# Therapeutic potential and health benefits of *Sargassum* species

**Subhash R. Yende, Uday N. Harle[1], Bhupal B. Chaugule[2]**

*Department of Pharmacology, Gurunanak College of Pharmacy, [1]Clinical Research Consultant, Nagpur, [2]Department of Botany, University of Pune, Pune, Maharashtra, India*

Submitted: 09-08-2013 Revised: 29-08-2013 Published: 20-01-2014

## ABSTRACT

*Sargassum* species are tropical and sub-tropical brown macroalgae (seaweed) of shallow marine meadow. These are nutritious and rich source of bioactive compounds such as vitamins, carotenoids, dietary fibers, proteins, and minerals. Also, many biologically active compounds like terpenoids, flavonoids, sterols, sulfated polysaccharides, polyphenols, sargaquinoic acids, sargachromenol, pheophytine were isolated from different *Sargassum* species. These isolated compounds exhibit diverse biological activities like analgesic, anti-inflammatory, antioxidant, neuroprotective, anti-microbial, anti-tumor, fibrinolytic, immune-modulatory, anti-coagulant, hepatoprotective, anti-viral activity etc., Hence, *Sargassum* species have great potential to be used in pharmaceutical and neutralceutical areas. This review paper explores the current knowledge of phytochemical, therapeutic potential, and health benefits of different species of genus *Sargassum.*

**Key words:** Brown seaweed, *Sargassum*, sulfated polysaccharide, therapeutic potential

## INTRODUCTION

As more than 70% of the world's surface is covered by oceans, the wide diversity of marine organisms offer a rich source of natural products, which make up approximately one half of the total global biodiversity and are rich reservoirs of structurally diverse bio-functional components. Among marine organisms, marine algae are rich sources of structurally diverse bioactive compounds with various biological activities.[1,2]

Marine algae are heterogeneous group of plants with a long fossil history. Two major types of algae can be identified: The macroalgae occupy the littoral zone, and the microalgae are found in both bentheic and littoral habitats and also throughout the ocean waters as phytoplankton. Marine macroalgae or seaweeds are found in the coastal region between high tide to low tide and in the sub-tidal region up to a depth where 0.01% photosynthetic light is available and can be classified into three classes: Brown algae (Phaeophyta), Green algae (Chlorophyta), and Red algae (Rhodophyta). Brown seaweeds are predominantly brown due to the presence of the carotenoid fucoxanthin, and the primary polysaccharides present include alginates, laminarins, fucans, and cellulose. Green seaweeds are dominated by chlorophyll a and b, with ulvan being the major polysaccharide component. While in Red seaweeds, principal pigments are phycoerythrin and phycocyanin and the primary polysaccharides are agars and carrageenans.[3,4] The importance of seaweeds for human consumption is well known since 300 BC in China and Japan. These two countries are the major seaweed cultivators, producers, and consumers in the world. In the Indian Ocean region countries like Malaysia, Indonesia, Singapore, Thailand, Korea etc., seaweeds are used in salad, jelly, soup etc., However, in India, seaweed consumption is negligible except in the preparation of porridge from *Gracilaria* species and *Acanthophora* species in coastal states of Kerala and Tamil Nadu.[5] Seaweeds are rich in soluble dietary fibers, proteins, minerals, vitamins, antioxidants, phytochemicals, and polyunsaturated fatty acids, with low caloric value.[6] They are an excellent source of vitamins A, $B_1$, $B_2$, $B_3$, $B_{12}$, C, D, E. Their amino acid content is well-balanced and contains all or most of the essential amino acids needed for life and health.[5] Moreover, biologically active compounds isolated from marine macroalgae exhibit various biological activities such as antioxidant,[7,8] anti-viral,[9] anti-allergic,[10] anti-inflammatory,[11,12] anti-cancer,[13] anti-coagulant[14] *etc.*

**Address for correspondence:**
Mr. Subhash R. Yende, Department of Pharmacology, Gurunanak College of Pharmacy, Nagpur, Maharashtra, India.
E-mail: subhashyende@gmail.com

**Access this article online**

Quick Response Code:

Website: www.phcogrev.com

DOI: 10.4103/0973-7847.125514

*Sargassum*, a genus of brown seaweed, commonly known as gulf-weed or sea holly belonging to family Sargassaceae, order Fucales, subclass Cyclosporeae, and class Phaeophyceae, contains approximately 400 species.[15,16] *Sargassum* species are found throughout tropical and subtropical areas of the world and are reported to produce metabolites of structural classes such as terpenoids, polysaccharides, polyphenols, sargaquinoic acids, sargachromenol, plastoquinones, steroids, glycerides etc., which possesses several therapeutic activities. As it possesses many pharmacological properties, it has been considered as a medicinal food of the twenty-first century, and research is being carried out on it to reveal its other pharmacological properties. This review focuses on pharmacological activities with potential health benefits of different *Sargassum* species.

