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Bioactive Compounds Derived from Microalgae Showing Antimicrobial Activities

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Abstract

Microalgae have been explored for their bioactive compounds with promising applications encompassing antibacterial, antiviral, antifungal and antialgal activities. Considering the present status of widely used treatment therapies and their limitations to tackle their adverse effects, the application of bioactive compounds derived from algae will prove beneficial and much more effective as compared with traditional treatment methods. Due to the emerging infectious diseases, viral infections (epidemic and pandemic) and raise in antibiotic resistant bacteria, there is an urgent need for development of alternative treatment therapies against infectious diseases. Present work provides a brief introduction about the algal bioactive compounds and their activities against various pathogens.

Keywords: Microalgae; Antibacterial; Antifungal; Antiviral; Antimicroalgal

Introduction

Algae has wide span of ecosystems contributes to the innumerable chemical compounds that they are able to synthesize. A number of antimicrobial compounds have been identified in miceoalgae as well as macroalgae [1]. More than 18,000 new compounds have been isolated from marine sources, yet majority of them have not yet been obtained nor characterized [2]. Therefore, microalgae represent a unique opportunity to discover novel metabolites. The rate of finding metabolites already obtained from other biological sources is less in microalgae as compared with other microorganisms [3]. Due to their metabolic plasticity under stressed vs. nonstressed conditions microalgae possess the extra advantage of triggering secondary metabolism [4]. As microalgae where potentially explored only after 1950s, they were not considered previously for therapeutic purposes. Extensive search is presently undergoing to find novel therapeutically useful agents [5-7]. Microalgae have meanwhile been found to produce antibiotics. A large number of microalgal extracts and/or extracellular products have proven antibacterial, antifungal, antiprotozoal and antiplasmodial [6-13]. Efforts to identify the compounds directly responsible for those antimicrobial features have been made, but are still embryonic.

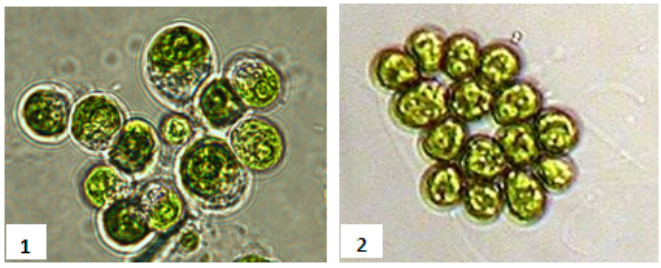

Figure 1: The microscopic images of *chlorella* sp. (1) and *Chlamydomonas* sp. (2).

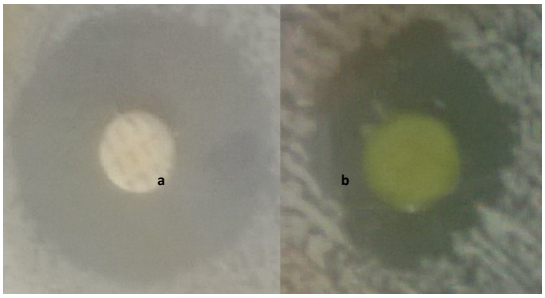

Figure 2: The antibacterial activity of *chlorella vulgaris* ethanol extract b) against *Staphylococcus* Sp. as compared with the control antibiotic streptomycin (a).

We have been working with algae like *Chlorella* and *Chlamydomonas* (Figure 1) isolated, maintained and extracted as described by Salem et al. [14]. These extracts were later used for antibacterial assay and determination of minimum inhibition concentration (MIC). Antibacterial activity of algal extracts determines the MIC of algae used in this study in vitro [14].

Algal cell-free extracts are already being tested [15-17]. Our aim is to provide information about the recent trends in the discovery of bioactive compounds derived from algae which have shown their potential as antimicrobial agents. We have briefly summarized the recent works carried out by the researchers globally in the field of algal antimicrobial activities.

Antimicrobial activities of algal extracts

Antibacterial activity of algae: The needs for development of alternative antibiotic agent were investigated since the emergence of antibiotic resistant microbes. Due to the emergence of drug-resistant pathogens they endanger people in affluent, industrial societies like the United States, as well as in less-developed nations.

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Examples of clinically important microbes that include *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Salmonella* or *E. coli* and infections transmitted healthcare malpractices enterococci, *Acinetobacter baumanii, Pseudomonas aeruginosa*, and *Klebsiella* spp [18]. The development in the field of algal therapeutic research has made it possible by their bioactive compounds which have been found effective against most of the pathogens (Figures 1 and 2). The list of some of the algal bioactive compounds is summarized in the Table 1 [19-24].

Antiviral activity of algae: The viruses have been the cause of mass epidemic and pandemic outbreaks of potentially harmful and deadly diseases like influenza, hepatitis, etc. Due to the unavailability of proper treatment facilities and precautionary measures they have been causing a great panic worldwide. Considering the present situation the discovery of antiviral compounds which were derived from algal bioactive compounds provide us a great relief. These compounds, which are tabulated in Table 2 [25-28] has a great prospective in the future.

