Edible brown seaweeds: a review

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Abstract

Seaweeds play a vital role as a source of food and ingredients in traditional Korean medicine. Koreans consume seaweed as fresh vegetables, salad, soups, or snacks. There are several edible brown seaweed species are abundant along the shores of the Korean peninsula, such as *Ecklonia cava*, *Hizikia fusiforme*, *Laminaria japonica*, *Pelvetia siliquosa*, *Sargassum fulvellum*, and *Undaria pinnatifida*. With the growing body of scientific evidence, it is clear that these brown seaweeds are not only good substitutes for land vegetables but also a good source of bioactive secondary metabolites. The secondary metabolites identified from edible Korean brown seaweeds (phlorotannins, sulfated polysaccharides, pigments, and sterols) have the potential to be developed as functional food ingredients. However, seaweeds consumption and their industrial level applications as functional materials are limited compared to the land vegetables. Insufficient awareness about health benefits of seaweeds might be the reason for this issue. Thus, in this review health promotion properties associated with edible Korean brown seaweeds are summarized. The present study might therefore increase consumption and industrial use of brown seaweeds.

Keywords: Seaweeds; Bioactive compounds; Functional foods.

1. Introduction

Seaweeds are important macroscopic marine organisms with great economic and ecological value. In East-Asia (Korea, China, and Japan) seaweeds serve as healthy food and medicinal ingredients (Jeong et al., 2015). The term "sea vegetable" is used to define seaweeds include approximately 50 different species of edible seaweeds in this region (Park et al., 2016). Besides the nutrient value, a growing body of scientific evidence indicates that the secondary metabolites present in seaweeds have great potential for developing active ingredients in functional products. Phlorotannins, sulfated polysaccharides, ergosterol, and some pigments isolated from seaweeds have been found to possess outstanding bioactive functionalities (antioxidant, anticoagulant, anticancer, anti-microbial, anti-diabetic, and anti-inflammatory activities) compared to the synthetic chemicals under *in vivo* and *in vitro* conditions (Jeong et al., 2015; Son et al., 2018).

Korea is one of the major seaweed producers and consumers in the global seaweed market and makes great contributions to the Korean economy. Seaweeds have more than thousands of year's history in Korea as food and medicinal ingredients, and increases the food security and healthy lifestyle of Koreans (Choi et al., 2012). During winter (December to February), Koreans enjoy seaweed as a vegetable substitute in the winter season (Park et al., 2016). Figure 1 graphically illustrates common seaweed applications including traditional meals, cosmeceutical and functional food ingredients found in Korea. On the basis of their color and appearance, seaweeds are categorized into three groups as brown, green, and red. All three seaweed types have been found to possess interesting bioactive properties and are useful for a range of industrial applications (Wijesinghe and Jeon, 2012a). However, in the present study, we have focused about the potential health promotion properties of edible brown seaweeds consumed in Korea including *Ecklonia cava, Hizikia fusiformis, Sargassum fulvellum, Laminaria japonica*, *Undaria pinnatifida*, and *Pelvetia siliquosa*.
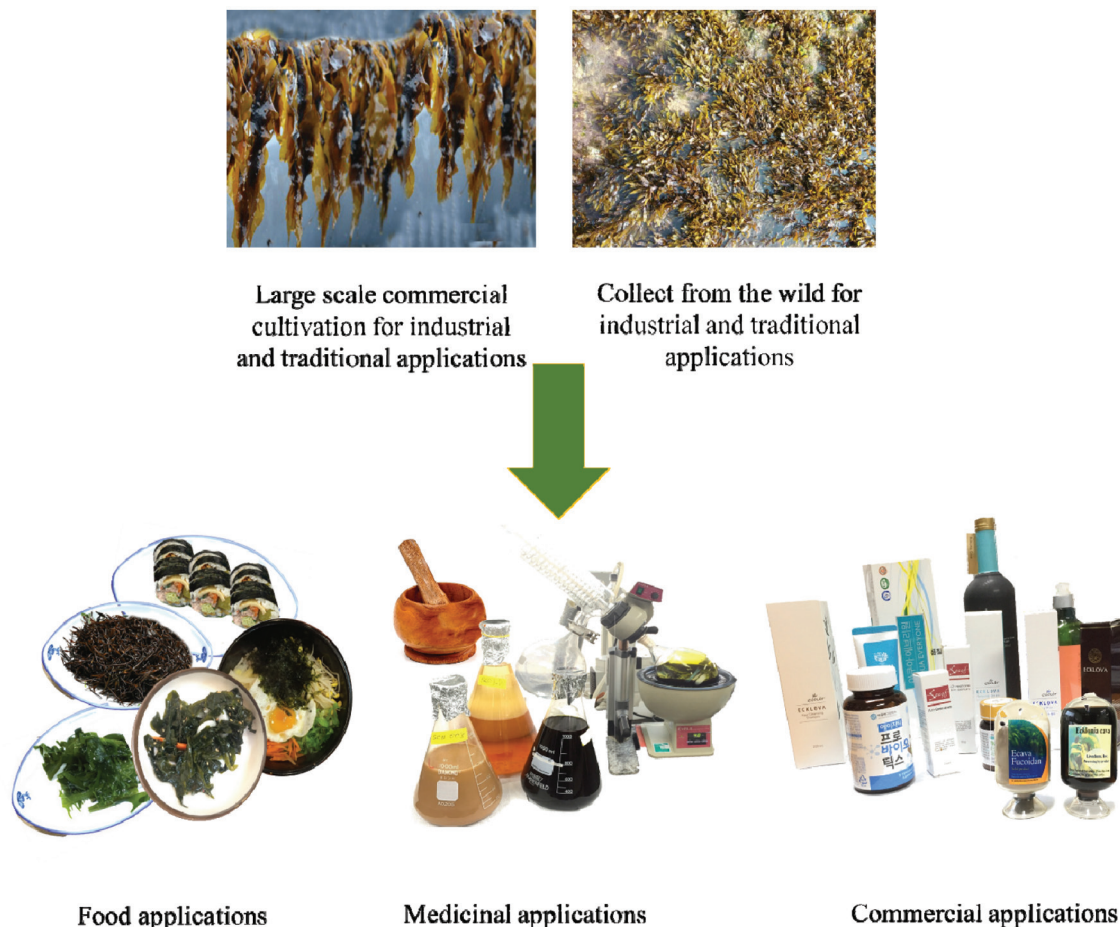
Figure 1. Common applications of seaweeds.

2. Brown seaweeds

2.1. Ecklonia cava (Kamthe)

Ecklonia cava is a brown alga, abundantly found in the subtidal regions of Jeju Island, Korea. *E. cava*, is popular as a food ingredient, fertilizer, as an ingredient in folk medicine, and animal feed stock in Korea and Japan (Le et al., 2009). Specifically, *E. cava*, is commercially cultivated to supply a summer feed for the abalone industry in Korea (Hwang et al., 2012a). *E. cava* has been identified as a potential source of a wide spectrum of secondary metabolites such as phlorotannins, sulfated polysaccharides, and carotenoids. The compounds isolated from this seaweed have shown interesting biological activities in vital industrial applications including functional foods, pharmaceuticals, cosmeceuticals, and nutraceuticals (Wijesinghe and Jeon., 2012a). Previously, a number of studies have reported that the secondary metabolites isolated from *E. cava* render bioactive properties such as antioxidant, anti-diabetes, anti-coagulative, anticancer, antimicrobial, anti-inflammatory, and anti-human immunodeficiency virus (HIV).

