Review

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Antioxidants from macroalgae: potential applications in human health and nutrition

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The underlying physiology of algal antioxidant compounds is reviewed in the context of seaweed biology and utilization. The application of seaweed antioxidants in foods, food supplements, nutraceuticals and medicine is considered from the perspective of benefits to human health. We advocate that direct consumption of seaweed products for their antioxidant composition alone provides a useful alternative to non-natural substances, while simultaneously providing worthwhile nutritional benefits. Economic utilization of seaweeds for their antioxidant properties remains in its infancy. This review provides examples ranging from laboratory studies through to clinical trials where antioxidants derived from seaweeds may provide major health benefits that warrant subsequent investigative studies and possible utilization.

Key Words: antioxidants; homeostasis; human health; oxidative stress; ROS

Abbreviations: CVD, cardiovascular disease; ROM, reactive oxygen metabolism; ROS, reactive oxygen species; RS, reactive species

INTRODUCTION

Responses of organisms to increased levels of oxidants are diverse (Halliwell and Gutteridge 1984, Yan et al. 1998). In a human context, the potential negative impacts of such compounds are widely recognized, and both modern science and 'folk remedy' utilization has responded by providing functional products that involve food, medicines and cosmetics. Consumption of products high in antioxidant compounds is thought to alleviate cellular stresses brought about by the influence of reactive species (Schwartz 1996, Halliwell and Gutteridge 2007). While antioxidant benefits associated with consuming various terrestrial plants (e.g., green vegetables and berries) have long been accepted, relatively little emphasis has been placed on the merits of consuming marine macroalgae for the same benefits. Appendix A summarizes the most relevant literature available to date in relation to seaweed. It provides the reader with information on a number and variety of species investigated and the potential applications of the antioxidant components detected. While research shows that many macroalgae possess considerable antioxidant activity, the diversity of assays used for detection and assessment make interpretation of many results problematic (Schwarz et al. 2001, Ou et al. 2002, Decker et al. 2005, Kranl et al. 2005, Dudonné et al. 2009, Barahona et al. 2011). Significant antioxidant capacity may be expected based on the ecology

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of seaweeds and metabolism (Table 1); however, there is considerable work remaining between merely establishing the occurrence of antioxidant activity and demonstrating that a beneficial response may be obtained by consumption or application of the putative compounds, particularly by humans. The numerous potential human health advantages associated with the utilization of marine macroalgae containing an assortment of antioxidant compounds depends upon both the respective intake of the plants, and the bioavailability of anticipated antioxidant activities (Manach et al. 2004). See Table 2 for a selection of perceived health benefits related to specific chemical components.

All energy-producing metabolic processes are intrinsically driven by an electron transport chain, maintenance of which is essential to the health and integrity of an organism. The hazards of a prolonged imbalance include formation of reactive species, unstable molecules or molecular fragments that, if not neutralized, can react with non-target molecules, causing a variety of (negative) cellular impacts (Dring 2005). These may include the initiation of increased cell proliferation, mitochondrial damage, excessive DNA strand breakage and deleterious chemical chain reactions leading to lipid peroxidation, enzyme inhibition and protein degradation (Halliwell and Gutteridge 1984, Yan et al. 1998, He and Häder 2002,

Table 1. The major groups of antioxidant compounds in macroalgae with specific examples and potential algal sources for utilization

General category	Example compounds	Algal source	Reference
Carotenoids	β-carotene	*Chondrus crispus* *Mastocarpus stellatus*	Lohrmann et al. 2004
	Fucoxanthin	Brown algae	Sachindra et al. 2007
	Antheraxanthin, lutein, violaxanthin, xanthophylls, zeaxanthin	Red algae	Schubert et al. 2006
Phenolic compounds	Stypodiol, isoepitaondiol, taondiol	*Taonia atomaria*	Nahas et al. 2007
	Terpenoids	*Cystoseira* sp.	Foti et al. 1994
Phycobilin pigments	Phycoerythrin, phycocyanin	Red algae in general	Romay et al. 2003, Sekar and Chandramohan 2008, Soni et al. 2009, Yabuta et al. 2010
Polyphenols	Catechin, epicatechin, gallate	*Halimeda* sp.	Devi et al. 2008
	Flavonoids	*Palmaria palmata*	Yuan et al. 2005*a*
	Phlorotannins	*Sargassum pallidum* *Fucus vesiculosus*	Ye et al. 2008 Díaz-Rubio et al. 2009
Sulphated polysaccharides	Fucoidan, alginic acid, laminaran	*Turbinaria conoides*	Chattopadhyay et al. 2010
	Fucoidan	*Laminaria japonica*	Luo et al. 2009
	Sulphated galactans (lambda carrageenan)	Some marine red algae	Rocha de Souza et al. 2007, Barahona et al. 2011
	Galactans	Most red algae	Costa et al. 2010
	Sulphated glycosaminoglycan	*Sargassum wightii*	Josephine et al. 2008
	Porphyran	*Porphyra* sp.	Athukorala et al. 2006
Vitamins	Ascorbate	*Chondrus crispus* *Mastocarpus stellatus* *Sargassum* sp.	Lohrmann et al. 2004 García-Casal et al. 2009
	Vitamin A	*Kappaphycus alvarezii*	Kumar et al. 2008

See Appendix A for species authorities.

Valko et al. 2007). In healthy biological systems, reactive oxygen species are continually produced (Alscher et al. 1997). Dring (2005) highlighted the role of reactive oxygen metabolism (ROM) in seaweeds, the stress factors that trigger it and details of the antioxidant response mechanisms. He emphasized the potential importance of ROM in seaweed ecophysiology and cautioned against making generalizations about the occurrence and function of antioxidants amongst various species. With this preface, this article reviews seaweed antioxidants in the context of human health.

