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Current Status and Prospects of Microalgae Bioactive Compounds for Anticancer and Antiviral Actions

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Abstract: *Introduction.* Microalgae, which include hundreds of thousands of varieties in both fresh and salt water, are the shortest link in aquatic food chains. Viral medication, cancer drugs, obesity treatment, skin treatment, and other uses are possible for pharmacologically active microalgae chemicals. *Objective*. To summarize the antiviral and anti-carcinogenic effect of microalgae that can be a promising way to drug development. *Method*. In this study, about 40 papers which are about microalgae, has been summarized and expressed in short summary. *Result*. Studies at the University of Verona in Italy have shown that algae called *Chlamydomonas reinhhardtii* trigger an antibody that is effective in suppressing the corona virus and also the cancer protection of Astaxanthin and Phycocyanin has been proved in mice test which can later be used to suppress cancer on a large scale. *Conclusion*. They will become one of the best means of making medicine in the future, as most of the medicines are now resistant, including antibiotic resistance and cancer drug resistance. So now is the time for us to look for other sources of drugs.

Keywords: Microalgae; Viral, Cancer; Nutrition; Bioactive compounds

1. Introduction

Microalgae are small, photosynthetic eukaryotic organisms that are high in dietary protein and nutrients. In current years, there has been a lot of buzz about microalgae and their prospective uses in the pharmaceutical and nutraceutical industries as a source of bioactive medical goods and food components with antioxidant, anti-inflammatory, anticancer, and anti-microbial qualities. Viral medication, cancer drugs, obesity treatment, skin treatment, and other uses are possible for pharmacologically active microalgae chemicals. This review compiles all research on the antiviral, anti-inflammatory, anticancer, and anti-obesity benefits of microalgae compounds. Furthermore, there is a rising demand for microalgae to be employed as nutraceuticals and dietary supplements [1].

Seaweeds are small single-cell organisms that are either prokaryotic or eukaryotic and may be found in both fresh water and salt water. They generate over half of the oxygen in the envionment and use the greenhouse gas carbon dioxide to develop photo-autotrophically. Microalgae, in collaboration with bacteria, supply energy to all trophic levels above them [1]. They generate a wide range of chemicals, including photosynthetic

pigments (carotenoids and chlorophylls), minerals, fiber, polysaccharides, enzymes,sterols, polyunsaturated fatty acids, vitamins, peptides, and toxins [2]. It is critical to stress that the properties of microalgae vary depending on the species and growing circumstances like as temperature, CO2 supply, lighting, pH, salt, and nutrients [3]. The primary groups of eukaryotic algae evolved through a sequence of endosymbiotic interactions, culminating in widely scattered and diversified lineages. The Chlorophyta, Rhodophyta, and Glaucophyta developed from a photosynthetic cyanobacterium, which arose to the chloroplast. Green algae subsequent endosymbiosis produced two main groupings, the Euglenophyta and photosynthetic Rhizaria, the Chlorarachniophyta [4].

During the last few years, huge money has been spent on screening microalgal bioactive metabolites [5]. Sulfated polysaccharides [6], different carotenoids, different carotenoids, omega-3 fatty acids [7], marennine [8] and polyphenols [9] have all been found and isolated from marine microscopic algae. Some of the compounds have shown biological activity, such as anticancer, strong antioxidant, antiviral, and anti-inflammatory characteristics. Polyphenols [10] and omega-3 [11] and several of these chemicals have shown biological activity, such as strong anti-inflammatory, antioxidant, anticancer, and virucidal characteristics. Nevertheless, there are emerging health and economic issues connected with massive microalgae development and the bioeconomy method that should be solved in order to secure the long-term development of large items with nutritional and medicinal advantages.

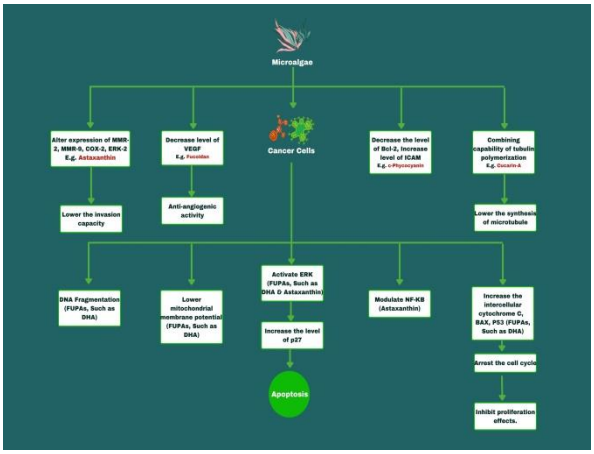

Figure 1*: Mode of action of microalgae*

The review expresses the effectiveness in our human body for altering the disease like cancer, infections, obesity and nutritive beneficiaries of these marine organisms. The cancerous diseases and viral contaminations have just emerged throughout the world. So, it is the time to pay attention for searching a new drug source.

