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Bioactive Compound from Micro Algae and their Anti-Cancer Properties

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ABSTRACT

According to the World Health Organization (WHO) 2020 statistics, cancer is a second leading cause of death before the age of 70 years in almost every country of the world. Know a day's; various allopathic drugs are used for the treatment of in cancer diseases, which causes side effects and many other complications. To overcome these issues, researchers' finding the alternative therapies based on has gained significance in recent times. Mainly they focused natural bioactive compounds with no side effects and higher therapeutic efficacy. The terrestrial and aquatic photosynthetic organisms are naturally rich in several types of bioactive compounds. Several species of microalgae are studied and found to be rich in Secondary metabolites such as Phenols, Flavonoids, Alkaloids and Tannins etc. Microalgae are unicellular, eukaryotic, photosynthetic organisms, which can easily grow in both marine as well as in freshwater environment. The secondary metabolites produced by microalgae have great therapeutic implications against several diseases and some of the compounds such as MAAs are already in the market and in phase III clinical trials. Here this review will summarize the anti-tumorigenic properties of bioactive compounds from microalgae and will also compare their other therapeutic properties for future drug development.

Introduction

Cancer is the second major causative disease globally. According to WHO statistical estimated 19.3 million new cancer cases and almost 10.0 million cancer deaths occurred in 2020. It has become increasingly recognized that cancer cases predispose to a variety of cancers, particularly Lung, Liver, colorectal and breast cancers [1]. The previous studies arereported on biological products having plenty of bioactive compounds and are playing their role in various medical activities. From ancient period plant product having rich of bio-metabolites as medicine and it use for human diseases, but this plant derived phytochemicals compound were screen and most of these are identified. In this regard, natural products might provide alternative drugs with better characteristics. Micro algae's are regular uptake through the diet hence some previous studies suggested that it having more biological activities than the terrestrial origin and also new path for novel pharmacological formulations. It might help to prevent the human disease [2]. Micro algae are potential sources of novel bioactive compounds and interestingly have biological effects, such as antibacterial, antifungal, antioxidant, anti-diabetic, and anti-inflammatory activities [3]. In many countries algae's prominently used as food and traditional medicine because it presence of micro, macro minerals, polysaccharides, essential amino acids, rich-fibers, proteins, essential fatty acids, among this it also having rich source of vitamins like A, B and C. [4]. Some of the marine algal strains are reported to have higher number of secondary metabolites like alkaloids, terpenes, steroids, polyketides, Phenolic compounds, tannins, fucoidans and polyphenols. These secondary metabolites can reduce the risk of chronic disorders such as cancer [5]. Hence,

in this review we will focus on micro algal bioactive compounds and their potentialactivities on different cancer cells.

Source of Micro Algae

Around 70% of our planet is occupied Bywater and it hosts a huge variety of marine organisms with large metabolite diversity [6]. Microalgae are microscopic organisms, it could be found over almost all ecosystems and habitats on the Earth, found in seawater as well as in freshwater. They may grow as free-floating or growing attached to substrates. Microalgae may even grow on fine sand, clay, or other material carried by running water and deposited as sediment, especially in a channel or harbor surfaces. There is a possibility of the well-founded opportunity for a larger range of microalgae species to be utilized for human nourishment. A wide variety of microphytes comprise very rich sources proteins for humans [7]. Micro algae can be classified as eukaryotic microorganisms or else prokaryotic cyanobacteria (blue-green algae), with more than 25,000 species already isolated and identified. These microorganisms perform photosynthesis, which is an important natural mechanism to reduce the atmospheric CO_2 concentration. Microalgae are also characterized by a short generation time, multiplying exponentially under favorable environmental conditions; microalgae can grow autotrophy, heterotrophy, and mixotrophy [8].

Bioactive Metabolites and Anticancer Efficacy of Micro Algae

The micro algae are rich in bioactive compounds as they can synthesize several stress specific natural secondary metabolites, with promising biomedical applications. The impact of marine algae in the area of traditional medicine is huge and they have been used as Aluredian Unani in various countries. Micro algae produce diversified compounds and rich sources of proteins, vitamins, essential fatty acids, and essential amino acids. Along with most promising bio active metabolites are present such as, Phenols, Alkaloids, Flavonoids, Carotenoids and other natural antioxidants. These metabolites act as free radical scavengers and prevent free-radical formation thus reduce the oxidative stress and help to prevent the diseases such as cancer, diabetes, early aging, and several other inflammatory diseases. Currently, cancer causes death rates increasing day by day, for everyone in seven deaths in the world is caused by cancer and it's far higher than AIDS, tuberculosis, and malaria's combined deaths rate [1]. Whole world understands the urgency of some drug, which can either help to prevent or cure the cancer. If this drug comes from natural compounds, then it will be affordable to all and will not have any side effect. Algal diversity is one of the hopes for finding such as natural drug and recently has being extensively explored. Below we have discussed some of the important algal species with promising anti cancerous properties.

Chlorella Species

Carotenoids such as lutein, zeaxanthin, beta-carotene and astaxanthin are commercially available, which are the main source of the *Chlorella ellipsoidea* and *C. vulgaris* (micro algae's) [9]. These metabolites are tested an anti-proliferative effect on a human colon carcinoma cell line (HCT116). As such as these active compounds are promoting apoptosis effectively in colon cancer.

Chaetoceros Calcitrans

Particularly Chaetoceroscalcitrans are studied for the cytotoxicity especially on mammarycarcinoma cell lines (MCF-7, MDA-MB), Adeno carcinoma cells, mammary epithelial (MCF-10A) and human peripheral blood mononuclear cells (PBMCs) [10].

