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Curing Functions and Medical Applications of Microalgae

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ABSTRACT

Microalgae are significant biological resources with numerous biotechnological uses. Microalgae like Spirulina and Chlorella are being mass-produced for health food due to their great nutritional content. A variety of high-value products including polyunsaturated fatty acids (PUFA), pigments such as carotenoids and phycobiliproteins, and bioactive compounds are useful as nutraceuticals and pharmaceuticals, as well as for industrial applications. Microalgae (prokaryotic and eukaryotic) consist of a wide range of autotrophic organisms that grow through photosynthesis just like land-based plants. Their unicellular structure allows them to easily convert solar energy into chemical energy through CO2 fixation and O2 evolution, being well adapted to capture CO2 and store it as biomass. Microalgae and cyanobacteria have an interesting and not yet fully exploited potential in biotechnology. They can be used to enhance the nutritional value of food and animal feed due to their chemical composition, playing a crucial role in aquaculture. Highly valuable molecules like natural dyes (e.g. carotenoids), polyunsaturated fatty acids, polysaccharides, and vitamins of algal origin are being exploited and can be applied in the nutritional supplements; cosmetics (e.g. phycocyanin), and, pharmaceuticals. In fact, microalgae and cyanobacteria are able to produce several biologically active compounds with reported antifungal, antibacterial, anticancer, antiviral (e.g. anti-HIV), immunosuppressive, anti-inflammatory, and antioxidant activity. Nowadays, there is a focus on using microalgae in renewable energy sources and environmental applications. The aim of this review is to discuss bioactive metabolites produced by microalgae for possible applications in the biotechnological fields.

INTRODUCTION

Microalgae are the ancestors of present-day land flora and the number one contributor of the aquatic ecosystem. Microalgae are unicellular microorganisms that can produce chemical energy from sunlight and engage in photosynthesis. A significant amount of oxygen can be produced by microalgae inside the atmosphere. These organisms have a fast boom and convey extra biomass rich in bioactive compounds in contrast with better flora. Microalgae have the most capacity to adapt to harmful environmental conditions, do not now compete with agricultural fields, and may even domesticate in sewage or salt water. Since early 1500 BC, algal biomass has been used as a primary nutritional factor and medicinal drug. The first microalgae were used as a medicinal drug dates returned in 2000 years to conquer famine disease (**Khatoon and Pal, 2015**). Microalgae have the capability to generate a whole lot of high-cost bioactive compounds like carbohydrates, proteins, lipids, important fatty acids, pigments, vitamins, antioxidants, etc. (**Udayan *et al.*, 2017**). For those reasons, microalga has been substantially utilized in food, cosmetics, biofuels, feed, nutraceutical, and pharmaceutical industries (**Fig. 1**) (**Wang *et al.*, 2015**).

It has additionally been utilized in bioremediation, CO_2 mitigation, bioremediation of wastewater, and biofuel manufacturing (**Uysal et al., 2016; Rashid *et al.*, 2018**). However, the production of strength derivatives using microalgae isn't necessarily environmentally friendly if it isn't also combined with the production of other high-priced metabolites. The predominant hazards of the commercialization of microalgal merchandise are small marketplace size, excessive value of manufacturing, low biomass, and product accumulation in large-scale cultivation, and excessive regulatory constraints (**Rajesh *et al.*, 2020**). However, recent financial analysis has demonstrated that the development of the microalgal industries is a field that is moving forward. The global marketplace of microalgal merchandise is anticipated to exceed $seventy-five million USD in sales via way of means of 2026 (**Microalgae marketplace, 2020**).

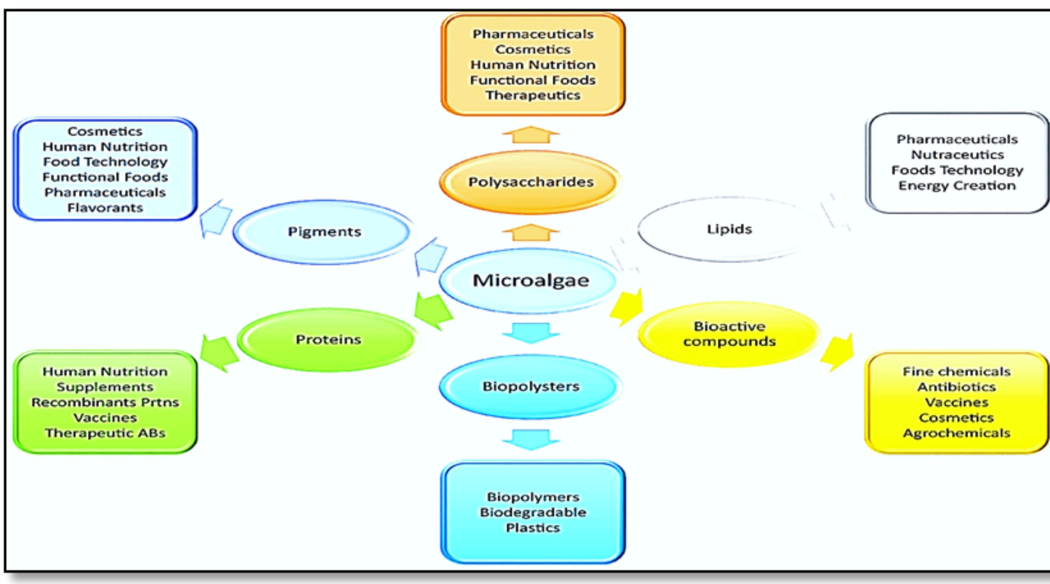

Fig. (1). Industrial applications of microalgae (**Wang *et al.*, 2015**).

Over the previous couple of years, microalgal bioactive compounds have attracted greater investment and study activities. The distinctive sorts of excessive-cost metabolites with nutraceutical and pharmaceutical significance extracted and purified from microalgae consist of polysaccharides, proteins, polyunsaturated fatty acids, polyphenols, vitamins, minerals, carotenoids, etc. (**Udayan et al., 2020)**. The metabolites derived from microalgae have validated roles for the remedy and prevention of many disorders situations as diabetes, cardiac, autoimmune, rheumatoid arthritis, anemia, obesity, dementia, and different neurodegenerative diseases (**Lordan *et al.*, 2011**).

From the literature, it's far obtrusive that microalgae had been taken into consideration as a meal complement from historical instances. During AD 1300, humans from Mexico decided to apply *Spirulina* as a meal component. It is likewise pronounced that humans from Africa have additionally protected *Spirulina* in their everyday diet. The population from South America, Mongolia, and China has been using *Nostoc* as a meal complement. In Spain, humans organized a dry cake recognized as 'tequila' from blue-inexperienced algae. From historical instances, *Spirogyra* has been used as a means component in international locations like India, Burma, and Vietnam (**Garcia *et al.*, 2017**). Japanese humans extensively utilized suitable for eating cyanobacteria to put together their local meals 'Suizenjinori'. Hence it's clear that cutting-edge biotechnological traits in the usage of microalgae commenced years ago.

In 1952, the University of Stanford in the United States performed the primary Algal mass lifestyle symposium which opened a brand new manner for the industrialization and commercialization of microalgae. In the 1960s, Japan commenced a corporation named Nihon *Chlorella* for the mass cultivation of *Chlorella* for meal packages. Then in the 1970s, a corporation named Sosa Texcoco S.A. commenced an *Arthrospira* cultivation facility in Lake Texcoco, Mexico. In Asia, forty-six large-scale microalgal cultivation factories commenced in the Eighties generating more than a thousand kg of microalgae in step per month. Then, the large-scale cultivation of *Dunaliella salina* changed into commenced for beta carotene manufacturing, ring and have become one of the predominant manufacturers of microalgal metabolites. India additionally commenced cultivating microalgae in large-scale industries (**Khatoon and Pal, 2015**).

In current years, there's a fast increase in the algal biotechnology industry. Microalgal biomass manufacturing marketplace has reached approximately 5000 lots of dry matter/12 months and has a turnover of ~ \$1.25 × 109 USD in step with 12 months (**Khatoon and Pal, 2015**). However the predominant drawback of large-scale microalgal cultivation structures is low biomass manufacturing and problems in product recovery, which will increase the value of cultivation and very last product prize. Researchers are nevertheless centered at the improvement of recent strategies to beautify the manufacturing of biomass from microalgae and reduce the economic cultivation value of microalgae (**Udayan *et al.*, 2017; Udayan *et al.*, 2020**). Collectively, the microalgal excessive-cost metabolites also are utilized in numerous industries for the improvement of nutraceuticals, pharmaceuticals, beauty merchandise, aquaculture and hen feed, and as biofertilizers (**Udayan *et al.*, 2018**). In addition, marine microalgae have several applications in biotechnology and are suitable hosts for the production of recombinant proteins/peptides, such as monoclonal antibodies and vaccines (**Khavari *et al.*, 2021**).

Thus, the current work illustrates the valuable characteristics of microalgal constituents and how they have essential roles in treating a lot of human diseases and possess significant applications in the medicinal sector.

1. Diversity of microalgal composition

Compared to terrestrial plants, microalgae are sustainable due to their rapid growth, ease of cultivation, and non-competition for arable land. Microalgae are unicellular aquatic microorganisms with over 50,000 classified species. Some notable examples include *Nostoc commune*, *Arthrospira platensis*, *Aphanizomenon flosaquae*, *Chlorella vulgaris,* and *C. pyrenoidosa* (**Nova *et al.*, 2020**). Besides their appreciable levels of primary metabolites (e.g. protein, carbohydrates, polyunsaturated fatty acids, and vitamins), the health benefits of microalgae are mainly correlated to the presence of high-value secondary metabolites. Secondary metabolites are non-nutritive compounds produced in plants as defense agents against environmental stress (**Ampofo and Ngadi, 2020**). Microalgae research has shown substantial concentrations of diverse secondary metabolites such as pigments (e.g., phenolics, carotenoids, etc.), phytosterols, and mycosporine-like amino acids (**Sidari and Tofalo, 2019**).

Algae species are known to vary widely in their chemical compositions, physical characteristics, and processing technologies required to fractionate their other constituents and will undoubtedly differ greatly in their nutritional value. Depending on species, environmental conditions, nutrient supply, and harvesting/processing techniques, whole biomass may be a highly attractive source of protein, essential amino acids, and other nutrients for terrestrial livestock and aquatic animals. This potential protein source from microalgae and algal co-products for nutrition applications has long been recognized, but commercial success has only been realized to a small extent for a few species (e.g., *Spirulina*, *Chlorella*, and *Dunaliella*) occupying niche markets (**Tibbetts *et al.*, 2015**). Clearly, *Spirulina* sp. is a blue-green microalga with high protein content, several vitamins, γ- linolenic acid, and tocopherol. In addition, spirulina has nutritional and therapeutic applications and is referred to as a 'superfood' (**Singh *et al.*, 2020**).