## THERAPEUTIC POTENTIAL OF *SARGASSUM* SPECIES

### *In vitro* antioxidant activity

Oxidative stress is the result of an imbalance between pro-oxidant and antioxidant homeostasis that leads to the generation of toxic reactive oxygen species (ROS).[17] ROS such as hydroxyl, super oxide, and peroxyl radicals are formed in human tissue cells, which attack macromolecules such as membrane lipids, proteins, and DNA, lead to many health disorders such as cancer, diabetes mellitus, age-related degenerative conditions, neurodegenerative and inflammatory diseases with severe tissue injuries.[18-20] Antioxidants may have a positive effect on human health as they can protect human body against damage by ROS. *In vivo,* cells have their own inherited antioxidative defense system, in the form of various enzymatic, as well as non-enzymatic pathways, for removing the ROS. Among enzymatic pathways, $O_2$ are dismutated by superoxide dismutase (SOD) to $H_2O_2$, catalase (CAT) reduces $H_2O_2$ to water and molecular oxygen. Glutathione peroxidase (GPX) catalyzes the reduction of $H_2O_2$ to water and organic peroxide to alcohols at the expense of reduced glutathione (GSH), while glutathione-S-transferase conjugates xenobiotics with glutathione for excretion. Among the non-enzymatic substances, β-carotene, vitamin-A, vitamin-E, and vitamin C scavenge free radicals.[21] Among the sources of natural antioxidants, marine seaweeds are now being considered to be a rich source of antioxidants. Antioxidant activities of *Sargassum* species have been determined by various methods such as 1,1-diphenyl-2-picryl hydrazyl (DPPH) radical scavenging, 2,2'-azinobis-3-ethylbenzo thizoline-6-sulfonate (ABTS) radical scavenging, NO scavenging, lipid peroxide inhibition, superoxide and hydroxyl radical scavenging assays.

Kim *et al.*[22] reported the sulfated polysaccharides of *Sargassum fulvellum* is more potent NO scavenging and DPPH scavenging activity than commercial antioxidants such as α-tocophorol. According to Hwang *et al.*,[23] the DPPH free radicals scavenging activity, superoxide anion scavenging activity measured using the xanthine- xanthine oxidase system and $Fe^{3+}$ reducing activity of hot-water extract from *Sargassum hemiphyllum* showed a linear dose-depending relationship with an $IC_{50}$ = 1.58 mg/ml, 2.41 mg/ml and 0.41 mg/ml, respectively. The antioxidant activities of *Sargassum hemiphyllum* may be due to high level of total phenolic compounds. The water-soluble natural antioxidants from another seaweed *Sargassum thunbergii* exhibited the DPPH free radical scavenging activities, and the scavenging activity of the radicals increased with increasing concentrations of the extract,[24] the thunbergols (tetraprenyltoluquinols) and sargothunbergol (chromene) isolated from the *Sargassum thunbergii* were scavengers of the DPPH radical.[25,26] Sargachromanols (meroterpenoids), isolated from the brown alga *Sargassum siliquastrum,* exhibited significant activity in the DPPH assay.[27] Also, extracts from *Sargassum siliquastrum* showed DPPH free radical scavenging activity, suppression of lipid peroxidation, and scavenging activity of superoxide radicals.[28] In addition, the plastiquinones, isolated from brown alga *Sargassum micracanthum,* displayed significant antioxidant activity.[29,30] Furthermore, total methanolic extract and ethyl acetate fraction of *S. marginatum* exhibited significant antioxidant activity in DPPH scavenging activity, deoxyribose scavenging activity, and hydroxyl radical scavenging activity in dose-dependent manner.[8]

### Cholinesterase inhibitory activity

Dementia is a chronic progressive mental disorder, which adversely affects memory, thinking, comprehension, calculation, and language. Some of the commonest types of dementia are Alzheimer's disease, Parkinsonism, and Myasthenia gravis.[31] Alzheimer's disease (AD) is an irreversible, progressive neurodegenerative disease, which resulting in memory loss, behavior disturbances, personality changes, and a decline in cognitive abilities.[32] Substantial reduction in activity of the enzyme choline acetyltransferase (ChAT) responsible for the synthesis of acetylcholine (ACh) is the key marker enzyme in AD. Parkinson's disease, a neurodegenerative disease of the substantia nigra (an area in the basal ganglia), which involves a breakdown of nerve cells in the motor area of the brain, is also characterized by reduction in ChAT activity.[33] Myasthenia gravis, a chronic autoimmune disorder, is characterized by reductions in levels of ACh at the neuromuscular junction.[34] All these disorders are related to abnormalities in the central cholinergic system, which shows a decline in ACh level. The inhibition of acetylcholinesterase (AChE) enzyme, which catalyzes the breakdown of ACh, may be one of the most realistic approaches to the symptomatic treatment of these disorders.[35]

