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Marine macroalgae: Biodiversity of Gulf of Mannar

Juhi Kataria[1&2], Louis Cojandaraj A[2], Gurpreet Kaur Gill[1],

[1] Department of Medical Lab Sciences, Khalsa College of Pharmacy & Technology Amritsar, Punjab India

[2]Department of Medical Lab Sciences, Lovely Professional University Phagwara Punjab India

Abstract:

Seaweeds have been extensively researched for more than seven decades by many researchers. Seaweeds have a high concentration of essential vitamins, trace elements, polysaccharides, enzymes, and variety of bioactive compounds. Each compound has properties such as antioxidant, antimicrobial, antiviral activities that can be exploited to enhance human health. The rationale of this review is to comprehend recent uses of algae in drug development, with the scope of replacing synthetic compounds and develop therapeutics for deadly diseases such as cancer, neurodegenerative disorders. Further research is needed to understand the mode of action of seaweed's compounds and to implement its potential in pharmaceutical companies and other applications with the final scope to produce sustainable and healthier products.

Keywords: Seaweeds, *Turbinaria decurrens*, Algae, anti-cancer, phlorotannin, phytosterol

Introduction:

Marine algae or 'Seaweed' has found its utilization widely through-out the world and is one of the main sources of income among people who live on the coast with high algae potential. Demand for algae is proportional to its usage as in industries, food, textiles, paper paint, cosmetics, and medicine (Atmaja, 1996). Seaweeds are the macroscopic algae that are found attached to the solid bottom substrates of the rock, pebbles, plant materials and shells. They are found at the depth of 180 meters in shallow waters, estuaries, intertidal and sea water. Seaweeds constitute of brown, green and red macroalgal, which are the great reservoir of natural anti-diabetic agents owing to the presence of polyphenols, vitamins, carotenoids, unsaturated fatty acids, pigments including phycoerythrin, phycobilins with barely any side effects (Satpati *et al.,* 2021).

Seaweed Diversity of India

India is one of the 12 mega-biodiversity nations in the world with coastline of 8100 km long and has an Exclusive Economic Zone (EEZ) of 2.17 million km^2 (equal to 66% of total mainland area). Approximately 30% of its human population is dependent on the rich exploitable coastal and marine resources (Ganesan *et al.*, 2019). The

Indian coastline having different coastal ecosystems that supports abundant growth of diverse seaweed populations with substantial economic significance. The CSMCRI team explored the seaweed diversity of the Gujarat and Tamil Nadu coasts known for their plenty of seaweeds. These two states are known as the home of 366 seaweed species that account for nearly half of India's total seaweed diversity (Jha *et al.*, 2009).

Tamil Nadu

Tamil Nadu has a diverse habitat and enriched with an abundant biodiversity from marine coastal systems inside the Gulf of Mannar to the Western Ghats. The location of Tamil Nadu is between 76° 14' and 80° 21 East longitudes and 8° 05' and 13° 34' North latitudes (Venkataraman and Wafer, 2005) and has a geographical area of 1,30,058 km^2, which entirely accounts for about 4% area of the total country (Zeitzchel, 1973).

The world's richest region of marine bio-diversity is Gulf of Mannar lying in the Indian coast between Rameswaram to Kanyakumari. The Gulf has 4,223 species of flora and animals representing from primary to higher forms. Due to the ecological and biological richness of the Gulf of Mannar, it has been declared as the first marine National Park of the country which includes 21 un-inhabited islands and their shallow waters around and the coastal regions of Ramanathapuram and Thoothukudi districts (Diaz and Rosenberg, 2008). The Gulf of Mannar Biosphere (GOMBR) covers an area of about 560 km^2 and extends up to 10,500 km^2 which includes the 21 islands of the national park. Reference required

The Gulf of Mannar exhibits different ecosystems like beach, island, Coral reefs, mudflats, mangrove and shallow waters and is abundant with sea grasses. There are about 147 species of seaweeds and all the 11 species of sea grass and all the mangrove species available in India. The country represents only smallest percentage of the globe's land but it comprises 7%–8% of total known plant and animal taxa globally. The greatest numbers of seaweeds are found in India in contrast to all other countries surrounding the Indian Ocean. Conservation efforts are crucial to protect the unique and fragile ecosystem of the Gulf of Mannar.

