International Journal of Research and Development in Pharmacy & Life Sciences

Review Article Open Access

A Review of Biological Activities of Genus Sargassum

Diana Al-Hashdy[1], Salwa Raweh[1], Amina El-Shaibany[1], Abdulrahman Humaid[2,3]* and Mahmoud El-Aasser[4]

[1]*Pharmacognosy Department, Pharmacy College, Sana`a University, Sanaa, Yemen*
[2]*Department of Biology, Faculty of Science, Sana`a University, Sanaa, Yemen*
[3]*Department of Pharmacy, Faculty of Medical Science, Modern Science University, Sana`a, Yemen*
[4]*The Regional Center for Mycology and Biotechnology, Al-Azhar University, 11787, Nasr City, Cairo, Egypt*

Abstract

Some important brown seaweed is Dictyota (Dictyotales) which are the most commonly found on European Atlantic coasts and the Mediterranean Sea. Laminaria, commonly known as kelps, represents the most complex and largest brown seaweed. Fucales order which contained Fucus (rockweed) and Sargassum (gulfweed) are two important brown seaweeds belonging to the order Faceless Seaweed produces several phytochemical compounds with different pharmacological activities including anticancer activity. This study attempted to investigate Sargassum Vulgare's biological activities (anti-cancer- anti-inflammatory, antioxidant, antiviral, and antimicrobial activities). Therapeutically, selected marine macroalgatoto to hathe the potential to be utilized in the treatments of cardiovascular diseases, diabetes, obesity, viral infection (especially HPV and HIV), cancers gastrointestinal tract disorders, hepatic diseases a an and flammatory diseases. Some seaweed also has been shoshowingti-coagulating and anti-hemorrhagic activity.

Keywords: Seaweed; Biological activities; Genus Sargassum

Introduction

Seaweeds are considered the most diverse group of organisms living in the oceans which represent almost 3/4 of the earth. They are located attached to rocks in the intertidal zone, washed up on tbeabeachesnd as giant underwater forests, as well as out patenting the ocean's surface. Sargassum C. Agardh is one of the most diverse and widely distributed genera of the Phaeophyceae. Sargassum is a genus of brown seaweed, commonly known as gulfweed or sea holly, and is considered one of the most complex Phaeophyceae genera. Sargassum was discovered by Agardh in 1820 and is reported to contain 537 species names in the algae database (Mattio and Payri 2011). In Asia, Sargassum species have many common names as Hai Zao or Hai Qian in Chinese,

Hondawara in Japanese, and Mojaban in Korean (L. Liu et al. 2012 [1]). Sargassum spp. has a broad geographical distribution from Central America, through Australia, New Zealand, Asia, Europe, and Africa (Gloria and Kweku 2016 [2]) spanning the three ocean basins of the Atlantic, Pacific, c, and Indian Oceans, inhabiting temperate, subtropic c, a,l and tropical habitats starting from the beach up to coral reefs along the littoral and sub-littoral areas (Yoshida 1989 [3]). Sargassum is highly tolerant to environmental parameters such as desiccation, full sunlight, and variations in salinity and temperature. This enables it to occupy a broad range of habitats from the upper intertidal, mainly rock pools to the subtidal and substrata from exposed rock to Eel-grass beds (Gloria and Kweku 2016 [2]). The genus has been considered to be the most species-rich genus of the marine macrophytes with 400 species being identified to date. The most recent taxonomy of the sargassum genus is as the following: Economicallysomee Sargassum species are important, particularly in Asian countries where they are used for agro-food, textile, cosmetic and pharmaceutical applications (Oo and Soe-Htun 2014 [4]).

Pharmacological activities of Sargassum seaweed

Sargassum is known to have several pharmacological activities Fitton concluded that the traditional Asian lifestyle of consuming brown seaweed as a diet is correlated to the low incidence of cancer when compared to the West region (Fitton 2003 [5]). Pharmacological properties of Sargassum species extracts, fractions, and isolated substances have been investigated. Among them, the Sargassum species demonstrated anticancer, anti-inflammatory, antiviral, antimicrobial, hypoglycaemic, liver protective, gastric protective, bone protective, skin-whitening, anti-Alzheim, er‟s and antioxidant activities (L. Liu et al. 2012[1]). Some of the Sargassum species' pharmacological activities are mentioned below.

Anti-Cancer Activity

Many Sargassum species have been proved to have anticancer activities on different cell lines in several studies. Generally, these studies divided them into groups as powders, crude extracts and their fractions, crude sulfated polysaccharides, and purified compounds. Many of them are mentioned below. Alginate obtained from Sargassum full vellum showed antitumor activity against Sarcoma-180 at doses of 50 mg/kg that exhibited d 38 % increase in life span, while doses of 6.3 and 25 mg/kg demonstrated no antitumor activity (Fujihara and Nagumo 1992 [6]). Sargassum horneri, Sargassum tortile, Sargassum ringgoldianum, Sargassum thunbergii, and Sargassum micracanthum powders showed significant activity against Ehrlich carcinoma with tumor inhibition growth rate of 38.6, 36.6, 46.5, 41.7, and 42.6%, respectively. On the contrary, Sargassum patens demonstrated no activity against Ehrlich carcinoma with a negative (-20.8%) inhibition tumor weight rate. Sargassum pates, Ssargassumm ringgoldian, Sargassum thunbergii, S, and sargassum micracanthum powders showed particular activity against Meth-A fibrosarcoma (55.5, 39.1, 35, 3 and 26.3% tumor inhibition growth rate, respectively). AdditionafucoidandanII isolated from Sargassum ringgoldianum exhibited higher activity against Meth-A fibrosarcoma (78.1% tumor

***Corresponding author:** Abdulrahman Humaid, Department of Biology, Faculty of Science, Sana`a University, Sanaa, Yemen, Tel: +96773191011, E-mail: humaidyemen@gmail.com

Received: 04-Jun-2022, Manuscript No: ijrdpl-22-68406, **Editor assigned:** 06-June-2022, PreQC No: ijrdpl-22-68406(PQ), **Reviewed:** 20-Jun-2022, QC No: ijrdpl-22-68406, **Revised:** 23-Jun-2022, Manuscript No: ijrdpl-22-68406(R) **Published:** 30-Jun-2022, DOI: 10.4172/2278-0238.1000130

Citation: Al-Hashdy S, Raweh S, El-Shaibany A, Humaid A, El-Aasser M (2022) A Review of Biological Activities of Genus Sargassum. Int J Res Dev Pharm L Sci, 8: 130.

