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Review Article

Therapeutic potential of seaweeds

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ABSTRACT

Seaweeds in general are known to contribute to the maintenance of health through their nutritional and medicinal properties and are served in soups and salads, cooked with grains, legumes or miso-soup broth, vegetable pies, stews and even consumed dried. The medicinal properties of seaweeds or vegetables have long been known in many cultures of people particularly those living in the coastal regions who are consuming these from centuries. Traditional Chinese dietotherapy (TCD) makes good use of natural marine nutrients and food to preserve health. Koreans wrap their bodies in seaweeds to get rid of deadly body toxins and Japanese who eat large quantities of seaweeds have very low incidence of cancers. The compounds with diverse biological activities such as antioxidant, antiviral, antifungal, antineoplastic, antimicrobial etc. have been isolated from the flora in the sea. A score of these bio-medicinal compounds are in different stages of clinical trials & analysis and are the focus of this article.

Keywords: Seaweeds or vegetables, Marine natural products, Marine pharmacology, Marine therapeutics

INTRODUCTION

The seaweeds or vegetables grow both on the rocks washed by the sea, on the sea floor in the inter-tidal zone and shallow sea water or at the narrow interface where the sea and land meets. Seaweeds belong to a group of plants known as algae which are classified as Rhodophyta (red algae), Phaeophyta (brown algae), or Chlorophyta (green algae) depending upon their nutrients and chemicals composition.

The seaweeds are rich in vitamins and minerals, dietary iodine, food pigments as anti-oxidants, phycocolloids-the long chain carbohydrates, proteins and even fats good for health. The edible sea weeds or sea vegetables such as nori and dulse (both red algae), sea palm and hijiki (brown algae), the large kelps (brown algae, mostly Laminaria species) and edible green algae sea lettuce (Ulva lactuca and Monostroma species), to name a few, are nowadays used as a regular part of the diet worldwide particularly in East Asian countries such as Japan, Korea and China. Some seaweeds are microscopic such as phytoplankton and diatoms, others are enormous like giant kelp but most are medium sized and come in the colors of green, red, brown and black.[1,2]

Seaweeds are considered as a source of bioactive compounds which are produced as a great variety of secondary metabolites characterized by a variety of broad spectrum of biological activities. Consequently, these have been used traditionally for the treatment of cough, asthma, hemorrhoid, boils, goiters, stomach ailments, ulcers, headaches, urinary diseases and in various cancers.

PHARMACOLOGICAL EFFECTS FOR BIO-ACTIVE COMPOUNDS FOUND IN SEAWEEDS

Seaweeds contain many polysaccharides such as alginic acid, laminarin, fucoxantin, fucoidan etc. which have tremendous biomedical potentials.[3] The Fucoidan is a

sulfated fucose (polysacchride) and is found in various species of brown sea weeds such as kombu (*Laminaria japonica*), limumoui, bladder wrack (*Fucus vesiculosus*), wakame, mozuku and hijiki. Fucoidan has been shown to induce apoptosis in lymphoma cell lines and also inhibit hyperplasia in rabbits.[4] Several brown algae including bladderwrack (*Fucus vesiculosus*) appear to suppress the growth of various cancer cells *in vitro* studies.[5-7] The intake of *Fucus vesiculosus* has shown to help women with abnormal menstrual cycling patterns and/or menstrual related disorders.[8-10]

Nori, a species of red algae genus Porphyra which includes most notably *Porphyra yezoensis* and *Porphyra tenera* is a rich source of vitamins A, B and C, iodine, protein, carotene and easily digestible dietary fibers. The vitamin C content in nori is even more than the raw oranges. A 14 kDa protein-PYP (Pyropia yezoensis protein) isolated from *Porphyra yezoensis* has recently been demonstrated to have a chemo-preventive effect against the acetaminophen induced liver injury in rats.[11]

Nori contains a sulfated polysaccharide called porphyran which is a complex galactone and is known to inhibit the growth of certain tumors as it prevents a purposely induced carcinogenesis. Nori, is also used to treat lower respiratory tract diseases. Another red marine alga, Dumontia is dried, powdered, encapsulated and used as a genital herpes suppressant.