Microalgae species producing bioactive compounds for inhibiting cancer

Carcinoma refers to a wide range of illnesses characterized by unregulated cell growth in the body. There are over 200 distinct forms of cancer, and certain tumors may gradually extend into other organs, creating fatal metastasis. During century, surgery, chemotherapy, radiation, and chemotherapy were the only options [29]. Analyses for the four most frequent kinds of cancer in 2012, according to the ECO (European Cancer Observatory), were as follows: There have been 342,137 instances of colon carcinoma, 309,589 cases of lung carcinoma (including trachea and bronchus cancer), 358,967 cases of breast carcinoma, and 82,075 cases of skin melanoma [28].

Microalgae are aquatic microorganisms that create biomass rich in primary and secondary metabolites including such fats, carbohydrates, enzymes, and carotenoids by consuming CO2, light, and mineral elements. HVCs such as lutein, zeaxanthin, and astaxanthin can be produced by microalgae. Tetraselmis suecica, a tropical green microalga of the Chlorophyceae class, is abundant in biomolecules, including 74 g of PUFAs per kilogram of collected microalgae. In vitro, it's aqueous extracts demonstrated high antioxidant and cell healing activities in the lung cancer cells cell line A549 [30].

Understanding the mechanisms by which various chemicals exert their effects is critical for designing medications to treat cancer and improving the lifestyle of individuals at risk. Different compounds exhibit reduction of tumor angiogenesis, enhancement of cell cycle arrest, induction of apoptosis or necrosis, and immune stimulation through a variety of pathways. The manner by which algal bioactives operate is mostly determined by their nature and chemical characteristics [30].

Astaxanthin

Astaxanthin is a kind of xanthophyll carotenoid found in plants and seafood. Carotinoids are mostly composed of hydrocarbons (-carotene, -carotene, -carotene, and lycopene) and oxidized compounds (violaxanthin, neoxanthin, fucoxanthin, zeaxanthin, astaxanthin, and canthaxanthin). AXT was determined as a new metastasis blocker using high-throughput drug screening, and the inhibitory impact of AXT on invadopodia development in carcinoma cells was verified. Moreover, AXT promotes the production of microRNA-29a-3p and miR-200a via transcriptional modification of the oncogenic transcriptional regulator MYC, ultimately inhibiting their downstream target genes, marker MMP2 and marker ZEB1, and thereby limiting EMT and metastasis [31].

Phycocyanin

Phycocyanin is an antioxidant that helps to preserve the liver by reducing hepatic lipid peroxidation. It also retrieves free radicals from injured nerve cells that might help to reduce DNA oxidative effects of free radicals and neuronal cell death [33]. Ever more studies have demonstrated that phycocyanin has an anti-cancer impact in numerous cancer cell types (such as liver cancer, lung cancer, colon cancer, breast canceria) in vitro and in vivo [32].

Stigmasterol

Utilizing chromatography (PTLC) techniques including such silica gel open column chromatography & sample preparation thin layer chromatography, Navicula incerta extracts were obtained. They tested the anti-proliferative impact of extracted stigmasterol on HepG2 cells at 5, 10, and 20 M. (liver cancer cell line). Immunomodulatory values of 40%, 43%, and 54%, correspondingly, were discovered, indicating a dose-dependent trend.

Table 1: Active microalgal species with anti-carcinogenic effects [12, 13]

Microalgae	Fraction	Target Cells	Mechanism	Refernce
Arthrospira platensis	Phycocyanin	Lung cancer - A549	Cell apoptosis/blebbing necrosis	[44]
Chlorella pyrenoidosa		Liver cancer, HepG2 cells	Apoptosis (morphology)	[12]

Chlorella ellipsoidea	Carotenoid extract	Colon carcinoma (HCT-116)	Anti-proliferation	[12]
Chlorella Vulgaris	Polyphenols, Flavonoid	Lung cancer (H1299, A549, and H1437)	Affects migration of cells, inhibits metastasis	[41]
Cocconeis scutellum	Eicosapentaenoic acid (EPA)	Breast carcinoma (BT20)		[43]
Dunaliella tertiolecta	Violaxanthin	Breast adenocarcinoma (MCF-7)		[42]
Dunaliella salina		Colon cancer, SW480 cells	Antiproliferation	[45]
Pavlova lutheri		Fibrosarcoma, HT1080 cells	Metastasis inhibition, MMP-9 inhibition	[12]
Synedra acus	Chrysolaminaran (polysaccharide)	Colorectal adenocarcinoma (HT-29 and DLD-1)		[12]