Typically, diverse bioactive compounds including phenolics, high-value polyunsaturated fatty acids, sterols, carotenoids, polysaccharides, minerals, vitamins, (e.g. vitamin B_{12}), peptides phycobilins, and other biologically active compounds have been detected in microalgal species. These bioactive compounds have been shown to possess positive health effects such as antihypertensive, anti-obesity, antioxidative, anticancer, and cardiovascular protection (Ampofo and Abbey, 2022). However, (**Fig. 2**) suggests a listing of important bioactive compound extracted from microalgae. Consequently, each of these components will be explained regarding its functions and applications in health caring and medical curing below as follows:

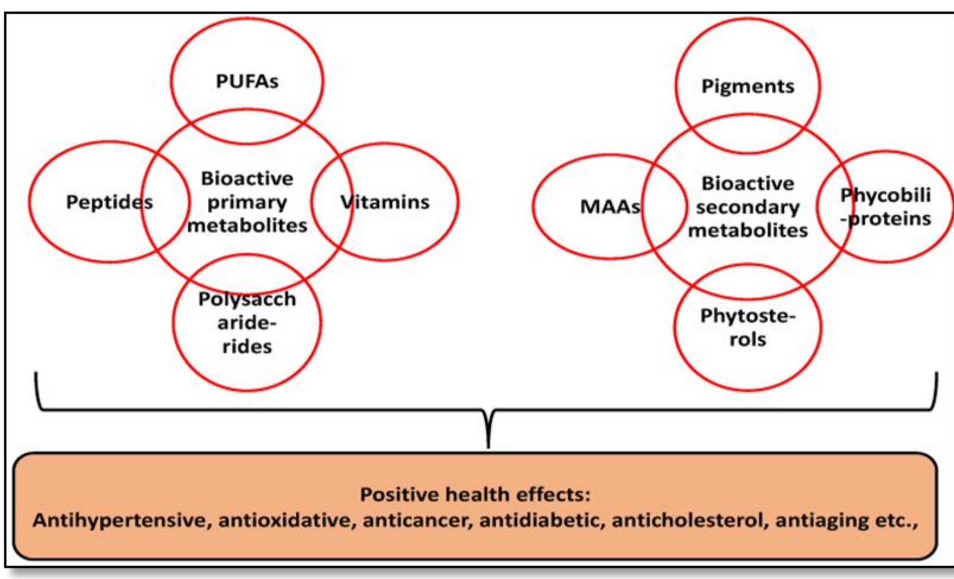

Fig. (2). Overall bioactive compounds obtained from microalgae biomass (**Ampofo and Abbey, 2022**).

Furthermore, the large biodiversity of microalgae available in nature and in culture collections still needs evaluation in terms of useful properties and safety before its exploitation in the food and feed sector. To obtain algae-based products and co-products, advancing our knowledge on the biochemical composition and digestibility of microalgae is the first key requirement (**Niccolai *et al.,* 2019**).

2.1. Microalgal polysaccharides and medical applications

A polysaccharide (PS) is a long-chain carbohydrate (e.g. starch, cellulose, or glycogen) made of smaller carbohydrates referred to as monosaccharides it is usually utilized by our bodies for electricity or to assist with cell structure. The cost of PSs varies in line with their use, availability, and purity. The variety of polysaccharides (PSs) produced via way of means of microalgae is large. Microalgae (e.g. *Porphyridium cruentum*) are commercially used to provide PSs. Under the proper conditions, 15 to 55% of the dry biomass weight of the microalgae may be extracted as PSs. Among numerous algal PS, sulfate PSs are the maximum vital from organic hobby factor of view and are a vital supply of bioactive herbal compounds displaying anticoagulant, antithrombotic, antitumor antimicrobial, antimutagenic, anti-inflammatory, immunomodulatory and antiviral sports (Mišurcováa et al., 2014).

The mobile partitions of the freshwater inexperienced algae of *Chlorella traces* are composed of as much as 80% PSs, which include cellulose (Mišurcováa et al., 2014). Several species of microalgae produced PS, sulfated EPSs in particular, containing sugars like glucose, an aldose, galactose, and xylose (**Raposo *et al.,* 2013**). The EPSs in microalgae consist of fucoidans, carrageenans, alginates, and EPS. They have been detected in microalgae as mobile wall additives, one component in cells peripheral to glycocalyx, or one of the polymers out of doors the cells or EPS. *Spirulina* affords organic sports useful for tissue engineering. It ought to produce nanofibers and additionally includes numerous biomass contents to deal with spinal wire damages or function of the matrix in stem mobile cultures (**De Morais *et al.,* 2010**).

The EPS remoted from *Spirulina platensis* is substantially applied as a meal additive or beauty colorant in Japan (**Liu *et al.,* 2016**). Amazingly, *S. platensis-derived* PS has been followed as a colorant for meals objects like ice sherbert, chewing gum, candy, popsicle, dairy product, gentle drinks, or jelly (Begum et al., 2016). High-molecular-weight (HMW) PS acquired from *P. cruentum* did now no longer show off the antioxidation impact, while the low-molecular- weight (LMW) fragments, following degradation, confirmed inhibition towards oxidative stress (OS). In *Porphyridium* sp., sulfated EPS sulfate confirmed an antioxidation impact on linoleic acid auto-oxidation, even as suppressed OS in 3T3 cells resulted from $FeSO_4$. The EPS from *Porphyridium* sp. inhibited oxidative harm relying on its dosage, which confirmed a high-quality correlation with sulfate tiers in EPS. The EPS acquired from *Rhodella reticulata* exhibited an antioxidation impact, and crude EPS confirmed an expanded cappotential without cost radical scavenging in addition to advanced antioxidation as compared to PS-changed samples (**Chen et al., 2010a & b**). Also, the same workers determined that extracellular crude EPS from *R. reticulata* ought to put off superoxide anion radicals and suppress linoleic acid auto-oxidation Depending on its dosage. Indeed, Tannin-Spitz et al. (2005) extracted EPS from the pink microalga, *Porphyridium* sp., and determined that even after the degradation of EPS, its additives ought to scavenge loose radicals.

Particularly, the calcium *spirulina,* as a PS isolated from *S. platensis,* inhibited lung metastasis of mouse B16 melanoma cells. Thus, PS, as well as phycocyanin and water-soluble components, may be responsible for anti-oxidant and anti-cancer effects in rodents. In humans, rough, spirulina was reported to alleviate oral leukoplakia in pan tobacco chewers (**Mathew *et al.*, 1995**). Frequently, water-soluble polysaccharides appear to participate in the anti-oxidant, anti-cancer, and anti-viral effects of spirulina. These reports, together with the finding of modulation of Toll signaling by the water extract in concert with immune modulation, imply that the target of spirulina-mediated immune activation is the innate immune system (**Medzhitov and Janeway, 1997**).

2.1.1. Antioxidant activity of microalgal polysaccharides

Microalgae are photoautotrophs below excessive publicity to oxidative pressure and radical pressure and as a result, collect the green antioxidative PS that defend their cells from harm. Successfully, **Sun et al. (2016)** used a hermetical microwave to degrade the EPS of *P. cruentum* from 2,918 to 256.2, 60.66, or 6.55 kDa. High-molecular-weight (HMW) PS acquired from *P. cruentum* did now no longer show off the antioxidation impact, while the low-molecular- weight (LMW) fragments, following degradation, confirmed inhibition in opposition to OS. In *Porphyridium* sp., sulfated exopolysaccharide sulfate confirmed an antioxidation impact on linoleic acid auto-oxidation, at the same time as suppressed OS in 3T3 cells resulting from $FeSO_4$. The EPS from *Porphyridium* sp. inhibited oxidative harm relying on its dosage, which confirmed a tremendous correlation with sulfate ranges in EPS. The EPS acquired from *R. reticulata* exhibited an antioxidation impact, and crude EPS confirmed an expanded capacity without spending a dime radical scavenging in addition to advanced antioxidation as compared to PS-changed samples (**Chen et al., 2010a**).

In addition, **Chen et al. (2010b)** located that extracellular crude PS from *R. reticulata* may want to take away superoxide anion radicals and suppress linoleic acid auto-oxidation relying on its dosage. Further, **Tannin-Spitz *et al.* (2005)** extracted EPS from the purple microalga, *Porphyridium sp.*, and located that even after the degradation of EPS, its additives may want to scavenge loose radicals.

2.1.2. Antitumor activity and immunoregulation of microalgal polysaccharides

The capacity hobby of PS is that it prevents the boom of most cancer cells. Exopolysaccharide named p-KG03 containing excessive sulfate may be generated through purple tide microalgae, *Gyrodinium impudicum* educate KG03. In general, p-KG03 confirmed immunostimulation hobby and promoted the tumor-killing consequences of herbal killer cells and macrophages in addition to suppressed tumor cellular boom *in vivo*. Early, **Hirahashi *et al.* (2002)** concluded that spirulina may be involved in the signaling responses through Toll in blood cells even when orally administered. These observations indicated that, in humans, Spirulina acts directly on myeloid lineages and either directly or indirectly on NK cells. The presence of co-operative IL-12 and IL-18 is critically important for NK-mediated IFN gamma production. In sucha manner, **Park et al. (2011)** also pronounced the characterization of the water-soluble polysaccharide from *Haematococcus lacustris* and decided on its immune stimulation activity. The outcomes indicated that PS had distinguished immune-stimulating hobby and inspired peritoneal macrophage RAW264.7 cells to boom the manufacturing of TNF-α

2.1.3. Antiviral and antibacterial activities of microalgal polysaccharides

Considerably, the antiviral hobby of sulfated polysaccharides can be the maximum investigated first-rate of marine microalgae. A marine microalga, *Cochlodinium polykrikoides*, generated sulfated polysaccharides outdoor the cellular. In particular, **Radonic et al. (2020)** recommended that *A. platensis* and *P. purpureum* launched PS inside the medium, which confirmed an antiviral impact at the *Vaccinia* and *Ectromelia* viruses, *in vitro* or *in vivo*. However, the mechanisms of this impact aren't but absolutely understood. In particular, *A. platensis* is a cyanobacterial species that is surmised to potentiate the immune system leading to suppression of cancer development and viral infection **(Hirahashi *et al.*, 2002).**

2.1.4. Anti -COVID-19 of microalgal polysaccharide

Currently, coronavirus disease (COVID-19) is the most important health issue across the world, and there is an urgent need to find effective treatments for this disease and prevent hundreds of thousands of deaths (**Talukdar *et al.*, 2020**). Studies have indicated that acute respiratory distress syndrome (ARDS) resulting from the cytokine storm syndrome is a major cause of death in COVID-19 patients. In cytokine storm, the level of pro-inflammatory cytokines (IL-1, IL-6, TNF-α) and chemokines (CCL2, CCL3, CXCL10, CXCL9) increase, thereby causing the hyperactivity of the immune system and acute lung injury (ALI) (**Yang *et al.*, 2020**).

