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Review

In vitro antioxidant properties of crude extracts and compounds from brown algae

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ABSTRACT

Research on the bioactives from seaweeds has increased in recent years. Antioxidant activity is one of the most studied, due to the interest of these compounds both as preservatives and protectors against oxidation in food and cosmetics and also due to their health implications, mainly in relation to their potential as functional ingredients. Brown algae present higher antioxidant potential in comparison with red and green families and contain compounds not found in terrestrial sources. *In vitro* antioxidant chemical methods, used as a first approach to evaluate potential agents to protect from lipid oxidation in foods, confirmed that the brown algae crude extracts, fractions and pure components are comparatively similar or superior to synthetic antioxidants. Particular emphasis on the fucoidan and phlorotannin polymeric fractions is given, considering variations associated with the species, collection area, season, and extraction and purification technologies.

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1. Introduction

The number of new compounds isolated from marine sources has been increasing steadily (Blunt, Copp, Keyzers, Munro, & Prinsep, 2012). Marine organisms possess great taxonomic diversity and synthesise metabolites with varied structures with interesting biological activities for food, cosmetics, biotechnology and pharmacy. Some macroalgae live in complex habitats exposed to extreme conditions that lead to the formation of free radicals and other oxidising agents. However, the absence of structural and photodynamic induced damage suggests that their cells possess mechanisms for a rapid adaptation, producing secondary metabolites, which protect them against oxidative stress (Batista González, Charles, Mancini-Filho, & Vidal Novoa, 2009; Jiménez-Escrig, Jiménez-Jiménez, Pulido, & Saura-Calixto, 2001). Natural antioxidants, the kind of compounds which have attracted major interest, may replace synthetic ones in prolonging the shelf life of food and cosmetics by delaying oxidation. They may also confer valuable properties to the product, acting against oxidation-associated diseases, ageing and skin UV-exposure. In recent years biologically active compounds from marine algae have been proposed for nutraceuticals and functional foods. Seaweeds are commonly classified into three groups based on their pigmentation: brown (Phaeophyceae), red (Rhodophyceae) and green (Chlorophyceae) algae. Phaeophyta have been reported to contain comparatively higher contents and more active antioxidants than green and red algae (Al-Amoudi, Mutawie, Patel, & Blunden, 2009; Costa et al., 2010; Cox, Abu-Ghannam, & Gupta, 2010; Kang et al., 2004; Kindleysides, Quek, & Miller, 2012).

The biological properties of algae have been summarised in numerous reviews. The most recent present the food and pharmacological applications (Cardozo et al., 2007; Chu, 2011; Lordan, Ross, & Stanton, 2011; Smit, 2004; Thomas & Kim, 2011), the potential of polysaccharides, polyphenolic compounds and terpenes (Chu, 2011; Gupta & Abu-Ghannam, 2011; Holdt & Kraan, 2011; Jiao, Yu, Zhang, & Ewart, 2011; Jiménez-Escrig et al., 2001; Mohamed, Hashim, & Rahman, 2012; Wijesekara, Kim, Li, & Li, 2011), and their nutritional and functional properties (Bocanegra, Bastida, Benedí, Ródenas, & Sánchez-Muniz, 2009; Kumar, Ganesan, Suresh, & Bhaskar, 2008). Recent reviews on macroalgae did not focus on antioxidants, but instead reviewed their composition, bioactivity and extraction methods (Herrero, Cifuentes, & Ibáñez, 2006; Plaza, Cifuentes, & Ibáñez, 2008), potential industrial utilisation (Ngo, Wijesekara, Vo, Van Ta, & Kim, 2011), properties of the liposoluble and hydrosoluble fractions for phytomedicinal uses (Batista González et al., 2009), and identification and extraction of antihypertensive and antioxidant components of green, red and brown algae (Tierney, Croft, & Hayes, 2010).

Antioxidants in a food system refer conventionally to compounds that inhibit lipid autoxidation; in a broader scope, dietary antioxidants are also considered. However, the beneficial effects of antioxidant therapy against oxidative stress are controversial (Halliwell, 2011), and antioxidant properties alone are not sufficient to explain their biological properties. The necessity of antioxidants in food and cosmetics is evident and the search for natural alternative sources is increasing. This work reviews recent publications in English, summarising the content and *in vitro* antioxidant properties of crude extracts, refined fractions and pure compounds, emphasising those found exclusively in brown algae. The *in vitro* antioxidant action is used as a first tool to select potential compounds for the protection from oil oxidation and for further formulation of functional foods. The major factors affecting the activity, such as species, environmental and seasonal conditions, and processing technologies are also discussed.

2. Major components of brown marine algae

Extraction from the algal biomass is usually not selective and the extracts are complex mixtures of the major compounds present in brown macroalgae: polysaccharides, phenolic compounds, polyunsaturated fatty acids, proteins, peptides, pigments, vitamins, terpenoids and sterols. Their content varies with season, age, species, geographical location and environmental factors. The structure, occurrence and bioactivity of the major components contributing to the antioxidant properties will be briefly discussed.

2.1. Polysaccharides

The cell wall of brown algae is mainly composed of fucoidan, alginate and laminarin (3:1:1) and their derivatives. These reserve polysaccharides provide strength and flexibility, maintain ionic equilibrium and prevent desiccation. They are suitable as thickeners and gelation agents. Comparative data on the polysaccharide content in brown algae (Holdt & Kraan, 2011; O'Sullivan et al., 2010; Zvyagintseva et al., 2003), their composition, functional and antioxidant properties have been reported (Cofrades et al., 2010; Elleuch et al., 2011; Rupérez & Saura-Calixto, 2001). Positive effects of seaweed crude and refined fractions in the gastrointestinal tract (Jiménez-Escrig & Sánchez-Muniz, 2000) were confirmed *in vitro* (Rupérez & Toledano, 2003) and with rats (Gudiel-Urbano & Goñi, 2002), pigs, lambs and cattle (O'Sullivan et al., 2010).

Alginic acid, a linear anionic polysaccharide containing 1,4-linked β-D-mannuronic acid and α-L-guluronic acid residues, is commercially used as a gelling agent. Laminarin, composed of (1,3)-β-D-glucopyranose residues, has a relatively low molecular weight and its structural features are species dependent. Laminarin is a modulator of intestinal metabolism (Deville, Gharbi, Dandrifosse, & Peulen, 2007), an activator of immune function (Choi, Kim, & Lee, 2011) but a less potent antioxidant than other components (Chattopadhyay et al., 2010).

Fucoidans are complex sulfated polysaccharides found in the cell walls of brown algae. They account for 10–20% dw, consisting mainly of sulfated L-fucose and small proportions of galactose, mannose, xylose, glucose, rhamnose and uronic acids (Pomin & Mourão, 2008; Usov & Bilan, 2009). Fucoidans are not found in other divisions of algae nor in land plants, and show more complex and heterogeneous composition and structure than the related polymers found in marine invertebrates (fucan sulfates), which contain only fucose and sulfate groups. Fucans are very soluble, do not develop highly viscous solutions and the technologies to obtain them can include (i) extraction of low molecular weight compounds, (ii) extraction with water, acid or calcium chloride, eventually aided by either hydrolytic enzymes, or ultrasound or microwave, (iii) precipitation and (iv) purification. Depolymerisation of crude fucoidans can be attained by chemical, physical, enzymatic (Anastyuk, Shevchenko, Nazarenko, Dmitrenok, & Zvyagintseva, 2009; Foley, Mulloy, & Tuohy, 2011) or radical induced (Hou, Wang, Jin, Zhang, & Zhang, 2012; Morya, Kim, & Kim, 2012) processes.

The composition, structures and pharmaceutical properties of fucoidans, including their tolerance and safe use have been reviewed (Berteau & Mulloy, 2003; Bilan & Usov, 2008; Holtkamp, Kelly, Ulber, & Lang, 2009; Jiao et al., 2011; Kusaykin et al., 2008; Li, Lu, Wei, & Zhao, 2008; Morya et al., 2012; Pomin & Mourão, 2008; Usov & Bilan, 2009; Wijesekara et al., 2011). The low molecular weight fractions are usually more biocompatible and active than the crude extract and preservation of the original structure and sulfation pattern is desirable (Anastyuk et al., 2009; Usov & Bilan, 2009), but there is no consensus on the optimal molecular size nor definitive correlation between structure and activity (Bilan & Usov, 2008; Li et al., 2008; Rocha et al., 2006).

Fucoidans frequently exert antithrombotic action (Berteau & Mulloy, 2003; Mourão, 2004), not directly related to anticoagulant activity, which has been extensively studied. Antitumour activity (Gamal-Eldeen, Ahmed, & Abo-Zeid, 2009; Ye et al., 2005) was confirmed in treatment and prevention of some cancers (Gamal-Eldeen et al., 2009; Kawamoto et al., 2006). Fucoidans have shown antiviral (Chen, Lim, Sohn, Choi, & Han, 2009; Hayashi, Nakano, Hashimoto, Kanekiyo, & Hayashi, 2008) and antiinflammatory (Abad, Bedoya, & Bermejo, 2008; Ananthi et al., 2010) actions, protection against radiation (Berteau & Mulloy, 2003; Lee, Bae, Cho, & Rhee, 2009), osteoarthritis (Myers et al., 2009) and gastric ulcers (Choi, Hwang, Kim, & Nam, 2009). Other uses have been proposed, e.g., growth stimulators and/or pesticides (Laporte et al., 2007), bone regeneration (Igondjo et al., 2008) and protection form oxidative damage (Hu, Liu, Chen, Wu, & Wang, 2010; Rupérez, Ahrazem, & Leal, 2002).

2.2. Phenolics and phlorotannins

Phenolics refer to monomeric, oligomeric or polymeric compounds with an aromatic ring bearing one or more hydroxyl substituents, and include simple phenols, coumarins, flavonoids, stilbenes, lignans, hydrolysable and condensed tannins, and phlorotannins. Phenolics play a primary role as structural components of cell walls and may have secondary roles in signalling, defence (Amsler & Fairhead, 2006) or in responses to environmental stress. Phlorotannins, produced by plant secondary metabolism in many Phaeophyceae (Kang et al., 2004; Koivikko, Loponen, Pihlaja, & Jormalainen, 2007; Serrano, Puupponen-Pimia, Dauer, Aura, & Saura-Calixto, 2009), are not found in terrestrial plants. They are oligomers or polymers of phloroglucinol (1,3,5-trihydroxybenzene), connected by aryl–aryl bonds (fucols), ether bonds (phlorethols, hydroxyphlorethols, fuhalols), or both (fucophlorethols) or with a dibenzodioxin linkage (eckols and carmalols) (Koivikko et al., 2007; Singh & Bharate, 2006). Flavonoids have not been found in brown algae, although phenolic acids and aldehydes have been identified (López, Rico, Rivero, & Suárez de Tangil, 2011; Onofrejová et al., 2010; Zubia et al., 2009). Marine algae bromophenols are probably associated with the perception of flavour (Da Silva et al., 2007).

Phlorotannins have a wide range of molecular sizes (400–400,000 Da) and can occur in variable concentrations (0.5–20% dw) in brown algae. The reported phenolic content of *Sargassum* and *Turbinaria* sp. (Stiger, Deslandes, & Payri, 2004) and comparative studies (Connan, Delisle, Deslandes, & Ar Gall, 2006; Cox et al., 2010; Nakai, Kageyama, Nakahara, & Miki, 2006) have been published. Whereas in some algae the phenolic and phloroglucinol derived fraction accounts for less than 1% dw, values close to 5% and higher were observed for *Ascophyllum nodosum* (Audibert, Fauchon, Blanc, Hauchard, & Ar Gall, 2010; Connan et al., 2006), *Cystoseira compressa* and *C. foeniculaceae* (Chkhikvishvili & Ramazanov, 2000), *Sargassum hemiphyllum*, *S. mangarevense*, *S. muticum*, *S. ringgoldianum* and *S. yezoense* (Boonchum et al., 2011; Connan et al., 2006; Le Lann, Jégou, & Stiger-Pouvreau, 2008; Nakai et al., 2006; Zubia, Payri, & Deslandes, 2008), *Turbinaria conoides* (Boonchum et al., 2011), and *Himanthalia elongata* (Cofrades et al., 2010; Cox et al., 2010).

Antimicrobial activity of phlorotannins against food-borne bacteria (Nagayama, Iwamura, Shibata, Hirayama, & Nakamura, 2002) and algae (Nagayama, Shibata, Fujimoto, Honjo, & Nakamura, 2003; Nagayama et al., 2002) have been reported. Anti-inflammatory properties (Kim & Bae, 2010; Kim & Kim, 2010; Lopes et al., 2012), therapeutic potential in arthritis treatment (Kang et al., 2004; Shin, Hwang, Kang, & Lee, 2006), antiphotocarcinogenic effect (Hwang, Chen, Nines, Shin, & Stoner, 2006) and protection against glucose-induced oxidative stress (Iwai, 2008; Lee et al., 2010) have also been reported. Hypopigmenting products from natural sources are increasingly demanded. Active whitening compounds can achieve the hypopigmenting effect by inhibiting tyrosinase or by blocking the upstream regulation points of melanogenesis. Phlorotannins are effective inhibitors of tyrosinase and melanin synthesis (Ahn, Jeon, Kang, Shin, & Jung, 2004) and absence of cytotoxic effects has been confirmed (Kim & Kim, 2010; Kim et al., 2009; Zou et al., 2008). Phlorotannins exhibit other activities, such as antioxidant, anticancer (Athukorala, Kim, & Jeon, 2006), antihypertension (Jung, Lee, & Choi, 2004), protection against vascular diseases (Kang et al., 2003a). Bromophenols also show some of these biological activities and could be used for pharmaceutical and medical applications (Liu, Hansen, & Lin, 2011).

2.3. Protein and peptides

The protein content of brown seaweed is generally low (6–13% dw) (Dawczynski, Schubert, & Jahreis, 2007; Hernández-Carmona et al., 2009; McDermid & Stuercke, 2003; Sánchez-Machado, López-Cervantes, López-Hernández, & Paseiro-Losada, 2004). The content of proteins, peptides and amino acids in seaweed has been reviewed (Harnedy & Fitzgerald, 2011; Holdt & Kraan, 2011). The protein content of marine algae varies greatly with species, seasons and nutrients (Stengel, Connan, & Popper, 2011).

Most seaweed proteins have a high nutritional value, being a rich source of aspartic acid, glutamic acid, and leucine, whereas threonine, lysine, tryptophan, sulphur amino acids and histidine are limiting, but at higher levels than those found in terrestrial plants (Dawczynski et al., 2007; Hernández-Carmona et al., 2009; Kolb, Vallorani, Milanović, & Stocchi, 2004). The protein digestibility (Fleurence, 1999; Wong & Cheung, 2001) is limited by the non-protein fraction (Dawczynski et al., 2007; Goñi, Gudiel-Urbano, & Saura-Calixto, 2002; Rupérez & Saura-Calixto, 2001), which accounts for 10–20% of the nitrogen content (Holdt & Kraan, 2011). The isolation of protein from algae is difficult due to viscous polysaccharides; the use of buffers and detergents for effective cell lysis and removal of polysaccharide was proposed (Kim, Kong, & Kim, 2010). Isolation of peptides from seaweeds has been addressed (Aneiros & Garateix, 2004). Their incorporation into an expanding variety of functional foods is suggested based on their antioxidative properties (Ngo et al., 2011) and hypotensive effects (Fitzgerald, Gallagher, Tasdemir, & Hayes, 2011).

2.4. Lipids

Lipid content in marine brown algae is low, 0.57–3.5% (dw), and wide variations among species have been observed (Aknin et al., 1992; Dawczynski et al., 2007; Hernández-Carmona et al., 2009; Holdt & Kraan, 2011; Khotimchenko & Kulikova, 2000; Kim et al., 2010; Kumari, Kumar, Gupta, Reddy, & Jha, 2010; Li, Fan, Han, & Lou, 2002; McDermid & Stuercke, 2003; Polat & Ozogul, 2008; Terasaki et al., 2009). Algal lipids have a higher proportion of polyunsaturated fatty acids (PUFA) than terrestrial plants. These PUFA are components of structural membrane lipids and are essential

for animal and human nutrition. The two classes of PUFA (ω3; ω6) have opposing physiological functions and their balance is important for normal growth and development. Brown algae have a balanced ω6/ω3 ratio (0.6–5.1:1), considering that in a healthy human diet the ratio of ω6/ω3 should not exceed 10:1. Differences in the fatty-acids composition among species and intraspecies variations with environmental and geographical factors (Li et al., 2002; Narayan, Miyashita, & Hosakawa, 2004), seasons (Terasaki et al., 2009), and algal parts (Khotimchenko & Kulikova, 2000) have been reported. Some PUFAs from algae can have anti-inflammatory (Khan et al., 2007) and anti-fouling actions, and prevent the undesirable accumulation of microrganisms, plants and invertebrates on artificial surfaces submerged in seawater (Plouguerné et al., 2010; Sidharthan, Viswanadh, Kyoung, Hyuk, & Shin, 2007), while some of the ω3 series are superoxide scavengers (Kim et al., 2010; Richard, Kefi, Barbe, Bausero, & Visioli, 2008).