inhibition growth rate)ththat'sowder, while fucoidan II fractions (A, B, and C) showed less growth inhibition activity against Meth-A fibrosarcoma (32.0, 26.2, 34.7%, respectively). Furthermore, neutral lipid, glycolipid, and phospholipid fractions from Sargassum ringgoldianum exhibited significant growth rate inhibition of Meth-A fibrosarcoma (42.6, 36.1, 47.1%, respectively) (Noda et al. 1990). Hydroxysargoquinone, sargasals-I and-II isolated from Sargassum tortile showed significant and marginal cytotoxicity against P-388 lymphocytic leukemia cells with ED50 values of 0.7, 5.7 and 5.8 μg/ml, respectively comparable to reference drug Etoposide (ED50 of 0.24 μg/ml) (Numata et al. 1992 [7]).Two polysaccharides fractions (GIV-A and GIV-B) were isolated from Sargassum thunbergii and showed markedly antitumor activity against Ehrlich ascites carcinoma (Zhuang et al. 1995 [8]). Polysaccharide (Sarg A) isolated from Sargassum stenophyllous showed significant inhibition of tumor growth in mice inoculated with B16F10 melanoma cells by approximately 55% and 7dosest dose 1.5 and 150 μg/animal, respectively, related to the control mice group. While SargA showed no effect on cell viability at doses from 50–2000 μg/well on B16F10 melanoma cells through MTT assay. After a 3-day treatment, SargA at a high tested concentration (2 mg/well) reduced the number of viable cells to about 21% compared to the control (medium only) (Dias et al. 2005 [9]). Sargassum vuVulgareow (SVLV) and high viscosity (SVHV) alginates inhibited the growth of sarcoma 180 in vivo. The oral route of administration was more effective for both alginates, resulting in an inhibition of 51.8% and 74.8% for SVLV at doses of 50 and 100mg/m2/day, respectively, and of 66.2% and 88.8% for SVHV at the same doses comparable with5-fluorouracil positive control (5-FU) 75.5% inhibition at 25 mg/m^2/day (A. P. A. De Sousa et al. 2007 [10]). Polysaccharide fractions (SP-1-1, SP-1-2, SP-2-1, SP-2-2, SP-2-3, SP-3-1and SP-3-2) obtained from Sargassum pallidum showed significant cytotoxic activity against human hepatoma cell line (HepG2), human lung cancer cell line (A549) and human gastric cancer cell line (MGC-803). SP-2-3 showed the highest antitumor activity only against HepG2 cells (81.4% at 1.000 mg/ml). SP-3-1 and SP-3-2 demonstrated particularly higher antitumor activity against HepG2 cells, A549 cells, and MGC-803 cells in vitro than did blank control groups with inhibition rates of SP-3-1 were 62.2%, 64.8%, and 79.6%, respectively and the inhibition rates of SP-3-2 were 63.5%, 67%, and 47.3%, respectively. SP-1-1 and SP-2-2 also showed antitumor activity against the HepG2 cells (59.7% and 63.0%, respectively). SP-2-1 exhibited obvious antitumor activity against the A549 cells (50.0%) at 1.000 mg/ml (Ye et al. 2008). Polysaccharides isolated from Sargassum latifolium (E1, E2 E3, E4) exhibited cancer chemo preventive activity. E1 and E4 polysaccharides demonstrated significant anti- initiation agents by their inhibition of carcinogen activator cytochrome P450 1A (IC50 2.54 and 10.30 μg/ml, respectively) and stimulate glutathione-S-transferases (carcinogen detoxification enzymes) 2.25-fold and 1.44-fold of the control cells, respectively. In addition, both E1 and E4 exhibited potential anti-promoting properties due to their anti-inflammatory activity by enhancing macrophage proliferation and dramatically inhibiting the stimulated NO, TNF-a, and COX-2. Among them, only E3 possessed a selective cytotoxic activity against only lymphoblastic leukemia(1301 cells) with an IC50 value of 17.18 μg/ml, while other fractions showed no cytotoxicity activity against hepatocellular carcinoma(Hep G2), colon carcinoma (HCT-116), and lymphoblastic leukemia (1301 cells) with IC50 values >40 μg/ml (Gamal-Eldeen et al. 2009 [11]). Cold aqueous extract of Sargassum oligocystum showed a cytostatic effect on human K562 (derived from human chronic myelogenous leukemia cells) and human Daudi (derived from Burkitt Lymphoma cells) cell lines at concentrations of 400 μg/ml and 500 μg/ml, respectively (Zandi et al. 2010 [12]). Fucoid fractions (ShF1, ShF2, ShF3) obtained from Sargassum hornery demonstrated no cytotoxic activity and no cell proliferation against human melanoma (SK-MEL-28) and human colon cancer cells (DLD-1) by MTS assay. While, when assayed with soft agar congenic assay, ShF2 and ShF3 particular inhibition of colony formation of DLD-1 cells and SK-MEL-28 by 32 and 33%, respectively. Meanwhile, ShF1 showed the highest inhibition potency of colony formation of DLD- 1 cells by 44%, on the other hand, it exhibited the lowest inhibition potency of colony formation of SK-MEL-28 (only 15%) (Ermakova et al. 2011 [13]). Hetrofucans (SF-0.5v, SF-0.7v, SF-1.0v, SF-1.5v, and SF-2.0v) obtained from Sargassum filipendula displayed anti-proliferative activity on human cervical cancer (HeLa), human prostate (PC3), and human hepatocellular (HepG2) cancer cell lines. SF-1.5v demonstrated no proliferation inhibition activity against HepG2 cells. All heterofucans exhibited moderate anti-proliferative activity against PC3 and HepG2 cells. SF-0.7v was the most [14-16] effective against HepG2 and PC3 by 38.1 and 31.0%, respectively. SF-0.5v, SF-0.7,v, and SF-2.0v showed moderate inhibition activity against HeLa cells while, SF-1.0v and SF-1.5v demonstrated the highest anti-proliferative activity with IC50 values of 15.69 and 13.83 μM, respectively related to doxorubicin and 5-fluorouracil with IC50 values 6.8 and 8.0 μM, respectively. Polysaccharides (SFPS), isolated from Sargassum fusiforme significantly inhibited the proliferation of lung adenocarcinoma (A549) bearing mice. SFPS had both direct cytotoxicity to the tumor cells and indirect anti-tumor accomplished by improving immune response via increasing the level of tumor necrosis factor (TNF)-α in serum, the level of the cytokines secreted by peritoneal macrophages, and splenocytes proliferation in A549-bearing mice. Crude fucoid an isolated from Sargassum plagiophyllum exhibited anticancer activity against diethyl nitrosamine-induced hepatocarcinogenesis in Wister rats via inhibition of carcinogen metabolic activation. Sulfated polysaccharides (PSV1 and SV1) isolated from Sargassum Vulgare exhibited antiangiogenic and cytostatic effects besides antiproliferative activity in the HeLa tumor cell line (PSV1 (50 μg/μl) inhibited around 47% of the proliferation of HeLa cells). Additionally, SV1 and PSV1 showed selective activity against cancer cell lines rather than normal endothelial cells. Sargassum Vulgare water extract only demonstrated significant anticancer activity against just HEP-2 (Human larynx epidermoid carcinoma) with IC50 18.7 μg/ml,while other extracts (dichloromethane, chloroform, methanol, ethanol) showed no activity against K562 (chronic myelocytic leukemia) and NCI-H292 (human lung mucoepidermoid carcinoma) cell lines with IC50 values more than 50 μg/ml according to Protocol of the American Cancer Institute (NCI). Sargassum muticum methanol extract(SMME) demonstrated anti-proliferative activity against MCF-7 and MDA-MB-231 breast cancer cell lines with IC50values 22 and 55 μg/ml, respectively with no cytotoxicity against normal Vero cell line. Moreover, SMME significantly reduces the angiogenesis processes in the chorioallantoic membrane (CAM) via decrease the length and the number of the vessel branches. Seven known meroterpenoids were isolated from 85% aqueous methanol fraction (most cytotoxic fraction) of Sargassum siliquastrum (which was collected off the shoJejuf Jeju Island, Korea in April 2005) and demonstrated strong cytotoxic activity against AGS (gastric cancer), HT-29 (colon cancer), HT-1080 (fibrosarcoma), and MCF-7 (breast adenocarcinoma) human cancer cells. All isolated meroterpenoids displayed strong cytotoxic activities against AGS, HT-29, HT-1080, and MCF-7 cell lines. In particular, Sargachromanols A, B, and K showed potent cytotoxicity to AGS, HT-29, HT-1080, and MCF-7 cell lines, with IC50 values of 0.7, 6.1, 0.7, and 28.1 μg/ml; 0.5,1.0, 3.3, and 23.6 μg /ml; and 5.7, 0.8, 1.8, and 10.3 μg/ml, respectively, related to paclitaxel and doxorubicin. Three meroterpenoids, sargachromanol J, sargachromanol Q, and sargachromanol R were isolated from Sargassum siliquastrum (which

