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Review Article

A Review Study on the Biomedical Potentials of Seaweeds Species

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ABSTRACT

Seaweeds have long been used in Asian nations as food and medicine due to their abundance of bioactive compounds that can treat diseases like cancer, inflammation, oxidative stress, allergies, diabetes, thrombosis, obesity, and hypertension. Algae extracts have been found to improve the activity of killer cells through various processes, including activation of the non-specific immune system, inhibition of cell growth, and induction of terminal differentiation and apoptosis. Endothelial cells exhibit greater sensitivity to inhibitors in cytotoxic and biomedical research due to their rapid genetic stability and high rate of proliferation. Compounds obtained from natural products have potential as anti-angiogenic, antioxidative, and anti-microbial agents due to their promising activities in overcoming the adverse effects posed by synthetic drugs on human health. Seaweed extracts contain various secondary metabolites, including polysaccharides, lipids, fatty acids, sterols, phenolic compounds, carotenoids, lectins, alkaloids, and terpenes, making them potential therapeutic agents largely screened for the development of antimicrobial drugs. Antioxidants are essential for health, with numerous health benefits including anti-aging and anti-inflammatory properties. Research is rapidly progressing to understand the antioxidant properties of natural foods, including seaweeds. Seaweed extracts have shown dose-dependent free radical scavenging effects, inhibiting lipid peroxidation and glutathione-S-transferase activities. Polysaccharides isolated from various seaweed species have shown anti-proliferative effects on human leukemia and Ca9-22 oral cancer cell lines. Marine algae are rich in antioxidants and have potential applications in pre-clinical research for drug development, treating various ailments and as food preservatives. Further investigation is required to determine the most effective agents.

Keywords: Biomedical, Seaweed, Disease, Anti-microbial, Anti-cancer.

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INTRODUCTION

A variety of ailments and disorders have been discovered and confirmed in numerous publications, and the list keeps growing. At least 2 million illnesses and 23,000 fatalities caused by antibiotic-resistant organisms occur each year, according to the Center for Disease Control (CDC).[1] Seaweeds have long been utilized as both food and medicine in Asian nations. According to[2] this is due to their abundance of bioactive compounds that can be utilized to treat diseases like cancer, inflammation, oxidative stress, allergies, diabetes, thrombosis, obesity, and hypertension as well as being rich in a variety of biomolecules as dietary sources.

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According to[2] an antioxidant study involving the use of algae improves the activity of killer cells through a variety of processes, including activation of the non-specific immune system, inhibition of cell growth and the intricate process of angiogenesis, induction of terminal differentiation and apoptosis, and many others, all of which are factors that can help algae extracts inhibit the process of carcinogenesis. Endothelial cells exhibit a greater sensitivity to inhibitors in cytotoxic and biomedical research because of their rapid genetic stability and high rate of proliferation. Clinical trials are being conducted on a large number of antiangiogenic medications, however there is a significant risk that they could have negative effects. Therefore, compounds obtained from natural products have potentials as anti-angiogenic, antioxidative and anti-microbial agents due to their promising activities in overcoming the adverse effects posed by the synthetic drugs on human health.[2]

The medications that are now used to treat cancer are also harmful and expensive because they affect both cancer cells

and healthy cells. Hence, identifying new, potent, and non-toxic chemicals from natural sources is more important than ever. As reported by,[3] marine macroalgae (seaweeds) have a variety of bioactive substances that may be used as functional components in products that are intended to improve both human and animal health. While bioactive chemicals are being screened, marine species are receiving greater attention nowadays. Despite this, seaweeds have been surprisingly well chosen as one of the main sources of biologically active ingredients because of their immense diversity and history as safe traditional Asian foods for a long time.

Seaweeds contain various secondary metabolites ranging from polysaccharides and derived oligosaccharides like alginates, carrageenans, galactans, laminarians, fucans and ulva,[4,5] lipids, fatty acids and sterols like phospholipids, glycolipids, carboxylic acids, fucosterol,[6] phenolic compounds,[7] carotenoids,[3] lectins,[8] alkaloids[9] and terpenes[10] which makes them become therapeutic agents largely screened for the development of antimicrobial drugs.[11] This review aims to reaffirm the significance of seaweeds as prospective biochemical agents and evaluate the various fields in which their biochemical use has been investigated.

Antimicrobial

Due to the ongoing spread of disease-causing organisms that are resistant to antibiotics, there is an increasing demand for alternative sources. Seaweed and their extracts are among the many photosynthetic species that have been identified as potential antibacterial agents.[12]

Investigated the antimicrobial activity of Sargassum sp. crude extract against 3 pathogenic bacteria, namely *S. aureus, B. subtilis*, and *E. coli*. Among the 3 strains tested, the extract of *Sargassum* sp. was more effective against *B. subtilis* and *E. coli*, at 4000 µg/100 µL concentration. The result shows that the methanol extract of *Sargassum* sp. possesses a strong antimicrobial activity against both gram-positive and gram-negative, bacteria (*E. coli*) when compared with Ampicillin as the standard antibiotic. *Sargassum aquifolium* ethanolic extract and column fractions according to the eluotropic series have been used as potential anti-bacterial agents against both Gram-positive and Gram-negative biofilm-forming human pathogenic bacteria.[13] *Listeria monocytogenes* and *Pseudomonas aeruginosa* were found to be the most susceptible and least susceptible organisms to the ethanolic and fractionated extracts respectively. *S. aquifolium* ethanolic extract showed synergistic activity with oxytetracycline, tetracycline and erythromycin antibiotics against *Staphylococcus aureus, Escherichia coli, L. monocytogenes* and *P. aeruginosa* at different concentrations.[13]