2.2. Hizikia fusiforme (Tot)

Hizikia fusiformis is a huge annual brown seaweed that grows in Korea, China, and Japan. *H. fusiformis* is abundant in southern coast, west coast, and Jeju Island in Korea. In the traditional Chinese medicine *H. fusiformis* have been used as an active ingredient for thousands of years (Park et al., 2017). *H. fusiformis* is a popular edible seaweed in East-Asian countries. Besides Korea, *H. fusiformis* is also popular in Japan and China as an edible seaweed (Choi et al., 2009). Tot grows from the foot of the eulittoral to the upper part of the sublittoral zone, around the Korean peninsula. Tot is preserved as a salad, fried with vegetables, and often used as an ingredient in bi-bim-bap. Bi-bim-bap is a mixture of seasoned vegetables, rice, and a paste prepared from chili paper. Recently, the market demand for food and other functional products prepared from *H. fusiformis* has increased due to the excellent nutritional value as well as health promotion properties associated with *H. fusiformis* (Hu et al., 2013). However, Nakamura et al. (2008) have reported that cooked tot also contains a considerable amount inorganic arsenic. Thus, the authors have proposed that the regular consumption of cocked tot might increase cancer risk due to the presence of inorganic arsenic in tot (Nakamura et al., 2008).

2.3. Laminaria japonica (Da-si-ma)

Laminaria japonica is an important seaweed cultured in Korea and commercially cultivated in the temperate seaside areas of northwest Pacific region. *L. japonica* is a popular sea vegetable in many
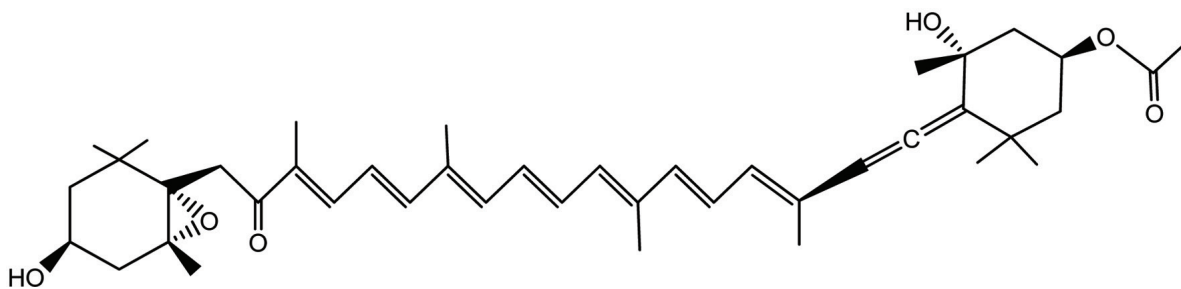
Figure 2. Chemical structure of fucoxanthin.

Asian and Pacific countries including Korea. *L. japonica* is used as an ingredient in traditional Korean medicine. A soup prepared from *L. japonica* is used to increase maternal health recovery of women after giving birth (Post-natal). (Choi et al., 2012; Islam et al., 2013). In addition, *L. japonica* use as a medicinal ingredient in traditional Japanese and Chinese medicine (anti-thrombosis, gall disease, hard lump, edema, anti-thyroid tumor, tuberculosis and beriberi drugs) to treat various disease conditions (Mei et al., 2017; Wang et al., 2018; Zeng et al., 2017). Sliced *L. japonica* (5–6 cm long strips) is boiled with hot water to prepare soup and dried *L. japonica* is used as a cookie with green tea, or pickled in vinegar. In addition, *L. japonica* is also mixed with various traditional Korean food products like bread, muffins, and cake to enhance flavor and quality of the food products (Choi et al., 2012).

2.4. Pelvetia siliquosa (Tumbugi)

Pelvetia siliquosa is another popular edible brown seaweed in Korea. *P. siliquosa* belongs to the family Fucaceae and abundantly grows in the rocky areas of the southern seashores of Korea. *P. siliquosa* is consider an important source of seafood and used as a source of alginic acid. Traditionally, *P. siliquosa* has been consumed as seasoned sea greens for religious services, as well as in soup or fresh seafood salad (Hwang et al., 2012b). A number of studies have reported that the metabolites present in tumbugi have bioactive properties such as anti-diabatic and antioxidant effects (Lee et al., 2003; Lee et al., 2004).

2.5. Sargassum fulvellum (Mo-Ja-ban)

Sargassum fulvellum is a popular seafood in the Korean food market. *S. fulvellum* is an abundant seaweed from southern coast to the eastern coast of Korea. People living in Jeju Island of Korea use this seaweed to prepare salad, soup (Mom-Guk) or use it to prepare side dishes (Choi et al., 2007a; Hwang et al., 2007). In addition to its food value, in the traditional medicine *S. fulvellum* is used as a medicine to treat diseases such as a dropsy, lump, swollen, painful scrotum, and to treat urination problems (Gwon et al., 2013; Kang et al., 2008). As claimed by the previous studies, *S. fulvellum* is a potential candidate for developing functional material due to the interesting bioactive properties such as antioxidant, anticancer, and anticoagulant (De Zoysa et al., 2008; Kang et al., 2008).

2.6. Undaria pinnatifida (Mi-Yeok)

Korea is one of the largest commercial cultivator of *U. pinnatifida* (Choi et al., 2007b). This seaweed has a long history in Korea and

Japan as an edible product. The coastal areas located in south part of Korea is popular for growth and cultivation of *U. pinnatifida*. Fucoxanthin is one of the major bioactive compounds present in Mi-Yeok. Fucoxanthin isolated from Mi-Yeok owing a number of bioactive properties such as antioxidative, anti-cancerous, anti-obesity, angiotensin-converting-enzyme inhibitory, and anti-inflammatory (Prabhasankar et al., 2009; Suetsuna and Nakano, 2000). *U. pinnatifida* is generally served in soup, salad, and side dishes (Kim, 2010). In addition, *U. pinnatifida* is a popular seafood among Korean mothers. Soup prepared from Mi-Yeok is served to lactating mothers to help to increasing postpartum convalescence (Cho et al., 2007).

3. Bioactive compounds reported from edible brown seaweeds

3.1. Carotenoids

Carotenoids are red, orange, and yellow color pigments present in plant leaves, fruits, and flowers. Plants, bacteria, fungi, and algae are the producers of carotenoids. However, carotenoids are also responsible for color spot present in birds, insects, fish, and crustaceans, because many animals incorporate carotenoids to their bodies from their diet (Stahl and Sies, 2003). Carotenoids in photosynthetic organisms help in photosynthesis, photo-protection, phototropism, and photo-reception, and act as a repellent for their natural enemies (Dembitsky and Maoka, 2007; Matsuno, 2001). The central chain of carotenoids is build up with cyclic end-groups substituted with oxygen-containing functional groups. According to their composition, carotenoids are divided into two groups as carotenes and oxocarotenoids or xanthophylls (Stahl and Sies, 2003). Fucoxanthin (Fig. 2) is a well-known carotenoid pigment present in brown seaweeds. Fucoxanthin accounts for around 10% of the total natural production of seaweed carotenoids (Matsuno, 2001). With interesting bioactive properties associated with fucoxanthin, which is a popular ingredient in industries like functional food, cosmeceutical, and nutraceuticals (Peng et al., 2011; Miyashita and Hosakawa, 2018).

