CHAPTER FOUR

Seaweed and seaweed-derived metabolites as prebiotics

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Contents

Abstract

Seaweeds and their bioactive compounds, particularly polysaccharides and phenolics can be regarded as great dietary supplements with gut health benefits and prebiotics. These components are resistant to digestion by enzymes present in the human gastrointestinal tract, also selectively stimulate the growth of beneficial gut bacteria and the production of fermentation products such as short chain fatty acids. Commonly, the health benefits of seaweed components are assessed by including them in an in vitro anaerobic fermentation system containing human fecal inocula that mimics the environment of the human large bowel. Regarding to the complex interactions between dietary components, gastrointestinal physiological processes, and gut microbiota are difficult to model in vitro. Consequently it is important to follow up the

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promising in vitro results with in vivo animal or human testing. The aim of this chapter is to have a comprehensive review on the application of seaweeds and seaweed-derived metabolites as prebiotics, and understand the trends, gaps and future directions of both scientific and industrial developments. This work contributes to develop and expand new platform of seaweed utilization for higher-value products, particularly to functional food and nutraceutical industries in order to serve the social demand for health awareness and support economic development.

1. Background

Marine macroalgae or seaweeds constitute approximately 25,000–30,000 species (Santos et al., 2015), with a great diversity of forms and sizes. They can be categorized into different taxonomic groups reflecting their pigmentation, including brown algae (Phaeophyceae), red algae (Rhodophyceae), and green algae (Chlorophyceae) (Mohamed, Hashim, & Rahman, 2012). Seaweeds have fast growth rates and do not require arable land, fresh water, and fertilizer, so they become an appealing source for commercialization (Lorbeer, Tham, & Zhang, 2013). The cultivation of seaweeds has been growing rapidly and is now practiced in about 50 countries. 28.5 million tonnes of seaweeds and other algae were harvested in 2014 to be used for direct consumption, or as a starting material for the production of food, hydrocolloids, fertilizers, and other purposes (FAO, 2016). Recently, the annual global production of alginate, agar, and carrageenan that are the most important seaweed hydrocolloids for various applications across the food, pharmaceutical, and biotechnology industries has reached 100,000 tonnes with a gross market value just above USD 1.1 billion (Rhein-Knudsen, Ale, & Meyer, 2015).

Seaweeds also contain a great variety of structurally diverse bioactive metabolites not produced by terrestrial plants (Gupta & Abu-Ghannam, 2011b). Seaweeds are rich in carbohydrates, proteins, polyunsaturated fatty acids (PUFAs) including omega-3 fatty acids, and minerals as well as polyphenols, pigments (chlorophylls, fucoxanthins, phycobilins), and mycosporine-like amino acids (MAAs). These compounds possess various biological functions including antioxidant, anti-HIV, anticancer, antidiabetic, antimicrobial, anticoagulant, antivirus, anti-inflammatory, immunomodulatory, prebiotic and cholesterol lowering effects (Holdt & Kraan, 2011). Although seaweed bioactive compounds are attractive for commercialization in different functional food and nutraceutical products, the use of seaweed for this purpose is still not extensive.

There are many publications reported on the functional properties of seaweed extracts. However, the efficiency of the extraction procedures for the retrieval of active compounds from seaweeds may be inhibited by the complex and heterogeneous structure and composition of seaweed cell walls in comparison to plants that have a cell wall mostly consisting of cellulose and hemicellulose. The main cell wall and storage polysaccharides of seaweeds vary with taxonomy. The structural polysaccharides of green seaweeds are sulfated polysaccharides, such as ulvans and sulfated galactans, xylans, and mannans, while the main storage polysaccharide is starch. Brown seaweeds contain laminarins as the storage polysaccharide, and the main cell walls are composed of alginic acids, fucoidans, and sargassans. On the other hand, red seaweed cell walls consist of agars, carrageenans, xylans, water-soluble sulfated galactans, and porphyrins (mucopolysaccharides), and the main storage polysaccharide is floridean starch (amylopectin-like glucan) (Kraan, 2012; Mišurcová, 2012). This is further complicated by a tightly-integrated network of biopolymers in seaweed cell walls, mainly polysaccharides, which are associated with proteins, proteoglycans, polymeric phenols, and various bound ions such as calcium and potassium (Jeon, Wijesinghe, & Kim, 2012; Synytsya, Čopíková, Kim, & Park, 2015). An example of the structure model of a brown seaweed cell wall is shown in Fig. 1. Although the complex structure of seaweed cell wall is the major obstacles for extraction process, these cell wall-derived polysaccharides can be regarded as great dietary fibers, as they are resistant to digestion by enzymes present in the human gastrointestinal tract, and selectively stimulate the growth of beneficial gut bacteria as prebiotics. The aim of this chapter is to have a comprehensive review on the application of seaweeds and seaweed-derived metabolites as prebiotics, and understand the trends, gaps and future directions of both scientific and industrial developments.

2. Introduction to seaweeds and their importance

2.1 Current commercially produced seaweeds

According to FAO (2018), from 2005 to 2015, the world production of seaweeds had doubled and reached 30.4 million tonnes, of which the marine aquaculture sector contributed about 29 million tonnes in about 50 countries. The top 10 producer are China, Indonesia, the Philippines, the Republic of Korea, the Democratic People's Republic of Korea, Japan Malaysia, Zanzibar, Madagascar and the Solomon Islands; while Chinese

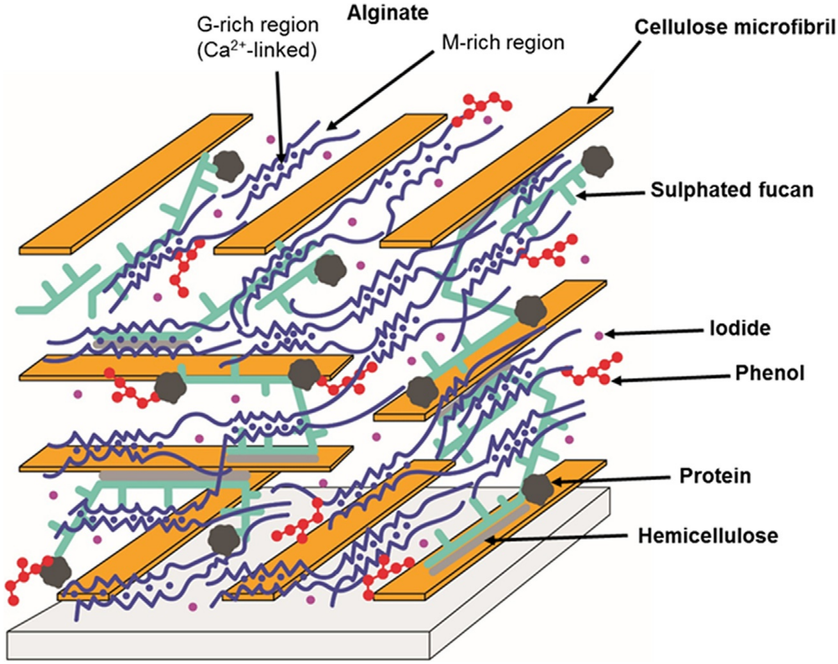

Fig. 1 Structure model of the brown seaweed cell wall; some sulfated fucans are tightly associated with cellulose microfibrils (flat ribbon-like shape), and they are embedded within the alginate network. Hemicellulose components (short chain form) link with the cellulose by hydrophobic interactions and connect with the sulfated fucans. Alginates and phenolic compounds are associated and can form high molecular weight complexes. Proteins are linked with sulfated fucans and covalently attached to phenolics. *Adapted from Kloareg, B., & Quatrano, R. S. (1988). Structure of the cell walls of marine algae andecophysiological functions of the matrix polysaccharides*. Oceanography and MarineBiology-an Annual Review, 26*, 259–315, Michel, G., Tonon, T., Scornet, D., Cock, J. M., & Kloareg, B. (2010). The cell wallpolysaccharide metabolism of the brown alga* Ectocarpus siliculosus. *Insights into theevolution of extracellular matrix polysaccharides in eukaryotes*. New Phytologist, 188*, 82–97, Deniaud-Bouët, E., Kervarec, N., Michel, G., Tonon, T., Kloareg, B., & Hervé, C. (2014). Chemical and enzymatic fractionation of cell walls from fucales: Insights into the structure of the extracellular matrix of brown algae.* Annals of Botany, 114*, 1203–1216, Charoensiddhi, S., Conlon, M. A., Vuaran, M. S., Franco, C. M. M., & Zhang, W. (2017). Polysaccharide and phlorotannin-enriched extracts of the brown seaweed* Ecklonia radiata *influence human gut microbiota and fermentation in vitro.* Journal of Applied Phycology, 29 (5)*, 2407–2416, Charoensiddhi, S., Conlon, M. A., Methacanon, P., Franco, C. M. M., Su, P., & Zhang, W. (2017). Gut health benefits of brown seaweed* Ecklonia radiata *and its polysaccharides demonstrated in vivo in a rat model.* Journal of Functional Foods, 37*, 676–684.*

output accounts for approximately 60% of the global volume. In terms of species produced, *Eucheuma* (10.2 million tonnes in 2015) was the most produced seaweed in the world, followed by Japanese kelp (8 million tonnes), *Gracilaria* spp. (3.9 million tonnes), *Undaria pinnatifid* (Japanese wakame) (2.3 million tonnes), *Kappaphycus* (1.8 million tonnes), and *Prophyra* spp. (Japanese nori) (1.2 million tonnes). In contrast to the seaweed aquaculture, species like *Lessonia nigrescens*, *Lessonia trabeculate*, *Graciliaria* spp., *Macrocystis* spp., *Saccharina japonica*, *Ascophyllum nodosum*, etc., are commercially harvested from wild; with relatively small combined quantity of 1–1.3 million tonnes annually.

The history of use of natural seaweeds as food for human nutrition can be traced back to several centuries ago in China, Japan and the Republic of Korea. Due to the migration of people from those regions, and the growing recognition of seaweed nutrition globally, many countries world-wide have nowadays had a strong tradition of using seaweed as food. The health and nutrition benefits of seaweed consumption include high complement of iodine, calcium, copper, iron, Vitamin C, Vitamin B12, Vitamin K and protein (Ferdouse, Holdt, Smith, Murúa, & Yang, 2018). More than 25 green algae (Chlorophyta) species, 40 brown algae (Phaeophyceae) species and 20 red algae (Rhodophyta) species are produced for food world-wide (Table 1).

