Plant Archives Vol. 26, Supplement 1, 2026 pp. 1477-1486 e-ISSN:2581-6063 (online), ISSN:0972-5210

Plant Archives

Journal homepage: http://www.plantarchives.org
DOI Url : https://doi.org/10.51470/PLANTARCHIVES.2026.v26.supplement-1.197

NATURAL SOURCES OF DRUG DISCOVERY FROM ALGAE AND FUNGI : A REVIEW

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(Date of Receiving : 08-09-2025; Date of Acceptance : 29-11-2025)

ABSTRACT

Algae and fungi have received growing attention as sources of bioactive metabolites and considered for the pharmaceutical industry in drug development. They have many convincing properties to make it stand out in front of synthetic drugs. The variety of species and the diversity of their habitats, some of them less exploited, allow the conclusion that they continue to be a rich source of new metabolites. Besides the conventional isolates, an increasing interest in endophytic and in marine-derived algae and fungi has been noticed. In addition new screening strategies based on innovative chemical, biological, and genetic approaches have led to novel fungal metabolites in recent years. This review focuses specifically on the potentials, properties, medicinal uses, applications of algal fungal molecules. This also focuses on the future aspects and challenges of algae and fungi in the pharmaceutical and nutraceutical area. Furthermore, synthetic products based on fungal metabolites as well as new developments in the uses or the biological activity of known compounds or new derivatives are discussed.

Keywords **:** Algae, Fungi, Natural products, Metabolites

Introduction

Nature sustains unlimited resources of novel bioactive molecules, and the study of these resources is very useful in the process of drug discovery (Ebada *et al*., 2008). These bioactive molecules are called natural products (NPs). Natural products originate as secondary metabolites from a myriad of sources, including terrestrial plants, animals, marine organisms, microorganisms, terrestrial vertebrates and invertebrates (Chin *et al.,* 2006). Natural products have played an intrinsic role in human life for thousands of years. Due to their low cost and availability, natural products have been used as a remarkable class of therapeutics to heal various ailments a source of medicine, especially in developing countries. Moreover, they are chemically diverse with various bioactivities and are the most valuable sources of drug discovery and development (Shen, 2015).

According to the World Health Organization (WHO), about 60% of the world's population depends on traditional medicine for their health care (El-Naggar *et al*., 2020, El-Sayed *et al*., 2020). It is possible that the use of natural products as medicinal agents predates the earliest recorded history when humans used various and specific plants to cure diseases (Barton, 1999). The oldest records dating to ancient Mesopotamia (2600 BC) described about 1000 plants and plant-derived materials, such as the oils of Cedrus species (cedar) and the juice of the poppy seed *Papaver somniferum* (Newman *et al*., 2000).

The discovery of penicillin from *Penicillium notatum* by Alexander Fleming in 1928 marked a significant shift from plants to microorganisms as a source of natural products (Fleming, 1944). Since then, microorganism-derived compounds have been utilized in medicine, agriculture, food industry and scientific research (Sanchez *et al*., 2012). The early years of antibiotic research discovered streptomycin from Streptomyces griseus (Waksman *et al*., 1946), gechlor etracycline from *Streptomyces aureofaciens* (Ehrlich *et*

al., 1947), cephalosporin C from *Cephalosporium acremonium* (newgeracimatsuand Abraham, 1955), erythromycin from Saccharopolysporaerythraea and vancomycin from *Amycolato psisorientalis* (Geraci *et al*., 1956). Given these historical successes, large pharmaceutical companies have continued to invest in this traditional domain (Dias *et al*., 2012). Currently, approximately 60% of approved small molecule medicines are related to natural products, and 69% of all antibacterial agents originate from natural products (Patridge *et al*., 2016, Matsumura *et al*., 2018). However, many natural compounds with potential as novel drug candidates occur in low concentrations in nature, often making drug discovery and development burdensome and economically impractical. Therefore, an emerging alternative solution is to express biosynthetic genes from the original producers in microbial hosts, notably bacteria and fungi (Song *et al*., 2014). Engineered microbes can produce appreciable amounts of scarce natural compounds, thereby facilitating the synthesis of the target novel compound and potent derivatives, as well as the validation of their activities (Matsumura *et al*., 2018). The natural product sector is not the only area that has undergone substantial growth or utilizes therapeutic products generated in/from living organisms. Prokaryotic and eukaryotic microbial cells, in combination with the advancement of recombinant DNA techniques, have been responsible for an explosion of biologics.