Volatile constituents, successive extracts, saponifiable matter and fatty acids obtained from marine algae *Sargassum asperifolium*, *Sargassum dentifolium*, and *Sargassum linifolium* were examined against many pure bacterial and fungal strains using the antibiotic assay method.[14] The test organisms include, *Bacillus cereus*, *Bacillus subtillis*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa, Pseudomonas fluorescens, Saccharomyces carles, Saccharomyces cerevisiae, Aspergillus flavus, Aspergillus niger*, and *Diplodia oryzea*. Different fractions of the *S. asperifolium, S. dentifolium* and *S. linifolium* showed significant degree of antimicrobial potency against the microbes in comparison with amoxicillin and canesten as standard antibiotics.[14]

The anti-bacterial effectiveness of some algae species, according to earlier research, is caused by the presence of a combination of fatty acids, specifically capric, lauric, linoleic, myristic, oleic, palmitic, and stearic acid.[14]

Sulfated polysaccharides are complex biologically active group of polymers which can be obtained from seaweeds. In a study conducted by[15] on the microbicidal and microbistatic activity of five fucose-rich fractions isolated from *Sargassum filipendula*, it was observed that two of the fractions inhibited the formation of biofilm by *Klebsiella pneumoniae* and the survival of *Trichomonas vaginalis*. One of the fractions also acted as a significant antibacterial against the growth of *S. aureus*.

It is crucial to manage and modify the conditions that these activities take place in order to achieve the ideal situation for a maximum antibiotic potential when evaluating biological molecules for their antibacterial activities. The antimicrobial potency of *S. fulvellum* ethanol extract has been investigated by the agar diffusion method to show strong and capable antimicrobial activity against *B. subtilis, C. perfringens, L. plantarum, S. aureus, L. monocytogenes, S. cerevisae* and *C. tropicalis.*[16] Furtherance to the anti-microbial screening, the effect of heat and pH stability was also conducted and it was established that the antibiotic activity remained stable at a temperature of 121°C for a period of 15 min and at pH of 2-10.

Seaweeds have been employed as anti-bacterial and anti-viral medicines in aquatic animals in addition to showing antimicrobial activity against human diseases. One of these studies examined the antibacterial properties of six different species of seaweed, including *Ulva pertusa, Ulva prolifera, Gloiopeltis furcata, Gracilariopsis lemaneiformis, Sargassum fusiforme*, and *Ishige okamurae.*[17] The *in vitro* investigation showed that the extracts, in particular *U. prolifera, G. lemaneiformis*, and *S. fusiforme*, were efficient against several bacterial strains and also improved the crab Scylla paramosain's immune response. This report and previous ones have also confirmed the potency of seaweed extract against *S. aureus, Vibrio aginolyticus* and *P. aeruginosa.*[17] Seaweeds have been found to contain a variety of biomolecules, some of which have been linked to seaweeds' effectiveness as anti-microbial agents. Polyphenols, fatty acids, polysaccharides,

flavonoids, terpenoids, and other physiologically active compounds are examples of these molecules (Figure 3).[18]

The method of extraction, sampling procedure and season have also been found to influence the course of biological activity of seaweeds.[19] Polysaccharide derivatives from *S. fusiforme* extract have displayed remarkable antimicrobial qualities.[17] The anti-bacterial and anti-fungal property of the brown alga, *S. glaucescense* extracts using the solvents methanol, ethyl acetate, hexane and chloroform were investigated in research Conducted by Jamili S.[1] While the other extracts showed considerable antimicrobial effect on just a few of the organisms, the methanolic extract exhibited significant antimicrobial potency against all the test organisms and that is really commendable. *S. polycystum, S. tenerrimum* and *Padina australis* extracts using different solvents have also been reported to display noteworthy activity against some bacteria and fungi.[11,20,21] Also have revealed the potentiality of *S. wightii*, *G. edulis*, *G. corticata* and *U. lactuca* to withstand the growth and spread of three human pathogenic bacteria namely, *P. aeruginosa*, *E. coli* and *S. aureus.* Ethyl acetate, butanol and methanol were used as extraction solvents and the extracts were shown to display different degrees of antimicrobial activity with respect to the different solvent used. The comparative antibacterial status of the four seaweeds revealed that all the seaweed extracts used have good capability to stop bacterial growth except the extract of *G. corticata.* A number of factors may be responsible for the differential anti-bacterial activity of the four seaweeds, the type of solvent used, mass of dried seaweed samples, environmental conditions of the habitat and herbivory have been listed among others.[11,22] Fucoidan, a bioactive compound was isolated from many brown seaweeds and it has reportedly been established to be of significant antibacterial value against some gram- positive bacteria.[23] Microbiological testing involving the crude solvent extracts of *S. ilicifolium, Kappaphycus alvarezii, S.linearifolium* and *Cystoseira crinita* was done and a wide range of antibacterial activity was reported.[24,25] A comparative biochemical analysis study carried out by[22] on the extracts *S. mangarevense* and *Turbinaria ornata* revealed the presence of alginate, mannitol and phenolic compounds in different degrees and the two extracts were also identified as anti-staphylococcal agents. A UGC (New Delhi) approved project carried out by Dr. K. Kolanjinathan and team in 2017 has identified the potential of ten seaweed extracts as antimicrobial agents. Various polar and non-polar solvents were used to isolate the phytochemical compounds in the seaweed samples and varying degrees of antimicrobial efficacy were documented against the test bacteria and fungi. The extracts also showed competing antimicrobial activities with standard antibiotic ampicillin. Sargassumone, a C_{11}-norisoprenoid derivative and other oxygenated cyclopentene norisoprenoids have been isolated from *S. naozhouense*. One of the norisoprenoids namely (+)-kjellmanianone was discovered to exhibit antimicrobial efficacy against resistant strains of *Candida albicans, S. aureus* and *E. coli.*[26] *S. oligocystum* hot and cold water-extracts were probed for their antibacterial property and it was ascertained that the hot water extract showed efficacy against the activities of *S. aureus, S. epidermidis* and *P. aeruginosa.*[27] The growth and activities of human skin pathogens such as *Propionibacterium acnes, S. epidermidis, S. aureus, P. aeruginosa* and *Candida albicans* which causes a range of acne and cutaneous candidiasis were inhibited by the ethanolic extract of *S. serratifolium*. The success recorded from this research was that the hexane-soluble fraction of the ethanolic extract showed a strong and synergistic antimicrobial activity with the commercial antibiotic against all the tested human skin pathogens at low concentrations. By using the disc diffusion antimicrobial screening method to evaluate the antibacterial and antifungal potentials of various seaweeds in relation to *T. conoides, P. gymnospora*, and *S. tenerrimum*,[28] found that *P. gymnospora* methanol and ethanol extract had notable antibacterial and antifungal activity against *Bacillus subtilis* and *Cryptococcus neoformans*, respectively. Possibly, the antimicrobial effect of seaweed extracts could be improved upon by using a combination of different solvent extracts. This was tested by[29] who combined the ethanol, ethylacetate and chloroform extracts of S. thunbergii and reporting a much higher anti-microbial activity. It is of paramount importance that in conducting an antimicrobial screening experiment, the process of drying the extract should be taken into consideration and done appropriately in order to preserve important bioactive components in the extract. In research conducted by,[30] it was reported that among fourteen brown seaweeds explored for their antimicrobial activities against some multi drug-resistant pathogens, only seven were potent against varying test organisms and this could be attributed to the elimination of active principles during the extracts drying process. Methanol extract of *T. ornata* and *S. wightii* were subjected to a comparative anti-microbial efficacy with standard Gallic acid against some human pathogenic microbes. The extracts reportedly showed significant activity against *Aeromonas hydrophila, Bacillus subtilis, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris, Pseudomonas aeruginosa, Shigella flexneri* and *Staphylococcus aureus*.[31]