The common food-seaweed species, such as, Nori or Purple laver (*Porphyra* spp.), Aonori or Green laver (*Monostroma* spp. and *Enteromorpha* spp.), Kombu or Haidai (*Laminaria japonica*), Wakame, Quandai-cai (*Undaria pinnatifida*), Hiziki (*Hizikia fusiforme*), Mozuku (*Cladosiphon okamuranus*), Sea Grapes or Green caviar (*Caulerpa lentillifera*), Dulse (*Palmaria palmata*), Irish moss or Carrageenan moss (*Chondrus crispus*), Winged kelp (*Alaria esculenta*), Ogonori or sea moss (*Gracilaria* spp.), *Callophyllis variegate* (McHugh, 2003), have been sustainably supplied to the global food industry.

Beside direct human consumption, many seaweeds are used as raw materials or feedstock for hydrocolloid extraction, mainly for agar and carrageenan's from red seaweed (>70 species) and alginates from brown seaweed (>30 species) (Tables 2–4, respectively).

Furthermore, seaweed can be processed and used in a broad variety of commercial applications, such as pharmaceutical, nutraceuticals, feeds, fertilizers, biofuels, cosmetics and medicines (Anis, Ahmed, & Hasan, 2017; Ferdouse et al., 2018; McHugh, 2003). For example, in agriculture sectors, seaweed is used in soil fertilizers because of its rich plant nutrients, such as potassium, nitrogen and phosphorus, as well as many growth factors (Verkleij, 1992). They are also used as key ingredients to formulate

Table 1 Seaweed species used worldwide as food (Arvinda Swamy, 2011; Blikra et al., 2019; Borderías, Pérez-Mateos, & Sánchez-Alonso, 2013; Buschmann et al., 2017; de Gaillande, Payri, Remoissenet, & Zubia, 2017; Delaney, Frangoudes, & Ii, 2016; Dominguez & Loret, 2019; Ferdouse et al., 2018; Fleurence, 2004; Forster & Radulovich, 2015; García, Palacios, & Roldán, 2016; Hardouin, Bedoux, Burlot, Nyvall-Collén, & Bourgougnon, 2014; Hwang, Amano, & Park, 2008; Lindsey White & Wilson, 2015; McHugh, 2003; Nguyen, Jung, & Kim, 2011; Ortiz et al., 2009; Raman, Rao, & Radhakrishnan, 2004; Shirosaki & Koyama, 2011; Venkatraman & Mehta, 2019; Wong & Cheung, 2000).

Taxa	Seaweed species	Country
Chlorophyta	*Capsosiphon fulvescens*	Korea
	Caulerpa bartlettii	Philippines
	Caulerpa intricatum	Philippines
	Caulerpa lentillifera	Philippines
	Caulerpa peltata	Philippines
	Caulerpa racemosa	Bangladesh, Fiji, Philippines, Vietnam
	Caulerpa sertularioides	Bangladesh, Philippines
	Caulerpa spp.	Malaysia
	Caulerpa taxifolia	Philippines
	Codium edule	Philippines
	Codium fragile	Korea
	Codium spp.	Bangladesh, Portugal
	Codium taylori	Israel
	Enteromorpha clathrata	Korea
	Enteromorpha compressa	Korea, Philippines
	Enteromorpha intestinalis	Japan, Korea
	Enteromorpha linza	Korea
	Enteromorpha prolifera	Japan, Korea
	Enteromorpha sp.	France
	Enteromorpha spp.	Bangladesh, Philippines, Portugal
	Monostroma grevillei	Korea
	Monostroma nitidum	Japan, Korea
	Ulva clathrata	China

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Taxa	Seaweed species	Country
	Ulva lactuca	Vietnam
	Ulva reticulata	Vietnam
	Ulva sp.	Bangladesh, France
	Ulva spp.	Brazil, Chile, Japan, Malaysia, Philippines, Portugal
	Ulva pertusa	Philippines, Taiwan
Phaeophyceae	*Alaria esculenta*	Ireland, United States of America
	Alaria marginata	Canada
	Chnoospora spp.	Bangladesh
	Cladosiphon okamuranus	Japan
	Cladosiphon sp.	Tonga
	Colpomenia sinuosa	Philippines
	Costaria costata	Korea
	Dictyota spp.	Bangladesh
	Durvillaea antarctica	Chile, New Zealand
	Ecklonia cava	Japan
	Ecklonia stolonifera	Korea
	Egregia menziesii	Canada
	Fucus distichus	Canada
	Fucus vesiculosus	Portugal
	Himanthalia elongata	France
	Hydroclathrus clathratus	Bangladesh, Philippines
	Laminaria hyperborea	France, Ireland, Norway, Russia, Spain
	Laminaria longipes	Russia

Continued

Table 1 Seaweed species used worldwide as food (Arvinda Swamy, 2011; Blikra et al., 2019; Borderías, Pérez-Mateos, & Sánchez-Alonso, 2013; Buschmann et al., 2017; de Gaillande, Payri, Remoissenet, & Zubia, 2017; Delaney, Frangoudes, & Ii, 2016; Dominguez & Loret, 2019; Ferdouse et al., 2018; Fleurence, 2004; Forster & Radulovich, 2015; García, Palacios, & Roldán, 2016; Hardouin, Bedoux, Burlot, Nyvall-Collén, & Bourgougnon, 2014; Hwang, Amano, & Park, 2008; Lindsey White & Wilson, 2015; McHugh, 2003; Nguyen, Jung, & Kim, 2011; Ortiz et al., 2009; Raman, Rao, & Radhakrishnan, 2004; Shirosaki & Koyama, 2011; Venkatraman & Mehta, 2019; Wong & Cheung, 2000).—Cont'd

Taxa	Seaweed species	Country
	Laminaria saccharina	Canada, France, Russia, Spain
	Laminaria setchellii	Canada
	Nemacystis decipiens	Japan
	Padina spp.	Bangladesh
	Pelvetia siliquosa	Korea
	Rosenvingea spp.	Bangladesh
	Saccharina angustata	Japan, Russia
	Saccharina cichorioides	Russia
	Saccharina diabolica	Japan
	Saccharina groenlandica	Canada
	Saccharina japonica	Russia, China, Japan, Korea, North Korea
	Saccharina latissima	Denmark
	Saccharina longicruris	United States of America
	Saccharina longissima	Japan
	Saccharina ochotensis	Japan
	Saccharina religiosa	Japan, Korea
	Sargassum fusiformis	Japan, Korea
	Sargassum horneri	Korea
	Sargassum spp.	Bangladesh, Brazil, Indonesia, Malaysia, Myanmar, Philippines, Vietnam
	Scytosiphon lomentaria	Korea
	Spatoglossum spp.	Bangladesh
	Undaria peterseniana	Korea
	Undaria pinnatifida	Australia, China, France, Japan, Korea

Table 1 Seaweed species used worldwide as food (Arvinda Swamy, 2011; Blikra et al., 2019; Borderías, Pérez-Mateos, & Sánchez-Alonso, 2013; Buschmann et al., 2017; de Gaillande, Payri, Remoissenet, & Zubia, 2017; Delaney, Frangoudes, & Ii, 2016; Dominguez & Loret, 2019; Ferdouse et al., 2018; Fleurence, 2004; Forster & Radulovich, 2015; García, Palacios, & Roldán, 2016; Hardouin, Bedoux, Burlot, Nyvall-Collén, & Bourgougnon, 2014; Hwang, Amano, & Park, 2008; Lindsey White & Wilson, 2015; McHugh, 2003; Nguyen, Jung, & Kim, 2011; Ortiz et al., 2009; Raman, Rao, & Radhakrishnan, 2004; Shirosaki & Koyama, 2011; Venkatraman & Mehta, 2019; Wong & Cheung, 2000).—Cont'd

Taxa	Seaweed species	Country
Rhodophyta	*Acanthophora spicifera*	Philippines, Vietnam
	Ahnfeltia tobuchiensis	Russia
	Asparagopsis taxiformis	Philippines, United States of America
	Betaphycus gelatinum	China, Vietnam
	Callophyllis variegata	Chile
	Catenella spp.	Bangladesh
	Chondracanthus chamissoi	Chile, Peru
	Chondrus crispus	France, Ireland, Spain, United States of America
	Eucheuma gelatinae	China, Japan, Philippines
	Eucheuma isiforme	Belize, Caribbean
	Eucheuma spp.	East Timor, Fiji, Philippines
	Gelidiella acerosa	India, Philippines, Vietnam
	Gelidiella spp.	Bangladesh
	Gelidium amansii	China, Japan, Korea
	Gelidium serrulatum	Caribbean
	Gelidium sp.	Bangladesh, Indonesia
	Ghondria crassicaulis	Korea
	Gloiopeltis furcata	Japan, Korea
	Gloiopeltis spp.	Vietnam
	Gloiopeltis tenax	Japan, Korea
	Gracilaria asiatica	Vietnam
	Gracilaria bursa-pastoris	Japan

Continued

Table 1 Seaweed species used worldwide as food (Arvinda Swamy, 2011; Blikra et al., 2019; Borderías, Pérez-Mateos, & Sánchez-Alonso, 2013; Buschmann et al., 2017; de Gaillande, Payri, Remoissenet, & Zubia, 2017; Delaney, Frangoudes, & Ii, 2016; Dominguez & Loret, 2019; Ferdouse et al., 2018; Fleurence, 2004; Forster & Radulovich, 2015; García, Palacios, & Roldán, 2016; Hardouin, Bedoux, Burlot, Nyvall-Collén, & Bourgougnon, 2014; Hwang, Amano, & Park, 2008; Lindsey White & Wilson, 2015; McHugh, 2003; Nguyen, Jung, & Kim, 2011; Ortiz et al., 2009; Raman, Rao, & Radhakrishnan, 2004; Shirosaki & Koyama, 2011; Venkatraman & Mehta, 2019; Wong & Cheung, 2000).—Cont'd

Taxa	Seaweed species	Country
	Gracilaria coronopifolia	United States of America, Vietnam
	Gracilaria domingensis	Caribbean
	Gracilaria eucheumoides	Vietnam
	Gracilaria firma	Philippines, Vietnam
	Gracilaria heteroclada	Philippines, Vietnam
	Gracilaria lemaneiformis	Japan
	Gracilaria parvispora	United States of America
	Gracilaria salicornia	Vietnam
	Gracilaria sp.	Bangladesh, Philippines
	Gracilaria spp.	Philippines, Portugal, Vietnam
	Gracilaria tenuistipitata	Philippines, Vietnam
	Gracilaria verrucosa	China, Italy, Japan, Korea
	Gracilaria spp.	Caribbean
	Grateloupia filicina	Japan, Philippines
	Grateloupia turuturu	Korea
	Halymenia durvillei	Philippines
	Halymenia spp.	Bangladesh
	Hydropuntia cornea	Caribbean
	Hydropuntia crassissima	Caribbean
	Hypnea muscoides	Vietnam
	Hypnea pannosa	Philippines
	Hypnea spp.	Bangladesh, China, Indonesia, Myanmar, Vietnam
	Hypnea valentiae	Vietnam

