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A study on the rich compounds and potential benefits of algae: A review

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Abstract
Researches on novel marine compounds has increased over the past decades in various areas such as medical, veterinary, pharmaceutical, cosmetics or bioenergy. Some compounds isolated from marine algae were revealed to have anti-aging, anti-cancer, anti-coagulant, anti-inflammatory, anti-microbial, anti-oxidant, anti-diabetic, anti-Alzheimer and anti-tuberculose activities. Algal secondary metabolites such as fatty acids, lipopeptides, alkaloids, steroids, terpenoids and most carotenoids, flavonoids with different potent activity have the potential to be produced commercially using bio-engineering techniques. This review provides an overview of novel publications related to the developments in these topics.

Keywords: Algae, seaweeds, veterinary, pharmaceutical, cosmetics or bioenergy

Introduction
Algae are photosynthetic organisms, with great diversity of forms from unicellular microalgae to multicellular macroalgae. Marine macroalgae, also called as seaweeds, can be classified into three groups, according to their pigmentation, brown (Phaeophyceae), red (Rhodo- phyceae) and green (Chlorophyceae) algae. Especially in some countries they have been used as food since ancient times. But nowadays, many natural bioactive substances obtained from algae as sustainable sources are exclusived to provide worldwide demand in different industrial area [1]. Some of algae and their bioactive compounds and their healt effects are depicit in Table 1.
Research on novel marine compounds has increased over the past decades for their application in various areas such as human or animal nutrition, pharmaceutical, cosmetics or bioenergy. Some compounds isolated from marine algae were reported to have anti-aging, anti-cancer, anti-coagulant, anti-inflammatory, anti-microbial, anti-oxidant, anti-viral, anti-diabetic, anti-Alzheimer, anti-tuberculosis, anti-fungal and anti-inseccidal activities [46, 47]. Some metabolites isolated from marine algae have already been reported for their potential health benefits such as on the immune and nervous system. Some algae and their possible healt effects are shown in Figure 1.

Existence of such variety in the algae species are due to the different living environments in which they live and survive in. Aquatic environments are variable systems, in order to survive, they must adapt rapidly to the new environmental conditions, producing a great variety of secondary metabolites which cannot be found in other organisms. Scientific studies on multi-functional therapeutic importance of algae with rich potential have been increasing in recent years [48]. Taking this into account, experimental production of some valuable metabolites such as astaxanthin has been increased in algae under laboratory conditions. This is a futuristic phenomenon in terms of sustainable usage and algae can potentially be considered for new therapeutic approaches to many global disease categories [49]. A br overview of the usage and benefits of algae in different areas has been targeted in this study.
Besides the conveniences of the twenty-first century, environmental problems, industrialization and its influences affect human health negatively. Algae at this point leads people who deal with many new diseases such as cardiovascular, obesity, diabetes, stress, cancer, hypertension, etc. to new therapeutic natural resources. The aim of this study is to draw attention once again to the multifunctional therapeutic importance of the algae in recent years with the prospect of rich potential ingredients.

Table 1: Some of algae and their bioactive compounds and their health effects

Source	Compound	Effect	Reference
Porphyra haitanesis (Rhodophyta)	Porphyran, shinorine	Anti-aging	[2]
Porphyra haitanesis (red alga)	Polysaccharide fraction	Anti-aging	[3]
Nannochloropsis sp	Fenolik compound	Anti-aging	[4]
Dunaliella tertiolecta	Fenolik compound	Anti-aging	[4]
Tetraselmis suecica	Fenolik compound	Anti-aging	[4]
Haematoccoccus pluvidis marine algae	Astaxantinin	Anti-aging	[5]
Cytophaga sp	Carrageenan, oligosaccharide	Anti-cancer	[6]
Fucus vesiculosus (brown seaweed)	Fucoidan (sulfated polysaccharide)	Anti-cancer	[7]
Porphyridium cruentum	Polysaccharide	Anti-cancer	[8]
Undaria pinnatifida	Fucoidans (sporophyll)	Anti-cancer	[9]
Costaria costata		Anti-cancer	[10]
Laminaria religiosa (kelp)	β-carotene	Anti-cancer	[11]
Sargassum horneri	Polysaccharide	Anti-coagulant	[12]
Arthrospira platensis (green algae)	Sulfated polysaccharide	Anti-coagulant	[13]
Laminaria japonica	Fucoidan	Anti-coagulant	[14]
Sargassum horneri	Proteinhydrolysates	Anti-coagulant	[15]
Laminaria japonica	Fucoidan	Anti-coagulant	[16]
Codium fragile	Polysaccharide	Anti-coagulant	[17]
Ishige foliacea (brown alga)	Phenolic compound	Anti-diabetic	[18]
Ecklonia kurome (brown alga)	Polyphenols	Anti-diabetic	[19]
Halimeda macroloba	α-glucosidase and dipeptidyl-peptidase	Anti-diabetic	[20]
Padina sulcata	α-glucosidase and dipeptidyl-peptidase	Anti-diabetic	[20]
Sargassum binderi	α-glucosidase and dipeptidyl-peptidase	Anti-diabetic	[20]
Turbinaria conoides	α-glucosidase and dipeptidyl-peptidase	Anti-diabetic	[20]
Ecklonia kurome (brown alga)	Polyphenols	Anti-diabetic	[19]
Ishige foliacea (brown alga)	Phenolic compound	Anti-diabetic	[18]
Gymnogongrus griffithsiae (Red seaweed)	Galactan sulfate	Anti-viral	[21]
Undaria pinnatifida	Sulfated polysaccharides	Anti-viral	[22]
Splachnidium rugosum	Sulfated polysaccharides	Anti-viral	[22]
Gigartina atropurpurea	Sulfated polysaccharides	Anti-viral	[22]
Plocamium cartilagineum	Sulfated polysaccharides	Anti-viral	[22]
Cryptonemia crenulata (Red seaweed)	Galactan sulfate	Anti-viral	[21]
Sargassum vulgare (brown seaweed)	Sulfoquinovosyldiacylglycerols (SQDGs)	Anti-viral	[23]
Spirulina platensis	Spirulan	Anti-viral	[24]
Arthrospira platensis	Spirulan	Anti-viral	[25]
Porphyra tenera (Asakusa-nori, edible red algae)	β-carotene,	Anti-oxidant	[26]
Porphyra haitanesis (Rhodopyta)	Polysaccharide fraction	Anti-oxidant	[3]
Ecklonia cava	Phlorotannin	Anti-oxidant	[27]
Sargassum horneri	Proteinhydrolysates	Anti-oxidant	[15]
Laminaria japonica	Polysaccharides	Anti-oxidant	[14]
seaweeds	Phenolic compounds	Anti-oxidant	[28]
Costaria costata		Anti-oxidant	[10]
Porphyra tenera (Nori, red algae)	Porphyran	Anti-oxidant	[29]
Cystoseira usneoides (Brown Algae)	Meroterpenoids	Anti-inflammatory	[30]
Ecklonia cava	Osteoarthritis	Anti-inflammatory	[27]
Ecklonia kurome (brown alga)	Phlorotannins	Anti-microbial	[31]
Scytosiphon lomentaria	Methanol extracted	Anti-microbial	[32]
Padina pavonica	Methanol extracted	Anti-microbial	[32]
Cystoseira mediterranea	Methanol extracted	Anti-microbial	[32]
Hypnea musciformis	Methanol extracted	Anti-microbial	[32]
Spyridia filamentosa	Methanol extracted	Anti-microbial	[32]
Callophycus sp. Fijian red alga	Bromophycoic acids	Anti-bacterial	[33]
Laurencia okamurai. red alga	Terpenoid	Anti-bacterial	[34]
Dictyosphaeria sp.		Anti-bacterial	[35]
Gracilaria salicornia		Anti-bacterial	[35]
Laurencia nidifica		Anti-bacterial	[35]
Liagora sp.		Anti-bacterial	[35]
Ulva sp		Anti-bacterial	[35]
Padina sp.		Anti-bacterial	[35]
Dilophus spiralis Brown Alga	Dolabellanes	Anti-bacterial	[36]
Chlamydomonas reinhardtii	Aqueous or methanolic and exanolic extracts	Anti-bacterial	[37]
Chlorella minutissima	Ethanolic extracts	Anti-bacterial	[38]
Chlorella pyrenoidosa	Various organic solvent extracts	Anti-bacterial	[39]
Porphyridium purpureum	Methanolic extracts	Anti-bacterial	[40]
Porphyridium aerugineum	Phycobiliproteins	Anti-bacterial	[41]
Chlorococcum humicola	Carotenoid, chlorophyll	Anti-bacterial	[42]
Chlorella vulgaris	Chlorellin	Anti-bacterial	[43]
Chlorella vulgaris	Aqueous or methanolic and hexanolic extracts	Anti-bacterial	[37]
Laurencia nidifica (Okinawan Red Alga)	Laurinterol	Anti-insecsidal	[44]
brown algae	Fucoxanthin	Anti-angiogenic	[45]