India's southeast coast is a distinctive coastal environment with a variety of seaweeds growing there. In order to investigate the bioactive potential of significant seaweeds, the Gulf of Mannar's southeast coast was used to collect the brown algae *S. wightii* and *T. ornata*. The effectiveness of both seaweeds' methanolic extracts against a range of Gram positive and Gram negative human pathogenic microorganisms was examined. According to the research, *T. ornata* methanol extracts are a good source of antibacterial agents for the pharmaceutical business. The dicholomethane fraction of 80% ethanol extract of *S. muticum* among other fractions have also proven to show remarkable antimicrobial activity against food spoilage bacteria such as *B. sublitis, Listeria monocytogenes, S. aureus, E. coli, S. enteritidis* and

P. aeruginosa and is hereby recommended as a food preservative agent.[32] In a similar experiment conducted by[33] to investigate the presence of phytochemicals and antimicrobial activity of sequential extraction of *S oligocystum* and *S. crassifolium* with different organic solvents in order of increasing polarity. It was exposed that among the tested extracts, the ethanolic extract showed the best antimicrobial activity and the seaweeds extracts were reported to contain different groups of secondary metabolites.[33,34] Similar to this, sequential extraction of powdered species of *S. polycystum, S. oligocystum, S. crassifolium*, and *S. cristaefolium* with various solvents was carried out and their antibacterial activity against specific strains of aquaculture pathogens was assessed. The strongest action against the test bacteria and fungus was specifically seen in the ethanol extracts of *S. polycystum*. It was advised, however, that the extract be used as a natural immunological booster in the aquaculture sector. The antimicrobial uses of the different types of seaweeds are captured in Table 1.

Antioxidant Study

Due to their numerous health advantages, including anti-aging and anti-inflammatory properties, antioxidants have emerged as scientifically intriguing substances and still employed today in numerous contexts. Antioxidants are a common addition in food technology to a variety of meals to improve the food and solve issues. As a result, research to ascertain the antioxidant properties of natural foods and their components is also progressing quickly.[35] Potential antioxidants have frequently been isolated from plant sources, including seaweeds, tested, and verified in studies.

Free radical scavenging potentials (DPPH and hydroxyl radicals), lipid peroxidation inhibition, and glutathione-S-transferase activities of *Sargassum* sp. extract were examined in a study by[12] DPPH and hydroxyl radicals were tested against the extract, and it was found to have a dose-dependent free radical scavenging effect. It was also discovered that as the concentration of seaweed extract rises, so does its ability to scavenge DPPH. In the study of how the extract may inhibit glutathione-S-transferase and lipid peroxidation in sheep liver microsomal fraction. An earlier study suggested that phenolic substances, such as tannic acid, may create hydrogen bonds with proteins, such as GST enzymes, producing steric hindrance and ultimately the inactivation of the enzyme.[36] Nevertheless, the mechanism by which *Sargassum* sp. extract might reduce GST activity has not yet been uncovered. With more research, the mechanism of inhibition can be uncovered, and this could provide important information for the study of tumor cells.[37]

Phenolic compounds are one of the most effective antioxidants in brown algae and it comprises of about 20–30% algae dry weight.[38,39] Catechin, phlorotannins, and quercetin were among the phenolic components in the sea weed, according to a previous absorption profile and spiking tests report on S. muticum methanolic extract by.[2] Of the three primary peaks, phlorotannins were one of the three that was found. According to reports, phlorotannins can be divided into three categories: soluble phlorotannin from the algal matrix, also known as cytoplasmic phlorotannin; phlorotannin that is bound to the cell wall and typically attaches to the membrane; and cell wall/exuded phlorotannin that is found to exude into the surrounding seawater.[2] Investigated the antioxidant activity of the methanolic extract of *S. muticum* using the Ferric Reducing Antioxidant Power (FRAP) assay and found 75.32 11.36 mmol Fe II and 78.95 4.33 mg gallic acid equivalents of total phenolic contents per 100 g dried plant. Phlorotannins, which have been discovered to be 10-100 times more potent, more stable, and having a better half-life as antioxidants than other substances, were found to be the primary cause of the antioxidative power of *S. muticum* methanolic extract.[40] Also, the ability of the fractionated 80% ethanol extract of *S. muticum* to scavenge DPPH and superoxide radicals as well as to inhibit xanthine oxidase was examined. The screening system revealed that the dicholomethane and ethylacetate fractions had high antioxidant properties with increase in dosage.[32]