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Taxa	Seaweed species	Country
	Kappaphycus alvarezii	Brazil, Caribbean, China, India, Indonesia, Kiribati, Madagascar, Malaysia, Myanmar, Philippines, Solomon Islands, Tanzania, Timor-Leste, Vietnam, Zanzibar
	Laurencia cartilaginea	Philippines
	Laurencia papillosa	Philippines
	Mastocarpus stellatus	Ireland, Portugal, Spain
	Mazzaella splendens	Canada
	Meristotheca papulosa	Japan
	Meristotheca procumbens	Fiji
	Meristotheca senegalensis	Senegal
	Nemalion vermiculare	Korea
	Osmundea pinnatifida	Portugal
	Palmaria hecatensis	Canada
	Palmaria mollis	Canada
	Palmaria palmata	Canada, France, Ireland, United States of America
	Porphyra abbottae	Canada
	Porphyra acanthophora	Brazil
	Porphyra columbina	Chile, Peru
	Porphyra conwayae	Canada
	Porphyra crispate	Vietnam
	Porphyra fallax	Canada
	Porphyra haitanensis	China

Continued

Table 1 Seaweed species used worldwide as food (Arvinda Swamy, 2011; Blikra et al., 2019; Borderías, Pérez-Mateos, & Sánchez-Alonso, 2013; Buschmann et al., 2017; de Gaillande, Payri, Remoissenet, & Zubia, 2017; Delaney, Frangoudes, & Ii, 2016; Dominguez & Loret, 2019; Ferdouse et al., 2018; Fleurence, 2004; Forster & Radulovich, 2015; García, Palacios, & Roldán, 2016; Hardouin, Bedoux, Burlot, Nyvall-Collén, & Bourgougnon, 2014; Hwang, Amano, & Park, 2008; Lindsey White & Wilson, 2015; McHugh, 2003; Nguyen, Jung, & Kim, 2011; Ortiz et al., 2009; Raman, Rao, & Radhakrishnan, 2004; Shirosaki & Koyama, 2011; Venkatraman & Mehta, 2019; Wong & Cheung, 2000).—Cont'd

Taxa	Seaweed species	Country
	Porphyra kuniedae	Korea
	Porphyra leucostica	Portugal
	Porphyra nereocystis	Canada
	Porphyra pseudolanceolata	Canada
	Porphyra seriata	Korea
	Porphyra sp.	France, Philippines
	Porphyra spiralis	Brazil
	Porphyra spp.	Israel, New Zealand, Philippines
	Porphyra suborbiculata	Korea, Vietnam
	Porphyra tenera	Japan, Korea, Taiwan
	Porphyra torta	Canada
	Porphyra umbilicalis	United States of America
	Porphyra yezoensis	China, Japan, Korea, United States of America
	Pterocladia capillacea	Korea, New Zealand, Portugal
	Scinaia hormoide	Philippines

aquafeeds or diets (Wan, Davies, Soler-Vila, Fitzgerald, & Johnson, 2018). Algins from brown seaweed have been widely used to produce paints, paper, cardboard, textile printing, personal lubricants, pesticides, and explosives. Furthermore, as a bio-filtering agent, seaweeds have strong capacity of removing ammonia, ammonium nitrate, nitrite, phosphate, iron, copper and carbon dioxide from water bodies (Mohd Udaiyappan, Abu Hasan, Takriff, & Sheikh Abdullah, 2017).

Table 2 Red seaweed species (Rhodophyta) used worldwide for agar production (Armisen, 1995; Armisén & Gaiatas, 2009; McHugh, 2003; Rebello, Ohno, Ukeda, & Sawamura, 1996).

Taxa	Red seaweed species	Country
Rhodophyta	*Ahnfeltia tobuchiensis*	Russia
	Chondracanthus exasperatus	Canada
	Gelidiella acerosa	India, Philippines, Vietnam
	Gelidium abbotiorum	South Africa
	Gelidium amansii	China, Japan, Korea
	Gelidium canariense	Morocco
	Gelidium chilense	Chile
	Gelidium corneum	Morocco
	Gelidium crinale	Morocco
	Gelidium japonicum	Japan
	Gelidium latifolium	Morocco, Spain
	Gelidium lingulatum	Chile
	Gelidium madagascariense	Madagascar
	Gelidium microdon	Morocco
	Gelidium pacificum	Japan
	Gelidium pristoides	South Africa
	Gelidium pteridifolium	South Africa
	Gelidium pulchellum	Morocco
	Gelidium pusillum	Morocco
	Gelidium rex	Chile
	Gelidium robustum	Mexico
	Gelidium sesquipedale	France, Portugal, Spain
	Gelidium sp.	Bangladesh, Indonesia
	Gelidium spinosum	Morocco
	Gelidium spp.	Malaysia, Philippines, Portugal, Taiwan
	Gelidium subcostatum	Japan

Continued

Table 2 Red seaweed species (Rhodophyta) used worldwide for agar production (Armisen, 1995; Armisén & Gaiatas, 2009; McHugh, 2003; Rebello, Ohno, Ukeda, & Sawamura, 1996).—Cont'd

Taxa	Red seaweed species	Country
	Gelidium vagum	Canada
	Gracilaria asiatica	Vietnam
	Gracilaria caudata	Brazil
	Gracilaria changii	Malaysia
	Gracilaria chilensis	Chile, New Zealand
	Gracilaria conferta	Morocco
	Gracilaria cornea	Brazil
	Gracilaria dura	Morocco
	Gracilaria edulis	India
	Gracilaria errucosa	Indonesia
	Gracilaria firma	Philippines, Vietnam
	Gracilaria gigas	Indonesia
	Gracilaria gracilis	Morocco, Namibia, South Africa
	Gracilaria heteroclada	Philippines, Vietnam
	Gracilaria longa	Italy
	Gracilaria pacifica	Canada
	Gracilaria sp.	Bangladesh, Philippines
	Gracilaria tenuistipitata	Philippines, Vietnam
	Gracilaria tenuistipitata var. *liui*	China
	Gracilaria vermiculata	Morocco
	Gracilaria vermiculophylla	China
	Gracilaria verrucosa	China, Italy, Japan, Korea
	Gracilariopsis andersonii	Canada
	Gracilariopsis howei	Peru
	Gracilariopsis lemaneiformis	Mexico, Morocco, Peru

Table 2 Red seaweed species (Rhodophyta) used worldwide for agar production (Armisen, 1995; Armisén & Gaiatas, 2009; McHugh, 2003; Rebello, Ohno, Ukeda, & Sawamura, 1996).—Cont'd

Taxa	Red seaweed species	Country
	Gracilariopsis longuissima	Morocco
	Gracilariopsis tenuifrons	Brazil
	Kappaphycus alvarezii	Brazil, Caribbean, China, India, Indonesia, Kiribati, Madagascar, Malaysia, Myanmar, Philippines, Solomon Islands, Tanzania, Timor-Leste, Vietnam, Zanzibar
	Mazzaella splendens	Canada
	Pterocladia capillacea	Korea, New Zealand, Portugal
	Pterocladia lucia	New Zealand
	Pterocladiella caerulescens	Morocco
	Pterocladiella capillacea	Brazil, Morocco

Table 3 Red seaweed species (Rhodophyta) used worldwide for carrageenan production (Hernández-Carmona, Freile-Pelegrín, & Hernández-Garibay, 2013; Levitt, Bolton, & Anderson, 1995; Lindsey White & Wilson, 2015; Parekh, Doshi, & Chauhan, 1989; Pereira, 2013; Pereira, Meireles, Abreu, & Paulo, 2015; Tasende, Cid, & Fraga, 2013).

Taxa	Red seaweed species	Country
Rhodophyta	*Acanthophora spicifera*	Philippines, Vietnam
	Agardhiella subulata	Italy
	Agardhiella tenera	Peru
	Ahnfeltia plicata	Chile
	Ahnfeltiopsis furcellata	Chile
	Betaphycus gelatinum	China, Vietnam
	Chondracanthus canaliculatus	Mexico
	Chondracanthus chamissoi	Chile, Peru
	Chondrus candiculatus	Peru
	Chondrus crispus	France, Ireland, Spain, United States of America

Continued

Table 3 Red seaweed species (Rhodophyta) used worldwide for carrageenan production (Hernández-Carmona, Freile-Pelegrín, & Hernández-Garibay, 2013; Levitt, Bolton, & Anderson, 1995; Lindsey White & Wilson, 2015; Parekh, Doshi, & Chauhan, 1989; Pereira, 2013; Pereira, Meireles, Abreu, & Paulo, 2015; Tasende, Cid, & Fraga, 2013).—Cont'd

Taxa	Red seaweed species	Country
	Chondrus spp.	Canada, Portugal
	Eucheuma arnoldii	Philippines
	Eucheuma denticulatum	Indonesia, Madagascar, Philippines, Tanzania, Zanzibar
	Eucheuma gelatinae	China, Japan, Philippines
	Eucheuma isiforme	Belize, Caribbean
	Eucheuma spinosum	Indonesia
	Eucheuma spp.	East Timor, Fiji, Philippines
	Eucheuma striatum	Madagascar
	Gigartina acicularis	Morocco
	Gigartina intermedia	Vietnam
	Gigartina pistillata	Morocco
	Gigartina skottsbergii	Chile
	Gigartina teedii	Morocco
	Gloiopeltis complanata	Japan
	Gloiopeltis furcata	Japan, Korea
	Gloiopeltis tenax	Japan, Korea
	Gymnogongrus furcellatus	Peru
	Hypnea musciformis	Brazil, Italy, Senegal
	Hypnea spp.	Bangladesh, China, Indonesia, Myanmar, Vietnam
	Kappaphycus alvarezii	Brazil, Caribbean, China, India, Indonesia, Kiribati, Madagascar, Malaysia, Myanmar, Philippines, Solomon Islands, Tanzania, Timor-Leste, Vietnam, Zanzibar
	Kappaphycus procrusteanum	Philippines

Table 3 Red seaweed species (Rhodophyta) used worldwide for carrageenan production (Hernández-Carmona, Freile-Pelegrín, & Hernández-Garibay, 2013; Levitt, Bolton, & Anderson, 1995; Lindsey White & Wilson, 2015; Parekh, Doshi, & Chauhan, 1989; Pereira, 2013; Pereira, Meireles, Abreu, & Paulo, 2015; Tasende, Cid, & Fraga, 2013).—Cont'd

Taxa	Red seaweed species	Country
	Kappaphycus striatum	Philippines
	Mastocarpus papillatus	Chile
	Mastocarpus stellatus	Ireland, Portugal, Spain
	Mazzaella laminarioides	Chile
	Mazzaella membranacea	Chile
	Prionitis decipiens	Peru
	Rhodoglossum denticulatum	Peru
	Sarcothalia crispata	Chile
	Solieria filiformis	Italy

Table 4 Brown seaweed species (Phaeophyceae) used worldwide for alginate production (Ang, 1984; Déléris, Nazih, & Bard, 2016; Draget, 2009; Kim & Bhatnagar, 2011; Lindsey White & Wilson, 2015; Pereira et al., 2015; Prameela, Murali Mohan, & Ramakrishna, 2018; Rhein-Knudsen, Ale, Ajalloueian, & Meyer, 2017; Ueno & Oda, 2014; Zou et al., 2019).