Nutrition value of Microalgae

Seaweeds are introduced as novel model organisms for a variety of biotechnological processes, involving biodiesel generation [14], wastewater bioremediation [15], and dietary supplements for animal and human nourishment. Recent economic feasibility studies have revealed that, due to restricted biodegradability and the expenses of commercial algae production, producing biofuels is not cost-effective because it is combined with the manufacturing of higher-value co-products [16].

For centuries, microalgae have been employed as a human food source or nutritional supplement. Around AD 1300, the Aztecs employed the cyanobacterium Spirulina from Lake Texcoco (Mexico). Local fishermen were recorded by Spanish chroniclers as taking bluegreen masses from the rivers and preparing them into a dry snack known as 'tecuitlatl.'[18] Currently, the filamentous green algae Spirogyra and Oedogonium are consumed as a dietary component in Thailand, Burma, Vietnam, plus India, while the species N. punctiforme, N. flagelliforme, and N. commune are ingested conventionally in China, Mongolia, Tartaria, and South America. Chlorella and Spirulina are now heavily marketed in health stores, garnering international appeal as one of the healthiest foods known to man. These microorganisms are also fed to a variety of mammals [17].

The nutritional content of any algal species for a certain organism is determined by its cell volume, accessibility, potentially toxic production, and metabolic makeup. Table 2 compares the gross composition of ten microalgae species. However, the contents of the micro-algal groups and species vary greatly, protein is always the most abundant biological ingredient, accompanied by lipid and finally carbohydrate. Protein, fat, and carbohydrate levels range from 12-35 percent, 7.2-23 percent, and 4.6-23 percent, proportionately, when shown as a percentage of total volume [19].

ICP analysis is the most used test to assess the bioactivity of a material through quantifying the changes in ion concentration in the solution. The highest ionic release of calcium and phosphorus by intervention group (contained bioglass filler) may be contributed to the release of calcium and phosphorus ions from bioactive glass compared to that of control group which did not contain any fillers[22]. SEM and EDX analysis that were carried out in order to assess the qualitative descriptive changes in surface morphology of the specimens and detection of any apatite precipitate. The spherical and irregular shaped beads region in the control group may be represent the pre-polymerized PMMA beads region which surrounded by in-situ PMMA. While, the white patches in the intervention group may be represent the calcium phosphate dense precipitate on the corner of PMMA beads which forming an apatite coating layer[22].

Nano-sized bio-ceramic particles serving as a reinforcing agent that could be enhance the mechanical and biological properties of the implants [23]. The improved compressive feature of the intervention group may be due to the reinforcement effect of the strong nano-sized bioglass ceramic fillers that the control group which composed only from a weak polymer[23,24].

Table 2: Nutritional value of species of micro-algae commonly used in aquaculture [19]

Microalgae	Protein	Carbohydrate	Lipid
Chaetoceros calcitrans	3.8	0.68	1.8
Chaetoceros gracilis	9.0	2.0	5.2
Dunaliella tertiolecta	20.0	12.2	15.0
Chroomonas salina	35.5	11.0	14.5
Nannochloropsis oculata	2.1	0.48	1.1
Tetraselmis suecica	52.1	20.2	16.8
Pavlova lutheri	29.7	9.1	12.3
Nannochloris atomus	30	23.0	21
Chroomonas salina	29	9.1	12
Tetraselmis suecica	31	12.0	10

If bioactive molecules are introduced to commonly recognized or normally consumed meals, it is feasible to supply bioactive compounds to the maximum of the population [20]. Whilst incorporation of peptides into meals has yet to be described, other

microalgae-derived substances and entire cells have been employed as culinary additives for a variety of applications [21]. Certain microalgae species have a favorable influence on the techno-functional and anti-oxidizing qualities of food emulsions [22]. Gels have been proposed as a medium for delivering important microalgae-based chemicals [23]. Numerous microalgae species were included into gels to enhance their structure and to deliver antioxidants and particular -3 PUFAs to potential customers. Similar research, although with different microalgae species, have been published.

