IJBPAS, January, 2025, 14(1): 97-116

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

PHARMACOLOGICAL ACTIVITIES FOR THE ALGAE SPIRULINA PLATENSIS– A REVIEW

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Received 24th Sept. 2023; Revised 25th Oct. 2023; Accepted 25th March 2024; Available online 1st Jan. 2025

https://doi.org/10.31032/IJBPAS/2025/14.1.8548

ABSTRACT

In the current era, there has been a growing global interest in microalgae due to their vast potential applications in the fields of renewable energy, pharmaceutical, and nutraceutical industries. Some specific microalgae varieties have been identified for their potential as value-added products with significant pharmacological and biological qualities. The exploitation of algae, mainly Spirulina, has garnered attention as a functional food source. It is renowned for its high protein content and amino acid profile, making it a valuable protein source with exceptional biological value. Spirulina has demonstrated potential in various health areas such as anticancer, arthritis, cataract, atherosclerosis, HIV, diabetes, and immuno modulating activities. The present review attempts to provide comprehensive information on morphology, cultivation and harvesting, microscopic study of Spirulina culture, profile of constituent phycocyanin, pharmacology, nutritional aspects and current research prospects of the herb.

Keywords: ***Spirulina platensis*****, phycocyanin, pharmacological activities, anticancer, nutritional aspects**

INTRODUCTION

Algae are plant-like protists that live in aquatic environments. These algae, like plants, are eukaryotes that have chloroplasts and photosynthesis. They can live in salt water, fresh water, wet soil, and on moist rocks. There are seven main types of algae, each with its own characteristics, function, and color. Chrysophyta is a group of algae characterized by its golden-brown coloration and the presence of diatoms. It is further subdivided into the following sub-divisions: pyrophyta (fire algae), chlorophyta (green algae), rhodophyta (red algae), paeophyta (brown algae), and xanthophyta (yellow-green algae) **[1]**. In 1967, Spirulina emerged as a potential food source for the future within the International Society for Applied Microbiology. It is a multi-celled, filamentous microalga characterized by its blue-green color. It is divided into two distinct genera: Spirulina and Arthrospira (Sasson, 1997). The first remarkable high protein content (roughly 60–70% of its dry weight) was the high quality of the proteins (balanced essential amino acids) found in Spirulina. A nutritional analysis of Spirulina was the first and, at the time, the leading source of cheap proteins—the so-called "single cell proteins" **[2]**. It represents a link between green plants and bacteria. It is widely distributed in the USA, China, Thailand, Mexico, and India **[3]**. *Arthrospira platensis* (*Spirulina*) is a spiral, unicellular microalgae that can thrive in freshwater as well as saltwater. The chemical constituents available in *Spirulina platensis* are as follows: Proteins (60–70%), phytocyanin (hydrophilic pigment), gamma linolenic acid, carbohydrates, and vitamins (A, B, E, and K). Spirulina consists of both essential and non-essential amino acids and grows best at pH 10–12 **[4, 5]**. It plays a vital role in therapeutic conditions like arthritis, cataracts, atherosclerosis, HIV, and diabetes. It also shows anticancer and immunomodulating activity **[6]**. Phycocyanin is a water-soluble pigment that is used as a dye in the pharmaceutical, cosmetic, and food industries. It has antioxidant activity and is used in the treatment of Parkinson's, Alzheimer's, and Huntington’s diseases **[7]**. Spirulina is also used to formulate candy and chocolate bars and has been officially recognized as a national food in the United States as well as in China. Additionally, it has been classified as (G.R.A.S. generally recognized As Safe **[8, 9]**. Amino acid indicates that the bioavailability of proteins is very high in Spirulina, and this can be achieved by adding a sufficient amount of sulphur-rich amino acids and possibly lysine, histidine, etc. So there are 8 amino acids that are not stored in the body but

found in Spirulina **[10]**. The essential amino acids, which cannot be synthesised by the body, are listed in **Table 1**.

Table 1: Essential amino acids that the body cannot synthesize:

Sr. No.	Amino acid	Role
1.	Isoleucine	Essential for growth
2.	Leucine	Stimulates brain functions
3.	Lysine	Required for antibody, enzyme and hormone production
4.	Methionine	Rich in sulphur and anti-oxidant properties
5.	Phenylalanine	Essential for the thyroid
6.	Threonine	Improves intestinal and digestive function
7.	Tryptophan	Serotonin regulator
8.	Valine	Natural mental and physical capacity stimulant

Plant Profile:

Kingdom : Bacteria

Covolie Smith

Subkingdom : Negibacteria

Domain : Bacteria

Phylum : Cyanobacteria

Class : Cyanophyceae

Order : Nostocales

Family : Oscillatoriaceae

Genus : Spirulina Turpin Ex Gomant 1893 Arthrospira

Species : Platensis, Maxima

Scientific Name : Arthrospira

Vernacular Name : Hindi – Shaiival : Marathi - Sheva

Macroscopy:

The colour of algae is bluish green; it forms gel with water and tastes like eggs. The blue-green is non-heterocystous, has vegetative filaments, and has a single-phase binary fissure with transparent cross-walls. The trichomes are defined by their length (50 µm to 500 µm) and width (3 µm to 4 µm). The trichomes, wrapped in a thin sheet, show more or less constriction at the cross-wall **[1]**. Spirulina's body surface is smooth and non-enveloped, making it easy for simple enzymes to break down. The primary photosynthetic pigment in it is phycocyanin, a blue pigment. In addition, it is also rich in chlorophyll and contains carotenoids, making it autotrophic **[11]**.

Microscopy:

Spirulina is a microscopic plant that grows in fresh water (planktonic form). It is in thallus form with filamentous, unbranched, and non-differentiated. It looks like tiny green spiral coils **[1]**. It is characterised by its nuclear structure and the absence of a membrane. It belongs to the family Cyanophyceae, a group of prokaryotes that includes blue-green algae. It doesn't have mitotic cell division and doesn't have the usual organic tissues of protoplasm. But it does have chlorophyll like all green plants because it stores it in platelets, which contain complex chlorophyll and are used for primary synthesis.

The cell size of cyanobacterium is 1 to 10 microns. The cell wall is a classic gram-

negative. The granules that contain the membrane are referred to as 'Phycobilisomes' and contain pigment. Cyanobacterium is visible under the microscope at 10X magnification and 40X magnification as unicellular spiral filaments. The trichomes are spiral filaments that are interlocked and have variable length (usually 100–200 microns) and diameter (8–10 microns), as shown in **Figure 1a** and **Figure 1b**. Cyanobacterium grows and develops rapidly (cell division, budding, or even fragmentation) under alkaline, warm, brackish water with blue-green slime. The unicellular filaments allow for on-site harvesting and strain **[12, 13]**.

Cultivation and Harvesting of Spirulina:

Cultivation and harvesting of Spirulina are carried out in two ways:

Commercial Production of Spirulina-

Species: *Spirulina plantensis* (98% of the commercial production).

Outdoor Commercial Cultivation: Land Selection: It should have good sunlight available, away from industries and pollution areas.

Requirement: The raceway tanks and square or rectangular tanks are required for cultivation. The dimensions required are length-width 4:1, height 30-45 cm, and a divider in the tank. Rotation of culture with paddle wheel, and in cases of high sunlight and heavy rains, sheds should be constructed to cover tanks. Culture should be developed in tubs before direct contact with sunlight **[14]**.

Harvesting

Spirulina harvesting requires skill and knowledge, as well as technique. This is a seasonal process, taking place after the last rains. The tools are prepared and ready for the arduous task ahead. At the end of the rainy season, the pools or wadis with valuable crops are located. The alga is collected by scooping it up and then filtered using doum palm baskets. In cases where the alga concentration is low, a finer mesh is employed during the initial stage of the harvest to expedite the drying process. Then, set up a sand filter and pour the concentrated solution into it. After 10–20 minutes, the suspension is sliced into a more rigid shape. The dried shapes are then lifted out for drying on frames, where they remain for a period of 5 to 6 days in the sun. The sand is then washed off the slabs. Finally, the slabs are packed into bags, ready for sale **[12]**.

Multiplication of Spirulina-

For multiplication of Spirulina, the ratio of water to culture is 9:1 in the evening. The optical density should be 0.2; the depth of the culture should be 18 to 20 cm. The dose for 1 litre of culture is depicted in **Table 2 [15, 16]**.

Factors affecting production: This technique shows some factors that affect

the production of Spirulina, as depicted in **Table 3**.

Daily Maintenance –

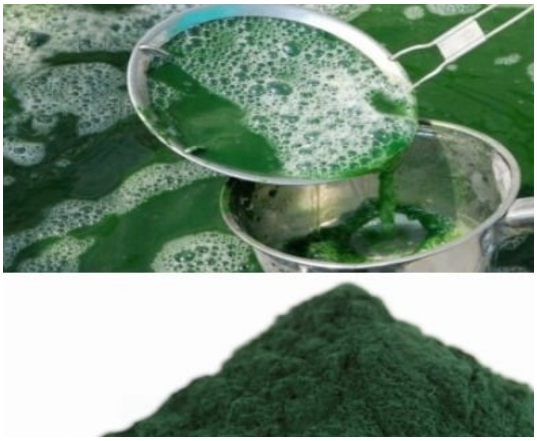
Maintain the depth of the culture, agitation by paddle wheel (6 to 8 hours minimum), dust and particles to be removed and shed, and use a net in high sunlight **[14, 15]**.