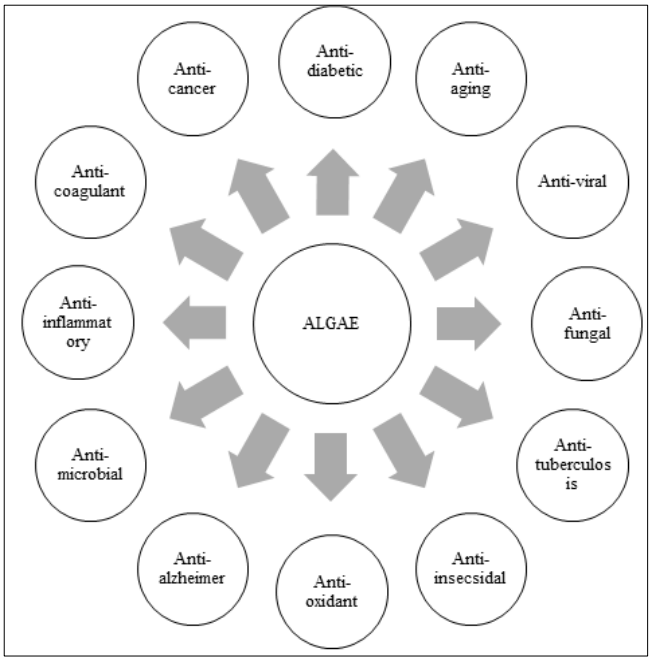

Fig 1: Some algae and their possible healt effects

Anti-diabetic effects

Diabetes mellitus is a metabolic disorder characterized by insufficient insulin secretion and variable degrees of insulin resistance leading to hyperglycemia. Generally treatments for diabetic patients include oral antidiabetic drugs and insulin injections. But, continuous use of these drugs causes lower healing with many side effects. That is why, preventive and therapeutic antidiabetic bioactive substances with minimum side effect are needed. At this point, among marine algae, brown and red algae are reported as promising sources due the therapeutic potential of compounds isolated from them to exhibit antidiabetic activity [50].

Endoplasmic reticulum stress has been expressed as a key connection between obesity, insulin resistance, and type 2 diabetes. It was reported that connection can be used for therapeutic purposes with orally active chemical chaperones. Özcan, *et al* [51] treated obese and diabetic mice with these compounds and normalization of hyperglycemia, restoration of systemic insulin sensitivity, resolution of fatty liver disease, and enhancement of insulin action in liver, muscle, and adipose tissues have been observed. So, results chemical chaperones enhance the adaptive capacity of the endoplasmic reticulum and act as potent anti-diabetic method with potential application in the treatment of type 2 diabetes.

The selection of the correct model animal is very important in studying metabolic diseases. It is reported that DM-II and KK-Ay mouse is considered as a suitable polygenic model for this human metabolic disease. There is intensive work on finding bioactive resources in this important issue that concerns human health. One of these is related to investigate the antidiabetic effect of algal polyphenols (E. Kurome, KPP) on KK-Ay mice. The antidiabetic effect of polyphenols from E. kurome (KPP) in KK-Ay mice has been studied. It was reported that KPP is effective against DM-II and might provide a source of therapeutic agents for DM-II. Xu *et al* [19] and Lee *et al*. [18] reported that Octaphlorethol A, a novel phenolic compound isolated from a brown alga, Ishige foliacea, is a potential novel anti-diabetic compound increases Glut4-mediated glucose uptake by activating PI3-K/Akt and the AMPK signaling pathway in skeletal muscle cells. It is explained as a novel target for the treatment of type 2 diabetes.

The information on marine polyphenols, with a particular focus on phlorotannins and their potential health benefits in relation to the prevention and treatment of risk factors for type 2 diabetes has been updated by Murray *et al* [52]. It was reported that astaxanthin had a protective effect against several deleterious effects caused by high glucose exposure and also restored the enzymatic antioxidant profile in salivary gland of alloxan-induced diabetic rats. Therefore, astaxanthin proposed as a potential antidiabetic remedy for the treatment of diabetic nephropathy [53, 54].

Anti-inflammatory and Immunologic effects

Cellular homeostasis can initiate inflammatory responses due to various stresses such as viral and bacterial infections, disturbance in protein production, mechanical restrictions, changes in the environment and nutrition mistakes. It is now reported that many diseases are associated with inflammation initiated by stressed cellular organelles but mechanisms are still poorly understood [55]. This is related with the immune defense capacity of the body and, consequently, many diseases. In this regard, positive results for some bioactive compounds of algae are found as important [30, 56-58].

For example, anti-inflammatory, 3-0-β-D-glucopyranosy-lstigmasta-5,25-diene have been isolated from the green alga *Ulva laetuea* by Awad [59]. Briefly, there is a remarkable increase in algal immunologic effect and anti-inflammatory research during recent year due to their rich bioactive content [60-63].

Anti-oxidant effects

Antioxidants are compounds capable to either delay or inhibit the oxidation processes which occur under the influence of atmospheric oxygen or reactive oxygen species called free radicals. Antioxidants can be subcategorized under two group, as endogenous and exogenous according to their source. Endogenous antioxidants are enzymes, like superoxide dismutase, catalase, glutathione peroxidase and nonenzymatic compounds, such as uric acid, bilirubin, albumin, metallothioneins. Exogenous antioxidants can derive from natural sources such as vitamins, carotenoids, flavonoids, anthocyanins, some mineral compounds and can also be synthetic compounds. When endogenous factors cannot make certain a careful control and a complete protection of the organism against the reactive oxygen species, the need for exogenous antioxidants emerges, as nutritional supplements or pharmaceutical products.