Comparison of natural products with chemically synthesized molecules reflects characteristics enriched for active target engagement including increased numbers of sp3-hybridized carbons and of chiral centres, fewer aromatic rings, larger macro cyclic aliphatic rings, lower nitrogen content and increased oxygen content, all contributing to more complex three dimensional structures. These properties enable natural products to more productively engage biological targets rather than the more planar and less stereo chemically complex features that dominate in synthetic compound libraries (Rodrigues *et al*., 2016). The beneficial chemical characteristics of natural products can be further elaborated in the lab though medical chemical strategies to produce compounds with improved drug-like properties. Despite their proven efficacy in drug discovery and development, the past 30 years have seen a steady decline in the number of new natural product-derived medicines entering into clinical use. This is the result of many factors. Changes in the process of drug discovery in the pharmaceutical industry in the 1980s and 90s saw a shift to automated assays enabling high throughput screening of thousands to millions of drug candidates. This change required equal access to vast libraries of com pounds that could be created with new synthetic strategies such as combinatorial chemistry, but not by traditional natural product extracts of plant or microbiological samples.

Herein, we will summarize the biological activities and applications of a variety of natural products and biologics and review the microbial systems used to produce these pharmaceutical compounds. We will also cover past and current attempts at improving the microbial production of these biological molecules and generating new molecules using diverse engineering approaches. In addition, we will discuss the challenges of the production of natural products and biologics in microbial systems and advances that can help overcome them for drug discovery and development. Future prospects for cutting-edge developments and technological advances in microbial production of bioactive natural products and recombinant proteins as the most valuable sources of therapeutics are also discussed**.**

Microbial cell factories

Selecting a suitable host strain is one of the most important aspects in the design of natural product and recombinant protein bioprocesses. We will review the characteristics of the algal and fungal strains used to produce natural products and biologics in this section. We will also present the tools and strategies that facilitate engineering of the hosts as microbial cell factories for the production of biopharmaceutical compounds.

1. Natural Products from Fungal Sources

Fungal-derived drugs include some of the most important medicines ever discovered, and have proved pivotal in treating chronic diseases. Not only have they saved millions of lives, but they have in some cases changed perceptions of what is medically possible**.** The idea that fungi contain biologically active compounds is not new and pre-dates the rise of scientific methodologies. Indeed, various cultures have long made use of fungi as medicines and hallucinogens (Guzman *et al.,* 1998). The isolation of pure chemical substances from fungi is not a recent endeavour either. Early examples of compound isolation date back to at least 1893 (Freedman *et al*., 2020). Despite this early knowledge of fungal bioactivity, the story of fungal drug discovery in many ways starts with the discovery of penicillin in the 1940s. A chance observation of antibiotic antagonism by a contaminant mould on a Petri dish resulted in the eventual discovery of a highly effective antibiotic that would change the course of history.

Obtaining Microorganism Strains for Biosynthesis of Bioactive Secondary Metabolites SMs

Figure 1 briefly illustrates a few steps from the isolation of a fungi strain to the development of a pharmaceutical product. The process begins with the isolation of the fungus strain from diverse environmental sources (e.g., water, plants, and soil), and the culture of the microorganisms. The product of the culture is processed for extraction and purification of the SM. Subsequently, biological assays and clinical trials are performed to define the possibility of future pharmaceutical applications of the SM (Figure 1).