2.5. Terpenoids and steroids

Terpenes are lipophilic secondary metabolites made up of isoprene units, and can be grouped into hemi-, mono-, sesqui-, di-, sester-, tri-, and tetraterpenoids (carotenoids). Some diterpenes exclusive to marine organisms have been suggested as taxonomic markers (Daoudi et al., 2001). Isolation of diterpenes from the genus *Bifurcaria* (Culioli, Di Guardia, Valls, & Piovetti, 2000; Daoudi et al., 2001), *Dictyota* (Abrantes et al., 2010) and *Sargassum* (Jang, Lee, Choi, Lee, & Shin 2005) has been reported (Khan, 2010; Plaza et al., 2008). Antioxidant activity (Jang et al., 2005) and antiviral action against herpes (Abrantes et al., 2010) have been reported.

Carotenoids are coloured terpenes with great structural diversity, and functional roles in hormone synthesis, photosynthesis, photomorphogenesis and photoprotection. Different carotenoids, such as α- and β-carotene, lutein, zeaxanthin, fucoxanthin, chlorophyll a and phaeophytin a, have been identified in seaweeds. Carotenoids play a role in human nutrition, providing provitamin A, preventing age-related macular degeneration and cerebrovascular diseases. The xanthophyll fucoxanthin is found in microalgae, brown macroalgae and diatomeae, and has protective and photosynthetic functions. Fucoxanthin content shows seasonal variations and values in the range 1–6 mg/g (de Quirós, Frecha-Ferreiro, Vidal-Pérez, & López-Hernández, 2010; Le Lann et al., 2012; Terasaki et al., 2009; Yan, Chuda, Suzuki, & Nagata, 1999), up to 16 mg/g for *Turbinaria* sp (Le Lann et al., 2012) and higher for *Undaria pinnatifida* and *Laminaria* sp (De Quirós et al., 2010) were reported. Fucoxanthin content and properties (Holdt & Kraan 2011; Le Lann et al., 2012; Lordan et al., 2011) and structural features in relation to activity and bioavailability (Heo et al., 2010; Peng, Yuan, Wu, & Wang, 2011) have been reviewed. Fucoxanthin protects from UV-B (Shimoda, Tanaka, Shan, & Maoka, 2010), and has shown antiangiogenic (Hosokawa, Okada, Mikami, Konishi, & Miyashita, 2009; Ishikawa et al., 2008), anti-inflammatory (Heo et al., 2010), antiobesity and antidiabetic (Maeda, Hosokawa, Sashima, Murakami-Funayama, & Miyashita, 2009) actions.

2.6. Other components

The predominant sterol in brown algae is fucosterol (Daoudi et al., 2001; Li et al., 2009; Plaza et al., 2008; Yan et al., 1999). Its sources (Terasaki et al., 2009), content and activity (Khan, 2010) have been reported. Fucosterol has beneficial effects, including inhibition of cholesterol absorption, anticancer, antioxidant (Lee, Yeon, Sang, Sam, & Kuk, 2003), antidiabetic, antiinflammatory, antibacterial, antifungicidal and antiulcerative (Plaza et al., 2008) actions. Ethylenecholesterol (Sánchez-Machado et al., 2004), cholesterol and ergosterol (Li et al., 2009) have also been found in brown algae.

Brown algae contain highly variable and seasonal dependent levels of vitamins (Hernández-Carmona et al., 2009; McDermid & Stuercke, 2003). Up to 1 mg vitamin C/g in *Eisenia arborea* (Hernández-Carmona et al., 2009), *Laminaria digitata* and higher content in *U. pinnatifida* (MacArtain, Gill, Brooks, Campbell, & Rowland, 2007) have been found. Vitamin E includes a family of tocopherols and tocotrienols and their ester derivatives, and is associated with membrane lipids or in storage stuctures. Tocopherol content is higher in brown than in red and green algae (Jiménez-Escrig & Goñi, 1999; Lordan et al., 2011), the principal isomer being α-tocopherol. Values in the range 1–1.5 mg/g were reported for *Laminaria* sp, *Fucus distichus*, *Desmarestia viridis*, *Chorda tomentosa* (Aguilera, Dummermuth, Karsten, Schriek, & Wiencke, 2002), *S. hemiphyllum* (Chan, Cheung, & Ang, 1997), *E. arborea* (Hernández-Carmona et al., 2009), *A. nodosum,* and *Fucus* sp (Le Tutour et al., 1998). Compiled data outlining Vitamin C and E levels in macroalgae are available (Lordan et al., 2011).

The mineral composition and content of brown algae, dependent on environmental, geographical and physiological factors (Funaki, Nishizawa, Sawaya, Inoue, & Yamagishi, 2001) and postharvest conditions have been evaluated (Kolb et al., 2004; Kuda & Ikemori, 2009; MacArtain et al., 2007; Rupérez & Toledano, 2003). Algae contain Se, Zn, Mn and Cu, which are structural components of some antioxidant enzymes and could contribute to their action once ingested (Batista González et al., 2009).

3. *In vitro* antioxidant properties of crude extracts, fractions and pure components from brown algae

3.1. Oxidation process and determination of antioxidant activity

Protection against oxidation is fundamental to maintain the nutritional and organoleptic properties of oil-containing foods. In these systems autoxidation of lipids is among the most important mechanisms, involving: (i) initiation, by chemical, thermal, electromagnetic and enzymatic means, leading to an increase in the number of free radicals; (ii) propagation by a radical chain reaction, and (iii) termination by producing non-radical compounds. The primary products are lipid hydroperoxides, which are very unstable and degrade to secondary oxidation products (aldehydes, ketones, alcohols, hydrocarbons) that affect food quality. Antioxidants can act by (i) scavenging species responsible for initiation, (ii) interrupting the chain reaction, (iii) singlet oxygen quenching, (iv) synergism increasing the activity of chain-breaking antioxidants, (v) reducing action, (vi) metal chelation or (vii) inhibiting specific oxidative enzymes. Antioxidants often act by mixed and cooperative mechanisms (Choe & Min, 2009; Craft, Kerrihard, Amarowicz, & Pegg, 2012).

Oxidation is also relevant at the biological level. Reactive species are collectively referred to as reactive oxygen species (ROS) and reactive nitrogen species (RNS). ROS include oxygen radicals and non-radical derivatives, which can be converted into radicals or act as oxidising agents. RNS includes nitrogen radical and non-radical species. Several ROS and NOS are relevant to food systems and metabolic processes: oxygen is essential for aerobic organisms and nitrogen is present in foods and *in vivo* in animals and plants; their intermediates may be essential for cellular functions, immune responses and redox regulation of signal transduction (Halliwell, 2002). There is a balance between generation and inactivation of ROS and RNS to minimise molecular, cellular and tissue damage. For this purpose cells have developed defence mechanisms, including metal chelators, low molecular weight antioxidants and enzymatic systems, and are also protected by chemical compounds and natural products. Under pathological conditions the imbalance between RS levels and antioxidant defences causes

oxidative stress, associated with the initiation and promotion of degenerative diseases.

Growing health concerns have increased the interest of finding safe and effective natural antioxidants to replace synthetics, which could have some harmful effects (Kahl & Kappus, 1993). Usually synthetic antioxidants are more eficient at lower doses, whereas natural extracts may be added in higher quantities and in many cases are generally recognised as safe (GRAS). The confirmed

Table 1
Pure compounds identified in brown algae and their *in vitro* action in relation to food protection from oxidation.

Compouds	Alga	Antioxidant activity reported	Reference
Carotenoids			
Fucoxanthin	*Sargassum* sp.	RSA: $ABTS^{\cdot+}$	
	Sargassum elegans	Oxidation potential	Ayyad et al. (2011), Ragubeer et al. (2012)
Meroterpenoids			
Fallahydroquinone, fallaquinone and fallachromenoic acid	*Sargassum fallax*	RSA: DPPH, $ONOO^-$	Reddy and Urban (2009)
Plastoquinones	*Sargassum micracanthum*	RSA: DPPH Inhibition of lipid peroxidation	Iwashima et al. (2005), Mori et al. (2005).
Tetraprenyltoluquinol derivatives (sargahydroquinoic acid, sargaquinoic acid, sargachromenol, thunbergol a, thunbergol b…)	*Cystoseira crinita*, *Sargassum thunbergii*, *S. elegans*	RSA: $ABTS^{\cdot+}$, DPPH, $O_2^{\cdot-}$, $ONOO^-$ Linoleic acid methyl ester peroxidation Oxidation potential	Fisch et al. (2003), Seo et al. (2004, 2006), Reddy and Urban (2009), Ragubeer et al. (2012)
Triprenyltoluquinol derivatives	*Cystoseira crinita*	RSA: DPPH, $O_2^{\cdot-}$, $ABTS^{\cdot+}$ Linoleic acid methyl ester peroxidation	Fisch et al. (2003)
Triprenyltoluquinone derivatives	*Cystoseira crinita*	RSA: DPPH, $O_2^{\cdot-}$, $ABTS^{\cdot+}$Linoleic acid methyl ester peroxidation	Fisch et al. (2003)
Mojabanchromanol	*Sargassum siliquastrum*	RSA: DPPH Chelating	Cho et al. (2008)
Sargachromanol a–p	*Sargassum siliquastrum*	RSA: DPPH	Jang et al. (2005)
Sargaol, sargaquinone	*Taonia atomaria*	RSA: DPPH, ·OH	Nahas et al. (2007)
Stypodiol, stypoldione	*Taonia atomaria*	RSA: DPPH, ·OH	Nahas et al. (2007)
Taondiol, isoepitaondiol	*Taonia atomaria*	RSA: DPPH, ·OH	Nahas et al. (2007)
Phloroglucinol derivatives			
2,7″-phloroglucinol-6,6′-bieckol	*Ecklonia cava*	RSA: alkyl, DPPH, ·OH, $O_2^{\cdot-}$, ROS	Kang et al. (2012)
6,6′-bieckol	*Hizikia fusiformis*, *Ishige okamurae*, *Ecklonia cava*, *Eisenia arborea*	RSA: alkyl, DPPH, ·OH, $O_2^{\cdot-}$, ROS	Kang et al. (2003a), Zou et al. (2008), Sugiura et al. (2008), Li et al. (2009)
6,8′-bieckol	*Eisenia arborea*	RSA: DPPH, $O_2^{\cdot-}$Protection against phospholipid peroxidationProtection against methyl α-linolenate oxidation	Nakamura, Nagayama, Uchida, and Tanaka (1996), Kang et al. (2003a), Shibata et al. (2008), Sugiura et al. (2008)
7-phloro eckol	*Ecklonia cava*	RSA: alkyl, DPPH, ·OH, $O_2^{\cdot-}$, ROS	Li et al. (2009)
8,8′-bieckol	*Ecklonia stolonifera*, *Ecklonia cava*, *Ecklonia kurome*, *Eisenia bicyclis*, *Eisenia arborea*	RSA: DPPH, $O_2^{\cdot-}$Protection against phospholipid peroxidationProtection against methyl α-linolenate oxidation	Nakamura et al. (1996), Kang et al. (2003a), Shibata et al. (2008), Sugiura et al. (2008)
Dieckol	*Ecklonia cava*, *E. stolonifera*, *E. kurome*, *Eisenia bicyclis*	RSA: alkyl, DPPH, ·OH, $O_2^{\cdot-}$, ROSProtection against lipid or phospholipid peroxidation	Ahn et al. (2007), Kang et al. (2003a, 2004, 2012), Kim et al. (2009), Li et al. (2009), Nakamura et al. (1996), Shibata et al. (2008)
Dioxinodehydroeckol	*Ecklonia stolonifera*	RSA: DPPH, ROS	Kim et al. (2009)
Diphlorethohydroxycarmalol	*Ishige okamurae*	RSA: ABTS, alkyl, DPPH, ·OH, $O_2^{\cdot-}$, ROS	Heo et al. (2008), Zou et al. (2008), Heo and Jeon (2009)
Eckol	*Ecklonia cava*, *Ecklonia kurome*, *Ecklonia stolonifera*, *Eisenia bicyclis*	RSA: alkyl, DPPH, ·OH, $O_2^{\cdot-}$, ROS Protection against lipid or phospholipid peroxidation	Nakamura et al. (1996), Kang et al. (2003a, 2004, 2005); Ahn et al. (2007); Shibata et al. (2008); Li et al. (2009)
Eckstolonol	*Ecklonia cava*, *Ecklonia stolonifera*	RSA: DPPH, ROS	Kang, Chung, Jung, Son, and Choi (2003b), Kang et al. (2004)
Flucol	*Fucus spiralis*	RSA: DPPH	Cérantola et al. (2006)
Flucophlorethol	*Fucus spiralis*	RSA: DPPH	Cérantola et al. (2006)
Fucodiphloroethol G	*Ecklonia cava*	RSA: DPPH, ·OH, alkyl, $O_2^{\cdot-}$, ROS	Li et al. (2009)
Fucotriphlorethol A	*Fucus vesiculosus*	RSA: DPPH, ROO·	Parys et al. (2010)
Phlorofucofuroeckol A	*Ecklonia cava*, *Ecklonia stolonifera*, *Ecklonia kurome*, *Eisenia bicyclis*	RSA: DPPH, ·OH, Alkyl, $O_2^{\cdot-}$, ROS Protection against lipid and phospholipid oxidation FRAP, Protection against lipid oxidation	Nakamura et al. (1996), Kang et al. (2003a), Kang et al. (2004), Nagayama et al. (2003), Shibata et al. (2008), Kim et al. (2009), Li et al. (2009)
Phloroglucinol	*Eisenia bicyclis*, *Ecklonia cava*, *Ecklonia stolonifera*, *Ecklonia kurome*, *Ishige okamurae*	RSA: DPPH, ·OH, Alkyl, $O_2^{\cdot-}$, ROS Protection against lipid and phospholipid oxidation	Nakamura et al. (1996), Kang et al. (2004), Kang et al. (2012), Ahn et al. (2007), Shibata et al. (2008), Zou et al. (2008), Li et al. (2009)
Pyro-phloroglucinol-6,6′-bieckol	*Ecklonia cava*	RSA: alkyl, DPPH, ·OH, $O_2^{\cdot-}$, ROS	Kang, Lee, Heo, Kim, and Jeon (2011)
Trifucodiphlorethol A	*Fucus vesiculosus*	RSA: DPPH, ROO·	Parys et al. (2010)
Trifucotriphlorethol A	*Fucus vesiculosus*	RSA: DPPH, ROO·	Parys et al. (2010)
Sterols			
Fucosterol	*Sargassum* sp.	RSA: $ABTS^{\cdot+}$	Ayyad et al. (2011)

RSA: Radical Scavenging Activity; $ABTS^{\cdot+}$ (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)) radical; DPPH: α,α-diphenylpicrylhydrazyl; ·OH; hydroxyl; ROO·: peroxyl; $O_2^{\cdot-}$, superoxide.
ROS: ROS generation inhibition.

Table 2
Some examples of the comparable *in vitro* antioxidant activity tests in non cellular systems of aqueous and organic crude extracts from brown algae.