In order to obtain natural and sustainable antioxidant sources, there are many studies aimed to being researched the relationship between the bioactives of algae such as carotenoid, phenolic acids and their antioxidant capacities. These carotenoids and phenolic compounds are involved in the defense mechanism of the organism against the pathologies associated to the attack of free radicals and they also avoid skin aging due to the presence of their antioxidant properties.

Therefore in recent years, there is an increasing interest in natural antioxidants from algae particularly in those have capacity to prevent deleterious effects of free radicals in the human body. For example, total carotenoid, phenolic acid, fucoxanthin contents and fatty acid profile of six species of algae (five microalgae and one macroalga) were quantified followed by bioactivity evaluation using four antioxidant assays by Foo *et al* [64].

There are many publications about the natural antioxidant content of algae in many countries of the World [63, 65-67]. Astaxanthin is a naturally occurring carotenoid with strong antioxidant properties both *in vitro* and in vivo [68] and retinal cells is protected against oxidative stress *in vitro* and in mice in vivo [69]. As observed by many researhers, today, algae sources are preferred around the world to obtain natural bioactive antioxidants from sustainable sources.

Anti-Alzheimer (AD) effect

Alzheimer's disease (AD) is a neurological irreversible disorder characterized by cognitive impairment, neuronal death, synapse and cholinergic neuron loss, brain damage. It is known that dementia is more common as people grow older, but it is not a normal part of aging [70]. There is no direct experimental evidence but the neuroprotective activities of most microalgal extracts have been attributed to bioactive compounds such as carotenoids, PUFAs, sterols and phenolic compounds. It was claimed that some carotenoid and isoflavone could be explored for nutraceuticals and pharmaceuticals for the treatment of Alzheimer's Disease. For example, Astanxathin and Biochanin A have been prposed as promising therapeutic agents and protect the brain against β-amyloid-induced neurotoxicity and neuronal damage. Microalgae species extracts such as those of *C. vulgaris, H. pluvialis, N. oculata, N. oleoabundans, and C. calcitrans* are rich in carotenoids and protect the brain against neuronal damage, cell death associated with oxidative stress.

Algae are known for their ability to synthesize complex and diverse compounds with specific enzyme inhibition properties. The pathophysiology connection of Glutaminyl cyclase enzymes to various diseases including Alzheimer's disease was described. Algae extracts from different species were investigated regarding their glutaminyl cyclase enzymes inhibiting activity and for the first time these enzyme inhibitors from algae were identified, characterized and isolated by Hielscher-Michael *et al* [71]. In addition, It has beeb pointed out by some scientists that the use of functional foods, dietary supplements and natural products with multi-neuroprotective activities could be an effective therapeutic intervention in the management of AD which pose little or no side effects compared to synthetic drugs.

Anti-aging and Cosmeceutical usage

Aging can be defined as the time-dependent decline of physiological functions of an organism. Aging is a the time-dependent degenerative change process of cell, tissue and organ functions of organisms. It is a multi-faceted process that is influenced by both genetic and environmental factors. It is known that a new urban life, working conditions and ecological effects in the 21st century caused metabolismal, cytotoxic and mutagenic damages in living organisms including humans. All of this listed factors increases the frequency of diseases like heart-vessel, cancer and triggers aging.

The details of the aging mechanisms are molecular but not clearly yet known [72]. It is reported that nutrition, living style and some environmental factors have an effect on aging[73]. In the scientific world, studies about the search for active substances from nature against aging have increased and for this reason rich and varied contents and algae have gained importance. Especially, anti-gerontological effect of some antioxidant rich algae is being investigated. It is known that natural antioxidants flavonoids, phenolic compounds, tannins and terpenes protect the cells by neutralizing the free radicals in the unstable structure in the cell. For this reason, biotechnological production of some algae, known as natural antioxidant sources, has recently been carried out due to their cell protective, restorative and anti-aging properties. For example, in some micro-algae cultured with special techniques, the amount of pigmented materials with strong antioxidant properties such as intense beta-carotene, astaxanthin, zeaxanthin, and lutein can be increased and used as productive organisms.

Aging is a phenomenon caused by cellular damage and insufficiency. Major causes of aging are known to include cellular oxidative stress and irreversible cellular demage. Algae biomass contain phenolic compounds such as tocopherols, polyphenols, tannins, and flavonoids and pigments such as carotenoids, astaxantin, lutein [74, 75]. It was reported that they all show diverse nutraceutical activities including protection agains toxidative cellular stress due to free radicals [76-78].

Studies on anti-aging effects of algae and bioactive compounds have gained importance. Some algae contain valuable antioxidants and the anti-gerontological role of these algae rich in antioxidants is an important issue. For example, it was reported that residual biomasses and protein hydrolysates of three green microalgae species exhibit antioxidant and anti-aging activity [4, 79]. Anti-aging, skin-whitening, and pigmentation reduction products have been announced using some bioactive from algae [80]. In recent years some positive results have been obtained from algae in lifetime studies with model animals.

Topic dermatitis and the possible role of matrix metalloproteinases in skin-related diseases have been studied for cosmeceutical products [81]. Some macroalgae attract attention in food, cosmetics, pharmaceuticals and nutraceutical industries [82]. Proper development of marine algae compounds would be beneficial in developing cosmeceutical products and in the development of cosmeceutical industry [83]. There are studies in which some algal secondary metabolites are quite protective for skin, including UV protection and prevention of wrinkles, etc.

Anti-cancer effect

Cancer is a major public health problem in Turkey. The rate of death due to cancer has been steadily increasing, similar traits can be observed all around the globe. There are many types of cancer, but all have a common cellular mechanism, which is the loss of cell division control. Cells that normally lose control or can not repair damage enter apoptosis. Apoptosis called as programmed cell death, which enables a cell to direct its own destruction. Apoptosis is a crucial factor for mammalian development and subsequent tissue homeostasis and karsinogenesis. Studies on the anti-carcinogenic effects of algal strains are gaining importance. For example, Kim *et al* [84] reported that fucoidan present in brown algae induces apoptosis of human colon cancer cells. Huang *et al* [85] examined the antitumor effect of marine algae (*Colpomenia sinuosa*, *Halimeda discoidae*, and *Galaxaura oblongata*) extracts on human hepatoma and leukemia cells. The results are were interpreted that reactive oxygen speciesis a key mediator in the apoptotic signaling pathway and algae extracts induce apoptosis in human leukemia cells through generation of reactive oxygen species.

Resent research shows that cancer can be caused by genetic and environmental factors. We may not be able to change our

genetic heritage, but it may be possible to protect ourselves from this disease with nutrition, living style and treatment methods. Antioxidant of algae[86] are found to be valuable for healthy nutrition and long life in some countries of the world. There are many studies on the anti-cancer effects of antioxidant ingredients of algae. For example, antioxidant and anticancer effect of fucoidan isolated from brown seaweed, *Sargassum polycystum*, was investigated by Palanisamy *et al* [87] and the results demonstrated that the isolated fucoidan from *S. polycystum* possessed potent antioxidant and anticancer properties.

