Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 **VOL14, ISSUE 10, 2023**

Nutrients Profile and Pharmacological activities of Spirulina – A Review

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ABSTRACT

Background - Freshwater microalgae called *spirulina* have been consumed for many years as a dietary supplement. This algae possesses a diversified concentration of nutrients and has been known as a wonder medicine due to its many applications. It promotes immunity and resistance to several illness. *Spirulina* possesses a high content of proteins, essential amino acid, lipids, polysaccharides, dietary minerals, vitamins, and fatty acids which is responsible for its pharmacological action like antimicrobial effect, anticancer and metaloprotective effect, potent immunostimulant and antioxidant effects.

Methodology- The experimental analysis and data reported on the species of *spirulina* were reviewed since the year 2005 to 2021.Various database were used as article source like Medline and Pubmed and literature review was done by using the key words *spirulina*, habitat, species, pharmacological action, toxicities and traditional uses.

Result - This article provides an outline of this algae's basic biochemical makeup before moving on to its potential uses in medicine. The fundamental description of the illness,

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the mechanism of harm, the specific *Spirulina* spp. content for therapy, in vivo and/or in vitro usage, variables related with therapeutic role, challenges encountered, and benefits are presented for each application.

KEYWORDS- Spirulina, chemical composition, pharmacological action, Immunomodulator, Antioxidant.

1. Introduction

Algae, a chlorophyll-containing organism made of one or more cells grouped together in colonies that are not closely linked to one another, which makes them polyphyletic in nature. Their derived products are economically important and widely consumed as dietary supplement in various countries, due to its potential source of fibre, minerals, proteins, antioxidants, pigments, lectins, polysaccharides, polyunsaturated fatty acid, lipids, halogenated compounds and vitamins (Afroz et al., 2021). Research revealed algae derived natural goods are widely used as human food supplement and for medical cure. Algae consists of vast range of neutraceutical value and natural pharmacological active compounds, which gives its products high market value. *Spirulina* is one such algae known for its vast therapeutic value in food industry mainly due to presence of high protein content, minerals, vitamins, essential amino acid, and fatty acids (Aditya et al., 2016).

Spirulina is a multicellular and filiform cyanobacterium (blue green algae) belongs to family *Oscillatoraceae*, photosynthetic in nature. It grows rapidly in strong sunlight and under high temperature and alkaline condition (Desai et al., 2004). This photosynthesizing cyanophyte is broadly utilised as a dietary source of supplement. It is rich in, essential fatty acids, proteins, carotenoids, vitamin B complex, vitamin E, and minerals (copper, manganese, magnesium, iron, selenium, and zinc). *Spirulina* is the collective term for 15 species of threadlike, multicellular, cyanobacterium that fall into two genera: *Spirulina and Arthrospira.* The diversity of (Voronichin),*S. platensis* NIES-39, *S. platensis* Geitler, *S. platensis* (Nordstedt) Geitler, *S. subsalsa* fo. *versicolor* (Cohn) Koster, *S. subsalsa* Oersted, *S. maxima* (as *S. geitleri*) (Setch. et Gardner), *S. subsalsa* Oersted ex Gomont, *S. major* Kützing, *Arthrospira fusiformis* (Voronichin), *A. maxima, A. jenneri* (Kützing), *S. labyrinthiformis, S. laxissima, S. lonar, S. nodosa, S. princeps , S. Laxa* (Afroz et al., 2021).

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Amoung all the species of *spirulina, S. platensis, S. maxima ad S. fusiforis* are broadly investigated and reported as edible source with high nutritional and potent therapeutic value. *S. platensis* is most widely used and accessible species. It has undergone extensive research in a variety of disciplines, particularly the food industry and medicine (Beheshtipour et al., 2012). It not only posseses high nutritional value but an excellent antioxidant source due to spirulans a sulphated polysaccharides, phenolics compounds, C- phycocyanin, allophycocyanin, and selenocompounds. *S.platensis* is used widely as dietary supplementation and its extract is used for treatment and prevention for diabetes, cancer, reduces blood cholesterol, and atherosclerosis (Desai et al., 2004). It is cultivated under controlled culture conditions still, certain other harmful cyanobacteria grow along with it, and contaminating it.

Microalgae *Spirulina's* chemical analysis reveals that it is an astounding source of some macro and micronutrient. *Spirulina* has a number of health benefits due to its high protein, dietary mineral, vitamin, essential amino acid, and fatty acid composition (Henrikson et al., 2009). Immunomodulation, anticancer, antioxidant, antiviral, and antibacterial activities are just a few of the potential health effects. Other benefits include protection against malnutrition, inflammatory allergic reactions, hyperlipidemia, obesity, anaemia, toxicity caused by heavy metals and chemicals, protection from radiation damage (Sow et al., 2021).

From the lakes of Mexico and Africa this algae was initially harvested, dried and gobble as food. Recently it is considered as major diet supplement for astronauts on space missions. As per NASA report *spirulina* is equal to 1000 kg of vegetable and fruits (Mishra et al.,2008).

2.Chemical composition

Spirulina has five times as much protein as meat, making it one of the natural sources with the greatest protein content. Most of the necessary and optional amino acids are found in *spirulina*. It has the excessive concentration of β-carotene (vitamin A forerunner), and a well-balanced amino acid composition (Jung et al., 2019). It is the only veggies source of vitamin B12 that contains 2.5 times as much of the nutrient as liver. It is a major source of linolenic acid, the essential fatty acid, which serves as a building block for hormones that control bodily processes. 50-70% of *spirulina* is

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composed of majorly protein, amino acids, minerals, fatty acids, polysaccharides, B vitamins (vitamin B12), β-carotene, and iron (Ravi et al.,2002).