Taxa	Brown seaweed species	Country
Phaeophyceae	*Durvillaea potatorum*	Australia
	Eisenia arborea	Mexico
	Fucus serratus	Ireland
	Hizikia fusiforme	China
	Laminaria bongardiana	Russia
	Laminaria digitata	Denmark, France, Iceland
	Laminaria gurjanovae	Russia
	Laminaria hyperborea	France, Ireland, Norway, Russia, Spain

Continued

Table 4 Brown seaweed species (Phaeophyceae) used worldwide for alginate production (Ang, 1984; Déléris, Nazih, & Bard, 2016; Draget, 2009; Kim & Bhatnagar, 2011; Lindsey White & Wilson, 2015; Pereira et al., 2015; Prameela, Murali Mohan, & Ramakrishna, 2018; Rhein-Knudsen, Ale, Ajalloueian, & Meyer, 2017; Ueno & Oda, 2014; Zou et al., 2019).—Cont'd

Taxa	Brown seaweed species	Country
	Laminaria longipes	Russia
	Laminaria ochroleuca	Spain
	Laminaria saccharina	Canada, France, Russia, Spain
	Lessonia nigrescens	Chile, Peru
	Lessonia trabeculata	Chile
	Macrocystis integrifolia	Canada, Chile, Peru
	Macrocystis pyrifera	Chile, Mexico, New Zealand, Peru, United States of America
	Saccharina angustata	Japan, Russia
	Saccharina cichorioides	Russia
	Saccharina japonica	Russia, China, Japan, Korea, North Korea
	Sargassum binderi	Philippines
	Sargassum cinctum	Philippines
	Sargassum crassifolium	Philippines
	Sargassum cristaefolium	Philippines
	Sargassum feldmannii	Philippines
	Sargassum hemiphyllum	Philippines
	Sargassum oligosystum	Philippines
	Sargassum paniculatum	Philippines
	Sargassum polycystum	China, Philippines
	Sargassum siliquosum	Philippines
	Sargassum spp.	Bangladesh, Brazil, Indonesia, Malaysia, Myanmar, Philippines, Vietnam
	Turbinaria spp.	Indonesia

2.2 Main metabolites from seaweeds

The bioactive metabolites of seaweeds have been studied and utilized globally, mainly including polysaccharides, phenolics, phlorotannins, proteins, peptides, amino acids, terpenes, terpenoids, lipids, and halogenated compounds. Carbohydrates account for the majority of seaweed biomass. Polysaccharides and oligosaccharides have therefore been the key focus of many studies looking at seaweed-derived bioactive/functional compounds. Beside those, phenolic compounds and proteins from seaweeds have also been widely studied as potential functional ingredients (Holdt & Kraan, 2011; Misra, Rai, & Hossain, 2015; Yu, Jantan, Ahmad, & Wong, 2014). These seaweed components possess several biological properties which may be exploited in functional food and nutraceutical applications (Gupta & Abu-Ghannam, 2011a), particularly polysaccharides and phenolics from brown seaweeds, as illustrated in Table 5.

2.2.1 Polysaccharides

From an economic perspective, seaweed polysaccharides are the most important products produced from seaweeds (Michalak & Chojnacka, 2015). As the major components in seaweeds, polysaccharides account for up to 76% of the dry weight (DW) (Holdt & Kraan, 2011). Seaweeds contain a high total dietary fiber content: 10%–75% for brown seaweed, 10%–59% for red seaweed, and 29%–67% for green seaweed. Seaweeds are particularly rich in soluble dietary fiber, which accounts for 26%–38%, 9%–37%, and 17%–24% in brown, red, and green seaweed, respectively (de Jesus Raposo, de Morais, & de Morais, 2016). Most of these polysaccharides can be fermented by gut microbiota, which may provide health benefit to humans though a prebiotic effect (O'Sullivan et al., 2010; Zaporozhets et al., 2014), which is the main subject of this chapter and will be discussed in more detail later. Additionally, sulfated polysaccharides have shown anti-inflammatory, antioxidant, antibacterial, and immunological activities. These include fucoidans (L-fucose and sulfate ester groups) from brown seaweeds, carrageenans (sulfated galactans) from red seaweeds, and ulvans (sulfated glucuronoxylorhamnans) from green seaweeds (Synytsya et al., 2015).

Agar and carrageenan are extracted primarily from red seaweeds. Low-value agars are used as thickeners, emulsifiers, and gelling agents in foods, while higher-value agars (those with a more idealized physicochemical structure) are used to make solid culture media for plant and bacterial propagation, and gels for the separation and analysis of molecules in molecular

Table 5 Bioactive compounds obtained from different brown seaweed species and their bioactivities.

Compound	Source of seaweed/ content (%DW)	Biological activity	Reference
Alginate	*Laminaria* 17%–46%, *Undaria* 24%, Sargassum 3.3%–41%, Fucus 18%–22%, *Ascophyllum* 24%–29% (Holdt & Kraan, 2011; Zubia, Payri, and Deslandes, 2008)	Antibacterial	Hu et al. (2005), Khan et al. (2012)
		Anticancer, Anti-tumor, Cholesterol-lowering effect	Murata and Nakazoe (2001), Paxman et al. (2008), Idota et al. (2016)
		Anti-hypertension	Holdt and Kraan (2011)
		Dietary fiber and prebiotic	Kuda, Yano, Matsuda, and Nishizawa (2005), Ramnani et al. (2012), Zhu et al. (2015), Li et al. (2016)
		Anti-diabetes	Holdt and Kraan (2011)
		Anti-obesity	Khoury, Goff, and Anderson (2015)
		Antioxidant	Hu, Geng, Zhang, and Jiang (2001), Şen (2011), Zhao, Li, Xue, and Sun (2012), Kelishomi et al. (2016)
		Anticoagulant	Ma et al. (2016)
Fucoidan	*Laminaria* 2%–5.5%, *Undaria* 1.5%, *Sargassum* 4.3%–26%, *Fucus* 16%–20%, *Ascophyllum* 4%–12%, (Holdt & Kraan, 2011; García-Ríos, Ríos-Leal, Robledo, & Freile-Pelegrin, 2012)	Anti-inflammatory	Cumashi et al. (2007), Fernando, Nah, and Jeon (2016)
		Prebiotic	Lynch, Sweeney, Callan, O'Sullivan, and O'Doherty (2010), Kong, Dong, Gao, and Jiang (2016), Shang et al. (2016)
		Anticoagulant	Li, Lu, Wei, and Zhao (2008), Wang, Zhang, Zhang, Song, and Li (2010), Jin, Zhang, Wang, and Zhang (2013), Zhang, Till, et al. (2015)
		Antibacterial	Shannon and Abu-Ghannam (2016)
		Anti-arteriosclerosis Antioxidant	Murata and Nakazoe (2001), Rupérez (2002), Xue et al. (2004), de Souza et al. (2007), Wang et al. (2009), Wang, Zhang, Zhang, and Li (2008), Huang, Wu, Yang, Kuan, and Chen (2016)
		Anticancer	Murata and Nakazoe (2001), Choi and Kim (2013), Moghadamtousi et al. (2014), Kalimuthu and Kim (2015), Anastyuk et al. (2017)

		Immunomodulator	Li, Lu, et al. (2008), Kawashima, Murakami, Nishimura, Nakano, and Obata (2012), Zhang, Oda, Yu, and Jin (2015)
		Antiviral	Besednova et al. (2016), Lee, Hayashi, Hashimoto, Nakano, and Hayashi (2004), Rabanal, Ponce, Navarro, Gómez, and Stortz (2014)
		Anti-HIV	Thuy et al. (2015), Dinesh et al. (2016)
		Improve metabolic syndrome	Shang et al. (2017)
		Neuroprotective effect	Fitton (2011)
		Anti-diabetes	Wang, Liu, Li, Zhang, and Zhang (2014), Shan et al. (2016)
Laminarin	*Laminaria* 0%–32%, *Undaria* 3%, *Sargassum* 0.3%, *Fucus* 0.04%–0.4%, *Ascophyllum* 1.2%–10% (Holdt & Kraan, 2011; Graiff, Ruth, Kragl, & Karsten, 2016)	Antibacterial	Shannon and Abu-Ghannam (2016)
		Antioxidant	Kadam, Tiwari, and O'Donnell (2015)
		Dietary fiber and prebiotic	Deville, Damas, Forget, Dandrifosse, and Peulen (2004), Deville, Gharbi, Dandrifosse, and Peulen (2007)
		Reduce cholesterol levels	Holdt and Kraan (2011)
		Anti-obesity	Nguyen et al. (2016)
		Immunostimulating	Holdt and Kraan (2011)
		Anticancer	Moussavou et al. (2014)
		Antiviral	Wang, Wang, and Guan (2012)

Continued

Table 5 Bioactive compounds obtained from different brown seaweed species and their bioactivities.—Cont'd

Compound	Source of seaweed/ content (%DW)	Biological activity	Reference
Phenolic compounds (mainly phlorotannin)	*Laminaria* 0.2%–5.3%, *Undaria* < 0.4%, *Sargassum* 1.1%–12.7%, *Fucus* < 0.4%–12.2%, *Ascophyllum* 0.5%–14% (Holdt & Kraan, 2011)	Antioxidant	Zubia et al. (2008), Li et al. (2011), Kirke, Smyth, Rai, Kenny, and Stengel (2017)
		Anti-diabetic	Lee and Jeon (2013), Lopes, Andrade, and Valentão (2017)
		Neuroprotective effect	Pangestuti and Kim (2013)
		Prevent cardiovascular disease	Murray, Dordevic, Ryan, and Bonham (2016)
		Antibacterial	Nagayama, Iwamura, Shibata, Hirayama, and Nakamura (2002), Eom, Kim, and Kim (2012), Lee et al. (2014)
		Anti-inflammatory	Dutot, Fagon, Hemon, and Rat (2012), Jung, Jin, Ahn, Lee, and Choi (2013), Wijesinghe et al. (2013)
		Antibiotic	Eom et al. (2013)
		Anticancer	Li, Wijesekara, Li, and Kim (2011), Namvar et al. (2012), Zenthoefer et al. (2017)
		Anti-HIV	Ahn et al. (2004), Artan et al. (2008), Vo and Kim (2010), Karadeniz, Kang, Park, Park, and Kim (2014)
		Hepatoprotective effect	Kang et al. (2012)
		Anti-allergic	Li, Lee, et al. (2008), Vo, Ngo, and Kim (2012)
		Prevent autoimmune disorder	Holdt and Kraan (2011)

biology research (Loth, 1993). Carrageenans are the most commonly used phycocolloids in the food industry, commonly employed as stabilizers and emulsifiers. They are often used in cosmetics, such as shampoos, skin creams and toothpastes, and a range of other gelatinous commodities including air fresheners and personal lubricants (McHugh, 2003).