Natarajan *et al.*[36] reported that methanolic extract of *Sargassum* showed strong inhibition at $IC_{50}$ value of 1 mg/ml and 0.6 mg/ml on Cholinesterase activity with Acetylthiocholine iodide (ATCI) and Butyrylthiocholine iodide (BTCI) as substrate. Two farnesylacetone derivatives (identified as (5E,10Z)-6,10,14-trimethylpentadeca-5,10-dien-2,12-dione and (5E,9E,13E)-6,10,4-trimethylpentadeca-5,9,13-trien-2,12-dione) were isolated from the Korean brown alga *Sargassum sagamianum* and showed moderate acetylcholinesterase and butyrylcholinesterase inhibitory activities with $IC_{50}$ values

of 65.0-48.0 and 34.0-23.0 mM, respectively.[37] However, two plastoquinones (sargaquinoic acid and sargachromenol), isolated from *Sargassum sagamianum,* showed moderate acetylcholinesterase inhibitory activity with $IC_{50}$ 23.2 and 32.7 μM respectively, and for butyrylcholinesterase, sargaquinoic acid showed potent inhibitory activity with $IC_{50}$ 26 nM.[38]

## Neuroprotective (Neurite outgrowth promoting) activity

The neurotrophic factor, nerve growth factor (NGF), is fundamentally important to the differentiation, survival, and maintenance by stimulating neurite outgrowth in neuronal and rat phaeochromocytoma (PC12) cells.[39,40] Reduction of NGF levels in the brain ultimately causing aging and neurodegenerative conditions such as Alzheimer's disease.[41] The use of NGF-potentiating substance with small molecular weight has been suggested for the treatment of neurodegenerative diseases.[42] Furthermore, numerous animal tests have also shown that the administration of NGF can significantly ameliorate the neuronal degeneration in rat cerebral cortex and hippocampus after ischemic insults.[43] These results underlie the rationale for the use of NGF to treat neurodegenerative diseases.

Neurite outgrowth is a fundamental neuronal feature and plays an important role in neuronal development during embryogenesis and in the adult brain.[44] Pheophytin A, purified from the Japanese brown alga *Sargassum fulvellum,* is a novel neuro-differentiation compound. Pheophytin A at 3.9 μg/mL was observed to synergize with NGF in promoting neurite outgrowth in rat pheochromocytoma PC12 cells by a mechanism that appeared to involve activation of mitogen-activated protein kinase signaling.[45] Sargachromenol isolated from *Sargassum macrocarpum* was shown to markedly promote NGF-dependent neurogenesis in PC12D cells ($ED_{50}$ 9 μM). Interestingly, mechanistic studies demonstrated that both the cyclic AMP-mediated protein kinase and mitogen-activated protein kinase 1/2 signal transduction pathways were required for neurite growth stimulated by sargachromenol.[46] Low molecular weight quinonic compound sargaquinoic acid isolated from *Sargassum macrocarpum* possesses a novel nerve growth factor-dependent neurite outgrowth promoting activity at the nanogram range. Kamei and Tsang investigated the signaling pathways involved using a pharmacological approach and concluded that sargaquinoic acid enhanced neurite outgrowth in PC-12 neuronal cells by involving both TrkA-mitogen-activated protein kinase and adenylate cyclase-protein kinase as a signal transduction pathways.[47] In a subsequent study, the neuroprotective effect of sargaquinoic acid was shown to be independent of nerve growth factor and phosphatidylinositol 3 kinase, a key signaling molecule.[48]

## Anti-cancer and cytotoxic activity

Cancer is a leading cause of death worldwide and a diverse group of diseases characterized by the uncontrolled proliferation of anaplastic cells, which tend to invade surrounding tissues and metastasize to other tissues and organs. Cancer results from a mutation in the chromosomal DNA of a normal cell, which can be triggered by both external factors (tobacco, alcohol, chemicals, infectious agents, and radiation) and internal factors (hormones, immune conditions, inherited mutations, and mutations occurring in metabolism).[49]

Zandi *et al.*[50] reported that the cold water extract of *Sargassum oligocystum* showed the reasonable anti-cancer activity against tumor cells replication. The most potent activity has been shown at concentrations 500 μg/ml and 400 μg/ml of extract on Daudi and K562 cell lines, respectively. Polysaccharides from *Sargassum fusiforme* showed significant anti-tumor activity both *in vitro* and *in vivo*, and improved the immune function in tumor-bearing mice.[51] Also, two polysaccharide fractions, SP-3-1 and SP-3-2 from *Sargassum pallidum,* showed significant *in vitro* anti-tumor activity against the HepG2 cells, A549 cells, and MGC-803 cells.[52] Khanavi *et al.*[53] found that the hexane fraction of methanol extract of *Sargassum swartzii* had *in vitro* cytotoxicity against Caco-2 and T47D cells and increased the percentage of apoptotic cells among these cells. The activity of this fraction may be due to the meroterpenoids. Hydroxysargaquinone and Sargasals I and II fraction of a methanolic extract of *Sargassum turtile* has demonstrated significant and marginal cytotoxicity against cultured P-388 lymphocytic leukemia cells.[54] Furthermore, polysaccharide E3 isolated from *Sargassum latifolium* showed a selective cytotoxicity against lymphoblastic leukemia 1301 cells.[55]