Gujarat:

The coast of Gujarat which is more than 1600 km long, is located in northwest India. This coastline has varied topography, geomorphology and has been widely segmented into five regions viz. the Rann of Kachchh, the Saurashtra coast, Gulf of Kachchh, Gulf of Khambhat and the South Gujarat coast. Among these regions, the Gulf of Kachchh which extends over 1000 km contains 42 islands, rocky intertidal regions and mangrove forests supporting rich seaweed diversity. The Gulf of Khambhat has several major rivers flowing into the sea, and this intertidal region comprises of mud and sand flats with meagre seaweed diversity. The survey revealed that there are 198 species seaweed in intertidal region of Gujarat coast entailing: Rhodophyta 109 species from 62 genera; Chlorophyta 54 species from 23 genera; Phaeophyceae 35 species from 16 genera. Gulf of Kachchh is the richest source of Seaweed totalling 130 species from Dani, Dhabdhaba, Kalubhar, Manmarodi, and Narara Islands. Species collected ranged from 93 species from Kalubhar Island to a minimum number of 14 species collected from Narara Island (*Jha et al.*, 2009).

Seaweeds- Classification and their Role

Seaweeds have recently gained significant importance due to their widespread distribution, ability to regenerate, and variety of uses. Seaweeds are renewable marine resources that can be consumed as nutritional supplements, as they contain vitamins, carbohydrates, proteins and minerals like sodium, calcium, magnesium, potassium, chlorine, sulphur, phosphorus and micronutrients such as iodine, iron, zinc, copper, selenium, molybdenum, fluoride, manganese, boron, nickel and cobalt are plenty in different species of seaweed. The calcium and protein content varies from species to species, where, green and red seaweed are high in protein content (up to 30%) and brown seaweed has lower protein content up to 15% (Paul *et al.*, 2007; Tagliapreta and Pedrosa, 2023; Sultana *et al.*, 2023).