The functional complexities associated with antioxidant defense mechanisms are diverse, and their relative importance against reactive species *in vivo* depends upon how, where and which reactive species (RS) is generated and what target of damage is measured. For example, polyphenols are well-known potent antioxidants, but their wide diversity and chemical complexity makes it challenging to correlate antioxidant potency *in vitro* with specific biological activity *in vivo* (Scalbert et al. 2005). In simplest terms, an antioxidant may be considered as an agent that delays, prevents, or removes oxidative damage from a target molecule (Halliwell and Gutteridge 2007). Biological systems strive for an intricate balance of electronically charged molecules necessary to maintain homeostasis, and selectivity in neutralizing specific RS is secondary to the activation of cellular defenses. If commercialization of seaweeds for their antioxidant activity is to be considered, additional research is required to establish bioavailability of specific compounds (Fran-

Table 2. Selected examples of perceived health benefits of specific antioxidant compounds from macroalgae

Antioxidant compound	Perceived health benefit	Reference
β-carotene, lutein	Antimutagenic Protective against breast cancer	Okai et al. 1996 Maruyama et al. 1991, Yang et al. 2010
Bromophenol	α-Glucosidase inhibition	Kim et al. 2010
Carrageenan, oligosaccharide	Anti-tumor	Haijin et al. 2003
Fucoidan	Anti-HIV	Béress et al. 1993, Witvrouw and De Clercq 1997
	Ameliorates hyperoxaluria	Veena et al. 2007
	Anticancer	Aisa et al. 2005, You et al. 2010
	Protection against neurodegenerative disorder	Luo et al. 2009
Fucophlorethols	Chemopreventive	Parys et al. 2010
Fucoxanthin	Antiangiogenic Protective effects against retinol deficiency	Sugawara et al. 2006 Sangeetha et al. 2009
Galactan sulfate	Anti-viral	Talarico et al. 2004, Yasuhara-Bell and Lu 2010
Phenolic functional groups and MAAs	Antiproliferative	Yuan et al. 2005*b*
Phlorotannins	Anti-inflammatory	Shin et al. 2006
	Bactericide	Nagayama et al. 2002
	Inhibits H_2O_2 mediated DNA damage	Ahn et al. 2007
	Hypertension	Cha et al. 2006
	Photochemopreventive	Hwang et al. 2006
Phycoerythrin	Amelioration of diabetic complications	Yabuta et al. 2010
Polyphenols	Vascular chemoprotection Antimicrobial α-Glucosidase inhibition	Kang et al. 2003 Jiménez et al. 2010 Apostolidis and Lee 2010
Porphyran, shinorine	Delays aging process	Zhang et al. 2003, Rastogi et al. 2010

Note: compound categories are not mutually exclusive.
MAAs, Mycosporine-like Amino Acids.

kel and Finley 2008) and to then guarantee production of standardized products containing them (Le Tutour et al. 1998, Jormalainen and Honkanen 2004, Díaz-Rubio et al. 2009). This review will focus primarily on the potential health benefits and therapeutic properties purported to be associated with consuming seaweed and seaweed based products (Table 2). Claims relating to other clinical aspects of seaweed utilization deserve a detailed and exclusive review beyond the scope of this paper.

MARINE ALGAE AND HOMEOSTASIS

The stress-coping mechanisms of intertidal algae are diverse and include antioxidant production, and free radical scavenging activities (Centeno and Ballantine 1999, Aguirre-von-Wobeser et al. 2000, Lohrmann et al. 2004, Martínez 2007, Nahas et al. 2007). Lohrmann et al. (2004) found that the activity of three antioxidant enzymes, superoxide dismutase (SOD), ascorbate peroxidase, and glutathione reductase in *Chondrus crispus* and *Mastocarpus stellatus* was greater in winter than in summer, suggesting that levels of reactive oxygen species (ROS) were also higher in winter as a result of cold stress. A gradual and continued accumulation of ROS in most macroalgae occurs as a result of environmental conditions such as dessication, freezing, low temperatures, high irradiance, ultraviolet radiation, heavy metals and salinity fluctuations (Harker et al. 1999, Collén et al. 2003, Dummermuth et al. 2003, Pinto et al. 2003, Lohrmann et al. 2004, Dring 2005, Connan et al. 2007). These stresses compromise photosynthesis, forming singlet oxygen that can cause damage to the photosynthetic apparatus (Dring 2005). To cope with such stresses, seaweeds deactivate the ROS by utilizing a high cellular content of antioxidant compounds, or by increasing the activity of antioxidant enzymes. This robust antioxidant potential of seaweeds helps minimize the hazardous effects of ultraviolet light or oxidation by ROS (Karentz et al. 1991, Garbary 2007, Yoshiki et al. 2009).

Marine macroalgae often experience exposure to high levels of both UVB and UVA radiation. While irradiance is required for the photosynthetic conversion of energy via light harvesting, electron transport, and ATP / NADPH synthesis, maintaining a metabolic oxidation / reduction balance is essential to the health and productivity of the system (Sinha et al. 1998). To quench the excess production of harmful radical species, seaweeds have evolved mechanisms such as photo-inhibition which leads to a slowly reversible reduction in photosynthetic rate from the maximum saturation level. This is brought about by either a reduction in the number of photosynthetic units, or by an increase in the maximum turnover time (Gröniger et al. 1999, Falkowski and Raven 2007). The up-regulation of antioxidants and antioxidant enzymes, such as carotenoids and SODs and methods of cellular repair by photo-reactivation and nucleotide excision are also strategies for maintaining homeostasis (Sinha et al. 1998, Martínez 2007, Jiang et al. 2008).

In a comprehensive literature review Yoshiki et al. (2009) identified a number of compounds in marine algae to which antioxidant activity has been attributed. These included polyphenols, phycocyanins, various enzymes, carotenoids, catechins, and ascorbic acid (Table 1).