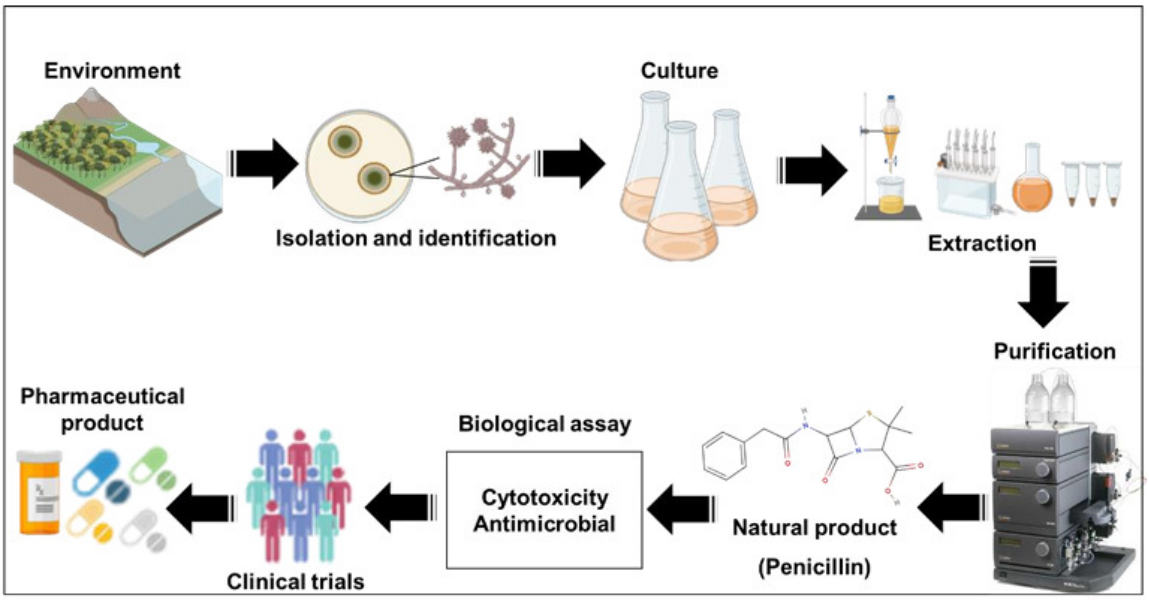

Fig. 1: Different steps for making pharmaceutical products from natural sources

Representation of fungal strain isolation and development of medicines containing natural products as the bioactive component. Penicillin is being used just as an example. (Source-Conrado *et al*. (2022), Prescott *et al.* (2023) have shown that despite the importance of fungal-derived drugs to the treatment of chronic diseases, in many cases their discovery is purely serendipitous or the result of random screening. The ability to gain clues to the mechanism of action of compounds produced by a given species before any chemical analysis has even taken place is proving to be a powerful investigational tool, and has attracted significant investment from the commercial sector. Even without these new experimental tools, research into previously known bioactive fungal metabolites has led to a range of fungal small molecules being tested in clinical trials, and a small number have recently received approval for use in humans. Future fungal drug discovery programs may benefit from a big picture view that takes into account patterns in the distribution of bioactive metabolites across the fungal kingdom, but this may involve examining traits such as fungal lifestyle and nutritional characteristics rather than simple taxonomic relationships. Taxonomic relatedness does not seem to be a good predictor, at least with the bioactivity data sets used. However, lifestyle flexibility may be a good indicator of bioactive metabolite production in the Ascomycota, but not in other groups. The fact that the fungal tree of life has so many unknowns andt hat so many bioactive species still have not been correctly placed, suggests that we may not yet be ready to use this type of information to guide drug discovery. Improved resolution of fungal genomic data combined with more densely sampled phylogenomic trees may help improve the situation.

