NUTRITIONAL VALUE OF SEAWEEDS AND THEIR POTENTIAL PHARMACOLOGICAL ROLE OF POLYPHENOLICS SUBSTANCES: A REVIEW

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ABSTRACT : seaweed shows extensive species diversity with inevitable ecological importance on marine biodiversity. It creates a unique marine ecosystem that acts as a shelter or nursery ground for marine organisms. Moreover, seaweeds are considered as vital sea food due to their richness of various food ingredients such as polysaccharides, dietary fiber, amino acids, minerals and vitamins, etc. They are available in different colors due to the presence of distinct pigments such as chlorophyll, fucoxanthin and phycoerythrin. In traditional Indian medical system, the dried or processed seaweeds are consumed as promising natural medicine for the treatment of various ailments. Seaweed contains various polyphenolic substances such as phlorotannins, phloroglucinol, eckol, dieckol, fucodiphloroethol, 7-phloroeckol, phlorofucofuroeckol and bieckol, which play a major role in human health. The preclinical studies proved that these compounds possess antimicrobial, antitumor, antioxidant activities and also reduce the risk of cardiovascular diseases. The present review deals with the nutritional value of seaweed and the importance of polyphenolic substances.

Key words: Seaweeds, phytochemistry, functional foods, polyphenolics, health benefits.

INTRODUCTION

As there is an increasing demand for search of therapeutic drugs from natural products, there is now a superior concern in marine organisms, especially seaweeds. It serves as a primary producer in water ecosystem and has both ecological and economic value. Seaweeds has been classified into three groups based on pigmentation into brown (Phaeophyta), red (Rhodophyta) and green (Chlorophyta) types. The green seaweeds are greenish in color due to the presence of chlorophyll pigments (Pangestuti and Kim, 2011). Brown seaweeds also contain chlorophyll, which are masked by other gold and brown pigments dominantly fucoxanthin (Airanthi *et al.,* 2011). Red seaweeds, in addition to chlorophyll, contain the phycocyanin and phycoerythrin as major pigments (McHugh, 2003). These marine macroalgae represent a source of potential bioactive compounds for variety of application in agro-food industry, cosmetics, pharmaceutical industries and more recently, in the field of functional food and chemistry (Holdt and Kraa, 2011; Gressler *et al.,* 2010). It has been exploited as an alternative source of food in Asian countries and represents a vegetative resource characterized by a high content of proteins, carbohydrates and minerals (Balboa et al., 2012; Patarra *et al.*, 2011). Seaweeds are also used in folk medicine for various diseases such as goiter, glandular problem, wounds, burns and rashes in many parts of the world (Aceves *et al.*, 2013). Metabolites derived from seaweeds have revealed the potential free radical scavenging activity, antibacterial, antiinflammatory, antidiabetic, antiproliferative, antihypertensive and antiallergic properties, as well as they are involved in hyaluronidase enzyme inhibition activity (Kolsi *et al.*, 2015; Ferreres *et al.,* 2012; Lordan *et al.*, 2011). The seaweeds are ubiquitous source for bioactive compounds. Among them, the phenolic substances are predominantly present in seaweeds. The phenolic substances are involved in variety of application and they are commonly used as nutrition enhancing materials or food ingredients, etc. The purpose of this review article is to discuss the nutritional value of marine algae and the recent progress in pharmaceutical application of polyphenolics isolated from seaweeds.

PHYTOCHEMISTRY

Seaweeds are a known source of bioactive compounds as they are able to produce a great variety of secondary metabolites including terpenes, acetogenins, alkaloids and polyphenolic substances. These molecules possess a broad spectrum of biological activities, which are shown in Table 1 (Venugopal, 2009; Watson and Cruz-Rivera, 2003).

TABLE 1 Nutritional value of some seaweed species

Constituents	*Laminaria digitata*	*L. saccharina*	*Himanthalia elongata*	*Palmaria palmata*	*Condrous crispus*
Protein (%)	8-14	6-11	6-13	12-21	11-18
Fat (%)	1	0.5	0.5	0.7-3	1-3
Carbohydrate (%)	48	61	65	46-50	55-66
Vitamin C (ppm)	12-18	13-18	11-18	150-280	10-30
Calcium (ppm*)	12400-13200	8910-9282	9110-9258	2000-8000	0.9-1.3%*
Iodine (ppm)	800-5000	800-4500	185	150-550	200-300
Iron (ppm)	50-70	22-40	31-40	56-350	170-210
Magnesium (ppm)	6400-7860	5670-6944	5790-6448	0.2-0.5	6710-8351
Manganese (ppm)	1-16	1-16	1-18	10-155	2-28
Sodium (%)	2-5.2	3-3.4	3-3.8	0.8-3	2-2.6