According to reports, *Callophyllis japonica* ethanolic extract has been shown to have antioxidant benefits by inhibiting apoptotic cells brought on by H_2O_2 and activating antioxidant enzymes within the cells.[41] Experiments have demonstrated that *Gracilaria tenuistipitata*[42] and the methanol extracts of *Fucus vesiculosus* and *F. serratus*[43] increase the process of recovery of H1299 and Caco-2 cell lines that were initially experiencing H_2O_2-induced DNA damage. Moreover, the aqueous extract of *Gracilaria tenuistipitata* decreased cell growth and stopped G2/M.[44] According to,[43] *Pelvetia canaliculata* methanolic extract can prevent Caco-2 cells from losing superoxide dismutase due to H_2O_2-induced oxidative stress. The *in vivo* antioxidant experiment utilizing the hot water extract of *Ulva reticulata* indicated the antioxidant potentials and the capacity to diminish hepatic oxidative stress- of various Ulva species.[45] Others have noted the presence of phytochemicals that are notable antioxidant agents, such as sesquiterpenoids in *U. fasciata*[46] and flavonoids in *U. lactuca*[47] and these are presented in Figure 3 Additionally, DPPH-radical scavenging assay has demonstrated the antioxidative potential of methanol extract from the Anabaena species *S. linearifolium* and *C. crinite*,[25,48] and the presence of phlorotannins in *Eisenia bicyclis, Ecklonia cava*, and *Ecklonia kurome* that have great antioxidant activity.[49] The Ascorbate/iron/H_2O_2 experiments also demonstrated that the naturally occurring phycobili-protein phycocyanin, which is present in *Spirulina platensis* extract, has antioxidant capabilities.[50] The pharmaceutical and food sectors may profit from derivatives of the polysaccharides isolated from *S. fusiforme* extract because they have shown impressive antioxidant properties.[17] The TPC, ABTS, and DPPH radical-scavenging activity of *S. polycystum*

Table 1: The Antimicrobial Uses of Different Types of Seaweeds.

Seaweed species	Test Organism	Activity
Sargassum sp.	*S. aureus* *B. subtilis* *E. coli*	Antibiotic effect
S. aquifolium	*L. monocytogenes* *P. aeruginosa* *S. aureus* *E. coli*	Synergistic antimicrobial activity with oxytetracycline, tetracycline and erythromycin.
S. asperifolium *S. dentifolium* *S. linifolium*	*B. cereus* *B. subtilis* *S. aureus* *E. coli* *P. aeruginosa* *P. florescens* *Saccharomyces carles* *S. cerevisiae* *A. flavus* *A. niger* Diplodia oryzea	Antimicrobial Effect
S. filipendula	K. pneumoniae T. vaginalis S. aureus	Antimicrobial activity
S. fulvellum	*B. subtilis* *C. perfringens* *Lactiplantibacillus plantarum* *S. aureus* *L. monocytogenes* *S. cerevisiae*	Heat and PH stability tested antimicrobial screening effect.
Ulva pertusa *U. prolifera* *Gloiopeltis furcate* *Gracilariopsis lemaneiformis* *S. fusiforme* *Ishige okamurae*	*S. aureus* *V. aginolyticus* *P. aeruginosa*	Antibacterial property
S. wightii *G. edulis* *G corticate* *U. lactuca*	*P. aeruginosa* *E. coli* *S. aureus*	Antibacterial potential
S. mangarevense *Turbinaria ornate*	*S. aureus*	Anti-staphylococcal effect
S. naozhouense	*C. albicans* *S. aureus* *E. coli*	Antimicrobial activity
S. oligocystum	*S. aureus* *S. epidermidis* *P. aeruginosa*	Antibacterial property
S. serratifolium	Propionibacterium acnes *S. epidermidis* *S. aureus* *P. aeruginosa* *C. albicans*	Anti-acne Anti-candidiasis
Padina gymnospora	*B. subtilis* *Cryptococcus neoformans*	Antimicrobial effect
T. ornata *S. wightii*	*Aeromonas hydrophila* *B. subtilis* *Enterococcus faecalis* *E. coli* *K. pneumoniae* *Proteus vulgaris* *P. aeruginosa* *Shigella flexneri* *S. aureus*	Antimicrobial activity
S. muticum	*B. subtilis* *L. monocytogenes* *S. aureus* *E. coli* *S. enteritidis* *P. aeruginosa*	Antimicrobial activity
Other seaweeds with varying antimicrobial activities includes: *S. polycystum* *S. oligocystum* *S. crassifolium* *S. ilicifolium* *S. linearifolium* *S. tenerrimum Antimicrobial activity* *S. fusiforme* *S.glaucescense* *Kappaphycus alvarezii* *Cystoseira crinite* *Padina australis*		