As with the other phycocolloids, alginates form viscous solutions and gels when dissolved in water. With a broad range of characteristics lend themselves to a wider spectrum of industrial applications, including the sizing of paper and textiles, water- and fire-proofing of fabrics, an additive to dehydrated products, a thickening agent in ice creams, jellies, soups, beverages and cosmetics and also as a slow-release vehicle for drugs in the pharmaceutical industry (Draget, 2009).

Fucoidans from a very wide range of brown seaweeds have also been shown to possess antiviral, anticancer, immunomodulatory, anti-inflammatory, anti-lipidemic and other activities, all of which have been comprehensively reviewed (Lorbeer et al., 2013). Similarly, interest in the laminarins from brown algae, and more-so the ulvans of green algae, has recently increased due to their biological activities. Alves and colleagues have provided a good review of ulvan research, listing anti-viral, anti-coagulant, anti-hyperlipidemic, immunostimulating, anti-cancer and antioxidant effects, again often being accredited to the sulfation of these polysaccharide molecules (Alves, Sousa, & Reis, 2013).

2.2.2 Phenolic compounds

Phlorotannins are the major phenolic compounds found in brown seaweeds, constituting up to 14% of dry seaweed biomass with lower amounts being found in some red and green seaweeds (Holdt & Kraan, 2011; Machu et al., 2015). Polyphenolic compounds, particularly those of the brown seaweeds (referred to as phlorotannins), have shown a great deal of promise as functional compounds. While Cystophora has been the most common source of isolation, phlorotannins are also widespread in seaweeds such as Ecklonia—these being predominant genera of brown algae found along the Southern coastline of Australia, New Zealand and Korea.

Phlorotannins are highly hydrophilic compounds formed by the polymerization of phloroglucinol (1,3,5-trihydroxybenzene) monomer units with a wide range of molecular weights between 126 Da and 650 kDa. They can be categorized into four groups based on their linkages which are fuhalols and phlorethols (ether linkage), eckols (dibenzodioxin linkage), fucophloroethols (ether and phenyl linkage), and fucols (phenyl linkage) (Li, Wijesekara, Li, & Kim, 2011). Phlorotannins have been explored as functional food ingredients with many biological activities such as antioxidant, anti-tumor, anti-inflammatory, antidiabetic, antihypertensive, and antiallergic activities (Freitas et al., 2015). Antibacterial activity is particularly common for phlorotannins. The bactericidal activity of phlorotannins from *Ecklonia kurome Okamura* against food borne pathogens including methicillin-resistant *Staphylococcus aureus Rosenbach* has been documented (Nagayama et al., 2002).

Meanwhile, an interesting cosmeceutical application of phlorotannins lies in their ability to induce depigmentation or whitening of the skin. This is achieved through the inhibition of melanogenesis, which is the process by which melanin is produced by cells known as melanocytes in the bottom epidermal layer of the skin, regulated by the enzyme tyrosinase (Wijesinghe & Jeon, 2011). A number of phlorotannins have been found to effectively inhibit tyrosinase, including 7-phloroeckol and dieckol from *Ecklonia cava* Kjellman and phloroglucinol derivatives from *Ecklonia stolonifera* Okamura (Lorbeer et al., 2013).

2.2.3 Proteins

Bioactive proteins and peptides from seaweeds have been demonstrated to have antioxidant, antihypertensive, and anticoagulant activities (Harnedy & FitzGerald, 2011). Generally, a higher content of proteins is found in red and green seaweeds (10%–47% of DW) compared to brown seaweeds (3%–15% of DW) (Wijesekara & Kim, 2015). Important bioactive proteins from red and green seaweeds include lectin and phycobiliprotein and bioactive peptides from brown seaweeds have been reported with angiotensin-I-converting enzyme (ACE-I) inhibitory potential (Fitzgerald, Gallagher, Tasdemir, & Hayes, 2011). Additionally, most seaweed species are a rich source of essential and acidic amino acids (Freitas et al., 2015).

Fleurence (1999) reviewed the composition and potential uses of seaweed proteins. In terms of protein content, that of brown algae is generally quite low (3%–15% dry weight) compared with the red and green seaweeds (10%–47% dry weight). In terms of higher-value products, the proteins of macroalgae are generally of little commercial significance. However, some exceptions exist, and functional macroalgal proteins, peptides and amino acids have been extensively reviewed (Harnedy & FitzGerald, 2011). Perhaps the most noteworthy use of seaweed proteins comes from the research industry's utilization of phycobiliproteins—the light-harvesting cellular machinery involved in the photosynthetic pathways of red algae and cyanobacteria. In many red algae the most common phycobiliprotein is known as R-phycoerythrin, which can account for the majority of soluble protein in the cells of some species when grown under optimal conditions. This highly fluorescent complex serves as a fluorescent tag with applications in flow cytometry, cell sorting, histochemistry and other fields, all of which are discussed in detail in the review (Glazer, 1994). Phycoerythrin has also been explored as a food dye, but this application is limited by its relative instability to heat (Fleurence, 1999).

2.2.4 Lipids

Even through the lipid content of seaweed are variable and generally from 1% to 10% of the dry weight, many studies demonstrated the potential use of seaweed lipids for food and nutritional benefit. For example, in the brown seaweed *Spatoglossum macrodontum*, 50% of these lipids are in the form of extractable fatty acids (Gosch, Magnusson, Paul, & de Nys, 2012). According to Kumari, the polyunsaturated fatty acid (PUFA) content is the same with or higher than the terrestrial plants (Kumari, Kumar, Gupta, Reddy, & Jha, 2010). In red seaweed, lipids and fatty acids are generally 1%–5%; however, the level of polyunsaturated fatty acids is higher than vegetables (Torres, Flórez-Fernández, & Domínguez, 2019).

2.3 Potential use of seaweed as functional foods and nutraceuticals

Increasing consumer awareness regarding the complex relationship between diet and health results in demand for new functional foods that can specifically contribute to health-promotion or disease prevention, beyond providing basic nutrition (Gul, Singh, & Jabeen, 2016). The global nutraceutical market, including functional foods and beverages as well as dietary supplements, was valued at around USD 250 billion in 2014. With the rapid increase in consumer demand, this market value is expected to reach around USD 385 billion by 2020 (Suleria, Osborne, Masci, & Gobe, 2015). Seaweeds are commonly used as general foodstuffs, such as flavorings for noodles, soups, and meals, as well as in snacks, salads, wrap-up vegetable, and pickled side-dishes, in Japan, China, Korea, and other coastal populations (Lee, 2008).

Many common edible seaweeds provide various natural nutraceutical benefits. For example, the Japanese nori or purple laver (*Porphyra* spp.) has extra low sugar level (0.1%) with significant amounts of Vitamins A, B1, B2, B6, B12, C, niacin and folic acid (Noda, 1993). Aonori or Green Laver (*Monostroma* spp. and *Enteromorpha* spp.) are high in protein, up to 20%, with low fat, low sodium and high iron and calcium content. The vitamin B-group content is generally higher than most vegetables (Mahadevan, 2015). Unlike other brown seaweed, wakame or Qundai-Cai (*Undaria pinnatifida*) is also rich in protein (up to 24%) (Dumay & Morançais, 2016) and the vitamin B group, especially niacin; and contains appreciable amounts of essential trace elements such as manganese, copper, cobalt, iron, nickel and zinc (Kolb, Luciana, Milanovi, & Stocchi, 2004).

While the recent studies on seaweed-derived functional food ingredients have shown that seaweeds are a rich source of bioactive compounds with a variety of potential health benefits, the volume of clinical research in humans into the health-promoting properties of seaweeds in food and nutraceutical applications is currently rather limited. Considering that data on the functional properties of brown seaweed components is now available, the potential applications of brown seaweeds and their extracts as functional ingredients in food products are summarized in Table 6. As shown in Table 6, most of the potential applications for brown seaweed ingredients have focused on improving the nutritional, textural, and sensory properties of food products, particularly meat, bakery, and dairy products. The reported effects of brown seaweed-derived food additives for specific health-promoting applications are still not extensive. In addition, the specific taste and aroma of seaweeds may affect consumer acceptance and limit the use of seaweeds as functional ingredients. However, it is interesting that the sensory characteristics of seaweed were reported to be acceptable when formulated into most food applications.

3. Overview of prebiotics

3.1 Concept, definition, and criteria of prebiotics

Interest in prebiotics as functional foods has increased due to their recognized health benefits. The global prebiotics market size was about 623.5 kilotons in 2015, and continued growth is expected due to rising consumer awareness of gut health issues (Grand View Research, 2018). The concept of "*Prebiotics*" started in 1995 as non-digestible food that stimulates the growth of bacteria that are responsible in improving human health. However, this was redefined as non-digestible carbohydrates that benefit gastrointestinal (GI) tract and overall immune system (Carlson, Erickson, Lloyd, & Slavin, 2018). The term "prebiotic" was defined as substrates that (1) are

Table 6 The effects associated with the incorporation of brown seaweeds and their extracts into food products, with regard to food properties and health benefits.