Carrageenan is a sulfated polysaccharide of microalgae origin, which is able to inhibit the attachment, transcription, and replication of viruses in host cells (Rosales-Mendoza et al., 2020). In a study, **Koenighofer *et al.* (2014)** produced a nasal spray containing zanamivir (antiviral drug), and carrageenan was reported to exert synergistic effects on the influenza virus. Studies have indicated that these microalgae have potent antiviral activities. Calcium *spirulina* is a polysaccharide derived from *Spirulina*, which inhibits the replication of several viruses, such as influenza, mumps, and HIV (**Singh *et al.*, 2020**).

2.1.5. Digestive performance of microalgal polysaccharides

Hopefully, many workers pronounced that Sprague-Dawley (SD) rats fed with PS from *Porphyridium sp*. brought about a good-sized boom in feces bulk in animals while reducing gastrointestinal transit time. Soluble EPS remoted from *Porphyridium sp*. might also additionally lower the plasma and duodenal mucosal contents of blood lipid alongside cholecystokinin, however boom fecal excretion of bile acid and impartial sterol. In addition, PS launched through such purple marine microalgae additionally caused morphological changes inside the colon and small gut in SD rats. A great lower in goblet cellular remember inside the mucosa layer changed observed, alongside improved fecal content material viscosity. Moreover, the Jejunal tunica muscularis morphology confirmed enlargement. These morphological changes may want to have taken location to triumph over the nutrient and mineral malabsorption problems (**De Jesus Raposo *et al.*, 2016**).

2.2. Microalgal proteins/peptides and medical applications

2.2.1. Proteins

The protein content material in microalgae can vary from 6 to 52% in their dwt. However, the protein content material in microalgae may be as excessive as 71% of the dwt (Zhu et al., 2014), however, those degrees can significantly be prompted through environmental factors, together with temperature, salinity, illumination, pH-value, mineral content material, CO_2 supply, populace density, boom section physiological status, the season and the species (Trivedi et al., 2015).

The first rate of meal protein relies upon on its crucial amino acids. Microalgae can gather excessive awareness of glutamic acid, aspartic acid, alanine, arginine, valine, leucine, lysine, threonine, isoleucine,a nd glycine, even though the fundamental amino acids are glutamine and aspartic acid. Glutamine and asparagine show off exciting homes in taste development. Amino acid composition of species of microalgae (*Spirulina* and *Chlorella*) may be determined in. Marine microalgae have attracted interest due to their abundance, quite cheap process, and a wealthy supply of proteins and peptides with organic function (**Rashidi *et al.*, 2019; Zhang *et al.*, 2019**).

Marine microalgae comprise many lively proteins with physiological capabilities. The fundamental capabilities of those lively materials consist of diazotrophic, antitumor, antioxidant, and immune-stimulating activities. They may be used as additives in medicinal cosmetics, and our bodies may be used as powerful adsorbents for heavy metals with inside the ocean (**Lee *et al.*, 2013**).

Generally, the principle additives in microalgae represent of carbohydrates, proteins, and lipids. Due to the variations amongst microalgal species and cultivation conditions, the proportions of cell additives (carbohydrate, lipid, and protein) in microalgae can vary significantly. Marine microalgae are excessive in protein content material, that is, 6-70% of its dry weight, and a majority having approximately 50%, as presented in (**Table 1**). High protein content material offers microalgae an excessive dietary value. Therefore, microalgal proteins may be used as a supplementary supply of nutritional protein, particularly in a few growing countries. Furthermore, the protein can be used as an element in wholesome meals or even purposeful meals. With the non-stop development in technology, lively proteins from microalgae confirmed remarkable capacity and feature come to be one of the studies focuses.

On focus, lectins are proteins that attach to specific mono and oligosaccharides. Cyanovirin-N is a lectin extracted from cyanobacteria (*Nostoc ellipsosporum*), which has exhibited anti-viral activities against HIV, influenza, and the Ebola virus (**Rosales-Mendoza *et al.*, 2020**). Further, *S. platensis* could activate the immune system against viruses through the activation of immune cells and inducing the production of interferon-gamma, which is an important cytokine with antiviral activity (**Singh *et al.*, 2020**).

2.2.2. Phycobiliproteins

Initially, phycobiliproteins, the water-soluble pigment–protein complicated, exist in Cyanobacteria in addition to a few algae. The complicated is shaped primarily based totally on apoprotein and covalently certain phycobilins serving because of the chromophores. Phycobiliproteins are categorized into 4 groups: phycocyanin (PC), phycoerythrin (PE), allophycocyanin (APC), and phycoerythrocyanin (PEC). Observably, PC turned into remoted from spirulina and especially exists in Cyanophyta, Rhodophyta, and Cryptophyta **(CHITOSE Group 2020**). It is generally divided into C-phycocyanin (C-PC) and R-phycocyanin (R-PC), wherein the previous is located in Cyanophyta, the latter in Rhodophyta, and each in Cryptophyta. PC is a protein–pigmented complicated that incorporates protein and nonprotein components, which take part in numerous organic consequences, inclusive of antioxidant, anti-unfastened radical, and antitumor activities. The PC also can save your OS by scavenging reactive oxygen species (ROS) in addition to reactive nitrogen species (RNS). In addition, **Liu *et al.* (2015)** investigated the recuperation consequences of PC at oxidative harm in mice as a result of X-ray radiation, anthe d effects proved that PC may want to efficaciously guard the body's antioxidant gadget and enhance its antioxidant capacity. Many sicknesses have resulted from oxidative harm to the human body. As well as PC may also want to, for this reason, act as a nutraceutical inside the medical practice. Also, PC, as an herbal blue pigment, has been broadly applied in cosmetics, inclusive of lipstick, eyeliner, nail polish, or eye shadow (**Jahan *et al.*, 2017**).

Table 1: Valuable percentages of protein in different microalgae strains.

Algal species	Protein %	References
Acutodesmus dimorphus	28.10	Tibbetts et al. (2015)
Botryococcus braunii	39.00	Tibbetts et al. (2015)
Chlorella pyrenoidosa	57.00	Hamed et al. (2016)
Chlorella vulgaris	31.17	Phusunti et al. (2018)
Chlorella sorokiniana	18.81	Chen et al. (2014)
Dunaliella tertiolecta	20–28	Welladsen et al. (2014)
Entomoneis punctulata	15–25	Welladsen et al. (2014)
Neochloris oleoabundans	30.10	Rashidi et al. (2019)
Scenedesmus almeriensis	42.80	Vizcaíno et al. (2019)
Spirulina platensis	46–63	Tibbetts et al. (2015)
Nannochloropsis oceanica	52.63	Zhang et al. (2019)
Nannochloropsis gaditana	44.90	Vizcaíno et al. (2019)

Specifically, C-PC, an herbal blue pigment, is regularly located in Cyanobacteria, and R-PC is remoted from pink algae. C-PC is famous for an antitumor effect. C-PC from *Oscillatoria tenuis* confirmed antioxidation and antiproliferation activity on human tumor cells through inducing apoptosis, inclusive of the consultant apoptotic characteristics, inclusive of mobileular contraction, membrane apoptosis, condensed nucleus, or DNA fragmentation (**Thangam *et al.*, 2013**). In addition, C-PC suppressed HepG2 (human hepatoma cells) increase and multiplication at 7.0 µg/ml with an LC50 below 1.75 µg/ml. Cyclooxygenase 2 (COX-2) is one of the precipitated enzymes with excessive expression in inflammatory and most cancer cells. Currently, COX-2 has been reported to be associated with colorectal most cancers (CRC), breast most cancers (BC), and gastric most cancers (GC) (**Cheng and Fan, 2013; Liu *et al.*, 2017**). A side of this is illustrated below in (**Fig.3**), (**Willemen *et al.*, 2021**).

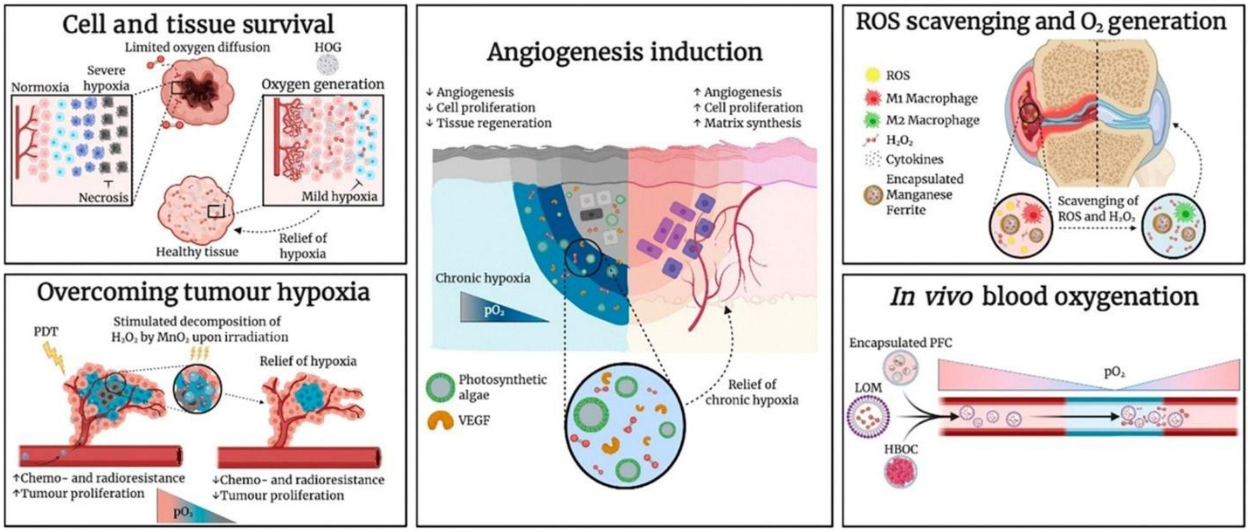

Fig. (3). Research Applications of Oxygen-Carrying and Oxygen-Generating Biomaterials (OCBs and OGBs) include microalgae. Hemoglobin-based oxygen carrier (HBOC), hydrophobic oxygen generator (HOG), lipid-based oxygen microbubble (LOM), photodynamic therapy (PDT), perfluorocarbon (PFC), partial pressure of oxygen (pO2), and vascular endothelial growth factor (VEGF) (31) (**Willemen *et al.,* 2021**).

Moreover, **Saini and Sanyal (2014)** recommended that C-PC, an inhibitor of COX-2, may want to lessen the tumor/lesion quantity and quantity with inside the DMH-precipitated CRC rat model. Afterward, **Jiang *et al*. (2018)** observed that C-PC suppressed BC MDA-MB-231 mobileular proliferation thru the activation of c-Jun N-terminal kinase (JNK) in addition to p38 mitogen-activated protein kinase (MAPK) sign transduction pathways and suppressing the extracellular sign-regulated kinase (ERK) sign transduction pathway. It reduced the COX-2 protein-degree at the same time as inhibiting MDA-MB-231 mobileular migration. Scientifically, R-PC is a member of the phycobiliprotein family, which has been constrained. Chang et al. (2011a) also assessed the R-PC remedy of allergic airway infection and stated accelerated IL-12 p70 ranges with inside the monocyte-derived dendritic cells in each wholesome human beings and sufferers with asthma.