was collected along the shore of Cheju Island, Korea in February 20077). Among them, sargachromanol R demonstrated the strongest cytotoxicity activity against stomach (AGS), colon (HT-29), and fibrosarcoma (HT-1080) cell lines with IC50 values of 6.5, 3.4, and 13.9 μg/ml, respectively, compared to paclitaxel and doxorubicin. On the contrary, sargachromanol Q and sargachromanol R show weaker activity against breast (MCF-7) cell lines with IC50> 50 μg/ml, while sargachromanol J revealed significant activity against breast (MCF- 7) with IC50 value 31.1 μg/ml comparable to paclitaxel and doxorubicin (IC50 15.6 and 23.7 μg/mL, respectively). Low molecular weight fucoidan (LMWF) isolated from Sargassum epiphyllum demonstrated anti-angiogenic activity in bladder cancer which may be related to the inhibition of hypoxia-inducible factors-1(HIF-1) accumulation, transcriptional activity vascular endothelial growth factor (VEGF) secretion, and the migration and invasion in hypoxic human bladder cancer cells (T24) cells HIF-1/VEGF-regulated signaling pathway. Fucoid a was obtained from Sargassum cristaefolium called crude fucoidan preparation (CFP) and purified fucoidan preparation (PFP). PFP, which contained more fucose and sulfate but less uronic acid, demonstrated stronger antioxidant activity and inhibition of human colon cancer (HT-29) proliferation than CFP, which contained less fucose and sulfate but more uronic acid. Fucoid and powder from Sargassum epiphyllum demonstrated inhibition of cell growth activity against human mammary gland epithelial adenocarcinoma (MCF-7 and MDA-MB-231) by 12 and 21%, respectively at 200 μg/ml concentration. Meanwhile, fucoidan exerted no inhibitory effect on the growth of the normal human breast cell line MCF-10A. Fucoid and FP08S2 isolated Sargassum fusiform, displayed significant inhibition of tube formation and migration of human microvascular endothelial cells (HMEC-1) in a dose-dependent manner (Cong et al. 2016[20]). Tuberatolide B(TTB), is a meroterpenoid isolated from Sargassum macrocarpum, exhibited growth inhibition activity against breast cancer cell lines (MDA-MB-231, MDA-MB-453, and MCF7), lung cancer (A549 and H1299), colon cancer (HCT116, SW620, and CT26), prostate cancer (PC3 and DU145), and cervical cancer (HeLa) cell lines through the inducing of apoptotic cell death. Therefore, TTB induction of ROS-mediated apoptosis by inhibiting STAT3 phosphorylation and enhancing of DNA damage. TTB demonstrated no cytotoxicity against normal monkey kidney epithelial cell viabilities (Vero cell lines). A sulfated fucoid an SHPPB2 isolated from Sargassum henslowianum showed significant immune-stimulant activity on gastric rats by promoting body weight, lymphocyte indices, splenocyte proliferation, and anti-inflammatory cytokines production .Sargassum angustifolium hexane, dichloromethane, and butanol partitions demonstrated cytotoxic activity against breast/cancer (MCF-7), cervical cancer (HeLa), and human umbilical vein endothelial cells (HUVEC). Among the three partitions dichloromethane showed the highest activity against MCF-7 than HeLa cell lines with media growthinhibitoryry (IC50) values of 36.18 and 62.52 μg/ml, respectively, on the other hand, it exhibited cytotoxic activity against human umbilical vein endothelial cells (HUVEC) with the median growth-inhibitory value of 88.14 μg/ml. Sargassum boveanum hexane, trichloroethane, chloroform, and butanol fractions demonstrated weak cytotoxicity activity against Hythe ela cell line with IC50values were 150.27, 437.02, 110.37 and 1025 μg/mL, respectively.Polysaccharide fractions (SWP1) were isolated from Sargassum weightier demonstrated a potential suppression of the proliferation of breast cancer cells (MCF7 and MDA-MB- 231) in a dose-dependent manner.SWP1 showed growth inhibition activity against MCF7 cells and MDA- MB-231 cells by 69% and 3%, respectively at 500 μg/ml concentration with IC50 values of 350 μg/ml against both cells lines. These cytotoxic activities were lower than cisplatin with an IC50valuefusee 200 μg/ml against MCF7 and MDA-MB-231 cells.

Anti-inflammatory activity:

Inflammation is a complex process known to be a protective strategy against any injury. Many threats causing inflammation as microbial infections, tissue stress, and certain injuries. Inflammatory response genera generated the recognition of different stimuli by a cellular trans-membrane receptor leads to the transactivation of several important transcription factors such as primarily nuclear factor-kB (NF-kB), mitogen-activated protein kinase pathways (MAPK). The overproduction of pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin (IL)- 1β, and IL-6, and inflammatory mediators including reactive oxygen species (ROS), nitric oxide (NO), and prostaglandin E2 (PGE2), generated by activated inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) by macrophages, plays a crucial role in inflammatory diseases. Sargassum heepiphyllumethanol extract had an inhibitory effect on the atopic allergic reaction via the regulation of inflammatory mediators such s interleukin (IL)-8 and tumor necrosis factor (TNF)-α. The dichloromethane extract of Sargassum full vellum exhibited potent-inflammatory activity through the inhibition of mouse ear edema (79.1%), while indomethacin exhibited 83.7% of ear edema inhibition. Meanwhile, the ethanol extract of Sargassum thunbergii showed anti-edema and anti- erythema activities at about 72.1% and 44.8%, respectively, while the indomethacin showed inhibition activity at about 83.7% and 62.1%, respectively . Hexane and chloroform fractions of Sargassum micracanthum ethanol extract demonstrated significantly inhibited of the production of the pro-inflammatory cytokines(IL-1ß IL-6 and TNF - a) and their mRNA expression by blocking of the NF-B signaling pathway and the possible inhibition of other transcription factors had not been excluded (YOON et al. 2009). Polysaccharides isolated from Sargassum latifolium (E1, E2, E3, E4) demonstrated anti-inflammatory activity through proliferative enhancement of the macrophage two folds more than control cells except for orE3, which had an insignificant decrease in macrophage growth. In addition, E1 and E4 possessed significant inhibition of stimulated NO (74.8 and 44.1%), TNF-α (60.3 and 46.4%), and COX-2 (20 and 18%), respectively (Gamal-Eldeen et al. 2009[11]). Sargassum epiphyllum hot aqueous extract demonstrated a slight immune-stimulating effect through proliferation and IgM secretion in HB4C5 Cells and proliferation and phagocytosis in J774.1 cells (murine macrophage-like cell line) assays. In HB4C5 cells, the highest relative activities of cell proliferation and IgM secretion were (174 and 132%, respectively) at 120 μg/ml. Meanwhile, In J774.1 cells, the maximum relative activities of cell proliferation and phagocytosis were (141 and 147%, respectively) at 80 μg/ml. Sargassum Swartz methanol extract demonstrated similarly maybe better anti-inflammatory activity than indomethacin standard drug. Is extract displayed acute anti-inflammatory activity by reducingcing paw edema in carrageenan-induced paw edema (52.12% at 175 mg/kg and 45.84% at 350 mgwhilehile indomethacin showed 33.145% at 25 mg/kg body weight)? In chronic anti-inflammatory, Sargassum Swartz extract (at175 and 350 mg/kg body weight) significantly reduced the weight of granulomas compared with control and better than prednisolone at 5 mg/kg dose. A novel anti-inflammatory substance Sargachromanol G (SG) was isolated from the chloroform fraction of Sargassum siliquastrum. SG showed a decrease in the pro-inflammatory mediators and cytokines levels after bacterial endotoxin lipopolysaccharide (LPS) stimulation. In addition, it demonstrated particularly suppression thof e production of pro-inflammatory mediators (NO, iNOS, PGE2, and COX-2) and pro-inflammatory cytokines (TNF-α, IL- 1β, and IL-6) in a concentration-