Product	Seaweed source	Seaweed-derived additive	Effect on food and health properties	Reference
Yoghurt	*Ascophyllum nodosum*, *Fucus vesiculosus*	Seaweed extract: 0.25% and 0.5%	– Increased yellowness and reduced levels of lipid oxidation – No negative effect on shelf life characteristics and sensory perspectives (color, flavor, and texture) – Did not alter cellular antioxidant status or protect against DNA damage	O'Sullivan et al. (2016)
	Himanthalia elongata, *Saccharina latissima*, *Undaria pinnatifida*	Seaweed powder: 0.5%	– *S. latissima* showed the lowest seaweed flavor and the highest flavor quality.	Nuñez and Picon (2017)
Milk	*Ascophyllum nodosum*, *Fucus vesiculosus*	Seaweed extract: 0.25% and 0.5%	– Extracts were stable in milk, and showed antioxidant activities before and after in vitro digestion. – Improved milk quality and shelf life characteristics.	O'Sullivan et al. (2014)

Continued

Table 6 The effects associated with the incorporation of brown seaweeds and their extracts into food products, with regard to food properties and health benefits.—Cont'd

Product	Seaweed source	Seaweed-derived additive	Effect on food and health properties	Reference
Bread	*Myagropsis myagroides*	Seaweed extract: 0.5%, 1%, and 2%	– Improved sensory acceptance with 0.5% supplementation and shelf life relative to the control – Decreased total microbial count with 2% supplementation	Lee et al. (2010)
	Himanthalia elongata	Seaweed powder: 5%–15%	– Predicted values from response surface methodology, 17.07% seaweed with 21.89% white flour provided the maximum total dietary fiber, phenolic, and antioxidant activity, while retaining acceptable sensory evaluation in the optimized sample.	Cox and Abu-Ghannam (2013a)
Pasta	*Undaria pinnatifida*	Seaweed extract: 5%, 10%, 20%, and 30%	– 20% Supplementation retained sensory acceptance, while improving bio-functional properties. – Extract-enriched pasta had an improved amino acid and fatty acid profile, and contained fucoxanthin and fucosterol. – Fucoxanthin was not degraded by the pasta making and cooking process.	Prabhasankar et al. (2009)

Pork product	*Himanthalia elongata*, *Undaria pinnatifida*	Seaweed powder: 2.5% and 5%	– Improved the water and fat binding properties – Chewiness and hardness of the cooked products was higher, while springiness and cohesiveness were lower. – Dietary fiber, antioxidant, polyphenol, and carotenoid content were higher.	Cofrades, López-López, Solas, Bravo, and Jiménez-Colmenero (2008)
	Himanthalia elongata	Seaweed powder: 3.4%	– Water/oil retention capacity, elastic modulus, and hardness were reinforced. – The presence of alginates prevented the thermal denaturation of proteins.	Fernández-Martín, López-López, Cofrades, and Colmenero (2009)
	Himanthalia elongata, *Undaria pinnatifida*	Seaweed powder: 5.6%	– Increased n-3 PUFA and reduced n-6/n-3 PUFA ratio – The thombogenic index decreased in *U. pinnatifida* added meat. – The concentrations of K, Ca, Mg, and Mn were increased, while Na was decreased. – *H. elongata* supplemented samples showed the greatest increase in polyphenol and antioxidant.	López-López, Bastida, et al. (2009)

Continued

Table 6 The effects associated with the incorporation of brown seaweeds and their extracts into food products, with regard to food properties and health benefits.—Cont'd

Product	Seaweed source	Seaweed-derived additive	Effect on food and health properties	Reference
	Laminaria digitata	Seaweed extract (containing 9.3% Laminarin and 7.8% Fucoidan): 0.01%, 0.1%, and 0.5%	– The laminarin/fucoidan extract at 0.5% showed the highest lipid pro-oxidant activity in fresh patties, but significantly reduced lipid oxidation in cooked patties. – 0.01% Supplementation showed no adverse effect on texture, color, lipid oxidation, and sensorial acceptance of pork patties.	Moroney, O'Grady, O'Doherty, and Kerry (2013)
		Seaweed extract: 3 and 6 mg/mL	– The laminarin/fucoidan supplemented product had higher antioxidant activity than the one supplemented only with fucoidan and control, after cooking and post digestion.	Moroney et al. (2015)

Beef product	*Undaria pinnatifida*	Seaweed powder: 3%	– Addition of seaweed and olive oil in water emulsion improved the binding properties and the cooking retention values of moisture, fat, fatty acid, and ash with acceptable sensory and good nutritional properties.	López-López et al. (2010) López-López et al. (2011)
	Himanthalia elongata	Seaweed powder: 10%–40%	– Reduced cooking losses, microbiological counts, and lipid oxidation, and increased the tenderness (∼50%), the dietary fiber and phenolic content, and the antioxidant activity – Patties supplemented with 40% seaweed had the highest overall acceptability (texture and mouthfeel).	Cox and Abu-Ghannam (2013b)
Chicken product	*Undaria pinnatifida*	Seaweed extract (fucoxanthin): 0.02%	– Enhanced color in ground chicken breast meat, and inhibited lipid peroxidation in chilling storage after cooking	Sasaki et al. (2008)
	Himanthalia elongata	Seaweed powder: 3%	– Reduced the cooking loss, while retaining sensory acceptance in low-salt restructured poultry steaks	Cofrades, López-López, Ruiz-Capillas, Triki, and Jiménez-Colmenero (2011)

Continued

Table 6 The effects associated with the incorporation of brown seaweeds and their extracts into food products, with regard to food properties and health benefits.—Cont'd

Product	Seaweed source	Seaweed-derived additive	Effect on food and health properties	Reference
Seafood product	*Fucus vesiculosus*	Seaweed extract (oligomeric phlorotannin-rich subfraction): 0.03%	– Demonstrated high potential for use as natural antioxidants in fish and fish products, with effectiveness comparable to 100 mg/kg of the positive control propyl gallate	Wang, Jónsdóttir, et al. (2010)
		Seaweed extract (phloroglucinol): 0.03%	– Demonstrated potential as natural antioxidants against lipid oxidation in fish muscle foods	Jónsdóttir et al. (2016)
Sausage	*Himanthalia elongata*	Seaweed powder: 5.5%	– Improved Na/K ratios, increased calcium, and increased fiber content	López-López, Cofrades, Ruiz-Capillas, and Jiménez-Colmenero (2009c)
		Seaweed powder: 5%	– Improved fat and water binding properties, decreased lightness and redness, increased the hardness and chewiness – Sensory acceptance was reduced by seaweed flavor.	López-López, Cofrades, and Jiménez-Colmenero (2009)
	Laminaria japonica	Seaweed powder: 1%, 2%, 3%, and 4%	– 1% Supplementation had the highest overall acceptability (physicochemical and sensory). – Improved cooking loss and emulsion stability, and increased hardness, gumminess, and chewiness	Kim et al. (2010)

resistant to gastrointestinal digestion and absorption, (2) can be fermented by the microbes in the large intestine, and (3) selectively stimulate the growth and/or activity of the intestinal microbes leading to health benefits of the host (Gibson, Probert, Van Loo, Rastall, & Roberfroid, 2004; Gibson et al., 2010). Gut microbiota is a key contributor to host metabolism and is considered potential source of an alternative therapy (Cani, 2018). The microbiota of a human adult approximately consists of 10^{14} bacterial cells, which is 10 times higher than the total number of human cells. A large number of microorganisms inhabit in the human colon up to 10^{12} bacteria per gram of colonic content (Duda-Chodak, Tarko, Satora, & Sroka, 2015). Prebiotics can be short-chain carbohydrates that plays a key role in enhancing the gut bacterial growth sourcing from natural food. These carbohydrates are non-digestible by digestive enzyme due to their backbone structure, which promotes the growth of selective bacteria that ferments these carbohydrates to short-chain fatty acids (Ashwini et al., 2019). This helps in stimulating the immune system by improving the digestion and absorption mechanism in the body.

The criteria which qualifies any substance prebiotic includes non-digestibility in human body, capability of getting fermented in GI tract and promotion of the growth of beneficial bacteria in the gut (Slavin, 2013). Prebiotics can also be categorized as dietary fibers that contain both polysaccharides and oligosaccharides either insoluble or soluble. Among them soluble fibers swell in stomach and cause decreased absorption in intestinal phase whereas insoluble added fecal bulk due to its capacity to hold water and has reduced absorption time in GI tract (Gurpilhares, Cinelli, Simas, Pessoa Jr., & Sette, 2019). However, their synergistic action provides better growth of gut microflora. Some of the commonly used prebiotic carbohydrates includes oligosaccharides, disaccharides, fructooligosaccharides, monosaccharides, polyols and xylooligosaccharides. Fruits and vegetables, legumes, wheat, barley, oatmeal, artichokes, berries are some of the rich sources of prebiotic fibers that add benefits to human body (Mohanty, Misra, Mohapatra, & Sahu, 2018).

3.2 Health-promoting benefits of prebiotics

The action of prebiotics on improved immune functions can occur directly or indirectly by increasing the microflora population, increasing the metabolism (fructooligosaccharide, maltooligosaccharide, flavonoids) and decreasing pathogenic organisms. Prebiotics studies conducted using combinations of *Bifidobacterium* and *Lactobacillus* report that they are capable of modulating the population of disease-causing microbes and improving the metabolism (Ashwar, Gani, Gani, Shah, & Masoodi, 2018; Dias et al., 2018; Tillmann & Wegener, 2018). The mechanism pathways of prebiotics include binding to G-protein receptors, changing cytokinin expression, inhibition of proinflammatory compounds, and varying gene expression (TLR2, TLR5, TLR7, CD4+ T cells, DP16, DP8 and DP4) (Khangwal & Shukla, 2019). Prebiotics play a vital role in increasing the metabolism and modulation gene expression which inactivates insulin inhibiting genes and thus helps in Type-2 diabetes regulation (Dávila et al., 2018). The addition of prebiotics in food can help prevention of irritable bowel syndrome which is caused by pathogenic bacteria *Helicobacter pylori* by manipulating the microflora in GI tract (Hennet, Mcconnell, Peilz, Salomonsson, & Vigsnæs, 2016). Gut microbiota are found to influence in overall lowering of body and fat mass by reduction in inflammation and glucose control (Klancic & Reimer, 2019). Oligo-fructose rich diets have been reported to decrease the body weight and fat mass, alter fecal bile acids and increase the microbiota composition of *Bifidobacterium* species (Nicolucci et al., 2017; Parnell & Reimer, 2009).

3.3 Prebiotic products in current market

The global market of prebiotics is segmented as fructooligosaccharides, galactooligosaccharides and inulin that are used as key ingredients in various prebiotics food products including dietary supplements, infant formulas, food and beverages and pharmaceuticals. The global market of prebiotics was estimated at 12.2% of Compound Annual Growth Rate (CAGR) from 2019 to 2024 and among that, Europe leads the market share with 43.3% of the global market (Mordor Intelligence, 2018). Inulin is the most utilized in food industry as a beneficial substitute to fat and sugar as it has shown prebiotics function to regulate diabetes. About 82% of global market of prebiotics is absorbed by food and beverage industry and the rest is contributed by dietary supplements and animal feed prebiotics. Some of the global companies that hold major market includes Kraft Foods, Beneo GmbH, Bright Food Corporation, Abott Laboratories (Grand View Research, 2018). The fructooligosaccharide market in 2016 was 1611.45 million USD in 2016 and the prebiotic application significantly increased in dairy products, infant formulas, nutrition bars and health drinks (Research and Markets, 2019). In 2017, the growth of prebiotic market was reported as $3.5 billion and expecting to rise-up to $7.7 billion by 2025 (Nutraceutical World, 2018).