## Anti-pyretic, analgesic, and anti-inflammatory activities

The inflammatory process involves a series of events that can be elicited by numerous internal or external stimuli. Therapy of inflammatory diseases is usually directed at the inflammatory processes. Anti-inflammatory refers to the property of a substance or treatment that reduces inflammation.[56]

Dar *et al.*[57] reported that butanolic extract of *Sargassum wightii* collected during winter season was most effective (86.7%) in reducing carrageenan-induced edema in rats at a dose of 100 mg/kg as compared to reference drugs aspirin (79.4%) and ibuprofen (57.3%). The dichloromethane extract of *Sargassum fulvellum* inhibited an inflammatory symptom of mouse ear edema by 79.1%. The ethanol extract of *Sargassum thunbergii* also inhibited edema by 72.1%, when evaluated against yeast-induced pyrexia, tail-flick test, and phorbol myristate acetate-induced inflammation (edema, erythema, and blood flow) in mice.[11] Also, methanolic extracts of *Sargassum swartzii* at the dose of 500 mg/kg body weight showed analgesic effects in both acetic acid-induced writhing and hot plate-induced pain models, acute anti-inflammatory effect in both edemas in hind paw induced by carrageenan and peritonitis models. Furthermore, *S. swartzii* extract showed chronic anti-inflammatory effects at the dose of 175 and 350 mg/kg body weight in amiant-induced granuloma model in mice.[58] According to Hwang *et al.*,[59] fucoidan (sulfated polysaccharide) from *Sargassum hemiphyllum* showed *in vivo* and *in vitro* anti-inflammatory activity.

### Hepatoprotective activity

Raghavendran *et al.*[60] reported the protective effects of *Sargassum polycystum* alcoholic extract on changes in liver mitochondrial enzymes against acetaminophen-induced toxic hepatitis in rats. Reports show that the *S. Polycystum* pre-treated rats showed an improved level of mitochondrial GSH, and prevented the excessive depletion of SOD and CAT with concomitant reduction in the levels of lipid peroxides when compared with acetaminophen-induced animals. Furthermore, extract prevent the severe impairment in the activities of tricarboxylic acid cycle enzymes, prevention in the excessive impairment of NADH dehydrogenase activity and improving the mitochondrial antioxidant defence system, thereby protecting the critical nucleophilic sites on the enzymes against toxic electrophilic metabolites. Sulfated polysaccharides from *Sargassum wightii* significantly restored the deformities due to cyclosporine A-induced oxidative liver injury in rats. Administration of sulfated polysaccharides repairs the activities of hepatic marker enzymes as it decreases the levels of lipid peroxidation, 8-hydroxy-2-deoxy guanosine and protein carbonyls, along with an increase in ATPase activities. Also, sulfated polysaccharides co-administration minimized the oxidants production by scavenging the free radicals.[61]

### Anti-viral activity

Iwashima *et al.*[62] discovered that three plastoquinones isolated from *Sargassum micracanthum* inhibited cytomegalo virus ($IC_{50}$ 0.49-2.6 μM) and measles virus ($IC_{50}$ 2.7-3.1 μM). A sulfated polysaccharide (SP-2a) from *Sargassum* patens was found to significantly inhibit the *in vitro* replication of both the acyclovir-sensitive and -resistant strains of Herpes simplex virus type 1 (HSV-1), in dose-dependent manners, with 50% inhibitions occurring with 1.5-5.3 μg/ml.[63] Also, a sulfated polysaccharide (SP2) isolated from *S*. patens inhibit the replication of herpes simplex virus type 2 (HSV-2) dose-dependently by 38.5-96.1% of the control level, after incubations with 0.78-12.5 μg/ml of the polysaccharide.[64] Polysaccharides, ST-F characterized fucoidan, from *Sargassum* trichophyllum showed anti-viral activity against herpes simplex virus type 2.[65] Sulfated polysaccharide, fucoidan, and a guluronic acid-rich alginate derived from *Sargassum tenerrimum* showed activity against herpes simplex virus type 1 (HSV-1). Their inhibitory concentration 50% (IC50) values were in the range 0.5-15 μg/ml.[66]

### Anti-coagulant activity

Disorders in blood coagulation can lead to an increased risk of bleeding (hemorrhage) or clotting (thrombosis).[67] Anti-coagulants are substances that prevent coagulation that is, they stop blood from clotting.[68] De Zoysa *et al.*[69] reported the isolation and characterization of fucose containing sulfated polysaccharide as an anti-coagulant agent from *Sargassum fulvellum*. Hot water extracts from *Sargassum horneri* showed high activated partial thromboplastin time (APTT) and exhibited the potent anticoagulant activity.[70]