dependent manner (Yoon et al. 2012). Sargassum pallidum aqueous extract demonstrated a stimulating effect on anti-inflammatory cytokines (interleukin (IL-2, L-4, and IL-10) production and inhibiting the production of the pro-inflammatory cytokines (interleukin IL-6 and IL-1β), tumor necrosis factor-alpha (TNF-α) levels. Additionally, it showed suppression of serum, gastric mucosa malondialdehyde (MDA) level and elevate of serum, gastric mucosa glutathione (GSH) level, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) which exerted a significant protective effect against N-methyl-N′-nitro-N- nitrosoguanidine (MNNG)-induced immunity damage and oxidative injury in gastric cancer rats. Sargassum fusiforme polysaccharides (SFPS) showed improving immune response by enhancing the release of tumor necrosis factor (TNF)-α in serum, cytokines secreted by peritoneal macrophages, and splenocytes proliferation in A549-bearing mice. Sargaquinoic acid, isolated from Sargassum siliquastrum, inhibited nitric oxide (NO) production through suppression of the nuclear factor (NF)-κB signaling pathway in RAW264.7 macrophages. Alginic acid isolated from Sargassum wightii showed a significant anti-inflammatory activity through reduction of paw edema volume (approximately 58, 65, and 79 % on days 8, 14, and 21, respectively) which is considered higher than indomethacin (about 39, 47 and 71% on the same days, respectively) along with reduced inflammatory enzymes activities and rheumatoid factor. Furthermore, alginic acid reduced lipid peroxidation and increases antioxidant enzyme activities. Sargachromanol Was isolated from Sargassum siliquastrum chloroform fraction and demonstrated anti-inflammatory activity using lipopolysaccharide (LPS) stimulated RAW 264.7 macrophages. The sargachromanol E significantly decreased the inflammatory response by reducing the pro-inflammatory cyclooxygenase-2, NO synthase, phosphate P38, phosphate ERK1/2, LPS-stimulated tumor-necrosis factor-alpha, interleukin-1 beta, and prostaglandin E2 release(via MAPK pathway). Sargassum cristaefolium polysaccharide(SCP) extract contained three polysaccharides fractions with average M.wts. of 1193.2, 864.4, and 386.1 kDa, respectively showed higher nitric oxide (NO) inhibitory activity than their four acid-degraded polysaccharides with M.ws. values of 106.3, 55.9, 15.4, and 1.9 kDa at 400 μg/ml. Moreover, SCP with M.ws. value of 386.1 kDa had the highest nitric oxide (NO) inhibition activity at 400 μg/ml in LPS-induced RAW264.7 cells than others. Nitric oxide (NO) secretion levels in RAW264.7 cells were 0.78 mm in the negative control, 9.53 mM in LPS-induced cells, and 2.47 mM (74.1% inhibition) at 400 μg/ml of SCP. In addition, SCP suppressed the LPS-induced MAPK and NF-kB signaling pathway in a dose-dependent manner (G. Wu et al. 2015). Fucan (SV1), sulfated polysaccharides obtained from Sargassum Vulgare,p ro moted a significant edema reduction in carrageenan-induced paw edema at a concentration of 10, 3,0, and 50 mg/kg with a significant difference related to carrageenan and no significant difference comparable to the saline negative control(Dore, Guerra, et al. 2013). Polysaccharides isolated from Sargassum horneri (SP) and their fractions F1 and F2 demonstrated potent anti-inflammatory activity against LPS-induced inflammation through suppression of the TNF-α secretion levels and inhibiting TNF-α/IL-10 ratio in a preventive and repair manner. Generally, F 1, at a high dose, of 200 μg/ml, exhibited higher anti-inflammatory activity against LPS-stimulated inflammation on RAW264.7 macrophages than F2 and SP (Wen et al. 2016). Crude polysaccharides from Cellules enzymatic digestion(CCP) of Sargassum horneri demonstrated the highest nitric oxide (NO) inhibition activity in lipopolysaccharides (LPS)-stimulated RAW 264.7 in vitro with IC50= 95.7μg/ml (in a dose-dependent manner) and suppressed prostaglandin (PGE2) secretions through inhibiting the secretion of the inducible nitric oxide synthase(iNOS) and cyclooxygenase-2(COX-2) as well as pro-inflammatory cytokines, including tumor necrosis factor (TNF)-α and interleukin (IL)-1β, compared to the only LPS-treated cells. Moreover, CCP inhibited the activation of the nuclear factor (NF)-κB, and mitogen-activated protein kinases (MAPKs) signaling pathway by down-regulating the phosphorylation of p38 and ERK and the translocation of NF-κB p50 and p65 protein that the o nucleus (Kapuge et al. 2017). Sargassum serratifolium ethanol extract (ESS) demonstrated down-regulation of melanin synthesis in melanocyte-stimulating hormone (α-MSH) -stimulated mouse melanoma cells (B16F10) with an IC50 value of 2.72 μg/ml. Additionally, sargahydroquinoic aid, sargachromenol, and sargaquinoic acid were isolated from the lipophilic fraction of ESSand displayed suppression of melanin production activity with IC50 values of 2.21, 51, and 1.97 μg/ml respectively. Sargachromenol (SCM), was isolated by a recycled high-performance liquid chromatography (HPLC) of Sargassum serratifolium ethanol extract, exhibited prevention of the vascular inflammation by suppression of nuclear factor (NF-κB) activation and via its intrinsic antioxidant activity in tumor necrosis factor (TNF)-α- stimulated human umbilical vein endothelial cells (HUVECs). Polysaccharide fractions isolated from Sargassum horneri cellular enzymatic extract chare characterized by different molecular weights. The f4 (M.wt >30 kDa) fraction demonstrated the superior nitric oxide (NO) inhibition activity with IC50 = 87.12 μg/ml compared to the other fractions in lipopolysaccharides (LPS)-stimulated RAW 264.7 in vitro. Additionally, f4 inhibited the production of prostaglandin E2, and pro-inflammatory cytokine via down-regulating of the nuclear factor-κB signaling pathway. Furthermore, f4 demonstrated the potential to down-regulate lipopolysaccharides (LPS)-induced toxicity, cell death, and nitric oxide (NO) production levels in lipopolysaccharides (LPS)-induced mortality, heart-beating levels, cell death rates, and against LPS-induced nitric oxide (NO) production in zebrafish embryos (in vivo). They have concluded that fucose-containing high molecular weight (>30 kDa) sulfated polysaccharide has the potential to act as an anti-inflammatory agent under in vitro and in vivo conditions. Meroterpinoid-rich fraction of Sargassum serratifolium ethanol extract (MES) showed significant prevention of vascular inflammation via suppressing chemokines in serum(in vitro) and a handling adhesion molecules and COX-2 in the aortic tissues of high cholesterol diet-fed mice(in vivo) . The isolated meroterpenoids had inhibitory effects on the adhesion molecules. MES, sargachromenol, and sargaquinoic acid showed intracellular adhesion molecule- 1(ICAM-1) inhibitory activity with IC50 values of 7.25 μg/mL, 22.04, and 7.75 μM, respectively, and the IC50 of vascular cell adhesion molecule inhibition(1VCAM-1) of MES, sargachromenol, and sargaquinoic acid were 6.67 μg/mL, 25.53 and 8.19 μM, respectively. In particular, sargahydroquinoic acid showed potent inhibition of VCAM-1 (IC50, 0.78 μM), but was not effective in the inhibition of ICAM-1 expression in tumor necrosis factor (TNF)-α-induced human umbilical vein endothelial cells (HUVECs), suggesting selective effects of VCAM-1. A grasshopper ketone(GK), Isolated from the n-hexane fraction of Sargasfull vellumllum ethanol extract, demonstrated anti-inflammatory properties via the inhibition of the nuclear factor (NF)-κB, and mitogen-activated protein kinases(MAPKs) pathways, which are correlated to the attenuation of cytokine secretion, demonstrated that n-hexane fraction Sargassum serratifolium showed 1.6-time and 1.8-time higher cell adhesion molecules suppression as intracellular adhesion molecule-1 and vascular cell adhesion molecule-1(ICAM-1 and VCAM-1) production, respectively than ethanol extract. While e n-butanol and water fractions showed no inhibited activity. Additionally ethyl-acetate fraction showed selectively higher inhibitory activity for intracellular adhesion molecule- 1(ICAM-1) production.