Furthermore**, Liu *et al.* (2015)** decided that R-PC had anti-allergy capacity after a test on mice or mast cells sensitized via way of means of antigens. It turned into additionally located that R-PC efficaciously decreased tropomyosin and histamine ranges and reduced interleukin four (IL-4) and IL-thirteen ranges in mice. In addition, this protein additionally inhibited pro-inflammatory elements and allergic reaction markers, for example, suppressing the manufacturing of IL-four collectively with tumor necrosis factor-α (TNF-α), lowering the histamine, β-hexosaminidase, or ROS launch in cells.

2.2.3. Collagen-like protein

Collagen bills for the most important structural protein with inside the area out of doors cells of various animal connective tissues that confirmed sizeable packages starting from meals to medicines. It also can be followed for burn or beauty operations (**Jérome *et al.,* 2015**). There are specific contributors with inside the collagen protein family, except many novel proteins are beneath Neath improvement via way of means of figuring out the collagen-like molecules inclusive of TrpA. Recently, TrpA has been found and tested in a marine cyanobacterium, *Trichodesmium erythraeum* IMS 101. The phylogenetic evaluation confirmed that the protein collection of TrpA confirmed a excessive courting with collagen proteins, now no longer forming fibril. Scanning electron microscopy (SEM) outcomes confirmed the expression of TrpA on trichome surface, without a regular localization pattern (**Price *et al.*, 2014**).

It has been mentioned that the TrpA gene confirmed expression at numerous boom stages, indicating its necessity for *T. erythraeu*m boom. TrpA protein performs a crucial position in preserving trichome structural integrity via way of means of adhering to cells. Frequently, *T. erythraeum* belonging to Cyanophyta, proliferates to shape purple tide algae in autumn and winter. The presence of this type of collagen gene with extraordinary duration in prokaryotes is probably associated with the functionality of *T. erythraeum* to shape blooms protecting the sea extensively. The collagen-like protein from marine microalgae ought to as a consequence be used for beauty and scientific formulation (**Price and Anandan, 2013).**

2.2.4. Bioactive peptides

Bioactive peptides (BP) as particular protein fragment play a crucial position in the physiological pastime of maximum-dwelling organisms. BP has been mentioned to have numerous healing activities, together with antioxidant, anti-inflammatory, antitumor, antiproliferative, antihypertensive, and antimicrobial properties, as proven in (**Table 2**). Actually, peptides derived from microalgae are recognized to expose excessive capacity with inside the fields of purposeful food, medicine, and cosmetics as a consequence of their selectivity, efficacy, protection, and right tolerance as soon as consumed. Furthermore, the hobby with inside the microalgae-derived bioactive peptides is growing rapidly. Several workers like **Chen *et al.* (2011b & c)** investigated the protecting outcomes of peptide received from *Chlorella* sp. on inhibiting MMP-1 manufacturing brought about via way of means of UVB and procollagen gene degradation in human pores and skin fibroblasts.

Additionally, **Shih and Cheng (2013)** tried to give an explanation for the mechanism of a peptide derived from Chlorella towards the cytotoxicity brought about via way of means of UVB. The outcomes confirmed that Chlorella-derived peptide ought to inhibit cytotoxicity as a result of UVC, lessen pFADD expression, lower cleaved PARP-1, and save you DNA harm and fragmentation.

As well as, **De Lucia *et al.* (2018)** remoted *Spirulina*-derived peptides as a singular biotechnological lively component that would growth hydration and decrease osmotic pressure in pores and skin cells. Recently, **Sedighi *et al.* (2019)** evaluated the antibacterial pastime of peptide fractions of *C. vulgaris*, which have been digested via way of means of pepsin and had antimicrobial pastime towards E. coli CECT 434. Moreover, **Guzmán *et al.* (2019)** mentioned antibacterial peptides from *Tetraselmis suecica*, particularly AQ-1766 peptide (LWFYTMWH), which had antimicrobial pastime towards the Gram-bad bacteria, inclusive of *E. coli*, *P. aeruginosa* and *S. typhimurium*, in addition to towards the Gram-effective bacterial strains, for example, *B. cereus, M. luteus, L. monocytogenes,* and *methicillin*-resistant *S. aureus*. Several researches have additionally verified that peptides from microalgae had antitumoral and antihypertensive pastime.

2.3. Microalgal lipids / fatty acids and medical applications

Some microalgae are wealthy in oil. However, the content material and composition of algal lipids range with species, geographical location, season, temperature, salinity, mild intensity, or mixture of those factors. In general, microalgae incorporate lipids from 2 to 23% of dry weight. The lipid content material of microalgae has been located to be very excessive (lipid content material > 60% of dry weight in some of marine species inclusive of *Dunaliella tertiolecta, Nannochloropsis sp.*, *Neochloris oleoabundans* and *Porphyridium cruentum*, and in a few freshwater species inclusive of *Botryococcus braunii, Chlorella emersonii* etc. (**Maity *et al.*, 2014**).

A mild lipid content material (40 - 60% of dry weight) has been located in numerous variety of marine microalgal species inclusive of *Crypthecodinium cohnii, D. salina, Isochrysis galbana, Nannochloris sp., Nannochloropsis oculata* NCTU-three, *Nitzschia sp., Phaeodactylum tricornutum, Schizochytrium sp., Skeletonema costatum* etc., and in some of the freshwater microalgae inclusive of *C. minutissima, C. protothecoides, C. vulgaris, Scenedesmus dimorphus,* and *S. obliquus* (**Mobin *et al.*, 2018**).

More data on the lipid content material of microalgae will be explored from (Mobin et al., 2018). Most of the alga's lipid content material is fabricated from polyunsaturated fatty acids (PUFAs), which can be critical vitamins for humans and should be received from food. They also are structural and purposeful additives of molecular membranes. The long-chain ω-three fatty acids eicosapentaenoic acid (EPA) (ω-three C 20:5) and docosahexaenoic acid (DHA) (ω-three C 22:6) have drawn extensive interest within the current years because of their contribution to the boom, nutrition, and healing and pharmaceutical benefits. An herbal supply of DHA is microalgae *S. platensis*, that may account for as much as 9.1% of the entire fatty acid content material. Further, the EPA content in numerous microalgae can range from 0.7 to 6.1% of overall lipid content material (**Fu *et al.*, 2017**).

Microalgal oil has attracted plenty of interest because of its brief breeding cycle, its capacity to seize carbon dioxide and acquire a massive quantity of lipids, and its wealthy omega-three long-chain polyunsaturated fatty acids. The fatty acids of microalgae oil in particular encompass saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids. Usually, polyunsaturated fatty acids in microalgae oil a massive percent of the entire fatty acid content material, particularly DHA and EPA. Basically, PUFA is a fatty acid that incorporates greater than double bonds in its backbone. According to the placement of the primary unsaturated bond, it's far divided into ω3, ω6, ω7, and ω9, from which ω3 and ω6 play a crucial position in frame physiological characteristic modulation. ω3 fatty acids have anti-inflammatory, antithrombotic, antiarrhythmic, decreasing blood lipid, and vasodilatation traits and also are critical for fetal and little one improvement, particularly the mind and imaginative and prescient improvement. The principal additives of ω3 encompass alpha-linolenic acid, and EPA at the side of DHA. The human frame no longer synthesizes those 3 PUFAs and as a consequence should be absorbed from the diet. Fishes of microalgae are the number one assets of ω3 PUFAs; microalgae-derived PUFAs are less expensive than fishes. Additionally, in comparison to fish oil, ω3 PUFA extracts from microalgae are odorless and do now no longer incorporate cholesterol (***Mimouni et al.*, 2012)**.

In the previous couple of years, the examination of microalgal PUFA has accrued hobby increasingly. Effectively, Ryckebosch et al. (2014) assessed the nutrient contents of the entire lipids remoted from the numerous PUFAs generated through microalgae. They used the microalgae, *Isochrysis sp., Nannochloropsis sp., Phaeodactylum sp., Pavlova sp*., and *Thalassiosira sp*. to supply ω3 PUFAs as a fish oil opportunity in meals. *Skeletonema costatum, Chaetoceros calcitrans*, and *Porphyridium cruentum*, in addition to *Nannochloropsis sp*., confirmed excessive EPA levels. High PUFA contents in those microalgae cause them to be a great complement to humans. In addition, the Food and Drug Administration tested the protection of DHA and oils wealthy in AA after extraction from *Crypthecodinium cohnii Javornicky* single-mobileular organism, a heterotrophic marine microalga, and advocated their use as dietary supplements for infants (**Martins *et al.*, 2013**).

Because fish oil cannot fulfill the developing necessities of purified PUFA, massive-scale cultivation of microalgae is a fantastic opportunity. Different microalgal strains, mainly diatoms, have been built to be the inventory cultures, amongst which 20 have been screened for boom charge and EPA/DHA contents, indicating their capacity for use in massive-scale manufacturing (**Steinrücken *et al.*, 2017**).

Structurally, the investigation of *Spirulina* sp. indicated that it contains glycolipids, such as O-b-D-galactosyl-(1-10)-20 ,30 -di-O-acyl-D-glycerol, which possess fatty acid moieties, palmitic acid and linoleic or linolenic acids (**Kataoka and Misaki, 1983**). It is currently accepted that lipid moieties of microbes often serve as ligands of Toll receptors. Thus, it is not surprising that *Spirulina* glycolipids serve as Toll ligands for stimulation of TLR2 and TLR4 together with BCG –CWS (**Means *et al.*, 1999**).

2.3.1. Antioxidant activity of microalgal ω3 PUFAs

The advocated nutritional consumption of ω3 PUFAs for the Chinese populace is 200 mg-1 g (Punia et al., 2019). An excessive dose of polyunsaturated fatty acids might also additionally cause oxidative pressure, however, a proper dose the has right antioxidant pastime. Interestingly, **Fu *et al.* (2016)** studied the impact of DHA algae oil contained in safe to eat oil at the antioxidant pastime of SD rats and outcomes confirmed that the right supplementation of DHA can decorate the antioxidant potential of the frame.

Additionally, **Zheng *et al*. (2017)** located that PUFA had a crucial impact with inside peroxidation–antioxidant stability. They investigated the impact of DHA algae oil on selling the frame antioxidation and inhibiting the peroxidation response via measuring the contents of malondialdehyde, overall antioxidant potential, and catalase pastime in cerebral cortex of SD rat. Results indicated that the mild-dose DHA alga oil performed an effective position in improving unfastened radical scavenging and lowering lipid peroxidation harm, however low and excessive doses confirmed destructive outcomes. Hence, the suitable nutritional consumption of ω3 PUFAs from microalgae can enhance the capacity of scavenging oxygen unfastened radicals and decrease peroxide harm of human frame.