Stadlerand Hoffmeister (2015) observed that there are three encouraging reasons why basidiomycetes advance mycology and natural product chemistry. Firstly, unique structures, e.g., the ones mentioned in the introduction, deserve elucidation of the biochemically and mechanistically intriguing basis behind their biogenesis. Secondly, fungi as such are a widely unexplored source for novel biotechnological products in general (cf. Rambold *et al*., 2013), and this especially holds true for the basidiomycetes. These two reasons alone justify new genomes to be sequenced. Finally, basidiomycetes are of outstanding ecological significance and may be key to answer the question as to why natural products exist. Due to their ability to

form mycorrhizae with conifers and deciduous trees, they are key elements of temperate and boreal climax vegetations. They efficiently degrade lignocellulose which makes them indispensable to keep the global carbon cycles going. The basidiomycetes and the existing genomes represent a good opportunity to follow a different approach, but still contributing substantially to natural product research: with perhaps a dozen of carefully chosen symbiotic, parasitic, and saprotrophic species and a concerted effort of mycologists, chemists, ecologists, biochemists and bioinformaticians we may come to a more profound understanding why these magnificent small molecules were evolved, beyond the established examples that they serve as defence agents and to compete with other microbes in their ecological niche.

Chugh *et al.* (2022) observed that in complement to its vital nutritional significance, numerous mushroom species of medicinal value have been identified as sources of bioactive chemicals. Incorporating entire mushrooms into one's diet could be beneficial as a nutritional supplement. The mushrooms with medicinal values contain a number of primary and secondary bioactive metabolites owing to which, the mushrooms possess various therapeutic activities such as anticancer, antiviral and anti-hypertensive actions. The same was envisaged from the clinical data as well. Also, the acute toxicity studies were performed on various mushrooms and it was evaluated that the most of the therapeutically active mushrooms are safe at a dose of 2000 mg/kg with mild side effects. Furthermore, high-quality, double-blind, randomized, long term, placebo-controlled human clinical investigations with big sample numbers and adequate power are required, as well as current statistical and bioinformatics tools.

Singh *et al.* (2019) fungal secondary metabolites production depends upon the growth condition. Compounds produced are of important chemical classes like alkaloids, terpenes, terpenoids, and sugar derivatives, for example, alliacol A, pasteurestins A and B, clavaric acid, helvolic acid, ergotamine, psilocybin, meleagrin, cyclophellitol, etc. They are reported to have a variety of biological properties antibacterial, anticarcinogenic, enzyme inhibitory, hepato protective, and others. However, at the laboratory level, the production of fungal secondary metabolite is very low; this leads to search alternative strategies to synthesize chemical compound in laboratory condition and at a higher rate of production. These objectives were somewhat achieved by chemical synthesis of compound. Moreover, total in vitro chemical synthesis does not always provide a way to produce chemical compounds at higher yield, however to overcome this problem, heterologous mode of producing secondary metabolite can be done. Heterologous expression of secondary metabolite is an effective strategy for describing cryptic gene, to achieve bioactive natural product clean background which aids to purification and down streaming of natural product.

Tehzeeb and Dhanabalan (2020) focused on antimalarial properties of natural products isolated from fungi. In present scenario, studies on isolation of fungal metabolite are more focused on marine fungi and endophytic fungi underestimating the potential of standard strains of pathogenic fungi. Considering large diversity of fungal species, only very few fungi have been studied and cultivated. This may account only to the surface of diverse world of fungi. Fungi irrespective of its pathogenicity may produce highly potent and widely accepted natural metabolites if properly cultured at optimum environmental conditions. Using the existing information and most widely use target of plasmodium, we have selected a standard strain of fungi such as Malassezia furfur is selected by cultivating it at different environmental conditions in a hope of finding potent antimalarial compounds. it at different environmental conditions in a hope of finding potent antimalarial compounds.

Shin (2020) marine fungi have been studied since the first record of the species Sphaeriaposidoniae (Halotthiaposidoniae) on the rhizome of the sea grass *Posidonia oceanica* by Durieu and Montagne in 1846, but they have largely been neglected, even though it is estimated that there are greater than 10,000 marine fungal species. To date, a relatively small percentage of described species are associated with marine environments, with ~1100 species exclusively retrieved from the marine environment, although estimates for the number of fungal species on the planet range from 1.5 to over five million, likely fewer than 10% of fungi have been identified so far. It is believed that the exploration of marine fungi that are living in new and extreme habitats will advance the isolation of novel marine fungi and, thus, might lead to the isolation of novel secondary metabolites.