A number of infectious diseases caused by viruses have re-emerged in recent years, new antiviral measures are necessary for those who are not exposed to them previously. Due to this microalgae have received a strong attention to be explored for potential antiviral agents [29].

Antifungal activity of algae: The study of resistance to antifungal agents has lagged far behind that of antibacterial resistance likely because fungi were not recognized as important pathogens [30,31]. The associated increase in fungal infections prompted search for newer and safer agents to combat fungal infections [32] and a few noteworthy results encompassing microalgae are listed in Table 3 [19,24,33].

Antialgal activity of algae: Inhibitory phenomena between microalgal cells have been reported in the past; Bagchi et al. [34] originally proposed that natural algaecides could effectively be applied in control of toxic algal blooms like *Isochrysis galbana* from cell-free filtrates *Dunaliella salina*, *Platymonas elliptica*, *C. vulgaris*, *Chaetoceros muelleri*, *Chlorella gracilis*, *Nitzschia closterium* and *P. tricornutum* [35].

Algal species	Extract source	Target bacteria	Reference
Pithophora oedogonium	Ethanol extract	*Salmonella*, *Staphylococcus* sp., 4978	[19]
Rivularia bullata, Nostoc spongiaeforme, Codium fragile, Colpomenia peregrina Sauvageau, *Cystoseira barbata, Zanardinia typus*	Methanol Chloroform Diethylether Dichloromethane Ethanol	Gram negative and Gram positive bacteria	[20]
Sargassum wightii, Chaetomorpha linum, Padina gymnospora.	Acetone, methonol	*P. aeruginosa* (ATCC27853), *S. typhi*-B, *Erwinia amylovora* (MTCC2760) (E. amylovora), Enterobacter aerogenes (MTCC111) (E. aerogenes), *Proteus vulgaris* (MTCC1771) (*P. vulgaris*), *Klebsiella pneumonia* (ATCC15380) (*K. pneumonia*) and *E. coli* (ATCC25922). gram-positive bacterial strains were Methicillin resistant *S. aureus*,	[21]
Asparagopsis taxiformis	Ethanol extract	*Vibrio alginolyticus, Vibrio vulnificus* and *Aeromonas salmonicida* subsp. *salmonicida Photobacterium damselae* subsp. *Damselae* and *Photobacterium damselae* subsp. *piscicida*, *Salmonella* sp., *Vibrio cholerae*, *Vibrio harveyi* and *Vibrio parahaemolyticus*	[22]
Chlorococcum humicola	Bioactive compounds	*Escherichia coli, Pseudomonas aeruginosa, Salmonella typhimurium, Klebsiella pneumoniae, Vibreo cholerae, Staphylococcus aureus, Bacillus subtilis, Candida albicans, Aspergillus niger* and *Aspergillus flavus.*	[23]
Gloeocapsa sp. *Synechocystis* sp. *Anabaena* sp. *Aphanizomenon flos-aquae*. *Nostoc* sp. *Nostoc entophytum*, *Nostoc muscorum*, *Scytonema ocellatum*, *Arthrospira fusiformis* (Voronich), *Scenedesmus obliquus*, *Coelastrella* sp. *Chlorella* sp. *Rhodella violacea*, *Porphyridium cruentum* (AG.) NAG	Ethanol extract	*Staphylococcus aureus* 209, *Streptococcus pyogenes* 981, *Bacillus cereus* 2421 *Escherichia coli* 3702, *Pseudomonas aeruginosa* 1396, *Salmonella typhimurium* 123, and *Yersinia enterocolitica* 623	[24]

Table 1: Antibacterial activity of selected compounds from microalgae.

Algal species	Extract source	Target Virus	Reference
Haematococcus Pluvialis and *Dunaliella salina*	Pressurized liquid extraction	Herpes simplex virus type 1	[25]
Gyrodinium Impudium (sulfated polysaccharide, p-KG03)	Sulfated polysaccharide	Influenza virus	[26]
Navicula directa	Polysaccharide	HSV1 & 2, Influenza A virus	[27]
Gyrodinium impudicum	p-KG03 exopolysaccharides	Encephalomyocarditis Virus	[28]

Table 2: Antiviral activities of selected compounds from microalgae.

Algal species	Extract source	Target fungi	Reference
Pithophora oedogonium	Ethanol extract	*Penicillium viridicatum* 1101, *Fusarium solini* 1127	[19]
Gloeocapsa sp.	Exopolysaccharides	*Candida albicans*	[24]
Haematococcus pluvialis	Butanoic acid and methyl lactate	*Candida albicans*	[33]

Table 3: Antifungal activities of selected compounds from microalgae.

However, Pratt [36] was the first to report that growth of *C. vulgaris* was depressed by a compound (chlorellin) that was produced and excreted into the medium - and several other extracellular metabolites able to inhibit their own growth and the growth of other species have meanwhile been reported [37].