Table 2: Multiplication of Spirulina

Sr. No.	Content	Multiplication (grams)	Harvesting (grams)
1.	Sodium bicarbonate ($NaHCO_3$)	8	650
2.	Sodium Chloride (NaCl) (salt)	5	-
3.	Urea (NH2)	0.2	30
4.	Potassium sulfate (K2SO4)	0.5	3
5.	Magnesium sulfate (MgSO4)	0.16	3
6.	Phosporic acid (H_3PO_4)	0.052	4ml
7.	Ferrous sulfate (FeSO4)	0.01	1ml

Table 3: Factors affecting production

Sr. No.	Factors	Level	Caution
1.	Temperature	20 to 35 degree	In low & high temperature growth slow down
2.	Sunlight	30 to 35 lux	Use shed, wooden to control
3.	Depth	18 to 20 cm	Sunlight reach to depth of tank



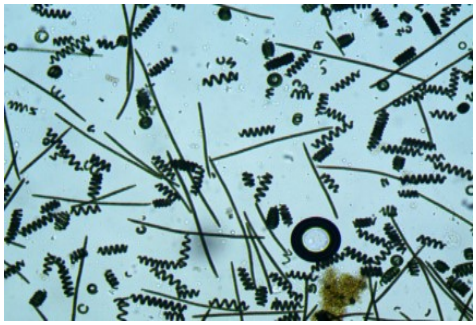


Figure 1a: Microscopic view under 10X

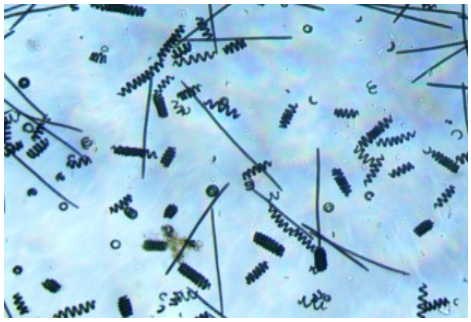


Figure 1b: Microscopic view under 40 X

Composition:

Spirulina is a remarkable natural source of several beneficial components. It boasts impressive protein content while being extremely low in calories and cholesterol. Additionally, it contains a wealth of essential enzymes, minerals such as iron, calcium, sodium, and magnesium, as well as phenolic acids, which act as potent antioxidants. Details are shown in **Table 4 [12]**.

Table 4: Chemical composition of Spirulina [17]

Sr. No.	Content	Amount
1.	Protein	6.5 g
2.	Beta carotene	14 mg
3.	Vitamin C	2 mg
4.	Thiamin (B1)	0.37 mg
5.	Riboflavin (B2)	0.46 mg
6.	Niacin	3mg
7.	Calcium	150 mg
8.	Iron	18 mg
9.	Vitamin E	0.4 mg
10.	Vitamin B 12	0.02 mg
11.	Magnesium	32 mg
12.	Copper	0.1 mg
13.	Chlorophyll	110 mg

Distribution-

Habitat: Numerous species of this organism inhabit diverse environments, including freshwater, brackish water, marine habitats, and mineral springs. Certain species are found in the benthic zones of freshwater bodies, while others thrive as plankton in saline lakes situated in California and Mexico **[13]**.

Phytochemical Screening:

The chemical constitution of algae is phycocyanin, gammalinolenic acid, proteins, carbohydrates, and vitamins (beta carotene). Vitamins' A, vitamin B (B1, B_2, B_6, B12), and proteins are widely available in *Spirulina* species **[18]**.

Phycocyanin:

Phycocyanin is a water-soluble protein that belongs to the phycobiliprotein family (deep and intense blue). It has high efficiency, low toxicity, and blocks the proliferation of cancer cells. The isoelectric point varies between 4.1 and 6.4, depending on the source of extraction and the extraction method. It consists of alpha- and beta-subunits. Alpha and beta subunits of phycocyanin have similar 3D structures, but their sequences are different. X-ray crystallography is used to determine structure. It is light- and heat-sensitive; therefore, it is preserved in the dark and purified at 4-5°C. Tetrapyrrole chromophore phycocyanobilin attaches to apopoprotein, giving blue colour to phycocyanin **[18, 19]**.