Studies Show that increased iodine levels can be contribute to hihher risk for thyroid cancer. Powdered tissue from 46 species of air-dried marine algae (four green, 21 brown and 21 red algae) were screened for antitumor activity and significant activity against Ehrlich carcinoma was found. In addition several glycolipid and phospholipid fractions from brown and red algae were found effective against Meth-A fibrosarcoma. The understanding that certain algal species have anticarcinogenic effects has further increased their importance in the future. There are studies on anti-cancerogenic effects of algae as raw materials for food and therapeutic drugs. Seaweed extracts have recently been found to have antioxidant and anti-tumor activities. A hot-water-soluble polysaccharide of the marine alga, *Capsosiphon fulvescens*, inhibits cell proliferation and induces apoptosis and inhibits gastric cancer [88]. Fucoidan a natural component of brown seaweed, has also anti-cancer activity against various cancer types by targeting key apoptotic molecules [89-91]. Astaxanthin is a red carotenoid pigment which has significant potential for antioxidant activity. The other example is fucoidan, a natural substance derived from marine algae, has immunomodulatory and cytotoxic activities and has been investigated as a potential anti-cancer agent [89, 92].

There are many other scientific studies that show the protective effects of algae on cancer. For example, the laminarin and fucoidan isolated from brown algae Sargassum duplicatum was found against colony formation of colon cancer cells *in vitro* [93]. Gonzalez-Ballesteros [94] reported that brown macroalgae, *Cystoseira baccata* (CB), extracts in obtaining gold nanoparticles has a significant potential for the treatment of colon rectal cancer. Fucoidan is a sulfated polysaccharide is extracted from marine brown seaweed has a wide range of bioactivities including anti-cancer. It was reported that fucoidan from *Padina* sp showed potential selective cytotoxicity, and promising for the development of an anti-cancer compound[95]. Intensive studies are still going on in this field of science.

Anti-microbial effects

Living organism (such as a bacteria, fungi, viruses) which are too small to be seen with naked eye but visible under a microscope are called microorganisms. An anti-microbial is any form of substance of natural, semisynthetic or synthetic origin that kills or inhibits the growth of microorganisms like the metronidazole, protozoa, yeast, fungi, viruses, algae, and some worms etc. But causes little or no damage to the host. The antibiotics are compounds which are able to fight just the bacteria. So, all antibiotics are antimicrobials, but not all antimicrobials are antibiotics.

Algae can survive in aquatic environments where microbial richness is present. It is also expected that they have a rich content against some harmful microorganisms due to adaptation. Seaweed derivatives are shown to be promising candidates for future antimicrobial drugs or their replacements [96]. It has been requently reported that an alternative to conventional antibiotics is needed as the microbial resistance to these drugs is increasing in humans and animals [97].

Numerous scientific studies have been conducted to research macroalgae and microalgae compounds as natural promising antimicrobial sources against human and animal pathogens. Many studies reported that antibacterialalgal natural products isolated from different algae, may contribute to the search for novel leads for developing newer drugs to treat drug-resistant bacterial infections. For examle, eight new antimicrobial natural products named chrysophaentins A−H belonging to a new structural class have been isolated from the marine chrysophyte alga *Chrysophaeum taylori* by Plaza, *et al*[98]. Thirteen new minor diterpenes were isolated from the organic extracts of the brown alga, *Dilophus spiralis* and the antibacterial activities were evaluated against six strains of *Staphylococcus aureus* [36].

It is well-known that the use of natural antimicrobial compounds in food has gained also much attention by the consumers and the food industry. This has prompted the food industry to look for alternative preservatives that can enhance the safety and quality of foods [99]. Results reported that some algal extracts from *Padina*and *Ulva* species and cyanobacterial compounds showed antimicrobial activity against Gram positive foodborne pathogens but none of the algal extracts or cyanobacterial isolates tested had antibacterial activity against Gram negative bacteria [35].

Some new bioactive substances from different marine algae have been reported as promising antiviral agents. For example, Anti-HIV compounds from red seaweeds were reported [100]. Two polybromocatechol compounds isolated from the red alga *Neorhodomela aculeate*, inhibited infection and cytopathic effects on a HeLa cell line by HRV2 and HRV3 which are causal agents of common colds due to respiratory infections. Their antiviral activity against human rhinoviruses [101] promises to be in a therapeutic struggle with this virus. Plouguerné *et al* [102]. characterized the antiviral activity of brown seaweed *Sargassum vulgare* for both HSV-1 and HSV-2 viruses. more potently than acyclovir, a clinically used antiherpetic agent.

In addition, antiviral activity sulfated fucans from *Stoechospermum marginatum* [103] sulfated polysaccharides from *Laminaria angustata* [104] anti-HSV-1 and HSV-2 activity of glycolipids from the marine algae *Osmundaria obtusiloba* [105] sulfated polysaccharides from *Sphacelaria indica* [106] and sulfated polysaccharide from *Agaricus brasiliensis* [107] have been reported.

Antifungal effects of algae with rich contents are also detected with different studies [108, 109]. Two new prenylated *para*-xylenes with broad spectrum of antifungal activity against *Candida glabrata*, *Trichophyton rubrum*, and *Cryptococcus neoformans*, were reported from the green algae *Caulerpa racemosa.* Scientist think that some novel marine algal compounds may contribute to ongoing research for clinically useful antifungal agents.

Considering the resistance to synthetic microbials, the results of the literature show that algae promises antimicrobial natural new sources for human and animal health. In addition, compounds derived from natural algal sources have also the potential to be used for food safety due to their antimicrobial properties against a broad range of foodborne pathogens.

Conclusion

Oceans, which have a rich diversity of marine life, cover more than 70% of the world's surface and offer a rich natural product line to humanity. Functional materials, including polyunsaturated fatty acids (PUFAs), polysaccharides, essential minerals and vitamins, antioxidants, enzymes and bioactive peptides are the first to come to mind [110]. Scientists from around the world have researched multifunctional rich contents of algae and their anti-oxidant, anti-microbial, anti-diabetic, anti-inflammatory, anti- Alzheimer, anti-aging, anti-cancer and other useful properties. For example, Mayer *et al* [46] have done a compilation work on this issue for an interval of two years and the peer-reviewed publications have been reviewed.

In addition, increasing consumers' awareness about potential negative impact of synthetic preservatives on human health and the benefits of natural additives has became a popular research interest.

Sustainable use of marine resources is crucial for humanity. For this reason, production studies of marine algae in different environments and conditions are being tried. For example, two green seaweeds Derbesia tenuissima and Ulva ohnoi were comparatively studied for yields of biomass and bioproducts (fatty acids, soluble fibres and amino acids) under controlled land-based culture by Wielgosz-Collin [111].

Scientists agree that algal biomass offers an innovative contribution to the challenge of providing sustainable bioenergy resources and secondary bioactive potential metabolites. Algae produce many secondary metabolites during growth because of their efforts to adapt to extreme conditions. These bioactive compounds with a great number of biological activities have been considered an important natural source of in different industrial area such as food, cosmetics, medicine, energy.