*unit of measurement, except where indicated differently; Ppm: parts per million

Phenolic compounds are the secondary metabolites of algae, which do not directly take part in physiological process such as photosynthesis, reproduction and cell division. They are biosynthesized through the shikimic acid and acetate–malonate pathways (Fernando *et al.*, 2016). The term "phenolic compound" describes an aromatic ring bearing one or more hydroxyl groups and their structures may range from that of a simple phenol to complex phenolic molecules. These structures determine the physicochemical and biological characteristics of polyphenols namely, phloroglucinol and phlorotannins (Gupta and Abu-Ghannam, 2011). Phlorotannins are phloroglucinol-based polyphenols, i.e. tannin compounds commonly found in brown seaweeds *viz*, *Eisenia bicyclis*, *Ecklonia cava*, *Ecklonia stolonifera*, *Undaria pinnatifida*, *Sargassum thunbergii*, *Ishigeo kamurae*, *Laminaria japonica* and *Himanthalia elongata* (Rajauria *et al.*, 2016; Perez *et al.*, 2016; Li *et al.*, 2011). Phlorotannins are formed by the polymerization of phloroglucinol (1,3,5-trihydroxybenzene) monomer units with molecular weights ranging from 126 to 650 kD. Based on the type of linkage, the phlorotannins can be classified into four subclasses namely, fuhalols, phlorethols (phlorotannins with an ether linkage), fucols (with a phenyl linkage), fucophloroethols (with an ether and phenyl linkage), and eckols (with a dibenzodioxin linkage) (Agregan *et al.*, 2016). Some of the pholorotannins are halogenated containing bromine, chlorine or iodine. Phloratannin ranges from 5 to 15 per cent of dry weight in seaweeds. Six phlorotannins namely phloroglucinol (0.7, 2.2%), phloroglucinol tetramer (3.4, 0.6%), eckol (7.5, 8.5%), phlorofucofuroeckol A (21.6, 27.6%), dieckol (21.9, 23.6%), 8,8'-bieckol (24.0, 6.8%) and other unknown compounds (20.9, 31.7%) were detected from the brown algae *Eisenia bicyclis* and *Eclonia kurome* (Sanjeewa *et al.*, 2016). In addition to that of phlorotannins, seaweed also contains high amount of other polyphenolics such as catechin, epicatechin, epigallocatechin, gallic acid and gallate (Yoshie-Stark *et al.*, 2003).

NUTRITIONAL VALUE:

Marine algae contain biologically active compounds (or substances), which possess many nutritional properties and are essential components of functional food. It considerably contributes to health when they are consumed regularly as part of a daily diet. It is well established that seaweeds have high concentration of polysaccharides, essential and non-essential amino acids, minerals, polyunsaturated fatty acids, polyphenolics, vitamins and dietary fibre (non starch polysaccharides) that are essential for normal growth and overall nutritional well-being (Garcia-Vaquero *et al.*, 2017; Garcia-vaquero and Hayes, 2016; Verma *et al.*, 2016; Robles-Sanchez *et al.*, 2013). The isolated compounds from seaweeds can be used as preservatives, nutrition enhancers, technologically characteristic products and healthy food source (Barba, 2016; Syad *et al.*, 2013; Rohani-Ghadikolaei *et al.*, 2012). Natural phytochemicals present in the seaweeds contains various benefits on its consumption such as on growth, body weight, mineral bioavailability, lipid metabolism, blood pressure and antioxidant properties (Yaich *et al.*, 2011; Bocanegra *et al.*, 2009). Green seaweeds *viz*, *Monostroma*, *Enteromorpha*, *Ulva*, *Caulerpa* and *codiumare* species are commonly used as source of food. Some of the brown seaweeds such as *Laminaria*, *Undaria*, *Sargassum*, *Cladosiphon*, *Turbinaria* and *Colpomenia* are widely consumed in the form of soup or stew in various countries. Red seaweeds namely *Acanthophora*, *Asparagopsis*, *Calophyllis*, *Hypnea* and *Laurencia* serve as raw or cooked savories and are widely used to prepare jellies (Indy *et al.*, 2009).