An edible red alga, *Palmaria palmata* which grows widely along the shorelines of North Atlantic is high in vitamins especially B, lot of fibers and proteins. Extracts from *Palmaria palmata* are known antioxidants and have anti-proliferative effects on HeLa cell proliferation *in vitro*.[12]

The accumulation of kainoids, the unusual excitatory amino acids from diatoms, in high concentration in shell fish are well known to cause Amnesic shellfish poisoning (ASP) when consumed by humans.[13]

The marine brown algae bull kelp (*Nereocystis luetkeana*) consumed in powdered form is effective in insomnia, hyperactivity, depression and schizophrenia. The brown algae Bladder Wrack (*Fucus vesiculosus*) is said to normalise enlarged prostrate in early stages. Its consumption also tends to lower blood pressure by inhibiting angiotensin converting enzyme (ACE), removes arterial plaque, possess antibacterial and anti-oxidative properties due to the high polyphenolic content. The regular consumption of brown algae hijiki (*Cystceria geminata*) and sargassum (*Sargassum muticum*) has been shown to improve overall lung functions.[14]

A study has shown that a microbicide, carragaurd or PC-515(a gel formulation) for vaginal use, made from a seaweed extract called carrageenan is known to provide protection from human paplioma virus (HPV) in addition to its protection against HIV infection.[15] The phase III clinical trials of testing carrageenan's efficiency against HIV infection are already underway. The carrageenans namely λ-carrageenan (2), possess potent antiviral activities against several strains of herpes simplex virus (HSV) types 1 and 2 genital infection.[16,17]

Carrageenan because of its microbiocidal properties is also used in the form of wound dressings for successful wound healing. Carrageenan, is a water-soluble mixture of sulfated polysaccharides extracted from a red algae *Chondrus crispus* (common name Irish moss or Carregeen moss) and other species such as Gigartina, Eucheuma, Furcellaria and Phyllophora. The studies are in progress on the use of Kappa-carrageenan as a potential biomaterial for skeletal regeneration.

A phycocolloid gel out of *Chondrus crispus* is effective in long term treatment of damage to lungs particularly after pneumonia, smoking and chronic bronchitis. According to ancient Irish folklore, it was carried on trips for protection and safety and was used widely in the treatment of tuberculosis and pneumonia.[18]

A polysaccharide having antiviral effect has been extracted from green alga *Ulva lactuca* and is known to provide nutrition to aging and environmentally damaged skin.[19]

A compound fucoxanthin (a subset of carotenoids) from the edible brown seaweed *Undaria pinnatifida*, has been shown to burn fatty tissue. It induces the expression of fat burning protein UCP1 (a member of uncoupling protein family in mitochondria) that accumulates in fat tissue around the internal organs.[20]

The capsules of *Undaria pinnatifida*, promote healing and inhibit the infection when given to patients suffering from viral infections such as herpes zoster (chicken pox) and Epstein - Barr virus (EBV). A major sulfated poly-anion characterized as galactofucan sulfate extract (GFS) from Tasmanian *Undaria pinnatifida* is shown to have immune stimulating qualities in vitro and is associated with healing and inhibition of reactivation of herpes.[21-24]

Most of the sea weeds or plants widely have sulpur containing but phosphorus free lipid namely sulfoquinovosyl diacylglycerol (SQDG) which is generally found in many photosynthetic organisms. One of the fatty acids component namely eicosapentaenoic acid of SQDG is a potent telomerase inhibitor and consequently a potent candidate for the therapeutic importance in cancer therapy.[25]

The hydrolysates of *Undaria pinnatifida* derived after treatment with proteases have shown anti-hypertensive effect via inhibiting angiotensin -1 converting enzyme (ACE) activity.[26-29]