### Immunomodulatory activity

Immunomodulation is explained as any change in the immune response and may involve induction, expression, amplification of any part or phase in the immune response. Modulation may be very specific limited to a given antigen/agent with a great effect on immune response.[71] *In vitro* and *In vivo* effect of ethyl acetate fraction *Sargassum ilicifolium* was tested for immunomodulatory activities. *In vitro* study revealed that *S. ilicifolium* has stimulated chemotatic, phagocytic, and intracellular killing of human neutrophils at a dose of 100 μg/ml. Whereas, *In vivo* studies have shown prominent immunostimulatory effect at a dose of 100 mg/kg p.o. The said activity was due to presence of terpenes and steroids.[72] The hot-water extract of *Sargassum hemiphyllum* showed the activity of cell proliferation (174%) at 120 μg/ml, and IgM secretion (132%) at 120 μg/ml when assayed in HB4C5 cells (human hybridomas producing monoclonal antibody against human lung cancer). Furthermore, extract showed significant proliferation activity (141%) and phagocytosis activity (148%) at 80 μg/ml when assayed in J774 (murine macrophage-like) cell line. These result revealed the significant immune-stimulating activity of *Sargassum hemiphyllum.*[23]

### Other biological activities

Other pharmacological activity includes fibrinolytic, anti-diabetic, anti-bacterial, anti-plasmodial, Skin-whitening, gastric-protective activity etc., Two bioactive products identified as 1-O-palmi toyl-2-O-oleoyl-3-O-(α-D-glucopyranosyl)–lycerol (POGG) and 1-O-myristoyl-2-O-oleoyl-3-O-(α-D-glucopyranosyl)–glycerol (MOGG) obtained from *Sargassum fulvellum* showed fibrinolytic activity in the reaction system of pro-u-PA and plasminogen.[73] According to Kim *et al.,*[74] Sargaquinoic acid and sargahydroquinoic acid from *Sargassum yezoense* able to increase Peroxisome proliferator-activated receptor α/γ (PPARα/γ) transcriptional activity. PPARs are members of the nuclear hormone receptor superfamily of ligand- activated transcription factors, and are currently appreciated as potential therapeutic targets for the treatment of diabetes and dyslipidemia. Hot water extract of *Sargassum polycystum* in dose of 100 mg/kg maintains the acidity of gastric juice and improves the gastric mucosal injury in rats.[75] Extracts of *Sargassum polycystum* and *Sargassum silquastrum* exerted *in vitro* inhibitory activity against tyrosinase and melanin production, which could be developed to a skin-whitening agent in cosmetics industry.[76,77]

## CONCLUSION

A large number of studies are reported that *Sargassum* species contain sulfated polysaccharide, plastoquinone, phlorotannins, flucoxanthin, fucoidan, sargaquinoic acid, sargachromenol, steroids, terpenoids, and flavonoids etc., Furthermore, these bioactive compounds and various extracts showed significant therapeutic potential and could be introduced for the preparation of novel functional ingredients in pharmaceuticals for the treatment and or prevention of several disorders. Therefore, further research studies are needed to exploit its maximum

therapeutic potential in the field of medicinal and pharmaceutical sciences for novel and fruitful application.

## ACKNOWLEDGMENT

Authors are thankful to Dr. A. M. Ittadwar, Principal, Gurunanak College of Pharmacy, Nagpur for his core guidance and necessary support.