ANTIOXIDANTS IN HUMAN HEALTH

ROS, along with reactive nitrogen species (collectively labelled RS) have been identified as agents in various pathogenic diseases and deleterious clinical conditions related to human health. These include cancer, cardiovascular disease, atherosclerosis, hypertension, ischemia / re-perfusion, diabetes mellitus, hyperoxaluria, neurodegenerative diseases such as Alzheimer's and Parkinson's diseases, rheumatoid arthritis and ageing (Cerutti 1985, Borek 1993, Hercberg et al. 1998, Cadenas and Davies 2000, Kang et al. 2003, Park et al. 2005, Valko et al. 2007, Veena et al. 2007, Halliwell 2009). RS have been implicated in over 150 human disorders, ranging from haemorrhagic shock, through cardio-myopathy, cystic fibrosis, AIDS and even male-pattern baldness (Halliwell and Gutteridge 2007). The defense response to excess RS metabolism can involve preventative mechanisms, repair mechanisms and up-regulation of endogenous antioxidant defenses (Demmig-Adams and Adams 2002, Valko et al. 2007).

Melanoma and non-melanoma skin cancers are among the most prevalent cancers in the human population. They are often caused by large, or prolonged doses of UV radiation that overwhelm the natural protective antioxidant capacity of the skin (Steenvoorden and van Henegouwen 1997, Sander et al. 2004). Using whole tissue extracts in a naked mouse study, polyphenols derived from certain brown algae (e.g., *Ecklonia* spp.; see Appendix A) and applied either topically or administered through the diet provided highly protective effects against UVB induced skin carcinogenesis (Hwang et al. 2006). Fuchs and Kern (1998) evaluated the dietary effects of non-seaweed derived commercial supplements of D-alpha-tocopherol and L-ascorbic acid on the sunburn reaction in humans, a potential elicitor for skin cancer. They determined that large doses of the two antioxidants acted synergistically to protect against sunburn damage. However, the effects of long-term administration of megadoses of these antioxidants requires more investigation.

In a study of female nurses and dietary intake of vitamins A, C, and E, folate and certain carotenoids, Fung et al. (2002) could not conclusively demonstrate that these antioxidants protected against basal cell carcinoma under their experimental conditions. More recently, Hercberg et al. (2007) suggested that regular dietary antioxidant supplementation may even be associated with harmful effects, especially in women. However, results of a two-year cohort study (Asgari et al. 2009) refuted this conclusion and that group observed no increased melanoma risk with supplementation of comparable doses of beta carotene and selenium. Although these trials relate to non-seaweed sources of antioxidants, marine macroalgae possess complements of such active compounds in various amounts and ratios (Yoshiki et al. 2009). Experiments showed human and monkey cancer cell lines were inhibited by extracts of various seaweeds, especially by the brown algae *Hydroclathrus clathratus* and *Padina arborescences* (Wang et al. 2008). The extracts, either in a crude state or after purification, demonstrated antioxidant activity and tumor suppression in a mouse model.

Cardiovascular disease (CVD) encompasses a broad range of primary and secondary conditions and its manifestation is a major cause of death – 30% worldwide (Halliwell and Gutteridge 2007). Risk factors for CVD include age, male gender, elevated low-density lipo-protein cholesterol levels, low high-density lipo-protein cholesterol levels, diabetes mellitus, smoking, chronic overeating and obesity. The adverse complications of obesity and unhealthy lifestyle factors are heightened by oxidative stress (Oben et al. 2007, Bocanegra et al. 2009, Riccioni 2009).

Extensive studies in patho-physiologic research clearly suggest that CVD represents a continuum of processes which include oxidative stress, endothelial dysfunction, inflammatory processes and vascular remodeling (Riccioni 2009). Foods rich in antioxidants have long been touted as aids in disease prevention. Shimazu et al. (2007) assessed the association between the traditional Japanese dietary patterns and CVD. They concluded that a diet high in antioxidant foods, including seaweeds, decreased the risk of CVD mortality. Kang et al. (2003) undertook an eight-week human clinical trial to assess the effect of orally administered polyphenolic compounds from brown algae on erectile dysfunction. Compounds from the five algae tested, *Eisenia bicyclis*, *Ecklonia stolonifera*, *Ecklonia cava*, *Ecklonia kurome*, and *Hizikia fusiformis* demonstrated positive effects against the risk factors associated with CVD. Deterioration of erectile function is a key *in vivo* indicator of cardiovascular health. Results from this trial showed significant improvement in erectile function and associated vascular health based on peripheral blood circulation.

Numerous studies into the synergistic effects of antioxidants and antioxidant enzymes and their interplay with RS suggest that the ideal protective mechanisms against clinical aspects of cellular damage should involve combinations, or whole suites of antioxidant compounds. Cellular homeostasis is thus more readily assured, and the possibility of profound imbalances brought about by high doses of single compounds can be effectively averted (Steenvoorden and van Henegouwen 1997).

Considerable research demonstrates the human health benefits of naturally occurring antioxidant compounds. Claims of anti-viral, anti-inflammatory, anticancer, anti-mutagenic, anti-tumour, and hepatoprotective properties have been substantiated, albeit mostly from *in vitro* trials (Yan et al. 1998, Yan et al. 1999, Yuan et al. 2005*a*, Hwang et al. 2006, Lim and Murtijaya 2007, Kumar et al. 2008, Yuan et al. 2009) (Table 2).

FOOD VALUE AND HEALTH POTENTIAL OF MARINE ALGAE

Intensive marketing programs and the popular health food press have raised the public profile of antioxidants considerably. However, clinical trials must be undertaken and publicized in order to educate and maintain consumer confidence. Aside from the direct health benefits, antioxidants from natural sources that combat lipid oxidation of foods, especially during processing and storage, are in high demand. The current use of synthetic antioxidants such as butylated hydroxyanisole, butylated hydroxytoluene, *tert* butylhydroxyquinone and propyl gallate is strictly regulated in many countries because they can in themselves pose potential health hazards, including carcinogenic effects (Matanjun et al. 2008, Wang et al. 2009).

Seaweeds are eaten as whole foods by a relatively small percentage of the world population (Yuan and Walsh 2006), in a relatively limited geography. Japanese form the largest consumer group eating on average, 1.6 kg dry weight per person, per year (Chandini et al.