Algae (solvent) Collection coast, date	Phenolic content (g/100 g extract)	*In vitro* antioxidant activity	Reference
Alaria esculenta (DCM:M 1:1) Brittany (France), May 2007	2.03 (Phl)	$EC_{50,\ DPPH^{\cdot}}$ = 6.43 mg/mL; RP: 38.71%; β-CB = 39.99% $EC_{50,\ DPPH^{\cdot},\ BHA}$ = 0.04 mg/mL; RP_{BHA} = 94.02%; β-CB_{BHA} = 87.18%	Zubia et al. (2009)
Alaria crassifolia (M) Hakodate (Japan), 2007	0.59	$RSA_{,\ DPPH^{\cdot}}$ = 9.43 mg Toc/g extract, $RSA_{ROO^{\cdot}}$ = 106 mg Toc/g	Airanthi et al. (2011)
Ascophyllum nodosum (W) (70% A) Hvassahraun (Iceland), May 2007	13.8 (Phl) 15.9 (Phl)	$EC_{50,\ DPPH^{\cdot}}$ = 0.025 mg/mL; ORAC = 1.35 mmol T/g; FICA = 95% $EC_{50,\ DPPH^{\cdot}}$ = 0.018 mg/mL; ORAC = 1.42 mmol T/g; FICA = 40% $EC_{50,\ DPPH^{\cdot},\ BHT}$ = 0.003 mg/mL; $EC_{50,\ DPPH,\ \alpha\text{-}T}$ = 0.006 mg/mL; $FICA_{AA}$ = 8.2%	Wang et al. (2009)
Ascophyllum nodosum (M) Bay of Brest (France), April 2007	1.5 (Phl)	$RSA_{ABTS^{\cdot}+}$ = 0.94 mmol T/L; $RSA_{ABTS^{\cdot}+,\ Q}$ = 2.16 mmol T/L; $RSA_{ABTS^{\cdot}+,\ Phl}$ = 1.26 mmol T/L	Audibert et al. (2010)
Ascophyllum nodosum (60% M) Galway (Ireland), Spring	0.45 (GA)	FRAP = 0.08 mM AA/g; RSA_{DPPH} = 25.6%; β-CB = 76.3%	O'Sullivan et al. (2011)
Bifurcaria bifurcata (50% M) Brittany (France), July 2007	–	$EC_{50,\ DPPH^{\cdot}}$ = 1.68 mg/mL; $EC_{50,\ \beta\text{-}CB}$ = 3.2 mg/mL	Le Lann et al. (2008)
Bifurcaria bifurcata (DCM:M, 1:1) Brittany (France), September 2007	0.96 (Phl)	$EC_{50,\ DPPH^{\cdot}}$ = 0.56 mg/mL; RP: 69.56%; β-CB = 39.99% $EC_{50,\ DPPH^{\cdot},\ BHT}$ = 0.06 mg/mL; RP_{BHT} = 90.18%; β-CB_{BHT} = 80.70%	Zubia et al. (2009)
Caulerpa lentillifera (M) East Sabah (Malaysia)	4.28 (Phl)	FRAP = 362.1 μM/mg; TEAC = 2.16 mM/mg $FRAP_{BHT}$ = 615.7 μM/mg; $TEAC_{BHT}$ = 3.74 mM/mg $FRAP_{Q}$ = 557.4 μM/mg; $TEAC_{Q}$ = 3.65 mM/mg	Matanjun et al. (2008)
Caulerpa racemosa (M) East Sabah (Malaysia)	4.04 (Phl)	FRAP = 355.4 μM/mg; TEAC = 2.01 mM/mg $FRAP_{BHT}$ = 615.7 μM/mg; $TEAC_{BHT}$ = 3.74 mM/mg $FRAP_{Q}$ = 557.4 μM/mg; $TEAC_{Q}$ = 3.65 mM/mg	Matanjun et al. (2008)
Colpomenia sinuosa (M) Leleiwi Beach Park (Hawaii), November 2009	–	FRAP = 3 mol/g	Kelman et al. (2012)
Cystoseira abies-marina (SW-100 °C) (SW-200 °C) Canary Islands (Spain)	0.684.81	$RSA_{ABTS^{\cdot}}$+= 0.16 mM T/g; ORAC = 276 μM T/g; $EC_{50,\ O2^{\cdot-}}$ > 50 mg/ mL$RSA_{ABTS^{\cdot}}$+= 1.01 mM T/g; ORAC = 1314 μM T/g; $EC_{50,\ O2^{\cdot-}}$ = 7.3 mg/mL	Plaza et al. (2010)
Cystoseira crinita (Chl) (EA) (M) Monastir (Tunisia), 2007	40.24 40.62 26.15	$EC_{50,\ DPPH^{\cdot}}$ = 0.10 mg/mL; FRAP = 3.58 mg GA/g $EC_{50,\ DPPH^{\cdot}}$ = 0.09 mg/mL; FRAP = 4.62 mg GA/g $EC_{50,\ DPPH^{\cdot}}$ = 0.11 mg/mL; FRAP = 1.26 mg GA/g $EC_{50,\ DPPH^{\cdot},\ T}$ = 0.09 mg/mL	Mhadhebi et al. (2011)
Cystoseira hakodatensis (M) Hakodate (Japan), 2007	3.13	$RSA_{,\ DPPH^{\cdot}}$ = 65.3 mg/g extract, $RSA_{ROO^{\cdot}}$ = 515 mg/g	Airanthi et al. (2011)
Cystoseira tamariscifolia (DCM:M 1:1) Brittany (France), April 2007	10.91 (Phl)	$EC_{50,\ DPPH^{\cdot}}$ = 0.49 mg/mL; β-CB = 52.79%; RP: 73.22% $EC_{50,\ DPPH^{\cdot},\ AA}$ = 0.06 mg/mL; RP_{AA} = 92.91%; β-CB_{BHT} = 80.70%	Zubia et al. (2009)
Desmarestia ligulata (DCM:M 1:1) Brittany (France), May 2007	1.22 (Phl)	$EC_{50,\ DPPH^{\cdot}}$ = 5.93 mg/mL; RP: 27.98% $EC_{50,\ DPPH^{\cdot},\ Toc}$ = 0.14 mg/mL; RP_{Toc} = 85.08%	Zubia et al. (2009)
Dictyopteris membranacea (DCM) (M) (DCM) Kolimbari and Marathi (Greece)	– –	$EC_{50,\ DPPH^{\cdot}}$ = 25.4 mg/g; $EC_{50,\ HO^{\cdot}}$ = 0.078 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 5.50 mg/g; $EC_{50,\ HO^{\cdot}}$ = 0.006 mg/mL	Nahas et al. (2007)
Dictyopteris membranacea (Chl) (EA) Mediterranean coast (Tunes)	8.49 (GA) 6.09 (GA)	$EC_{50,\ DPPH^{\cdot}}$ = 0.09 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 0.11 mg/mL; $EC_{50,\ DPPH^{\cdot},\ T}$ = 0.09 mg/mL	Aoun, Said, and Farhat (2010)
Dictyota dichotoma (DCM:M 1:1) Brittany (France), May 2007	1.88 (Phl)	$EC_{50,\ DPPH^{\cdot}}$ = 4.73 mg/mL; RP: 27.59% $EC_{50,\ DPPH^{\cdot},\ BHA}$ = 0.04 mg/mL; β-CB_{BHA} = 87.18%; RP_{BHA} = 94.02%	Zubia et al. (2009)
Ecklonia cava (Enz, crude extract) (Enz phenolic fraction) Jeju Island (Korea), March–October 2004	–	$RSA_{DPPH^{\cdot}}$ = 50.3%; $RSA_{O2^{\cdot-}}$ = 10.3%; RSA_{H2O2} = 10.2%; $RSA_{HO^{\cdot}}$ = 10.2% $RSA_{DPPH^{\cdot}}$ = 70.1%; $RSA_{O2^{\cdot-}}$ = 31.3%; RSA_{H2O2} = 17.0%; $RSA_{HO^{\cdot}}$ = 10.2% BHA: $RSA_{DPPH^{\cdot}}$ = 60.2%; $RSA_{O2^{\cdot-}}$ = 50.1%; RSA_{H2O2} = 42.1%; $RSA_{HO^{\cdot}}$ = 42.1% BHT: $RSA_{DPPH^{\cdot}}$ = 68.3%; $RSA_{O2^{\cdot-}}$ = 51.0%; RSA_{H2O2} = 38.5%; $RSA_{HO^{\cdot}}$ = 35.1%	Athukorala et al. (2006)
Ecklonia cava (70% M) (70%M-EA) Jeju Island (Korea), March–October 2004	8.30 (GA) 5.05 (GA)	$EC_{50,\ DPPH^{\cdot}}$ = 0.02 mg/mL; $EC_{50,\ O2^{\cdot}-}$ = 0.05 mg/mL; $EC_{50,\ H2O2}$ = 0.06 mg/mL $EC_{50,\ HO^{\cdot}}$ = 0.02 mg/mL; $EC_{50,\ NO^{\cdot}-}$ = 0.04 mg/mL; $EC_{50,\ metal\ chelating}$ = 0.44 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 0.04 mg/mL; $EC_{50,\ O2^{\cdot}-}$ = 0.37 mg/mL; $EC_{50,\ H2O2}$ = 0.06 mg/mL $EC_{50,\ HO^{\cdot}}$ = 0.07 mg/mL; $EC_{50,\ NO^{\cdot}-}$ = 0.39 mg/mL; $EC_{50,\ metal\ chelating}$ = 1.2 mg/mL BHT: $EC_{50,\ DPPH^{\cdot}}$ = 0.36 mg/mL; $EC_{50,\ O2^{\cdot}}$ = 0.16 mg/mL; $EC_{50,\ H2O2}$ = 0.073 mg/mL BHT: $EC_{50,\ HO^{\cdot}}$ = 0.02 mg/mL; $EC_{50,\ NO^{\cdot}-}$ = 1.59 mg/mL; $EC_{50,\ metal\ chelat.}$= 1.6 mg/mL αT: $EC_{50,\ DPPH^{\cdot}}$ = 0.01 mg/mL; $EC_{50,\ O2^{\cdot}-}$ = 1.3 mg/mL; $EC_{50,\ H2O2}$ = 0.13 mg/mL αT: $EC_{50,\ HO^{\cdot}}$ = 0.05 mg/mL; $EC_{50,\ NO^{\cdot}-}$ = 2.1 mg/mL; $EC_{50,\ metal\ chelat.}$= 1.72 mg/mL	Senevirathne et al. (2006)
Ecklonia cava (W) (30% E) Jeju Island (Korea)	20.7 (GA) 45.3 (GA)	$RSA_{,\ DPPH^{\cdot}}$ = 48.4%; FRAP = 210 μM Vit C $RSA_{,\ DPPH^{\cdot}}$ = 58.3%; FRAP = 238 μM Vit C BHA: $RSA_{,\ DPPH^{\cdot}}$ = 83.4%; FRAP = 1212 μM Vit C C: $RSA_{,\ DPPH^{\cdot}}$ = 84.6%; FRAP = 748 μM Vit C	Shin et al. (2006)
Ecklonia cava (80% E) Jeju Island (Korea)	28.9 (GA)	$EC_{50,\ DPPH^{\cdot}}$ = 0.01 mg/L; $EC_{50,\ HO^{\cdot}}$ = 0.09 mg/L; $EC_{50,\ alkyl^{\cdot}}$ = 0.04 mg/L Vit C: $EC_{50,\ DPPH^{\cdot}}$ = 0.009 mg/L; $EC_{50,\ HO^{\cdot}}$ = 0.03 mg/L; $EC_{50,\ alkyl^{\cdot}}$ = 0.02 mg/L	Wijesinghe et al. (2012)
Ecklonia kurome (W) (80% E) Noto (Japan), March 2006	9.7 (Phl) 6.2 (Phl)	$RSA_{,\ DPPH^{\cdot}}$ = 28 mg C/g; $RSA_{,\ O2^{\cdot}-}$ = 240 mg C/g; FRAP = 52 mg C/g $RSA_{,\ DPPH^{\cdot}}$ = 23 mg C/g; $RSA_{,\ O2^{\cdot}-}$ = 190 mg C/g; FRAP = 51 mg C/g	Kuda et al. (2007)
Ecklonia cava (Enz)	–	$RSA_{,\ DPPH^{\cdot}}$ = 62.9%; $RSA_{,\ O2^{\cdot}-}$ = 67.1%; $RSA_{,\ HO^{\cdot}}$ = 16.3%;$RSA_{,\ H2O2}$ = 72.9%	Heo et al. (2005)

(*continued on next page*)

Table 2 (*continued*)

Algae (solvent) Collection coast, date	Phenolic content (g/100 g extract)	*In vitro* antioxidant activity	Reference
Jeju Island (Korea), October 2002–March 2003		α-T: $RSA_{,DPPH\cdot}$ = 89.6%; $RSA_{,O2\cdot-}$ = 41.1%; $RSA_{,HO\cdot}$ = 78.9%; $RSA_{,H2O2}$ = 64.1% BHT: $RSA_{,DPPH\cdot}$ = 56.0%; $RSA_{,O2\cdot-}$ = 24.7%; $RSA_{,HO\cdot}$ = 46.9%;$RSA_{,H2O2}$ = 50.3%	
Ecklonia radiata (lipid solubles) Commercial (AgriSea New Zealand, New Zealand)	3 (Phl)	$RSA_{,DPPH\cdot}$ = 97%; ORAC = 360 μM T/g $RSA_{,DPPH\cdot,BHT}$ = 64%; $ORAC_{,BHT}$ = 580 μM T/g	Kindleysides et al. (2012)
Ecklonia stolonifera (W) (80% E) Noto Peninsula (Japan), March 2006	7.4 (Phl) 7.3 (Phl)	$RSA_{,DPPH\cdot}$ = 17 mg C/g; $RSA_{,O2\cdot-}$ = 230 mg C/g; FRAP = 35 mg C/g $RSA_{,DPPH\cdot}$ = 24 mg C/g; $RSA_{,O2\cdot-}$ = 170 mg C/g; FRAP = 90 mg C/g	Kuda et al. (2007)
Ecklonia stolonifera (W) (M) Sea near Oma (Japan)	8.21 (GA) 30.30 (GA)	$EC_{50,HO\cdot}$ = 4.18 mg/mL; $EC_{50,O2^{-}}$ = 0.68 mg/mL $EC_{50,HO\cdot}$ = 1.85 mg/mL; $EC_{50,O2^{-}}$ = 0.38 mg/mL $EC_{50,HO\cdot,AA}$ = 0.49 mg/mL; $EC_{50,O2^{-},AA}$ = 0.01 mg/mL	Iwai (2008)
Eisenia bicyclis (M) Hakodate (Japan), 2007	0.77	$RSA_{,DPPH\cdot}$ = 58.6 mg/g extract, $RSA_{ROO\cdot}$ = 25 mg/g	Airanthi et al. (2011)
Eucheuma cotonii (M) Sabah (Malaysia)	2.25 (PG)	FRAP = 225.0 μM/mg; TEAC = 1.63 mM/mg $FRAP_{BHT}$ = 615.7 μM/mg; $RSA_{ABTS\cdot,BHT}$ = 3.74 mM T/mg $FRAP_{Q}$ = 557.4 μM/mg; $RSA_{ABTS\cdot,Q}$ = 3.65 mM T/mg	Matanjun et al. (2008)
Eucheuma spinosum (M) Sabah (Malaysia)	1.58 (PG)	FRAP = 153.9 μM/mg; $RSA_{ABTS\cdot}$+ = 1.54 mM T/mg $FRAP_{BHT}$ = 615.7 μM/mg; $RSA_{ABTS\cdot+,BHT}$ = 3.74 mM T/mg $FRAP_{Q}$ = 557.4 μM/mg; $RSA_{ABTS\cdot+,Q}$ = 3.65 mM T/mg	Matanjun et al. (2008)
Fucus ceranoides (DCM:M, 1:1) Brittany (France), March 2006	5.47 (Phl)	$EC_{50,DPPH\cdot}$ = 0.46 mg/mL; β-CB = 18.42%; RP: 42.74% $EC_{50,DPPH\cdot,BHA}$ = 0.04 mg/mL; $β\text{-}CB_{BHA}$ = 87.18%; RP_{BHA} = 94.02%	Zubia et al. (2009)
Fucus serratus (W) (70% A) Hvassahraun (Iceland), March 2007	16.9 (Phl) 24.2 (Phl)	$EC_{50,DPPH\cdot}$ = 0.02 mg/mL; ORAC = 2.10 mmol T/g; FICA = 96% $EC_{50,DPPH\cdot}$ = 0.01 mg/mL; ORAC = 2.54 mmol T/g; FICA = 38% $EC_{50,DPPH\cdot,AA}$ = 0.002 mg/mL; $FICA_{EDTA}$ = 99.8%	Wang et al. (2009)
Fucus serratus (DCM:M, 1:1) Brittany (France), March 2007	2.82 (Phl)	$EC_{50,DPPH\cdot}$ = 5.51 mg/mL; β-CB = 17.83%; RP: 35.03% $EC_{50,DPPH\cdot,BHT}$ = 0.06 mg/mL; $β\text{-}CB_{BHT}$ = 80.70%; RP_{BHT} = 90.18%	Zubia et al. (2009)
Fucus vesiculosus (W) (HCl) (KOH) Commercial (Algamar C. B., Spain) Pontevedra (Spain), Spring 1998	1.5–2.7 (GA) 0.1 (GA) 1.1 (GA)	FRAP = 54.5–97.5 μM T/g FRAP = 123.0 μM T/g FRAP = 80.0 μM T/g	Rupérez et al. (2002)
Fucus vesiculosus (30–35% E) (50–70% E) North Coast (France), late winter/spring and late summer	27.7 (Phl) 16.3 (Phl)	RP = 1.5 mmol Q/g; $EC_{50,DPPH}$ = 0.12 mg/mL; $EC_{50,O2\cdot-}$ = 0.18 mg/mL RP = 1.0 mmol Q/g; $EC_{50,DPPH\cdot}$ = 0.03 mg/mL; $EC_{50,O2\cdot-}$ = 0.69 mg/mL RP_{Phl} = 8.5 mmol Q/g; $EC_{50,DPPH\cdot}$ = 0.02 mg/mL; $EC_{50,O2\cdot-}$ = 0.09 mg/mL	Zaragozá et al. (2008)
Fucus vesiculosus (W) (70% A) Hvassahraun (Iceland), March 2007	17.6 (Phl) 24.2 (Phl)	$EC_{50,DPPH\cdot}$ = 0.02 mg/mL; ORAC = 2.25 mmol T/g E; FICA = 97% $EC_{50,DPPH\cdot}$ = 0.01 mg/mL; ORAC = 2.57 mmol T/g E; FICA = 54% $EC_{50,DPPH\cdot,α\text{-}T}$ = 0.006 mg/mL; $FICA_{CA}$ = 21.5%	Wang et al. (2009)
Fucus vesiculosus (60% M)	0.25 (GA)	FRAP = 109.8 μM AA/g; RSA_{DPPH} = 31.2%; β-CB = 71.2%	O'Sullivan et al. (2011)
Fucus serratus (60% M) Galway (Ireland), Spring	0.40 (GA)	FRAP = 113.4 μM AA/g; RSA_{DPPH} = 5.5%; β-CB = 62.2%	O'Sullivan et al. (2011)
Halidrys siliquosa (DCM:M 1:1) Brittany (France), May 2007	1.60 (Phl)	$EC_{50,DPPH\cdot}$ = 0.21 mg/mL; β-CB = 76.04%; RP: 83.77% $EC_{50,DPPH\cdot,BHT}$ = 0.06 mg/mL; $β\text{-}CB_{BHT}$ = 80.70%; RP_{BHT} = 90.18%	Zubia et al. (2009)
Halopteris scoparia (M) (DCM) Kolimbari and Marathi (Greece)	– –	$EC_{50,DPPH\cdot}$ = 45.5 mg/g; $EC_{50,HO\cdot}$ = 0.22 mg/mL $EC_{50,DPPH\cdot}$ = 9.80 mg/g; $EC_{50,HO\cdot}$ = 0.03 mg/mL	Nahas et al. (2007)
Himanthalia elongata (50% M_{ac}–70% Ac) Commercial (Algamar C.B., Spain) Pontevedra (Spain)	–	FRAP = 46.81 μg Trolox /g; $RSA_{ABTS\cdot}$ = 14.05 μM T/g	Cofrades et al. (2010)
Himanthalia elongata (M) Commercial (Quality Sea Veg., Co, Ireland), June, September 2008	8.1 (C + Q)	$EC_{50,DPPH\cdot}$ = 0.125 μg/mL	Cox et al. (2010)
Himanthalia elongata (60%M) Commercial (Quality Sea Veg., Co, Ireland)	8.9 (GA)	$EC_{50,DPPH\cdot}$ = 0.10 mg/mL; ; $EC_{50,H2O2}$ = 0.30 mg/mL; $EC_{50,LP}$ = 0.53 mg/mL FRAP = 5 mg T/g $EC_{50,DPPH\cdot,BHT}$ = 0.02 mg/mL; $EC_{50,H2O2,BHT}$ = 0.16 mg/mL $EC_{50,LP,AA}$ = 0.09 mg/mL	Rajauria et al. (2010)
Hizikia fusiformis (Enz) Jeju Island (South Korea), February 2004	16.0 (GA) 18.2 (GA)	$EC_{50,DPPH\cdot}$ = 1.90 mg/mL; $EC_{50,H2O2}$ = 0.99 mg/mL $EC_{50,DPPH\cdot}$ = 2.04 mg/mL; $EC_{50,H2O2}$ = 1.01 mg/mL	Siriwardhana et al. (2008)
Ishige okamurae W (Enz) Jeju Island (South Korea), October 2002–March 2003	–	$RSA_{,DPPH\cdot}$ = 23.0%; $RSA_{,O2\cdot-}$ = 37.1%; $RSA_{,HO\cdot}$ = 25.3%; $RSA_{,H2O2}$ = 18.0% α-T: $RSA_{,DPPH\cdot}$ = 89.6%; $RSA_{,O2\cdot-}$ = 41.1%; $RSA_{,HO\cdot}$ = 78.9%; $RSA_{,H2O2}$ = 64.1% BHA: $RSA_{,DPPH\cdot}$ = 87.4%; $RSA_{,O2\cdot-}$ = 34.8%; $RSA_{,HO\cdot}$ = 56.4%; $RSA_{,H2O2}$ = 67.4%	Heo et al. (2005)
Kjellmaniella crassifolia (M) Hakodate (Japan), 2007	0.99	$RSA_{,DPPH\cdot}$ = 33.5 mg/g extract, $RSA_{ROO\cdot}$ = 146 mg/g	Airanthi et al. (2011)
Laminaria digitata (60% M) Commercial (Quality Sea Veg., Co, Ireland)	6.4 (GA)	$EC_{50,DPPH\cdot}$ = 0.62 mg/mL; $EC_{50,H2O2}$ = 0.29 mg/mL; $EC_{50,LP}$ = 0.75 mg/mL FRAP = 3 mg T/g $EC_{50,DPPH\cdot,AA}$ = 0.037 mg/mL; $EC_{50,H2O2,BHT}$ = 0.16 mg/mL $EC_{50,LP,AA}$ = 0.094 mg/mL	Rajauria et al. (2010)
Laminaria hyperborea (M) Ireland, Galway (NUI Galway), Spring	0.15 (GA)	FRAP = 25.6 μM AA/g; β-CB = 50.0%	O'Sullivan et al. (2011)
Laminaria japonica (DE) Qingdao (China)	–	β-CB = 57.0%; $β\text{-}CB_{BHT}$ = 84.8%	Huang and Wang (2004)
Laminaria saccharina (60% M) Commercial (Quality Sea Veg., Co, Ireland)	7.6 (GA)	$EC_{50,DPPH\cdot}$ = 0.48 mg/mL; $EC_{50,H2O2}$ = 0.31 mg/mL; $EC_{50,LP}$ = 0.71 mg/mL FRAP = 4 mg T/g	Rajauria et al. (2010)