3.2. Polyphenols

Polyphenols are water-soluble chemical compounds present in cell vacuole (Harborne, 1998; Manach et al., 2005). Polyphenols are capable of reacting or pairing with one-electron oxidants formed during biological processes. Due to their high electron donating ability, polyphenols are considered as one of the best class of bioactive compounds present in nature (Handique and Baruah, 2002). Polyphenols reported from land plants are polymers of flavonoids and gallic acid and similarly occur in brown seaweeds (phlorotannins) as
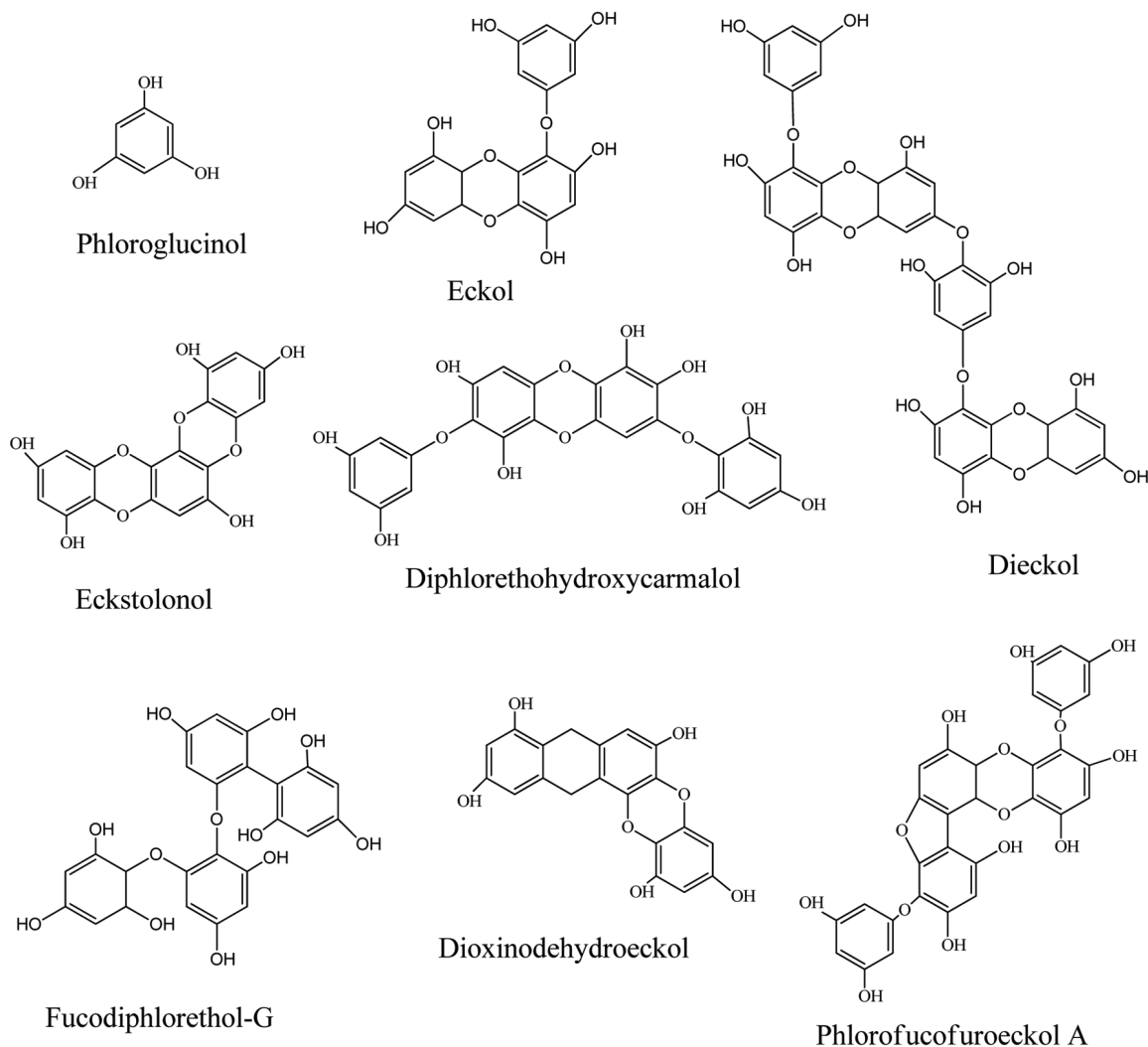
Figure 3. Bioactive phlorotannins isolated from brown seaweeds.

chains of 1,3,5-trihydroxybenzene formed in the acetate-malonate pathway (Li et al., 2011). Phlorotannins produced by brown seaweeds act as herbivore deterrent, digestive inhibitor, UV screen, and antibacterial agents that protect seaweeds from their natural enemies (Targett and Arnold, 1998). In addition, some studies have confirmed that, phlorotannins render a range of bioactive properties such as antioxidant, anticancer, ant-inflammation, anti-allergic, antibacterial, and matrix metalloproteinase inhibition (Wijesinghe and Jeon, 2012b). Due to these diverse bioactive properties, phlorotannins have been identified as an important seaweed metabolite to use as a functional ingredient in food products, pharmaceuticals, and cosmeceuticals (Li et al., 2011). Figure 3 illustrates the structures of some phlorotannins isolated from brown seaweeds.

3.3. Polysaccharides

3.3.1. Alginic acid

Alginic acids are high-molecular-weight polysaccharides reported from the brown seaweed cell wall. Alginic acids are alkali-solu-

ble polysaccharide where the other cell wall constitutes such as fucoidan and laminarin are water-soluble. In water, alginic acid forms a mechanically stable porous hydrogel. Moreover, seaweeds contain approximately 10–40% of alginic acid from on a dry weight basic. Growing depth and seaweed growth season determine the amount of alginic acid in the seaweed biomass (Marriott et al., 2016; Rioux et al., 2007). Alginic acid comprises two kinds of hexuronic acids including α-1,4-linked L-guluronic acid and β-1,4-linked D-mannuronic acid residues arranged in homopolymeric blocks separated by regions of alternating sequences of the two monomers (Fig. 4) (Marriott et al., 2016). In the food industry, alginates are used as thickening agents or metal ion chelators (Gupta and Abu-Ghannam, 2011). In addition, alginates have also been used as an immune-stimulant in aquaculture to increase disease resistance and non-specific immune responses in aquatic species such as abalone, shrimp, and grouper (Lee et al., 2017).

3.3.2. Fucoidans

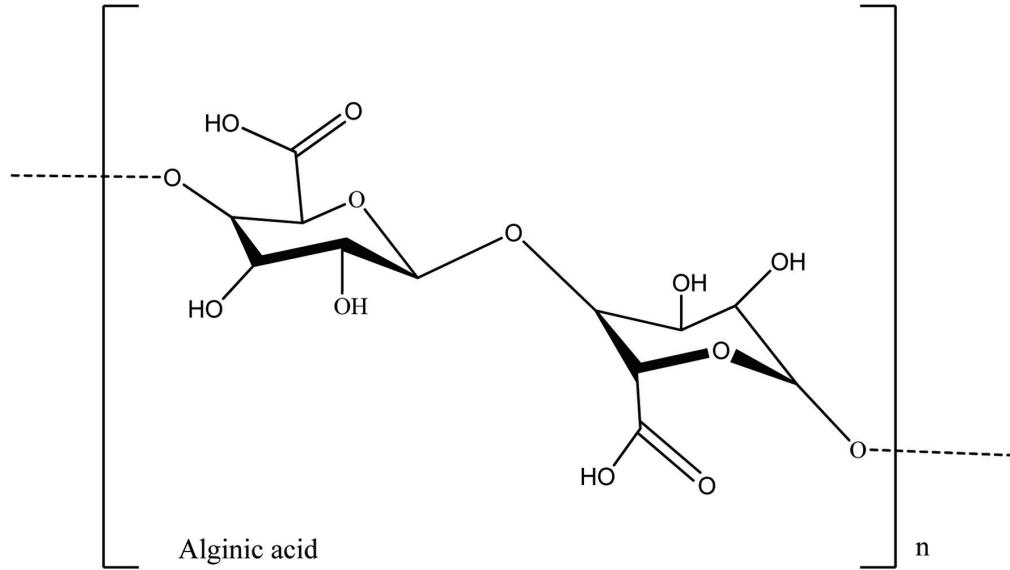Fucoidans are a class of sulfated polysaccharide extracts from

Figure 4. The chemical structure of alginic acids present in brown seaweeds.

brown seaweeds. During the past few decades, fucoidan has gained considerable attention in the biomedical research studies due to its diverse bioactive properties like anti-coagulant, antioxidant, anti-cancer, anti-inflammatory, and immune-modulatory effects (Sanjeewa et al., 2017). Classically, backbone of fucoidan is made of α(1 → 3)-L-fucopyranose residues or alternating α(1 → 3) and α(1 → 4)-linked L-fucopyranosyls or both forms. Moreover, fucoidans contain monosaccharides such as fucose (mainly), mannose, galactose, glucose, arabinose, uronic acids, and xylose (Sanjeewa et al., 2017). Due to the significant differences in fucoidan structure

(fucose linkage, sulfate position, and sugar composition), they are very diverse (Fig. 5) and their structures depend on the species, season, location, and growth stage of the seaweed (Fletcher et al., 2017).