Despite the fact that a certain path has been taken to obtain natural and renewable algal compounds by sustainable methods it is already seen that great developments will take place in this issue with cooperation of science and technology in near future.

References

1. El Gamal AA. Biological importance of marine algae. Saudi Pharmaceutical Journal. 2010; 18(1):1-25.
2. Huangfu J, Liu J, Sun Z, Wang M, Jiang Y, Chen ZY, *et al*. Antiaging effects of astaxanthin-rich alga Haematococcus pluvialis on fruit flies under oxidative stress. Journal of agricultural and food chemistry. 2013; 61(32):7800-7804.
3. Zhang Q, Li N, Zhou G, Lu X, Xu Z, Li Z. In vivo antioxidant activity of polysaccharide fraction from Por¬phyra haitanesis (Rhodophyta) in aging mice. Pharmacological Research. 2003; 48:151-155.
4. Norzagaray-Valenzuela CD, Valdez-Ortiz A, Shelton LM, Jiménez-Edeza M, Rivera-López J, Valdez-Flores MA, *et al*. Residual biomasses and protein hydrolysates of three green microalgae species exhibit antioxidant and anti-aging activity. Journal of Applied Phycology. 2017; 29(1):189-198.
5. Chen Yong, Xue Yuqin, Hao Yuyang. Anti-aging effects of marine algae and their application on skin care products [OL]. [28 January 2016] http://www.paper.edu.cn/lwzx/en_releasepaper/content/4676919
6. Haijin M, Xiaolu J, Huashi G. A k-carrageenan derived oligosaccharide prepared by enzymatic degra¬dation containing anti-tumor activity. Journal of Applied Phycology. 2003; 15:297-303.
7. Aisa Y, Miyakawa Y, Nakazato T, Shibata H, Saito K, Ikeda Y, *et al*. Fucoidan induces apoptosis of human HS-Sultan cells accompanied by activation of caspase-3 and down-regulation of ERK pathways. American Journal of Hematology. 2005; 78:7-14.
8. You SG, Yang C, Lee HY, Lee BY. Molecular characteristics of partially hydrolyzed fucoidans from sporophyll of Undaria pinnatifida and their *in vitro* an¬ticancer activity. Food Chemistry. 2010; 119:554-559.
9. Gardeva E, Toshkova R, Minkova K, Gigova L. Cancer protective action of polysaccharide derived from microalgaPorphyridiumcruentum—A biological background. Biotechnology & Biotechnological Equipment. 2009; 23:783-787.
10. Lee JM, You SG, Kim SM. Functional activities of low-molecular-weight peptides purified from enzymatic hydrolysates of seaweeds. Journal of the Korean Society of Food Science and Nutrition. 2005; 34:1124-9.
11. Maruyama H, Watanabe K, Yamamoto I. Effect of dietary kelp on lipid peroxidation and glutathione per¬oxidase activity in livers of rats given breast carcinogen DMBA. Nutrition and Cancer. 1991; 15:221-228.
12. Athukorala Y, Lee KW, Kim SK, Jeon YJ. Anticoagulant activity of marine green and brown algae collected from Jeju Island in Korea. Bioresource Technology. 2007; 98:1711-6.
13. Majdoub H, Ben Mansour M, Chaubet F, Roudesli MS, Maaroufi RM. Anticoagulant activity of a sulfated polysaccharide from the green alga Arthrospira platensis. Biochimica et Biophysica Acta. 2009; 1790:1377-81.
14. Wang J, Zhang Q, Zhang Z, Song H, Li P. Potential antioxidant and anticoagulant capacity of low-molecular-weight fucoidan fractions extracted from Laminaria japonica. International Journal of Biological Macromolecules. 2010; 46:6-12.
15. Harnedy PA, FitzGerald RJ. Bioactive proteins, peptides, and amino acids from macroalgae. Journal of Phycology. 2011; 47:218-32.
16. Wijesekara I, Pangestuti R, Kim SK. Biological activities and potential health benefits of sulfated polysaccharides derived from marine algae. Carbohydrate Polymers. 2011; 84:14-21.
17. Zhang J, Tiller C, Shen J, Wang C, Girouard GS, Dennis D, *et al*. Antidiabetic properties of polysaccharide- and polyphenolic-enriched fractions from the brown seaweed Ascophyllum nodosum. Can. J Physiol. Pharmacol. 2007; 85:1116-1123.
18. Lee SH, Kang SM, Ko SC, Lee DH, Jeon YJ. Octaphlorethol A, a novel phenolic compound isolated from a brown alga, Ishige foliacea, increases glucose transporter 4-mediated glucose uptake in skeletal muscle cells. Biochemical and biophysical research communications. 2012; 420(3):576-581.
19. Xu HL, Kitajima C, Ito H, Miyazaki T, Baba M, Okuyama T, *et al*. Antidiabetic effect of polyphenols from brown alga Ecklonia kurome in genetically diabetic KK-Ay mice. Pharmaceutical biology. 2012; 50(3):393-400.
20. Chin YX, Lim PE, Maggs CA, Phang SM, Sharifuddin