Antioxidant activity:

Antioxidant activities of various Sargassum species were conducted by several methods including lipid peroxidation and radical scavenging activity. Sargassum horneri ethanol extract showed the highest potent lipoxygenase inhibition activity about 80% inhibition followed by Sargassum macrocarpum Sargassum siliquastrum ethanol extract. Additionally, Sargassum siliquastrum aqueous extract demonstrated the most effective DPPH radical scavenging activity followed by Sargassum macrocarpum and Sargassum thunbergii. Sargassum micracanthum methanol extract demonstrated potent lipid peroxidation inhibitory activity with an IC50 value of 0.77μg/ml more than vit. E and vit. C (IC50 values 34 and 28 μg/ml, respectively). Additionally, their isolated plastoquinones compound 1, 2, and chrome derivatives3 demonstrated strong lipid peroxidation inhibitory effect with IC50 values of 0.11, 1.0, and 0.28μg/ml, respectively, which were approximately ten to hundredfold stronger than the positive controls. Contrary, Sargassum micracanthum methanol extract and their isolated compounds 1, 2, and 3 showed week to moderate DPPH radical scavenging activity with IC50 values of 34, 11, 400, and 10.7 μg/ml, respectively lower than commercial antioxidants (Vit. E and vit. C) With IC50 values of 10.0 and 2.5 μg/ml, respectively. Sargassum ringgoldianum, Sargassum confusum, Sargassum expense, Sargassum epiphyllum, and Sargassum micracanthum had anti-oxidative activity against the superoxide anion radical and hydroxyl radical scavenging activity. Among them, Sargassum ringgoldianum 50% ethanol extract had the most potent scavenging activity against the superoxide anion radical (88.4%) and hydroxyl radical(78.8%) with an IC50 value of 5.1 mg/ml against the superoxide anion radical scavenging activity due to its highest content of phenolic compounds, 383.0 mg catechin equivalents/g of dry extract. Phlorotannin was isolated from the ethyl acetate fraction from Sargassum ringgoldianum demonstrated the strongest superoxide anion radicals scavenging activity with an IC50 value ue 1.0 mg/ml, whiwasere approximately five times stronger than catechin (IC50 value of 4.6 mg/ml). The polysaccharide fraction of Sargassum fulvellulm exhibited high DPPH radical scavenging activity (> 90% at 10mg/ml) but not more than α –tocopherol and butylated hydroxytoluene (BHT) at 2 mg/ml. In addition, Sargassum fulvellulm polysaccharides showed good hydrogen peroxide scavenging activity approximately 70-80%. Moreover, this polysaccharide showed poor superoxide (about 30%) and hydroxyl radical scavenging activity (about 10%) comparable to α –tocopherol and BHT(about 50 and 55% respectively). While the nitric oxide scavenging activity of the polysaccharide was more active (70%) than that of α –tocopherol and butylated hydroxytoluene (BHT) (about 28, 30% respectively). Sargassum dentifolium ethanol and dichloromethane extract demonstrated high free radical scavenging activity 82 and 86% at 100 μg/ml, respectively comparable to Silymarin, reference control, 92%. In addition, Sargassum dentifolium ethanol and dichloromethane extract demonstrated lipid peroxidation inhibition activity of 68.50 and83.44% at 1.0 mg/ml, respectively comparable to Silymarin 96.50% . Hydro-methanolic (50%) extract of Sargassum mangarevense demonstrated a great DPPH radical scavenging antioxidant activity (84%).The antioxidant activity of the main crude polysaccharides (SP-1, SP-2, and SP-3) obtained from Sargassum pallidum represented weak DPPH free radical-scavenging activity at 3.8 mg/ml (17.8%, 19.1%, and 10.2%, respectively). While, SP-1-1, SP-1-2, SP-2-1and SP-2-2, polysaccharide fractions purified by DEAE-52 anion-exchange chromatography, exhibited lower antioxidant activities at 5mg/ml than the crude polysaccharides (3.55, 3.26, 3.60, and 4.94%, respectively). The DPPH radical scavenging radical antioxidant activity of the polysaccharides (E1, E2, E3, and E4), isolated from Sargassum latifolium, showed no antioxidant activity due to the high SC50 (half-maximal scavenging concentration) values of E1, E2, E3, and E4 were 205.61, 234.7, 139.32, and 286.53 μg/ml, respectively, while the SC50 value of ascorbic acid was 7.85 μg/ml. Sargassum epiphyllum aqueous extract demonstrated a significant DPPH radical scavenging activity, superoxide anion scavenging, ferrous chelating activity, and ferric reducing power activity with IC50 values of 1.58, 2.41, 2.07, and 0.41 mg/ml, respectively. Heterofucans (SF-0.5v, SF-0.7v, SF-1.0v, SF-1.5v, and SF-2.0v) isolated from Sargassum filipendula demonstrated no to moderate total antioxidant capacity (TAC), scavenging hydroxyl and superoxide radicals, reducing power and ferrous chelating, except SF-1.0v which showed the most significant antioxidant activity with 90.7 ascorbic acid equivalents in a total antioxidant capacity test and similar activity to vitamin C in a reducing power assay. Hydro-alcohol and chloroform fractions of Sargassum swartzii represented the highest ferric reducing power activity (FRAP) 73.92, 55.32 mmol FeII / 100 g dried sample, respectively. While, hexane fraction showed moderate antioxidant activity (19.62 mmol FeII /100g dried sample) and the ethyl-acetate fraction showed the lowest antioxidant activity (0.56 mmol FeII / 100 g dried sample). Polysaccharides isolated from Sargassum graminifolium aqueous extract exhibited dose-dependent superoxide anions scavenging and DPPH radicals scavenging activity with IC50= 1.9 and 0.6 mg/ml, respectively. Sargassum siliques dichloromethane fraction showed the highest hydroxyl radical scavenging activity, nitric oxide scavenging activity, and hydrogen peroxide scavenging activity with IC50value of 0.28, 0.29, and 2.27 mg/mL, respectively comparable to ascorbic acid. Sargassum muticum methanol extract (SMME) displayed 75.32 ± 11.36mmol, Fe II per 100 g dried plant ferric reducing antioxidant power (FRAP) activity. Intact Fucoidan(IF) isolated from Sargassum tenerrimum demonstrated a significant DPPH radical scavenging, superoxide anion scavenging, and total antioxidant assay(approximately 83, 81, 41%, respectively) rather than other fucoidan fractions (F1, F2, and F3). Methanol extract of Sargassum polycystum showed significant DPPH (2, 2- diphenyl- 1-picryl hydrazyl) value 0.14mg Ascorbic acid/g extract and ABTS (2, 2-Azino-bis3-ethylbenzthiazoline-6-sulfonic) value of 0.03mg Trolox/g extract antioxidant activity. The ferric reducing power (FRAP) of methanol extract was 4.618 mg Fe^{2+}/g DW. Among fractions (F1,F2,F3, and F4), obtained through column chromatography, F2 showed the highest anti-oxidant potency with DPPH value 16.567mg Ascorbic acid/g extract; ABTS value 4.075 mg Trolox/g extract ; FRAP value175.481± 16.206 mg Fe^{2+}/g extract Sargassum polycystin, Sargassum aquifolium, Sargassum ilicifolium water, methanol (50%), ethanol (75%), Viscozyme, and Protamex enzymatic extract demonstrated weak DPPH radical scavenging activity compared to the standards, BHA and BHT. On the other hand, Sargassum ppolycystinaqueous extract demonstrated the highest reducing power activity with 43.5 ± 0.7 μM Eq Fe^{2+}, followed by Sargassum aquifolium Viscozyme enzymatic extract with 33.2±2.5 μM Eq Fe^{2+} comparable to vitamin C with reducing power 58.1 ± 0.7 μM Eq Fe^{2+}. On contrary, Sargassum ilicifolium ethanol (75%) extract demonstrated inferior reducing power activity 7.9 ± 1.2 μM Eq Fe^{2+} .The DPPH radical scavenging activity of ethyl acetate fraction obtained from Sargassum fusiforme ethanol extract showed the strongest radical scavenging activity than the crude ethanol extract (30%),1-butanol fraction, and aqueous residue. Additionally, the ethyl acetate fraction of Sargassum fusiforme exhibited higher DPPH radical scavenging activity than Trolox (a synthetic antioxidant analogous to vitamin E), and commercially available tea polyphenols with IC50 14.61, 15.62, and18.42 μg/ml, respectively. Total phlorotannin content was found the highest in the ethyl acetate fraction with a value of 88.48 mg of phloroglucinol equivalents /100 mg of extract, then the crude ethanol, 1-butanol