3.3.3. Laminaran

Laminaran is a major storage polysaccharide present in brown seaweeds (Fig. 6). Laminaran represents 35% of seaweed on a dry
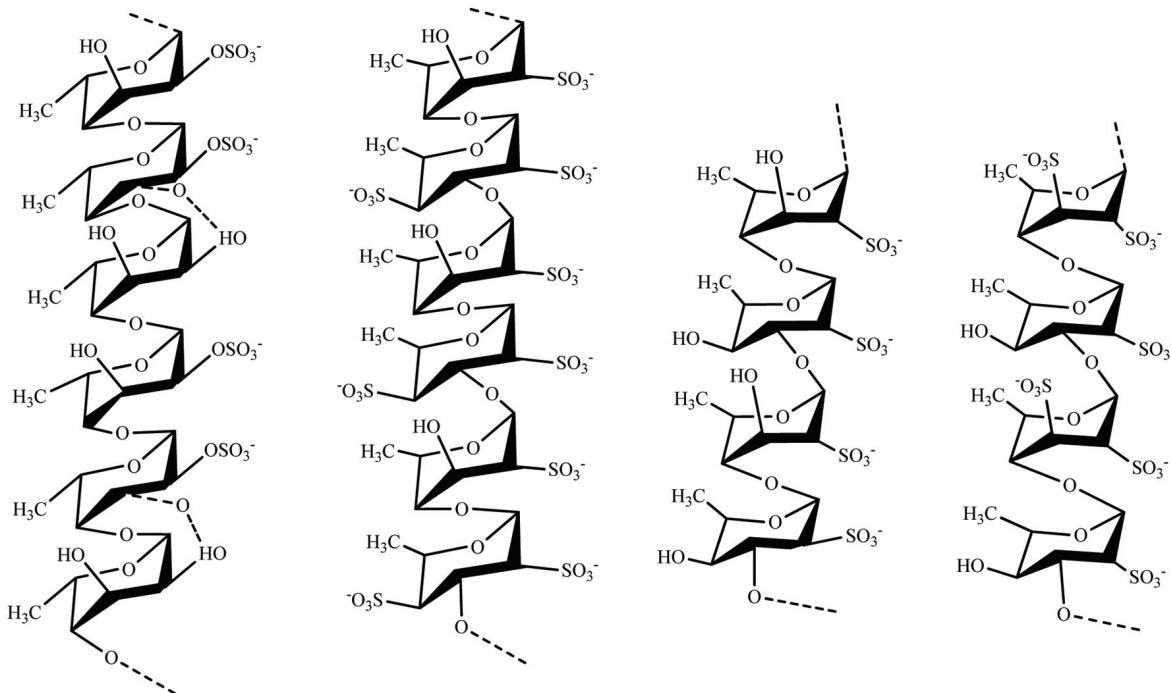

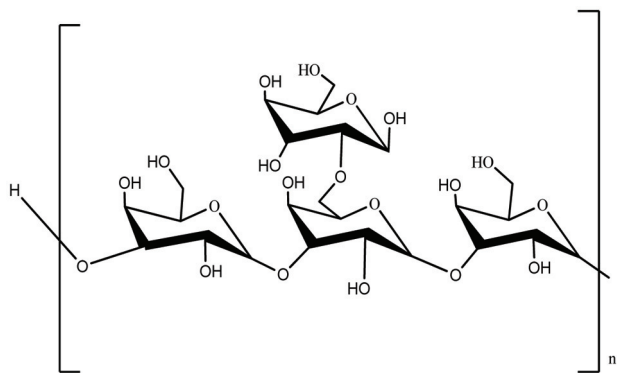**Figure 5. Structural motifs of fucoidans present in brown seaweeds.**

Figure 6. Chemical structure of laminarin presents in brown seaweeds.

weight basis. The percentage of laminaran depends on seaweed species, harvesting time, and extraction method (Yin et al., 2014). Laminaran consists of glucose monomers joined together mainly by (1,3)-β-D-glucan backbone with β (1,6) glycosidic bonds. Laminarans may be separated into two groups as G and M chains, where M chains end with a mannitol as the terminal reducing end and glucose is attached to the end of the G chains. It has been reported that laminaran possesses interesting bioactive properties such as antioxidant, antitumor, anti-inflammatory, and anticoagulant activities (Sanjeewa et al., 2017).

3.4. Sterols

Sterols are major components in the plasma membranes of all eukaryotes (20–30%) but are absent in prokaryotes. Cholesterol is the major sterol in animals, fungi, and yeast capable to produce ergosterol. Other than that phytosterols and fucosterol are major sterols present in higher plants and seaweeds, respectively (Mouritsen et al., 2017; Sanjeewa et al., 2016). Sterols in seaweeds serve as a substantial source of bioactive ingredients. A number of studies have reported that sterols such as ergosterol and fucosterol (Fig. 7) have the potential to be incorporated as an active ingredient in functional food products (Kim and Ta, 2011).

4. Bioactivities of brown seaweed polysaccharides

4.1. Antioxidant ability

According to the previous reports, edible seaweeds grow along the shores of the Korean peninsula, *H. fusiformis*, *L. japonica*, and *E. cava* bio-synthesize secondary metabolites with strong antioxidant properties. Some antioxidant properties of edible brown seaweeds growing along the shores of the Korean peninsula are discussed here.

Siriwardhana et al. (2003) studied the reactive oxygen species (ROS) scavenging and lipid peroxidation inhibition activities of water and organic extracts separated from *H. fusiformis* respectively. According to the results, water extract of *H. fusiformis* had the highest DPPH radical scavenging activity among the other tested extracts (methanol and ethanol). Additionally, the authors reported, that the radical scavenging activities of water extract were stronger than those of the commercial antioxidant (BHA, BHT, and α-tocopherol) under tested conditions (Siriwardhana et al., 2003). Tong et al. (2012) evaluated the antioxidant properties of the extracts separated from three seaweeds including *H. fusiforme, Capsosiphon fulvescens,* and *U. pinnatifida* collected from Wando, Korea. Among the tested seaweed extracts, *H. fusiforme* had a better DPPH radical scavenging activity (90.12%, at a 0.32 mg/mL concentration), followed by *U. pinnatifida*. Additionally, the reducing power of extract of *U. pinnatifida* and *H. fusiforme* had better effects compared to *Capsosiphon fulvescens* (Tong et al., 2014). Lee and Kang (2015) evaluated DPPH radical scavenging effect of 70% ethanolic extract separated from *H. fusiformis*. According to the authors, *H. fusiformis* extract significantly scavenged DPPH radicals with IC_{50} of 9.64 ± 0.78 μg/mL (Lee and Kang, 2015). Wu et al. (2016) reported a novel lectin (65 kDa) isolated from *H. fusiformis* which has the potential to incorporate it as an active ingredient in functional food products. At 1.6 mg/mL concentration, the isolated lectin inhibited DPPH and hydroxyl radicals by 77.23 and 33.65%, respectively (Wu et al., 2016). However, compared to the DPPH inhibitory effect of 70% ethanolic extract (reported by Lee and Kang 2015), the inhibitory effect of lectin was very low. Kim (2010) evaluated the total phenolic contents and antioxidant activities of *U. pinnatifida* and *Capsosiphon fulvescens* under different drying conditions. The authors reported that radical scavenging
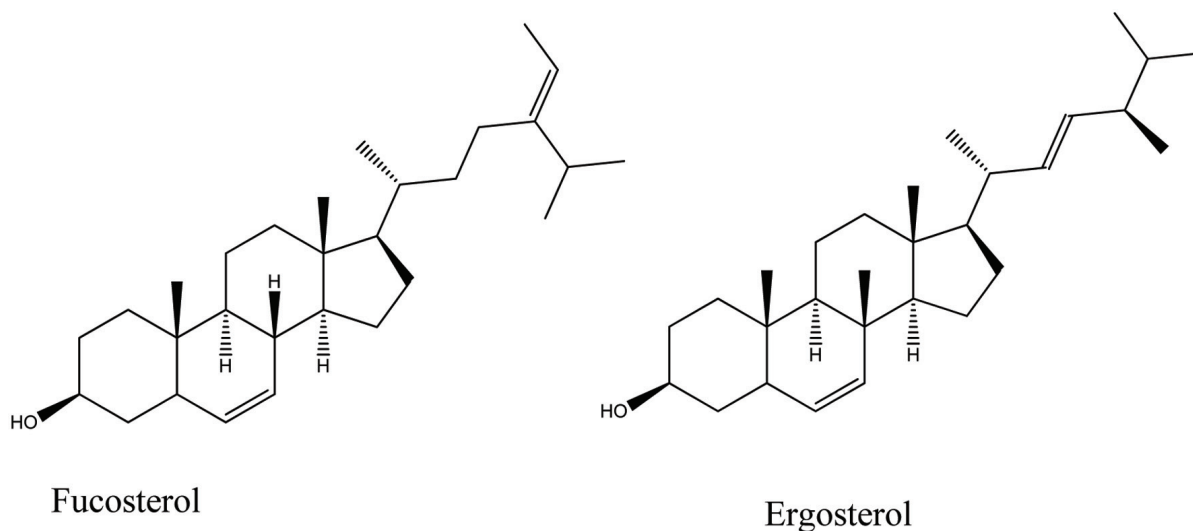