Phenolic compounds are aromatic secondary metabolites of plants and marine algae which play a significant role in color, sensory and nutritional qualities of food (Fleurence and Levine, 2016; Peinado *et al.*, 2015; Misurcova *et al.*, 2012). Phenolics such as flavonoids and phenolic acids in seaweeds behave as natural antioxidants and therapeutic medicines due to their nutraceutical and health properties (Thomas and Kim, 2011). Seaweeds contain pectin, cellulose, and hemicelluloses, which are resistant to breakdown by digestive enzymes and therefore are candidate source of dietary fibres (Gomez-Ordonez *et al.*, 2010; Ruperez and Saura-Calixto, 2001). Dietary fiber contains beneficial human health effects such as antioxidant potential (Wang *et al.*, 2016; Wijesekara *et al.*, 2011), hypoglycemic effects (Cao *et al.*, 2015), cholesterol lowering (El- Gamal, 2012; Chan et al., 2014) and their consumption can reduce the occurrence of some chronic diseases such as diabetes, obesity and cancer in human. Along with the nutritional function, the fibre can be used for technological purposes such as a bulking agent or fat substitute because of the physicochemical properties such as water- and oil-holding capacities, absorption of organic molecules, bacterial degradation, cation-exchange capacity and antioxidant activity (Chan *et al.*, 2016; Syad *et al.*, 2013). Seaweeds are rich in sulfated and non sulfated polysaccharides such as agar, alginates, laminaran, fucoidans and carageenans that are used in food, pharmaceuticals and other products for human health exhibiting antioxidant, anticoagulant, antiinflammatory and antithrombic activities (Isaka *et al.*, 2015; Wijesinghe and Jeon, 2012; Barahona *et al.*, 2011; Sokolova et al., 2011; Wijesekara *et al.*, 2011). Polysaccharides of seaweeds are mostly composed of galactose, mannose, fucose, xylose and glucose (Elleuch *et al.*, 2011; Venugopal, 2009).

The presence of nutrients, proteins, vitamins and polyunsaturated fatty acids help to prevent unwanted damage to cell membranes and other structures of the body by neutralizing free radicals. Antioxidants in these algae possess antitumor and antimetastasis activity (Blunt *et al.*, 2015; Nwosu *et al.*, 2011; Kim *et al.*, 2010). The consumption of seaweeds may significantly improve the bone quality due to the presence of vitamins and its bioactive compounds preserve bone calcium concentration (Misurcova, 2014). Seaweeds contain all the essential amino acids and are a rich source of the aspartic and glutamic acid which are widely served as salads (Barbarino and Lourenco, 2005; Fleurence, 2004). The presence of essential and non-essential, saturated and unsaturated fatty acids in marine algae are highly acceptable for consumption than vegetables. In addition, seaweeds are rich source of vitamin C, vitamin B-complex and vitamin A precursors (Kadam and Prabhasankar, 2010). Seaweeds are also good source of vitamin C which plays a crucial role in the suppression of superoxide radicals (Eom *et al.*, 2013a; Zhang *et al.*, 2012). Like most other whole foods, seaweeds also contain an impressive list of other essential nutrients, including glycaemic and non-glycaemic carbohydrate, potassium, folate, calcium, thiamin, niacin, vitamin B_6, phosphorus, magnesium, copper, riboflavin, pantothenic acid and a variety of phytochemicals (Suleria *et al.*, 2015; Kumar *et al.*, 2011). Natural foods, especially seaweeds, play a major role in human nutrition as excellent sources of free radical scavenger and contain a variety of sugars, citric acid, vitamin C, B, P and carotenoids, mineral substances (nutritive value of 100gm of various seaweeds are denoted in **TABLE 2**) (Morrissey *et al.*, 2001).

TABLE 2 Some bioactive compounds from seaweeds and their functions

Seaweed species	Ingredient	Potential Health Effects
Sargassum vulgare	Alginic acid, xylofucans	Antiviral activity
Himanthalia elongata	PUFAs, α-tocopherol, sterols, fibre	Reduction of total and low density lipoprotein (LDL) cholesterol
Undaria pinnatifida	PUFAs, α-tocopherol, sterols. Fibre, folate, fucoxanthin	Reduction of total and LDL cholesterol and certain types of cancer, antiviral activity
Chondrus crispus	PUFAs, α-tocopherol, sterols. fibre, folate, fucoxanthin	Reduction of total and LDL cholesterol, reduction of cardiovascular disease
Ulva spp.	Sterol	Reduction of total and LDL Cholesterol

Seaweeds consist of the macromolecules such as iodine, sodium, calcium, iron, potassium, manganese and magnesium (Saravana *et al.*, 2016; Anuradha *et al.*, 2014).