Extraction of algal pigments

Three different techniques used for the extraction of phycocyanin from Spirulina are as follows:

1. Freeze thawing
2. Mechanical shaking
3. Soxhlet extraction

1. **Freeze thawing**

   The dried spirulina powder was mixed in a 1:25 ratio with distilled water. The powder was frozen at -21°C for 24 hours. It was then thawed at room temperature and centrifuged at 5000 rpm for 15 min. Phosphate buffer was also used during the extraction (0.1M).

2. **Mechanical shaking at room temperature:**

   The mixture of dried powder of Spirulina and distilled water was combined by mechanical shaking at 150 rpm for 24 hours. 0.1M phosphate buffer was used for extraction and centrifuged for 15 min at 5000 rpm.

3. **Soxhlet Extraction:**

   The dried spirulina powders (5 grams) placed separately into a thimble and run through five cycles with three different solvents—acetone, methanol, and chloroform (all having a different boiling point). Rotary evaporators are used to recover the extracted solvents.

   In contrast to the Soxhlet method, which does not allow for pigment extraction, the freeze-thaw and mechanical shaking methods were effective in extracting the phycocynin **[18, 19, 20]**.

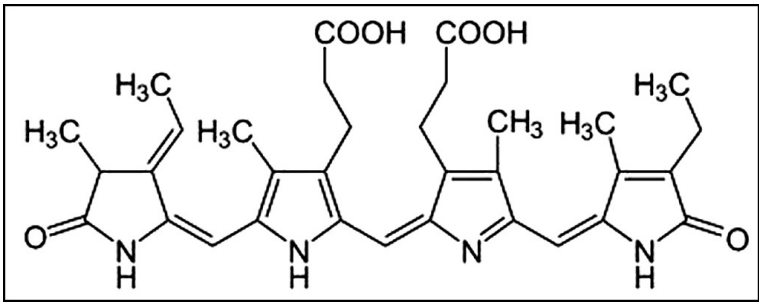


Figure 2: of C-Phycocyanin

Pharmacological application:

Spirulina platensis has pharmacological activities like arthritis, cataracts, atherosclerosis, diabetes, anticancer, and immunomodulating activity **[6]**.

Rheumatoid arthritis:

Systemic inflammation, persistent synovitis, and the creation of autoantibodies are the characteristics of rheumatoid arthritis (RA). The problems

that arise due to RA are anti-inflammatory, progressive, and debilitating autoimmune disease, joint degeneration, disability, and cardiovascular issues. It has physical and emotional effects. Spirulina is a unicellular blue-green alga that has recently been discovered to be an anti-angiogen, antioxidant, and anti-inflammatory agent. It is used as a dietary supplement for both humans and animals. It develops naturally in warm locations. It contains high levels of fatty acids, beta-carotene, and amino acids, as well as minerals and phenolic acids. Tocopherols and vitamins with antioxidant properties are also found in it. The alga is recognised to have a variety of biological activities. Current studies reveal that this alga may have a number of health advantages and curative characteristics. The active ingredient in Spirulina is C-phycocyanin, which has been shown to have anti-cancer, anti-inflammatory, and neuroprotective properties, as well as immunomodulatory properties. *Spirulina platensis* was tested in the current study using a complete Freund's adjuvant-induced arthritis (CFA)-AIA model in rats. This model was used to assess the anti-inflammatory and immunomodulatory as well as anti-angiographic properties of Spirulina. Its anti-angiogenic, immunomodulatory, and antioxidant benefits towards CFA-induced arthritis in rats have been examined. Spirulina treatment improved survival rates while also lowering the RA clinical score in a dose-dependent manner. The alga delayed the onset of arthritis and stopped the progression of macroscopy and microscopy signs in CIA (collagen-induced arthritis) rats. The survival rate of rats treated with Spirulina was higher than that of rats treated with Indomethacins. The clinical RA score decreased dose-dependently with Spirulina **[21]**.

Cataract:

Spirulina, a blue-green microalga, contains carotenoids such as zeaxanthin, which is a major xanthophyll found in the human eye. It has been suggested that zeaxanthin may be protective against cataracts and age-related macular degeneration. Spirulina, an algal food, is rich in zeaxanthin and other carotenoids. Humans cannot synthesise xanthophylls; it is essential that we consume foods high in xanthophylls to give our bodies' access to these phytonutrients. Since dietary intake that contains xanthophyll is essential for providing our bodies with these phytonutrients **[22]**.