## REFERENCES


1. Pomponi SA. The bioprocess-technological potential of the sea. J Biotechnol 1999;70:5-13.
2. Wijesekara I, Pangestuti R, Kim SK. Biological activities and potential health benefits of sulfated polysaccharides derived from marine algae. Carbohydr Polym 2011;84:14-21.
3. Garson MJ. Marine natural products. Nat Prod Rep 1989;6:143-70.
4. El Gamal AA. Biological importance of marine algae. Saudi Pharm J 2010;18:1-25.
5. Dhargalkar VK, Pereira N. Seaweed: Promising plant of the millennium. Sci and Cult 2005;71:60-6.
6. Khotimchenko SV, Vaskovsky VE, Titlyanova TV. Fatty acids of marine algae from the Pacific coast of North California. Bot Mar 2005;45:17-22.
7. Yuan YV, Walsh NA. Antioxidant and antiproliferative activities of extracts from a variety of edible seaweeds. Food Chem Toxicol 2006;44:1144-50.
8. Chandini SK, Ganesan P, Bhaskar N. *In vitro* antioxidant activities of three selected brown seaweeds of India. Food Chem 2008;107:707-13.
9. Artan M, Li Y, Karadeniz F, Lee SH, Kim MM, Kim SK. Anti-HIV-1 activity of phloroglucinol derivative, 6,6'-bieckol, from *Ecklonia cava*. Bioorg Med Chem 2008;16:7921-6.
10. Li Y, Lee SH, Le QT, Kim MM, Kim SK. Anti-allergic effects of phlorotannins on histamine release via binding inhibition between IgE and Fc epsilon RI. J Agric Food Chem 2008;56:12073-80.
11. Kang JY, Khan MN, Park NH, Cho JY, Lee MC, Fujii H, *et al*. Antipyretic, analgesic, and anti-inflammatory activities of the seaweed *Sargassum fulvellum* and *Sargassum thunbergii* in mice. J Ethnopharmacol 2008;116:187-90.
12. Kim MM, Rajapakse N, Kim SK. Anti-inflammatory effect of *Ishige okamurae* ethanolic extract via inhibition of NF-kappaB transcription factor in RAW 264.7 cells. Phytother Res 2009;23:628-34.
13. Kong CS, Kim JA, Yoon NY, Kim SK. Induction of apoptosis by phloroglucinol derivative from *Ecklonia cava* in MCF-7 human breast cancer cells. Food Chem Toxicol 2009;47:1653-8.
14. Pushpamali WA, Nikapitiya C, Zoysa MD, Whang I, Kim SJ, Lee J. Isolation and purification of an anticoagulant from fermented red seaweed *Lomentaria catenata*. Carbohydrate Polymers 2008;73:274-9.
15. Blunt JW, Copp BR, Hu WP, Munro MH, Northcote PT, Prinsep MR. Marine natural products. Nat Prod Rep 2008;25:35-94.
16. Mattio L, Payri CE. 190 years of *Sargassum* taxonomy, facing the advent of DNA phylogenies. Bot Rev 2011;77:31-70.
17. Barnham KJ, Masters CL, Bush AI. Neurodegenerative diseases and oxidative stress. Nat Rev Drug Discov 2004;3:205-14.
18. Frölich L, Riederer P. Free radical mechanisms in dementia of Alzheimer type and the potential for antioxidative treatment. Arzneimittelforschung 1995;45:443-6.
19. Yang CS, Landau JM, Huang MT, Newmark HL. Inhibition of carcinogenesis by dietary polyphenolic compounds. Annu Rev Nutr 2001;21:381-406.
20. Aruoma IO. Antioxidant action of plant foods: Use of oxidative DNA damage as a tool for studying antioxidant efficacy. Free Radic Res 1999;30:419-27.
21. Halliwell B, Gutteridge JM. Free Radicals in Biology and Medicine. Oxford: Clarendon Press; 1986.
22. Kim SH, Choi DS, Athukorala Y, Jeon YJ, Senevirathne M, Rha CK. Antioxidant activity of sulfated polysaccharides isolated from *Sargassum fulvellum*. J Food Sci Nutr 2007;12:65-73.
23. Hwang PA, Wu CH, Gau SY, Chien SY, Hwang DF. Antioxidant and immune-stimulating activities of hot-water extract from seaweed *Sargassum hemiphyllum*. J Mar Sci Technol 2010;18:41-6.
24. Park PJ, Heo SJ, Park EJ, Kim SK, Byun HG, Jeon BT, *et al*. Reactive oxygen scavenging effect of enzymatic extracts from *Sargassum thunbergii*. J Agric Food Chem 2005;53:6666-72.
25. Seo Y, Park KE, Kim YA, Lee HJ, Yoo JS, Ahn JW, *et al*. Isolation of tetraprenyltoluquinols from the brown alga *Sargassum thunbergii*. Chem Pharm Bull (Tokyo) 2006;54:1730-3.
26. Seo Y, Park KE, Nam TJ. Isolation of a new chromene from the brown alga *Sargassum thunbergii*. Bull Korean Chem Soc 2007;28:1831-3.
27. Jung M, Jang KH, Kim B, Lee BH, Choi BW, Oh KB, *et al*. Meroditerpenoids from the brown alga *Sargassum siliquastrum*. J Nat Prod 2008;71:1714-9.
28. Lim SN, Cheung PC, Ooi VE, Ang PO. Evaluation of antioxidative activity of extracts from a brown seaweed, *Sargassum siliquastrum*. J Agr Food Chem 2002;50:3862-6.
29. Iwashima M, Mori J, Ting X, Matsunaga T, Hayashi K, Shinoda D, *et al*. Antioxidant and antiviral activities of plastoquinones from the brown alga *Sargassum micracanthum*, and a new chromene derivative converted from the plastoquinones. Biol Pharm Bull 2005;28:374-7.
30. Mori J, Iwashima M, Wakasugi H, Saito H, Matsunaga T, Ogasawara M, *et al*. New plastoquinones isolated from the brown alga, *Sargassum micracanthum*. Chem Pharm Bull (Tokyo) 2005;53:1159-63.
31. Holden M, Kelly C. Use of cholinesterase inhibitors in dementia. Adv Psychiatr Treat 2002;8:89-96.
32. Pietrini P, Alexander GE, Furey ML, Hampel H, Guazzelli M. The neurometabolic landscape of cognitive decline: *In vivo* studies with positron emission tomography in Alzheimer's disease. Int J Psychophysiol 2000;37:87-98.
33. Whitehouse PJ, Hedreen JC, White CL 3rd, Price DL. Basal forebrain neurons in the dementia of Parkinson disease. Ann Neurol 1983;13:243-8.
34. Mukherjee PK, Kumar V, Mal M, Houghton PJ. Acetylcholinesterase inhibitors from plants. Phytomedicine 2007;14:289-300.
35. Pangestuti R, Kim SK. Neuroprotective properties of chitosan and its derivatives. Mar Drugs 2010;8:2117-28.
36. Natarajan S, Shanmugiahthevar KP, Kasi PD. Cholinesterase inhibitors from *Sargassum* and *Gracilaria gracilis*: Seaweeds inhabiting South Indian coastal areas (Hare Island, Gulf of Mannar). Nat Prod Res 2009;23:355-69.
37. Ryu G, Park SH, Kim ES, Choi BW, Ryu SY, Lee BH. Cholinesterase inhibitory activity of two farnesylacetone derivatives from the brown alga *Sargassum sagamianum*. Arch Pharm Res 2003;26:796-9.
38. Choi BW, Ryu G, Park SH, Kim ES, Shin J, Roh SS, *et al*. Anticholinesterase activity of plastoquinones from *Sargassum sagamianum*: Lead compounds for Alzheimer's disease therapy. Phytother Res 2007;21:423-6.