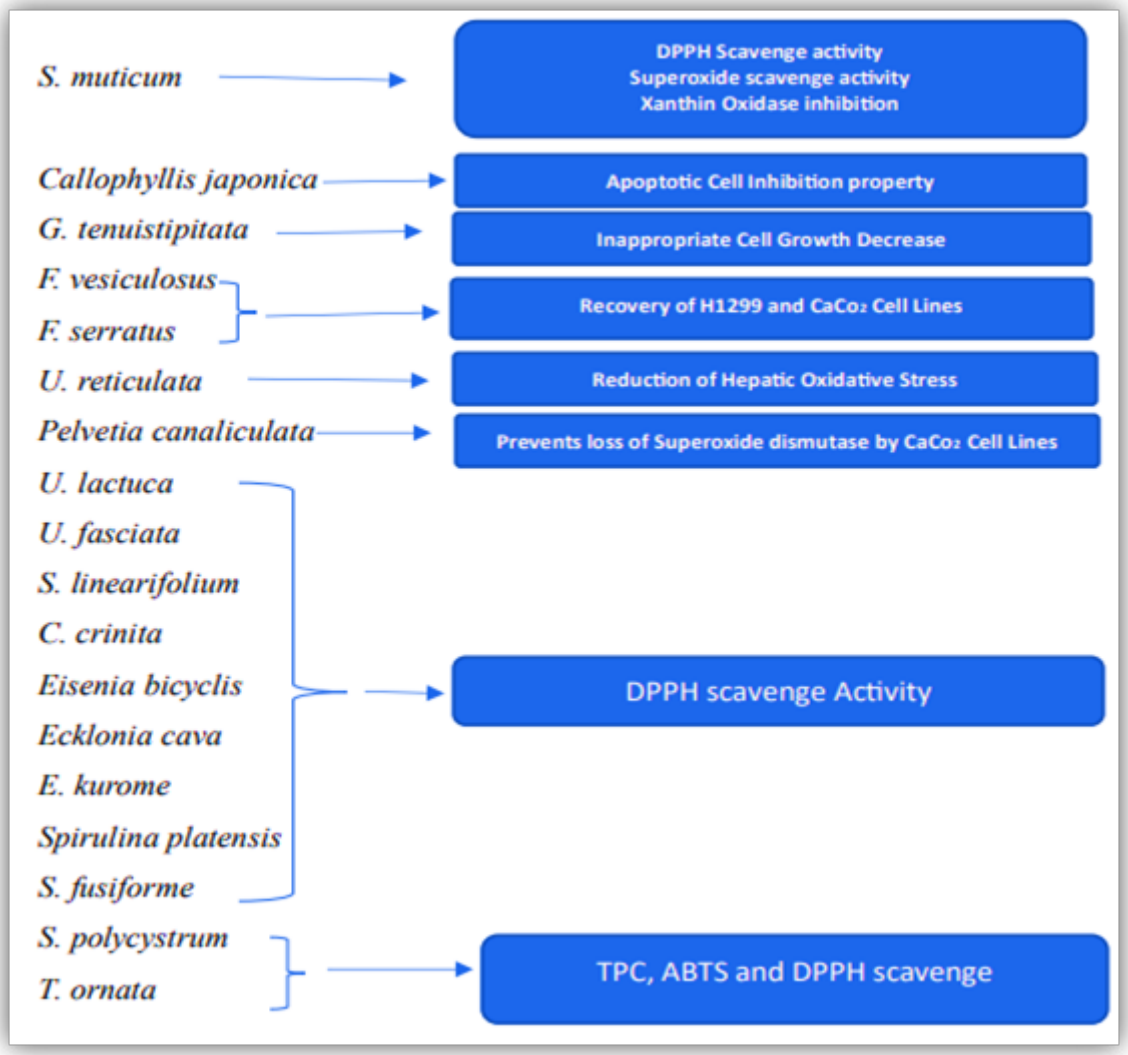

Figure 1: The Antioxidative Activity of Seaweeds.

and *Turbinaria ornata* was evaluated, and it was discovered that the extracts can scavenge the radicals and also diminish their power however in a dose-dependent manner.[51] As highlighted in Figure 1 below, the summary of various seaweeds that have proven as potential antioxidants is hereby presented.

Anti-nociceptive and Anti-inflammatory properties

Anti-inflammatory properties report on different species of seaweeds and other algae is quite robust while only minimal reports have been collated on the antinociceptive activities. According to Figure 2 below and as evident in various reports, seeaweeds have been found to contain varying degree of antinociceptive and anti-inflammatory properties.

As of 2011,[52] asserted that only *G. verrucosa* and *G. textorii* have been shown to have anti-inflammatory characteristics following a thorough biological assessment of the *Gracilaria* spp. However, *G. tenuistipitata* aqueous extract was later found to suppress inflammation brought on by viral infection,[53] as well as the replication of retroviruses by a polysaccharide obtained from *Porphyridium* sp.[54] and *Polyopes affinis* ethanolic extract being found to be an anti-asthmatic reaction substance.[55,56] studied *Neorhodomela aculeata* methanol extract for its anti-inflammatory effects in neurological illnesses and found that the extract could reduce the formation of ROS and lipid peroxidation caused by H_2O_2.[56]

Many other seaweeds with their naturally obtained phytochemicals have shown varying degrees of anti-inflammatory reactions which have been documented (Figure 3).[57] For example neorogiotrol, a diterpenoid derived from *Laurencia glandulifera*,[58] C15 acetogenins, (12Z)-cis-maneonene-D and (12E)-cis-maneonene-E derived from *Laurencia obtuse*,[59] a glycoprotein from *Porphyra yezoensis*,[60] (*E*)-10-Oxooctadec-8-enoic acid and (*E*)-9-Oxooctadec-10-enoic acid obtained from *Gracilaria verrucosa*,[29] aquamin with multiminerals gotten from *Lithothamnion corallioides* and Sulfated polysaccharides from *Delesseria sanguinea*.[61] *Dunaliella*