It was grown in a nutrient solution containing water to identify carotenoids and determine the Zeaxanthin bioavailability for dietary supplementation. In the clinical trials, 14 healthy male volunteers (four Americans and ten Chinese) ingested single servings of 2H-labelled Spirulina (4.0–5.0 g) containing

2.6–3.7 mg of Zeaxanthin along with 12 g of dietary fat. To collect blood samples, 45 days were needed. High-Pressurised Liquid Chromatography (HPLC) was used to quantify the total amount of Zeaxanthin present in the serum, and LC-Atmospheric Pressure Chemical Ionisation-MS (CPCI-MS) was used to assess the concentration of labelled Zeaxanthin. The study showed that up to 45 days after ingestion of the algae, Spirulina naturally labelled Zeaxanthin was present in the circulatory system at concentrations as low as 10% of its total content. According to these studies, which included Chinese as well as American volunteers, *spirulina* increases the mean serum Zeaxanthin concentration in humans between 0.06 and 0.15 mol/l. For a single dose, the average 15-day area under the serum zeaxanthin response curve was 293 nmol/mol (range: 254–335) among American individuals and 197 nmol/mol (range: 154–285) for Chinese subjects. It is concluded that with the use of 2H labelling and the LC-API-MS technique, the relative bioavailability of zeaxanthin can be characterised with high sensitivity and specificity. Thus, in humans, S*pirulina* can be a valuable source of nutritional Zeaxanthin **[22]**.

Atherosclerosis:

Spirulina platensis (anti-atherogenic) properties were studied using the New Zealand White (NZW) rabbit model. The animal was fed a high-cholesterol diet (HCD) supplemented with 1% or 5% Spirulina for an additional 8 weeks before developing hypercholesterolemia. The HCD covered 0.5% cholesterol for the first 4 weeks. In comparison to HCD, Spirulina supplementation decreased the intimal surface area of the aorta by 32.2–48.3%. In *Spirulina* groups, serum triglycerides (TG) and total cholesterol (TC) have decreased. After 8 weeks, blood low-density lipoprotein cholesterol (LDL-C) was extensively reduced in SP1 and SP5 in comparison to HCD with the aid of 26.4% and 41.2%, respectively. However, from 2 to 8 weeks, high-density lipoprotein cholesterol (HDL-C) levels in SP1 and SP5 were significantly greater than in the HCD group. These results suggested that *Spirulina* supplementation can lower hypercholesterolemic atherosclerosis and decrease serum TC, TG, and LDL-C, as well as increase HDL-C levels. Therefore, *Spirulina* would help prevent atherosclerosis and be a relatively low-risk factor for cardiovascular disorders **[23]**.

Diabetes:

A microscopic, filamentous cyanobacterium called Spirulina. It is rich in antioxidants, amino acids, fatty acids, minerals, and vitamins. The objective of the study was to evaluate the effects of Spirulina on Korean patients with type 2 diabetes. The study included 37 patients

with this condition. They were randomly allocated to the Spirulina *(*8 g/day) or control groups when they were visiting a diabetic clinic in Seoul. Participants were told to stick to their regular diets during the 12-week intervention period and were not allowed to consume any functional foods or dietary supplements. As a functional food, Spirulina (*Arthrospira platensis*) has generated a lot of interest because of its potential to reduce cholesterol and exhibit immunomodulatory and antioxidant properties. It helps to prevent cancer, diabetes, arthritis, anaemia, and chronic iseases. *Spirulina* supplementation decreased plasma triglycerides and LDL-cholesterol, blood pressure, and elevated antioxidant and inflammatory conditions in healthy older individuals. This concluded that *Spirulina* is a functional diet for the population. This study determines how well type 2 diabetic Korean patients could benefit from *Spirulina* as a functional diet **[24]**.

Hyperlipidemia

Hyperlipidemia is one of the top causes of coronary heart disease, which is the most common type of heart disease. Coronary heart disease stands as the leading cause of death, trailed by stroke, atherosclerosis, and hyperlipidemia. Elevated serum total cholesterol, low-density lipoprotein, and decreasing levels of high-density lipoprotein are all signs of hyperlipidemia. Lipid disorders associated with hyperlipidemia are the major contributors to atherosclerosis, and the primary objective of treatment in patients with hyperlipids is to reduce the risk of ischemic heart disease (IHD) or other cardiovascular diseases or stroke. Drugs that have arrived on the market have a number of adverse reactions **[19]**. When synthetic drugs are taken, it leads to hyperuricaemia, diarrhoea, nausea, and myositis. It also leads to stomach irritation, bloating, dry skin, and poor liver function. Cardiovascular disorders may be prevented with the use of Spirulina. Studies have demonstrated that oral Spirulina intake has a positive effect on blood pressure as well as plasma lipid levels, particularly triglycerides and LDL cholesterol. Additionally, it has been found to have a moderate effect on total cholesterol and HLDL cholesterol levels. By inhibiting the activity of pancreatic lipases, the Spirulina water extract has the potential to inhibit the intestinal uptake of dietary fat. Recent work has been proposed to assess the lipid-controlling action of *Spirulina platensis* in triton-induced hyperlipidemia in Wistar albino rats. *Spirulina maxima (a* species of Arthrospira) protects against significant changes in lead-acetate-induced plasma and liver lipids. It demonstrates a protective impact on the kidney and liver **[25]**.