2008). Scientists in Asian countries have demonstrated the health benefits derived from eating seaweeds (Nisizawa 2002), and the official Japanese Food Guide (see Rhatigan 2009 for discussion) promotes seaweed as a nutritional foodstuff. Research is advancing into using marine macroalgae for production of novel foods, such as health beverages and processed meat products. The objective is to take advantage of their naturally occurring antioxidant compounds and other nutritive components (Nagai and Yukimoto 2003, López-López et al. 2009). This is a more holistic approach, based upon the observation that supplements of manufactured vitamins do not significantly decrease levels of oxidative damage in well-nourished individuals who already eat a balanced diet (Halliwell and Gutteridge 2007, Halliwell 2008). Hwang et al. (2006) demonstrated that extracted brown algal polyphenols from *Ecklonia* sp. decreased UVB-induced skin tumor development in mice regardless of whether the polyphenols were administered topically, or ingested as a dietary component, suggesting that the viability of these seaweed based antioxidants is unaffected by digestive processes. A growing awareness of the functionality of seaweeds beyond basic nutritive value will enhance the development of science and technology in this area of study (Holdt and Kraan in press).

FINAL PERSPECTIVES

The publication of Gerschman et al.'s (1954) free radical theory of metabolic oxygen toxicity instigated significant interest in ROS and the various mechanisms associated with redox homeostasis within biological systems. Since then, volumes have been written and commercialization of antioxidants has evolved to include functional foods, beverages, cosmeceuticals, nutraceuticals and health supplements. However, much work remains before we are able to establish and target site-specific reactions within biological systems, much less determine what, if any, synergistic effects may occur in the process (Le Tutour et al. 1998). Indeed, it could be challenging to aim for a targeted antioxidant response, considering the potential complexities of *in vivo* associations and interactions of the numerous compounds and metabolites that contribute to the biological efficacy of cells.

The potential for commercialization of seaweed based, antioxidant compounds as food supplements or nutraceuticals ensures continued dedicated efforts to eventually develop functional, condition-specific, antioxidant products. Seaweeds are indeed suitable natural agents for producing and delivering these products based on the multi-functional aspects of secondary seaweed metabolites and the presence of a wide variety of associated non-toxic antioxidants (Smit 2004, Bocanegra et al. 2009). Such relatively non-toxic associations can enhance the synergistic effects of multiple antioxidants and provide buffering capacity if necessary for those compounds which may have been intentionally increased. Algae are efficient harvesters and proficient managers of electromagnetic energy and as highly nutritional foodstuffs, can be regularly consumed without fear of metabolic toxicities. As part of a balanced diet, seaweeds can provide fibre, protein, minerals, vitamins and low fat carbohydrate content (Yuan and Walsh 2006). The versatility of algae as food allows consumption in fresh, dried, pickled or cooked forms and as a component in a wide assortment of other products. We advocate the regular consumption of a variety of marine algae, primarily for their anticipated *in vivo* antioxidant capacities and associated synergistic effects. Rather than striving for targeted cause and effect mechanisms, which are developed in isolation and are generally fraught with the complexities of endogenous cellular activities, a diet rich in a diversity of seaweeds would provide healthy, whole food sustenance and competent antioxidant balance. Ideally, algae destined for human use would be derived from managed, sustainable sources, thus ensuring traceability and a high level of food safety and security. Core research avenues should include investigations into the bioavailability of seaweed based antioxidants (Frankel and Finley 2008). Organisms do not normally function in isolation at any metabolic level, and oxidation-reduction reactions and subsequent cellular exposures to RS are fundamental to all living things. It is the imbalance of RS that can compromise homeostasis, and it is a legion of relevant seaweed antioxidants that may mitigate, and even help reduce the impacts of cellular impairment.

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Appendix A. Algal species evaluated for antioxidant activity and potential applications of detected compounds. With each application category R indicates Rhodophyta, P indicates Phaeophyta and C indicates Chlorophyta