Singh *et al.* (2021) highlighted the prospects of endophyte dependent biosynthesis of such plant-derived pharmacologically active compounds and the bottlenecks in the commercialization of this novel approach in the area of drug discovery. After recent updates in the field of 'omics' and 'one strain many compounds' (OSMAC) approach, fungal endophytes have emerged as strong unconventional source of such prized products.

Schueffler and Anke (2014) observed approximately 100 000 fungal species are known although far more than one million are expected. The variety of species and the diversity of their habitats, some of them less exploited, allow the conclusion that fungi continue to be a rich source of new metabolites. Besides the conventional fungal isolates, an increasing interest in endophytic and in marine-derived fungi has been noticed. In addition new screening strategies based on innovative chemical, biological, and genetic approaches have led to novel fungal metabolites in recent from 2009 to 2013 highlighting the originality of the structures and their biological potential.

According to Wang *et al*. from 1998 to 2019, 272 antimicrobial compounds were obtained from marine fungal strains isolated from sediments, sponges, algae, mangroves, and corals. China was the country responsible for the discovery of the majority of these compounds, which were obtained mainly from *Aspergillus* sp. followed by *Penicillium* sp. In spite of the fact that 207 compounds showed antibacterial activity and 68 were antifungal agents, none of them are in clinical trials. In a wider period, between 1981 and 2019, among 164 new antimicrobial drugs approved, 36 were of biological origin, of which 89% were prophylactic agents. In the same period, although fungal diseases were frequently reported, only two antifungal drugs were approved, both of synthetic origin (Newman and Cragg, 2020). In addition to the indiscriminate use of antibiotics by the population around the world, microorganisms' resistance to antimicrobials is also related to the high demand for animal protein for human consumption due to the regular use of antimicrobials in the modern production of this food.

According to Van Boeckel *et al*., the global average consumption of antimicrobials is from 45 to 172 mg/kg of animal produced per year, considering cattle, chicken, and pigs. In this sector, globally, the use of antimicrobials tends to increase by 67% in developed countries between 2010 and 2030, while in countries with low Human Development Index (HDI), such as Brazil, Russia, India, China, and South Africa, this rate may increase, reaching 99% . Historically, it is clear that drug discovery is still not enough to attend to the high demand for new antimicrobial and antitumor agents, evidencing the relevance of intensifying studies in order to have a sustainable use of the huge world biodiversity, as well as of microorganisms.

Natural Products from Algae

Algae are a very simple chlorophyll-containing organism composed of one or group of cells together in colonies which are basically not much related to each other making it polyphyletic in nature (Montessar *et al.,* 2016). Natural products from algae have been widely explored, since long time, for human use as food and as medical treatments. Many chemicals and products from algae have economic importance and are broadly used as it is a good source of fibre, minerals, antioxidants, vitamins, pigments, steroids, lectins, halogenated compounds, polysaccharides, proteins, polyunsaturated fatty acids and other lipids; thus, they are even consumed in many countries (Mehta *et al.,* 2016, Muraleedhara *et al*., 2016). Algae are a rich and varied source of pharmacologically active natural products and nutraceuticals. Currently these products are very valuable in the market. Even marine algae which are categorised into micro/macro algae are being very beneficial to the pharmaceutical industries. Marine algae are potential sources of highly bioactive secondary metabolites that might represent useful leads in the development of new pharmaceutical requirements (Suryanarayanan and Johnson, 2014, Raja *et al*., 2014, Gede Suantika *et al*., 2013). Many studies are now being carried out on the chemicals which are being extracted from marine algae for human benefits and welfare. After biofuel many researchers are working on production of biologic drugs by coaxing therapeutic pharmaceuticals to replace expensive drugs (Suryanarayanan and Johnson, 2014, Raja *et al*., 2014).