4. Prebiotic effect of seaweeds and seaweed-derived metabolites

4.1 Influence of seaweeds on gastrointestinal microbiome and short chain fatty acids (SCFA) production

The potential of using seaweeds as mediators of gut microbes has been investigated in several studies due to the reported gut health beneficial effect of their bioactive compounds especially polysaccharides. There are no genes identified for the enzymes which are able to digest seaweed polysaccharides in human body (Hehemann et al., 2010; Michel & Macfarlane, 1996; O'Sullivan et al., 2010), so the metabolism of these polysaccharides is manipulated by gut microbiota. Gut microbes play an important role by producing different hydrolytic enzymes to degrade the complex structures and macromolecules of seaweed carbohydrates. The gut microbiota genome composes of several genes that encode diverse carbohydrate-active enzymes (CAZymes) (El Kaoutari, Armougom, Gordon, Raoult, & Henrissat, 2013). CAZymes could digest and ferment the seaweed polysaccharides in the gut. Commonly, the insoluble carbohydrates are firstly digested by gut microbes *Bacteroides* sp. and *Ruminococcus* sp. Then, oligosaccharides are further fermented by *Bifidobacterium* sp. and *Lactobacillus* sp. (Yadav, Verma, & Chauhan, 2018). However, the type and structure of seaweed carbohydrate substrates also affect the manipulation of microbial composition and activity.

The fermentation of seaweed by gut bacteria has also been shown to generate beneficial metabolites mainly short chain fatty acids (SCFA) such as butyrate, acetate, and propionate, apart from gas generation such as H_2, CO_2, and methane (de Jesus Raposo et al., 2016). The beneficial effects of SCFA on host health include protection from obesity, chronic respiratory disease or asthma, cancer, and inflammatory bowel, as well as modulation of immunity, glucose homeostasis, lipid metabolism, and appetite regulation (Bultman, 2016; Dwivedi, Kumar, Laddha, & Kemp, 2016; Koh, De Vadder, Kovatcheva-Datchary, & Bäckhed, 2016; Morrison & Preston, 2016). Butyrate is the primary energy source of cells lining in the colon, and helps maintain colonic tissue integrity through stimulation of apoptosis in cells with high levels of DNA damage (Canani et al., 2011). Butyrate producers include members of Clostridium cluster XIVa which produce the butyrate by the CoA transferase or by butyrate-kinase activity (Louis et al., 2004). Butyrate is also produced by Firmicutes such as

Faecalibacterium prausnitzii and *Lachnospiraceae*, *Eubacterium hallii*, *Clostridium indolis* and *Anaerostipes caccae* using lactate as substrates (Duncan, Louis, & Flint, 2004). Propionate produced in the gut may also influence hepatic cholesterol synthesis (Raman, Ambalam, & Doble, 2016). Bacteroidetes, *Roseburia inulinivorans*, and *Negativicutes* are bacteria species that produce propionate using succinate, propanediol, as well as succinate and acrylate pathway, respectively (Mortensen & Clausen, 1996; Reichardt et al., 2014). Apart from both SCFA, acetate can inhibit the growth of enteropathogenic bacteria (Fukuda et al., 2011). It is quite likely that the metabolite of one microbial population acts as the substrate for the subsequent ones as a co-culture and series fermentation. For instance, *Bifidobacterium longum* could produce acetate, which is used by *Roseburia intestinalis* (Falony, Vlachou, Verbrugghe, & De Vuyst, 2006). Also, *B. longum* produces lactate and that is used by *Eubacterium hallii* to produce butyrate as it is unable to grow alone on carbohydrate substrate (Belenguer et al., 2006).

4.1.1 Seaweed-derived polysaccharides and oligosaccharides

Dietary habits influence the composition and metabolic activity of the human gut microbiota (Conlon & Bird, 2015; Flint, Duncan, Scott, & Louis, 2015). Several studies have demonstrated that a higher intake of plant dietary fiber affects the makeup of beneficial intestinal microbiota and metabolites, and inhibits the growth of potential pathogens compared with animal-dominated diets richer in fat and protein (Claesson et al., 2012; David et al., 2014; Wu et al., 2011; Zimmer et al., 2012). de Jesus Raposo et al. (2016) suggested that most seaweed polysaccharides such as alginates, fucoidans, laminarins, porphyrins, ulvans, and carrageenans can be regarded as dietary fibers, as they are resistant to digestion by enzymes present in the human gastrointestinal tract, and selectively stimulate the growth of beneficial gut bacteria (Fig. 2). Brown seaweed is of particular interest as it contains polysaccharides such as fucoidan, laminarin and alginate which are all reported to have impacts on gut health.

Alginate is generally fermented by a specific gut bacterium, *Bacteroides ovatus* (Salyers, Palmer, & Wilkins, 1978). Apart from *B. ovatus*, alginate is also used by other bacteria in the gut. So, Wang, Han, Hu, Li, and Yu (2006) and Ramnani et al. (2012) demonstrated that alginate and its low molecular weight derivatives could stimulate the growth of *Bifidobacterium* spp. and *Lactobacillus* spp. in the gut. In addition, depolymerized alginate could inhibit the adhesion and invasion of the pathogenic bacterium *Salmonella Typhimurium* in both human enterocyte and BALB/c mice (Kuda et al., 2017).

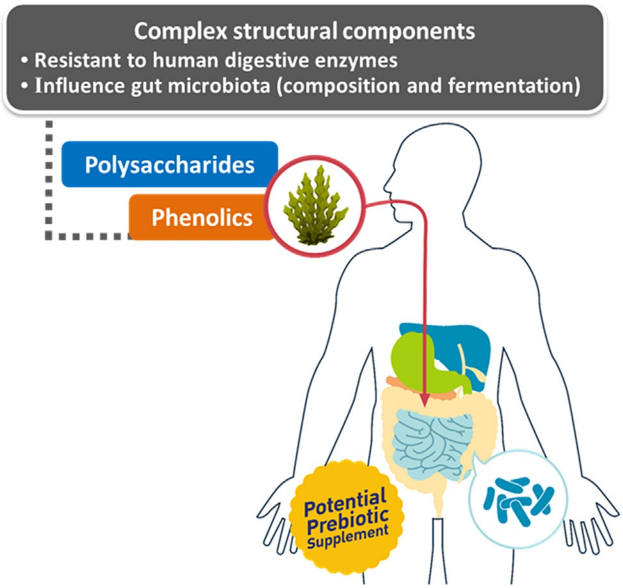

Fig. 2 Seaweed components and their potential health benefits though prebiotic effects (Charoensiddhi, Conlon, Methacanon, et al., 2017; Charoensiddhi, Conlon, Vuaran, et al., 2017).

In contrast to alginate, Shang et al. (2018) reported the potential use of fucoidan as a gut microbiota modulator for health promotion and potential treatment of intestinal dysbiosis. Although fucoidan cannot be fermented by intestinal microbes, it can change the bacterial composition and fermentation ability of gut microbiota and confer benefits to the host. A study in pigs (Lynch et al., 2010) demonstrated that a fucoidan-supplemented diet increased *Lactobacillus* populations and SCFA production. Shang et al. (2016) demonstrated that fucoidan increased the abundance of *Lactobacillus* and *Ruminococcaceae*, and decreased the number of *Peptococcus* in mice.

Regarding the structure of laminarin as a linear polysaccharide, it is easily fermented by gut microbiota. Salyers, Palmer, and Wilkins (1977), Salyers, Vercellotti, West, and Wilkins (1977) demonstrated that specific gut bacteria in the genus of *Bacteroides* such as *B. thetaiotaomicron*, *B. distasonis* and *B. fragilis* could metabolize laminarin by producing laminarinase and β-glucosidase. Several studies provided the beneficial effects of laminarin on gut health. Kuda, Enomoto, and Yano (2009) report that laminarin from seaweeds enhanced the growth of *Bifidobacterium* spp. and *Lactobacillus* spp. in the gut.

4.1.2 Phenolic compounds

Ingested polyphenols with complex structures can also reach the large intestine where they can be converted by microorganisms into beneficial bioactive metabolites (Cardona, Andrés-Lacueva, Tulipani, Tinahones, & Queipo-Ortuño, 2013). The types of polyphenols particularly their presence, metabolism, and roles are variable. Major categories are phenolic acids, flavonoids, stilbenes, and lignans. Polyphenols may be associated with carbohydrates and organic acids, and most of them enter the colon without being absorbed in the small intestine (Manach, Scalbert, Morand, Rémésy, & Jiménez, 2004). This has been shown to occur for phlorotannins from brown seaweed (Corona et al., 2016) as Fig. 2. Charoensiddhi, Conlon, Methacanon, et al. (2017), Charoensiddhi, Conlon, Vuaran, et al., 2017) reported the fermentation of the phlorotannin enriched fraction from brown seaweed *Ecklonia radiata* resulted in a decrease in the numbers of *Enterococcus* which are often linked to poor gut health outcomes. However, low levels of SCFA were produced in comparison to other seaweed fractions and controls. Phlorotannins in brown seaweed appear to have some antibacterial activities (Dierick, Ovyn, & De Smet, 2010) which could explain the low SCFA production although the inhibition of gut bacteria growth occurs for selected populations. Generally, *Bacteroides distasonis*, *Bacteroides ovatus*, *Bacteroides uniformis*, *Enterococcus casseliflavus*, *Eubacterium cellulosolvens*, *Eubacterium ramulus* and *Lachnospiraceae* CG191 are the primary polyphenol degrading bacteria. Monomers and the aglycones are then metabolized *via* decarboxylation and ring-cleavage to form simpler forms such as hydroxyphenyl propionic acid and hydroxyphenyl acetic acids. These reactions have been reported for flavonoids, lignans and phenolic acids (Braune & Blaut, 2016; Braune, Engst, & Blaut, 2016; Marín, Miguélez, Villar, & Lombó, 2015).

4.1.3 Proteins and peptides

Generally, approximately 66%–95% of proteins are absorbed before entering the large intestine depending on genetics and other dietary factors (He, Marco, & Slupsky, 2013). Phlorotannins and high polysaccharide content in seaweeds are the main factors which negatively affect the digestibility of algal proteins (Bleakley & Hayes, 2017). The dietary fiber fermentation demonstrates several gut health benefits including the generation of SCFA and the manipulation of gut microbiomes, while the relationship between gut health and protein fermentation has not been comprehensively studied. Most investigations have been mostly limited to in vitro studies. *Bacteroides*, *Clostridium*, *Propionibacterium*, *Fusobacterium*, *Lactobacillus*, and *Streptococcus* are responsible for proteolysis (Macfarlane & Macfarlane, 2006). The fermentation of aspartate, alanine, threonine, and methionine generates propionate, whereas the fermentation of glutamate, lysine, histidine, cysteine, serine, and methionine leads to the formation of butyrate (Yadav et al., 2018). Propionate and butyrate are produced as a result of amino acid and peptide fermentation by Bacteroidetes and Firmicutes (Scott, Martin, Campbell, Mayer, & Flint, 2006). A fermentation process mainly occurs in the distal colon. The complex proteins are first digested by bacterial exo and endopeptidases to release free amino acids and short peptides (Macfarlane & Macfarlane, 2006). Amino acids and short peptides then undergo fermentation to generate branched chain fatty acids (2-methyl butyrate, isobutyrate, isovalerate), organic acids, gases (H_2 and CO_2) and potentially toxic metabolites such as phenols, amines, indoles, sulfides, and ammonia (Windey, De Preter, & Verbeke, 2012). This is associated with the consumption of high intake of red and processed meat which may increase the risk of colon cancer (Chao et al., 2005). However, Cian, Drago, de Medina, and Martínez-Augustin (2015) demonstrated the proteins and derived peptides together with polysaccharides and minerals could balance the intestinal mucosal barrier function, acting as prebiotics, regulating intestinal epithelial cell, macrophage and lymphocyte proliferation and differentiation, and modulating the immune response.