39. Connor B, Dragunow M. The role of neuronal growth factors in neurodegenerative disorders of the human brain. Brain Res Rev 1998;27:1-39.
40. Greene LA. Nerve growth factor prevents the death and stimulates the neuronal differentiation of clonal PC12 pheochromocytoma cells in serum-free medium. J Cell Biol 1978;78:747-55.
41. Heese K, Low JW, Inoue N. Nerve growth factor, neural stem cells and Alzheimer's disease. Neurosignals 2006-2007;15:1-12.
42. Diaz BR, Yamazaki RS. Advances and challenges in the prevention and treatment of Alzheimer's disease. Pharm Res 1998;15:386-98.
43. Buchan AM, Williams L, Bruederlin B. Nerve growth factor: Pretreatment ameliorates ischemic hippocampal neuronal injury. Stroke 1990;21:177-95.
44. Khodosevich K, Monyer H. Signaling involved in neurite outgrowth of postnatally born subventricular zone neurons *in vitro*. BMC Neurosci 2010;11:18.1-18.11.
45. Ina A, Hayashi KI, Nozaki H, Kamei Y. Pheophytin a, a low molecular weight compound found in the marine brown alga *Sargassum fulvellum*, promotes the differentiation of PC12 cells. Int J Dev Neurosci 2007;25:63-8.
46. Tsang CK, Ina A, Goto T, Kamei Y. Sargachromenol, a novel nerve growth factor-potentiating substance isolated from *Sargassum macrocarpum*, promotes neurite outgrowth and survival via distinct signaling pathways in PC12D cells. Neurosci 2005;132:633-43.
47. Kamei Y, Tsang CK. Sargaquinoic acid promotes neurite outgrowth via protein kinase A and MAP kinases-mediated signaling pathways in PC12D cells. Int J Devl Neurosci 2003;21:255-62.
48. Tsang CK, Kamei Y. Sargaquinoic acid supports the survival of neuronal PC12D cells in a nerve growth factor-independent manner. Eur J Pharmacol 2004;488:11-8.
49. Zong A, Cao H, Wang F. Anticancer polysaccharides from natural resources: A review of recent research. Carbohydr Polym 2012;90:1395-410.
50. Zandi K, Ahmadzadeh S, Tajbakhsh S, Rastian Z, Yousefi F, Farshadpour F, *et al*. Anticancer activity of *Sargassum oligocystum* water extract against human cancer cell lines. Eur Rev Med Pharmacol Sci 2010;14:669-73.
51. Chen X, Nie W, Yu G, Li Y, Hu Y, Lu J, *et al*. Antitumor and immunomodulatory activity of polysaccharides from *Sargassum fusiforme*. Food Chem Toxicol 2012;50:695-700.
52. Ye H, Wang K, Zhou C, Liu J, Zeng X. Purification, antitumor and antioxidant activities *in vitro* of polysaccharides from the brown seaweed *Sargassum pallidum*. Food Chem 2008;111:428-32.
53. Khanavi M, Nabavi M, Sadati N, Shams AM, Sohrabipour J, Nabavi SM, *et al*. Cytotoxic activity of some marine brown algae against cancer cell lines. Biol Res 2010;43:31-7.
54. Numata A, Kanbara S, Takahashi C, Fujiki R, Yoneda M, Usami Y, *et al*. A cytotoxic principle of the brown alga *Sargassum tortile* and structures of chromenes. Phytochemistry 1992;31:1209-13.
55. Gamal-Eldeen AM, Ahmed EF, Abo-Zeid MA. *In vitro* cancer chemopreventive properties of polysaccharide extract from the brown alga, *Sargassum latifolium*. Food Chem Toxicol 2009;47:1378-84.
56. Kazłowska K, Hsu T, Hou CC, Yang WC, Tsai GJ. Anti-inflammatory properties of phenolic compounds and crude extract from *Porphyra dentata*. J Ethnopharmacol 2010;128:123-30.
57. Dar A, Baig HS, Saifullah SM, Ahmad VU, Yasmeen S, Nizamuddin M. Effect of seasonal variation on the anti-inflammatory activity of *Sargassum wightii* growing on the N. Arabian Sea coast of Pakistan. J Exp Mar Bio Ecol 2007;351:1-9.
58. Hong DD, Hien HM, Anh HT. Studies on the analgesic and anti-inflammatory activities of *Sargassum swartzii* (Turner) *C. Agardh* (Phaeophyta) and *Ulva reticulata* Forsskal (Chlorophyta) in experiment animal models. African J Biotechnol 2011;10:2308-14.
59. Hwang PA, Chien SY, Chan YL, Lu MK, Wu CH, Kong ZL, *et al*. Inhibition of lipopolysaccharide (LPS)-induced inflammatory responses by *Sargassum hemiphyllum* sulfated polysaccharide extract in RAW 264.7 macrophage cells. J Agric Food Chem 2011;59:2062-8.