Anticancer activity:

Spirulina plays a vital role in the treatment of breast, liver, lung, colon, and bone marrow cancer. Laser-induced cytotoxicity (LIT) of Phycocyanin is the first known way to kill tumour cells with minimal damage to normal tissue. Phycocyanin causes cell apoptosis and has the following characteristics: bubbling of the cell membrane, shrinking of cells, and cytoplasmic coagulation. The side effects of chemotherapy are diarrhoea, hair loss, mouth sores, nausea and vomiting, and a lack of appetite. In humans, Spirulina affects NK cells either directly or indirectly and myeloid linkages directly **[21]**. Spirulina may have a chemopreventive effect on cancer, according to reports. Before the start of cancer, certain medicines (natural or synthetic) can block or reverse carcinogenic stages. Spirulina extract, according to Grawish, had a tumour-suppressing impact on the hamster cheek pouch mucosa by repairing the DNA that had been damaged. A bifunctional enzyme called cyclooxygenase (Cox, PGs Hsynthase) catalyses the biosynthesis of PGs using arachidonic acid as a substrate. These two variants of the bifunctional enzyme, cyclooxygenase-1 (Cox-1) and cyclooxygenase-2 (Cox-2), have been identified. Normal physiologic function is maintained by Cox-1 (a constitutive enzyme), and the PGs that are produced serve as a protective mechanism. The creation of PGs in areas of inflammation is caused by Cox-2 (as an inducible form whose stimulators are mitogens, oncogenes, tumour promoters, and growth factors). It has been proven that human gastric and breast cancers, as well as colorectal cancer, indicate increased Cox-2 (and not Cox-1) activity. C-phycocyanin is a specific inhibitor of Cox-2 produced by S. platensis. It was recently discovered that *S. platensis* enriched in selenium inhibited the growth of MCF-7 human breast cancer cells **[26]**. The various biological properties and their effects are shown below in **Table 5**.

Table 5: Biological properties and their effects with bioactive components

Sr. No.	Biological properties	Specific effect	Bioactive component
1)	Anticancer	Repairing of damaged DNA	Polysaccharide
		Selective inhibition of cyclooxygenase-2	C-Phycocyanin
		Induction of G1 Cell cycle arrest, mitochondria mediated apoptosis in MCF-7 human breast carcinoma	Se-enriched spirulina
2)	Antiviral	Blocking virus adsorption and protection into vero cells	Calcium spirulan
		Inhibition of the DNA polymerase activity	Sulfolipid
		Inhibition of enterovirus 71 –induced cytopathic effect, viral plaque formation and viral induced apoptosis	Protein bound pigment allophychocyanin
3)	Metalloprotective	Inhibiting lipid peroxidation, scavenging free radicals, enhancement of the activity of GSH peroxidase and superoxide dismutase	Antioxidant components
4)	Antioxidant	Metal chelating activity, free radical scavenging activity	Carotenoids, Vit. E, Phycocyanin and chlorophyll

Radiation protection:

The observed radiation protection effect in Spirulina is credited to its higher concentrations of phytopigments, including carotenoids, chlorophyll, and phycocyanin. These compounds are believed to play a significant role in providing the radiation-protective properties of Spirulina **[27]**.

Nephrotoxicity Effects:

Spirulina fusiformis protects mice's livers from damage caused by GalN. After treatment, the values returned to normal, likely due to liver cell regeneration, showing the protective ability of *Spirulina fusiformis*. Histological tests confirmed this protection, and various components in *Spirulina fusiformis* might be responsible for its liver-protecting properties **[28]**.

Antiviral effects:

Nearly 40 years ago, researchers discovered that the polysaccharides from marine algae inhibited the replication of viruses. Algal polysaccharides showed antiviral efficacy against the mumps and influenza B viruses. Aqueous extracts from *S. platensis* were also found to have anti-HSV-1 action. Spirulina's sulfated polysaccharide shows antiviral effects, blocking the growth of viruses like herpes simplex, human cytomegalovirus, influenza A, measles, mumps, human immunodeficiency virus (HIV), and white spot syndrome **[29]**. It contains essential components such as phycocyanin protein, a sulphate compound, a glycerol derivative, GLA (a type of glucosyl alcohol), and various sulfolipid compounds. The predominant polymer found in *S. platensis* resembles glycogen in its structure. 11.4–2600 g/mL of calcium Spirulina is the effective concentration that can limit viral multiplication by 50%. The alga is commonly acknowledged to contain approximately 2-5% sulfolipid molecules, known for their strong antiviral activity against the Human Immunodeficiency Virus (HIV) by selectively inhibiting the activity of DNA polymerase **[30]**.