Fucosterol

Ergosterol

Figure 7. Chemical structure of two major sterol present in seaweeds.

Table 1. Antioxidant properties reported from edible Korean brown seaweeds

Seaweed	Active compound/fraction	Effect	Reference
H. fusiformis	Water extract	DPPH radical scavenging	Siriwardhana et al., 2003
	Crude phenolic	DPPH radical scavenging	Tong et al., 2014
	70% Ethanolic extract	DPPH radical scavenging	Lee and Kang, 2015
	70% Ethanolic extract	Protective effect against radiation-induced damage in splenocytes	Kim et al., 2015
	Polysaccharides	Protection against CCL_4 induced liver damage in BALB/c mouse	Wu et al., 2013
	Lectin (65 kDa)	DPPH radical and hydroxyl radical scavenging	Wu et al., 2016
L. japonica	Low molecular weight Polysaccharides	Superoxide radical scavenging properties	Zha et al., 2016
	Crude polysaccharide	oxygen radical absorbance capacity and ABTS radical scavenging	Cui et al., 2016
	Crude polysaccharides	oxygen radical absorbance capacity and ABTS radical scavenging	Yao et al., 2017
	Fucoidan	DPPH radical and hydroxyl radical scavenging	Zhao et al., 2018
E. cava	Phlorotannins	DPPH and hydroxyl radical scavenging	Cha et al., 2012
	Fucoidan	Protective effect against hydrogen peroxide-induced cytotoxicity in PC-12 and MC-IXC neuronal cells	Park et al., 2018
S. fulvellum	Sulphated polysaccharides	DPPH radical scavenging	Choi et al., 2007a
U. pinnatifida	Crude phenolic extracts	DPPH radical scavenging	Kim, 2010
	Ethanolic extract	Hypoxia/reoxygenation-induced oxidative stress inhibition in neuronal cells	Mohibbullah et al., 2015
	Crude phenolic	DPPH radical scavenging activity	Tong et al., 2014
	Fucoidan	DPPH, hydroxyl radical scavenging, and iron chelating ability	Phull et al., 2017

activity and phlorotannins contents were comparatively high in the extracts separated from vacuum dry method compared to the hot air dry method. Thus, the antioxidant properties of seaweeds extracts depended on the processing method employed (Kim, 2010). Zha et al. (2016) evaluated the antioxidant properties of different molecular weight polysaccharides separated from *L. japonica* using superoxide radical scavenging properties of polysaccharides. Their results confirmed, that the low-molecular-weight polysaccharide fraction had a better superoxide radical scavenging effect than the high-molecular-weight fraction (Zha et al., 2016). Cui et al. (2016) reported that a polysaccharide [mole ratio of galactose, mannose and fucose (26.1:1.3:1) and 1,3- and 1-linked galactose] separated from *L. japonica* had remarkably high oxygen radical absorbance capacity (1247.22 μmol trolox equants g^{-1}) and ABTS (−70% at 4mg/mL) scavenging activities (Cui et al., 2016). In another similar study, antioxidant effect of polysaccharide separated from *L. japonica* was documented by Yao et al. (2017). In this study, the authors compared the antioxidant capacity of polysaccharide extracted from different extraction methods such as water extraction and acidic extraction (citric acid, sulfuric acid, hydrochloric acid, and phosphoric acid). According to the results, polysaccharides from citric acid aided extraction method had good ABTS radical scavenging activity (IC_{50} = 1.06 mg/mL) and oxygen radical absorbance capacity (341.87 μmol trolox equants g^{-1}) under the test conditions (Yao et al., 2017). In addition, antioxidant properties of pigment-free fucoidan separated from *L. japonica* was also reported (Zhao et al., 2018). The results revealed *L. ja-*

ponica fucoidan had the potential for developing as antioxidant materials. Under the test conditions, the isolated fucoidans had a better DPPH radical scavenging (IC_{50} = 4.64 mg/mL) and hydroxyl radical scavenging activity. A sulfated polysaccharide fraction (529 kDa) from *S. fulvellum* possessed a strong hydrogen peroxide scavenging activity compared to the commercial antioxidant such as BHA and α-tocopherol. Additionally, the separated polysaccharides inhibited the superoxide radicals, nitric oxide radicals, and DPPH in a dose-dependent manner (Choi et al., 2007a).

Other than the radical scavenging effects, some studies reported that extracts and pure compounds separated from edible brown seaweed render strong antioxidant properties under *in vitro* and *in vivo* conditions. Here we briefly introduce a few curious studies reporting *in vitro* and *in vivo* antioxidant properties of edible Korean brown seaweeds. Cha et al. (2012) studied the protective effect of *E. cava* phlorotannins on UV-induced ROS production in *in vivo* zebrafish model. The results confirmed that, pretreatment of eckol, eckstolonol, phloroglucinol, and triphlorethol-A (50 μM) protect zebrafish against UV-induced ROS generation, NO production, and cell death. In addition, the authors also studied the Inhibitory effect of phlorotannins on UV-B-induced hyperpigmentation in zebrafish embryos. Further they have reported that phlorotannins inhibited the UV-B induced melanin production in zebrafish embryos (Cha et al., 2012). Later, Wu et al. (2013) proclaimed that the water-soluble polysaccharides isolated from *H. fusiformis* had a protective effect on CCL_4 induced liver damage in BALB/c mouse. In relation to the results, administration of separated polysaccharide at a rate of 200

Table 2. Anticancer properties reported from edible Korean brown seaweeds

Seaweed	Active compound/fraction	Cell line and effect	Reference
H. fusiformis	Ethanolic extract	Induce apoptosis via upregulating Tumor necrosis factor-related apoptosis-inducing ligand. *AGS human gastric adenocarcinoma cells	Kim et al., 2009
	Ethanolic extract	Inhibit matrix metalloproteinase and tumour invasiveness and metastasis-related genes in Hep3B human hepatocarcinoma cells	Kim and Choi, 2010
	Ethanolic extract	pre-neoplastic lesions progression in the colon	Son et al., 2018
	Ethanolic extract	Apoptosis cell death in human leukaemia U937 cells	Kang et al., 2011
	5-Hydroxy-3,6,7,8,3′,4′-hexamethoxyflavone	Induction of expression death receptor-associated apoptosis mediators *AGS and DR4 cancer cells	Kim et al., 2012
L. japonica	Crude polysaccharides	Apoptotic cell death. Cervical carcinoma cells (HeLa and U14)	Zhai et al., 2014)
	Crude polysaccharides	Inhibitory effect on tumor growth (nasopharyngeal cancer cell transplanted BALB/C nude mouse)	Zeng et al., 201
	Water soluble polysaccharide	Induced the expression levels of interleukin-2 (IL-2), TNF-α and inhibited the expression of vascular endothelial growth factor	Zhu et al., 2016
	Fucoxanthin	Up-regulated expression of p53, $p21^{waf1/cip1}$, PUMA, and FAS and the down-regulated expression of Bcl-2 in lung cancer cells including A549, H460, SPC-A1, and H1299	Mei et al., 2017
E. cava	Fucoidans	Inhibited the colony formation of skin melanoma cell (SK-MEL-28) and the colon cancer cells (DLD-1)	Ermakova et al., 2011
U. pinnatifida	Fucoidans	Induce apoptosis in cancer cells including HeLa, PC-3, A549, and HepG2.	Synytsya et al., 2010