2.3.2. Antimicrobial activity of microalgal fatty acids

Microalgae has the capacity to restrict microbial contamination in aquaculture and has outstanding utility prospects as an herbal antibiotic. Now more than one research has proven that brief-chain fatty acids and unsaturated chain fatty acids remoted from microalgae had antibacterial pastime (**Falaise *et al.*, 2016**). Successfully, Alsenani et al. (2020) recognized the dominant compounds of 3 microalgae, *Isochrysis galbana, Scenedesmus sp*., and *Chlorella sp*. included, as DHA, EPA linoleic acid, and oleic acid, and the extracts of those fatty acids ought to inhibit the boom of gram-effective bacteria.

2.3.3. Anti-inflammatory activity of microalgal ω3 PUFAs

Long-chain PUFA has healing outcomes on numerous inflammatory sicknesses, like lupus, arthritis, or Alzheimer's disease (AD). Several animals and *in vitro* experiments supported the microalgal oil impact on irritation. Regarding Nauroth et al. (2010), docosapentaenoic acid (DPA) inhibited the secretion of IL-1β and TNF-α via way of means of human monocytes in peripheral blood via in vitro LPS stimulation. Algal oil, which contained DPA (16% overall fatty acids TFAs) in addition to DHA (forty%), notably decreased inflammatory reaction with inside the version rats with foot edema in comparison to the manipulate group. Both **Banskota *et al*. (2013a & b**) have already advised that a lipid extract remoted from *Nannochloropsis granulate* in RAW264.7 macrophage cells having pastime towards irritation contained mono-and di-galactosyldiacylglycerols.

Afterward, **Dawczynski *et al.* (2018**) have been the primary to discover the scientific parameters in sufferers with rheumatoid arthritis, who have been allotted to devour microalgae oil from *Schizochytrium sp,* containing 2.1 g DHA/day. So, outcomes confirmed that supplemented DHA microalgae oil ought to ameliorate the nation of contamination in sufferers at the side of rheumatoid arthritis, destroy the stability of AA- and DHA-derived lipid mediators, and offer an anti-inflammatory/pro-resolving nation.

2.4. Microalgal vitamins and medical applications

Microalgae are plentiful reasserts for nearly all crucial nutrients and minerals and are wealthy in Cu, I, Fe, K, Zn, etc. (**Christaki *et al.*, 2011**). Besides, selenium (Se) is an integral detail in the creation of glutathione peroxidase. Glutathione peroxidase participates with inside the antioxidant technique of the human frame, prevents the oxidation of unsaturated fatty acids, and avoids the manufacturing of a few poisonous metabolites, thereby lowering the danger of cancers and preserving the homeostasis inside the human frame. In addition, Se additionally participates with inside the immune reaction via way of means of enhancing the proliferation and organic pastime of B cells, enhancing the physiological characteristic of T cells, and shielding the frame's immune device via way of means of fending off oxidative harm to cells. The nutrients located in microalgae encompass diet B1, diet B2, diet B6, diet B12, diet C, diet E, niacin, biotin, and folic acid (**Raposo and de Morais, 2015**).

Essentially, vitamin E (VE), known as tocopherol, is a crucial fat-soluble antioxidant synthesized handiest via way means of photosynthetic organisms. Microorganisms are a fantastic supply of herbal VE. However, the handiest photosynthetic algae, inclusive of microalgae, can synthesize VE, which in particular encompass *Spirulina platensis, Dunaliella tertiolecta, Synechocystis aquatilis,* *Nannochloro oculate, Tetraselmis suecica, Chlamydomonas, Ochromonas, Euglena gracilis,* etc. The VE content material in microalgae relies upon on many factors, inclusive of genotype, boom stage, dietary status, and mild intensity (photosynthetic charge). Vitamin B12 has additionally been located in a few macro and microalgae (**Edelmann *et al.*, 2019**).

Recently, **Edelmann *et al.* (2019)** measured the diet B12 content material in microalgae powders, while *Chlorella sp.* And *N. gaditana* powders entirely contained lively diet B12 as much as 2.1 μg/g. In addition, a few nutrients were proven to be produced via way of means of microalgae in current years. The deficiency and insufficiency of diet D, belonging to a collection of lipid-soluble sterols, are customary trouble in the world. For example, a couple of billion humans are brief of diet D3, particularly around 13% European populace on a yearly basis **(Ljubic *et al*., 2020).**

Actually, microalgae have to be capable of synthesize 7-dehydrocholesterol, which will synthesize diet D3 via way of means of ultraviolet radiation with short wavelength (UVB) publicity, in the event that they use the identical metabolic pathway as vertebrates. So, Ljubic et al. (2020) focused on 4 microalgal species to supply diet D3 via way of means of publicity of synthetic UVB, together with *C. minutissima*, *N. oceanica*, *Arthrospira maxima*, and *Rhodomonas salina.* Results confirmed completely *N. oceanica* ought to produce diet D3 with a yield asof much as 1 ± 0. three g/g DM. In addition, growing the dose of the UVB turned into capin a position to seriously decorate the manufacturing of diet D3. Hence, *N. oceanica* uncovered to synthetic UVB will be used as a brand new herbal supply of diet D3. Recently, diet K1 has been recognized as a crucial nutrient to save you the continual sicknesses, particularly a few sicknesses related to aging, inclusive of osteoporosis and cardiovascular disease. Vitamin K1 is normally produced through chemical synthesis. However, currently, the use of microalgae to supply diet has a great utility prospect.

Valuable data were obtained by **Taranto *et al.* (2018),** who screened seven specific species of microalgae to supply diet K1. Their results confirmed that *Anabaena cylindrical* turned into recognized because of the richest supply of diet K1. Marine microalgae can synthesize all nutrients that better plant life produce. The diet accumulation of microalgae is more than that of soybeans and cereals however can range consistent with algal species, season, alga boom stage, and environmental parameters (**Mishra *et al.*, 2015**). In any case, Table 2 shows the diet profile of specific microalgae (in mg kg^{-1} until in any other case stated).

2.5. Microalgal pigments and medical applications

Natural pigments play an important position at some stage in algae photosynthetic metabolism and pigmentation. Microalgae account for the number one photosynthesizes that generate numerous critical pigments, together with chlorophyll, β-carotene, phycobiliproteins, astaxanthin, and xanthophylls with packages in meals, nutraceutical, pharmaceutical, aquaculture, and beauty industries (**Table 3**). Chlorophylls, and carotenoids, collectively with phycobiliproteins, are the 3 number one lessons of photosynthetic pigments of microalgae (**Begum *et al.*, 2016**). Occasionally, **Nemoto-Kawamura *et al.* (2004)** suggested that phycocyanin enhances biological defense activity against infectious diseases through sustaining functions of the mucosal immune system and reduces allergic inflammation by the suppression of antigen-specific IgE antibodies.

Most pigments are biologically active, with antiobesity, anti-inflammatory, and anticancer consequences, especially because of their powerful antioxidant pastime hired to guard the frame from OS (**Guedes *et al.*, 2011; Ciccone *et al.*, 2013**). Phycobiliproteins are broadly utilized in commercial and immunological research. As fluorescent markers, they're usually utilized in immunoassays and as fluorescent dyes in molecular biology (**Banskota *et al.*, 2013a & b**). Chlorophyll is a fat-soluble pigment with a porphyrin ring, which bills for 0.5%~1% of the dry weight of microalgae. Studies have discovered that chlorophylls have physiological consequences like antimutagenesis and anticancer. Carotenoids, as critical nutrients, are especially utilized in nutritional supplements, fortified foods, meal dyes, animal feeds, pharmaceuticals, and cosmetics (**Vílchez *et al.*, 2011**).

Table 2: Vitamin profile of two species of microalgae (in mg kg^{-1} unless otherwise stated) (Adapted from Borowitzka, 2013).

Vitamin ($IUkg^{-1}$)	*Spirulina* sp.	*Chlorella* sp.
Provitamin A	2330000	55500
Beta-Carotene	1400	1808
Vitamin E	100	<10
Thiamin B1	35	15
Riboflavin B2	40	48
Niacin B3	140	238
Vitamin B6	8	17
Vitamin B12	3.2	1259
Inositol	640	1650
Folic acid	0.1	209
Biotin	0.05	1916
Pantothenic acid	1	13

Carotenoids additionally display organic consequences with the aid of using affecting molecular boom modulation, modulating gene stage, or immune response (**Kalra *et al.*, 2020**). Epidemiological research confirmed that accelerated carotenoid intake and tissue stage have been associated with the reduced dangers of malignancies and cardiovascular diseases. Broadly, it's been broadly used as a complicated fitness product because of its pastime to guard the coronary heart and liver. Additionally, carotenoids have been utilized in lotions and creams for solar safety as stabilizers and preservatives. Humans and animals can't synthesize carotenoids and depend upon their diets for those critical nutrients. Thus, microalgae had been cautioned to be a candidate supply for carotenoids (**Nascimento *et al.*, 2020**).

Astaxanthin is a carotenoid with anti-inflammatory, immunomodulatory, and antioxidative properties, as well as other therapeutic activities. For instance, *H. pluvialis* is a microalgae and a natural source of astaxanthin. Studies have indicated that the administration of this carotenoid to COVID-19 patients could alleviate cytokine storm, thereby preventing acute respiratory distress syndrome (ARDS) and acute lung injury

(ALI) (**Talukdar *et al.*, 2020**). Furthermore, phycocyanin is also a pigment obtained from spirulina and an inhibitor of NADPH oxidase with anti-inflammatory activity. It seems that microalgae are effective candidates for the adjuvant therapy of COVID-19 patients (**Singh *et al.*, 2020**).

Table 3: Pigments from different microalgae (**Begum *et al.*, 2016**).

Microalgae	Division	Pigments
Green microalgae	Chlorophyta	Chlorophylls, β-carotene, prasinoxanthin, siphonaxanthin, astaxanthin
Brown microalgae	Bacillariophyta	Chlorophyll a and c, β-carotene, fucoxanthin, Diadinoxanthin
Blue-green microalgae	Cyanophyta	Chlorophyll a, xanthophylls, phycobiliproteins
Dinoflagellates	Dinophyta	Chlorophyll a and c, β-carotene, peridinin

2.5.1. Chlorophylls

There are 5 styles of chlorophyll in microalgae, along with chlorophyll a, b, c, d, and e. Chlorophyll a is the number one photosynthetic pigment, ample in cyanobacteria and Rhodophyta. Chlorophyll b exists in Chlorophyta and Euglenophyta, whilst chlorophylls c, d, and e are located inside the freshwater diatoms (**Begum *et al.*, 2016**). *Spirulina* sp. is the maximum critical chlorophyll supply, generating 2–three instances greater chlorophyll than different plants. In addition, the chlorophyll in Spirulina includes porphyrin, much like the heme in humans and animals. It is a right away complement of the heme in human beings and animals, and thus, chlorophyll is called "inexperienced blood." Since spirulina is rich in iron, the appropriate mixture of chlorophyll and iron is the first-class remedy for iron deficiency anemia. Recently, chlorophyll has drawn extensive interest for getting used as a most cancers preventative agent.