According to Aditya *et al*. (2016) marine algae have received growing attention as sources of bioactive metabolites and have convincing properties to make it stand out in front of synthetic drugs. The therapeutic drugs prepared from algae which exist on both sunlight and carbon dioxide in the air will be manufactured at one-thousandth of today's costs, which makes it cheaper. Microalgae is being widely used for nutraceutical supplements, species of *chlorella*, *Dunaliella*, *Haematococcus*, Spiirulina, *Aphanizomenon*, are widely evaluated by researchers for its potential. It generally depends on the protein content of the species which determines its credibility towards nutraceutical development. Extracts of *chlorella*, *Spirulina* have good antioxidant, anti-inflammatory, antitumor properties. Haematococcus has many vitamins in it which makes it more interesting towards nutraceutical development. Aphanizomenon plays a huge role in cholesterol controlling, stimulation of liver functions and also is a cure for many dermatological problems (Aajjane *et al*., 2014, Farfour and Al-Saman, 2014).

Farid Menaa (2021) concluded Marine algae are rich in bioactive nutraceuticals (e.g., carbohydrates,

proteins, minerals, fatty acids, antioxidants, and pigments). Biotic (e.g., plants, microorganisms) and abiotic factors (e.g., temperature, pH, salinity, and light intensity) contribute to the production of primary and secondary metabolites by algae. Easy, profitable, and sustainable recovery methods include novel solid-liquid and liquid-liquid extraction techniques (e.g., supercritical, high pressure, microwave, ultrasound, enzymatic). The spectacular findings of algal mediated synthesis of nanotheranostics has attracted further interest because of the availability of microalgae-based natural bioactive therapeutic com pounds and the cost effective commercialization of stable microalgal drugs. Algal extracts can serve as stabilizing/capping and reducing agents for the synthesis of thermodynamically stable nanoparticles (NPs). Different types of nanotherapeutics have been synthesized using physical, chemical, and biological methods. Marine algae are a fascinating source of lead theranostics compounds, and the development of nanotheranostics has been linked to enhanced drug efficacy and safety. Indeed, algae are remarkable nanobiofactories, and their pragmatic properties reside in their (i) ease of handling; (ii) capacity to absorb/accumulate inorganic metallic ions; (iii) cost-effectiveness; and (iv) capacity of eco-friendly, rapid, and healthier synthesis of NPs. Preclinical and clinical trials shall enable to really define effective algal based nanotherapies.

Ajit Kumar *et al*. (2025) Marine algae offer an attractive, environmentally friendly, and valid platform for the production of biopolymers that contain antiviral and anticancer compounds with the potential to solve major global health issues. Their bioactive molecules, such as polysaccharides, polyphenols, alkaloids, and terpenoids, possess various mechanisms of action, including antiviral activity, the induction of cancer cell apoptosis, and immune modulation. However, the ecological benefits of algae farming, including the ability to grow them in uncultivated land and use seawater, contribute to making them a sustainable resource. Nevertheless, challenges remain, such as the difficulty in separating specific bioactive compounds, production scalability, and concerns regarding toxicity and bioavailability. Developments in biotechnology, including genetic manipulation and bioreactor systems, together with further understanding of the unique marine ecosystem, will be essential for the exploitation of the full pharmaceutical value of marine algae. Through the integration of interdisciplinary methods, marine algae may become the cornerstone of novel, potent, and environmentally friendly therapies for viral infections and cancer

Boopathy and Kathiresan (2010) Marine floras, such as bacteria, actinobacteria, cyanobacteria, fungi, microalgae, seaweeds, mangroves, and other halophytes are extremely important oceanic resources, constituting over 90% of the oceanic biomass. They are taxonomically diverse, largely productive, biologically active, and chemically unique offering a great scope for discovery of new anticancer drugs. The marine floras are rich in medicinally potent chemicals predominantly belonging to polyphenols and sulphated polysaccharides. The chemicals have displayed an array of pharmacological properties especially antioxidant, immune stimulatory, and anti-tumour activities. The phytochemicals possibly activate macrophages, induce apoptosis, and prevent oxidative damage of DNA, thereby controlling carcinogenesis. In spite of vast resources enriched with chemicals, the marine floras are largely unexplored for anticancer lead compounds.