Anti-inflammatory effects:

Bilirubin, referred to as free bilirubin, acts as a potent oxidase inhibitor for NADPH oxidase. Spirulina contains a chromophore called Phycocyanobilin (PCB). PCB is a potent enzyme complex inhibitor. In mammalian cells, phycocyanorubin bears structural similarity to bilirubin. Phycocyanin (a holoprotein that contains PCB, orally administered) has anti-inflammatory activity **[31]**.

Antioxidant activity:

Phycocyanin, a constituent of *Spirulina plantensis,* inhibits hepatic lipid peroxidation and helps in liver protection. It scavenges free radicals from damaging nerve cells. It also prevents neuronal cell apoptosis and is a reason for free radical scavenging activity [24]. The antioxidant effects of ß-carotene, tocopherols, and phenolic acids found in spirulina are well

documented. The antioxidant activity of Spirulina platensis ethanolic and aqueous extracts, as well as its bioactive components such as phycocyanin, phycocyanopeptide, and phycocyanobilin, has been observed based on their ability to scavenge 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals. In the DPPH test, a mixture of 0.5 ml of 50 M DPPH in ethanol and 1 ml of the sample was incubated in the dark for 30 minutes. At 517 nm, the mixture's absorbance was measured, and as positive controls, a standard concentration of vitamin C (5–30 g/ml) was utilized. Using the following formula, the radical scavenging activity was calculated based on the percentage of inhibition **[32]**.

Radical Scavenging Activity (%) = [(A control – A sample) / A control] x 100 (7)

In the formula,

A control represents the absorbance of the control (vitamin A), and

A sample represents the absorbance of the sample

In vitro and *in vivo* studies show the antioxidant activity of spirulina. Due to its high protein, fat, mineral (zinc, manganese, magnesium, and selenium), and vitamin contents, it has protective benefits against CCl4-induced liver damage. The protein extract of *S. platensis* displayed an inhibitory effect against lipid peroxidation and scavenged hydroxyl and peroxyl radicals. A living organism can effectively prevent oxidative stress by allowing *S. platensis to* scavenge these free radicals **[32]**.

Effects of Probiotics:

Probiotic bacteria are "living microbial food" that has been consumed by humans as dietary supplements for decades. Probiotics benefit their host animals because they contain more nutrients. Spirulina improves the microbial balance and serves as a valuable probiotic for lactic acid bacteria. *Spirulina platensis* also has potent antibacterial properties against various human pathogens **[33, 34]**.

From malnutrition to HIV:

The true global health challenge is malnutrition, not hunger. A deficiency in micronutrients (essential amino acids, minerals, and vitamins) causes this pathological condition, hindering the body from sustaining growth and crucial functions. Malnutrition has a number of negative effects on young children, including an increased risk of mortality, weak immune defences, slower motor development, and lower cognitive and learning capacities in school. Spirulina has an advantage in fighting against chronic malnutrition due to its ~~microcontainment~~ composition. After mother's milk, the second source for gammalinolenic acid *(a* fatty acid precursor of mediators involved in anti-inflammatory and immune

processes) is *Spirulina platensis.* Spirulina, which is effective in the treatment of malnutrition, also has clinically significant anti-viral and immunostimulatory effects in HIV patients. Spirulina has at least fifteen pigments, including chlorophyll and phycocyanin (anti-inflammatory, antioxidant, antitumoral, etc.) **[35]**.

Immunostimulant effects of Spirulina:

Spirulina boosts active peritoneal macrophages, promotes antibody production, and stimulates the proliferation of spleen cells. The inclusion of the Spirulina extract in the grown spleen cells increased the production of IL-1 and antibodies. Macrophages are Spirulina's first cell targets. It exhibits an additive effect on the cytokine production pathways mediated by the Toll-like receptor (TLR) in myeloid cells. Spirulina glycolipids work like Toll ligands, activating TLR2 and TLR4, similar to the BCG cell wall skeleton **[36, 37]**.

Hepatotoxicity:

This study aimed to explore the potential protective effects of Spirulina fusiforms in Swiss albino mice against galactosamine-induced toxicity. The study involved assessing various parameters, including serum glutamate oxaloacetate transferase (SGOT), serum glutamate pyruvate (SGPT), alkaline phosphatase (ALP), serum bilirubin (SBLN), antioxidant status, and TNF-α levels. These evaluations were then compared with the effects of the standard reference drug, Silymarin.