Table 2 (*continued*)

Algae (solvent) Collection coast, date	Phenolic content (g/100 g extract)	*In vitro* antioxidant activity	Reference
		$EC_{50,\ DPPH^{\cdot},\ BHT}$ = 0.024 mg/mL; $EC_{50,\ H2O2,\ BHT}$ = 0.016 mg/mL $EC_{50,\ LP,\ AA}$ = 0.094 mg/L	
Macrocystis pyrifera (lipid solubles) Commercial (Valére™ NZ Kelp Ltd., New Zealand)	2.4 (Phl)	$RSA_{,\ DPPH^{\cdot}}$ = 92%; ORAC = 480 μM T/g $RSA_{,\ DPPH^{\cdot},\ BHT}$ = 64%; $ORAC_{,\ BHT}$ = 580 μM T/g	Kindleysides et al. (2012)
Padina antillarum (50% M) Teluk Kumang (Malaysia), October–December, 2005	–	$EC_{50,\ DPPH^{\cdot}}$ = 0.337 mg/mL; FRAP = 15.7 mg GAE/g; $\beta\text{-}CB_{1\ mg}$ = 35% $EC_{50,\ AA}$ = 0.004 mg/mL; $\beta\text{-}CB_{Q0.01\ mg}$ = 63%	Chew et al. (2008)
Pelvetia canaliculata (60% M) Galway (Ireland), Spring	0.40 (GA)	FRAP = 0.071 μM AA/g; $RSA_{DPPH^{\cdot}}$ = 7.3%; β-CB = 53.9%	O'Sullivan et al. (2011)
Petalonia binghamiae (W) (E) Wajima (Japan), April 2004	0.93 (Phl) 0.27 (Phl)	RP = 0.09 mmol Phl/g; $RSA_{,\ DPPH^{\cdot}}$ = 2.73 mmol Phl/g; $RSA_{,\ O2^{\cdot-}}$ = 80.0 mmol Phl/g RP = 0.02 mmol Phl/g; $RSA_{,\ DPPH^{\cdot}}$ = 0.53 mmol Phl/g; $RSA_{,\ O2^{\cdot-}}$ = 5.9 mmol Phl/g	Kuda et al. (2006)
Sargassum binderi (W) (E) Salak Phet (Thailand)	0.03 (GA) 0.01 (GA)	$EC_{50,\ DPPH^{\cdot}}$ = 0.13 mg/L; $EC_{50,\ ABTS}$ = 5.29 mg/mL; $EC_{50,\ LP}$ = 155.8 mg/mL $EC_{50,\ O2^{\cdot-}}$ = 2.07 mg/mL; $EC_{50,\ RP,\ 700\ nm}$ = 2.14 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 113.9 mg/L; $EC_{50,\ ABTS}$ = 96.2 mg/mL	Boonchum et al. (2011)
Sargassum boveanum (W) (E) Bushehr (Iran), May 2006	1.70 (C) 0.09 (C)	$EC_{50,\ DPPH^{\cdot}}$ = 0.4 mg/mL; $EC_{50,\ LP}$ = 3.82 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 18 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 0.015 mg/mL; $EC_{50,\ LP,\ C}$ = 0.07 mg/mL	Zahra et al. (2007)
Sargassum echinocarpum (M) Richardson's Ocean Park (Hawaii), September, 2004	–	FRAP = 3 mol/g	Kelman et al. (2012)
Sargassum hyxtrix (M-NaOH)(M) (NaOH) Gunung Kidul (Indonesia), October 2009	1.21 9.95	$EC_{50,\ DPPH^{\cdot}}$ = 13.86 mg/mL; FICA = 0.84% $EC_{50,\ DPPH^{\cdot}}$ = 1.01 mg/mL; FICA = 12.65% $EC_{50,\ DPPH^{\cdot},\ BHT}$ = 0.10 mg/mL; $FICA_{,\ BHT}$ = 95.00%	Budhiyanti et al. (2011)
Sargassum horneri (MC) Zhoushan Archipelago (China), Summer 2009	12.2	RP = 0.75; $RSA_{DPPH^{\cdot\cdot}}$ = 43.8%; $RSA_{HO^{\cdot}}$ = 57.9% RP_{GA} = 0.79; $RSA_{DPPH,\ GA^{\cdot}}$ = 92.4%; $RSA_{\ HO^{\cdot},\ GA}$ = 53.5%	Luo et al. (2010)
Sargassum horneri (M) Hakodate (Japan), 2007	2.08	$RSA_{,\ DPPH}$ = 28.5 mg/g extract, $RSA_{ROO^{\cdot}}$ = 477 mg/g	Airanthi et al. (2011)
Sargassum kjelmanianum (MC) Zhoushan Archipelago (China), Summer 2009	16.3	RP = 0.98; $RSA_{DPPH^{\cdot}}$ = 58.2%; $RSA_{\ HO^{\cdot}}$ = 67.6% RP_{AA} = 0.71; $RSA_{DPPH^{\cdot},\ AA}$ = 93.7%; $RSA_{\ HO^{\cdot},\ AA}$ = 32.4%	Luo et al. (2010)
Sargassum micracanthum (M) (M–C:M) Himi City (Japan), September 1995	– –	$EC_{50,\ DPPH^{\cdot}}$ = 34 μg/mL; $EC_{50,\ LP}$ = 0.7 μg/mL $EC_{50,\ DPPH^{\cdot}}$ = 37 μg/mL; $EC_{50,\ LP}$ = 0.7 μg/mL BHT: $EC_{50,\ DPPH^{\cdot}}$ = 43.3 μg/mL; $EC_{50,\ LP}$ = 0.11 μg/mL Toc: $EC_{50,\ DPPH^{\cdot}}$ = 6 μg/mL; $EC_{50,\ LP}$ = 34 μg/mL AA: $EC_{50,\ DPPH^{\cdot}}$ = 2.5 μg/mL; $EC_{50,\ LP}$ = 28 μg/mL	Mori et al. (2003)
Sargassum muticum (50% M) Brittany (France), July 2007	–	$EC_{50,\ DPPH^{\cdot}}$ = 1.45 mg/mL; $EC_{50,\ \beta\text{-}CB}$ = 3.1 mg/mL	Le Lann et al. (2008)
Sargassum muticum (SW 100 °C) (SW 200 °C) Freeze-dried extract, Las Palmas de Gran Canaria Univ. (Spain)	1.07 5.87	$RSA_{,\ DPPH^{\cdot}}$ = 0.30 mM T/g; ORAC = 284.17 μM TE/g; $EC_{50,\ O2^{\cdot-}}$ > 50 mg/mL $RSA_{,\ DPPH^{\cdot}}$ = 1.05 mM T/g; ORAC = 1449.34 μM/g; $EC_{50,\ O2^{\cdot-}}$ = 3.56 mg/mL	Plaza et al. (2010)
Sargassum muticum (SW 190 °C) Pontevedra (Spain), June 2010	14	$EC_{50,\ DPPH^{\cdot}}$ = 1 g/L BHA: $EC_{50,\ DPPH^{\cdot}}$ = 0.24 mg/mL; BHT: $EC_{50,\ DPPH^{\cdot}}$ = 2.79 mg/mL	González-López et al. (2012)
Sargassum horneri (Enz) Jeju Island (Korea) October 2002–March 2003	–	$RSA_{,\ DPPH}$ = 11.2%; $RSA_{,\ O2^{\cdot-}}$ = 58.6%; $RSA_{,\ HO^{\cdot}}$ = 24.1%; $RSA_{,\ H2O2}$ = 90.9% α-T: $RSA_{,\ DPPH^{\cdot}}$ = 89.6%; $RSA_{,O2^{\cdot-}}$ = 41.1%; $RSA_{,\ HO^{\cdot}}$ = 78.9%; $RSA_{,\ H2O2}$ = 64.1% BHT: $RSA_{,\ DPPH^{\cdot}}$ = 56.0%; $RSA_{,O2^{\cdot-}}$ = 24.7%; $RSA_{,\ HO^{\cdot}}$ = 46.9%; $RSA_{,\ H2O2}$ = 50.3%	Heo et al. (2005)
Sargassum polycystum (M) Seribu Islands (Indonesia)		PF = 1.49	Anggadiredja et al. (1997)
Sargassum polycystum (M) Tanjung Aru (Malaysia)	4.5 (Phl)	FRAP = 366.7 μM/mg; $RSA_{ABTS^{\cdot+}}$ = 1.86 mM T/mg $FRAP_{BHT}$ = 615.7 μM/mg; $RSA_{ABTS^{\cdot+},BHT}$ = 3.74 mM T/mg $FRAP_{Q}$ = 557.4 μM/mg; $RSA_{ABTS^{\cdot+},Q}$ = 3.65 mM T/mg	Matanjun et al. (2008)
Sargassum siliquastrum (E) Pusan (South Korea)	–	$RSA_{,\ DPPH^{\cdot}}$ = 94.75%; IOEO = 72.11%; FICA = 4.8%; RP = 0.13 $RSA_{,\ DPPH^{\cdot},\ BHT}$ = 93.02%; $IOEO_{BHT}$ = 87.90%; $FICA_{EDTA}$ = 4.8% $RSA_{,\ DPPH^{\cdot},\ AA}$ = 14.50%; $IOEO_{BHT}$ = 32.18%; RP_{AA} = 0.68	Cho et al. (2008)
Sargassum thunbergii W (Enz) Jeju Island (Korea), October 2002–March 2003	–	$EC_{50\ DPPH^{\cdot}}$ = 0.001 mg/mL; $EC_{50\ alkyl}$ = 0.018 mg/mL; $EC_{50,\ HO^{\cdot}}$ = 0.007 mg/mL $EC_{50\ DPPH^{\cdot},\ Vit\ C}$ = 0.85 μg/mL; $EC_{50\ alkyl,\ Vit\ C}$ = 6.23 μg/mL $EC_{50\ HO^{\cdot},\ Vit\ C}$ = 12.18 μg/mL	Park et al. (2005)
Sargassum thunbergii (85% M) Youngdo Island (Korea), December 2001	–	$ONOO^{-}$ = 84%; $ONOO^{-}_{AA}$ = 99%	Seo et al. (2004)
Sargassum thunbergii W (Enz)Jeju Island (Korea), October 2002–March2003	–	$RSA_{,\ DPPH^{\cdot}}$ = 16.8%; $RSA_{,\ O2^{\cdot-}}$ = 47.1%; $RSA_{,\ HO^{\cdot}}$ = 26.8%; $RSA_{,\ H2O2}$ = 30.0% BHA: $RSA_{,\ DPPH^{\cdot}}$ = 87.4%; $RSA_{,\ O2^{\cdot-}}$ = 34.8%; $RSA_{,\ HO^{\cdot}}$ = 56.4%;$RSA_{,\ H2O2}$ = 67.4%	Heo et al. (2005)
Sargassum thunbergii (MC) Zhoushan Archipelago (China), Summer, 2009	11.5	RP = 0.61; $RSA_{DPPH^{\cdot}}$ = 38.55%; $RSA_{HO^{\cdot}}$ = 57.66% RP_{GA} = 0.79; $RSA_{DPPH^{\cdot},\ GA}$ = 92.43%; $RSA_{OH,\ GA}$ = 53.52%	Luo et al. (2010)
Sargasum vulgare (M-DCM) (M) (DCM) Kolimbari and Marathi (Crete, Greece)	–	$EC_{50,\ DPPH^{\cdot}}$ = 60.2 mg/g; $EC_{50,\ HO^{\cdot}}$ = 0.294 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 15.6 mg/g; $EC_{50,\ HO^{\cdot}}$ = 0.051 mg/mL	Nahas et al. (2007)
Sargassum vulgare (SW 100 °C) (SW 200 °C) Freeze-dried algae (Las Palmas de Gran Canaria Univ., Spain)	2.64 7.09	$RSA_{ABTS^{\cdot+}}$ = 0.85 mM T/g; ORAC = 439.53 μM T/g; $EC_{50,\ O2^{\cdot-}}$ = 11.42 mg/mL $RSA_{ABTS^{\cdot+}}$ = 1.56 mM T/g; ORAC = 1742.67 μM T/g; $EC_{50,\ O2^{\cdot-}}$ = 4.39 mg/mL	Plaza et al. (2010)

(*continued on next page*)

Table 2 (*continued*)