2.5.2. Carotenoids / β-Carotene

Ordinarily, carotenoids are a chief magnificence of fat-soluble pigments and effective antioxidants that play a key function in oxygenic photosynthesis (**Fu *et al.*, 2017**). They can't switch daylight power immediately to the photosynthetic pathway however byskip their absorbed power from one chlorophyll molecule to another. The common awareness of carotenoids in maximum algae varies from 0.1 to 2% of dry weight (**Suganya *et al.*, 2016**). Among four hundred acknowledged carotenoids, just a few have extensive industrial importance (β-carotene, astaxanthin) and others have much less importance (lutein, zeaxanthin, lycopene, and bixin) (**Suganya *et al.*, 2016**).

Basically, the carotenoid composition of microalgae may be stimulated through the physico-chemical parameters of the aquatic surroundings together with water temperature, salinity, mild, and availability of nutrients. Most of the environmental parameters vary with the season, which can in the long run stimulate or inhibit the biosynthesis of carotenoids. For example, *Dunaliella salina beneathneath* nutrient stress, excessive salt and excessive-mild situations can acquire β-carotene as much as 14% of its dry weight. This discovery brought about the industrial derivation of herbal β-carotene from this organism. A range of researchers have investigated the specific developing situations that are capable of maximizing the manufacturing of β-carotene at commercial scale (**Hochman *et al.,* 2014**).

Like *D. salina*, beneath Neath strain circumstance the inexperienced microalgae *Haematococcus pluvialis* can acquire huge portions of carotenoid (astaxanthin), as much as 2–three% of dwt. Until the early 1980s, industrial manufacturing of β-carotene turned into artificial. The rate of extracted and purified herbal β- carotene turned into about 2.5 instances better than that of artificial β-carotene in the 1980s. Natural β-carotene is advanced to artificial β-carotene. Specifically, herbal β-carotene is fat-soluble, and it includes admixtures of carotenoids and nutrients, which can be absent in artificial β-carotene (**Varfolomeev and Wasserman, 2011**).

Particularly, astaxanthin is a type of carotenoid now no longer belonging to provitamin A. Additionally, *H. pluvialis* is the number one supply of astaxanthin. In addition, *Chlorella zofingiensis*, *Chlorococcum sp.*, *Neochloris wimmeri*, *Catenella repens*, and *Coelastrella striolata* have additionally been said to comprise astaxanthin in decreased content material. The antioxidant overall performance of astaxanthin is higher than that of β-carotene, zeaxanthin, canthaxanthin, nutrition C, and nutrition E. It can relieve photooxidative strain and inhibit photosensitive action. In addition, astaxanthin proved to have a sturdy anticancer impact, which can lessen the range and length of liver most cancers and lung tumor lesions, and it additionally has an apparent inhibitory impact on bladder most cancers, oral cancers, and colon most cancers cells (**Sathasivam and Ki, 2018).**

2.6. Microalgal fine chemicals and medical applications

2.6.1. Phenolic compounds

Phenols are a critical organization of herbal products (produced through microalgae as secondary metabolites) with antioxidant and different organic sports, and those compounds play a critical function in algal defense towards abiotic and biotic strain. However, those compounds aren't immediately worried in algal number one techniques together with photosynthesis and reproduction (**Suganya *et al.,* 2016**).

Wonderfully, the purified phenolic compounds showcase many sports together with antioxidant, anti-radical, UV-protection, steel chelation e.g. copper and anti-fouling (Suganya et al., 2016). However, the primary bioactivity related to phenolic compounds is antioxidant activity. It has been said that a few algal phenolic compounds were related to anti-inflammatory activity, together with rutin, hesperidin, morin, caffeic acid, catechol, catechin, and epigallocatechin gallate and this phenolic compound has the capability to combat unfastened radicals (**Morais *et al.,* 2015**).

2.6.2. Minerals

Microalgae are acknowledged to be excessive in mineral content material. More than 6.7% of the dwt of microalgae Spirulina is ash. The mineral content material in widespread is and relatively depending on the environmental developing situations, together with the season, temperature, physiological state, geographic versions, etc. (**Herrero *et al.,* 2013**). Collectively, (**Table 4**) indicates the mineral content material of microalgae.

Table 4: Mineral content of two species of microalgae -Adapted from (**Herrero *et al.*, 2013**).

Microalgae	**Na**[a]	**K**[a]	**Mg**[a]	**Ca**[a]	**P**[a]	**F**[b]	**Zn**[b]	**Cu**[b]	**Mn**[b]	**Cr**[b]	**B**[b]
Chlorella sp.	10.4	11	3.53	2.3	19.2	1,185	24.7	6.21	77.8	1.38	27
Spirulina sp.	10.1	14.9	4.76	2.96	12.6	1,480	59.2	7.26	240	1.08	33

3. High-value commercial microalgal bioproducts

Microalgae stay in a completely unique environment, in which they compete for area and vitamins and feature the incredible variation method for dwelling in special physicochemical conditions. Hence, they have got developed with a splendid protection method, and bring novel secondary metabolites (herbal bio-merchandise). Generally, the manufacturing of those bio-merchandise varies from species to species or even with inside identical species of algae. The manufacturing of bioproducts (Bioactive natural products) relies upon elements like environmental conditions, seasons, geographic locations, and the level of lifestyles cycle, etc. (**Anbuchezhian *et al*., 2015).**

Bioactive compounds (bioproducts) are physiologically lively materials with useful houses with inside the human body. Microalgae were defined as authentic herbal reactors for generating bioactive herbal compounds and are a great opportunity for chemical synthesis for sure bioactive herbal compounds of industrial interest. There is incredible enthusiasm for the improvement and manufacture of numerous bioactive compounds that could probably be used as useful ingredients, which include carotenoids, PC, polyphenols, fatty acids, and polyunsaturated compounds. Bioactive compounds of microalgal origin, which include proteins, fatty acids, vitamins, and pigments, may be sourced without delay from number one metabolism or may be synthesized from secondary metabolism. In maximum microalgae, the bioactive compounds are accrued inside the biomass; however, in a few cases, those metabolites are excreted into the medium (**Morais *et al.*, 2015).**

3.1. Microalgae as a source of prebiotics

Commercially available nutritional supplements based on microalgae that are approved to be edible by FDA, like *S. platensis* and *C. vulgaris* become widely attractive. Microalgae are rich in carbohydrates, proteins, and polyunsaturated fatty acids that have high bioactivity. Recently, scientists are studying the microalgae polysaccharides (PS) or their derivatives (as dietary fibers) for their potential action as a novel prebiotic source for functional foods. Besides, the microalgae prebiotic PS are used for medication due to their antioxidant, anticancer, and antihypertensive bioactivities (**Gouda et al., 2022**) (**Fig. 4**).

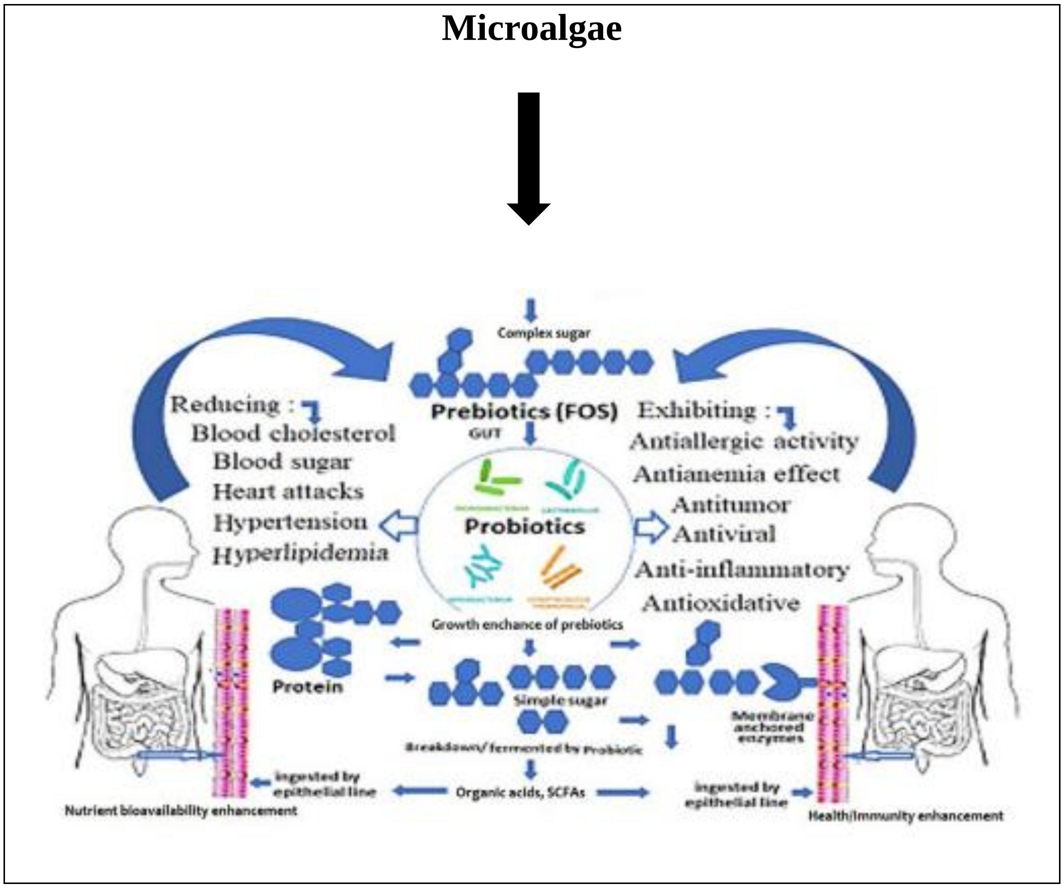

Fig. (4). Microalgae as prebiotics improving the probiotics properties and hence their medical functions (**Gouda *et al.,* 2022**).

Microalgae is an important source of prebiotics that defined as potential native and modified forms of PS such as xylooligosaccharides (XOS), galacto-oligosaccharides (GOS), alginate oligosaccharide (ALGOS), neoagaro-oligosaccharides (NAOS), galactans, arabinoxylans, and β-glucan. These microalgae PS are against the digestion process by the metabolic enzymes in the human gut. Therefore, they could be used as dietary prebiotics and able to augment the growth of probiotics bacterial in the gut and colon (Suwal et al., 2019). Recently, de Medeiros et al. (2021) used the prebiotic score (P. Score) technique to investigate the different tolerance abilities of microalgae against the digested through a method of an *in vitro* colonic fermentation.