mg/kg/day significantly reduced the CCl_4 induced liver damage compared to the control group (Wu et al., 2013). Mohibbullah et al. (2015) compared the neuroprotective effect of 23 ethanolic extracts separated from seaweed against hypoxia/reoxygenation-induced oxidative stress in cultured hippocampal neurons. According to the authors, *Gracilariopsis chorda* (red alga) had the highest neuroprotection at 15 µg/mL, followed by *U. pinnatifida*. (Mohibbullah et al., 2015). Kim et al. (2015) also evaluated the protective effect of *H. fusiforme* extract on radiation-induced damage in splenocytes (C57BL/6 mouse). In this study the authors demonstrated pre-incubation of splenocytes with *H. fusiforme* (3.1–25 µg/mL) extract prior to gamma-ray irradiation (1.5 Gy) which had the potential to increase cell viability and proliferation by reducing elevated ROS levels in gamma irradiated splenocytes compared to the control group (Kim et al., 2015). In addition, fucoidan separated from *E. cava* was also found to possess protective effect against hydrogen peroxide-induced cytotoxicity in PC-12 and MC-IXC neuronal cells (Park et al., 2018). The isolated fucoidan restored mitochondrial damage by increasing the mitochondrial membrane potential ($\Delta\psi$m) and ATP levels as well as regulating mitochondrial-mediated proteins (p-AMPK and BAX). The aforementioned antioxidant properties are summarized in Table 1.

4.2. Anticancer activity

Induction of apoptosis in cancer cells is a major strategy for eliminating cancer cells. Tumor necrosis factor-related apoptosis-inducing (TNFAI) ligand is a transmembrane protein which capable of binding to its membrane-bound death receptors. Coupling

of TNFAI and its receptor transmit an apoptotic signal via their intracellular death domains. Which can induce apoptosis in cancer cells (Kim et al., 2009). Kim et al. (2009) evaluated the anticancer effects of ethanolic extract separated from *H. fusiforme* on AGS human gastric adenocarcinoma cells. The results revealed that *H. fusiforme* extract (0–25 µg/mL) had the potential to induce apoptosis in cancer cells via up-regulating tumor necrosis factor-α (TNF-α) expression in cancer cells (Kim et al., 2009). Later, Kim and Choi (2010) reported ethyl alcohol fraction separated from *H. fusiforme* has a potential to inhibit matrix metalloproteinase (MMP) activity and regulates tight junction related protein expression in Hep3B human hepatocarcinoma cells. In this study, the authors demonstrated the regulation of MMP activity related genes (MMP-1, MMP-2, TIMP-1, and TIMP-2) and tumor invasiveness and metastasis-related genes (claudins, E-cadherin, IGF-1R, and TSP-1) are responsible for induce apoptosis in cancer cells (Kim and Choi, 2010). In addition, 5-hydroxy-3,6,7,8,3′,4′-hexamethoxyflavone isolated from 80% ethanolic extract of *H. fusiforme* was also found to possess promising anticancer properties against human AGS carcinoma cells and DR4 in cancer cells (Kim et al., 2012). The isolated compound dose-dependently increased (1–10 µg/mL) the death receptor-associated apoptosis mediators including Fas, Fas L, FADD, TRADD. In addition, Son et al. (2018) proclaimed that ethanol extract from *H. fusiforme* had the potential to reduce azoxymethane-induced colonic aberrant crypt foci (ACF) formation in F344 male rats (5 weeks, 150 g). ACF is a term used to describe the pre-neoplastic lesions in the colon which progress into colorectal cancers (Son et al., 2018). Kang et al. (2011) noted that ethyl alcohol extract of *H. fusiforme* had the potential to induce apoptosis in human leukemia U937 cells. Their

results indicated that the down-regulated expression of IAP family members such as IAP-1, IAP-2, and XIAP, as well as inhibition of Bcl-2 proteins were responsible for the apoptotic cell death of U937 cells (Kang et al., 2011).

Ermakova et al. (2011) attempted to studied the anticancer properties of fucoidans isolated from three seaweed species grown in the Korean costs including *S. hornery*, *E. cava*, and *Costaria costata*. According to their results, fucoidans (100 μg/mL) inhibited the colony formation of skin melanoma cell (SK-MEL-28) and the colon cancer cells (DLD-1). Cervical carcinoma is a major cancer in women globally and threatens the health of females who are in the reproductive age (Zhai et al., 2014). Crude polysaccharides from *L. Japonica* were evaluated against two cervical carcinoma cells (HeLa and U14) to explore the potential of *L. Japonica* polysaccharides to develop as anticancer drugs (Zhai et al., 2014). According to the results, *L. Japonica* polysaccharide induced apoptosis in HeLa and U14 cells with IC_{50} values of 85.74 and 76.91 μg/mL, respectively. The nasopharyngeal carcinoma cells inhibitory effect of a polysaccharide separated from *L. Japonica* was recently documented by Zeng et al. (2017). In this study, the authors demonstrated that the administration of 12.5–50 mg/kg polysaccharide had significant inhibitory effect on tumor growth (nasopharyngeal cancer cell transplanted BALB/C nude mouse). In another recent study, fucoxanthin isolated from *L. Japonica* was evaluated for its anticancer effect on lung cancer cells including A549, H460, SPC-A1, and H1299. In this study, the up-regulated expression of p53, $p21^{waf1/cip1}$, PUMA, and FAS and the down-regulated expression of Bcl-2 were found to be responsible for inducing apoptosis in tested cancer cells (Mei et al., 2017). In addition to fucoxanthin, a water-soluble polysaccharide separated from *L. Japonica* was found to possess anticancer properties in mouse (female kunming mouse) bearing H22 liver cancer cells as well as *in vitro* in H22 hepatoma cells. Moreover, they found that administration of polysaccharides induced the expression levels of interleukin-2 (IL-2), TNF-α and inhibited the expression of vascular endothelial growth factor (Zhu et al., 2016).

Synytsya et al. (2010) evaluated the anticancer properties of fucoidan isolated from *U. pinnatifida* using four cancer cell lines, including cervical cancer cells (HeLa), prostate cancer cells (PC-3), carcinomic human alveolar basal epithelial cells (A549), and hepatocellular carcinoma cells (HepG2). According to the results, fucoidans had considerable anticancer effect against all tested cancer cells at concentrations of 0–0.8 mg/mL. However, the authors reported that fucoidans from *U. pinnatifida* had slightly lower activity than the commercial fucoidan against PC-3 and A549 cancer cells (Synytsya et al., 2010). Other than the aforementioned studies, Cho et al. (1997) studied anti-mutagenic and anticancer properties of 9 seaweeds collected from Korean peninsula including ceylon moss, chlorella, sea lettuce, sea mustard, sea tangle, sporophyll of sea mustard, and purple laver. The authors assessed the anticancer effect of 20% methanolic extracts collected from the aforementioned seaweeds on *Salmonella typhimurium* TA100 cells and human colon cancer (HT-29) cells. The 20% methanol extracts had strong anti-mutagenic activity against aflatoxin B_1 and N-methyl -N′-nitro-N-nitrosoguanidine in *S. typhimurium* TA100. Moreover, sea mustard extracts, and sea tangle had cytotoxic effects on HT-29 human colon carcinoma cells at the 0.2 mg/mL (Cho et al., 1997). Table 2. represent some anticancer properties reported in edible Korean seaweeds.