Amphidinium Carterae

This micro alga extracted bioactive compounds are shows the anti-proliferative, apoptosis and cell growth inhibition activity on various tumorigenic cell lines such as human promyelocytic leukemia cells (HL-60), mouse melanoma tumor cells(B16F10), and Adenocarcinomic human alveolar basal epithelial cells(A549). Cytotoxicity assays were also carried out using the mouse monocyte macrophage cell line (RAW 264.7) [11].

Skeletonema Marinoi

Thisclass of microalgae are identified by microscopic studies and they derived more than the 32 species. The compound resin was isolated from this class of microalgae, and this metabolic compound obtains hydrophobic fractions which are from *Alexandriumminutum*, *Alexandriumtamutum*, *Skeletonemamarinoi* and *Alexandriumersoni* were active against on melanoma cancer cell line [12].

Chlorella Sorokiniana

The chlorella speciesbiomass is widely using as nutrition supplement in many Asian countries. *Chlorella sorokiniana* active compounds effect on lung adenocarcinoma cell lines and which are also inhibit main cell pathways activation of caspase 9 and caspase 3 involved and to promotingapoptosis in mitochondrial pathway [13].

Thalassiosirarotula, Skeletonemacostatum and Pseudonitzschiadelicatissima

These microalgae show anti-proliferative activity on the human colon adenocarcinoma cell line (Caco-2) which is isolated three polyunsaturated aldehydes (PUAs) such as, 2-trans-4-cis-7-cisdecatrienal; 2-trans-4-trans-7-cis-decatrienal and 2-trans-4-trans-decadienal had [14].

Synedra Acus

The well common water-soluble biopolymer such as Chrysolaminaran Polysaccharide, isolated from chrysolaminaran family of marine micro algae (Synedra acus), chrysolaminaran is promoting anti-cancer activity on human colon cancer cells (HTC-116 and DLD-1) [15].

Phaeodactylum Tricornutum

Nonyl 8-acetoxy-6-methyloctanoate (NAMO) isolated from *Phaeodactylum tricornutum* it was tested as anti-malignant activity on humanleukemia cell line (HL-60) and lung carcinoma cell line (A549). It occurs proportionally to the concentration of NAMO, inhibits the stage of G1 phase in the Cell cycle and also observed activation of the pro-apoptotic protein Bax, suppression of the anti-apoptotic protein Bcl-x. It increases in the expression of tumor suppressor proteins like caspase-3 and p53 proteins [16].

Phaeodactylum Tricornutum

Monogalactosyl Glycerols isolated from *Phaeodactylum tricornutum* and tested iton mouse epithelial cells (W2 and D3). The W2 epithelial cell line is a wild type, while D3 epithelial cells have the apoptosis function disabled through gene deletion, this assay is one of the approaches for the study of apoptosis and its role in cancer and tumorogenesis [17].

Bio Active Compounds from Other Marine Micro Algae

The marine micro algal potential species, major sources of anti-tumorbioactive compounds, available in the market and under Phase III clinical trials (Table 1) [18-23]. At present days, several allopathic drugs are used in the cancer treatment to reduce oxidative stress. The natural bioactive compounds have represented, and they still do an important source of drugs with high therapeutic efficacy. In condition, terrestrial and aquatic photosynthetic organisms have been shown to be an essential source of natural compounds, some of which might play a leading role in drug development. Plants, algae, seaweeds, and seagrasses are the first reported sources of natural products for discovering novel pharmacophores among this micro algae's are contain rich sources of bioactive metabolites (secondary metabolic) compounds were extracted from natural and genetically modified micro algae's, in response to treatment of several cancers activity with subsequent acquisition of invasive behavior both *in vitro* and *in vivo* studies [24].

Table 1: Micro algae, active compounds and the target cancer cell lines.

Micro-Algal Species	Active Compounds	Target Cells	Reference
Ecteinascidia turbinate	Ecteinascidin/ Trabectedin (alkaloid)	MCF7 A549	[18]
Symploca species/ Dolabellaauricularia VP642	Brentuximabvedotin (antibody conjugated drug)	Lymphoma cells	[19]
Halichondriaokadai	Eribulinmesylate (macrolide)	DLD-1 LNCaP HL-60 (*Prostate cancer*)	[20]
Cryptothecacrypta	Cytarabine (nucleoside)	Acute Myeloid Leukemia cells	[21]
Aspergillus sp. CNC139	Plinabulin (diketopiperazine)	Multiple myeloma cells	[22]
Aplidiumalbicans	Plitidepsin (depsipeptide)	MCF-7 (Mammary cancer cells)	[23]

Summary and Conclusion

This article reviewed the effect of algal extracts as a medicine for cancer. Since ancient era, natural plant or algal extracts have been used for treating various diseases. Natural products are known to have large number of nutraceuticals and pharmaceuticals properties. The bioactive compounds from micro algae can play an important role in human health and disease prevention and cure. Algal extracts are used in traditional medicine and recent studies investigated the beneficial effects of their secondary metabolites, such as reduction of oxidative stress and modulation of apoptosis and cell cycle. The exploitation of algal diversity might help to develop novel algal dietary supplements and pharmaceuticals to prevent or treat chronic diseases such as cancer. In conclusion, we can say that micro algae offer a great variety of bioactive molecules with potential health benefits. Several types of micro algae are already consumed as food additives and nutritional supplements. However, there is an impelling necessity of considering the algal bioactive compounds in drug discovery programs and to investigate their biological effects in deeper detail. This will for sure, help to find new pharmaceuticals with preventive and therapeutic efficacy to treat diseases like cancer.

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