A red alga, an agarophyte *Gracilaria tenuistipitata*, found in Caribbean islands is known to be a potent virility tonic helpful in erectile dysfunction (ED) in males and is

consumed as a "Seaweed drink" or "Sea moss tea" in the Caribbean. Gracilaria is a gem of red algae (Rhodophyta). Its species are also notable for its economic importance as an agarophyte and are commonly used for the treatment of gastrointestinal disorders. Notable genera of commercially valuable agarophytes are Gracilaria, and Gelidium.[30]

The list of medicinal compounds from seaweeds is endless and many more sea weed species are on the bench top of biomedical researchers to look out for novel compounds having therapeutic value. A few of bioactive compounds with their structures (Figure A, B) and corresponding therapeutic activities are discussed in successive section.[31-3]

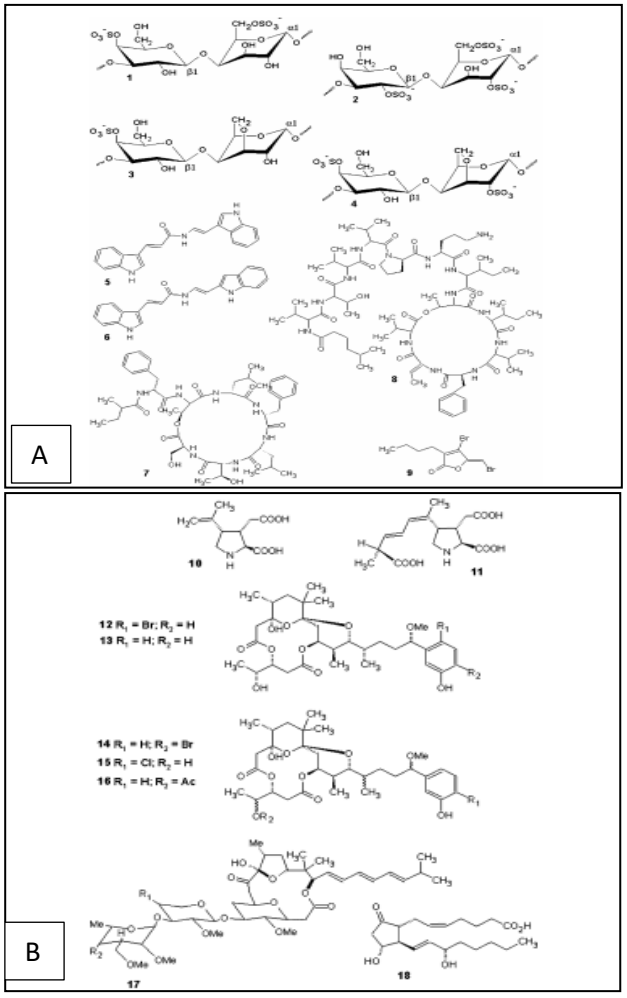

Figure 1: (A and B) The chemical structures of µ-carrageenan (1); λ-carrageenan (2); κ-carrageenan (3); ´ı-carrageenan (4); chondriamide A (5); chondriamide C (6); kahalalide A (7); kahalalide F (8); (5Z)-4-bromo-5-(bromomethylene)-3-butyl-2(5H)-furanone (9); α-kainic (10); domoic acid (11); aplysiatoxin (12); debromoaplysiatoxin (13); manauealide A (14); manauealide B (15); manauealide C (16); polycavernoside A (17) and prostaglandin E2 (18).

Structure-activity relationship of bio-active compounds[31-33]

Some carrageenans such as µ-carrageenan (1), λ-carrageenan (2), κ-carrageenan (3) and ´ı-carrageenan (4) have potent antiviral activities against several strains of HSV types 1 and 2.

Chondriamide A (5) from *Chondria atropurpurea* shows antiviral activity against HSV type II and cytotoxicity against human nasopharyngeal and colorectal cancer cells. Chondriamide C (6), also from *Chondria atropurpurea*, displays cytotoxic and in vitro anthelmintic properties.