Algae (solvent) Collection coast, date	Phenolic content (g/100 g extract)	*In vitro* antioxidant activity	Reference
Scytosiphon lomentaria (Enz) Jeju-Do Island (Korea), March, October 2002	–	$EC_{50,\ HO^{\cdot}}$ = 0.05 mg/mL; $EC_{50,\ alkyl^{\cdot}}$ = 0.02–0.07 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 0.02–0.08 mg/mL	Ahn et al. (2004)
Scytosipon lomentaria (Enz) Jeju Island (Korea), October 2002–March 2003	–	$RSA_{,\ DPPH^{\cdot}}$ = 16.0%; $RSA_{,\ O2^{\cdot-}}$ = 47.1%; $RSA_{,\ HO^{\cdot}}$ = 26.1%;$RSA_{,\ H2O2}$ = 10.8% BHA: $RSA_{,\ DPPH^{\cdot}}$ = 87.4%; $RSA_{,\ O2^{\cdot-}}$ = 34.8%; $RSA_{,\ HO^{\cdot}}$ = 56.4%;$RSA_{,\ H2O2}$ = 67.4%	Heo et al. (2005)
Stypocaulon scoparium (E) (W) (50% M)Canary Island (Spain), March–April 2008	0.12 (GA) 0.33 (GA) 0.29 (GA)	$RSA_{DPPH^{\cdot}}$ = 17.0% $RSA_{DPPH^{\cdot}}$ = 47.9% $RSA_{DPPH^{\cdot}}$ = 38.6%	López et al. (2011)
Taonia atomaria (M-DCM) (M) (DCM) Kolimbari and Marathi (Greece)	–	$EC_{50,\ DPPH^{\cdot}}$ = 5.10 mg/g; $EC_{50,\ HO^{\cdot}}$ = 0.017 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 1.00 mg/g; $EC_{50,\ HO^{\cdot}}$ = 0.003 mg/mL	Nahas et al. (2007)
Turbinaria conoides (W) (E) Nang Rong (Thailand)	0.11 (GA) 0.02 (GA)	$EC_{50,\ DPPH^{\cdot}}$ = 0.84 mg/L; $EC_{50,\ ABTS^{\cdot}}$ = 15.2 mg/mL; $EC_{50,\ LP}$ = 218.3 mg/mL $EC_{50,\ O2^{\cdot-}}$ = 9.2 mg/mL; $EC_{50,\ RP,\ 700\ nm}$ = 15.6 mg/mL $EC_{50,\ DPPH^{\cdot}}$ = 45.0 mg/L; $EC_{50,\ ABTS^{\cdot}}$ = 36.6 mg/mL	Boonchum et al. (2011)
Turbinaria ornata (M) Richardson's Ocean Park (Hawaii), August 2004	–	FRAP = 7.4–10.2 mmol/mg	Kelman et al. (2012)
Undaria pinnatifida (Enz) Commercial (Sealight Co. Ltd., Wando, Korea)	–	$RSA_{DPPH^{\cdot}}$ = 47%; $RSA_{HO^{\cdot}}$ = 70%	Je et al. (2009)
Undaria pinnatifida (50% M_{ac}–70% Ac) Commercial (Algamar C.B., Spain) Fresh: Pontevedra (Spain)	–	FRAP = 17.57 μg T/g; $RSA_{ABTS^{\cdot}}$ = 1.81 μM T/g	Cofrades et al. (2010)
Undaria pinnatifida (DE) Qingdao (China)	–	β-CB = 29.7%; $\beta\text{-}CB_{BHT}$ = 84.8%	Huang and Wang (2004)
Undaria pinnatifida (SW 100 °C) (SW 200 °C) Freeze-dried algae (Las Palmas de Gran Canaria Univ., Spain)	0.38 6.71	TEAC = 0.05 mM/g; ORAC = 45.36 μM T/g; $IC_{50,\ O2^{\cdot-}}$ > 50 mg/mL TEAC = 1.51 mM/g; ORAC = 1522.69 μM T/g; $IC_{50,\ O2^{\cdot-}}$ = 5.37 mg/mL	Plaza et al. (2010)

AA: Ascorbic acid; BHA: Butyl hydroxyanisol; BHT: Butyl hydroxytoluene; C: catechin; C: Citric Acid; GA: Gallic acid; Phl: Phloroglucinol; Q: Quercetin; TA: Tannic acid; Toc = Tocopherol; TA: Tocopherol acetate; T: Trolox equivalents.
A: Acetone; ACN: Acetonitrile; C: Chloroform; DE: diethylether; E: Ethanol; EA: Ethyl acetate; Enz: Enzymatic treatment; W: water; M: methanol; M_{ac}: acidified methanol; SW-T: Subcritical Water-Temperature.
Solvents separated by ":" means a mixture; solvents separated by "–" means a sequence.
FICA: Ferrous Ion Chelating Ability; LP: lipid peroxidation; IOEO: Inhibition of oil emulsion oxidation.
$EC_{50,LP}$: efficient concentration for 50% inhibition of lipid peroxidation.

therapeutic potential of natural products includes actions such as (i) protection from cellular or molecular damage by free radicals, (ii) reduction of the radical-induced tissue injuries and (iii) retardation in the progress of chronic diseases, However, these effects cannot be ascribed exclusively to the antioxidant properties, but also to other complex of beneficial actions.

The need for simple and reliable *in vitro* antioxidant tests is widely acknowledged (Antolovich, Prenzler, Patsalides, McDonald, & Robards, 2002; Craft et al., 2012; Magalhães, Segundo, Reis, & Lima, 2008; Prior, Wu, & Schaich, 2005; Sánchez-Moreno 2002). The most widely used *in vitro* assays for determining antioxidant activity have been grouped based on mechanisms such as the ability to quench free radicals by hydrogen donation, the ability to transfer one electron, and other assays (Huang, Ou, & Prior, 2005). *In vitro* antioxidant capacity is useful to compare the potential of different components, but do not necessarily predict the performance in food systems. These are complex heterogeneous systems influenced by the type of substrate, the antioxidant solubility and phase distribution, the interaction with food constituents and the environmental conditions (Decker, 1998).

This review is focused on the potential food uses of compounds exclusively found in brown algae, with particular emphasis on those from the polymeric fraction. The compilation of the *in vitro* available data is presented with the aim of exploring the potential of this bioresource as an alternative to synthetic antioxidants and to present preliminary information for selecting brown seaweed extracts useful for food protection. The *in vitro* methods have been grouped in an operative rather than in a mechanistic classification, including the reducing power, the scavenging of radicals and reactive species, the chelating properties and the protection of lipid oxidation.

3.2. Antioxidant activity of algal components

Several compounds with antioxidative action have been isolated from brown algae, most of them belonging to the phenolic fraction (Table 1). A joint summary of the total phenolic content and activity of brown algal extracts has been published (Holdt & Kraan, 2011; Tierney et al., 2010). Information presented in Table 2 confirms the potential of algal species from different geographical origin, Indonesia (Anggadiredja, Andyani, & Hayati, 1997), Japan (Kuda & Ikemori, 2009; Kuda, Kunii, Goto, Suzuki, & Yano, 2007; Matsukawa et al., 1997; Nakai et al., 2006; Yan et al., 1999), the Canary Islands (Chkhikvishvili & Ramazanov, 2000), Norway (Aguilera et al., 2002), the Brittany coast (Connan et al., 2006; Plouguerné et al., 2006; Zubia et al., 2009), the Aegean Sea (Caki, Ozturk, Taskin, & Taskin, 2011; Demirel, Yilmaz-Koz, Karabay-Yavasoglu, Ozdemir, & Sukatar, 2009; Nahas et al., 2007), Korea (Kim et al., 2008), Iceland (Wang, Jónsdóttir, & Ólafsdóttir, 2009), Saudi Arabia (Al-Amoudi et al., 2009), Thailand (Yangthong, Hutadilok-Towatana, & Phromkunthong, 2009), Mexico (Hernández-Carmona et al., 2009), Ireland (Cox et al., 2010; O'Sullivan et al., 2011; Rajauria, Jaiswal, Abu-Gannam, & Gupta, 2012), Brazil (Costa et al., 2010), China (Luo, Wang, Yu, Qu, & Su, 2010), Hawaii (Kelman et al., 2012) and New Zealand (Kindleysides et al., 2012). The fucoidan fraction content and structure is highly dependent on the extraction and depolymerisation process; data on the composition and *in vitro* antioxidant properties of crude fucoidan and fractions are summarised in Table 3.

Table 3
Examples of the radical scavenging by polysaccharide fractions from brown algae.

Alga	Composition information Total sugars/Uronic acids/Sulphate/Protein/Polyphenols (weight% or *molar ratio*) (Molar ratio of sugars = Gal:Fuc:Glc:Ara:Rha:Xyl:Man)	*In vitro* antioxidant properties	Reference
Caulerpa sertularoides	Total sugars/sulfate: 0.90	RP = 60%; $RSA_{\cdot HO}$ = 11.8%; $RSA_{O2\cdot-}$ = 23.3%; FICA = 58% $RSA_{\cdot HO, GA}$ = 93.7%; $RSA_{O2\cdot-, GA}$ = 86.3%; $FICA_{EDTA}$ = 97%	Costa et al. (2010)
Canistrocarpus cervicornis	12.2/–/0.6/2.8/– (0.5/1.0/0.5/–/–/0.5/0.5) 33.4/–/0.5/3.9/– (–/1.0/–/–/–/0.5/–) 33.2/–/0.4/19.2/– (–/1.0/nd/–/–/0.5/–) 41.8/–/0.3/16.5/– (0.5/1.0/nd/–/–/0.5/–) 21.8/–/0.2/7.8/– (2.5/1.0/nd/–/–/0.5/–) 19.9/–/0.2/20.1/– (2.0/1.0/nd/–/–/0.5/0.5)	$RSA_{\cdot HO}$ = 1.0%; $RSA_{O2\cdot-}$ = 18.0% $RSA_{\cdot HO}$ = 0.5%; $RSA_{O2\cdot-}$ = 13.0% $RSA_{\cdot HO}$ = 0.9%; $RSA_{O2\cdot-}$ = 18.4% $RSA_{\cdot HO}$ = 3.0%; $RSA_{O2\cdot-}$ = 0.3% $RSA_{\cdot HO}$ = 3.0%; $RSA_{O2\cdot-}$ = 43.1% $RSA_{\cdot HO}$ = 2.9%; $RSA_{O2\cdot-}$ = 13.1% $RSA_{\cdot HO, GA}$ = 43.6%; $RSA_{O2\cdot-, GA}$ = 41.8%	Camara et al. (2011)
Dictyota mertensii	Total sugars/sulfate: 0.36	RP = 72%; $RSA_{\cdot HO}$ = 8.7%; $RSA_{O2\cdot-}$ = 16.8%; FICA = 24% $RSA_{\cdot HO, GA}$ = 93.7%; $RSA_{O2\cdot-, GA}$ = 86.3%; $FICA_{EDTA}$ = 97%	Costa et al. (2010)
Dictyopteris delicatula	89.1/–/14.1/0.1/– (2.0:1.0:0.3:–:–:0.7:0.5) 70.0/ –/17.8/0.3/–(3.0:1.0:0.4:–: –:1.5:0.6) 65.0/ –/19.0/0.5/– (1.9:1.0:0.2:–:–:0.8:0.5) 68.2/–/14.5/0.1/– (2.4:1.0:0.3:–:–:0.6:0.2) 61.3/–/15.4/0.1/– (1.6:1.0:0.2:–:–:1.3:0.4) 64.3/–/16.0/0.7/– (1.8:1.0:0.2:–:–:1.6:0.4)	RP = 7%; $RSA_{\cdot HO}$ = 14.4%; $RSA_{O2\cdot-}$ = 5.7% RP = 9%; $RSA_{\cdot HO}$ = 15.6%; $RSA_{O2\cdot-}$ = 4.8% RP = 42%; $RSA_{\cdot HO}$ = 17.0%; $RSA_{O2\cdot-}$ = 0.0% RP = 54%; $RSA_{\cdot HO}$ = 0.0%; $RSA_{O2\cdot-}$ = 0.0% RP = 37%; $RSA_{\cdot HO}$ = 0.0%; $RSA_{O2\cdot-}$ = 13.4% RP = 6%; $RSA_{\cdot HO}$ = 93.7%; $RSA_{O2\cdot-}$ = 86.3%	Magalhães et al. (2011)
Dictyota menstrualis	Total sugars/sulfate: 0.23	RP = 63%; $RSA_{\cdot HO}$ = 7.5%; $RSA_{O2\cdot-}$ = 9.0%; FICA = 43% $RSA_{\cdot HO, GA}$ = 93.7%; $RSA_{O2\cdot-, GA}$ = 86.3%; $FICA_{EDTA}$ = 97%	Costa et al. (2010)
Fucus vesiculosus	33.3/ 39.1/ 6.4/ 1.4/ 1.5 (2.3:14.1:6.5: –:–:2.8: –) 25.3/ 36.8/ 5.1/ 4.2/ 2.7 (2.5:8.1:4.6: –:–:2.4: –) 48.4/ 8.8/ 11.5/ –/0.1 (2.2:33.5:0: –:–:2.3: –) 18.9/ 52.8/ 2.4/ 6.1/ 1.1 (2.1:6.5:2.8: –:–:1.7: –)	FRAP = 54.5 μM T/g FRAP = 97.5 μM T/g FRAP = 123.0 μM T/g FRAP = 80.0 μM T/g	Rupérez et al. (2002)
Fucus vesiculosus	55.2/–/44.1/0.80/– (0.0:1.0:0.0:–:–:–:–) 80.2/–/18.4/0.90/– (0.6:1.0:0.0:–:–:0.5:–) 70.1/–/27.6/2.56/– (0.3:1.0:0.0:–:–:0.6:–)	$EC_{50, HO\cdot}$ = 0.16 g/L; $EC_{50, O2\cdot-}$ = 0.06 g/L; $EC_{50, LP}$ = 1.25 g/L $EC_{50, O2\cdot-}$ = 0.24 g/L; $EC_{50, LP}$ = 2.75 g/L $EC_{50, HO\cdot}$ = 0.35 g/L; $EC_{50, O2\cdot-}$ = 0.24 g/L; $EC_{50, LP}$ = 23.9 g/L	Rocha de Souza et al. (2007)
Laminaria japonica	33.4/19.2/19.9/–/– (0.01:0.00:0.29:0.04:1.00:0.49:0.06)	$RP_{700\ nm,\ 1\ g/L}$ = 0.2; $RSA_{\cdot HO}$ = 70%; $RSA_{O2\cdot-}$ = 85%	Zhang et al. (2010)
Laminaria japonica	–/3.65/30.1/–/– (32.7:51.5:9.01:1.54:3.07:–:2.13) –/6.01/32.8/–/– (31.9:42.6:12.4:3.17:4.23:–:5.71)	$RP_{700\ nm,\ 6\ g/L}$ = 1.7; $RSA_{\cdot HO}$ = 30%; $RSA_{O2\cdot-}$ = 90% $RP_{700\ nm,\ 6\ g/L}$ = 1.9; $RSA_{\cdot HO}$ = 28%; $RSA_{O2\cdot-}$ = 90%	Wang et al. (2010)
Laminaria japonica	42.2/4.2/30.8/–/– (0.10:1.00:0.05:–:0.01:0.03:0.08) 49.2/4.6/32.1/–/– (0.13:1.00:0.03:–:0.01:0.02:0.06) 60.3/5.3/34.7/–/– (0.15:1.00:0.03:– :0.02:0.03:0.10) 66.9/ 6.2/ 30.3/–/– (0.15:1.00:0.04:–:0.02:0.03:0.09) 66.5/6.1/30.1/–/– (0.16:1.00:0.07:–:0.02:0.04:0.10) 63.5/6.6/33.0/–/– (0.16:1.00:0.06:–:0.02:0.04:0.11) 67.5/6.7/30.6/–/– (0.18:1.00:0.06:–:0.02:0.04:0.12)	$RP_{700\ nm}$ = 1.56; $RSA_{\cdot HO}$ = 85%; $RSA_{O2\cdot-}$ = 55% $RP_{700\ nm}$ = 1.21; $RSA_{\cdot HO}$ = 92%; $RSA_{O2\cdot-}$ = 71% $RP_{700\ nm}$ = 0.54; $RSA_{\cdot HO}$ = 91%; $RSA_{O2\cdot-}$ = 89% $RP_{700\ nm}$ = 0.22; $RSA_{\cdot HO}$ = 17%; $RSA_{O2\cdot-}$ = 87% $RP_{700\ nm}$ = 0.38; $RSA_{\cdot HO}$ = 25%; $RSA_{O2\cdot-}$ = 89% $RP_{700\ nm}$ = 0.40; $RSA_{\cdot HO}$ = 62%; $RSA_{O2\cdot-}$ = 85% $RP_{700\ nm}$ = 0.52; $RSA_{\cdot HO}$ = 44%; $RSA_{O2\cdot-}$ = 88%	Hou et al. (2012)
Lobophora variegata	46.6/–/22.7/0.12/–	$RP_{700\ nm,\ 1\ g/L}$ = 0.74; $RSA_{\cdot HO}$ = 96%; $RSA_{O2\cdot-}$ = 80%	Paiva et al. (2011)
Turbinaria conoides	37/–/4/nd/–	RP = 0.16 mmol T/g $RSA_{\cdot DPPH,\ 2\ g/L}$ = 70%; $RSA_{DPPH,\ BHA,\ 0.5\ g/L}$ = 55%	Chattopadhyay et al. (2010)
Turbinaria ornata	53.88/–/–/10.64/–	RSA_{DPPH} = 80.21%; $RSA_{NO\cdot}$ = 26.43%; LP = 69.96% Q: RSA_{DPPH} = 63.53%; $RSA_{NO\cdot}$ = 82.72%; LP = 89.98%	Ananthi et al. (2010)

AA: Ascorbic acid; GA: Gallic acid; AA: Ascorbic Acid; T: Trolox.
nd: not detected.
Gal (Galactose): Fuc (Fucose): Glc (Glucose): Ara (Arabinose): Rha (Rhamnose): Xyl (Xylose): Man (Manose).

