IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
June 2017 Vol.:9, Issue:3

Therapeutic Uses of *Sargassum Species*: A Review

IJPPR
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ISSN 2349-7203
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Submission: 4 June 2017
Accepted: 10 June 2017
Published: 25 June 2017

Keywords: *Sargassum* species, medicinal, phytochemical, pharmacological.

ABSTRACT

Sargassum species are brown macroalgae found in shallow marine meadows. These are nutritious and rich source of several bioactive compounds. These isolated active compounds exhibit diverse biological activities like antioxidant, anti-inflammatory, antipyretic, analgesic, antiviral, antidiabetic, hepatoprotective, anti-obesity, cholinesterase inhibitory activities etc. This makes the *Sargassum* species to be used in pharmaceutical and nutraceutical areas. This review focuses mainly on the phytochemical, therapeutic potential and health benefits of different *Sargassum* species.

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INTRODUCTION

Sargassum (Family Sargassaceae, Order Fucales) represents the most common species of brown macroalgae in tropical to warm temperate waters. It is the most diverse genus of marine macrophytes with more than 130 described species.[1]*Sargassum* contains higher amounts of protein, essential and non-essential amino acids, essential fatty acids, and minerals. *Sargassum* also contains phycocolloids and bioactive compounds (e.g., alginic acid and fucoidan) and polyphenols, which may have potential nutraceutical and medical applications.

Findings of *in-vitro* studies show that *Sargassum* species have several therapeutical uses as anti-tumor, antioxidant, antiviral, antibacterial, antifungal and anti-inflammatory activities. The aim of this study was to investigate the beneficial uses of *Sargassum* species on human health.[2]

THERAPEUTIC USES

In-vitro antioxidant activity

Oxidative stress is formed due to the result of imbalance between preoxidant and antioxidant homeostasis which leads to the formation of toxic reactive oxygen species (ROS).[3] ROS such as hydroxyl, superoxide and peroxy radicals are formed in human tissue cells. These ROS may attack macromolecules such as membrane lipids, proteins and DNA which leads to many health disorders such as cancer, diabetes mellitus, age related degenerative conditions etc. Antioxidants may protect human tissue cells from ROS. *In-vitro* cells have their own inherited antioxidant defense system in the form of various enzymatic as well as non-enzymatic pathways for removing the ROS.[4]

Marine seaweed is considered to be the best source of natural antioxidant. 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-ethybenzothiazoline-6-sulfonate (ABTS) radical scavenging, NO scavenging, lipid peroxide inhibition, superoxide and hydroxyl radical scavenging assays. Compared to the commercial antioxidant such as α-tocopherol, the sulfated polysaccharides of *Sargassum fulvellum* have more potent NO scavenging and DPPH scavenging activity.[5] The hot H_2O extract from *Sargassum hemiphyllum* show DPPH free radical scavenging activity, superoxide anion scavenging

activity measured using the xanthine-xanthine oxidase system and Fe^{3+} reducing activity.[6] Due to high level of total phenolic content, the *Sargassum hemiphyllum* shows high antioxidant activity. The thunbergols (tetraprenyltoluquinols) and sargothunbergol (chromene) isolated from the *Sargassum thunbergii* shows DDPH free radical scavenging activity.[6] Also, the extracts from *Sargassum siliquastrum* showed DPPH free radical scavenging activity suppression of lipid peroxidation and scavenging activity of superoxide radicals.[7] The total methanolic extract and ethyl acetate fraction of *Sargassum 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 thinking, memory, comprehension and language. Alzheimer's disease, Parkinsonism, and Myasthenia gravis are some of the commonest types of Dementia. These disorders are due to the abnormalities in central cholinergic system which shows decline in Ach level. The symptomatic treatment of these disorders is done by the inhibition of acetylcholinesterase (AChE) enzyme, which catalyzes the breakdown of Ach.[9] The two farnesyl acetone derivatives such 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 isolated from *Sargassum sagamianum* show moderate acetylcholinesterase and butyrylcholinesterase inhibitory activity.[10] The two plastoquinones such as sargaquinoic acid and sargachromenol isolated from *Sargassum sagamianum* showed moderate acetylcholinesterase inhibitory activity and sargaquinoic acid showed moderate acetylcholinesterase inhibitory activity.[11]