PHARMACOLOGICAL POTENTIAL OF SEAWEEDS

Research in natural products of marine algae has made significant advances in recent years. Seaweed has been shown to produce a variety of compounds and it possesses biological activity of potential pharmaceutical value. Over the past decades, the isolated polyphenolic compounds from marine algae and their extracts have generated an enormous amount of interest in the pharmaceutical industry. The health benefits of polyphenolic compounds in edible seaweeds and their role in disease prevention has been illustrated in **TABLE 3**. This review will cover areas related to antimicrobial, antiinflammatory, antidiabetic, antitumor, tyrosinase enzyme inhibitory and antioxidant activity of seaweed polyphenolics constituents that can be supported through science and claims substantiation.

TABLE 3 List of phenolic compounds and their beneficial activity for human

S. No	Phenolic compound	Source	Activity	Reference
1	Phlorotannins	*Sargassum thunbergii Sargassum kjellmanianum*	Anticoagulant	Li *et al*. (2007); Wei *et al*. (2003)
		Sargassum ringgoldianum	Free radical scavenging	Nakai *et al*. (2006)
		Saccharina japonica	Anti-proliferative	He *et al*. (2013)
		Sargassum muticum	against HT-29 adenocarcinoma colon cancer cells	Montero *et al*. (2015)
		Sargassum muticum	Against lung adenocarcinoma A549 cells , against colon carcinoma HCT-116 cells.	Casas *et al*. (2016)
		Fucus distichus	Inhibit carbolytic enzyme	Kellogg *et al*. (2014)
2	Dieckol	*Ecklonia cava, Ecklonia stolonifera*	Tyrosinase inhibition	Lee *et al*. (2015); Kang *et al*. (2004)
		Ecklonia bicyclis and *Ecklonia kurome*	Hyaluronidase Inhibition	Shibata *et al*. (2002)
		Ecklonia cava	Anti-proliferative	Li *et al*. (2011); Oh *et al*. (2011)
		Ecklonia stolonifera	Matrix metalloproteinase inhibition	Joe *et al*. (2006)
		Ecklonia stolonifera	Anti-hyperlipidemic	Yoon *et al*. (2008)
		Ecklonia cava	Antioxidant	Heo *et al*. (2009)
		Ecklonia cava	Anti-allergic	Le *et al*. (2009)
		Eisenia bicyclis	Inhibit α-amylase	Okada *et al*. (2004)
		Ecklonia cava	Inhibit α-amylase and α-glucosidase	Lee *et al*. (2010)
3	Phlorofucofuroeckol	*Eisenia arborea*	Anti-allergic	Sugiura *et al*. (2008)
		Ecklonia stolonifera	Anti-inflammation	Lee *et al*. (2012)
		Eisenia arborea	Inhibitory effects on histamine release	Sugiura *et al*. (2006)
		Ecklonia cava	Anti-viral	Ahh *et al*. (2004)
		Eisenia bicyclis and *Ecklonia kurome*	Hyaluronidase Inhibition and Antioxidant	Shibata *et al*. (2002)
		Palmaria palmata	Antioxidant	Yuan *et al*. (2005)
		Ecklonia stolonifera	AGEs inhibition	Jung *et al*. (2008)
4	Eckol	*Eisenia bicyclis*	Inhibit α-amylase	Okada *et al*. (2004)
		Ecklonia cava	Anti-proliferative	Li *et al*. (2011)
		Ecklonia cava	Inhibit α-amylase and α-glucosidase	Lee *et al*. (2009); Lee *et al*. (2010)
		Eisenia bicyclis	Inhibit pancreatic lipase	Eom *et al*. (2013b)
5	7-phloroeckol	*Ecklonia stolonifera*	Inhibit α-glucosidase	Moon *et al*. (2011)
		Ecklonia cava	Inhibit α-glucosidase	Lee *et al*. (2009)
		Eisenia bicyclis	Inhibit pancreatic lipase	Eom *et al*. (2013b)
		Eisenia arborea; Eisenia bicyclis	Anti-inflammatory	Jung *et al*. (2013)