Prebiotic was described by the Association of Probiotics and Prebiotics (ISAPP) as a non-digestible carbohydrate group, such as short and long-chain β-fructans [Fructooligosaccharide (FOS) and inulin], and GOS that beneficially affects the human by stimulating the growth of probiotics bacteria (like *Lactobacillus* spp., *Bifidobacterium* spp., *Streptococcus* spp., *Lactococcus* spp., and *Saccharomyces* spp.), and release some essential metabolites that could improve the human gut health (e.g., enhance the gut permeability through the released butyric acid) (**Szentirmai *et al.,* 2019**). These beneficial compounds are classified based on their resistance to the acidic pH and hydrolyze enzymes, absorption in the gastrointestinal tract, and fermentation potential by the intestinal microbiota (**Davani-Davari *et al.,* 2019**). For instance, oligosaccharide carbohydrates (OSCs) are a good prebiotic family-like Fructans that consists of inulin and

FOS or oligofructose. Their structure is a linear chain of fructose with $\beta(2 \rightarrow 1)$ linkage (**Louis *et al.*, 2016**). In which, the specific structure of these molecules like, the length of fructans chain, is play a key role in their bacterial selection that can ferment them to the beneficial secondary metabolites (**Scott *et al.*, 2014).**

3.2. In complementary baby food

The World Health Organization considers its "superfood" and the best food for the future because of its nutritional value is very high. **Sharoba (2014)** designed and prepared 16 food formulas for as complementary food babies (1-3 years of age) by using spirulina at 0, 2.5 0.5, and 7.5% for the production of two types of baby food one of them is ready-to-eat by using some fruits and vegetables. The second type of baby food formula was production by using cereals, legumes and some dried green vegetables. The chemical composition indicated that these formulas were suitable as a food supplement for children aged 1-3 years. On the other hand, the same workers estimated that these formulas were economic cost and could be produced on the scale of domestic and industrial scale, as well as can be exported to the outside.

3.3. In wound healing

Basically, wound healing is a complicated process, in which oxygen as a crucial molecule participates in cell metabolism, signaling, and many reparative activities, like cell proliferation, collagen synthesis, re-epithelialization, and anti-bacterial immune response (**Farris *et al.*, 2015**). However, vascular disruption and vasoconstriction lead to an insufficient oxygen supply, inducing hypoxic tissue, which is unfavorable for the healing process (**Rothenberg *et al.*, 2014**). So, increasing the O_2 supply to the hypoxic tissues has become an effective strategy to promote wound healing.

Indeed, **Li *et al*. (2020)** developed an algal hydrogel composed of *S. platensis* and natural polymer carboxymethyl chitosan (called SP gel), which could simultaneously maintain the oxygen production capacity of algae and promote their adhesion to the infected wound. Moreover, the SP gel could generate ROS by the released chlorophyll from algae under a 650 nm laser irradiation, thus photodynamic killing bacteria in the infected area. SP gel combined with the laser irradiation treatment showed strong *in vitro* antibacterial activities against two representative strains Gram-positive *S. aureus* and Gram-negative *E. coli*. In the *S. aureus*-infected mouse model, the SP gel + laser group showed better wound recovery than the other groups, demonstrating the excellent wound healing effects of SP gel-mediated PDT. Besides, this gel has also been studied to treat wounds that are more difficult to recover, such as chronic wounds in diabetes.

Experimentally, **Chen *et al.* (2020)** reported a patch-like wound dressing named alga-gel patch (AGP), in which the filled gel beads contained bioactive *Synechococcus elongates* PCC7942, ensuring the dissolved oxygen delivery to the wound site. The AGPs could produce continuous oxygen, effectively penetrate the skin, and were effective in various hypoxic chronic wounds. Notably, PCC79422 might contain growth factors that further stimulate cell proliferation and migration for promoting wound healing. In addition to being used as wound dressings and patches, microalgae can also be incorporated into surgical sutures to improve healing capacities. **Cerdas *et al*. (2018)** seeded *C. reinhardtii* in polyglactin sutures to fabricate the photosynthetic sutures. In addition to possessing basic functional like mechanical fixation, they were capable of locally and stably releasing oxygen and recombinant human growth factor [VEGF, platelet derived growth factor (PDGF-BB), or stromal cell-derived factor 1A (SDF1A)] at the wound site. These algal agents have demonstrated their feasibility for commercial and clinical use in wound healing.

3.4. As anti-obesity agents

In general, obesity is the over-accumulation of adipose tissues (fats) in the body. Obesity is considered a multifactorial metabolic disorder linked to many complications and diseases, such as cancer, cardiovascular disease, diabetes mellitus, and aging (**Khan *et al.*, 2018**). The overgrowth of adipose tissue occurs because of adipogenesis, so obesity can be controlled by guarding the cells against adipogenesis (**Wang *et al.*, 2008**). Research has revealed various anti-hyperlipidemic and fat-lowering agents from natural sources, such as medicinal plants. Microalgae are now being studied as potential sources of these products. Moreover, ROS has been reported to be involved in the progression of obesity. Thus, antioxidants can be used to control the free radical–induced accumulation of fats. Fucoxanthin and fucoxanthinol can inhibit the differentiation of 3T3- L1 cells to adipocytes. Besides, both inhibit adipocyte differentiation by down-regulating peroxisome proliferator–activated receptor-c (**Hayato *et al.*, 2006**).

In addition, **Okada *et al.* (2008)** reported that neoxanthin and fucoxanthin inhibited the accumulation of fats and stated that allenic and hydroxyl groups must be present to differentiate adipocytes. These compounds are reportedly crucial for lowering fat in high-fat mouse feeds (**Maeda *et al.*, 2007a**). In obese mice, fucoxanthin suppresses adiposity by activating the mitochondrial protein UCP1 (Uncoupling protein1) in abdominal WAT (**Miyashita, 2014**). Fucoxanthin signifcantly reduced body fat in obese individuals in a clinical trial by Abidov et al. (2010) *Cylindrotheca closterium* and *Phaeodactylum tricornutum* are the two microalgae species that produce fucoxanthin, (**Kim *et al.*, 2012**), which shows potential as an anticancer, anti-oxidant, anti-obesity, anti-diabetic, and anti-inflammatory agent (**Maeda *et al.*, 2007b**).

3.5. In the drug delivery system

Principally, **Zhong *et al.* (2020)** used *S. platensis* as a drug carrier to fabricate a Doxorubicin (DOX)-loaded system for lung-targeted delivery. In such a system, positively charged DOX molecules were firstly loaded to negatively charged *S. platensis* by noncovalent electrostatic interactions. In addition, drug loading efficacy was further improved as small DOX molecules were allowed to enter the cell envelope through the continuous water channels and junctional pores (15 nm) on the *S. platensis* cell membrane. The micrometer-sized and spiral-shaped *S. platensis* carriers were easily trapped by pulmonary capillaries, allowing them to passively target the lungs. The fabricated DOX-loaded *S. platensis* (SP@DOX) system exhibited obvious killing ability to 4T1 and CT26 tumor cells in vitro. Subsequently, the targeted chemotherapeutic efficacy of SP@DOX was confirmed in a 4T1 breast cancer mouse model of lung metastasis.

Moreover, magnetic *S. platensis* could magnetically target the tumor site under an external magnetic field and generate O_2 in situ to improve the local O_2 concentration in the tumor, so as to realize an enhanced RT on the 4T1 tumor-bearing mouse model. Furthermore, chlorophyll released from algae could be used as photosensitizer for successive PDT, which greatly promoted the anticancer effect by synergistic RT/PDT treatment. Importantly, these MSPs exhibited the capability of fluorescence and photoacoustic imaging based on chlorophyll and magnetic resonance imaging based on Fe_3O_4 NPs to potentially monitor the tumor therapeutic procedure by such tri-modality imaging. In contrast, chlorella, a much smaller alga, has also been widely studied as a highly efficient oxygen-generating agent for the treatment of hypoxic-associated cancer (**Zhong *et al.*, 2020**).

Amazingly, **Zhou *et al.* (2019**) reported an autotrophic light-triggered green-affording oxygen engine (ALGAE) system, which was composed of *C. pyrenoidosa* and calcium alginate, achieving nearly three times oxygen production compared to inorganic oxygen production materials. The calcium alginate in this system could prevent the chlorella from the phagocytosis of macrophage, making a long period for oxygen affording *in vivo* for the repeated PDT. The ALGAE were implanted around the tumors of 4T1 tumor-bearing mice in a minimally invasive way to stay a long period around the tumor tissues to afford sufficient oxygen. The hypoxia-resistant PDT induced by ALGAE, not only effectively ablated tumor tissues but also successfully inhibited tumor progression and metastasis. To resolve the tumor-targeting issue and maintain the O_2-producing activity *in vivo*, a series of surface modifications have been applied to *Chlorella* sp. for intravenous injection. **Li *et al.* (2020)** reported a biohybrid Algae@SiO_2 system, by modifying the *C. vulgaris* with silica by a one-step biomimetic solidification method. As a protective shell, the SiO_2 layer outside the algae could significantly reduce the cytotoxicity and improve their tolerance and bioactivity in the tumor area. Algae@SiO_2 could reach the tumor site and mediate RT and PDT combined therapy to inhibit tumor growth in 4T1 tumor-bearing mice after intravenous administration, indicating their high bioactivity *in vivo*.

Recently, **Qiao *et al*. (2020)** modified the surface of *C. vulgaris* with a red blood cell membrane (RBCM) to protect it from the clearance from many mononuclear phagocyte system organs. The RBCM-engineered algae (RBCM-algae) showed greater stability and higher tumor uptake than unmodified native algae. With the aid of x-ray and 650 nm laser irradiation, RBCM-algae significantly suppressed the tumor growth in both 4T1 breast tumor and SKOV3 ovarian tumor mouse models, attributing to the enhanced radio-sensitizing and photodynamic effect. In addition, the relevant molecular mechanism underlying RBCM-algae-mediated abrogation of hypoxia-dependent radio-resistance was also elucidated to further verify the reliability of algal therapy for hypoxic tumors. They found that the combination of RBCM-algae + RT + laser therapy resulted in tumor regression, by inhibiting angiogenesis and proliferation and inducing apoptosis, including the down-regulation of HIF1α and VEGF levels, followed by a remarkable decrease of CD31 and Ki67 expression and increase of cleaved Caspase3. These findings provide proof-of-concept evidence for the future development of algae-mediated hypoxic-associated tumor therapy.