Upon administering galactosamine, there was a significant increase in SGOT, SGPT, SBLN, and TNF-α levels in the serum, accompanied by a decrease in antioxidant status in the liver. However, when *Spirulina fusiformis* was administered, these parameters were positively affected and brought closer to normal levels. These findings strongly suggest that *Spirulina fusiformis* possesses hepatoprotective activity against galactosamine-induced toxicity in mice **[38]**.

Nutritional aspect:

Spirulina has been helpful in preventing cadmium and arsenic-induced toxicity, as well as cataract acute allergic rhinitis (seasonal allergy), cerebral ischemia (ischemic strokes), and vascular reactivity (responsiveness of the blood vessel to specific stimuli). By modifying glial activation, Spirulina platensis successfully reduced peripheral sensitization and enhanced motor recovery in collagen-induced arthritic rats **[39]**.

Consumption by Humans:

Spirulina can treat a variety of disorders in addition to conventional treatments, according to clinical investigations. The use of Spirulina supplements has been demonstrated to enhance immunological function, reduce cholesterol levels in the blood, and decrease white blood cell count

after radiotherapy and chemotherapy. Since the 1980s, it has also been employed in feed, biochemical products, and healthy foods **[40, 41]**.

Use as Additives and Feed for Animals:

Along with other components, *Spirulina* is also used to prepare cuisine. For instance, instant noodles, fashionable noodles, healthy blocks, drinks, and cookies are prepared by this alga. Additionally, research on microalgae biomass has been done on a number of food items, including vegetable puddings, cookies, pastas, and oil-in-water emulsions **[42]**. The impact of microalgae concentration on the product's colour characteristics and stability throughout processing and storage were also examined. The tasty Spirulina, with its lovely blue-green hue, was advertised as being included in a variety of foods marketed to children. Include it in milkshakes, jams, cookies, or cakes **[43–45]**.

Spirulina Use in Poultry:

Spirulina is used as a high-quality feed for poultry. The addition of *Spirulina* to the diets of laying hens considerably increased the colour of the egg yolk **[46]**.

Spirulina Use in Aquaculture:

It was discovered that *Spirulina*-containing feed decreased scallop cultivation time and mortality while increasing shell thickness. The haliotis midae abalone's survival rate increased by 37.4%. The high-value fish's survival rate increased from 15 to 30 percent as a result of *Spirulina* consumption. This improvement was attributed to the fish's improved illness resistance **[47]**.

Phycocyanin as dye:

Phycocyanin is a pigment protein complex synthesised from *Spirulina platensis.* It is utilised as a natural dye in the food industry. Natural dyes, pigments, and colourants derived from minerals, animals, or plants have gained popularity in recent times due to growing concerns about health and the environment. These eco-friendly alternatives can be obtained from various parts of plants, such as leaves, fruits, twigs, seeds, flowers, bark, and roots, and are used to impart colour in various applications **[48]**.

The production of plant pigments has two notable drawbacks: land requirements for cultivation and CO2 emissions. However, algae, being photosynthetic organisms, offer a solution as they are rich in photosynthetic pigments **[49]**. Macroalgae, in particular, contain phycoerythrins and carotenoids, which are essential pigments in the textile finishing industry. Phycoerythrin, a water-soluble light-harvesting protein, plays a crucial role in the energy transfer chain. Algal pigments can fulfil this function while also exhibiting antimicrobial activity **[50, 51]**.

Adverse effects

Spirulina causes a sensation of sickness, an upset stomach, and minor diarrhea. Gastric overacidity and poor digestion may cause nausea and constipation. People with hypoglycemia and anaemia may experience adverse symptoms such as feeling hungry, light headed, and low on energy. The body's increased fat burning could be the cause of excitement and sleep issues. Poor digestion might cause brief and infrequent healing crises in the form of typically short-lived headaches. Depending on the degree of toxification throughout the detoxification, perspiration may fluctuate for a while **[51]**.

CONCLUSION:

From the review of the present work, it was concluded that microalgae has tremendous potential in various fields. However, their value-added products remain relatively unexplored. In the current era, it is crucial to tackle new challenges to address contemporary inquiries related to the quality and efficacy of herbal medicinal products. These inquiries encompass aspects such as cultivation, harvesting, processing, storage, major phytochemicals, and pharmacological applications. Consequently, this study focuses on investigating the morphology, cultivation, and harvesting of Spirulina, as well as conducting a microscopic examination of Spirulina culture. Additionally, the study explores the profile of the constituent phycocyanin and its associated pharmacological activities.

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