Y, Green BD. Anti-diabetic potential of selected Malaysian seaweeds. Journal of applied phycology. 2015; 27(5):2137-2148.
21. Talarico LB, Zibetti RGM, Faria PCS, Scolaro LA, Duarte MER, *et al*. Anti-herpes simplex virus activity of sulfated galactans from the red seaweeds Gymnogongrus griffithsiae and Cryptonemia crenulata. Int. J Biol. Macromol. 2004; 34:63-71.
22. Harden EA, Falshaw R, Carnachan, SM, Kern ER, Prichard MN. Virucidal activity of polysaccharide extracts from four algal species against herpes simplex virus. Antiviral research. 2009; 83(3):282-289.
23. Plouguerne E, de Souza LM, Sassaki GL, Cavalcanti JF, Villela Romanos MT, da Gama BA, Pereira RC, Barreto-Bergter E. Antiviral Sulfoquinovosyldiacylglycerols (SQDGs) from the Brazilian brown seaweed Sargassum vulgare. Marine Drugs. 2013; 11:4628-4640.
24. Hayashi K, Hayashi T, Kojima I. A natural sulfated polysaccharide, calcium spirulan, isolated from Spirulina platensis: *In vitro* and ex vivo evaluation of anti-Herpes simplex virus and anti-human immunodeficiency virus activities. AIDS Research and Human Retroviruses. 1996; 12:1463-71.
25. Rechter S, K¨onig T, Auerochs S, Thulke S, Walter H, D¨ornenburg H, Walter C, Marschall M. Antiviral activity of Arthrospira-derived spirulan-like substances. Antiviral Research. 2006; 72:197-206.
26. Okai Y, Higashi-Okai K, Yano Y, Otani S. Identi¬fication of antimutagenic substances in an extract of edible red alga, Porphyra tenera (Asakusa-nori). Cancer Letters. 1996; 100:235-240.
27. Shin HC, Hwang HJ, Kang KJ, Lee BH. An antioxidative and anti-inflammatory agent for potential treatment of osteoarthritis from Ecklonia cava. Archives of Pharmacal Research. 2006; 29:165-171.
28. Jiménez, Carlos, Belén R. Cossí, and F. Xavier Niell. "Relationship between physicochemical variables and productivity in open ponds for the production of Spirulina: a predictive model of algal yield." Aquaculture 200; 221.1:331-345.
29. Lordan S, Ross RP, Stanton C. Marine bioactives as functional food ingredients: potential to reduce the incidence of chronic diseases. Marine Drugs. 2011; 9:1056-100.
30. De Los RC, Zbakh H, Motilva V, Zubia E. Antioxidant and anti-inflammatory meroterpenoids from the brown alga Cystoseira usneoides. Journal of Natural Products. 2013; 76:621-629.
31. Nagayama K, Iwamura Y, Shibata T, Hirayama I, Na¬kamura T. Bactericidal activity of phlorotannins from the brown alga Ecklonia kurome. Journal of Antimicrobial Chemotherapy. 2002; 50:889-893.
32. Taskin E, Caki Z, Ozturk M, Taskin E. Assessment of *in vitro* antitumoral and antimicrobial activities of marine algae harvested from the eastern Mediterranean sea. African Journal of Biotechnology. 2010; 9:4272-4277.
33. Teasdele, Margaret E, *et al*. Bromophycoic acids: bioactive natural products from a Fijian red alga Callophycus sp. The Journal of organic chemistry. 2012; 77.18:8000-8006.
34. Li L, Gao N, Deng Y, Yao J, Zhang, K. Characterization of intracellular & extracellular algae organic matters (AOM) of Microcystic aeruginosa and formation of AOM-associated disinfection byproducts and odor & taste compounds. Water Research. 2012; 46.4:1233-1240.
35. Dussault D, Vu KD, Vansach T, Horgen FD, Lacroix M. Antimicrobial effects of marine algal extracts and cyanobacterial pure compounds against five foodborne pathogens. Food chemistry. 2016; 199:114-118.
36. Ioannou E, Quesada A, Rahman MM, Gibbons S, Vagias C, Roussis V. Structures and Antibacterial Activities of Minor Dolabellanes from the Brown Alga *Dilophus spiralis*. European Journal of Organic Chemistry. 2012; 5:177-5186.
37. Ghasemi Moradian, A Mohagheghzadeh A, Shokravi S, Morowvat MH, Antifungal, and antibacterial activity of the microalgae collected from paddy fields of Iran: Characterization of antimicrobial activity of Chroococcus dispersus. J Biol. Sci. 2007; 7:904-910.
38. Ördög V, Stirk WA, Lenobel R, Bancír˘ová M, Strnad M, van Staden J, Szigeti J, Németh L. Screening Microalgae for Some Potentially Useful Agricultural and Pharmaceutical Secondary Metabolites. Journal of Applied Phycology. 2004; 16:309-314.
39. Abedin R, Taha H. Antibacterial And Antifungal Activity Ofcyanobacteria and Green Microalgae. Evaluation Of Medium Components by Plackett-Burman Design for Antimicrobial Activity of *Spirulina platensis*. Global Journal Biotechnolgy. Biochemistry. 2008; 3:22-31.
40. Mudimu O, Rybalka N, Bauersachs T, Born J, Friedl T, Schulz R. Biotechnological Screening of Microalgal and Cyanobacterial Strains for Biogas Production and Antibacterial and Antifungal Effects. Metabolites. 2014; 4:373-393.
41. Najdenski HM, Gigova LG, Iliev II, Pilarski PS, Lukavský J, Tsvetkova IV, Ninova MS, Kussovski VK. Antibacterial and Antifungal Activities of Selected Microalgae And Cyanobacteria. International Journal Food Science and Technology. 2013; 48:1533-1540.
42. Bhagavathy S, Sumathi P, Jancy Sherene Bell, I. Green algae Chlorococcum humicola—A new source of bioactive compounds with antimicrobial activity. Asian Pacific. J Trop. Biomed. 2011; 1:S1-S7.
43. Pratt R, Daniels TC, Eiler JJ, Gunnison JB, Kumler WD, Oneto JF, *et al*. Chlorellin, an antibacterial substance from Chlorella. Science. 1944; 99:351-352.
44. Ishii T, Nagamine T, Nguyen BCQ, Tawata S. Insecticidal and Repellent Activit ies of Laurinterol from the Okinawan Red Alga Laurencia nidifica. Records of Natural Products. 2017; 11(1):63.
45. Sugawara T, Baskaran V, Tsuzuki W, Nagao A. Brown algae fucoxanthin is hydrolyzed to fucoxanthinol during absorption by Caco-2 human intestinal cells and mice. The Journal of Nutrition. 2002; 132.5:946-951.
46. Mayer A, Rodríguez AD, Taglialatela-Scafati O, Fusetani N. Marine Pharmacology in 2012–2013: Marine Compounds with Antibacterial, Antidiabetic, Antifungal, Anti-Inflammatory, Antiprotozoal, Antituberculosis, and Antiviral Activities; Affecting the Immune and Nervous Systems, and Other Miscellaneous Mechanisms of Action. Marine Drugs. 2017; 15(9):273.
47. Hoseini SM, Khosravi-Darani K, Mozafari MR. Nutritional and medical applications of spirulina microalgae. Mini Reviews in Medicinal Chemistry. 2013; 13(8):1231-1237.
48. Pal A, Kamthania M, Kumar A. Bioactive Compounds and Properties of Seaweeds—A Review. Open Access Library Journal. 2014; 1:1-17.