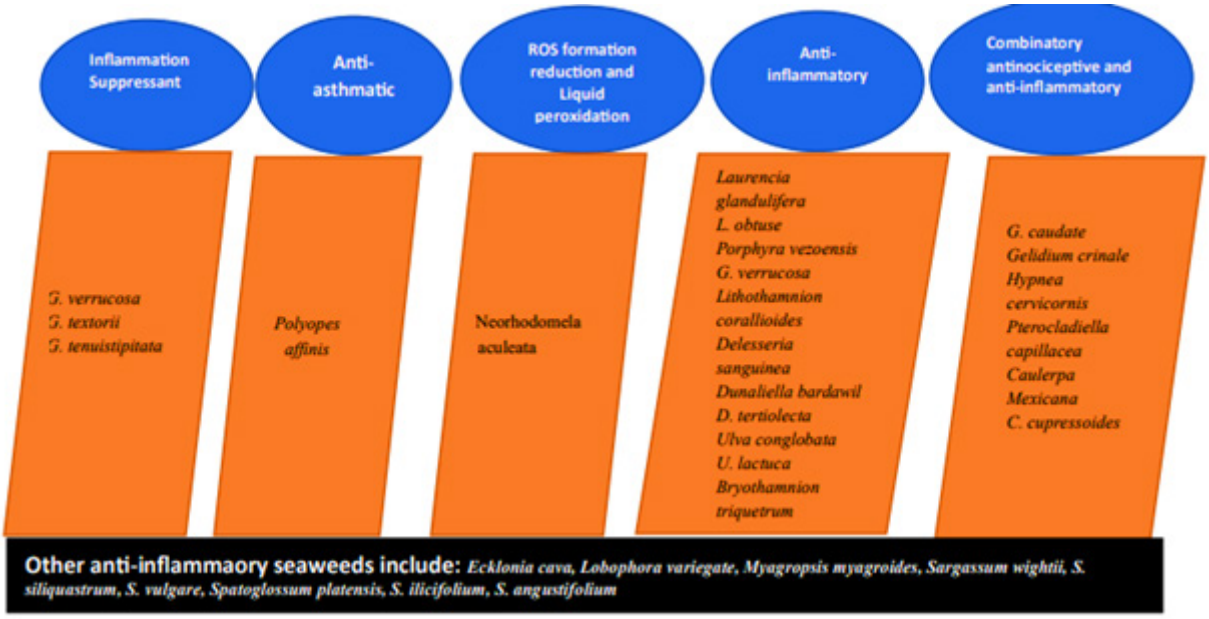

Figure 2: Examples of seaweeds with varying anti-inflammatory properties.

bardawil and *Dunaliella tertiolecta* have both shown a protective ability against inflammation induced by acetic acid[62] and cytokine production induced inflammation[63] respectively. Similarly, *Ulva conglobata* and *U. lactuca* have been reported by[64] to have anti-inflammatory effects in an assay where a murine hippocampal HT22 cell line was used.[64]

The combinatory antinociceptive and anti-inflammatory activities of some red seaweeds have been reported by earlier scientists.[65] investigated and confirmed by acetic acid-induced writhing test, a hot-plate test, and glutamate-/formalin-induced nociception using Swiss mice, the antinociceptive properties of *Bryothamnion triquetrum* methanolic extract. However, the anti-inflammatory potency was confirmed by zymosan A-induced peritonitis test. Some other algae which antinociceptive and anti-inflammatory activities have also been reportedly confirmed includes; *Gracilaria caudate*,[66] *Gelidium crinale*[67] *Hypnea cervicornis*,[68] *Pterocladiella capillacea*,[65] *Caulerpa Mexicana*,[69] *Caulerpa cupressoides*.[70]

Also, against the inflammation of the human endothelial cells, the ethanolic extract of *Ecklonia cava* have shown some inhibitory potentials by reducing allergic airways reactions.[71] The brown and blue-green seaweeds with their corresponding active principles that also have anti-inflammatory property includes; *Lobophora variegata* extract revealed the presence of sulfated galactofucan,[72,73] *Myagropsis myagroides* shows the presence of carotenoid fucoxanthin,[16] *Sargassum wightii* contains alginic acid,[74] *Sargassum siliquastrum* contains sargachromanol G[75] and *Lobophora variegate*,[76] *Sargassum vulgare*,[77] and *Spatoglossum schroederi*[78] which all contain fucan and has anti-inflammatory activity as earlier reported. The blue green alga spirulina, aside having anti-oxidative potentials, also have shown anti-inflammatory effects when investigated by using a non-alcoholic steatohepatitis model.[79] Especially, *Spirulina platensis*, with the compound C-phycocyanin,[80] a biliprotein have been able to suppress inflammation from earlier reports. DPPH, superoxide-hydroxyl radical scavenging, chelating ability and reducing power of fucoidan isolated from *S. ilicifolium* and *S. angustifolium* was assessed and reported to be considerable and positive when correlated with sulfate and phenol content.[23]

Anti-cancer properties

Table 2 below is composed of various seaweeds that have anticancer properties. There have been many reports earlier published about the potentiality of crude seaweed extracts as anticancer agents but much attention has not been given to that area of research until recently. One of the most frequent issues in medicine are antitumor medication resistance and antitumor compound side effects. Consequently, it would be intriguing to discover novel anticancer medications with minimal side effects. In 2013, a group of researchers reported the antiproliferative and anti-angiogenesis activities of extracts from the Persian Gulf brown seaweed (*S. muticum*) methanolic extract. The cytotoxicity test conducted by cellular morphological change observation showed that the seaweed extract did not have any toxic effect on normal cell Vero cell line, but was able to inhibit the proliferation of two breast cancer cell lines when the inhibition potential was monitored and the experiment was found to be dose and time dependent. The treatment was done for just 24 hr and IC_{50} values were calculated for *S. muticum* methanolic extract. It was discovered that MCF-7 and MDA-MB-231 cells showed IC_{50} values of 20±0.1 and 55±0.2 μg/mL respectively, confirming that the methanolic extracts of seaweeds can selectively inhibit the growth of specific cell or tumor types. Another report by[25]

Table 2: Examples of Different Seaweeds with Anticancer Property.

