found both in acidic and salt forms. The acid form, known as an alginic acid, is a polymer consisting of two types of hexuronic acid monomers linked by 1–4 bonds: β-D-mannuronic acid and α-L-guluronic acid. They have thickening, stabilizing and general colloidal properties, but also strong antibacterial and anti-inflammatory activities [42], [44] , [43], [64] , [65] .

3.3.5. Polyphenols and Antioxidants

Polyphenols are produced by most plants, including seaweeds. Among polyphenols phenolic acids, flavonoids, isoflavones, cinnamic acid, benzoic acid, quercetin and lignans can be mentioned. Polyphenols are strong antioxidants. Reactive oxygen species, generated in organisms as an integral part of metabolism, are highly reactive and can cause cell dysfunction and cytotoxicity. Polyphenols can donate hydrogen to free radicals and produce non-reactive radicals. Phlorotannins are the group of tannin compounds, which belong to the polyphenolic substances formed by polymerization of phloroglucinol (1, 3, 5-trihydroxybenzene) through the acetate-malonate pathway. These polymers have many biological activities in organisms, eg, are involved in host defense mechanisms. Phlorotannin content varies from 1 to 10% of the algal dry mass. The molecular skeleton of phlorotannins consists of even 8 phenol rings, while terrestrial plants produce tannins consisting of only 3 to 4 rings. Phenol rings act as electron traps for free radicals. Consequently, phlorotannins have very strong antioxidant properties and antimicrobial activities 10 times higher antioxidant activity in comparison with ascorbic acid and α-tocopherol because of their unique structure. They can attack microbiological proteins, which can result in inhibition of bacteria [43], [63], [66] . Seaweeds, especially their polyphenolic extracts constituents, have exhibited strong inhibitory activity against both α-glucosidase and α-amylase [67], [68] , [69] . Carotenoids are natural pigments derived from five-carbon isoprene units that are polymerized enzymatically to form regular highly conjugated 40-carbon structures (with up to 15 conjugated double bonds). At least 600 different carotenoids exercising important biological functions in bacteria, algae, plants and animals have been identified to date [*70*], [*15*]. Different species of algae contain different kinds of Carotenoids', are generally powerful antioxidants and have reported anti-cancer activities, anti-obesity activity. The antioxidant properties are based on the fact that they are able to quench singlet oxygen and scavenge free radicals. The most important carotenoids are β-carotene, fucoxanthin and tocopherol. [*43], [46*], [*71*]. Phycobiliproteins are water soluble pigments produced by cyanobacteria (blue-green algae), red algae and crypto monads. Phycobiliproteins have many functional properties such as anti- oxidation, and radical scavenging activities, anti- tumor, anti-virus, anti-inflammation, liver-protection, neuro-protection, UV protection, antiviral, atherosclerosis and skin function activating have been demonstrated [43], [72], [46], [71] . Recent studies indicated that PBP even has potential applications for enhancement of memory and disposal of optics message, fast photoelectricity detection and manual nerve network [72], [71]. Antioxidants are free radical scavengers (FRS) which postpone the oxidation and block the chain initiated by high energy molecules and other consequent reactions. Although many synthetic antioxidants are promising for various human ailments, their pro-oxidant or cytotoxic nature at higher concentration prevents them from long term use. Natural antioxidants, the kind of compounds which have attracted major interest, may replace synthetic ones in prolonging the shelf life of food and cosmetics by delaying oxidation [42] . More recent reports revealed marine algae are rich sources of antioxidant compounds with potential free radical scavenging activity [*59*], [*73*] . Therefore, algal species as alternative materials to extract natural antioxidative compounds have attracted much attention of biomedical scientists. There are some evidences that seaweeds contain compounds with a relatively high antioxidant and antipro-liferative activity [7] , [33] , [63], [74], [75].

3.3.6. Polyunsaturated Fatty Acids

Phospholipids and glycolipids are the main classes of lipids found in seaweeds. When the decrease of environmental temperature occurs, seaweeds can accumulate polyunsaturated fatty acids (PUFAs). The species that live in cold regions contain more PUFAs than species living in higher temperatures [7], [43] , [76] , [65] . Long chain PUFAs (LC-PUFAs) play key roles in cellular and tissue metabolism, including the regulation of membrane fluidity, electron and oxygen transport, as well as thermal adaptation. In addition, public perception of healthy food and life style has brought them to the attention of the consumer [61], [70]. In particular, there is increasing interest in a typical PUFA family (ω-3) named eicosapentaenoic acid (EPA, C20:5Δ5, 8, 11, 14, 17, 20:5 ω-3) [61], [70], because they are very important for human health maintenance and they are synthesized only by plants [*7*], [*43*] , [*76*], [*65*]**.** . EPA is a fatty acid 20 carbons in length with five double bonds from the carboxy [Δ]terminus or with the I^{st} double bond located at third carbon from the methyl (ω) terminus [7], [43], [46], [61], [65], [70] , [76] .

3.3.7 Minerals & Vitamins

Algae are rich in iodine, iron, potassium, magnesium, calcium, selenium, and phosphorus – minerals that are widely used in health beneficial supplements. Iodine, in particular, plays an important role in the functioning of the thyroid [77]. Their content in the biomass is sometimes as high as 40%. This is because seaweeds accumulate metal ions from salt water and concentrate those substances as carbonate salts in their fronds [*43*]. Vitamins are essential nutrients found in foods. They perform specific and vital functions in a variety of body systems, and are crucial for maintaining optimal health [78]. Marine algae is a rich source of vitamins A, B1, B2, B3, B9, C, and E. Vitamins C, and E are potent antioxidants. Vitamin A plays an important role in cell growth and differentiation, and B vitamins are precursors for enzyme cofactors [77] .

3.2.8 Therapeutic uses of sea weeds

Functional food for prevention of chronic diseases is one of this century's key global challenges[79]. In the last few decades, discovery of pharmacologically active metabolites from the seaweeds has increased tremendously those can be used against several diseases like cancer, diabetes, infectious diseases etc. Seaweeds or marine algae have been reported to contain many important compounds such as antioxidants and polyphenols , several oligo and polysaccharides , Carrageenans and alginate which act as antibiotics, laxatives, anticoagulants, anti-tumor, anti-ulcer products and suspending agents in radiological preparations [27], [37] , [80] and have been used for decades in medicine and pharmacy . Fibers perform varied range of anti-mutagenic; also plays an important role in modification of lipid metabolism in the human body[*81*]. More and more chemist and biologist pay attention to the

constituents of the algae; if their natural products are explored, they may lead to an efficient lead for the discovery of new drug molecules against several pathogens causing infectious diseases [26],[38] . High intake of calcium, potassium and sodium are associated with lower mean systolic pressure and lower risk of hypertension. All seaweeds offer an extraordinary level of potassium that is very similar to our natural plasma level. Worldwide research indicated that seaweed extract is similar to human blood plasma. Two Japanese surgeons used a novel technique of mixing seaweed compounds with water to substitute whole blood in transfusion and this was successfully tried in over 100 operations [*81*].

4. Conclusion

Functional foods provide health benefits over and above normal nutrition. Functional foods are different from medical foods and dietary supplements, but they may overlap with those foods developed for special dietary uses and fortified foods. The demand for bioactive ingredients will continue to grow as the global market for functional foods and preventative or protective foods with associated health claims continues to rise. Over the last decade, there has been significant research and development in the areas of bioactive discovery and development of new materials, processes, ingredients and products that can contribute to the development of functional foods for improving the health of the general population. Seaweeds have been increasingly viewed as potential sources of bioactive compounds with immense pharmaceutical, biomedical and nutraceutical importance.

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