49. Lee JC, Hou MF, Huang H W, Chang FR, Yeh CC, Tang JY, *et al*. Marine algal natural products with anti-oxidative, anti-inflammatory, and anti-cancer properties. Cancer Cell International. 2013; 13(1):55.
50. Unnikrishnan SP, Jayasri AM. Marine algae as a prospective source for antidiabetic compounds-A brief review. Current Diabetes Reviews, 2016.
51. Özcan U, Yilmaz E, Özcan L, Furuhashi M, Vaillancourt E, Smith RO, Hotamisligil GS. Chemical chaperones reduce ER stress and restore glucose homeostasis in a mouse model of type 2 diabetes. Science. 2006; 313(5790):1137-1140.
52. Murray M, Dordevic AL, Ryan L, Bonham MP. An Emerging Trend in Functional Foods for the Prevention of Cardiovascular Disease and Diabetes: Marine algal polyphenols. Critical Reviews in Food Science and Nutrition, 2016.
53. Kim YJ, Kim YA, Yokozawa T. Protection against oxidative stress, inflammation, and apoptosis of high-glucose-exposed proximal tubular epithelial cells by astaxanthin. Journal of Agricultural and Food Chemistry. 2009; *57*:8793-8797.
54. Leite MF, Lima AM, Massuyama MM, Otton R. Astaxanthin restores the enzymatic antioxidant profile in salivary gland of alloxan-induced diabetic rats. Archives of Oral Biology. 2010; 55:479-485.
55. Martinon F. Inflammation initiated by stressed organelles. Joint Bone Spine, 2017.
56. Yang YI, Shin HC, Kim SH, Park WY, Lee KT, Choi JH. 6,6′-Bieckol, isolated from marine alga *Ecklonia cava*, suppressed LPS-induced nitric oxide and PGE(2) production and inflammatory cytokine expression in macrophages: The inhibition of NFkappaB. International Immunopharmacology. 2012; 12:510-517.
57. Jung HA, Jin SE, Ahn BR, Lee CM, Choi JS. Anti-inflammatory activity of edible brown alga Eisenia bicyclis and its constituents fucosterol and phlorotannins in LPS-stimulated RAW264. 7 macrophages. Food and Chemical toxicology. 2013; 59:199-206.
58. Okai Y, Higashi-Okai K. Potent anti-inflammatory activity of pheophytin a derived from edible green alga, Enteromorpha prolifera (Sujiao-nori). International Journal of Immunopharmacology. 1997; 19(6):355-358.
59. Awad NE, Biologically active steroid from the green alga *Ulva lactuca*. Phytotherapy Research. 2000; 14:641-643.
60. Brito da Matta CB, De Souza ÉT, De Queiroz AC, De Lira DP, De Araújo MV, Cavalcante-Silva LHA, Alexandre-Moreira MS. Antinociceptive and anti-inflammatory activity from algae of the genus Caulerpa. Marine drugs. 2011: 9(3):307-318.
61. Chae D, Manzoor Z, Kim, SC, Kim S, Oh TH, Yoo ES, Kang HK, Hyun JW, Lee NH, Ko MH. Apo-9′-fucoxanthinone, isolated from *Sargassum muticum*, inhibits CpG-induced inflammatory response by attenuating the mitogen-activated protein kinase pathway. Marine Drugs. 2013; 11:3272-3287.
62. Speranza L, Pesce M, Patruno A, Franceschelli S, de Lutiis MA, Grilli A, *et al*. Astaxanthin treatment reduced oxidative induced pro-inflammatory cytokines secretion in U937: SHP-1 as a novel biological target. Marine Drugs. 2012; 10:890-899.
63. Ananthi S, Raghavendran HRB, Sunil AG, Gayathri V, Ramakrishnan G, Vasanthi HR. *In vitro* antioxidant and in vivo anti-inflammatory potential of crude polysaccharide from Turbinaria ornata (Marine Brown Alga). Food and Chemical Toxicology. 2010; 48(1):187-192.
64. Foo SC, Yusoff FM, Ismail M, Basri M, Yau SK, Khong NM, Ebrahimi M. Antioxidant capacities of fucoxanthin-producing algae as influenced by their carotenoid and phenolic contents. Journal of Biotechnology. 2017; 241:175-183.
65. Farasat M, Khavari-Nejad R, Nabavi BMS, Namjooyan F. Antioxidant properties of some filamentous green algae (*Chaetomorpha* Genus) Brazilian Archives of Biology and Technology. 2013; 56(6):1678-4324.
66. Marudhupandi T, Kumar TA, Senthil SL, Devi KN. *In vitro* antioxidant properties of fucoidan fractions from Sargassum tenerrimum. Pakistan Journal of Biological Sciences. 2014; 17(3):402.
67. Nursid M, Marasskuranto E, Atmojo KB, Hartono MP, Meinita MDN, Riyanti R. Investigation on Antioxidant Compounds from Marine Algae Extracts Collected from Binuangeun Coast, Banten, Indonesia. Squalen Bulletin of Marine and Fisheries Postharvest and Biotechnology. 2017; 11(2):59-67.
68. Naguib YM. Antioxidant activities of Astaxanthin and Related Carotenoids. Journal of Agricultural and Food Chemistry. 2000; 48:1150-1154.
69. Nakajima Y, Inokuchi Y, Shimazawa M, Otsubo K, Ishibashi T, Hara H. Astaxanthin, a dietary carotenoid, protects retinal cells against oxidative stress *in vitro* and in mice in vivo. Journal of Pharmacy and Pharmacology. 2008; 60:1365-1374.
70. Olasehinde TA, Olaniran AO, Okoh AI. Therapeutic Potentials of Microalgae in the Treatment of Alzheimer's Disease. Molecules. 2017; 22(3):480.
71. Hielscher-Michael S, Griehl C, Buchholz M, Demuth HU, Arnold, N, Wessjohann LA. Natural Products from microalgae with potential against Alzheimer's Disease: Sulfolipids are potent glutaminyl cyclase inhibitors. Marine drugs. 2016; 14(11):203.
72. Çakir Ş. Genetics and Some Aging-Related Mechanisms. Turkish Journal of Zoology. 2000; 24(2):183-190.
73. Sarıkaya R, Çakır Ş, Solak K. The Effects of Food Preservatives on The Longevity of *Drosophila Melanogaster* (MWHXFLR). Kastamonu Eğitim Dergisi. 2006; 14(1):173-184.
74. Li X, Gutierrez DV, Hanson MG, Han J, Mark MD, Chiel H, Herlitze S. Fast noninvasive activation and inhibition of neural and network activity by vertebrate rhodopsin and green algae channelrhodopsin. Proceedings of the National Academy of Sciences of the United States of America. 2005; 102(49):17816-17821.
75. Goiris K, Muylaert K, Fraeye I, Foubert I, De Brabanter J, De Cooman L. Antioxidant potential of microalgae in relation to their phenolic and carotenoid content. Journal of Applied Phycology. 2012; 24(6):1477-1486.
76. Plaza M, Santoyo S, Jaime L, Reina GGB, HerreroM, Señoráns FJ, Ibáñez, E. Screening for bioactive compounds from algae. Journal of pharmaceutical and biomedical analysis. 2010; 51(2):450-455.
77. Goiris K, Muylaert K, Fraeye I, Foubert I, De Brabanter J, De Cooman L. Antioxidant potential of microalgae in relation to their phenolic and carotenoid content. Journal of Applied Phycology. 2012; 24(6):1477-1486.