4.3. Anti-inflammatory activity

Senevirathna et al. (2012) studied the nitric oxide (NO) inhibi-

tory effect of *L. japonica* enzymatic digests on lipopolysaccharide (LPS)-stimulated RAW 264.7 cells. According to the results, Celluclast- and AMG enzyme-assisted digests had more than 60% NO inhibition at concentrations between 50 and 500 μg/mL compared to the LPS-stimulated RAW 264.7 cells (Sevevirathne et al., 2012). Jung et al. (2013) attempted to evaluate the *in vitro* anti-inflammatory activities of fucosterol and seven phlorotannins (phloroglucinol, eckol, dieckol, phlorofucofuroeckol-A, dioxinodehydroeckol, 7-phloroeckol) collected from edible brown seaweed *E. bicyclis*. The results revealed that the seven phlorotannins isolated from *E. bicyclis* effectively inhibited the LPS-Induced NO production via down-regulating inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2) protein expression in LPS-stimulated RAW 264.7 cells. Additionally, fucosterol inhibited tert-butylhydroperoxide-induced ROS production and down-regulated the expression of iNOS and COX-2 protein expressions (Jung et al., 2013). Gwon et al. (2013) investigated the anti-inflammatory effect of the hexane fraction of *S. fulvellum* in LPS-induced RAW 264.7 cells and phorbol 12-myristate 13-acetate (PMA)-induced mouse-ear edema. The results revealed that *S. fulvellum* extracts had the potential to inhibit the LPS-induced inflammatory responses in macrophages by reducing NF-κB transcriptional activity and NF-κB translocation into the nucleus by inhibiting phosphorylation of inhibitor κB-α. Additionally, down-regulated expression of Akt and mitogen-activated protein kinases (MAPKs) in the LPS-stimulated RAW 264.7 cells was also observed in this study. In addition, *S. fulvellum* extracts suppressed PMA-induced mouse-ear edema.

Cho et al. (2007) studied the anti-inflammatory effect of dichloromethane, ethanol, and boiling water extracts of the brown seaweeds *U. pinnatifida* and *L. japonica* using a BALB/c mouse model. The ethanol and dichloromethane (0.4 mg/ear) extracts of *U. pinnatifida* inhibited inflammatory symptoms induced by phorbol 12-myristate 13-acetate (PMA) in mouse ear edema by 95.3 and 65.5%, respectively (Cho et al., 2007). Furthermore, Khan et al. (2009) studied the protective effect of *U. pinnatifida* methanol extracts on PMA induced ear edema in BALB/c mouse model. According to the results, the methanol extract of the seaweed had considerable protective effect in ear edema induced by PMA, with an IC_{50} of 10.3 mg/mL. Nevertheless, compared to the study carried out by Cho et al. (2006) the ethanol extract of *U. pinnatifida* had more than 25 times activity against PMA induced ear edema in BALB/c mouse compared to the methanol extract of *U. pinnatifida*. In contrast to the organic solvent extraction methods, supercritical fluid extraction (SFE) method is a novel green extraction technique which has the potential to increase the bioactive compounds recovery, reduce the environmental pollution, and enhance the extraction rates (da Silva et al., 2016). Kang et al. (2016) attempted to evaluate the anti-inflammatory effects of *U. pinnatifida* using SFE in a BALB/c mouse (8–10 weeks old, 20–25 g body weight) model. In this study, the authors reported that the essential oil from *U. pinnatifida* had a protective effect against BALB/c mouse ear inflammation induced by PMA, with IC_{50} values of 87, 134, and 158 μg per ear for edema, erythema, and blood flow, respectively (Kang et al., 2016). Fucoidan isolated from *U. pinnatifida* also possessed anti-inflammatory properties against IL-1β-induced COX-2 expression in rabbit articular chondrocytes in a dose-dependent (0–100 μg) and time-dependent (0–48 h) manner (Phull et al., 2017).

Microglial cells (BV-2) are specialized macrophage-like immune cells present in the central nervous system, which are involved in the initiation of innate immune responses. Specifically, the activated cells are responsible for the production of pro-inflammatory mediators such as NO, prostaglandin E2 (PGE_2), and

TNF-α (Kang et al., 2013). Jung et al. (2007) reported that the methanolic extract obtained from *H. fusiforme* had a suppressive effect on TNF-α production in LPS-stimulated BV-2 cells. According to the results, pre-incubation of *H. fusiforme* extract together with BV-2 cells prior to LPS stimulation inhibited the LPS-induced TNF-α production by inhibiting the nuclear factor-κB (NF-κB) translocation (Jung et al., 2007). Kang et al. (2013) evaluated the anti-inflammatory effects of 5-hydroxy-3,6,7,8,3′4′-hexamethoxyflavone isolated from *H. fusiforme*. In this study the authors demonstrated that the isolated compound had the potential to suppress NF-κB associated proteins in LPS-induced BV-2 cells. Lee and Kang (2015) attempted to evaluate the anti-inflammatory effects of 70% ethanol extract collected from *H. fusiformis* using BV-2 microglial cells. Accordingly, pretreatment of *H. fusiformis* extract (0–100 μg/mL) inhibited the activation of BV-2 cells through down-regulation of inflammation-related gene expression (iNOS) and inhibiting pro-inflammatory cytokine production including TNF-α and IL-6.

4.4. Immunomodulation properties

Other than anti-inflammatory properties, some brown seaweed metabolites were found to possess immunomodulatory properties under *in vitro* and *in vivo* conditions. Park et al. (2017) attempted to study the immunomodulatory properties of extract separated from *H. fusiforme* using RAW 264.7 macrophage and using seven weeks old male C57BL mouse model (Park et al., 2017). According to the results, pre-incubation of *H. fusiforme* extract with RAW 264.7 cells increased the production of NO, PGE$_2$, and TNF-α activity in murine macrophage cells at concentrations of 0–200 μg/mL without altering cell viability. Specifically, the authors found that the active compound in the extract was fucosterol which was responsible for the immunomodulatory properties of Khan the extract. Jeong et al. (2015) attempted to evaluate the immunomodulatory properties of polysaccharides separated from *H. fusiforme* using murine macrophage and splenocytes. According to the results, the polysaccharides exposed cells dose-dependently induced the production of NO, iNOS, and inflammation related cytokine production from macrophage cells (Jeong et al., 2015). In another study, Feng et al. (2015) reported the immunomodulatory effects of a homogeneous polysaccharide (molecular mass of 2.24×10^6 Da) separated from *L. japonica*. The isolated polysaccharide induced the activation of macrophage cells by up-regulating inflammation associated signal pathways such as NF-κB and MAPK (Fang et al., 2015). In addition, Zha et al. (2015) also reported a polysaccharide isolated from *L. japonica* (molecular mass of 2.89×10^6 Da) has a potential to act as immunostimulaory agent. Specifically, in this study the authors observed that the isolated polysaccharide had the potential to upregulate proteins associated with NF-κB and MAPKs signaling pathways in RAW 264.7 cells (Zha et al., 2015). Table 3. illustrates some anti-inflammatory and immune-modulatory properties reported from edible Korean brown seaweeds with their references.