Neuroprotective (Neurite outgrowth promoting) activity

The reduction in nerve growth factor (NGF) levels in brain cause aging and neurodegenerative conditions such as Alzheimer's disease.[12] For the treatment of neurodegenerative diseases, NGF-potentiating substance with low molecular weight can be used.[13] Neurite outgrowth is a fundamental neuronal feature which plays an important role in neuronal development during embryogenesis and in the adult brain.[14] Pheophytin A, isolated from *Sargassum fulvellum* is a neurodifferentiation compound which synergizes with NGF in promoting neurite outgrowth in rat pheochromocytoma PC 12 cells by a mechanism involved in activation of mitogen-activated protein kinase signaling.[15] The Sargachromenol isolated

from *Sargassum macrocarpum* was shown to markedly promote NGF-dependent neurogenesis in PC12D cells. Sargaquinoic acid a low molecular weight quinovic compound isolated from *Sargassum macrocarpum* possesses a novel nerve growth factor dependent neurite outgrowth promoting activity at the nanogram range. The neuroprotective effect of sargaquinoic acid was found to be independent of nerve growth factor and phosphatidylinositol 3 kinases, a key signaling molecule.[16]

Anti-cancer and cytotoxic activity

Cancer results from a mutation in the chromosomal DNA of a normal cell, which can be triggered by both external factors and internal factors. The cold water extract of *Sargassum oligoccystum* shows reasonable anti-cancer activity against tumor cells replication. The polysaccharides obtained from *Sargassum fusiforme* shows anti-cancer activity both *in vitro* and *in vivo* and improved the immune function in tumor bearing mice.[17] Hydroxysargaquinone and Sargasala I and II compounds obtained from the methanolic extract of *Sargassum turtile* has shown significant and marginal cytotoxic activity against cultured P-388 lymphocytic leukemia cells. Also polysaccharide E_3 isolated from *Sargassum latifolium* shows cytotoxic activity against lymphoblastic leukemia 1301 cells.[18]

Antipyretic, analgesic and anti-inflammatory activities

Anti-inflammatory means the property of a substance to reduce inflammation. The butanolic extract of *Sargassum wightii* was most effective (86.7%) in reducing carrageenan-induced edema in rats at a dose of 10 mg/kg as compared to reference drugs aspirin (79.4%) and ibuprofen (57.3%). On mouse ear edema 79.1% dichloromethane extract of *Sargassum fulvellum* shows anti-inflammatory action. The ethanolic extract of *Sargassum thunbergii* inhibits edema by 72.1%, when evaluated against yeast-induced pyrexia, tail-flick test and phorbol myristate acetate-induced inflammation in mice.[19] In both acetic acid induced writhing and hot plate-induced pain models the methanolic extracts of *Sargassum swartzii* at the dose of 500 mg/kg body weight show analgesic effect, also acute anti-inflammatory effect in both edemas in hind paw induced by carrageenan and peritonitis models. The extract of *Sargassum swartzii* shows chronic anti-inflammatory effects at a dose of 175 and 350 mg/kg body weight in amiant induced granuloma model in mice. Fucidin, a sulfated polysaccharide obtained from *Sargassum polycystum* show *in-vivo* and *in-vitro* anti-inflammatory activities.[20]

Hepatoprotective activity

The alcoholic extract of *Sargassum polycystum* shows changes in liver mitochondrial enzymes against acetaminophen-induced toxic hepatitis in rats. The deformat is due to cyclosporine A-induced oxidative liver injury in rats has been restored by sulfated polysaccharides from *Sargassum wightii*.[21]

Anti-viral activity

The three plastoquinones isolated from *Sargassum micracanthum* inhibit cytomegalovirus and measles virus. Sulfated polysaccharide obtained from *Sargassum patens* was found to inhibit *in vitro* replication of both the acyclovir-sensitive and resistant strains of Herpes simplex virus type 1 in a dose dependent manner. A sulfated polysaccharide, fucoidan and a guluronic acid-rich alginate obtained from *Sargassum tenerrimum* showed activity against herpes simplex virus type 1 (HSV-1).[22]

Anticoagulant activity

Anticoagulants are substances which prevents coagulation. The hot water extracts of *Sargassum horneri* shows high activated partial thromboplastin time (APTT) and exhibited the potent anticoagulant activity.[23]

Anti-diabetic activity

Fucoidan, a newly found α-D-glucosidase inhibitor obtained from *Sargassum wightii* has been used for the treatment of type 2 diabetes mellitus. Thunberol is another new sterol isolated from the *Sargassum thunbergii* has been used in the management of diabetes mellitus.[24]

Anti-obesity activity

Sargassum polycystum showed the best anti-obesity agent.[24]

CONCLUSION

In conclusion, marine seaweeds are a valuable source of bioactive compounds and could be utilized for the preparation of novel functional ingredients for functional food and also a good approach for the treatment or prevention of chronic diseases. The *Sargassum species* contain

different chemical constituents such as plastoquinones, phlorotannins, sulfated polysaccharides, phlorotannins, fucoxanthin, fucoidan, sargaquinoic acid, sargachromenol, steroids, terpenoids and flavonoid etc. These chemical compounds have several activities like antioxidant activity, cholinesterase inhibitory activity, neuroprotective activity, anticancer, antiviral, antidiabetic, hepatoprotective, analgesic, anti-inflammatory, antipyretic activity etc, for the treatment of several chronic disorders.

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