ANTIMICROBIAL ACTIVITY

Seaweeds have been recognized as potential sources of antimicrobial active compounds (Chiheb *et al.,* 2009). Seaweeds possess various secondary metabolites which have a wide spectrum of biological activities. The bioactive secondary metabolites of seaweeds such as phenolic compounds exhibit the antimicrobial activities (Smit, 2004). Those compounds from green, brown and red algae exhibit cytostatic, antiviral, anthelminthic, antifungal and antibacterial activities (Daglia, 2012; Chakraborthy *et al.*, 2010). Antimicrobial substance from seaweeds may be incorporated in medicine and pharmacotheraphy due to the bacteriostatic and bactericidal properties (Gorban *et al.*, 2003). Jaswir *et al.*, 2014) screened the antibacterial activity of some selected brown seaweeds from Malaysia. The authors have reported that methanolic extract of the seaweed exhibited strongest antibacterial activity and the least activity was reported in chloroform extract. Shimaa *et al.,* 2015) evaluated the antibacterial activity of diethyl ether, methanol, ethanol and chloroform extracts of various red seaweeds such as *Ceramium rubrum*, *Sargassum vulgare*, *S. fusiforme* and *Padina pavonia*. Their results showed significant inhibitory potential of diethyl extract of *S. fusiforme* and ethanol extract of *S. vulgare* against multi drug resistant bacteria such as *Staphylococcus aureus* and *Klebsiella pneumoniae*. These activities were confirmed by the presence of bioactive compounds such as terpenes, acetogenins, indoles, fatty acids and volatile halogenated hydrocarbons along with phenolic subtances. Moubayed *et al.*, (2017) demonstrated the higher antibacterial activity of methanol and acetone extracts from brown algae *viz*, *Sargassum latifolium* B and *S. platycarpum* A than green algae *Cladophora socialis* and also had higher activity in comparison with standard antibiotics. Antimicrobial activities of phenolic compounds from seaweeds were demonstrated as a potent pharmaceutical alternative for the treatment of various microbial infections.

ANTIINFLAMMATORY ACTIVITY

Inflammatory activities of phenolic compounds represent a large and diverse group of secondary metabolites comprising of one or more phenol groups. Marine algae, especially the brown algae have extensively been studied as a rich source of bioactive phenolic compounds (Thomas and Kim, 2011). Many researchers have examined the antiinflammatory potential of phenolic compounds from marine seaweeds as drugs in the pharmaceutical field. Especially the phlorotannins from brown algae has been reported to be inhibitors of proinflammatory cytokines such as inducible nitric oxide synthase, cyclooxygenase-2, tumor necrosis factor α, interleukin-1 β and interleukin-6 in lipopolysaccharides (LPS) stimulated microglial cells (Kim and Kim, 2010). Kazlowska *et al*., (2015) investigated the antiinflammatory activity of isolated phenolic compounds such as catechol, rutin and hesperidin from methanolic extract of *Porphyra dentate*. They also evaluated their effect on nitric oxide/inducible nitric oxide synthase transcription pathway in LPS-stimulated RAW 264.7 cells. Their results confirmed that the red seaweed is more potent suppressors of iNOS promoter and NF-κB enhancer by catechol than rutin and hesperidine.

ANTIDIABETIC ACTIVITY

Phenolic acids and flavonoids of seaweeds possess antidiabetic effects due to their ability to inhibit the major digestive enzymes namely α-amylase and α-glucosidase. Polyphenols from marine algae have the antidiabetic potential through modulation of glucose-induced oxidative stress and inhibition of starch-digestive enzymes (Hemlatha *et al.*, 2017; Lee *et al.*, 2010). Phlorotannins are tannin like components and have particular affinity for inhibition of α-amylase and α-glucosidase enzyme. Purified phlorotannins from brown algae, *Ecklonia cava* have the α-amylase inhibiting potential at IC_{50} value of 90 µg/ml (Lee *et al.*, 2009). Phenolic compounds from *Ascophyllum nodosum* was confirmed to have the α-glucosidase inhibiting potential at 1.34 µg phenol/ml when compared with acarbose, a known inhibitor of α-amylase and α-glucosidase enzyme (Apostolidis and Lee, 2010). The polyphenolic compounds of *Ascophyllum* extract were tested for inhibition of α-amylase and the extract abolished activity at the concentration of 50 µg/ml (Nwosu *et al.*, 2011). Similarly, polyphenolic enriched fractions from the brown seaweed *Ascophyllum nodosum* showed inhibitory activity of α-glucosidase and promising antidiabetic effects in mouse models (Zhang et al., 2007). Lee *et al*., (2010) examined the antidiabetic activity of purified phlorotannins such as dieckol and diploroetohydroxycarmalol compounds isolated from *Ecklonia cava*, which significantly suppressed post-prandial glucose levels in streptozotocin induced diabetic mice. Pantidos *et al.*, (2014) studied the potential antihyperglycemic activity of phenolic-rich *Ascophyllum nodosum* extract which inhibited the α-amylase and α-glucosidase enzymes.