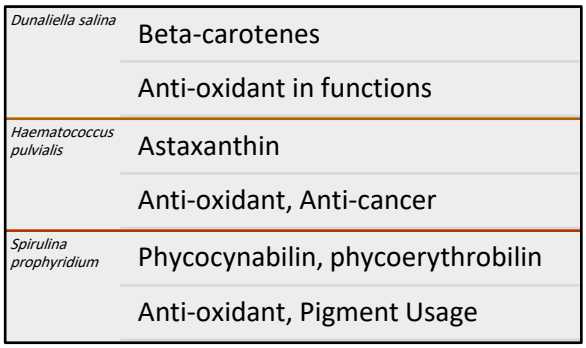

Figure 2: Bioactive compounds from microalgae

Milk products would also be combined with sea algae to offer bioactive substances [24]. Few scientists believe that definite species, including such Arthrospira spp., can boost the aggrandizement of desirable good bacterial fragments in food products and milk, enhancing the sustainability of the probiotics [25]. The appearance of trace minerals, vitamins, and many other bioactive components in microalgae granules encourages the growth of desirable microorganisms. Bread and cookies are appropriate categories for delivering microalgae-based components. Factors include flavor acceptability, variety, ease of preservation and transit, consistency, and appearance. As Chlorella vulgaris has been utilized in desserts as a coloring agent and more also a possible antioxidant and multivitamins [26].

Considering the phytonutrients properties of Chlorella and Arthrospira, consumers typically regard changes in color and flavor in meals as unfavorable [27]. The greenish color of microalgae restricts its usage in everyday items since it influences customers' perceptions of flavor and purity.

Antiviral Effects of Microalgae

Following the COVID pandemic, which resulted in a large number of deaths and the global financial meltdown in 2020, science has spent the previous year focused on the study of anti-virally active chemicals in general [34]. Viruses are the tiniest and most numerous organisms on the planet. Their distinctiveness stems from the fact that they can only proliferate within the organisms of other living beings. They are devided as non-living because they are composed of a center of genetic material, whether DNA or RNA, surrounded by an outer protein covering known as a capsid [35].

Seaweeds, also known as phytoplankton by scientists, are very microscopic plant-like creatures with diameters ranging from 1 to 50 μm with no roots, stems, or foliage. Microalgae, which include hundreds of thousands of varieties in both fresh and salt water, are the shortest link in aquatic food chains. In modern eras, algae have yielded the discovery of over 15,000 novel chemical compounds. It has been revealed that the maximum of bio chemicals derived from microalgae have antiviral properties. Despite substantial study on the bactericidal, antioxidant, and antifungal activities of these bioactive metabolites, there has been little research on their antiviral effects [34].

Seaweeds and cyanobacteria are among the greatest production house of biologically active chemicals with antimicrobial and pharmacological activity [36]. Flavonols flavanones, and alkaloids have been express to suppress proteins associated in COVID-19 proliferation such as 3CLpro, TMPRSS2, and ACE2.

Sulphated fucans from the brown seaweeds D. mertensii, L. variegata, F. vesiculosus, and S. schroederi have been shown to protect against HIV transmission by inhibiting reverse transcriptase actions [37]. Cladosiphon okamuranus fucan polysaccharide prohibits DENV-2 proliferation in renal cell (BHK-21) cell line [38].

Table 3: Viruses are prevented from entering the body by algal chemicals [39].

Species	Fraction	Inhibiting mode of entry	Virus	Reference
Kjellmaniella crassifolia	Fucoidan	Respiratory epithelia	IAV-A	[46]
Undaria pinnatifida	Fucoidan	Alimentary epithelia	IAV-A, Avian IAV-A	[47]
Durvillaea antarctica	Protein extract	Dermal lesion	HSV-1, HSV-2	[48]
Macrocystis pyrifera	Protein extract	Dermal lesion	HSV-1, HSV-2	[48]
Symphyocladia latiuscula	Bromophenols	Dermal lesion	HSV-1	[49]

2. Results

Studies at the University of Verona in Italy have shown that algae called Chlamydomonas reinhhardtii trigger an antibody that is effective in suppressing the corona virus [40]. Another study found that oral vaccines could be developed from genetically modified algae. Moreover, the cancer protection of Astaxanthin and Phycocyanin has been proved in mice test which can later be used to suppress cancer on a large scale.

3. Conclusions

In our world, new types of cancer are constantly appearing and at the same time, the types of viruses are also becoming very different. But drug inventions are not accelerating with such rapid variation of disease. So, perhaps, microalgae will become one of the best means of making medicine in the future, as most of the medicines are now resistant, including antibiotic resistance and cancer drug resistance. So now is the time for us to look for other sources of drugs. Moreover, through genetic engineering, it will be possible to easily develop more advanced drugs from these microalgae, which may become anticancer or antiviral drugs in the future.

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