Application (Phylum) species	Reference
Antiangiogenic activity (P) *Undaria pinnatifida* (Harvey) Suringar	Sugawara et al. 2006
Antiaging (R) *Porphyra haitanensis* Chang & Zheng	Zhang et al. 2003
Antibacterial (P) *Colpomenia peregrina* Sauvageau; *Cystoseira crinita* Duby; *Punctaria latifolia* Greville; *P. plantaginea* (Roth) Greville; *Scytosiphon lomentaria* (Lyngbye) Link; *Stilophora tenella* (Esper) Silva; *Zanardinia prototypus* (Nardo) Nardo (R) *Bangia fuscopurpurea* (Dillwyn) Lyngbye; *Callithamnion granulatum* (Ducluzeau); *Ceramium diaphanum* var. *elegans* (Roth) Roth; *Chondrophycus papillosus* (C. Agardh) Garbary & Harper; *Corallina elongata* Ellis & Solander; *Gelidium spinosum* (Gmelin) Silva; *Haliptilon virgatum* (Zanardini) Garbary & Johansen; *Laurencia coronopus* J. Agardh; *Polysiphonia denudata* (Dillwyn) Greville ex Harvey; *P. denudata* f. *fragilis* (Sperk) Voronikh	Kamenarska et al. 2009
Anticancer (P) *U. pinnatifida*; *Fucus vesiculosus* Linnaeus	Aisa et al. 2005, You et al. 2010
Anticoagulant (R) *Acrosorium flabellatum* Yamada; *Ahnfeltiopsis flabelliformis* (Harvey) Masuda; *Carpopeltis affinis* (Harvey) Okamura; *Chondria cassicaulis* Harvey; *Chondrophycus undulatus* (Yamada) Garbary & Harper; *Chondrus crispus* Stackhouse; *Gelidium amansii* (Lamouroux) Lamouroux; *Gloiopeltis furcata* (Postels & Ruprecht) J. Agardh; *Gracilaria textorii* (Suringar) De Toni; *G. verrucosa*; *Grateloupia elliptica* Holmes; *G. lanceolata* (Okamura) Kawaguchi; *Halymenia dilatata* Zanardini; *Laurencia okamurae* Yamada; *Lithophyllum okamurai* Foslie; *Lomentaria catenata* Harvey; *Martensia denticulata* Harvey; *Prionitis cornea* (Okamura) Dawson; *Pterocladiella capillacea* (Gmelin) Santelices & Hommersand; *Schizymenia dubyi* (Chauvin ex Duby) J. Agardh; *Scinaia okamurae* (Setchell) Huisman; *Sinkoraena lancifolia* (Harvey) Lee, Lewis, Kraft & Lee	Lee et al. 2008
Antidiabetic (P) *Ascophyllum nodosum* (Linnaeus) Le Jolis	Zhang et al. 2007*a*
Anti inflammatory (osteoarthritis) (P) *Ecklonia cava* Kjellman	Shin et al. 2006
Anti inflammatory (R) *Gracilaria verrucosa* (Hudson) Papenfuss	Dang et al. 2008
Antimicrobial (P) *Cystoseira mediterranea* Sauvageau; *Padina pavonica* (Linnaeus) Thivy; *Scytosiphon lomentaria* (Lyngbye) Link (R) *Hypnea musciformis* (Wulfen) Lamouroux; *Spyridia filamentosa* (Wulfen) Harvey	Taskin et al. 2010
Antiproliferative (P) *E.* cava; *Laminaria setchellii* Silva; *Macrocystis integrifolia* Bory; *Nereocystis luetkeana* (Mertens) Postels & Ruprecht (R) *Palmaria palmata* (Linneaus) Weber & Mohr	Yuan et al. 2005*b*, Athukorala et al. 2006, Yuan and Walsh 2006
Antiretroviral (HIV-1) (P) *Adenocystis utricularis* (Bory) Skottsberg; *Fucus vesiculosus* Linnaeus	Béress et al. 1993, Trinchero et al. 2009
Antitumoural (P) *Alaria esculenta* (Linnaeus) Greville; *Asperococcus bullosus* Lamouroux; *Bifurcaria bifurcata* Ross;	Ye et al. 2008, Zubia et al. 2009,

Cystoseira mediterranea Sauvageau; *C. tamariscifolia* (Hudson) Papenfuss; *Desmarestia ligulata* (Stackhouse) Lamouroux; *Dictyota dichotoma* (Hudson) Lamouroux; *Fucus ceranoides* Linnaeus; *F. serratus* Linnaeus; *Halidrys siliquosa* (Linnaeus) Lyngbye; *Padina pavonica* (Linnaeus) Thivy; *Saccorhiza polyschides* (Lightfoot) Batters; *Sargassum pallidum* (Turner) C. Agardh; *Scytosiphon lomentaria* (Lyngbye) Link (R) *Hypnea musciformis* (Wulfen) Lamouroux; *Spyridia filamentosa* (Wulfen) Harvey	Taskin et al. 2010
Antiviral (P) *Colpomenia peregrine* Sauvageau; *Cystoseira crinita* Duby; *Punctaria latifolia* Greville; *P. plantaginea* (Roth) Greville; *Scytosiphon lomentaria* (Lyngbye) Link; *Stilophora tenella* (Esper) Silva; *Zanardinia prototypus* (Nardo) Nardo (R) *Bangia fuscopurpurea* (Dillwyn) Lyngbye; *Callithamnion granulata* Ducluzeau; *Ceramium diaphanum* var. *elegans* (Roth) Roth; *Chondrophycus papillosus* (C. Agardh) Garbary & Harper; *Corallina elongata* Ellis & Solander; *Gelidium spinosum* (Gmelin) Silva; *Haliptilon virgatum* (Zanardini) Garbary & Johansen; *Laurencia coronopus* J. Agardh; *Polysiphonia denudata* (Dillwyn) Greville ex Harvey; *P. denudata* f. *fragilis* (Sperk) Voronikh	Kamenarska et al. 2009
Chemopreventive (P) *Fucus vesiculosus* Linnaeus	Parys et al. 2010
Cytotoxic activity (P) *Colpomenia peregrina* Sauvageau; *Cystoseira crinita* Duby; *Punctaria latifolia* Greville; *P. plantaginea* (Roth) Greville; *Scytosiphon lomentaria* (Lyngbye) Link; *Stilophora tenella* (Esper) Silva; *Zanardinia prototypus* (Nardo) Nardo (R) *Bangia fuscopurpurea* (Dillwyn) Lyngbye; *Callithamnion granulata* Ducluzeau; *Ceramium diaphanum* var. *elegans* (Roth) Roth; *Chondrophycus papillosus* (C. Agardh) Garbary & Harper; *Corallina elongata* Ellis & Solander; *Gelidium spinosum* (Gmelin) Silva; *Haliptilon virgatum* (Zanardini) Garbary & Johansen; *Laurencia coronopus* J. Agardh; *Polysiphonia denudata* (Dillwyn) Greville ex Harvey; *P. denudata* f. *fragilis* (Sperk) Voronikh	Kamenarska et al. 2009
Dietary antioxidants (P) *Chorda filum* (Linnaeus) Stackhouse; *Colpomenia sinuosa* (Mertens ex Roth) Derbès & Solier; *Desmarestia viridis* (Müller) Lamouroux; *Dictyopteris divaricata* (Okamura) Okamura; *Dictyota cervicornis* Kützing; *D. dichotoma* (Hudson) Lamouroux; *D. ciliolate* Sonder ex Kützing; *D. crenulata* J. Agardh; *Ecklonia cava*; *F. vesiculosus*; *Laminaria japonica* Areschoug; *L. ochroleuca* Linneaus; *Leathesia difformis* Areschoug; *Lobophora variegata* (Lamouroux) Womersley ex Oliveira; *Myelophycus simplex* (Harvey) Papenfuss; *Padina gymnospora* (Kützing) Sonder; *Padina* spp.; *Petalonia binghamiae* (J. Agardh) Vinogradova; *Punctaria plantaginea* (Roth) Greville; *Sargassum kjellmanianum* Yendo; *S. polycystum* C. Agardh; *S. pteropleuron* Grunow; *S. ramifolium* Kützing; *S. thunbergii* (Mertens ex Roth) Kuntz; *Sargassum* sp.; *Scytosiphon lomentaria* (Lyngbye) Link; *Turbinaria tricostata* Barton; *Undaria pinnatifida* (R) *Acanthophora spicifera* (Vahl) Børgesen; *Bryothamnion triquetrum* (Gmelin) Howe; *Ceramium boydenii* Gepp; *C. nitens* (C. Agardh) J. Agardh; *C. kondoi* Yendo; *Champia salicornioides* Harvey; *Chondria atropurpurea* Harvey; *C. baileyana* (Montagne) Harvey; *Chondrophycus papillosus* (C. Agardh) Garbary & Harper; *C. poiteaui* (Lamouroux) Nam; *Chondrus crispus* Stackhouse; *Corallina pilulifera* Postels & Ruprecht; *Digenea simplex* (Wulfen) C. Agardh; *Eucheuma cottonii* Weber-van Bosse; *E. isiforme* (C. Agardh) J. Agardh; *Gelidium amansii* (Lamouroux) Lamouroux; *Gloiosiphonia capillaries* (Farlow) J. Agardh; *Gracilaria bursa-pastoris* (Gmelin) Silva; *G. caudata* J. Agardh; *G. cornea* J. Agardh; *G. cylindrica* Børgesen; *G. tenuistipitata* var. *tenuistipitata* Chang & Xia *G. tikvahiae* McLachlan; *Gracilaria verrucosa*; *Gracilariopsis tenuifrons* (Bird & Oliveira) Fredericq & Hommersand; *Halymenia durvillaei* Bory; *H. floresii* (Clemente & Rubio) C. Agardh; *Heterosiphonia gibbesii* (Harvey) Falkenberg; *Hyalosiphonia caespitosa* Okamura; *Hypnea spinella* (C. Agardh) Kützing; *Laurencia intricata* Lamouroux; *L. obtusa* (Hudson) Lamouroux; *Laurencia surculigera* Tseng; *Liagora ceranoides* Lamouroux; *Nemalion helminthoides* (Velley) Batters; *Polysiphonia urceolata* (Lightfoot ex Dillwyn) Greville; *Porphyra umbilicalus* (Linnaeus) J. Agardh; *Rhodomela confervoides*; *R. teres* (Perestenko) Masuda	Yan et al. 1998, Jiménez-Escrig et al. 2001, Rupérez et al. 2002, Kuda et al. 2006, Zubia et al. 2007, Matanjun et al. 2008, Yangthong et al. 2009