78. Goiris K, Van Colen W, Wilches I, León-Tamariz F, De Cooman L, Muylaert K. Impact of nutrient stress on antioxidant production in three species of microalgae. Algal Research. 2015; 7:51-57.78.
79. German-Báez LJ, Valdez-Flores MA, Félix-Medina JV, Norzagaray-Valenzuela CD, Santos-Ballardo DU, Reyes-Moreno C, *et al*. Chemical Composition and Physicochemical Properties of Phaeodactylum Tricornutum Microalgal Residual Biomass. Food Science and Technology International, 2017.
80. Wang HMD, Chen CC, Huynh P, Chang JS. Exploring the potential of using algae in cosmetics. Bioresource technology. 2015; 184:355-362.
81. Thomas NV, Kim SK. Beneficial effects of marine algal compounds in cosmeceuticals. Marine drugs. 2013, 11(1):146-164.
82. Vo TS, Ngo DH, Kim SK. Marine algae as a potential pharmaceutical source for anti-allergic therapeutics. Process Biochemistry. 2012; 47:386-394.
83. Ariede MB, Candido TM, Jacome ALM, Velasco MVR, de Carvalho JCM, Baby AR. Cosmetic attributes of algae-A review. Algal Research. 2017; 25:483-487.
84. Kim EJ, Lee JY, Park JHY, Park SY. Fucoidan present in brown algae induces apoptosis of human colon cancer cells. BMC Gastroenterology. 2010; 10(1):96.
85. Huang HL, Wu SL, Liao HF, Jiang CM, Huang RL, Chen YY, *et al*. Induction of apoptosis by three marine algae through generation of reactive oxygen species in human leukemic cell lines. Journal of Agricultural and Food Chemistry. 2005; 53(5):1776-1781.
86. Drum Ryan. Sea vegetables for food and medicine. Well being Jornal, 2013. http://www.eidon.com/SeaweedArticle.pdf 2003.
87. Palanisamy S, Vinosha M, Marudhupandi T, Rajasekar P, Prabhu NM. Isolation of fucoidan from Sargassum polycystum brown algae: Structural characterization, *in vitro* antioxidant and anticancer activity. International Journal of Biological Macromolecules. 2017; 102:405-412.
88. Kwon MJ, Nam TJ. A polysaccharide of the marine alga Capsosiphon fulvescens induces apoptosis in AGS gastric cancer cells via an IGF-IR-mediated PI3K/Akt pathway. Cell Biology İnternational. 2007; 31(8):768-775.
89. Atashrazm F, Lowenthal R M, Woods GM, Holloway AF, Dickinson JL. Fucoidan and Cancer: A Multifunctional Molecule With Anti-Tumor Potential. Marine drugs. 2015; 13(4):2327-2346.
90. Kwak JH, Baek SH, Woo Y, Han JK, Kim BG, Kim OY, *et al*. Beneficial immunostimulatory effect of short-term Chlorella supplementation: enhancement of Natural Killer cell activity and early inflammatory response (Randomized, double-blinded, placebo-controlled trial). Nutrition journal. 2012; 11(1):53.
91. Kimura R, Rokkaku T, Takeda S, Senba M, Mori N. Cytotoxic effects of fucoidan nanoparticles against osteosarcoma. Marine Drugs. 2013; 11(11):4267-4278.
92. Atashrazm F, Lowenthal RM, Dickinson JL, Holloway AF, Woods GM. Fucoidan enhances the therapeutic potential of arsenic trioxide and all-trans retinoic acid in acute promyelocytic leukemia, *in vitro* and in vivo. Oncotarget. 2016a; 7(29):46028.
93. Usoltseva RV, Anastyuk SD, Shevchenko NM, Surits VV, Silchenko AS, Isakov VV. Ermakova SP. Polysaccharides from brown algae Sargassum duplicatum: the structure and anticancer activity *in vitro*. Carbohydrate Polymers. 2017; 175:547-556.
94. Gonzalez-Ballesteros N, Prado-López S, Rodriguez-Gonzalez JB, Lastra M, Rodríguez-Argüelles MC. Green synthesis of gold nanoparticles using brown algae Cystoseira baccata: Its activity in colon cancer cells. Colloids and Surfaces B. Biointerfaces. 2017; 153:190-198.
95. Isnansetyo A, Lutfia FNL, Nursid M, Susidarti RA. Cytotoxicity of Fucoidan from Three Tropical Brown Algae Against Breast and Colon Cancer Cell Lines. Pharmacognosy Journal. 2017; 9(1).
96. Shannon E, Abu-Ghannam N. Antibacterial derivatives of marine algae: An overview of pharmacological mechanisms and applications. Marine Drugs. 2016; 14(4):81.
97. Falaise C, François C, Travers MA, Morga B, Haure J, Tremblay R, Leignel V. Antimicrobial Compounds from Eukaryotic Microalgae against Human Pathogens and Diseases in Aquaculture. Marine drugs. 2016; 14(9):159.
98. Plaza A, Keffer JL, Bifulco G, Lloyd JR, Bewley CA. Chrysophaentins A− H, antibacterial bisdiarylbutene macrocycles that inhibit the bacterial cell division protein FtsZ. Journal of the American Chemical Society. 2010; 132(26):9069-9077.
99. Gyawali R, Ibrahim SA. Natural products as antimicrobial agents. Food control. 2014; 46:412-429.
100. Bourgougnon N. Anti-HIV compounds from red seaweeds. Biomaterials and bioprocessing, Vol. 9. Recent advances in marine biotechnology. Science Publishers, Enfield. 2003; 165-206.
101. Park SH, Song JH, Kim T, Shin WS, Park GM, Lee S, Kwon DH. Anti-human rhinoviral activity of polybromocatechol compounds isolated from the Rhodophyta, Neorhodomela aculeata. Marine drugs. 2012; 10(10):2222-2233.
102. Plouguerné E, Ioannou E, Georgantea P, Vagias C, Roussis V, Hellio C, *et al*. Anti-microfouling activity of lipidic metabolites from the invasive brown alga Sargassum muticum (Yendo) Fensholt. Marine Biotechnology. 2010; 12(1):52-61.
103. Adhikari U, Mateu CG, Chattopadhyay K, Pujol CA, Damonte EB, Ray B. Structure and antiviral activity of sulfated fucans from *Stoechospermum marginatum*. Phytochemistry. 2006; 67:2474-2482.
104. Saha S, Navid MH, Bandyopadhyay SS, Schnitzler P, Ray B. Sulfated polysaccharides from *Laminaria angustata*: Structural features and *in vitro* antiviral activities. Carbohydrate Polymers. 2012; 87:123-130.
105. De Souza LM, Sassaki GL, Romanos MT, Barreto-Bergter E. Structural characterization and anti-HSV-1 and HSV-2 activity of glycolipids from the marine algae *Osmundaria obtusiloba* isolated from Southeastern Brazilian coast. Mar. Drugs. 2012, 10:918-931.
106. Bandyopadhyay SS, Navid MH, GhoshT, Schnitzler P, Ray B. Structural features and *in vitro* antiviral activities of sulfated polysaccharides from *Sphacelaria indica*. Phytochemistry. 2011; 72:276-283.
107. Cardozo FT, Camelini CM, Mascarello A, Rossi MJ, Nunes RJ, Barardi CR, de Mendonça MM, Simões CM. Antiherpetic activity of a sulfated polysaccharide from *Agaricus brasiliensis* mycelia. Antiviral Research. 2011; 92:108-114.

108. Kaaria PK, Matiru VN, Wakibia JG, Ndung'u M W, Bii CC. Evaluation of antibacterial and antifungal activity of macro algae associated microbes from the Northern and Southern coast of Kenya. Journal of Microbiology and Biotechnology Research. 2017; 5(5):7-13.
109. Liu AH, Liu DQ, Liang TJ, Yu XQ, Feng MT, Yao LG, *et al*. Caulerprenylols A and B, two rare antifungal prenylated para-xylenes from the green alga Caulerpa racemosa. Bioorganic & Medicinal Chemistry Letters. 2013; 23(9):2491-2494.
110. Kim SK, Wijesekara I. Development and Biological Activities of Marine-Derived Bioactive Peptides: A review. Journal of Functional Foods. 2010; 2(1):1-9.
111. Wielgosz-Collin, G, Kendel M, Couzinet-Mossion A. Lipids, Fatty Acids, Glycolipids, and Phospholipids. In Seaweed in Health and Disease Prevention. 2016, 185-221.