3.2.1. Reducing capacity

The reducing capacity assay provides a measure of the ability of a compound to donate electrons and to reduce the oxidised intermediates of the peroxidation process, and has been used as a comparative tool among foods and algae. It can be determined by simple methods: (i) the FRAP assay, based on the reduction of the Fe^{3+}/tripyridyltriazine complex (Benzie & Szeto, 1999), (ii) the direct reduction of Fe^{3+}-ferricyanide complexes, (iii) the Folin–Ciocalteu method for total phenolic compounds, and (iv) electrochemical methods, based on the fact that most low molecular weight antioxidants are reducing agents able to donate electrons to reactive oxygen species. This latter technique is relatively rapid, cheap, clean, and used for rapid screening of marine algae antioxidants (Ragubeer, Beukes, & Limson, 2010; Ragubeer, Limson, & Beukes, 2012).

Reducing activity or FRAP values are available for dried and boiled products (Kuda et al., 2007), nutraceuticals (Díaz-Rubio, Pérez-Jiménez, & Saura-Calixto, 2009; Kang et al., 2003a), crude solvent extracts (Athukorala et al., 2006; Kuda, Hishi, & Maekawa, 2006; Murat et al., 2009; Shin et al., 2006; Zubia et al., 2009), and

solvent fractions (Senevirathne et al., 2006) rich in phlorotannins. Reducing power of crude polysaccharides and fractions has been reported for species from *Ecklonia* (Athukorala et al., 2006), *Laminaria* (Hou et al., 2012; Zhang et al., 2010), *Dictyota*, *Dictyopteris*, *Sargassum* and *Spatoglossum* (Costa et al., 2010; Magalhães et al., 2011; Zhang, Wu, Wang, & Lan, 2012). Fucoidan has shown higher activity than other polysaccharide fractions, i.e., alginate and laminaran (Chattopadhyay et al., 2010) and higher than organic extracts, containing mainly apolar components (Rupérez et al., 2002).

3.2.2. Scavenging of free radicals and reactive species

Radical scavenging is one of the mechanisms by which antioxidants inhibit oxidation, and a wide variety of *in vitro* methods has been used for algae, including free radicals, such as $ABTS^{\cdot+}$ radical cation, DPPH radical, and reactive species, such as superoxide anion, hydrogen peroxide, peroxyl radicals, hydroxyl radical, singlet oxygen and peroxynitrite, which are responsible for oxidative damage in the human body, but have also been proposed for food samples (Craft et al., 2012; Huang et al., 2005).

α,α-Diphenylpicrylhydrazyl (DPPH) is a stable free radical widely used for evaluating natural antioxidants, algae or algal products (Kang et al., 2003a; Kuda et al., 2007) due to its stability, simplicity and reproducibility. Some antioxidants may react slowly or be inert to DPPH (Huang et al., 2005). Crude extracts, most of them in water or in ethanol, showed antioxidant capacity using this method, including solvent extracts from *Scytosiphon* (Kuda, Tsunekawa, Hishi, & Araki, 2005), *Petalonia* (Kuda et al., 2006), *Sargassum* (Boonchum et al., 2011; Zahra, Mehrnaz, Farzaneh, & Kohzad, 2007), *Turbinaria* (Zubia et al., 2008), *Dictyota*, *Padina* and *Halopteris* (Murat et al., 2009; Zubia et al., 2009). Extracts and solvent fractions (methanol, chloroform/methanol, and ethyl acetate) have been evaluated, such as those from *Ascophyllum* (Audibert et al., 2010), *Ecklonia* (Kindleysides et al., 2012; Senevirathne et al., 2006), and *Sargassum* (Budhiyanti, Raharjo, Marseno, & Lelana, 2011; Mori, Matsunaga, Takahashi, Hasegawa, & Saito, 2003). The enzymatic extracts from *Sargassum horneri* (Park, Shahidi, & Jeon, 2004), *S. thunbergii* (Park et al., 2005) and *Ecklonia cava* (Athukorala et al., 2006; Shin et al., 2006), and boiled, autoclaved and subcritical water extracts from *C. racemosa* and *Sargassum* sp. (González-López, Moure, & Domínguez, in press; Plaza, Amigo-Benavent, del Castillo, Ibáñez, & Herrero, 2010; Yangthong et al., 2009) were active.

The DPPH radical scavenging assay was also used for pure compounds, those from the phlorotannin fraction of *Eisenia bicyclis*, *E. cava* and *Ecklonia kurome* (Ahn et al., 2007; Li et al., 2009; Shibata, Ishimaru, Kawaguchi, Yoshikawa, & Hama, 2008), phlorethols (Parys et al., 2010) and tetramer and hexamers from *Fucus vesiculosus* (Wang et al., 2012) being the most studied (Table 1). Among the active pure compounds isolated can be mentioned phloroglucinol, triphlorethol-A (Kang et al., 2005), eckol, dieckol, 6,6′-bieckol, 8,8′-bieckol (Kang et al., 2005; Senevirathne et al., 2006; Shibata et al., 2008; Zou et al., 2008), phlorofucofuroeckol A, dioxinodehydroeckol (Kim et al., 2009) and diphlorethohydroxycarmalol (Heo et al., 2008; Zou et al., 2008). The combination of pentamer and hexamers of phloroglucinol with soybean protein enhanced activity (Shibata et al., 2008).

Water-soluble crude polysaccharides from *Petalonia binghamiae* and *Scytosipon lomentaria* (Kuda et al., 2006) and from *Turbinaria ornata* (Ananthi et al., 2010) were less potent scavengers than the phenolic fraction (Athukorala et al., 2006). Concentration-dependent radical scavenging was reported for polysaccharides from *Turbinaria* (Ananthi et al., 2010; Chattopadhyay et al., 2010), *Sargassum graminifolium* (Zhang et al., 2012) and *Sargassum pallidum* (Ye, Wang, Zhou, Liu, & Zeng, 2008). Other compounds that exhibit DPPH radical-scavenging activity are nahocols and isonahocols (Jung et al., 2008), meroterpenoids (Fisch, Böhm, Wright, & König, 2003), sargachromanols (Jang et al., 2005), chromenes (Cho, Cho, Kang, Hong, & Ahn, 2008; Jang et al., 2005) and fucoxanthin (Nomura, Kikuchi, Kubodera, & Kawakami, 1997).

In Table 2, the phenolic content of the extracts is indicated, although a comparison on this basis is difficult, since other components could be active. Generally, the results are reported as the efficient concentration (EC_{50}), the amount of antioxidant necessary to scavenge by 50% the initial radical. According to the radical scavenging capacities or to the EC_{50} values, in most studies the standard antioxidants BHA, BHT, ascorbic acid and tocopherol were superior than the algal extracts. However, some solvent extracts and their fractions and some enzymatic extracts and subcritical water extracts were comparable or superior to BHT, Trolox, ascorbic acid and tocopherol. Table 4 summarises the EC_{50} values reported for compounds isolated from the phenolic fraction of brown algae. As a general trend, pure phloroglucinol derivatives are more potent than standard antioxidants. Bromophenols (EC_{50} = 7.5–24.7 μM) are more active than BHT ($EC_{50,BHT}$ = 81.8 - μM) (Liu et al., 2011).

ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) radical is oxidised to the radical cation ($ABTS^{\cdot+}$), its decolorisation being used to measure the antioxidant capacity in both water-soluble and lipid-soluble food samples and is expressed as TEAC (Trolox equivalent antioxidant capacity) (Huang et al., 2005). This activity was reported for commercial algal products (Cofrades et al., 2010; Díaz-Rubio et al., 2009), aqueous and ethanol extracts of different algae, including *Colpomenia*, *Dictyota*, *Petalonia*, and *Sargassum* (Boonchum et al., 2011; Demirel et al., 2009), subcritical water extracts from *Cystoseira*, *Sargassum* (Plaza et al., 2010) and *Undaria* (Onofrejová et al., 2010). Methanolic extracts of brown algae showed high antioxidant capacity (TEAC = 1–3), but lower than BHT and quercetin (Matanjun, Mohamed, Mustapha, Muhammad, & Ming, 2008). Water-soluble crude polysaccharide from *T. ornata* (Ananthi et al., 2010), *F. vesiculosus* (Díaz-Rubio et al., 2009) and *Lessonia vadosa* (Barahona, Chandía, Encinas, Matsuhiro, & Zúñiga, 2011), and terpenoid derivatives from *Cystoseira crinita* (Fisch et al., 2003) were active. Data in Table 2 confirm the comparable or slightly lower potency of algal extracts compared to phloroglucinol, Trolox, BHT and quercetin.

Superoxide anion ($O_2^{\cdot-}$) is biologically produced by the enzyme NADPH oxidase in metabolic processes to protect against invading pathogens. Since superoxide is toxic, most organisms living in the presence of oxygen contain isoforms of the superoxide dismutase. The superoxide anion can be produced *in vivo* as a result of the donation of one electron to oxygen, either in metabolic processes or following oxygen activation by irradiation. The reactivity of superoxide anion is low, but it is the precursor of H_2O_2, HO^- and $^1O_2$, which induce oxidative damage in lipids, proteins and DNA. The ability to scavenge superoxide anions is an important property for a therapeutic compound, but also has been applied to natural extracts and foods. Superoxide anion radical can be generated by the xanthine–xanthine oxidase system. A variety of methods for determination the superoxide scavenging activity are available, including the reduction of nitroblue tetrazolium (NBT) or cytochrome c into products which can be monitored spectrophotometrically or by gas chromatography, the use of hydroethidine has been proposed to follow an oxidised fluorescent product (Huang et al., 2005) and ESR spectrometry was also used to measure the scavenging capacity against this radical.

The superoxide radical scavenging capacity was reported for algal products (Kuda et al., 2005, 2006, 2007), boiling and autoclave water extracts (Yangthong et al., 2009), subcritical water extracts (Plaza et al., 2010), solvent extracts (Nakai et al., 2006), and solvent fractions (Senevirathne et al., 2006). Different purified compounds, such as diphlorethohydroxycarmalol and 6,6′-bieckol (Zou et al., 2008), phlorofucofuroeckol A, dieckol and 8,8′-bieckol, were as

Table 4
EC_{50} values for the DPPH radical scavenging activity of pure compounds isolated from brown algae. In parenthesis and italic the value for the standard compounds used as reference expressed in the same units.

Compound	DPPH	Hydroxyl	Peroxyl	Superoxide	Reference
6,6′-Bieckol	8.69–9.1 μM (α-T = 45.3)	28.7–29.7 μM	17.1 μM	15.4–15.9 μM	Li et al. (2009), Zou et al. (2008)
8,8′-Bieckol	15 μM (Toc = 52)			6.5 μM (Toc = 12)	Shibata et al. (2008)
Dieckol	6.2–13 μM (Cat = 32)(AA = 10.3)	28.6 μM	14.5 μM	7.6–16.2 μM (Cat = 5.2)	Kim et al. (2009), Li et al. (2009), Shibata et al. (2008)
Dioxinodehydroeckol	8.8 μM (AA = 10.3)				Kim et al. (2009)
Diphlorethohydroxycarmalol	3.4–10.5 μM (AA = 19.9) (Toc = 45.3)	27.1–114.8 μM (AA = *69.7*)		16.7 μM	Heo et al. (2008), Zou et al. (2008)
Eckol	22.9–26 μM (Cat = 32)	51.8 μM	28.4 μM	26.5–107 μM (AA = 62)	Shibata et al. (2008), Li et al. (2009)
Isoepitaondiol	0.07 mg/g DPPH (T = 0.12)	0.5 mg/L (T = 0.7)			Nahas et al. (2007)
Fucophlorethols	10–14 μg/mL				Lee, Park, and Choi (1996)
Fucodiphloroethol g	14.72 μM	33.5 μM	18.1 μM	18.6 μM	Li et al. (2009)
Fucotriphlorethol a	10 μg/mL (Vit C = 3.6 μM)		3.3 μg/mL		Parys et al. (2010)
7-Phloro eckol	18.64 μM	39.6 μM	22.7 μM	21.9 μM	Li et al. (2009)
Phlorofucofuroeckol a	4.7–17.7 μM (AA = 10.3–30)	39.2 μM	21.4 μM	8.4–21.6 μM (AA = 62)	Kim et al. (2009), Li et al. (2009), Shibata et al. (2008)
Phloroglucinol	13.2 μg/mL (Vit C = 0.14)	392.5–408.5 μM	128.9 μM	115.2–124.7 μM	Li et al. (2009), Parys et al. (2010), Zou et al. (2008)
Taondiol	0.10 mg/g DPPH (T = 0.12)	0.4 mg/L (T = 0.12)			Nahas et al. (2007)
Sargaol	0.20 mg/g DPPH (T = 0.12)	2.4 mg/L (T = 0.12)			Nahas et al. (2007)
Sargaquinone	0.20 mg/g DPPH (AA = 0.25)	0.8 mg/L (AA = 1.2)			Nahas et al. (2007)
Stypodiol	0.21 mg/g DPPH (Q = 0.06)	1.0 mg/L (Q = 0.3)			Nahas et al. (2007)
Stypoldione	0.18 mg/g DPPH (T = 0.12)	0.8 mg/L (T = 0.7)			Nahas et al. (2007)
Trifucodiphlorethol A	14.4 μg/mL (Vit C = 0.14)		3.5 μg/mL		Parys et al. (2010)
Trifucotriphlorethol A	13.8 μg/mL (Vit C = 0.14)		3.2 μg/mL	152.9 μg/mL	Parys et al. (2010)

AA: ascorbic acid; BHT: butylated hydroxytoluene; Cat: catechin; Q: quercetin; T: Trolox; Toc: α-tocopherol; Vit C: vitamin C.

active as catechin, epigallocatechin gallate, resveratrol and more active than ascorbic acid and α-tocopherol (Shibata et al., 2008). Inhibition of superoxide radical formation was reported for sulfated polysaccharides from *U. pinnatifida* (Hu et al., 2010), *F. vesiculosus* (Rupérez et al., 2002), *Dictyota sp* and *Dictyopteris delicatula* (Costa et al., 2010; Magalhães et al., 2011), *Canistrocarpus cervicornis* (Camara et al., 2011), *Lobophora variegata* (Paiva et al., 2011), *Laminaria japonica* (Hou et al., 2012; Zhao, Li, Xue, & Sun, 2012) and *S. graminifolium* (Zhang et al., 2012). Sulfated polysaccharides showed higher antioxidant potential than sulfated galactans and gallic acid. *F. vesiculosus* fucoidan and some fucoidan fractions of *Padina gymnospora* were more active than the kappa, iota and lambda carrageenans (Rocha De Souza et al., 2007), but *E. cava* extracts showed higher antioxidant capacity for the phenolic fraction than for the highly sulfated polysaccharidic fraction (Athukorala et al., 2006).

Hydrogen peroxide (H_2O_2), a non-radical reactive species, is rather inert at low concentrations, but converts into singlet oxygen ($^1O_2$) and hydroxyl radicals ($HO^{\cdot}$), which are powerful oxidising agents, since they can cross membranes and may oxidise a number of compounds. The scavenging assay commonly used is based on the oxidation of scopoletin with horseradish peroxidase to a nonfluorescent product. The ability to scavenge peroxyl radicals was reported for several brown seaweed solvent extracts (Le Tutour et al., 1998) and the enzymatic extracts from *S. thunbergii* (Park et al., 2005), *E. cava*, *Sargassum* sp, *S. lomentaria* (Heo, Park, Lee, & Jeon, 2005) and *Ishige okamurae* (Heo & Jeon, 2009a, 2009b). The aqueous ethyl acetate, chloroform fractions and methanol extract of *E. cava* showed strong scavenging activities, comparable or higher than those of commercial antioxidants BHT and α-tocopherol (Senevirathne et al., 2006). Also the crude polysaccharide and crude polyphenolic fractions of *E. cava* were active (Athukorala et al., 2006). No clear trend can be established for the extracts summarised in Table 2, but in most cases enzymatic extracts were less efficient than BHT, BHA and tocopherol and different values in relation to BHT were observed for solvent extracts.

Hydroxyl radical ($HO^{\cdot}$) is generated at a biological level, when hydrogen peroxide reacts with Fe^{2+} (Fenton reaction). This radical is an extremely reactive and short-lived species that can hydroxylate DNA, proteins, and lipids, being the most reactive and harmful ROS in living cells. Its direct scavenging by dietary antioxidants in a biological system is unrealistic as the cellular concentration of dietary antioxidants is negligible compared with other biological molecules. At least two mechanisms occur *in vitro*: hydroxyl trapping and metal chelation, since it is possible to prevent the formation of hydroxyl radicals by chelating metal ions. Hydroxyl radical scavenging was reported for extracts from *C. racemosa* and *Sargassum* sp (Yangthong et al., 2009), *S. thunbergii* (Park et al., 2005) and *E. cava* (Athukorala et al., 2006), for enzymatically prepared extracts from *S. horneri* (Park et al., 2004), and for fractions, i.e., the aqueous chloroform fraction, 70% methanol extract and the *n*-hexane fraction of *E. cava*, with activities similar to that of BHT (Senevirathne et al., 2006). Pure phenolic compounds, such as phloroglucinol (Ahn et al., 2007; Kang et al., 2003a; Zou et al., 2008), eckol (Kang, Chung, Jung, Son, & Choi, 2003b, 2005; Ahn et al., 2007), dieckol (Ahn et al., 2007), 6,6′-bieckol (Zou et al., 2008), and diphlorethohydroxycarmalol (Heo et al., 2008), were active. The hydroxyl radical-scavenging effect was observed for fucoidan (Barahona et al., 2011; Camara et al., 2011; Costa et al., 2010; Magalhães et al., 2011; Paiva et al., 2011; Rocha De Souza et al., 2007) and low-MW sulfated polysaccharides (1–10 kDa) (Hou et al., 2012; Wang, Zhang, Zhang, Song, & Li, 2010; Zhang et al., 2010; Zhao et al., 2012). Whereas the hydroxyl radical scavenging assay in crude sulfated polysaccharides was lower than for standard antioxidants (Camara et al., 2011; Costa et al., 2010; Magalhães et al., 2011), polysaccharides with high content of uronic acid have shown good antioxidant potential, and alginates of 1–10 kDa from *L. japonica* exhibited higher scavenging potency than ascorbic acid and carnosine (Zhao et al., 2012).