S. muticum	Breast cancer cell anti-proliferation and apoptosis induction
S. linearifolium *C. crinita*	Cytotoxic
Corallina pilulifera	Cytotoxic anti-cervical adenocarcinoma.
L. japonica *Pyropia tenera* *Capsosiphon fulvescens*	Induced apoptotic activity of breast cancer cells.
G, corticate *Amphira sonata*	Selective cytotoxic agents.
G. corticate *S. oligocystum* *G. tenuistipitata*	Anti-proliferative effect on human leukemia and Ca9-22 oral cancer cell.
Costaria costata	human colon anti-cancer
Ecklonia cava	Cervical anti-cancer
S. hornery	Prostate anti-cancer
S. filipendula	Anti-cancer of the liver
S. swartzii *S. wightii* *S. vulgare*	Anti-cancer
S. integerrimum	Anti-cancer of the human lung
S. oligocystrum	Anti-tumor
U. lactuca *Codium tomentosum* *Cystoseira crinite* *Cystoseira stricta* *S. vulgare* *Gelidium latifolium* *Hypnea musciformis* *Jania rubens*	Caco-2 cell anti-proliferation.

supported this claim by investigating the cytotoxic effect of *S. linearifolium* and *C. crinita* crude extract against the growth of MCF-7 cells and they were evidently found to induce apoptosis and autophagy in MCF-7 cells.

The study also reported an increase in apoptotic cells in response to increase in dose after exposure to *S. muticum* methanolic extract for 48 hr which indicates the extract as a potential apoptosis-inducing agent. A polysaccharide fraction has also been reported earlier as an active ingredient in some hot water extracts of many brown algae and it was found to be effective against cancer cells in mouse.

In a report published by[81] on the cytotoxic activity of ethanolic extracts of *Corallina pilulifera* against human cervical adenocarcinoma cell line, HeLa. It was observed that *Corallina pilulifera* ethanolic extract was able to induce apoptosis in HeLa cells whereas the process of cell cycle was not arrested.[81] A similar report also indicated that the water extract of *Laminaria japonica* induced apoptosis when tested on human breast cancer cell lines[82] Polyphenols are a kind of bioactive components obtained from algae and have been found to play a special role as anticarcinogens and antiproliferative agents. This claim has been verified by[83] who investigated the antitumour promotion activity of Laminariales sp. and *Pyropia tenera* methanolic extract against ornithine decarboxylase induction by tumour promoter 12-O-tetradecanoylphorbol-13-acetate (TPA) in BALB/c 3T3 fibroblasts. An inhibition rate of 75–87% was achieved by *Laminariales sp.* and 92% inhibition by *P. tenera*.[83]

Red algae *Gracilaria cortica* and *Amphiroa sonata* MeOH extracts were reportedly found to be remarkable as selective cytotoxic agents compared to other algae in many experiments.[84] Also,[84] confirmed in an experiment how several species of seaweeds were able to display strong cytotoxic activity against L1210 cells with minimal effect on normal cells. The active principle found in the seaweeds extracts was said to bind with the receptor molecules of the cancer cells thereby initiating cancer cell death. Aside this, the chemical properties of the bioactive component show that it is very different from some substances especially the polysaccharide derived from other algae in that it is heat stable and water/organic solvent soluble and has a molecular weight of less than 3000kg/mol.[85]

Antioxidants have very vital role to play in carcinogenesis because they modulate ROS[86] and when human cells are exposed to metals from the environment, ROS are induced. Meanwhile, the excess production of ROS may result in damage to cells which is caused by genomic instability.[87] Several other results have suggested that ROS and miRNAs are also involved in carcinogenesis[88] When anti-cancer drugs are to be selected, priority is given to pro-oxidant natural products because there is a link between inflammation and development of cancer cells.[89,90]

Gracilaria corticate[91] and *Sargassum oligocystum*[92] aqueous extracts and methanol[44] extract of *Gracilaria tenuistipitata* have demonstrated anti-proliferative effect on human leukemia and Ca9-22 oral cancer cell lines respectively. A green algae *Capsosiphon fulvescens* hot water extract was reported by [Park et 2006] to induce apoptosis in gastric cancer cells. One tertiary sulfonium metabolite Dimethy-lsulfoniopropionate, found in algae species have exhibited anti-cancer properties.[93] *Laminaria japonica* contains glycoproteins,[82] fucoidans isolated from *Costaria costata, Eclonia cava* and *S. hornery*[94] and