More recently, **Khavari *et al.* (2021)** explained why silica-based nanoparticles obtained from diatoms (called also golden microalgae) are used as drug delivery carriers owing to their biodegradability, easy functionalization, low cost, and simple features compared to synthetics, which make these agents proper alternatives for synthetic silica nanoparticles. Therefore, diatom-based nanoparticles are a viable option for the delivery of anti-cancer drugs and reducing the side effects of cancer chemotherapy.

3.6. In skin care and protection

Marine algae have gained much importance in cosmeceutical product development due to their rich bioactive compounds. Nowadays, marine algal compounds (phlorotannins, sulfated polysaccharides and tyrosinase inhibitors) have been discussed toward cosmeceutical application. In addition, atopic dermatitis and the possible role of matrix metalloproteinase (MMP) in skin-related diseases have been explored extensively for cosmeceutical products. The proper development of marine algae compounds will be helpful in cosmeceutical product development and in the development of the cosmeceutical industry (**Thomas and Kim, 2013**).

Compared to the terrestrial plants and animal-based foods, seaweed is rich in some health-promoting molecules and materials such as, dietary fiber, ω-3 fatty acids, essential amino acids, and vitamins A, B, C, and E (Rajapakse and Kim, 2011), which is essential for cosmeceutical product development (**Kim *et al.*, 2008**)

For instance, **Ragusa *et al. (*2021)** stated that *Spirulina* sp. stands out as a sustainable bioactive microalga with health-promoting properties, and an important active ingredient of natural cosmetics products. Currently, *Spirulina* sp., mainly *S. platensis* and *S. maxima*, has been incorporated in topical skin-care formulations, such as a moisturizing, anti-wrinkles, antiaging and anti-acne agent. Furthermore, this microalga is used by cosmetic formulators to promote healthy sunscreen protection, to treat skin pigmentation disorders and to heal wounds. Most of commercial cosmetics claim a large range of Spirulina properties, including antioxidant, revitalizing, remineralizing, moisturizing, protecting alongside cleansing and shining action, both for hair and for skin.

In vitro-studies on methanol extract from marine alga *Corallina pilulifera* have revealed that CPM has the ability to prevent UV-induced oxidative stress and also the expressions of matrix metalloproteinase (MMP-2 and MMP-9) in human dermal fibroblast (HDF) cells. This clearly suggests the role of phenolic compounds from marine algae as potential MMP inhibitors (**Ryu *et al.*, 2009**). As it is evident that unregulated expression of MMPs leads to photoaging, many research groups are emphasizing their research goals to check the ability of marine-derived phlorotannins as potential anti-photoaging agents (**Pallela *et al.*, 2010; Cha *et al.*, 2012**).

Moreover, the ROS including hydrogen peroxide, hydroxyl radical and superoxide anion are involved in metabolic diseases, especially chronic inflammation. In chronic inflammation, pro-inflammatory cytokines induce MMPs that degrade the extracellular matrix and contribute to several inflammatory disorders. Skin whitening has been in practice around the world, with Asia as its largest market. Tyrosinase inhibitors are the most common approach to achieve skin hypo-pigmentation, as this enzyme catalyzes the rate-limiting step of pigmentation. Despite the large number of tyrosinase inhibitors in vitro, only a few are able to show induced effects in clinical trials. Actually, fucoxanthin isolated from *Laminaria japonica* has been reported to suppress tyrosinase activity in UVB-irradiated guinea pig and melanogenesis in UVB-irradiated mice. Oral treatment of fucoxanthin significantly suppressed skin mRNA expression related to melanogenesis, suggesting that fucoxanthin negatively regulated melanogenesis factor at transcriptional level (**Shimoda *et al.*, 2010**).

3.7. As anti-skin diseases

The encounter between humans and infectious agents has been recognized since ancient times. There are various types of infectious agents, such as bacteria, viruses, and fungi, which cause various types of diseases in humans, and the outcome of the disease symptoms is contingent upon the disease-causing agents (**Nene, 2007**). Humans have produced various types of treatments/remedies for different types of bacterial diseases since ancient times by using a variety of practices, such as Ayurveda, depending on the availability of the natural resources in those countries (**Gopal *et al.*, 2008**). Bioactive sesquiterpenes isolated from red algae species *Laurencia rigida*; *L. luzonesis* yielded deschloroelatol, elatol, luzonenone, luzofuran, 3,4-epoxypalisadin, 1,2-dehydro-3,4-epoxypalisadin B, and 15-hydroxypalisadin; and a new diterpene former has shown antibacterial action on *Bacillus megaterium*, and also possesses antifungal action (**Kuniyoshi *et al.*, 2005**). Crude extracts, purified diverse phlorotannins extracted from brown algae, *Ecklonia kurome* tested on multiresistant *S. aureus* and food-borne pathogens, exhibited the antibacterial activity on Gram-positive bacteria, *S. aureus*, and *B. cereus*, and Gram-negative bacteria, *C. jejuni, E. coli, S. Enteritidis, S. typhimurium,* and *V. parahaemolyticus* (Nagayama et al., 2002).

In a study carried out by **Tuney *et al.* (2006**), diethyl ether (DEE) extracts of seaweeds *Cystoseira mediterranea, Enteromorpha linza, Ulva rigida, Gracilaria gracilis,* and *Ectocarpus siliculosus* are isolated from the Urla coast (Turkey) showed effective results against all test organisms such as *Candida sp., Enterococcus faecalis, S. aureus, Streptococcus epidermidis, Pseudomonas aeruginosa,* and *E. coli*). Fresh weights of algae extracted using DEE showed the strong broad spectrum antibiotic activity against the tested bacterial strains; moreover, they have shown more activity against the Gram-positive bacteria, which was more when compared to the Gram-negative bacteria. The latest improvements in science and technology explored the untapped potentials of marine resources.

3.8. In treating atopic dermatitis

In general, atopic dermatitis (AD) is a pruritic inflammatory skin disorder associated with a personal or family history of allergy. It can occur at any age; most often, it affects infants and young children. In some instances, it may persist into adulthood or actually appear only later in life (**Niggemann *et al.*, 2008**). The fundamental lesion in AD is a defective skin barrier that results in dry itchy skin and is aggravated by mechanical injury inflicted by scratching. This allows entry of antigens via the skin and creates a milieu that shapes the immune response to these antigens. Clinical observations suggest that AD is the cutaneous manifestation of a systemic disorder that gives rise to asthma, food allergies, and allergic rhinitis (**Oyoshi *et al.*, 2009**).

Marine brown algae-derived phlorotannins have been investigated for their human beneficial aspects that include anti-inflammatory, and hyaluronidase inhibitory activities. *In vitro* studies with the methanol extracts from marine brown algae *Eisenia arborea* have shown good inhibition of histamine release from rat basophile leukemia cells (RBL-2H3) sensitized with antidinitrophenyl (DNP) IgE and stimulated with DNP-BSA. These observations suggest that methanol extract which is rich in phlorotannins exhibits the potential to treat histamine-related inflammatory diseases that include AD (Sugiura *et al*., 2006a). Six phlorotannins: phloroglucinol, an unknown tetramer, equol (a trimer), phlorofucofuroeckol A (a pentamer), dieckol and 8,8′-bieckol (hexamers), obtained from brown algae *E. bicyclis* and *Ecklonia kurome* were tested *in vitro* for their ability to inhibit hyaluronidase activity. It was reported that these crude phlorotannins had a stronger inhibitory effect on hyaluronidase than well-known inhibitors such as catechins and sodium cromoglycate. According to these findings, 8,8′-bieckol has shown stronger hyaluronidase inhibition with an IC50 value of 40 μm, which was about seven times stronger than that of DSCG (a major and active component of anti-allergic drugs) (**Shibata *et al.*, 2002).** Due to the abundant content of phloroglucinol derivatives in *Ecklonia cava*, it is used as a food ingredient and folk medicine against allergic diseases in Asian countries. Crude extract from *E. cava* was investigated for its anti-allergic activity by **Le *et al.* (2009).**

Additionally, a new phlorotannin, phlorofucofuroeckol-B, was isolated from *Eisenia arborea*, edible brown algae that is occasionally used as a folk medicine in gynecopathy in Japan. The *in vitro* studies on rat basophile leukemia (RBL)-2H3 cells confirmed that this phlorotannin is capable of inhibiting histamine release assuring the anti-allergic property (**Sugiura *et al.*, 2006b**).

On the other hand, the effects of 80% methanol extracts from frozen samples of 41 macroalgae collected in the Ise-Shima region of Japan were investigated on histamine release from rat basophile leukemia cells (RBL-2H3) sensitized with antidinitrophenyl (DNP) IgE and stimulated with DNP-BSA. Of the 21 brown, 5 green, 15 red algae extracts only from seven brown algae showed histamine release inhibitory activity from RBL cells (**Sugiura *et al.*, 2006a**).

This unique feature of phlorotannins in repairing skin damage from various allergens could be exploited for the better treatment of ever-challenging AD. More studies have to be focused in the screening of novel compounds from marine algae that could find themselves a prominent place in the treatment of not only AD but also various other skin inflammations. In addition, as the marine environment includes sponges, mollusks, bryozoans, coelenterates, echinoderms, tunicates, and other marine microorganisms, and reports suggest that most of them do possess anti-inflammatory substances within themselves, a wide choice of cosmeceutical compounds that could cure AD are proposed to researchers.

In skin-related diseases, UV-B reduces type I procollagen levels increases MMP-1 levels in human skin, and plays a major role in the process of photoaging (Wijesinghe and Jeon, 2012). Fucoidan inhibits UVB-induced MMP-I expression at the protein and mRNA levels in human skin fibroblasts (HS68). Fucoidan treatment also increased type I procollagen mRNA and protein expression in a dose-dependent manner compared to the control. These data indicate that fucoidan may prevent UVB-induced MMP-I expression and inhibit downregulation of type I procollagen synthesis. So, fucoidan may be a potential therapeutic agent to prevent and treat skin photoaging. Further, two phlorotannins, namely dieckol and 1-(3′, 5′-dihydroxy phenoxy)-7-(2′,4′,6′-trihydroxyphenoxy) 2,4,9-trihydroxydibenzo-1,4, -dioxin, isolated from the methanol extract of the marine brown alga, *Ecklonia cava*, have been reported to suppress both the protein and gene expression levels of MMP-1, MMP-3, and MMP-13 in human osteosarcoma cells (MG-63) (**Moon *et al.*, 2013).**

4. Remarkable conclusion

The aim of this paper is to review the microalgal metabolites, the source for bioactive compounds present in indifferent microalgae. This paper also deals with the ability of microalgae to produce bioactive compounds that make it an important tool in various sectors of biotechnology. Microalgae have long been used as nutritional supplements or food and feed sources. Many of the pharmaceutically interesting compounds in cyanobacteria are peptides, including cyanobacterial toxins and important candidates for anti-cancer drugs. A clear picture of the ability of microalgal bioactive compounds to tackle various diseases has been put forth in this paper. The cultivation of microalgae is known to be the most profitable in the biotechnological industry

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