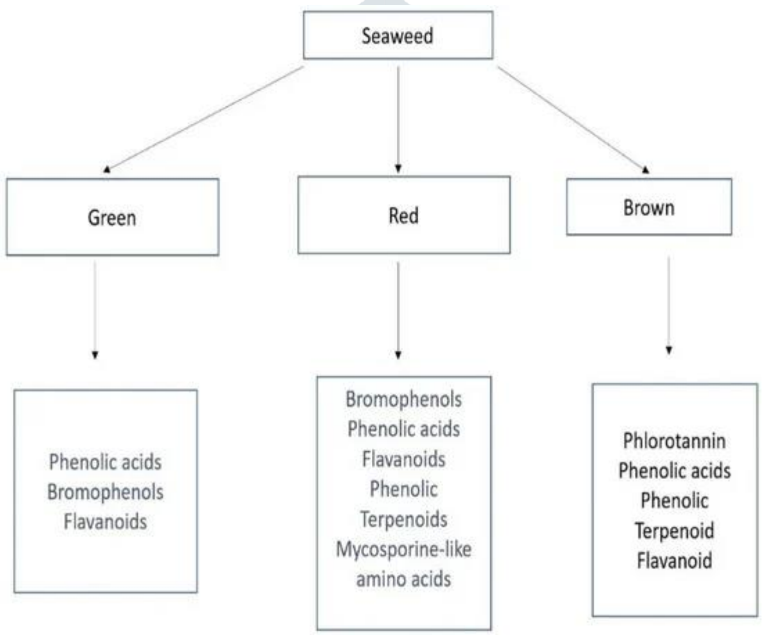

Figure 1: Classification of Seawed

Seaweeds, belongs to three taxonomic groups due to different pigment composition: green algae (Chlorophyta), red algae (Rhodophyta), and brown algae (Ochrophyta) (Figure 1). Green algae are primarily characterized by their green coloration due to the dominance of chlorophyll a and chlorophyll b pigments. Microscopic unicellular forms to large multicellular range of green algae can be seen in the environment. They are mostly found in fresh water and marine habitats. Red algae have red pigments and appear in shades of red, pink and purple (Delwiche *et al.*, 2011). They are usually multicellular and can grow at various depths, including deep sea regions. Brown algae get their pigments from fucoxanthin. They are found primarily in marine and include some of the largest seaweeds. They are eco-friendly for providing food sources for marine life (Din *et al.*, 2022). Brown algae indeed encompass a wide variety of species, and they have been recognized for their rich nutritional content and potential therapeutic properties (Li *et al.*, 2021).

Polysaccharides, which are complex carbohydrates, are particularly abundant in brown algae and contribute to their unique characteristics. The diverse structures of polysaccharides found in brown algae contribute to their range of physical and chemical properties. These properties enable them to interact with biological systems in ways that can have positive impacts on human health. Polysaccharides from brown algae may influence the immune system's response, potentially enhancing its ability to defend against infections and diseases. Some polysaccharides have demonstrated antibacterial properties, which could be valuable in preventing and treating bacterial infections. Brown algae polysaccharides can act as antioxidants, helping to neutralize harmful free radicals in the body and potentially reducing the risk of oxidative stress-related diseases (Ismail *et al.,* 2022; Ismail *et al.,* 2023). Some polysaccharides may serve as prebiotics, promoting the growth and activity of beneficial gut bacteria and contributing to gut health. Certain compounds in brown algae may have antihypertensive effects, which could be beneficial for individuals with high blood pressure (Lopez *et al.*, 2020). They might also play a role in managing blood sugar levels and reducing the risk of diabetes.

One of commonly found brown algae species in marine water is *Turbinaria decurrens* (Phaeophyta). It is a genus of brown algae that is found primarily in tropical marine waters and grows on rocky substrates (Blomquist, 1945). It is distributed in tropical coral reefs and also found in the subtropics and temperate regions. Southeast Asia as well as the Indian Ocean contains the highest diversity of the genus. This genus can survive in different habitats such as tide pools, rocky intertidal zones, and forereefs, up to depths of 30 meters and in habitats with varying levels of exposure (Zubia *et al.*, 2020). *Turbinaria* contains fucoxanthin a type of carotenoid pigment found in all brown algae. Its functions lie in the harvesting of light and energy transfer. The genus has high levels of iron and has an affinity for arsenic and nickel, depending on the concentrations in the environments in which they grow (Zubia *et al.*, 2020). According to the studies, *Turbinaria decurrens* has the ability to capture free radicals, act as natural antioxidant and has anti-cancer properties (Myerscough, 2003; Nursid *et al.,* 2007; Fajarningsih *et al.,* 2008).The Genus *Turbinaria* is still unexplored both chemically and pharmacologically. Therapeutic potentials of the compounds isolated from the Genus *Turbinaria* has antiproliferative, antipyretic, anti-inflammatory, immunostimulatory, anti-diabetic, anti-obesity, antiviral, antimicrobial, cardioprotective, hepatoprotective and hypolipidemic properties (Rushidi *et al.,* 2021). There are 32 species of *Turbinaria* on algae base: *Turbinaria capensis*, *Turbinaria conoides*, *Turbinaria conoides f. retroflexa*, *Turbinaria costata*, *Turbinaria crateriformis*, *Turbinaria decurrens*, *Turbinaria denudata*, *Turbinaria elatensis*, *Turbinaria filamentosa* and many more (Guiry, 2014).