Cyclic depsipeptides kahalalide A (7) and F (8) are produced by a species of Bryopsis. Both show in vitro activity against *Mycobacterium tuberculosis*. Kahalalide F has anti-HIV qualities which are being further studied in clinical trials and its effectiveness as treatment of lung cancers and tumours are also being studied.

(5Z)-4-bromo-5-(bromomethylene)-3-butyl- 2(5H)-furanone (9) is a halogenated compound from *Delisea pulchra* which displays strong antifouling properties.

α-Kainic (10) and domoic acids (11) are pyrrolidine dicarboxylates with excitatory and excitotoxic activities. Kainoids occur in some pennate diatoms where they cause amnesic shellfish poisoning, but they are also produced by some members of the Ceramiales. They are used as tools in research into neurophysiological disorders such as Alzheimer's and Parkinson's disease, and epilepsy. Domoic acid-containing extracts of *Digenea simplex* and *Chondria armata* have been used by the Japanese as anthelmintic agent, and it also has insecticidal properties.

Aplysiatoxin (12) and debromoaplysiatoxin (13) are potent tumour promoters used in medical research, and are responsible for non-fatal poisonings associated with eating *Gracilaria coronopifolia*.

Manauealide A (14), manauealide B (15) and manauealide C (16) compounds corresponding to debromoaplysiatoxin extracted from a red alga *Gracilaria coronopifolia* were shown to induce diarrhea in mice and were considered to be the causative toxins of food poisoning in Hawaii.

Polycavernosides (17) isolated from the red alga *Polycavernosa tsudae* are complex glycosidic toxins belonging to a class of macrocyclic lactones and are the causative agents for the fatal human poisonings following consumption of *Polycavernosa tsudae*.

Prostaglandin E2 (18) is a product of PUFA metabolism in some species of *Gracilaria* and is the causative agent responsible for the fatal 'ogonori' poisoning resulting from their consumption.

Summary of biological activities of bio compounds from seaweeds[34-35]

- Antioxidant activity (Fucoxanthin, phycoerythrobilin, chlorophyll-a and derivatives)
- Antiviral activity (Sulfated glucuronogalactan, sulphated galactans, sulphated fucans, carrageenan)
- Cardiovascular protection (Carotenoids, sterols, cardiac glycosides, eicosapentaenoic acid, docosa-hexaenoic acid)
- Cytotoxicity, antimitogenic, anticancer and antitumour properties (Fucoidans, glucans, phloroglucinol, stypoldione, sesquiterpene elatol, carotene, lutien)
- Antithrombic and anticoagulant activities (Galactans/Carrageenan, fucoidans, heparins, phlorotannins, phloroglucinol)
- Toxins-vermifuges, insecticides, ichthyotoxins, neurotoxins
- Anti-inflammatory activity and effects on the immune response (Marine terpenes, bioactive peptides, sulfated polysaccharides, fucoidan, ascophyllan, algal polyphenols, phlorotannins, terpenes and steroids, alkaloids, commercially produced microalgal PUFAs)
- Agglutination, coagulation and the stimulation of cell migration
- Mitogenic activity.

CONCLUSION

Seaweeds which are consumed worldwide are now under consideration for medicinal value and future therapies besides their use in commercial goods. Many of the biomolecules extracted from the seaweeds are potent drug candidates and are in pre-clinical or early clinical development stages. The sulphated polysaccharides as antiviral substances, halogenated furanones from *Delisea pulchra* as antifouling compounds, and *kahalalide F* from a species of bryopsis as a possible treatment for lung cancer, tumors and AIDS are gaining attention from pharmaceutical companies. The indiscriminate collection or harvesting of the marine flora however, may unbalance the marine ecosystems. The sustainable management of seaweeds to conserve them for posterity is of utmost importance considering their ecological and medicinal value. It is high time to identify the genes that produce the desired bioactive compounds in the sea weeds and to transfer those genes to the microorganisms such as *Escherichia coli* that are easy to culture in the lab for medical pursuits.

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