(C) *Acetabularia schenckii* Möbius; *Avrainvillea longicaulis* (Kützing) Murray & Boodle; *Caulerpa ashmeadii* Harvey; *C. cupressoides* (West in Vahl) C. Agardh; *Caulerpa lentillifera* J. Agardh; *C. paspaloides* (Bory) Greville; *C. prolifera* (Forsskål) Lamouroux; *C. racemosa* (Forsskål) J. Agardh; *Caulerpa racemosa* var. *macrophysa* (Sonder ex Kützing) Murray; *C. sertularioides* (Gmelin) Howe; *C. taxifolia* (West in Vahl) C. Agardh; *Cladophora prolifera* (Roth) Kützing; *C. vagabunda* (Linnaeus) Hoek; *Codium decorticatum* (Woodward) Howe; *Halimeda monile* (Ellis & Solander) Lamouroux; *H. tuna* (Ellis & Solander) Lamouroux; *Penicillus dumetosus* (Lamouroux) Blainville; *P. pyriformis* Gepp & Gepp; *Udotea conglutinate* (Ellis & Solander) Lamouroux; *Ulva intestinalis* Linnaeus [as *Enteromorpha intestinalis* (Linnaeus) Nees]; *U. lactuca* Linnaeus; *U. pertusa* Kjellman; *U. prolifera* O. F. Müller [as *Enteromorpha prolifera* (O. F. Müller) J. Agardh]	
Food preservatives (P) *F. vesiculosus*; *Padina antillarum* (Kützing) Piccone; *P. gymnospora*; *Turbinaria conoides* (J. Agardh) Kützing (R) *Eucheuma cottonii* Weber-van Bosse; *Euchema spinosum* J. Agardh; *Gigartina acicularis* (Roth) Lamouroux; *Gigartina pistillata* (Gmelin) Stackhouse; *Kappaphycus alvarezzi* (Doty) Doty ex Silva; *Palmaria palmata*; *Polysiphonia urceolata* Lightfoot ex Dillwyn (C) *Caulerpa racemosa* (Forsskål) J. Agardh	Yuan et al. 2005*a*, 2005*b*, Duan et al. 2006, Rocha de Souza et al. 2007, Chew et al. 2008, Chattopadhyay et al. 2010
Functional foods (P) *Desmarestia viridis* (Müller) Lamouroux; *Dictyopteris divaricata* (Okamura) Okamura; *D. membranacea* (Stackhouse) Batters; *Dictyota cervicornis* (Kützing); *D. delicatula* (Lamouroux); *D. menstrualis*; *D. mertensii* (Martius) Kützing); *Ecklonia cava*; *Ectocarpus siliculosus* (Dillwyn) Lyngbye; *F. vesiculosus*; *Halopteris scoparia* (Linnaeus) Sauvageau; *Himanthalia elongata* (Linnaeus) Gray; *Hizikia fusiformis* (Harvey) Okamura; *Ishige okamurae* Yendo; *Laminaria japonica* Areschoug; *Padina antillarum* (Kützing) Piccone; *P. tetrastromatica* Hauck; *Sargassum coreanum* J. Agardh; *S. filipendula* C. Agardh; *S. fullvelum* (Turner) C. Agardh; *S. horneri* (Turner) C. Agardh; *S. marginatum* (C. Agardh) J. Agardh; *S. thunbergii* (Mertens ex Roth) Kuntz; *S. vulgare* C. Agardh; *Sargassum* sp.; *Scytosiphon lomentaria* (Lyngbye) Link; *Spatoglossom schroederi* (C. Agardh) Kützing; *Taonia atomaria* (Woodward) J. Agardh; *Turbinaria conoides*; *Undaria pinnatifida* (R) *Ahnfeltiopsis flabelliformis* (Harvey) Masuda; *Amphiroa cryptarthrodia* var. *verruculosa* (Kützing) Hauck; *Amphiroa* sp.; *Ceramium kondoi* Yendo; *Chondria crassicaulis* Harvey; *C. tenuissima* (Withering) C. Agardh; *Corallina elongata* Ellis & Solander; *Gelidium amansii* (Lamouroux) Lamouroux; *Gloiopeltis tenax* (Turner) Decaisne; *Gracilaria caudata* J. Agardh; *Grateloupia elliptica* Holmes; *Kappaphycus alvarezzi*; *Laurencia obtusa*; *Laurencia papillosa* (C. Agardh) Greville; *Liagora* sp.; *Peyssonnelia harveyana* Crouan & Crouan ex J. Agardh; *Porphyra* sp.; *Rhodothamniella floridula* (C) *Caulerpa cupressoides* (West) C. Agardh; *C. prolifera* (Forsskäl) Lamouroux; *C. racemosa* (Forsskål) J. Agardh; *C. sertularioides* (Gmelin) Howe; *Cladophora vagabunda* (Linnaeus) Hoek; *Codium fragile* (Suringar) Hariot; *C. isthmocladum* Vickers; *Ulva pertusa* Kjellman; *Ulva fasciata* Delile; *Ulva* sp.	Yan et al. 1999, Rupérez et al. 2002, Nagai and Yukimoto 2003, Fayaz et al. 2005, Heo et al. 2005, Ahn et al. 2007, Nahas et al. 2007, Zhang et al. 2007*b*, Chandini et al. 2008, Chew et al. 2008, Kumar et al. 2008, García-Casal et al. 2009, Chattopadhyay et al. 2010, Costa et al. 2010, Plaza et al. 2010
Health related functions (P) *Padina australis* Hauck; *Sargassum polycystum* C. Agardh; *Turbinaria conoides* (C) *Caulerpa sertularoides* (Gmelin) Howe; *Halimeda macroloba* Decaisne; *Ulva reticulata* Forsskål	Gunji et al. 2007
Hepatoprotective properties (P) *Myagropsis myagroides* (Mertens ex Turner) Fensholt; *Sargassum henslowianum* (R) *Callophyllis japonica* Okamura C. Agardh; *S. siliquastrum* (Turner) C. Agardh	Wong et al. 2000, Park et al. 2005
Hyperoxaluria inhibition (P) *F. vesiculosus*	Veena et al. 2007
Hypertension and vascular health (R) *Ahnfeltiopsis flabelliformis* (Harvey) Masuda; *Bonnemaisonia hamifera* Hariot; *Carpopeltis affinis* (Harvey) Okamura; *Chondria crassicaulis* Harvey; *Chondrophycus undulatus* (Yamada) Garbary & Harper; *Chondrus crispus* Stackhouse; *Gelidium amansii*; *Gloiopeltis furcata* (Postels & Ruprecht) J. Agardh; *Gracilaria textorii* (Suringar) De Toni; *G. verrucosa*; *Grateloupia elliptica* Holmes; *G. filicina* (Lamouroux) C. Agardh; *G. lanceolata* (Okamura) Kawaguchi; *Halymenia dilatata* Zanardini;	Cha et al. 2006