Compounds of different seaweeds:

Turbinaria contain Sulfated polysaccharide known as fucoidan that includes various monosugars such glucuronic acid, xylose, and galactose in addition to fucose, which basically serves as the main fundamental sugar. Its potential health benefits on cancer have drawn the attention of scientists working in the field of medicine. Brown algae also contains carotenoid fucoxanthins, a bioactive compound with maximum health benefits such as anti-inflammatory (Huang *et al.,* 2016; Rodrigueze *et al.,* 2019), anti-obesity (Meada *et al.,* 2005; 2007), antiangiogenic (Ganesan *et al.,* 2013) and anticancer properties which can be exploited for pharmaceutical purposes. Studies showed that fucoxanthin extracts from *Laminaria japonica* inhibits the tumour growth in lung cancer (Mei *et al.,* 2017), while growth of B16-F10 melanoma cells implanted in albino mice showed inhibition owing to fucoxanthin isolated from the marine alga *Ishige okamurae* (Kim *et al.,* 2013; Chung *et al.,* 2013). Another study revealed positive results of fucoxanthin isolated from *Colpomenia sinuosa* and *Sargassum prismaticum* against cancer activity in HCT-116 (colon adenocarcinoma), MCF-7 (breast adenocarcinoma) and HepG-2 (liver adenocarcinoma) cell lines showing reduction in growth (Atya *et al.,* 2021).

Fucoidans exhibits several pharmacological properties such as antiproliferative activity against human lung adenocarcinoma cell line A549 (Boo *et al.,* 2011; Kalimuthu *et al.,* 2015]. Apart from this, fucoidans extracted from *Cladosiphon okamuranus*, exhibits the antimicrobial activity during *Helicobacter pylori* infection (Shibata et al., 2003). The mechanism of defence is due to the inhibition of urease enzyme avoiding the *Helicobacter pylori* adhesion to the gastric mucosa. In another study by Liu *et al.,* 2017), depolymerized compounds of fucoidans extracted from *Laminaria japonica* possessed good antibacterial activity both against *Escherichia coli* and *Staphylococcus aureus*. Depolymerized fucoidans when combine with the membrane proteins, cause a membrane-disrupting effect, resulting in collapse of membrane structure and eventually leads to cell death. Fucoidans isolated from *Undaria pinnatifida* possesses anti-diabetic activity against three starch hydrolysing enzymes, α-amylase, α-glucosidase and amyloglucosidase. Oral administration of polysaccharides restrained loss of weight and increased water intake, significantly controlling the increase of levels of blood glucose, triglyceride and total cholesterol in diabetic rats (Lomartier *et al.,* 2022). Therefore, polysaccharides from brown seaweeds could be promising candidates as natural medicines and functional foods for the improvement of diabetes problems.

Secondary Metabolites of Brown Algae

Secondary metabolites are present in brown algae that plays role in defence against pathogens such as Phlorotannin, phytosterol, and polyphenol.

Phlorotannins

Phlorotannins, present in seaweeds and synthesized by the acetate-malonate pathway also known as polyketide pathway produced by the polymerization of phloroglucinol. They are extremely hydrophilic components with a molecular size range between 126 kDa and 650 kDa (Ragan *et al.,* 1986). Phlorotannins have different biological activities such as anti-diabetic, antioxidant, anti-proliferative, anti-HIV, and skin protection, radioprotective, and anti-allergic activities (Weijeskara *et al.,* 2010; Sugiura *et al.,* 2021).