ANTI TUMOR ACTIVITY

Phenolic compounds and flavonoids from marine algae have been reported to inhibit cancer cells by altering the activation of xenobiotic metabolizing enzymes, alter hormone production and inhibit aromatase to prevent the development of tumor cells (Fernando *et al.*, 2016). Phenolic compounds isolated from marine algae showed antioxidant activity acting as chemopreventive agent in the inhibition of carcinogenic process (Padua *et al.*, 2015). Zhang *et al.*, (2012) reported the phloroglucinol derivative such as Dryofragin, isolated from *Dryopteris fragrance*, which showed potential antiproliferative activity in human breast cancer cell MCF-7 through ROS-mediated mitochondrial pathway. Yuan *et al.*, (2005) examined the antiproliferative activity of *Palmaria palmata* and the polyphenolic compounds showed the ability of inhibiting cancer cell proliferation. Two phlorotannins (dioxinodehydroeckol and 1-(3′,5′-dihyroxyphenoxy)-7-(2′′,4′′,6-trihydroxyphenoxy)-2,4,trihydroxybenzo-1,4-dioxin from edible marine algae *E. cava* were evaluated for inhibition of human breast cancer cells (Kong *et al.*, 2009). Yang et al. (2010) reported the antiproliferative effect of phlorotannin extract of *Laminaria japonica* on human hepatocellular carcinoma cells (IC_{50}-200 µg/mL) and murine leukemic cells (IC_{50}-120 µg/mL). The presence of phlorotannins and polyphenols in seaweeds exhibited the antiproliferative activity and they were positively correlated with total polyphenolic contents ($p<0.05$). Nwose *et al.*, (2011) reported anti-proliferative effect of polyphenolics from *Palmaria palmata*, *Ascophyllum nodosum* and *Alaria esculenta* extract against colon cancer cells.

TYROSINASE INHIBITORY ACTIVITY

Tyrosinase is a polyphenols oxidase with a dinuclear copper active site and responsible for the formation of mammalian melanin pigments, enzymatic browning of fruits and vegetables. Over-activity of this enzyme leads to hyperpigmentation of the skin. Tyrosinase inhibitors suppress melanogenesis and can be clinically useful for the treatment of some dermatological disorders associated with melanin hyperpigmentation (Lee *et al.*, 2015). Phlorotannins isolated from seaweeds have the potential property to inhibit the tyrosinase enzyme activity. Dieckol, eckol, eckstolonol, phlorofucofuroeckol A and phloroglucinol compounds from *Ecklonia stolonifera* were reported to possess the tyrosinase inhibitory activity (IC_{50} values such as 2.16, 33.2, 126, 177 and 92.8 µg/ml respectively) using mushroom tyrosinase with L-tyrosine as a substrate (Kang *et al.*, 2004). 4-hydroxyphenethyl alcohol compound from hot water extract of *Hizikia fusiformis* has been reported to have *in vitro* and *in vivo* whitening effect on B16 melanoma cells and promote the depigmentation of UVB-induced hyper pigmented spots on brown guinea pigs (Jang *et al.*, 2014). 7-phloroeckol from *Ecklonia cava* showed more potent melanin inhibitory activity (IC_{50} value 0.85µM) in B16F10 mouse melanoma cancer cell than phloroglucinol and 3-isobutyl-1-methylxanthine (Yoon *et al.*, 2008).