Laurencia okamurae Yamada; *Lithophyllum okamurai* Foslie; *Lomentaria catenata* Harvey; *Martensia denticulata* Harvey; *Phacelocarpus* sp.; *Polysiphonia japonica* Harvey; *Porphyra tenera* Kjellman; *Prionitis cornea* (Okamura) Dawson; *Pterocladiella capillacea* (Gmelin) Santelices & Hommersand; *Schizymenia dubyi* (Chauvin ex Duby) J. Agardh; *Scinaia okamurae* (Setchell) Huisman; *Sinkoraena lancifolia* (Harvey) Lee, Lewis, Kraft & Lee

Inhibition of H_2O_2 mediated DNA damage — Ahn et al. 2007

(P) *Ecklonia cava*

Medical effects — Zubia et al. 2007

(P) *Dictyota cervicornis* Kützing; *D. ciliolate* Sonder ex Kützing; *D. crenulata* J. Agardh; *Lobophora variegata* (Lamouroux) Womersley ex Oliveira; *Padina gymnospora* (Kützing); *Sargassum pteropleuron* Grunow; *S. ramifolium* Kützing; *Turbinaria tricostata*

(R) *Acanthophora spicifera* (Vahl) Børgesen; *Bryothamnion triquetrum* (Gmelin) Howe; *Ceramium nitens* (C. Agardh) J. Agardh; *Champia salicornioides* Harvey; *Chondria atropurpurea* Harvey; *C. baileyana* (Montagne) Harvey; *Chondrophycus papillosus* (C. Agardh) Garbary & Harper; *C. poiteaui* (Lamouroux) Nam; *Digenea simplex* (Wulfen) C. Agardh; *Eucheuma isiforme* (C. Agardh) J. Agardh; *Gracilaria bursa-pastoris* (Gmelin) Silva; *G. caudata* J. Agardh; *G. cornea* J. Agardh; *G. cylindrica* Børgesen; *G. tikvahiae* McLachlan; *Gracilariopsis tenuifrons* (Bird & Oliveira) Fredericq & Hommersand; *Halymenia floresii* (Clemente & Rubio) C. Agardh; *Heterosiphonia gibbesii* (Harvey) Falkenberg; *Hypnea spinella* (C. Agardh) Kützing; *Laurencia intricata* Lamouroux; *L. obtusa* (Hudson) Lamouroux; *Liagora ceranoides* Lamouroux; *Nemalion helminthoides* (Velley) Batters