Phlorotanin likes phloroglucinol triacetate, diphlorethol pentacetate, and triphlorethol-A-heptacetate is present in *Cystophora congesta* (Young *et al.,* 2007) Extracts of which are good antioxidants and have cytotoxic effects, which can suggested that it can be used in the synthesis of the cytotoxic drug (Yoon *et al.,* 2008) and have bieckol, fucophloroethol, 7-phloroeckol, and phlorofucofuroeckol compound (Shibata *et al.,* 2012). It was noticed that different species of *Ecklonia* have antioxidant, anti-cancer, and anti-diabetic properties due to the presence of different phlorotannin compounds like fucodiphlorethol G, phloroglucinol, eckol, dieckol, and phlorofucofuroeckol A (Nagayama *et al.*, 2003; Jung *et al.*, 2006; Joe *et al.*, 2006; Ismail *et al.*, 2022). Edible brown algae *Eisenia arborea* was used in folk medicine and showed anti-allergic properties owing to the phlorofucofuroeckol B compound (Heo *et al.*, 2009). Presence of phloroglucinol in *Himanthalia elongates* showed high anti-microbial and antioxidant activity (Afsana *et al.*, 2016).

Phytosterol

Phytosterols, present in plants, (Pirronen *et al.*, 2003) are the bioactive compound in marine algae, terrestrial, and marine plants. About 200 types of phytosterol have been found (Lagarda *et al.*, 2006), entailing Stigmasterol and sitosterol (Abidi 2001). Most of the brown seaweeds contain fucosterol and fucosterol derivatives, bioactive compounds which are important because of the beneficial health effects. Bioactive compound fucosterol played role as anti-proliferative and cytotoxic properties in *Padina sanctae-Crucis* and *Dictyota ciliolate* (Murugan *et al.*, 2014). Similarly, *Padina gymnospora* and *Sargassum angustifolium* are having great antioxidant activity and it has been testified that they have a good source of fucosterol, brassicasterol, cholesterol, and stigmasterol (Ayad *et al.*, 2003). *Sargassum asperifolium* have important phytosterol compound like fucosterol, stigmasterol, saringosterone, and saringosterol (Xiao *et al.*, 2013), which gave good biological activities to it.

Polyphenols

Polyphenols are a group of secondary metabolites, supports the plant in structural development and protect the algae from biotic and abiotic stress condition (Aires *et al.*, 2017). Polyphenols and phlorotannin compound are a class of these polyphonic compound present in brown algae (Yajing *et al.*, 2017).These compounds are formed under harsh condition and able to absorb UV-radiation and repair wounds (Cruces *et al.*, 2016). Polyphenols are used as major ingredients for cosmeceutical and nutraceutical products (Sanjeewa *et al.*, 2016), have therapeutic properties such as anti-oxidative, anti-bacterial, anti-cancer, anti-allergic, anti-diabetes, anti-aging, anti-inflammatory, and anti-HIV activities (Lee *et al.*, 2011; Thomas *et al.*, 2011). Different brown algae showed antioxidant activity. It has been reported that *Fucus* species, *Sargassum multicum, Saccharina latissima* and *Laminaria digitata* contains gallic acid, protocatechuic acid, genistic, vanillic acid, and caffeic acid, protocatechuic acid, syringic (Sudha *et al.*, 2013). *Padina pavonica* was found to have polyphenol compounds like kaempferol, tannic acid, caffeic acid, quercetin, and epigallocatechin, and FTIR analysis confirmed the presence of various groups like phenol, alkanes, alcohol, and aromatic compounds (Sabeena *et al.*, 2013). Different species of *Sargassum* also shown to have polyphenolic compound like gallic acid and P-hydroxybenzoic acid, the presence of this compound was confirmed by RP-HPLC method (Al-Gamal, 2010).