60. Raghavendran BH, Sathivel A, Devaki T. Antioxidant effect of *Sargassum polycystum* (Phaeophyceae) against acetaminophen induced changes in hepatic mitochondrial enzymes during toxic hepatitis. Chemosphere 2005;61:276-81.
61. Josephine A, Nithya K, Amudha G, Veena CK, Preetha SP, Varalakshmi P. Role of sulphated polysaccharides from *Sargassum Wightii* in Cyclosporine A-induced oxidative liver injury in rats. BMC Pharmacol 2008;8:1-9.
62. Iwashima M, Mori J, Ting X, Matsunaga T, Hayashi K, Shinoda D, *et al*. Antioxidant and antiviral activities of plastoquinones from the brown alga *Sargassum micracanthum*, and a new chromene derivative converted from the plastoquinones. Biol Pharm Bull 2005;28:374-7.
63. Zhu W, Chiu LC, Ooi VE, Chan PK, Ang PO Jr. Antiviral property and mechanisms of a sulphated polysaccharide from the brown alga *Sargassum* patens against Herpes simplex virus type 1. Phytomedicine 2006;13:695-701.
64. Zhu W, Chiu LC, Ooi VE, Chan PK, Ang PO Jr. Antiviral property and mode of action of a sulphated polysaccharide from *Sargassum patens* against herpes simplex virus type 2. Int J Antimicrob Agents 2004;24:279-83.
65. Lee JB, Takeshita A, Hayashi K, Hayashi T. Structures and antiviral activities of polysaccharides from *Sargassum trichophyllum*. Carbohydr Polym 2011;86:995-9.
66. Sinha S, Astani A, Ghosh T, Schnitzler P, Ray B. Polysaccharides from *Sargassum tenerrimum*: Structural features, chemical modification and anti-viral activity. Phytochemistry 2010;71:235-42.
67. Guerra-Rivas G, Gómez-Gutiérrez CM, Alarcón-Arteaga G, Soria-Mercado IE, Ayala-Sánchez NE. Screening for anticoagulant activity in marine algae from the Northwest Mexican Pacific coast. J Appl Phycol 2011;23:495-503.
68. Desai UR. New antithrombin-based anticoagulants. Med Res Rev 2004;24:151-81.
69. De Zoysa M, Nikapitiya C, Jeon YJ, Jee Y, Lee J. Anticoagulant activity of sulfated polysaccharide isolated from fermented brown seaweed *Sargassum fulvellum*. J Appl Phycol 2008;20:67-74.
70. Athukorala Y, Lee KW, Kim SK, Jeon YJ. Anticoagulant activity of marine green and brown algae collected from Jeju Island in Korea. Bioresour Technol 2007;98:1711-6.
71. Sell S. Immunomodulation. In: Immunology Immunopathology and Immunity. New York: Elsevier Science Publishing Co. Inc; 1987. p. 655-83.
72. Chandraraj S, Prakash B, Navanath K. Immunomodulatory activities of ethyl acetate extracts of two marine sponges *Gelliodes fibrosa* and *Tedania anhelans* and brown algae *Sargassum ilicifolium* with reference to phagocytosis. Res J Pharm Biol Chem Sci 2010;1:302-7.
73. Wu W, Hasumi K, Peng H, Hu X, Wang X, Bao B. Fibrinolytic compounds isolated from a brown alga, *Sargassum fulvellum*. Mar Drugs 2009;7:85-94.
74. Kim SN, Choi HY, Lee W, Park GM, Shin WS, Kim YK. Sargaquinoic acid and sargahydroquinoic acid from *Sargassum yezoense* stimulate adipocyte differentiation through PPAR α/γ activation in 3T3-L1 cells. FEBS Lett 2008;582:3465-72.

75. Raghavendran HR, Sathivel A, Devaki T. Efficacy of brown seaweed hot water extract against HCl-ethanol induced gastric mucosal injury in rats. Arch Pharm Res 2004;27:449-53.
76. Cha SH, Ko SC, Kim D, Jeon YJ. Screening of marine algae for potential tyrosinase inhibitor: Those inhibitors reduced tyrosinase activity and melanin synthesis in zebrafish. J Dermatol 2011;38:354-63.
77. Chan YY, Kim KH, Cheah SH. Inhibitory effects of *Sargassum polycystum* on tyrosinase activity and melanin formation in B16F10 murine melanoma cells. J Ethnopharmacol 2011;137:1183-8.

**How to cite this Article:** Yende SR, Harle UN, Chaugule BB. Therapeutic potential and health benefits of *Sargassum* species. Phcog Rev 2014;8:1-7.

**Source of Support:** Nil, **Conflict of Interest:** None declared