4.5. Antidiabetic and Anti-obesity activities

Kim and Lee (2012) evaluated the anti-obesity properties of fucoidan isolated from *U. pinnatifida*. The authors evaluated the obesity-specific therapeutic property of fucoidan in 3T3-L1 adipocytes. According to the results, exposure of adipocytes to fucoidan (1–100 μg/mL) inhibited the activation of key markers in adipocyte differentiation including CCAAR/enhancer-binding

protein α, PPARγ, and adipocyte protein-2 proteins as well as activation of TNFα, MCP-1, and PAI-1 in 3T3-L1 cells (Kim and Lee, 2012). Kim et al. (2014) reported *in vivo* anti-obesity effect of fucoidan purchased from a commercial outlet (Haewon Biotech, Seoul, Korea). The authors studied the anti-obesity activity using a high fat diet (HFD)-induced obesity in C57BL/6 mouse model. Their results revealed that, HFD + 1% fucoidan and HFD + 2% fucoidan suppressed mRANA expression of aP2, PPARγ, and ACC in epididymal fat tissues compared to the only HFD administrated group (Kim et al., 2014). Oh et al. (2016) studied the anti-inflammatory and anti-diabetic effects of four brown seaweeds (*U. Pinnatifida*, *L. Japonica*, *S. fulvellum*, and *H. fusiforme*) in a high-fat diet-induced obese mouse. The authors reported that mouse fed *L. Japonica* with HFD had improved insulin resistance and reduced circulating pro-inflammatory cytokines despite being obese. In addition, supplementation of HFD with *U. Pinnatifida*, *S. fulvellum*, and *H. fusiforme* reduced inflammation in the absence of decreased adipose depot mass and improvement of insulin resistance male C57BL/6N mouse (Oh et al., 2016). Polysaccharide isolated from *L. japonica* was also found to possess antidiabetic properties in mouse with alloxan-induced diabetes (Jia et al., 2014). According to the authors, administration of *L. japonica* (200 mg/kg for 28 days) prevented body-weight loss, fasting blood glucose levels, and increased serum insulin levels in diabetic mouse. In addition, the tested polysaccharide decreased the total cholesterol, triglycerides, and low-density lipoprotein-cholesterol levels, and increased high-density lipoprotein-cholesterol levels in diabetic mouse.

4.6. Anti-microbial properties

Thompson and Dragar (2004) attempted to evaluate antiviral properties of a galactofucan isolated from *U. pinnatifida* against herpes simplex virus (HSV). In this study, the authors evaluated, antiviral activity of 32 clinical strains of HSV which included 14 strains of HSV-1 and 18 strains of HSV-2. Enterovirus 71 is a major etiological agent of hand, foot, and mouth disease as well as being is responsible for severe neurological symptoms developed in young children (Yue et al., 2017). Recently, Yue et al. (2017) assessed inhibitory effects of a polysaccharide purified from *L. japonica* against Enterovirus 71 (E71). In this study, the authors reported that the incubation of RD cells with isolated polysaccharides had the potential to reduce infection of E71 to human RD cells in a dose- and time-dependent manner. Cao et al. (2016) reported that polysaccharide separated from *L. japonica* has inhibitory effect on respiratory syncytial virus. The results revealed the polysaccharide extracted from *L. japonica* had a dose-dependent inhibitory effect on respiratory syncytial virus replication (Cao et al., 2016). In addition to antiviral activity, Liu et al. (2017) reported that depolymerized fucoidans separated from *L. japonica* had the potential to suppress the growth of *Staphylococcus aureus* and *Escherichia coli* at concentrations between 5 and 10 mg/mL (Liu et al., 2017). Additionally, methanolic extract separated from *H. fusiformis* were found to possess antibacterial properties against several pathogenic bacterial strains including *Escherichia coli*, *S. aureus*, *Bacillus subtilis*, *Enterobacter aerogenes*, and *Shewanella* sp (Ming-Jiang et al., 2016).

Antimicrobial properties of ethanolic extract separated from *S. fulvellum* were previously assessed by Yoon et al. (2010). The authors reported that, *S. fulvellum* extract inhibited the growth of several bacterial pathogens including, *B. subtilis*, *Clostridium perfringens*, *Lactobacillus plantarum*, *S. aureus*, *Listeria monocytogenes*, *Saccharomyces cerevisae*, and *Candida tropicalis* at a concentration of 4 mg/mL (agar diffusion assay) (Yoon et al., 2010).

Table 3. Anti-inflammatory and immune-modulatory properties reported from edible Korean brown seaweeds

Seaweed	Active compound/fraction	Effect	Reference
L. japonica	Celluclast enzyme assisted extract	Nitric oxide (NO) inhibitory properties on LPS-stimulated RAW 264.7 cells	Sevevirathne et al., 2012
	Boiling water extracts	Inhibitory effect on PMA induced inflammation in mouse model	Cho et al., 2007
	Purified sulphated polysacharide	Induced activation of NF-κB and MAPK signal pathways	Zha et al., 2015
	Homogeneous polysaccharide (2.24×10^6 Da)	Induced activation of NF-κB and MAPK signal pathways	Fang et al., 2015
H. fusiforme	Methanolic extract	Suppressive effect on TNF-α production in LPS-stimulated BV-2 cells	Jung et al., 2007
	70% ethanolic extract	Inhibit TNF-α and IL-6 production in LPS-induced BV-2 cells	Lee and Kang, 2015
	5-Hydroxy-3,6,7,8,3'4'-hexamethoxyflavone	Suppress NF-κB associated proteins in LPS-induced BV-2 cells	Kang et al., 2013
	Fucosterol rich extract	Induced production of NO, PGE_2, and TNF-α from macrophage cells	Park et al., 2017
	Crude polysaccharides	induced the production of NO, iNOS, and inflammation related cytokine production from macrophage cells	Jeong et al., 2015
S. fulvellum	Hexane fraction	Inhibitory effect on NF-κB associated signal molecule expression	Gwon et al., 2013
E. cava	Ethanolic extracts	Suppressor of cytokine signalling	Kim et al., 2008
	Phlorotannins	Inhibits histamine release on human basophilic leukamia (KU812) and rat basophilic leukamia (RBL-2H3)	Le et al., 2009
U. pinnatifida	Boiling water extracts	Inhibitory effect on PMA induced inflammation in mouse model	Cho et al., 2007
	Methanol extract	Protective effect against mouse ear edema induced by PMA	Khan et al., 2009
	Supercritical fluid extracts	PMA induced ear edema, erythema, and blood flow in mouse model	da Silva et al., 2016
	Fucoidan	IL-1β-induced COX-2 expression in rabbit articular chondrocytes	Phull et al., 2017

4.7. Anti-coagulant properties

Heparin is a well-known commercial anticoagulant drug available in the market. However, oral administration of heparin and low-molecular-weight heparin is limited because the enzymes secreted by bacteria in the gut increase the degradation and desulfation before those anticoagulants enter to the blood circulation (Zhao et al., 2016). Zhao et al. (2016) evaluated the antithrombotic activity of orally administered low-molecular-weight fucoidan isolated from *L. Japonica*. According to the authors, the low-molecular-weight fucoidan (7.6 kDa) had better absorption and antithrombotic activity in male wistar rats than the medium-molecular-weight fucoidan (35 kDa). Specifically, oral administration of the low-molecular-weight fucoidan at 400–800 mg/kg prolonged the activated partial thromboplastin time (APTT) and thrombin time (TT) in male wistar rats. Anticoagulant properties of a sulfated polysaccharide isolated from *E. cava* and commercial fucoidan was earlier assessed by Wijesinghe et al. (2011). The results revealed the polysaccharide isolated from *E. cava* had strong anticoagulant activity compared to that of a commercial fucoidan in APTT, TT, and prothrombin time (PT) clotting assays *in vitro* (Wijesinghe et al.,

2011).

5. Conclusions

Edible brown seaweeds are abundant in the coastal areas of the Korean peninsula and its Islands such as Jeju. This review reports on the available edible Korean brown seaweeds, dealing with health promotion properties and compounds being isolated from Korean edible brown seaweeds. Most of the studies reported that, the isolated compounds and crude extracts isolated from these seaweeds exhibited promising bioactive properties such as antioxidant, anti-cancer, anti-inflammatory, immunomodulatory, anti-diabetic, anti-microbial, and anti-coagulant effects. Some comparative studies reported the secondary metabolites present in these edible seaweeds which are more active than the commercial drugs. However, most of the studies limited to cultured cells and/or with laboratory animals like zebrafish or mouse models. Lack of clinical trials and detail investigations with those extracts reduced the industrial level applications of this untapped resource. Therefore, continued research with those identified compounds is required to develop

functional products such as cosmeceuticals, nutraceuticals, functional foods, and commercial drugs. In addition, dissemination of scientific results to general population is an important requirement to increase seaweed consumption all around the world. Future research work dealing with edible Korean seaweed bioactivities should be focus to explain the mode of action of isolated compounds under *in vivo* conditions. These approaches will be a useful approach to develop industrially useful products.

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