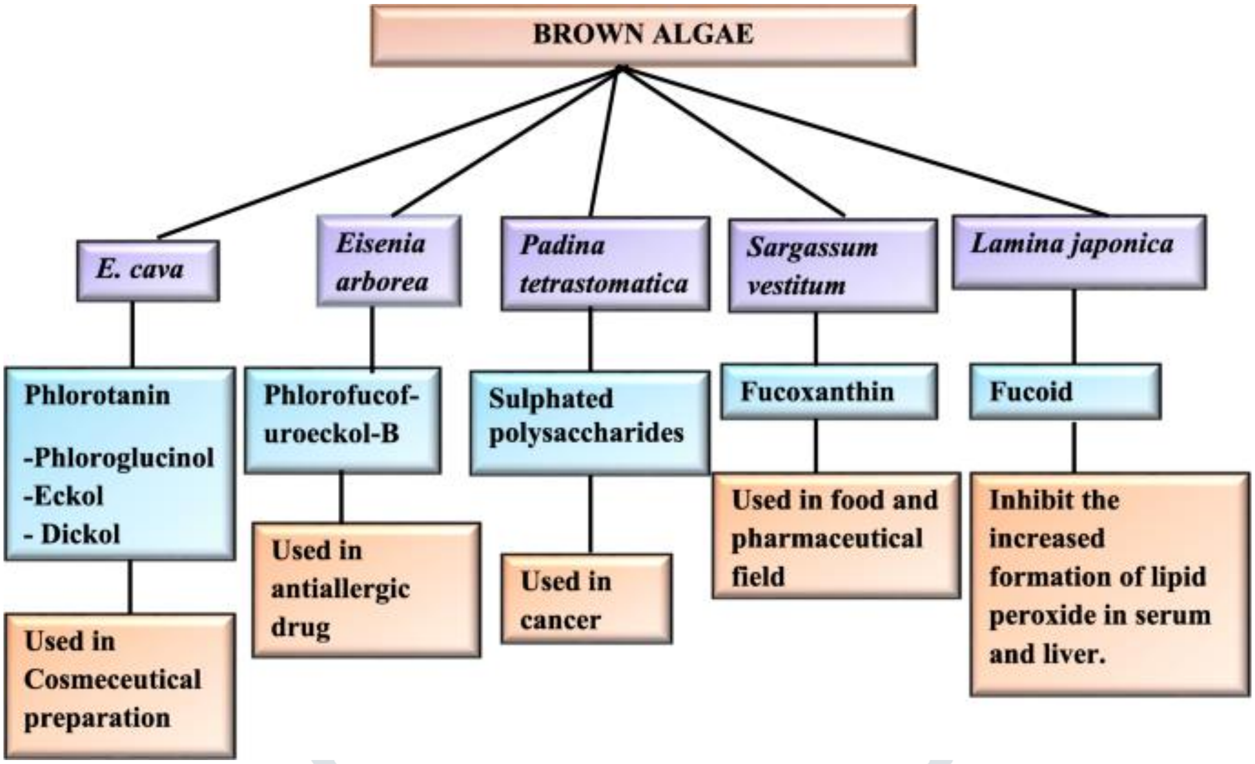

Figure 2: Schematic diagram showing applications of brown algae depending on its bioactive compounds (Hakim *et al.*, 2020)

Biological properties of algae:

Anticancer Activity

Cancer is one of the main diseases detected globally. Various treatments have been development to cure this disease but all are with some side. To curb this, new therapies need to be found to help alleviate these side effects. The polysaccharides present in the seaweeds could be an alternative, as they have some anticancer activity against some types of cancer. These polysaccharides effect tumor cells by several modes of action, such as cell cycle arrest, depolarization of mitochondrial membrane, DNA damage, and nitric oxide production (Bilal *et al.*, 2020). Numerous studies have indicated that antioxidants such as β-carotene, is beneficial in the treatment of precancerous conditions such as oral leukoplakia, a possible precursor of oral cancer (Sithranga and Kathiresan, 2010). Fucoidan being L-fucose-rich sulphated polysaccharide exhibits several anticancer effects, including induction of apoptosis and inhibition of tumor-induced angiogenesis (Van Weeldan *et al.*, 2019), effects on hepatocarcinoma and melanoma cancer bladder, breast, colon, liver, lung, and prostate cells (Arumugan *et al.*, 2019). The polysaccharides compose of the fiber are potentially beneficial in gastrointestinal health, contributing towards positive influence in the prevention of colon cancer. Hasan *et al.*, 2022 develop a green synthesis of AuNPs using hydromethanolic extract (HME) of *T. decurrens* and confirmed that the antioxidant and anticancer activities of HME and its AuNPs, and their potential as a therapeutic candidate in the treatment of oxidative stress diseases specifically cancer.