fraction, and aqueous residue where their total phlorotannin compounds values were 13.52,20.67, and 6.96 mg of phloroglucinol equivalents/100 mg of extract, respectively. Sargassum tenerrimum aqueous extract demonstrated the highest total antioxidant activity, total phenol content, and FRAP activity. Moreover, Sargassum tenerrimum aqueous and methanol extracts exhibited the strongest DPPH radical scavenging activities with IC50 0.76 and 0.78 mg/ml.

Anti-viral activity:

Infectious diseases cause one-third of all deaths around the globe. Although the last decade has yielded significant advances in the treatment of infectious diseases, new therapies for viral, fungal, bacteria, rial and parasitic infections are needed (Martinez et al. 2005). Fucan sulfated polysaccharide was isolated from hot water extract of Sargassum horneri and showed potent antiviral activity against herpes simplex virus type1, human immunodeficiency virus type 1, and human cytomegalovirus with IC50 values of 1, 1.2, and 3.3 μg/ml, respectively compared to dextran sulfated with IC50 values of 1.9, 2.8 and 2.9 μg/ml, respectively. Two plastoquinones and chromene-3 compounds were obtained from Sargassum micracanthum methanol extract and demonstrated potent antiviral activity against only human cytomegalovirus with a selectivity index(SI) of more than 10, for plastoquinone2 and a chromene whereas plastoquinone1 SI approximately of 4. Crude sulfated polysaccharides(SP) and their fractions (SP-I, SP-II, and SP-III, I isolated from Sargassum latifolium, showed antiviral activity against herpes simplex virus type-1 and hepatitis A virus. SP-III had the highest inhibition activity against HSV-1 and HAV (81 and 85% at 40 μg/ml, respectively). They reported that the antiviral activity related to the higher molecular weights and sulfate contents (Mohsen et al. 2007). The aqueous extract of Sargassum epiphyllum exhibited moderate anti-herpes simplex virus1 and 2 activity (EC50 =19.1 and 12.5 μg/ml, respectively) but its selective index (SI) was low (6 and 10) due to the high cytotoxicity on Vero cells (CC50=125 μg/ml). They reported that its antiviral activity was related to its cellular toxicity to the host cells (Wang et al. 2008). Anti-viral activity of polysaccharides (alginic acid and fucoidan obtained from Sargassum tenerrimum and their chemically sulfated derivatives (BS and CS)) against herpes simplex virus type 1 (HSV-1) demonstrated that fucoidan has a higher activity than alginic acid with IC50 15 and 1.4 μg/ml, respectively. Additionally, the chemically sulfated fucan (CS) is the most potent anti-HSV-1 compound with IC50 0.5 μg/ml which is considered 30-fold more active than fucoidan (C) against HSV-1. The sulfated water-soluble polysaccharides isolated from Sargassum naozhouense showed strong antiviral activity against herpes simplex virus type 1 strain F (HSV-1) at ≥12.5 μg/mL (EC50 = 8.92 μg/mL) comparable to acyclovir (ACV) displayed more than 75% cellular protection at 20 μg/mL with selectivity index more than 22. Crude fucoidan fraction (CFF), and their fractions (FF1 and FF2) isolated from Sargassum Swartz exhibited a significant reduction of human immunodeficiency virus type 1 at a concentration of 25 μg/ml. FF2 demonstrated the maximum inhibition activity of 95.6%, related to Azidothymidine (positive control) 97.2% inhibition activity at 10 μM. Moreover, FF2 demonstrated maximum inhibition activity of 78.9% at 25 μg/ml against HIV, whereas CFF and FF1 showed minimal inhibitory activity (54.9 and 67.9%, respectively) comparable to azidothymidine (95.5%). Polysaccharides isolated from Sargassum fluitans exhibited significantly higher antiviral activity against herpes simplex virus type-I with EC50 of 42.8 μg/ml, comparable to acyclovir EC50 of 15.4 μg/ml with no cytotoxicity against normal Vero cell lines (CC50 >200 μg/mL). Only Neutrase and Alcalase Sargassum muticum protease enzymatic extract demonstrated anti-viral activity with EC50 of 430.1 ± 16.3 and 225.1±23.3 μg/ml respectively, meanwhile, the positive control, Zovirax, EC50 was 0.7±0.3 μg/ml rather than other Sargassum muticum enzymatic extract, with no cytotoxicity on Vero cell lines CC50>500 μg/ml(Maya Puspita et al. 2017[46, 47].