ANTIOXIDANT ACTIVITY

Phenolic compounds are commonly found in plants, including seaweeds (Manach *et al.*, 2004; Duan *et al.*, 2006). Phlorotannins from brown seaweed are considered to be the electron rich compounds and have been reported to possess strong antioxidant activity and their free radical scavenging potential is more powerful than that of other polyphenols derived from terrestrial plants (Ahn *et al.*, 2007). Radical scavenging activity of phenolic compounds also depends upon their unique phenolic structure and the number and location of the hydroxyl groups (Brand-Williams *et al.*, 1995). Phenolic compounds found in seaweed contribute to beneficial health effects such as it can serve as antioxidants by chelating metal ions, protective agents against free radical-mediated disease processes, preventing radical formation and improving the antioxidant endogenous system (Al-Azzawie and Mohamed-Saiel, 2006). Phenolic compounds from seaweeds are responsible for antioxidant activities and protective effect against free radical induced cell damage. Al-Amoudi *et al.*, (2009) proved the antioxidant potential of seaweeds by measuring various radical scavenging activity such as DPPH and superoxide anion radical scavenging activity, total content of phenolic compounds and inhibition of lipid peroxidation.

Ethanolic extract of *Euchema kappaphycus*, *Gracilaria edulis* and *Acanthophora spicifera* were evaluated for antioxidant potential. *G. edulis* exhibited higher phenolic content (16.26 mg gallic acid equivalent/g) in petroleum ether fraction than other red seaweed (Ganesan *et al.*, 2008). Sachindra *et al.*, (2010) reported higher ABTS radical scavenging activity of brown seaweeds and the activity are correlated to the high polyphenol content in the seaweeds. The total flavonoid content and *in vitro* antioxidant activity of methanolic extract of two seaweeds *Ulva lactuca* and *Sargassum wightii* were evaluated by Meenakshi *et al.*, (2009). The authors observed the higher phenolic content in brown seaweeds than the green seaweeds. Methanolic extract of six species of edible Irish seaweeds viz, *Laminaria digitata*, *L. saccharina*, *Himanthalia elongata*, *Palmaria palmata*, *Chondrus crispus*
and *Enteromorpha spirulina* were reported to possess phenolic content and DPPH radical scavenging activity (Cox *et al.*, 2010). Farvin and Jacobsen (2013) reported the total phenolic content of sixteen brown algal species, which ranged from 11.5 to 607.7 mg/100 g dried seaweed in water and from 32.4 to 1920 mg/100 g in ethanol. The ethanolic extract of red algae *Polysiphonia fucoides* contained significantly ($P<0.001$) higher levels of phenolic compounds when compared with other extracts followed by ethanolic extracts of other brown algal species. Khairy *et al.*, (2015) observed the maximum value of phenolic contents in seaweeds during summer and minimum values during winter that indicated a significant increase in total phenolic content (0.75 mg /100 g) in red algae, *Jania rubens* during summer time than the *Ulva lactuca*, and *Pterocladia capillacea*. Aqueous extract of three different seaweeds, *Ascophyllum nodosum*, *Bifurcaria bifurcata* and *Fucus vesiculosus* exhibited the total phenolic content of 0.96 to 1.99 gm of phloroglucinol/100 gm of extract (Agregan *et al.*, 2016). Further, they analyzed the phenolic compounds from three marine algae by liquid chromatography-diode array detection coupled to negative electrospray ionization-tandem mass spectrometer with the interest to evaluate their potential application as functional ingredients. Wang *et al.*, (2009) reported the Total Phenolic Content (TPC) in 70% acetone extract and water extract of various seaweeds. Among these, acetone extract of *Ascophyllum nodosum*, *Fucus serratus* and *F. vesiculosus* were 15.9, 24.0 and 24.2 g phloroglucinol/100 g extract than water extract.

CONCLUSIONS

Seaweeds are popular food dishes and additives that are unique source of many compounds with diverse structure. It is a multifaceted nutritious sea food with a great variety of pharmaceutical applications. Here, an attempt was made to address nutritional property of seaweed, phytochemistry and pharmacological role of polyphenolic substances of marine algae. It is quite evident from this review that seaweeds are significant in various applications, which are being utilized in the field of Ayurveda, Siddha and other pharmaceutical systems. It contains a number of phytoceuticals, which are the key factors in the field of nutritional and health aspects. Crude extracts and isolated compounds from three different classes of seaweeds as reviewed here have been found to have many pharmacological activities such as antimicrobial, antiinflammatory, antitumor, antidiabetic, tyrosinase inhibitory and antioxidant activity. Quite a significant amount of work has been done on the biological activity and possible application of these compounds. Hence, extensive investigation on its pharmacology and clinical trials is needed to explore their therapeutic utility to cure various diseases.

CONFLICTS OF INTEREST

The authors declare no conflict of interests.

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