Antiprotozoal and Antiplasmodial activity of algae: The antiprotozoal activities algal extracts have recently been discovered against *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi* and *Leishmania donovani* and were found effective. The development of antiprotozoal algal extracts may prove effective in controlling various protozoan diseases and their preventive measures [38]. The crude seaweed extracts from green marine algae *Cladophora rupestris*, *Codium fragile ssp. tomentosoides*, *Ulva intestinalis* and *Ulva lactuca* have shown anti protozoan activity against *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, *Leishmania donovani* [39]. Ciau et al. [40] studied the antiprotozoal activity of brown alga *Lobophora variegata* against *Giardia intestinalis*, *Entamoeba histolytica* and *Trichomonas vaginalis*. They have extracted antiprotozoal compound by chloroform, the major compounds included -O-palmitoyl-2-O-myristoyl-3-O-(6'''-sulfo-a-D-quinovopyranosyl)-glycerol; 1,2-di-O-palmitoyl-3-O-(6'''-sulfo-a-D-quinovopyranosyl)-glycerol and a new compound identified as 1-O-palmitoyl-2-O-oleoyl-3-O-(6'''-sulfo-a-Dquinovopyranosyl)-glycerol [40]. The ethanolic extracts of freshwater macrophytes *Potamogeton perfoliatus*, *Ranunculus tricophyllus* and *Cladophora glomerata* as well as marine macroalgae *Dictyota dichotoma*, *Halopteris scoparia*, *Posidonia oceanica*, *Scinaia furcellata*, *Sargassum natans* and *Ulva lactuca* are assayed for their in vitro antiprotozoal activity against *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, *Leishmania donovani* and *Plasmodium falciparum* [41].

Trypanosomiasis is one of the most important parasitic diseases worldwide. The undesirable side effects and low efficacy of classical trypanocidal drugs underline the necessity of the development of new drugs from natural products. Although marine algae have been recognized as attractive sources of known and novel bioactive compounds, very little research has been focused on antiprotozoal activity. Aqueous and organic extracts of Rhodophyta, Phaeophyta and Chlorophyta were evaluated for their antiprotozoal activity in vitro against Trypanosoma cruzi trypomastigotes. The organic extracts from *Dictyota caribea, Lobophora variegata*, *Turbinaria turbinata Linnaeus*, and *Laurencia microcladia Kützing* possess promising in vitro activity against *T. cruzi trypomastigotes*. *Laurencia microcladia* is effective against *Artemia salina* and the high cytotoxicity exhibited by *T. turbinate* is required to be investigated further [42].

Red alga from genus Chondria produces cyclic polysulfides, terpenoids, amino acids and amines. Domoic acid derivatives from *Chondria armata* show larvicidal and blood pressure lowering activity [43]. The algal extracts have also been explores for their antiplasmodial activities, [38]. The *P. falciparum* (Erythrocytic stages), *T. cruzi* (Trypomastigotes) and *L. donovani* (Axenic amastigotes) are growth inhibited with the ethanol and ethyl acetate extract of algae belonging to Chlorophyta, Heterokontophyta and Rhodophyta. Antimalarial leads from marine algae, four metabolites, sargaquinoic acid, sargahydroquinoic acid, sargaquinal and fucoxanthin, were isolated from the *Sargassum heterophyllum*. Fucoxanthin and sargaquinal showed good antiplasmodial activity toward a chloroquine-sensitive strain of *Plasmodium falciparum* [44] Ethylacetate (EtOAc) extract of *Sargassum swartzii* and *Chondria dasyphylla* were investigated for larvicidal activities in larvae of malaria vector *Anopheles stephensi* and the mortality rate of *Anopheles stephensi* was 96 and 95%, respectively [45]. The endemic marine red alga *Plocamium cornutum* (Turner) *Harvey* show antiplasmodial activity in organic extracts. Interestingly, compounds bearing the 7-dichloromethyl substituent showed significantly higher antiplasmodial activity toward a chloroquine sensitive strain of *Plasmodium falciparum* [46].

Conclusion

We have screened the antibacterial activities of organic extracts of isolated culture of algal species and had evaluated them by agar well diffusion method. Methanol extract and ethyl acetate extract of algae were effective against few bacterial species including *Staphylococcus spp.* and *E.coli*. Methanol extracts were more effective as compared with ethyl acetate extract of algae. The antibacterial and antifungal activities were seen predominantly from the *chlorella* sp. as well as *Chlamydomonas* sp. Our work clearly summarizes the importance of microalgal extracts which have potential implication as antibacterial, antiviral, antifungal, antimicroalgal antiprotozoal as well as antiplasmodial agents. This information can prove very helpful in further research and discovery of new drugs. The work briefly explains the work carried out by various researchers, clearly elaborating the important implications of algal bioactive compounds for the application against infectious diseases and as an antimicrobial therapy.

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