Neuroprotective activity

Parkinson's disease is one of the common neurodegenerative disease associated with movement difficulties and characterized by the accumulation of Lewy bodies, loss of dopaminergic neurons in the substantia nigra of pars compacta (SNpc), and depletion of the neurotransmitter dopamine. Apart from this, Alzheimer's disease is also quite common among the people of all ages. It was found that brown seaweed *Saccharina japonica* has anti-Alzheimer's, anti-inflammatory, and antioxidant properties (Sevevirathne *et al.*, 2012). Also, Phloroeckol and a tetrameric phloroglucinol of *Macrocystis pyrifera* (Phaeophyceae) have antidiabetic and anti-alzheimer's effect, and antiallergic effect, respectively. Cha *et al.*, 2016 noticed the potential use of the edible brown seaweed *Ecklonia cava* as therapeutic agent for the prevention of Parkinson's disease. Its anti-neurodegenerative activity could be linked with the antioxidant activity of dieckol in dopaminergic neuronal cells. The vulnerability of these cells to oxidative stress gives rise to intracellular toxic events, which result in protein aggregation, leading to cell death and the appearance of Parkinson's disease. This polyphenol isolated from the seaweed prevents α-synuclein aggregation (Cha *et al.*, 2016).

Tissue Engineering

It has been found that fucoidan-enriched seaweed extracts are used in osteoarthritis treatment as they contribute to mineral deposition in bones, increasing the activity of alkaline phosphatase and the level of osteocalcin (Cho *et al.*, 2009). Alginate-based biocompatible hydrogels are used in the stem-cell transplantation and greatly impact several organ, bone, and cartilage defects (Barralet *et al.*, 2005). Polysaccharide laminaran obtained from the brown algae *Saccharina longicruris* increases the tissue-generation process (Ayoub *et al.*, 2015). Repairing affects by low-molecular-weight polysaccharides of *Betaphycus gelatinus* (formerly *Eucheuma gelatinum*), *Gracilariopsis lemaneiformis* (formerly *Gracilaria lemaneiformis*), *Pyropia yezoensis* (formerly *Porphyra yezoensis*) (Rhodophyta), *Saccharina japonica* (formerly *Laminaria japonica*), *Sargassum fusiforme*, and *Undaria pinnatifida* (Phaeophyceae) on kidney epithelial cells was reported by Bhadja *et al.*, 2016.

Other Activity

Algae have a high proportion of soluble fiber which is known by its ability to increase viscosity, reduce glycemic response and plasma cholesterol. Apart from this, they have positive effects on reducing the risk of cardiovascular diseases (Sirot *et al.*, 2012), triglyceride levels (Kris-Etherton *et al.*, 2009), pregnancy, lactation and development of nervous system ad retina, postpartum and depression as well (Hiblon *et al.*, 2009).

Conclusion:

Seaweeds are primary resource of essential vitamins, trace elements, proteins, lipids, polysaccharides, enzymes and minerals. Seaweed and its products are widely used in variety of application in pharmaceutical, clinical and industrial sector; however, regular uptake of seaweed may not be safe as it could be contaminated by heavy metals. The brown algae contain heavy metals such as high iodine content which may lead to toxic. Regular uptake of brow algae results in the abnormalities in thyroid, acne-type skin lesions, increased salivation, and stomach irritation and may also and may affect the blood sugar level. Medicinal plants and seaweeds available in the marine environment is ideal for the discovery of various medicines with biological activities such as antibacterial, anticancer, antifungal, antidiarrheal, analgesics, anti- diabetic, anti- inflammatory and antioxidant agent. Hence, we can use these herbal plant and their products to cure different diseases as it has no side effect as compared to allopathic drugs.

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