4.2 Case studies: Prebiotic properties of seaweed and seaweed-derived metabolites

Accumulating evidence provides the basis for the use of seaweeds as prebiotics. Table 7 summarizes up to date the investigation of prebiotic properties from both in vitro and in vivo studies.

4.2.1 In vitro studies

In vitro batch fermentation models commonly use anaerobic human fecal fermentation for 24 h as a model for gut fermentation processes. Using this approach, Deville et al. (2007) reported that laminarin could stimulate the production of SCFA; especially butyrate and propionate. Low molecular weight (MW) polysaccharides from the red seaweed *Gelidium sesquipidale* caused a significant increase in populations of *Bifidobacterium*, as well as an increase in acetate and propionate (Ramnani et al., 2012). Rodrigues et al. (2016) obtained a similar result using an extract from the brown seaweed *Osmundea pinnatifida*. Charoensiddhi, Conlon, Vuaran, Franco, and Zhang (2016), Charoensiddhi, Conlon, Methacanon, et al. (2017),

Table 7 Summary of fermentation performance of different seaweed dietary fibers by in vitro and in vivo models of gut microbiota reported from 2016 to 2019.

Polysaccharides	Fermentation models	SCFA	Microbiota composition changes	Reference
Alginate	In vitro	↑Total SCFA	↑*Bacteroides* (*Bacteroides finegoldii*)	Ai et al. (2019)
Alginate	In vitro	↑Propionate ↑Butyrate ↑Total SCFA	↑*Bacteroides*	Bai et al. (2017)
Alginate (Alg) Mannuronic acid Oligosaccharides (MO) Guluronic acid Oligosaccharides (GO) Propylene glycol alginate Sodium sulfate (PSS)	In vitro	Alg, MO, GO: ↑Acetate ↑Propionate ↑Butyrate ↑Total SCFA	Detection of *Bacteroides xylanisolvens*, *Clostridium clostridioforme/Clostridium symbiosum*, *Bacteroides finegoldii*, *Shigella flexneri/E. coli/E. fergusonii*, and *Bacteroides ovatus*	Li et al. (2016)
Alginate	In vivo (cecum)	↓Indole	↑*Catabacter hongkongensis* ↑*Stomatobaculum longum* ↓*Adlercreuzia* ↓*Helicobacter*	Nakata, Kyoui, Takahashi, Kimura, and Kuda (2016)
Fucoidan	In vivo (feces)	–	↓Bacteroidetes ↑Firmicutes ↑Prevotella	Xue et al. (2018)

Fucoidan + Alginate	In vivo (cecum)	↑Acetate ↑Propionate ↑Butyrate ↑Total SCFA ↓Phenol ↓*p*-cresol	↑*Faecalibacterium prausnitzii*	Charoensiddhi, Conlon, Methacanon, et al. (2017)
Fucoidan	In vivo (cecum)	–	↑*Lactobacillus* ↑*Ruminococcaceae* ↓*Peptococcus*	Shang et al. (2016)
Laminarin	In vitro	↑Acetate ↑Propionate ↑Total SCFA	↑*Bifidobacteria* ↑*Bacteroides*	Seong et al. (2019)
Laminarin	In vivo (cecum)	↑Lactic acid ↓Indole	↑*Lactobacillus* ↑*Porphyromonas* ↑*Coprobacillus* ↑*Oscillibacter valericigenes* ↓*Parabacteroides* ↓*Helicobacter*	Nakata et al. (2016)
Laminarin	In vivo (feces)	–	↑Bacteroidetes ↓Firmicutes	Nguyen et al. (2016)
Agarose (Neoagarotetraose)	In vivo (feces)	↑Total SCFA	↑*Bifidobacterium* ↑*Lactobacillus* ↑*Prevotella*	Zhang et al. (2017)

Continued

Table 7 Summary of fermentation performance of different seaweed dietary fibers by in vitro and in vivo models of gut microbiota reported from 2016 to 2019.—Cont'd

Polysaccharides	Fermentation models	SCFA	Microbiota composition changes	Reference
Porphyran	In vitro	Not significant difference	↑ *Bifidobacteria* ↑ *Bacteroides*	Seong et al. (2019)
Porphyran	In vitro	↑ Acetate ↑ Propionate ↑ Butyrate ↑ Total SCFA	↑ Bacteroides thetaiotaomicron ↑ Bacteroides ovatus ↑ Defluviitalea saccharophila ↑ Faecalibacterium prausnitzii	Xu et al. (2019)
Carrageenan	In vitro	↑ Total SCFA	↑ *Prevotella* ↓ *Bacteroides* ↓ *Parabacteroides*	Sun et al. (2019)
Ulvan	In vitro	↑ Acetate ↑ Lactate	↑ *Bifidobacteria* ↑ *Lactobacillus*	Seong et al. (2019)

Charoensiddhi, Conlon, Vuaran, et al. (2017) demonstrated that extracts from the brown seaweed *Ecklonia radiata* stimulated the production of SCFA and the growth of beneficial microbes such as *Bifidobacterium* and *Lactobacillus*. In addition, Kuda et al. (2015) demonstrated that sodium alginate and laminaran from brown seaweeds inhibited the adhesion and invasion of pathogens (*Salmonella* Typhimurium, *Listeria monocytogenes*, and *Vibrio parahaemolyticus*) in human enterocyte-like HT-29-Luc cells. The effect of whole brown seaweed *Ascophyllum nodosum* on piglet gut flora was studied by simulating small intestinal and caecal conditions, with antibacterial effects, especially on *E. coli*, and also observing a decrease in fermentative activity (Dierick et al., 2010).

To simulate the physiological fermentation, in vitro conditions in the oral, gastric, and small intestine were performed prior to the in vitro batch fermentation. The digestibility of seaweed components can be determined whether they are decomposed by human digestive enzymes, and thus their likelihood of reaching the large bowel and its resident microbiota. Neoagaro-oligosaccharides and glycerol galactoside from red seaweeds, for instance, have shown that they were not digestible by enzymes typically present in the small intestine (Hu et al., 2006; Muraoka et al., 2008).

Several studies used another model called in vitro dynamic continuous culture systems or multi-stage dynamic in vitro models. The simulator of the TNO in vitro model of the colon (TIM) and the human intestinal microbial ecosystem (SHIME®) are typical representative models. Most of the dynamic fermentation models mimic the conditions of stomach, small intestine, and colon (proximal, transverse and distal colon) (Wang et al., 2019). However, only a few studies investigated these colonic fermentation models in seaweeds. Torres-Escribano et al. (2011) reported static and dynamic models which mimic human physiological conditions to evaluate bioaccessibility of elements in seaweed *Fucus* sp., IAEA-140/TM.

4.2.2 In vivo animal studies

The complex interactions between dietary components, gastrointestinal physiological processes, and gut microbiota are difficult to model in vitro. Therefore, it is important to follow up promising in vitro results with in vivo studies. The health benefits attributed to oligosaccharides and polysaccharides derived from seaweeds have been demonstrated by in vivo animal models. Most such studies have investigated prebiotic effects in rats or mice being fed a seaweed-supplemented diet. The germ-free mice is another animal model that allows to study the absence of microbes or the gnotobiotic animals exclusively colonized by known microbes. The dominant gut bacteria in human are Firmicutes and Bacteroidetes, and the baseline of gut microbiota in mice is not exactly the same as human. Therefore, humanized germ-free rats inoculated with fecal microbiota from human donors have been found to show more similar Firmicutes: Bacteroidetes phylogenetic ratios than mice (Turner, 2018). However, the generation and maintenance require specialized facilities, high costs, and skilled persons leading to the limited use of this mice model in many research (Kennedy, King, & Baldridge, 2018).

Results from Liu et al. (2015) showed an increase in the abundance of beneficial gut microbes such as *Bifidobacterium breve* and a decrease in pathogenic bacteria such as *Streptococcus pneumonia* and *Clostridium septicum* in rats supplemented with the red seaweed *Chondrus crispus*. Furthermore, an increase in SCFA production and colonic growth was observed, as well as an improvement of host immunity modulation though elevation of the plasma immunoglobulin levels. Supplementation of diets with the brown seaweeds *Undaria pinnatifida* and *Laminaria japonica* has resulted in suppressed weight gain of rats, influenced the composition of gut microbial communities associated with obesity by reduction in the ratio of *Firmicutes* to *Bacteroidetes*, and reduced populations of pathogenic bacteria including *Clostridium*, *Escherichia*, and *Enterobacter* genera (Kim et al., 2016). The oral administration of fucoidan extracts has been shown to reduce the inflammatory pathology associated with DSS-induced colitis in mice, indicating its potential for treating inflammatory bowel disease (Lean, Eri, Fitton, Patel, & Gueven, 2015). In addition, Kuda et al. (2005) reported that rats fed with a diet containing laminarin and low MW alginate suppressed the production of indole, *p*-cresol, and sulfide which are the putative risk markers for colon cancer. Neoagaro-oligosaccharides derived from the hydrolysis of agarose by β-agarase resulted in an increase in the numbers of *Lactobacillus* and *Bifidobacterium* in the feces or cecal content of mice, along with a decrease in putrefactive bacteria (Hu et al., 2006).

5. Concluding remarks

Seaweeds are valuable sources of bioactive compounds including polysaccharides, polyphenols, and proteins for potential gut health benefits. The application of these seaweed-derived compounds in functional foods and nutraceuticals is being increasingly recognized, particularly with regard to prebiotic supplements. Most seaweed polysaccharides can be regarded as dietary fiber that are resistant to digestion by enzymes present in the human gastrointestinal tract, and selectively stimulate the growth of beneficial gut bacteria. Increasing scientific evidence from both in vitro and in vivo studies provides encouraging data to support the utilization of seaweeds and their-derived compounds to modulate the formation of SCFA and gastrointestinal microbiome. Despite the evidences, there are still lack of clinical studies using in vivo human models to validate the results obtained by the in vitro and in vivo animal studies.

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