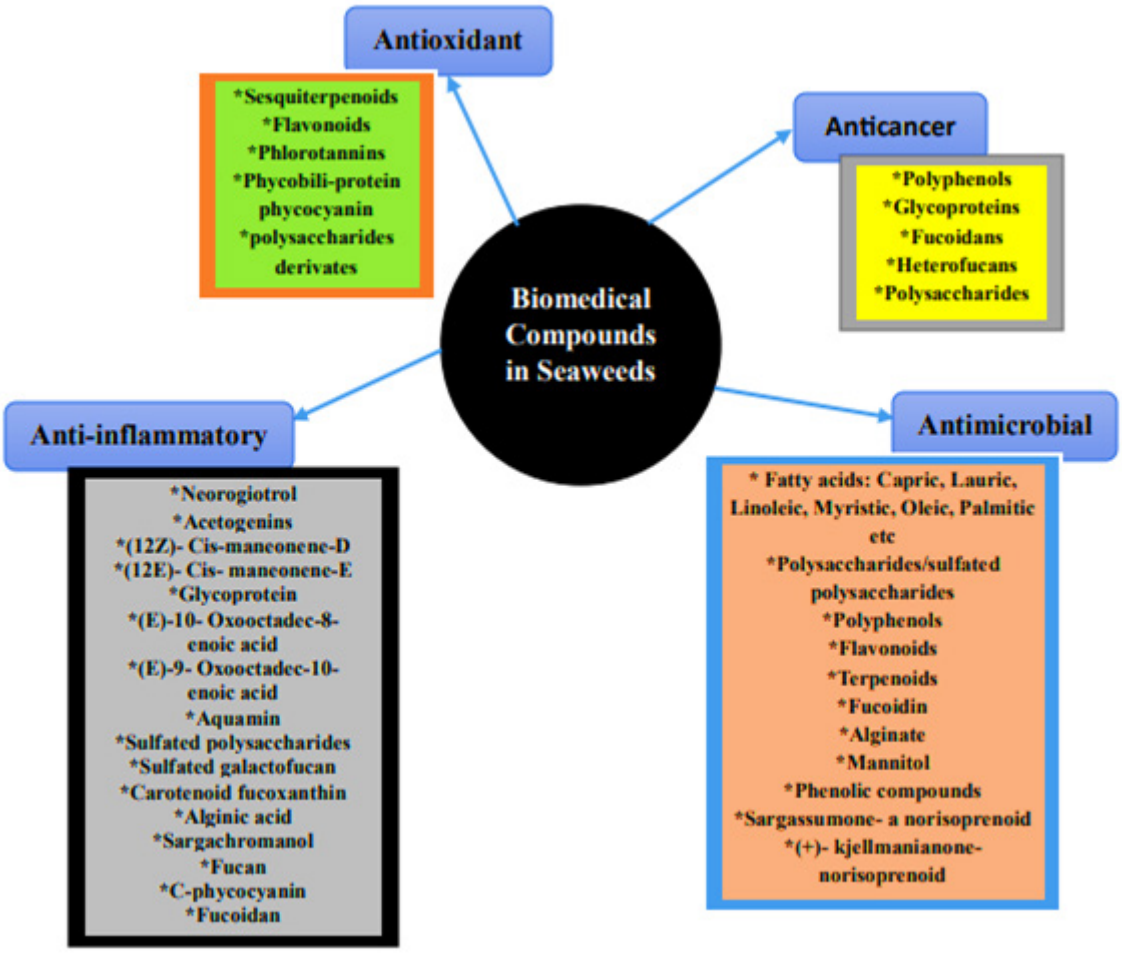

Figure 3: Different Active Ingredients Contained in Seaweeds Used for Biomedical Activities.

heterofucans contained in *S. filipendula*[95] also have anti-cancer potentials on human colon, cervical, prostate and liver cancer cells in different reports earlier published. These and other phytochemical compounds obtained from seaweeds and possess anticancer properties are portrayed in Figure 3.[96] Gave some *in vitro* evidence of polysaccharides isolated from *S. swartzi* and *S. wightii* which were tested for their effectiveness as colloidal drugs in cancer cell treatment. It was confirmed that the two polysaccharides have an m/z ratio of around 6349 and 6873 and were conclusively recommended as potential anti-cancer agents. Another study involving the use of ethanol extract of *S. wightii* against the spread and increase of DAL cell lines in mice have also supported the above evidence that *S. wightii* extract is a potential anticancer agent because the extract was able to show inhibitory effect on DAL cancer cell lines.[97,98] A novel polysaccharide named SPS was isolate from *S. integerrimum* and discovered to exhibit significant anticancer efficacy in a human lung cancer cell line A549 *in vitro* and *in vivo.* SPS responded to the cancer cells by significantly reducing the viability of A549 cells in a dose-time dependent MTT assay. An *in vitro* antitumor potential of *S. oligocystum* extract against K562 and Daudi human cancer cell lines was reported by.[92] The most effective activities were recorded at the concentration of 500 µg/mL and 400 µg/mL which is an indication that the anticancer potential of *S. oligocystum* extract is dose dependent. The anticancer potential of *S. oligocystum* was remarkable and it was suggested that further fractionation and purification of isolated compounds as well as the *in vivo* biomedical activity can be done in order to formulate and ascertain an anticancer natural product.[92] In very recent research conducted by,[99] *Sargassum* sp. extract was discovered to significantly inhibit the viability and spread of MCF-7 human cancer cells in a time and dose dependent MTT assay study with 24 hr treatment. *Ulva lactuca*, *Codium tomentosum, Cystoseira crinita*, *Cystoseira stricta, Sargassum vulgare, Gelidium latifolium*, *Hypnea musciformis*, and *Jania rubens* have been explored for their *in vitro* potential inhibition of Caco-2 cell proliferation. When the cells were exposed to various concentrations of the extracts, it was discovered that there was a significant reduction in cell proliferation and this effect has a correlation with the content of their polyphenols and flavonoids.[100] The cytotoxic activity of *S. vulgare* against Jurkat human cancer cell line particularly have also been investigated by trypan exclusion test. The different

crude extracts were administered synergistically at different ratio and very considerable IC_{50} values were obtained after 72 hr of treatment.[101]

CONCLUSION

Natural products identified from marine algae are abundant in antioxidants. In actuality, certain sea algae are edible. According to the specifics of the fractionation of crude extracts detailed by different researchers, oxidative stress as well as illnesses and malignancies connected to oxidative stress have been strongly modulated by these extracts and their bioactive components. Researchers have looked at the anti-microbial, anti-inflammatory, anti-nociceptive, and anti-cancer characteristics of many types of algae as reviewed here. The marine algae-derived materials and chemicals can be employed more frequently in pre-clinical research for the development of new drugs in the future. Overall findings have shown that this seaweed may be utilized to prevent or treat a number of ailments as well as preservatives in the food processing business. Certain compounds obtained especially from *Sargassum* spp. might be the most suitable for further research to deal with selective antitumor active substances to human cancer especially breast cancer. There have also been predictions regarding the synergistic effectiveness of specific antibiotic combinations with seaweed extracts against pathogenic bacteria. To determine the precise agent that can receive the biomedical award, more research must be done on the separation, purification, and identification of the active elements.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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