Anti-microbial activity:

Sargassum dentifolium dichloromethane and ethanol (70%) extracts showed antimicrobial activity against Bacillus subtilis, Escherichia coli, Staphylococcus albus , Streptococcus fuels, Candida albicans (inhibition zone in a range of 10-12mm), and no activity against Aspergillus flavus (Shanab 2007). Ethanol and aqueous extracts of Sargassum mangarevense demonstrated antibacterial activity against only Staphylococcus aureus (12.5mm and 9.5mm inhibition zone, respectively) with no activity shown against Escherichia coli, Pseudomonas aeruginosa, Candida albicans and Aspergillus niger. Sargassum wightii methanol extract showed strong growth inhibition against Escherichia coli and Aeromonas hydrophila (18 and 15mm, respectively) compared to ampicillin standard (24 and 22 mm, respectively). Moreover, the methanol extract demonstrated mild activity against Bacillus subtilis and Pseudomonas aeruginosa (12 mm, against both) related to the standard (28 and 16, respectively), and weak activity against Enterococcus faecalis, Klebsiella pneumonia, Proteus Vulgaris, Shigella flexneri and Staphylococcus aureus (6,10, 8, 10, and 9mm, respectively)comparable to the ampicillin. Antibacterial and antifungal activities of different extracts of Sargassum tenerrimum showed different activities against the different human pathogens, but it was concluded that the methanol extract showed the best activity among other extracts. Sargassum wightii methanol extract showed the highest inhibition zones (10 mm) against Rhizoctonia solani, Aspergillus niger, and Candida albicans, followed by diethyl ether extract against Candida albicans (8mm) and aqueous extract against Rhizoctonia solani (8 mm). The lowest inhibition zones (2 mm) exhibited in acetone extract against Fusarium udum, Candida albicans, methanol extract against Botrytis cinerea, chloroform extract against Candida krusei, Aspergillus niger, hexane extract against Aspergillus flavus, water extract against Fusarium udum, Candida krusei. Ethyl acetate extract of Sargassum wightii displayed no activity against all tested pathogens. Sargassum polycystin methanol extract demonstrated the highest bactericidal inhibitory activity against Propionibacterium acnes with a minimum inhibitory concentration (MICof) of 1.25 mg/ml and minimum bactericidal concentration (MBC) of 2.50 mg/ml comparable to gentamycin and ampicillin < 0.31 mg/ml for MIC and MBC for both STD than hexane and ethyl acetate extracts. The methanol extract fractions (F1–F4), F1 displayed the highest inhibition activity against P. acnes (MIC= 0.25 mg/ml, MBC=0.50 mg/ml) followed by F2 (MIC= 0.50 mg/ml, MBC=2.00 mg/ml). Moreover, F1 displayed the highest Propionibacterium acnes lipase inhibition 71.90% when compared to tetracycline (reference drug) 97.99%. Low molecular weight phlorotannins (LMPs) from Sargassum thunbergii demonstrated significant antibacterial effect against Vibrio parahaemolyticus by inhibition of the tested bacteria growth, preventing cell division, damaging the cell membrane and cell wall through increased membrane permeability, and fluidity leading to leakage of cytoplasm and disintegration of cell. Sargassum muticum enzymatic extracts demonstrated no to weak antibacterial activity against Staphylococcus hominis, Bacillus subtilis, Pseudomonas aeruginosa, and Escherichia coli in the agar diffusion method when compared to standard drugs phosphomycin, ampicillin, and streptomycin antibiotics which had substantial antibacterial. Antibacterial activity of solid-liquid extraction (SLE) and enzyme-assisted extraction(EAE) of Sargassumpolycystinm, Sargassum aquifoliu,m, and Sargassum ilicifolliu against Bacillus

subtilis, Pseudomonas aeruginosa and Escherichia coli demonstrated that the tested bacteria were sensitive only to SLE methods That' s means that the enzymatic extracts represented no inhibition activity against the bacterial growth. It was assumed that the sugar contained in the enzymatic extracts might provoke growth instead of inhibiting the bacteria. Sargassum boveanum methanol: ethyl-acetate (1:1) extract demonstrated no growth inhibition activity against Mycobacterium tuberculosis (M. tuberculosis) at 50 µg/ml comparable to rifampicin, streptomycin, isoniazid, ofloxacin, and ethambutol.

Hypolipidemic Activity

Sargassum polycystin extract showed some protective activity against the hyperlipidemia induced during toxic hepatitis in rats. They suggested that anti-hyperlipidemic activity is due to the presence of sulfated polysaccharides. ulfated polysaccharides (SPS) obtained from Sargassum wightii demonstrated a reduction in serum lipid levels and restored the abnormalities of inflammatory complications of hypercholesterolemia include plasma tumor necrosis factor-alpha (TNF-alpha), C-reactive protein (CRP), fibrinogen, inducible nitric oxide synthase (iNOS), nitric oxide (NO), cyclooxygenase (COX-2) and lysosomal enzymes . Sargassum polycystin ethanol and aqueous extract showed lipid reduction levels in the diabetic type2 rat model after 22 days of treatment. Sargassum polycystin ethanol and aqueous extract (at doses 300 and 150 mg/kg) decreased total blood cholesterol, triglycerides, and lipoprotein-cholesterol comparable to the metformin standard and the diabetic control group . Fucoidan isolated Sargassum henslowianum demonstrated hypolipidaemic activity at the dose of 100 mg/kg P/day, through lowering cholesterol compared with the high-fat diet (HFD) group. The triglyceride and LDL-cholesterol decreased (6.35% and 18.74%, respectively) compared with the high-fat diet mice group . Phytosterols isolated from Sargassum fusiforme demonstrated a strong cholesterol-lowering agent through induced higher expression levels of liver X receptor (LXR) target genes including key players in reverse cholesterol transport. Among them, 24(S)-saringosterol had a selective LXRβ agonist activity . A meroterpenoid-rich fraction of Sargassum serratifolium ethanol extract (MES) dietary supplementation exhibited significant protective effects on lipid accumulation in the liver, epididymal, and subcutaneous fat tissues through regulation of β-oxidation, lipolysis, cholesterol synthesis, lipogenesis, and hepatic lipid synthesis. MES decreased the high-fat diet-induced obesity and hepatic steatosis without changes in food intake (Kwon et al. 2018).

Anticoagulant activity:

Sargassum, an acid-extractable, water-soluble polysaccharide, isolated from Sargassum linoleum demonstrated high anticoagulant activity, hence the time required for the blood plasma clotting was 72 h, compared to 1 h for heparin (standard solution) (Abdel-Fattah et al. 1974) [1]. Six fucoid an fractions (F1-F6) isolated from Sargassum stenophyllous demonstrated week anticoagulant activity. In particular, F5 and F6 showed higher activated partial thromboplastin time (APTT) and thrombin time (TT) than those of F1 to F4, despite the that these activities are low in comparison to heparin (APTT and TT times higher than 120 and 100 s at 4 and 5 mg/mL, respectively). Sarg A, a polysaccharide isolated from Sargassum stenophyllous demonstrated weak anticoagulant activity via increasing thrombin time (TT) significantly to 23.34 and 44.25 s at 0.5 and 5 mg/ml, respectively related to heparin(reference drug) thrombin time (TT) at approximately 120 s at 5µ g/ml . A sulfated polysaccharide (ASP) isolated from the fermented Sargassum full vellum demonstrated lower anticoagulant activity than heparin due to its low molecular weight. In inactivated partial thromboplastin time (APTT) and prothrombin time (PT) assays, ASP at 180 mg/ml showed prolonged coagulation time, whereas no clotting inhibition was observed in thrombin time (TT) assays at the same concentration. While the positive controls, heparin at 60 mg/ml prolonged the coagulation time over 1,000 s in both APTT and TT assays, and prolonged coagulation time to19.7 s in PT assay. All hetero furans obtained from Sargassum filipendula showed no anticoagulant activity when tested by activated partial thromboplastin time (PTT) and prothromb in time (PT) Assays. Fucan (SV1), sulfated polysaccharides isolated from Sargassum Vulgare, exhibited a significant anticoagulant activity. SV1 showed a maximum increase in clotting time, examined via activated partial thromboplastic time (aPTT, intrinsic coagulation pathways) at 50 and 100 µg/ml. SV1 and Purified SV1 showed no anti-clotting effect when tested by the prothrombin time (PT, extrinsic coagulation pathways) test. PSV1 fraction showed no anticoagulant effect. Moreover, SV1 demonstrated strong antithrombotic activity in vivo equal to heparin when used at ten time's higher concentration (10µg/g) meanwhile, this activity was reduced at 5µg/g comparable to the control. Sargassum fusiform polysaccharides (SFP) and their low-molecular-weight SFP (LSFP) demonstrated prolonged clotting time idose-dependent manner. SFP (sulfate 24.73%, MW 227 kDa) showed the highest anticoagulant activity.