A dose-dependent activity has been reported and examples of this behaviour for crude extracts and for polysaccharide fractions are shown in Fig. 1. Different extracts show a typical behaviour

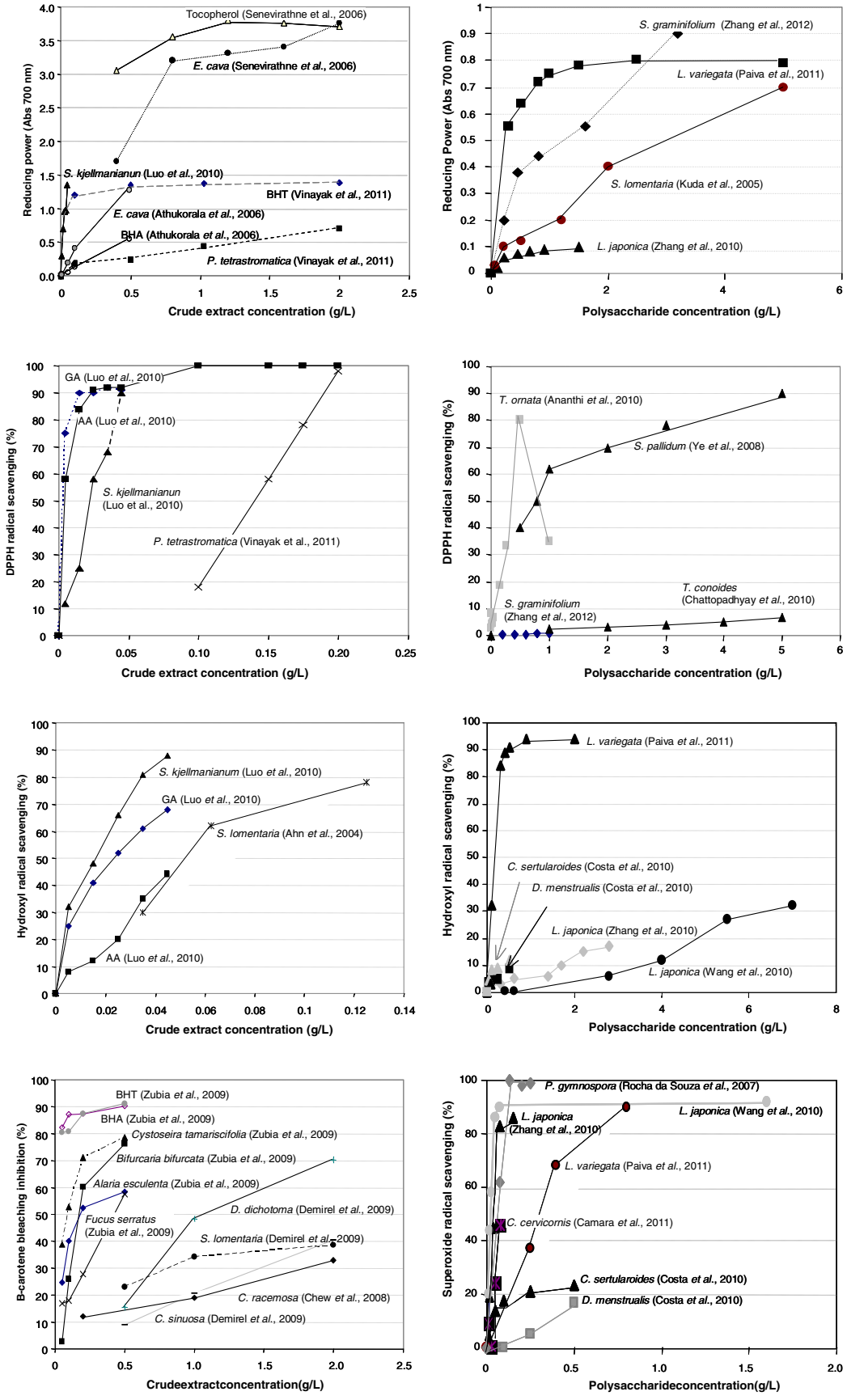

Fig. 1. Effect of concentration of crude extracts and crude polysaccharides from brown algae on *in vitro* antioxidant properties.

reaching a plateau at a given concentration, but the concentration of phenolics to achieve maximum protection can be achieved at lower values than for the oligosaccharide components. A similar behaviour for synthetic and standard antioxidants can be observed, but the plateau was reached at lower concentrations in the case of synthetic compounds. Higher efficiency of algal components was noticed in some cases.

Singlet oxygen scavenging capacity assay Singlet oxygen ($^1O_2$) is an excited state of molecular oxygen that has no unpaired electrons and does not react via radical mechanisms. It is a powerful oxidising agent reacting directly with a wide range of biomolecules, mostly by the addition to double bonds, forming endoperoxides that can be reduced to alkoxy radicals, which initiate radical chain reactions (Prior et al., 2005). Singlet oxygen is normally generated in the presence of light and photosensitisers (Choe & Min, 2009), in the absence of light, extracellular $^1O_2$ production could be a result from the spontaneous dismutation of superoxide anion and it can be chemically generated from the non-photochemical decomposition of hydrogen peroxide by metals or hypochlorite. Singlet oxygen can interact with molecules by direct reaction or by transfer of its excitation energy to other molecules and a return to the ground state (quenching of singlet oxygen). The decay rates of phosphorescence have been used to measure singlet oxygen quenching ability. Meroditerpenoids from *Cystoseira sp* (Foti, Piattelli, Amico, & Ruberto, 1994) and the butanol and aqueous fractions from *Sargassum hystrix*, particularly those from the membrane bound fraction (Budhiyanti et al., 2011), were $^1O_2$ quenchers comparable to α-tocopherol.

Oxygen radical absorbance capacity (ORAC), is used to determine the ability to scavenge certain peroxyl radicals that induce oxidation in the presence of fluorescein. Frequently 2,2-azobis-(2-amidinopropane) dihydrochloride (AAPH) is used as a peroxyl radical generator. Despite the limitations in lipophilic samples, the ORAC assay is widely accepted as a standard assay for the antioxidant capacity when multiple constituents and complex reaction mechanisms are involved, e.g., food, nutraceuticals (Huang et al., 2005) and algae (Price, Sanny, & Shevlin, 2006). This activity was reported for *F. vesiculosus* products (Díaz-Rubio et al., 2009) and crude extracts from *Fucus sp., A. nodosum* and *L. hyperborean* in acetone (Wang et al., 2009), from *Sargassum sp*, *Cystoseira abies-marina*, *U. pinnatifida* in subcritical water (Plaza et al., 2010) and the lipid fraction from *Macrocystis pyrifera* and *Ecklonia radiata*, with effects comparable to that of BHT (Kindleysides et al., 2012). Trifucodiphlorethol A, trifucotriphlorethol A, fucotriphlorethol A and phloroglucinol scavenged peroxyl radicals in the ORAC assay more efficiently than Trolox (Parys et al., 2010), and fucoidan from *L. vadosa* was also active (Barahona et al., 2011). For crude algal extracts, ORAC values in the range 50–80% of those for Trolox were reported for subcritical water extracts and solvent fractions.

Alkyl radicals are a primary intermediate in many hydrocarbon reactions (Choe & Min, 2009), and in studies with algal extracts alkyl radicals are generated *via* AAPH. The spin adduct was recorded using a ESR spectrometer. A strong radical scavenging effect on alkyl radicals was reported for *S. horneri* (Park et al., 2004) and *S. thunbergii* enzymatic extracts (Park et al., 2005). Phloroglucinol, eckol and dieckol (Ahn et al., 2007), diphlorethohydroxycarmalol (Heo et al., 2008), 2,7′-phloroglucinol-6,6′-bieckol (Kang, Heo, Kim, Lee, & Jeon, 2012) and 6,6′-bieckol exhibited stronger alkyl radical scavenging capacity than epigallocatechin gallate (Zou et al., 2008), and diphlorethohydroxycarmalol showed a dose-dependent higher potency than ascorbic acid (Heo et al., 2008).

Peroxynitrite ($ONOO^-$) can be formed by reaction of superoxide and nitric oxide, which is not a strong oxidant. The protonated form, peroxynitrous acid (ONOOH), is a very strong oxidant. Under physiological conditions, these species cause the nitration or hydroxylation of aromatic compounds, particularly tyrosine (to nitrotyrosine). Peroxynitrite formation *in vivo* is implicated in numerous human diseases and has been evaluated in different foods. Two methods are used for $ONOO^-$ scavenging measurements: inhibition of tyrosine nitration and inhibition of dihydrorhodamine 123 oxidation. The organic solvent and the aqueous fractions from *I. okamurae*, *S. hemiphyllum* (Lee et al., 2004) and *Sargassum thunbergii*, which showed activities comparable to those of L-ascorbic acid and penicillamine (Seo et al., 2004), and phlorotannin rich extracts of *E. cava* (Shin et al., 2006) were active against peroxynitrite.

Nitric oxide (·NO) is a potent mediator of physiological processes, with functions related to cell signalling and vasodilation, protecting organs from ischaemic damage, and also shows antimicrobial and antitumor activities. It is a highly reactive and diffusible free radical. The toxicity and damage caused by nitric oxide and superoxide anion is multiplied as they produce reactive peroxynitrite, which leads to serious toxic reactions with biomolecules, like protein, lipids and nucleic acids. Several methods can be used for the quantification of ·NO-scavenging capacity, including a simple amperometric sensor, ESR spectrometry to detect a spin adduct formed when ·NO is oxidised to NO_2, the Griess reaction for *in vitro* determinations, and a fluorescent method for *in vivo* detection (Magalhães et al., 2008). Ethyl acetate and aqueous chloroform fractions of *E. cava* showed stronger activities on ·NO scavenging than standard antioxidants (Senevirathne et al., 2006), and crude polysaccharide from *T. ornata* (Ananthi et al., 2010) was also active.

3.2.3. Metal-ion chelating ability

Secondary or preventive antioxidative action by metal-ion chelating reflects the inhibition of an interaction between metals and lipids through the formation of insoluble metal complexes or generation of steric resistance without directly interacting with oxidative species. The presence of ionic transition metals, such as Cu^{2+}, Fe^{2+}, Fe^{3+}, in a system can induce the initiation and accelerate the rate of oxidation, either by promoting the decomposition of hydroperoxides or through the production of hydroxyl radicals by the Fenton reaction. Lipids in foods are often present as emulsions; in these systems, transition metals ions are the major prooxidants and primarily promote oxidation by decomposing lipid hydroperoxides located at the droplet surface into free radicals. The most important type of secondary antioxidants are those that chelate transition metal ions by decreasing metal reactivity or by physically partitioning the metal away from the lipid (McClements & Decker, 2000; Waraho, McClements, & Decker, 2011). Spectrophotometric methods are used to determine the metal-ion chelating activity of phenolic compounds, using a strong chelator such as EDTA as control.

Dried *S. lomentaria* (Kuda et al., 2005), the methanol extract and some solvent fractions of *E. cava* (Senevirathne et al., 2006; Shin et al., 2006), *S. hystrix* (Budhiyanti et al., 2011) and *F. vesiculosus* (Wang et al., 2012) were active. Literature presents contradictory reports regarding metal chelating capacities of brown algal polyphenols, some studies have demonstrated they are potent ferrous ion chelators (Chew, Lim, Omar, & Khoo, 2008; Senevirathne et al., 2006) dependent upon their structure and the number and location of the hydroxyl groups. Data in Table 2 show values comparable to or higher than ascorbic acid and citric acid, similar to BHT and tocopherol, and similar or lower than EDTA. High molecular weight peptides and proteins might be more effective than low MW peptides and amino acids (Wang et al., 2009). Water-soluble polysaccharides, such as alginate, fucoidan and laminaran, are dose dependent and stronger ferrous ion chelators than ethanol extracts (Kuda et al., 2006). This activity was reported for water extracts and polysaccharides from *F. serratus*, *A. nodosum* and *Laminaria* sp (Wang et al., 2009), *Dictyota cervicornis*, *D. mertensis* (Costa et al., 2010), *L. japonica* (Zhang et al., 2010), *D. delicatula*

(Magalhães et al., 2011), *F. vesiculosus* (Wang et al., 2012) and *C. cervicornis* (Camara et al., 2011).

In addition to the previously mentioned chemical tests valuable for their simplicity, other assays more oriented to the final practical use should also be considered. Since in most food products, the major concern is to avoid and minimise oxidation, assays evaluating the lipid protection are desired.

3.2.4. Protection against lipid oxidation

Oil stability tests provide an evaluation of the protection from oil peroxidation, although most methods involve unrealistic conditions by using radical initiators and accelerated storage at elevated temperature. Different analyses can be performed, including peroxide value (a measurement of the content in hydroperoxide, primary products of lipid oxidation), conjugated dienes (an indication of fatty acids autoxidation), the *p*-anisidine value (measuring secondary products, generated by hydroperoxide decomposition), thiobarbituric acid-reactive substances (TBARS, to quantify malonaldehyde and secondary decomposition products of PUFAs) and volatile compounds (secondary oxidation products, related to the product quality and the development of off-flavours) (Antolovich et al., 2002; Choe & Min, 2009; Craft et al., 2012).

Several extracts proved efficient against model lipids oxidation, such as linoleic acid and methyl linoleate, e.g., the water and ethanol extracts from *Sargassum polycystum* (Anggadiredja et al., 1997), *A. nodosum* and *Fucus vesiculosum* (Le Tutour et al., 1998), *E. cava* and *H. fusiformis* (Siriwardhana et al., 2004), *S. lomentaria* (Kuda et al., 2005), *Sargassum vulgare* and *S. angustrifolum* (Rastian, Mehranian, Vahabzadeh, & Sartavi, 2007), and *S. boveanum* (Zahra et al., 2007). Crude polysaccharide and crude polyphenolic fractions of *E. cava* (Athukorala et al., 2006; Li et al., 2009), pure compounds isolated from *Sargassum siliquastrum* (Cho et al., 2008) and terpenoid derivatives from *C. crinita* (Fisch et al., 2003; Foti et al., 1994) were active.

Food systems with vegetable oils have also been investigated, e.g., *L. digitata* and *H. elongata* extracts were effective for preservation of sunflower oil (Le Tutour, 1990). Fish oil, rich in ω3 long-chain PUFA, and highly susceptible to oxidation was protected by organic fractions of *E. cava* and *H. fusiformis* (Siriwardhana et al., 2004); *E. cava* organic fractions showed higher potency than α-tocopherol and were comparable to BHT (Senevirathne et al., 2006). *E. radiata* and *M. pyrifera* extracts were more effective than BHT (Kindleysides et al., 2012). *E. radiata* extract also protected eicosapentaenoic, docosapentaenoic and docosahexaenoic acids. The formulation of entirely marine-based food products or nutraceuticals, using brown algae extracts at an optimum dose, to avoid off-flavours conferred by the extracts, is claimed (Kindleysides et al., 2012).

Another important application is to protect oxidation in emulsion, common both in food and cosmetics, although the oxidation mechanism in emulsions differs from that in bulk oil (Waraho et al., 2011). Protection of model emulsions, such as β-carotene/linoleic acid bleaching, was investigated with extracts from *L. japonica* and *U. pinnatifida* (Huang & Wang, 2004), *Colpomenia sinuosa*, *Dictyota dichotoma*, *Petalonia fascia* and *S. lomentaria* (Demirel et al., 2009), and real systems, such as tuna eyeball oil emulsion (Cho et al., 2008).

Other systems include the liposome as a model of the cell membrane for *in vitro* biochemical research. Phlorotannins have high affinity for lipid bilayers, and oligomers of phloroglucinol isolated from *Eisenia bicyclis*, *E. cava* and *E. kurome*, showed potent inhibition of phospholipid peroxidation in the liposome system (Shibata et al., 2008), while alginate fractions from *L. japonica* inhibited yolk homogenate lipid peroxidation (Zhao et al., 2012). Oxidation in model cells has also been used, e.g., the solvent fractions from *S. siliquastrum* to protect rat brain homogenate (Lim, Cheung, Ooi, & Ang, 2002), and the solvent extracts from *Sargassum micracanthum* (Mori et al., 2003) and *T. ornata* crude polysaccharides (Ananthi et al., 2010) to protect rat liver homogenates. Lipid oxidation in steaks was limited by supplementation of feed diets with a *L. digitata* extract containing laminarin and fucoidan (Moroney, O'Grady, O'Doherty, & Kerry, 2012). It is not the in scope of this review, but at biological level lipid peroxidation is involved in damage to cell membranes, altering both lipids and proteins, and a number of studies have investigated the protection of other lipid substrates with biological implications, e.g., the oxidation of LDL (low density lipoproteins).