(C) *Acetabularia schenckii* Möbius; *Avrainvillea longicaulis* (Kützing) Murray & Boodle; *Caulerpa ashmeadii* Harvey; *C. cupressoides* (West in Vahl) C. Agardh; *C. paspaloides* (Bory) Greville; *C. prolifera* (Forsskål) Lamouroux; *C. sertularioides* (Gmelin) Howe; *C. taxifolia* (West in Vahl) C. Agardh; *Cladophora prolifera* (Roth) Kützing; *C. vagabunda* (Linnaeus) Hoek; *Codium decorticatum* (Woodward) Howe; *Enteromorpha intestinalis* (Linnaeus) Nees; *Halimeda monile* (Ellis & Solander) Lamouroux; *H. tuna* (Ellis & Solander) Lamouroux; *Penicillus dumetosus* (Lamouroux) Blainville; *P. pyriformis* Gepp & Gepp; *Udotea conglutinate* (Ellis & Solander) Lamouroux; *Ulva intestinalis* Linnaeus [as *Enteromorpha intestinalis* (Linnaeus) Nees]

Nutraceuticals — Fayaz et al. 2005, Kumar et al. 2008, Díaz-Rubio et al. 2009

(R) *Kappaphycus alvarezii*; *Fucus vesiculosus* Linnaeus

Parkinson's disease (protective effects) — Luo et al. 2009

(P) *Laminaria japonica* Areschoug

Peroxynitrite inhibition (pharmaceutical) — Lee et al. 2004

(P) *Colpomenia bullosa* (De A. Saunders) Yamada; *C. sinuosa* (Mertens ex Roth) Derbès & Solier; *Derbesia marina* (Lyngbye) Solier; *Dictyota dichotoma* (Hudson) Lamouroux; *Hizikia fusiformis* (Harvey) Okamura; *Ishige okamurai* Yendo; *Myelophycus simplex* (Harvey) Papenfuss; *Sargassum confusum* C. Agardh; *S. hemiphyllum* (Turner) C. Agardh; *S. horneri* (Turner) C. Agardh; *S. thunbergii* (Mertens ex Roth) Kuntz; *Sargassum* sp.; *Scytosiphon lomentaria* (Lyngbye) Link

(R) *Carpopeltis affinis* (Harvey) Okamura; *C. cornea* (Okamura) Okamura; *Chondria crassicaulis* Harvey; *Chondrus ocellatus* Holmes; *Corallina pilulifera* Postels & Ruprecht; *Corallina* spp.; *Gelidium amansii* (Lamouroux) Lamouroux; *Gigartina intermedia* Suringar; *Gigartina tenella* Harvey; *Gloiopeltis furcata* (Postels & Ruprecht) J. Agardh; *Grateloupia turutura* Yamada; *Gymnogongrus flabelliformis* (Harvey) Masuda; *Halymenia acuminata* (Holmes) J. Agardh; *Lomentaria catenata* Harvey; *L. hakodatensis* Yendo; *Pachymeniopsis lanceolata* (Okamura) Yamada ex Kawabata; *Plocamium telfairiae* (Hooker & Harvey) Harvey ex Kützing; *Porphyra suborbiculata* Kjellman; *Symphyocladia latiuscula* (Harvey) Yamada

(C) *Codium adhaerens* C. Agardh; *Enteromorpha linza* (Linnaeus) J. Agardh; *Ulva pertusa* Kjellman

Pharmaceuticals — Heo et al. 2005, Nahas et al. 2007, Chandini et al. 2008,

(P) *Dictyopteris membranacea* (Stackhouse) Batters; *Dictyota cervicornis* Kützing; *D. delicatula* Lamouroux;

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D. menstrualis (Hoyt) Schnetter; *D. mertensii* (Martius) Kützing; *Ecklonia cava*; *Halopteris scoparia* (Linnaeus) Sauvageau; *Ishige okamurae* Yendo; *Laminaria japonica* Areschoug; *Padina tetrastromatica* Hauck; *Sargassum coreanum* J. Agardh; *S. filipendula* (C. Agardh); *Sargassum fullvelum* (Turner) C. Agardh; *S. horneri* (Turner) C. Agardh; *S. marginatum* (C. Agardh) J. Agardh; *S. thunbergii* (Mertens ex Roth) Kuntz; *S. vulgare C.* Agardh; *Spatoglossom schroederi* (C. Agardh) Kützing; *Taonia atomaria* (Woodward) J. Agardh; *Scytosiphon lomentaria* (Lyngbye) Link; *Turbinaria conoides* (R) *Amphiroa cryptarthrodia* var. *verruculosa* (Kützing) Hauck; *Amphiroa* sp.; *Corallina elongata* Ellis & Solander; *Gracilaria caudata* J. Agardh; *Laurencia obtusa*; *L. papillosa* (C. Agardh) Greville; *Liagora* sp.; *Peyssonnelia harveyana* Crouan & Crouan ex J. Agardh; *Rhodothamniella floridula* (C) *Caulerpa cupressoides* (West) C. Agardh; *C. prolifera* (Forsskäl); *C. sertularioides* (Gmelin) Howe; *Codium isthmocladum* Vickers	Zhao et al. 2008, Costa et al. 2010
Promotes cellular homeostasis (R) *Callophyllis japonica* Okamura	Kang et al. 2005
Vascular chemoprotection; Improved peripheral blood circulation (P) *Eisenia bicyclis* (Kjellman) Setchell; *Ecklonia cava*; *E. kurome* Okamura; *E. stolonifera* Okamura; *Hizikia fusiformis* (Harvey) Okamura	Kang et al. 2003