Anti-diabetic activity:

Crude extracts of Sargassum siliquosum and Sargassum polycystin showed efficient angiotensin-converting enzyme inhibitory activity (IC50 values 0.42 and 0.03 mg/ml, respectively) comparable to gallic acid standard (IC50 value 0.52 mg/ml). Meanwhile, fucoxanthin-rich fractions of Sargassum siliquosum and Sargassum polycystin showed inferior activity than that of crude extracts and gallic acid (IC 50 0.94 and1.53 mg/ml, respectively) In α- Amylase inhibitory assay, the crude extracts of Sargassum siliquosum and Sargassum polycystin displayed the most effective activity against α- amylase inhibitory assay with IC50 0.58 mg/ml for both when compared to reference drug Voglibose (IC50value 0.61mg/ml), while fucoxanthin-rich fractions of Sargassum siliquosum and Sargassum polycystin had significantly higher IC50 values(0.68 and 0.71 mg/ml, respectively). On the contrary, the α-glucosidase inhibitory activity of fucoxanthin-rich fractions of Sargassum siliquosum and Sargassum polycystin showed higher activity (IC50 0.50and 0.53 mg/ml, respectively) than that of the crude extracts of Sargassum siliquosum and Sargassum polycystin (IC50 0.57and 0.69 mg/ml, respectively) comparable to the reference drug. Sargassum polycystin ethanol (150 and 300 mg/kg dose) and aqueous extract (only at300 mg/kg dose) demonstrated particular blood glucose reduction and glycosylated hemoglobin (HbA1C) (32, 30, and31%) comparable to the metformin standard (23%). Sargassum polycystin hypoglycaemic activity is caused by increased insulin sensitivity for glucose utilization in insulin-target tissues, not by enhancing insulin secretion.

Conclusion

Seaweed e considered a r a renewable reservation with enormous potential for the production of an unlimited variety of bioactive compounds due to their wide ecological diversity company an sensitive adaptation environmental conditions. In the present review, we systematically summarized the pharmacological effects of the genus Sargassum.

As aan an antimicrobial bialrobialntioxidant, and anticancer antidiabetic anti-inflammatory, hypolipidemic, anticoagulant, and antiviral activities, sargassum species may be considered as future potential medicines for many illnesses.

Acknowledgment

The authors are grateful to The Regional Center for Mycology and Biotechnology, Al-Azhar University, Cairo, Egypt.

Conflict of Interest

The authors declare that they have no competing interests.

References

1. Liu L, Heinrich M, Myers S, Dworjanyn SA (2012) 'Towards a better understanding of medicinal uses of the brown seaweed Sargassum in Traditional Chinese Medicine: A phytochemical and pharmacological review'. J Ethnopharmacol 142:pp. 591–619.
2. Gloria NDA, Kweku AA, deGraft-J (2016) 'Preliminary investigation into the chemical composition of the invasive brown seaweed Sargassum along the West Coast of Ghana'. African Journal of Biotechnology, 15:pp. 2184–2191.
3. Yoshida T (1989) 'Taxonomy of Sargassum'. The Korean Journal of Phycology 4: pp. 107–110.
4. Mon-Oo H, Soe-Htun U (2014) 'The Morphotaxonomy and Phytogeographical Distribution of the Genus The Morphotaxonomy and Phytogeographical Distribution of the Genus Sargassum C . Agardh (Fucales Phaeophyta) from Kampani Coastal Areas'. Mawlamyine University Research Journal 6:pp. 143–168.
5. Fitton JH (2003) 'Brown marine algae: A survey of therapeutic potentials'. Alternative & Complementary Therapies, 9, pp. 29–33.
6. Fujihara M, Nagumo T (1992) 'The effect of the content of d-mannuronic acid and l-guluronic acid blocks in alginates on antitumor activity. Carbohydrate Research 224: pp. 343–347.
7. Numata A, Kanbara S, Takahashi C, Fujiki R, et al. (1992) 'A cytotoxic Principle of the Brown Alga sargassum tortilla: and Structures of Chromenes'. Phytochemistry 31:pp. 1209–1213.
8. Zhuang C, Itoh H, Mizuno T, Ito, H (1995) 'Antitumor Active Fucoidan from the Brown Seaweed, Umitoranoo(Sargassum thunbergii).' Biosci Biotechnol Biochem 59:pp. 563–567.
9. Dias PF, Siqueira JM, Vendruscolo LF, Neiva TDJ, et al. (2005) 'Antiangiogenic and antitumoral properties of a polysaccharide isolated from the seaweed Sargassum stenophyllum.' Cancer Chemother Pharmacol 56:pp. 436–446.
10. Torres, MR, Sousa APA, Silva Filho EAT, Melo DF, et al. (2007) 'Extraction and physicochemical characterization of Sargassum Vulgare alginate from Brazil.' Carbohydrate Research, 342, pp.2067–2074.
11. Gamal-Eldeen AM, Ahmed EF , Abo-Zeid MA (2009) 'In vitro cancer chemopreventive properties of a polysaccharide extract from the brown alga, Sargassum latifolium.', Food and Chemical Toxicology, 47(6), pp. 1378–1384.
12. Zandi K, Ahmadzadeh S, Tajbakhsh S, Rastian Z, F. Yousefi, et al. (2010) 'Anticancer activity of Sargassum oligocystum water extract against human cancer cell lines.' Eur Rev Med Pharmacol Sci 14: pp. 669–673.
13. Ermakova S, Sokolova R, Kim SM, Um BH, et al (2011) 'Fucoidans from brown seaweed sargassum hornery, Colonia cava, costars costata: Structural characteristics and anticancer activity. Applied Biochemistry and Biotechnology, 164(6), pp. 841–850.
14. Costa LS, Fidelis GP, Telles CBS, Dantas-Santos N, Rafael Barros Gomes Camara, et al. (2011) 'Antioxidant and antiproliferative activities of heterofucans from the seaweed Sargassum filipendula.' Mar Drugs 9:pp. 952–966.
15. Chen X, Nie W, Yu G, Li Y, et al. (2012) 'Antitumor and immunomodulatory activity of polysaccharides from Sargassum fusiform. Food Chem Toxicol 50: pp. 695–700.
16. Suresh V, Anbazhagan C, Thangam R, Senthilkumar D, Wisln M, et al. (2013) Stabilization of mitochondrial and microsomal function of fucoidan from Sargassum plagiophyllum in diethylnitrosamine induced hepatocarcinogenesis. Carbohydr Polym 92:pp. 1377–1385.