Ferdous and Yusof (2021) showed that over the last few decades, there have been several in vitro and in vivo studies regarding the antioxidant therapies which have shown that daily intake of a specific dosage of antioxidant nutraceuticals is inversely related to cancer risk as well as enhances the treatment efficacy, nonetheless, randomized clinical trials have shown mixed results which are considered as a real conundrum for the extensive use of antioxidant supplements in cancer therapy. These inconsistent outcomes can be directed by several factors, such as dose, synergism, the bioavailability of antioxidants used, patients'health status, type of cancer, lifestyle, tendency to supplement intake, and the duration of studies with other variables involved.

Musale *et al.* (2021) observed that present COVID-19 pandemic has highlighted the importance and priority of discovery compounds from marine natural resources for the prevention and treatment of severe and acute viral infections. To the best of our knowledge, Macro algae, micro algae, Cyanobacteria and diatoms are excellent source of antiviral activity. Several cyclic or linear peptides and depsipeptides isolated from Cyanobacteria are protease inhibitors, which is considered as significant antiviral candidate. Numerous in vitro or in vivo studies has shown the potential of algae against wide range of viruses. The use of natural products in the manufacturing of drugs is an ancient and well-established practice. The pharmaceutical potential of marine algae deserves more scientific attention, inter disciplinary research along with its diverse habitat explorations to find novel compounds to control viral diseases in humans and probably in recent pandemic, COVID-19.

Khavari (2021) Microalgae are microorganisms and biorefinery factories for the production of recombinant proteins. In addition, diatom shells have unique 3D structures and are used for the production of NPs for drug and biomolecule delivery. Different morphology and functionalization could enhance drug loading and release from DE NPs. Several studies have investigated modified DEMPs for the specific delivery of drugs (DOX, camptothecin, paclitaxel) in the treatment of colon and breast cancer, proposing positive outcomes.

Torresa *et al*. (2014) concluded macroalgae are the main organisms responsible for nitrate assimilation, the most abundant form of nitrogen found in the marine environment. Additionally, algae are photosynthetic organisms, primarily responsible for production of O_2, and simultaneous take up of CO_2. Algae are at the bottom of the food chain, and this position means that the nutritional composition of macroalgae plays an essential role in the food chain. The biochemical composition of macroalgae, including the levels of fatty acids, sterols, amino acids, sugars, minerals and vitamins, determine the food quality transferred to other trophic levels. The search for natural products in different environments, together with the traditional knowledge of tribes and ethnic groups, plays an invaluable role and clue in the current drug discovery process. The investigation of marine macroalgal chemical compounds has proven to be a pomising area of pharmaceutical study, resulting in new drugs with leishmanicidal and trypanocidal activity. Although the study and use of algal compounds against NTDs are recent, many reports have already been published describing isolated compounds from several algae with strong antiprotozoal activity and low toxicity. Therefore, the discovery of novel molecules with a high therapeutic potential from marine macroalgae is very welcomed.

Table 1 : Biologically active compounds extracted from micro and macroalgae (Slusarczyk *et al*., 2021)