4. Composition and structure–activity relationships

The structure–activity relationships of the active compounds present in marine seaweed is comparatively a less studied field, and further work is required to evaluate this relationship, which may vary depending on the protocol employed. In this section a summary of the results on the two major polymeric fractions in brown algae will be discussed. The effect of structure on the radical-scavenging activity of nahocols and isonahocols (Jung et al., 2008) or bromophenols (Liu et al., 2011) has also been studied.

4.1. Correlation between total phenolics and antioxidant activity

In many studies the antioxidant activity of whole algae, their parts, extracts and fractions has been ascribed to the phenolic compounds. However, the observed activity could be a result of the complex composition of the macroalgal extracts. Positive correlations between phenolic content and scavenging capacity have been reported, mostly with $DPPH^{\cdot}$, for example for crude extracts from *E. stolonifera* (Iwai, 2008), *Stypocaulon scoparium* (López et al., 2011), *H. elongata* and *Laminaria sp.* (Rajauria, Jaiswal, Abu-Ghannam, & Gupta, 2010), *C. racemosa* and *Sargassum* sp (Yangthong et al., 2009), and for fractions from *Cystoseira sedoides* (Mhadhebi, Laroche-Clary, Robert, & Bouraoui, 2011), *A. nodosum* (Audibert et al., 2010) and *F. vesiculosus* (Wang et al., 2012). Correlation of the phenolic content with the reducing power (Kuda & Ikemori, 2009; Wang et al., 2010; Zubia et al., 2009, 2012), metal chelating (Senevirathne et al., 2006), protection in emulsion (Zubia et al., 2008) and the scavenging of other radicals, including superoxide anion (Nakai et al., 2006; Yangthong et al., 2009), $ABTS^{\cdot+}$ (Audibert et al., 2010) and hydroxyl (Yangthong et al., 2009) radicals has also been found.

Since the phenolic content in algal extracts is lower than in those from other terrestrial sources, the value obtained with the Folin–Ciocalteau reagent could be a measure of the reducing capacity, and similar results with other methods based on similar redox reactions (DPPH, FRAP, TEAC) are expected (Huang et al., 2005). The phenolic content correlated with some activities but not with others, i.e., with the reducing power but not with TEAC values (Matanjun et al., 2008). With $DPPH^{\cdot}$ and hydroxyl radical-scavenging capacity the correlations were strong, but with superoxide anion radicals was lower (Kuda et al., 2005, 2006; Kuda & Ikemori, 2009), with $DPPH^{\cdot}$ and with reducing potential, but not with chelating capacity (Wang et al., 2012). When comparing extracts from different solvents, due to the different composition, this correlation was found only with some of them, i.e., with the DPPH and peroxyl radical scavenging capacity for acetone extracts (Wang et al., 2009). Different behaviour depending on the type of extraction process was observed, e.g., the antioxidant potency correlated with the phenolic content for autoclave extracts but not for boiling extracts (Yangthong et al., 2009). Several extracts with low phenolic content have displayed higher activity than expected, suggesting that other compounds were also responsible for the action,

e.g., extracts from *T. conoides* (Boonchum et al., 2011). *Cystoseira sp.* (Chkhikvishvili & Ramazanov, 2000), *P. binghamiae* (Kuda et al., 2006), *Sargassum sp* (Rastian et al., 2007), *S. boveanum* (Zahra et al., 2007), *S. ringgoldianum* (Nakai et al., 2006), and *E. radiata* and *M. pyrifera* (Kindleysides et al., 2012). The compounds responsible could be ascorbic acid, proteins or peptides, fucoxanthin, sterols, sulfated polysaccharides, Maillard reaction products (Boonchum et al., 2011; Peng et al., 2011; Plaza et al., 2010), mycosporines-like amino acids in *S. hystrix* (Budhiyanti et al., 2011), and hydrocarbons and terpenes in *Colpomenia sinuosa*, *Dictyota dichotoma*, *Petalonia fascia* and *S. lomentaria* (Demirel et al., 2009). Synergistic effects with extracts from brown algae and α-tocopherol and non-polar pigments have been observed (Le Tutour, 1990; Le Tutour et al., 1998).

No correlation was observed between phenolic content and activity for fractions from the *S. siliquastrum* dichloromethane extract in lipid oxidation assays (Lim et al., 2002), for DPPH· of brown seaweeds (Airanthi, Hosokawa, & Miyashita, 2011), for chelating ability of *F. vesiculosus*, *F. serratus* and *A. nodosum* (Wang et al., 2009), for crude extracts from *C. tamariscifolia* and *F. ceranoides* and DPPH radical scavenging, reducing activity or β-carotene protection in emulsion, although in this case the most active extracts presented high phenolic content (Zubia et al., 2009). Similarly, no correlation was found between lipoxygenase inhibition and radical-scavenging activities of *Sargassum sp*. (Matsukawa et al., 1997).

In extracts from terrestrial plants the correlation between phenolic content and antioxidant activity is almost always linear. This comparison would also be reasonable for phenolic–enriched fractions from seaweeds. However, due to the complexity of crude algal extracts, a simple correlation between the phenolic content and the antioxidant properties is not informative. A detailed characterisation of both the active components and other substances are needed.

4.2. Structure–activity of the phenolic fraction

Abundant studies on the influence of the structural features and antioxidant activity of phenolics from terrestrial sources can be found, but the structure–activity relationships in phlorotannins are less studied. Phlorotannins possess strong antioxidant potency in the presence of oxidising agents and produce phenoxyl radical species, stabilised by resonance delocalisation of the unpaired electron and by hydrogen bonding with an adjacent hydroxyl group (Ahn et al., 2007; Shibata et al., 2008; Singh & Bharate, 2006; Zou et al., 2008). Phlorotannins from brown algae have up to eight interconnected rings, and thus are more potent radical scavengers than other polyphenols from terrestrial plants. In this sense, polymeric phlorotannins of the fucol and fucophlorethol classes exhibited greater antioxidant activity than phloroglucinol (Cérantola, Breton, Gall, & Deslandes, 2006). The influence of the molecular weight of brown algae extracts has been confirmed, e.g., on the DPPH· and $ABTS^{\cdot+}$ radical scavenging capacity for *A. nodosum* (Audibert et al., 2010) and DPPH· and reducing power for *F. vesiculosus* (Wang et al., 2012). Identification of the major moieties in the active compounds and studies with structurally related model compounds, to clarify the effect of substituents and active groups are needed in order to define their effect on the activity and to propose practical uses.

4.3. Structure-activity of the fucoidan fraction

The relationship between the molecular weight of oligosaccharides, sulfation and acetylation degree and their antioxidant action is not simply linear (Barahona et al., 2011; Hou et al., 2012; Kuda et al., 2006; Zhang et al., 2010). The reducing potential (Magalhães et al., 2011), free radical quenching and the chelating effect (Zou et al., 2008) of the crude polysaccharide has been ascribed to the presence of sulfate groups (Ananthi et al., 2010; Rocha de Souza et al., 2007; Rupérez et al., 2002). However, the activities of fucoidans also depend on their structural features and the spatial patterns of sulfate groups and esteric hindrance (Ananthi et al., 2010; Barahona et al., 2011; Jiao et al., 2011; Wang et al., 2010). The low-MW sulfated polysaccharides could be readily incorporated into the cells. Despite their low molecular weight sulfated polysaccharides have shown more potent radical scavenging capacity (Choi et al., 2009; Wang et al., 2009; Zhang et al., 2012), and reducing power (Zou et al., 2008) than high molecular weight; no clear effect of the MW of polysaccharides was seen in other cases (Barahona et al., 2011; Camara et al., 2011; Costa et al., 2010; Hou et al., 2012; Kuda et al., 2006; Magalhães et al., 2011) or contradictory results, which suggests that the conformation of the fucoidan, composition and sequence of monosaccharides, configuration and position of glycosidic linkages, position of branching points could be determinant, and more studies are needed (Morya et al., 2012).

5. Major variables affecting *in vitro* antioxidant activity

The content and antioxidative properties of extracts and fractions isolated from brown algae are highly dependent on fractions associated with the natural variability and to processing factors. Some of the most relevant aspects in relation to the *in vitro* activity will be briefly commented on.

5.1. Natural variability

A systematic review of variability in macroalgal composition (Stengel et al., 2011) considered changes due to i) spatial and temporal environmental aspects and responses of different compounds to environmental parameters (light, nutritients, salinity, temperature, pH, and contaminants), ii) variations within thalli, with function and position and iii) impacts of biotic interactions. The influential spatial and temporal aspects would include: fluctuations in physicochemical characteristics, biotic impacts due to grazers, spatial and population differences due to genetic and ambient variability, and physiological changes in response to seasonal and diurnal variations and to reproductive development. A similar study on antioxidant properties is not available and published information on the variables associated with natural factors will be briefly discussed.

Seasonal variations in population structure and composition have been reported for brown seaweeds growing in the same area (Gorham & Lewey, 1984; Stiger et al., 2004). The chemical composition of macroalgae varies strongly with growth cycle and maturity (Le Tutour et al., 1998; Murakami et al., 2011), the pattern being not the same in all species (Lewey & Gorham, 1984). Spatial, depth and temporal variations on the phenolic composition and DPPH radical scavenging activity have been observed (Zubia et al., 2008). Seasonal variations in levels and composition of commercially important phycocolloids have been most studied, but information on fucoidans is scarce. Temporal variation in phenolics has also been attributed to developmental stage and light environment. In addition to seasonal changes over several months, short-term fluctuations in pigment levels may occur within a daily cycle (Stengel et al., 2011). Light, and UV exposure impacts on levels and composition of various components, particularly, pigments, polysaccharides and phlorotannins. Salinity is mostly studied in relation to ionic composition, protein and phenolic levels (Connan & Stengel, 2011). Temperature effects on the production of stress metabolites and the interactive effects with UV-radiation and nutrients has also been considered (Stengel et al., 2011). The levels

of phenolics are associated with environmental stress conditions (salinity and nutrient availability), although additional variations can also occur within individuals and with life stages. The activity of reactive oxygen scavenging enzymes in response to temperature has been reported (Collén & Davison, 2001), although in some *Fucus* sp the content of antioxidants (ascorbate, glutathione, carotenoids, and tocopherols) and protective enzymes (catalase, superoxide dismutase, ascorbate peroxidase, and glutathione reductase) were not correlated with stress tolerance (Collén & Davison, 1999).

Variation within different functional regions of macroalgae (holdfast, stipe and blade) are due to exposure to different microhabitats. Intra-thallus radical-scavenging activity variations for *A. nodosum* and *Laminaria sp.* (Connan et al., 2006), and *Ecklonia* and *Sargassum sp* (Kuda & Ikemori, 2009) have been observed. The variations cannot be observed in all species; no significant differences in the phenolic levels were found within the vegetative cells, with species, stage of growth or organ in *Eisenia bicyclis*, *E. cava* and *E. kurome* (Shibata et al., 2004) or between vegetative and reproductive parts of *A. nodosum* (Connan et al., 2006). Phlorotannins tend to accumulate in the outer cortical layers and their content shows variation with age, length and tissues (Amsler & Fairhead, 2006; Shibata et al., 2004; Zubia et al., 2008). Environmental contaminants such as heavy metals can also induce changes in the chemical composition and in the endogenous compounds produced to control the induced oxidative stress and also polysaccharides and phenolics, owing to their metal-complexing properties (Connan & Stengel, 2011).

The macroalgal defence against biotic attacks is based on signalling, responses and synthesis of secondary metabolites, such as phlorotannins, fatty acid-derived compounds, terpenoids and halogenated compounds. Since the synthesis of metabolites and components with relevant antioxidant action is dependent on several spatial and temporal factors, it is difficult to assess the direct influence of each one of them, since simultaneous influence of various components can occur. The correct interpretation of their presence, levels and composition is considered a challenge to attain a more profound understanding of these effects and would aid future exploitation of algal resources (Stengel et al., 2011).

5.2. Processing factors

Considering the utilisation of brown algae as a source of food antioxidants, either as a whole or as crude extracts, fractions or components, the most relevant processing stages are drying the raw material, and the selective solvent extraction of the active components. In the case of polysaccharides, the depolymerisation occurring during extraction or in subsequent stages would also be influential, although no systematic information is yet available.

The drying stage can determine the nutritional properties, since some components are more sensitive than others, e.g., the protein and lipid content in sun-, oven- and freeze-dried *S. hemiphyllum* were unaffected, whereas amino acids, polyunsaturated fatty acids, and vitamin C values were higher in freeze-dried algae, and ash, mineral, and total vitamin C were lower in sun-dried seaweed (Chan et al., 1997). Fucoxanthin is heat and light sensitive and phenolic compounds can be degraded during drying, as reported for oven-drying (Anggadiredja et al., 1997; Balboa, Moure, & Domínguez, unpublished data; Jiménez-Escrig et al. 2001; Wong & Cheung, 2001) and greenhouse-drying (Le Lann et al., 2008). Thermosensitive products can be preserved during freeze-drying, but destabilisation of the native conformation may decrease bioactivity. The different effects of drying on the phenolic content may be caused by the structure of phenolic compounds, the morphology of the seaweeds and also by the endogenous enzymes (Le Lann et al., 2008; Rastian et al., 2007). The drying and storage processes may destroy the alcohol- rather than the water-soluble antioxidants (Kuda et al., 2005).

The extraction solvent affects the total phenolic extraction yield and antioxidant activity (Demirel et al., 2009; Kindleysides et al., 2012; López et al., 2011; Matsuka, Ninomiya, Mitou, & Kawakubo, 1995; Mhadhebi et al., 2011; Zubia et al., 2008). Aqueous extraction showed higher phenolic extraction and radical scavenging activity than organic solvents (Boonchum et al., 2011; Jiménez-Escrig et al. 2001; Kuda & Ikemori, 2009; Kuda et al., 2005; López et al., 2011; Senevirathne et al., 2006). However, the opposite trend was also observed (Ananthi et al., 2010; Iwai, 2008; Matsukawa et al., 1997; Mhadhebi et al., 2011). The contents of fucoidan and phenolic compounds for dried and for boiled products of *E. stolonifera* and their properties were affected by processing (Kuda et al., 2007). Autoclave and subcritical water extraction at temperatures 100–300 °C enhanced the cell wall degradation, facilitating the release and extraction of antioxidants, an effect that increased with temperature (González-López et al., 2012; Plaza et al., 2010; Yangthong et al., 2009). Although heating at 85 °C caused a reduction in the total phenolic content in water extracts of *P. binghamiae* and *S. lomentaria*, increased yields and DPPH radical-scavenging activities were obtained at 121 °C, probably due to the Maillard reaction and the formation of novel active compounds (Kuda et al., 2006; Plaza et al., 2010). Thermal stability at 100 °C of enzyme extracts from *S. horneri* (Heo et al., 2005) and *E. cava* (Athukorala et al., 2006) was reported.

In comparison with solvent extracts from some terrestrial sources the phenolic content of crude extracts from algae are relatively low (see Table 2). Further solvent fractionation of the crude extracts provides additional enrichment, ethyl acetate usually providing the most active fractions (Audibert et al., 2010; Senevirathne et al., 2006; Wang et al., 2012). For example, the methanol/chloroform extracts of *Sargassum sp.* showed lower DPPH radical-scavenging activity than gallic acid and ascorbic acid, but purification with ethyl acetate yielded fractions with higher activity (Luo et al., 2010). The selective removal of sugar components by fermentation with *Candida utilis* of *Eisenia bicyclis* water extracts (Eom et al., 2011) and *E. cava* processing by-product obtained after polyphenolic extraction (Wijesinghe et al., 2012) enhanced the phenolic content and DPPH scavenging activity without affecting the lipid, protein and ash contents. In the production of refined extracts and/or components, the physicochemical stages are relevant to maintain structures and bioactivities, particularly the exposure to high temperatures.

6. Conclusions and future trends

Marine brown macroalgae produce a variety of highly bioactive secondary metabolites, with structures that cannot be found in other organisms. Different components and fractions in brown macroalgae have great potential as antoxidant food additives suitable for commercial exploitation, the most promising being polysaccharides, phlorotannins and terpenoids. In this review, a comparison of the *in vitro* activities of brown macroalgae crude extracts, fractions and components is presented in relation to synthetic and standard antioxidants. From the available information it can be inferred that there are many potentially useful algae as sources of bioactive components with antioxidant action.

A key application of antioxidants is their inclusion in food products as preservatives to extend shelf-life and to maintain quality; in this sense the *in vitro* antioxidant action can be explored as a preliminary tool for screening purposes. A recommendation on the most suited algaes should not be based on preliminary *in vitro* tests, but also in assays in model systems similar to the foods that they should protect. In order to propose an active

antioxidant from algal biomass, in addition to the protective properties, different aspects should be considered, including the possibility of using either a crude extract, or fractions or components, the organoleptic and functional properties they can confer on the final product and the lack of toxic elements or contaminants. Additional considerations on the availability, seasonal production and processing are also important. The possibility of valorising other fractions for alternative products is encouraged in order to achieve a sustainable and integral use of raw materials.

Although some natural extracts are less efficient than synthetic extracts, the legal requirements could allow their use at higher levels, and supplementation of fish oil and marine products with algal extracts would be functionally and organoleptically favourable. The future development of this area is encouraged, and the wide variety and complex chemical structures found in the crude extracts makes necessary their processing to isolate and characterise the active fractions. Further knowledge of the properties, mechanisms of action and performance in practical systems will provide a better understanding of their antioxidant contribution. The synergistic effects of mixtures could favour the further development of seaweed antioxidants based not only on pure components but also on mixtures or crude extracts.

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