Compounds	Microalgae	Macroalgae references
Proteins	Ulvales	Glutamic acid (*Pyropia yezoensis*) Rhodophyta
Lipids	DHA EPA (*Trachydiscus minutus*, *Odontella aurita*, *Phaeodactylum tricornututum*)	Fatty acids (rhodophyta, phaeophyta)
Minerals	Aquamin	Rhodophyta
Vitamins	Tocopherol Riboflavin (*Chlorella stigmatophora*) cobalamin (*Dunallel latertiolecta*) thiamine (*Volvox carten*) Ascorbic acid	*Macrocystis pyrifera, Pyropia yezoensis, Porphyra umblicalis*
Polysaccharides	Ulvans (*Ulvales, chlorophyta*)	Alginate (*Laminaria* sp.) agar (*Gracilaria cornea*) fucoidans (*Phaeophyta*) laminarans (*Phaeophyta*) caarageenans (*Gelidiales, gigartinales, gracilariales*) porphyran (*Rhodophyta*)
Antioxidants	Astaxanthin (*Haematococcus pluialis, Chlorella zofingiensis*)	ascorbate glutathione
bioflavonoids	Rutin Quercetin Kaempherol	
Polyphenols	Carboxylic acid, Bacillariophyceae, (*Eustigmatophyceae, Chlorophyta*) hydroxycinnamic, Acids (*Chlorella vulgaris, Haemalococcus pluvialis*)	*Phlorotannin phaeophyta* Catechins, flavonoids, tannis, lignans, mycosporine, bromphenols (Rhodophyta)
pholorotannins		*Phaeophyta, Ascophyllum nodosum*
pigments	Chlorophyll b (green algae)	*Fucoxanthin phaeophyta, Perdinindino flagellale, Phycoerythrin rhodophyta, Phycocynin rhodophyta*
Unsaturated fatty acid	Green alga (ulvalactuca)	
sterols	Diatoms (Gomphonema), Green algae (Ankistrodesmus), Monoraphidium, Scenedesmus	*Brassica sterol, palmaraia decipiens, Fuscosterol, rhodophyta, phaeophta*
phytohormones	Auxins, abscisic acid, cytokinin (Chlorophyta)	

Minhas *et al.* (2024) stated cancer therapy aims to eradicate tumour cells, and chemotherapy drugs are often paired with numerous adverse side effects. Therefore, natural substances are very effective and have fewer side effects than traditional chemotherapeutic drugs. Prokaryotic and eukaryotic algae offer various organic anti-cancer compounds that could be administered to treat multiple cancers. Algae species conserved include *Fucus vesiculosus, Lyngbyaboulloni, Nostoc linckia, Symplocahydnoides,* and *Lyngbya* majuscule and their phytochemicals such as symplo statins, cryptophycin, apratoxin A, curacin A, and fucoidan effectively treat cancer in vitro. Such compounds effectively treat melanoma, leukemia, colon carcinomas, kidney tumours, brain meningiomas, and breast cancer. It is expected that using these natural resources will not only revolutionize the fields of drug discovery and development but also serve the masses by curing cancers and improving their lifestyle. Hence, algae derived phytochemicals offer a new direction for effective cancer treatment using natural and renewable resources.

Conclusion

In recent years, polysaccharides with immune regulatory and anticancer properties contained in some fungi and algae have been intensively researched. Thanks to their ability to activate the immune system, these can support the treatment of cancer. An additional advantage of naturally derived polysaccharide compounds is the fact that they often buffer the side effects of chemotherapy, and that they do not exhibit toxic effects on the human body. The positive effects of fungi and algae result from the interaction of various active ingredients contained in their organisms. It is also possible to use ready-made preparations of fungal origin in the form of capsules or tablets containing purified fungal or algae extracts, treated as dietary supplements. They are most often used as preparations to strengthen the immune system and prevent cancer. Preparations of this type are mainly produced from such species of medicinal fungi as *Ganoderma lucidum* (lacquered bracket or reishi), *Lentinula edodes* (shiitake), *Grifolafrondosa* (hen-of-the-woods), *Trametes versicolor* (turkeytail), *Ophiocordy cepssinensis* (caterpillar fungus), and in the case of algae from genera such as *Chlorella* and *Spirulina*. There are also preparations containing extracts from various species of fungi, including lichens species such as *Cetrariaisla indica*, *Umbilicaria esculenta* and species from genera *Cladonia*, *Usnea* and many others. The natural organisms, such as fungi, lichens, fungi and algae, could be used as supplementary medicine, in the form of pharmaceutical preparations and food sources. Further advanced studies are required on the pharmacological properties and bioactive compounds of these organisms. The impact of fungi and algae on human health can be beneficial, opening up new perspectives for studying their biological properties. Due to bioactive properties of these organisms, it may contribute to health benefits for consumers.

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