The desiccated cell weight of *spirulina* is composed of 55-70% protein and 5-6% lipid. In this alga, the proportion of polyunsaturated fatty acids (PUFAs) to total lipids ranges from 1.5 to 2%. *Spirulina* supplement majorly consists linolenic acid (36% of the total PUFAs), vitamins (B1, B2, B3, B6, B9, B12, vitamin C, D and E), minerals (potassium, Cacium, Cromium, Copper, iron, Manganese, Magnesium, Phosphorus, Selenium, and Zn), pigments (chlorophyll a, echinenone, allophycocyanin, xanthophyll, canthaxanthin. betacarotene, phycobiliproteins, myxoxantβhophyll, zeaxanthin, ,diatoxanthin, 3-hydroxyechinenone, beta-cryptoxanthin, oscillaxanthin, and C-phycocyanin) and enzymes (e.g. lipase) (Khan et al., 2005; Ama Moor et al., 2016).

TABLE 1: General Composition of Spirulina (Desai et al., 2007**)**

Protein	60 % - 69 %
Carbohydrates	16 % - 20 %
Lipids	5% - 7 %
Minerals	6 % - 9%
Moisture	2.5% - 6.0%

Spirulina composition may vary according to the culturing conditions, and the methods of analysis.

3. Macronutrient profile

3.1 Protein and amino acid

Protein makes up 60 to 70 percent of the dry weight of *spirulina*. This is a remarkable ratio considering that only roughly 35% of plant-based foods, including those that are regarded as "good protein sources," have this amount. In fact, C-phycocyanin, a compound that makes about 20% of the dry weight of the algae and contains phycocyanobilin, a biliverdin homolog, is one of the main proteins in *spirulina*. (Demir et al., 2010 ; Kulshreshtha et al., 2008 ; Pawar et al., 2020)

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3.2 Lipids

A lipid portion of about 5–10% of the dry weight of *spirulina* is present. The fact that the majority of the fats in this fraction are necessary lipids for humans is crucial in this regard. Therefore, gamma-linolenic, linoleic, and oleic acids are thought to be present in *spirulina* in good amounts. The first one has drawn a lot of interest because few foods contain a considerable amount; in fact, *spirulina* is thought to be the vegetable source with the highest quantity (representing around 20% of its total fatty acid content) **(**Ismail et al., 2015 ; Seyhaneyildiz et al., 2017)

4.Micronutrient profile

4.1 Vitamins

The extraordinary amount of vitamin B12 present in *spirulina.* Foods with an animal origin typically contain the vitamin B12 alone. Because vegans don't eat any foods with animal origin, this alga could be thought of as a useful source for them **(**Belay 2002 ; Salmeán et al., 2015**)**. *Spirulina* is nurtured as the wealthiest complete-food source of provitamin A (carotene) and vitamin B12 (corrinoid forms, analogs, and pseudovitamin B12). The body can get all the vitamin B1 (thiamine), B2 (riboflavin), and B3 (niacin) it needs from just 20g of these microalgae (Hoseini et al., 2013; Mendiola et al. 2008; Michael et al., 2019; Kumar et al., 2018)

Spirulina does not fulfil the exact functional roles that vitamin B12 plays in humans but it does not affect the way that B12 is metabolised in mammals **(**Jung et al., 2019; Sharma, 2011**)**. According to a highly sensitive microbiological test, 36% of the vitamin B12 molecules found in *Spirulina* spp. are functional in humans **(**Watanabe et al., 2002**)** Methyl cobalamin, a physiologically active form of vitamin B12, is present in *S. platensis* at concentrations of 35 to 38 g per 100 g of dry *spirulina* biomass **(**Sharma et al., 2019**)**.

4.2 Minerals

Compared to cereals, which are typically regarded as good sources of iron, blue-green algae have an iron concentration that is significantly higher, ranging from 580 to 1800 mg/kg. Algae do not contain phytates or oxalates that could bind iron and reduce its absorption because they do not have a pericardium (unlike grains *spirulina* contains

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high concentrations of a number of micronutrients, particularly minerals,which makes it an ideal dietary supplement for vegetarians. (Babadzhanov et al., 2008**)**.

Table 3: Mineral component of spirulina (g/kg) (Kumudha et al., 2010)

Component	Quantity
Iron	0.55-1.5
Calcium	1.2-15
Phosphorus	6.5-9.2
Potassium	6.8-15.7

Spirulina's mineral content consequently varies on its source and cultivation environment. Comparable amounts to those found in milk are present for calcium, phosphorus, and magnesium. *Spirulina* is considered as the highest iron rich food as compared with other typical iron supplements. Iron from *spirulina* is absorbed 60% more readily than iron from ferrous sulphate, which is included in iron supplements **(**Michael et al., 2019**;** Kumudha et al., 2010).

Table 2: Composition of Phytopigments of *spirulina* (mg / 100g) (Watanabe et al., 2002; Sharma et al.,2019)

Total Carotenoids	400 – 650
BCarotene	150 – 250
Phylloxanthine	250 – 470
Zeaxanthin	125 – 200
Chlorophyll	1300 – 1700
Phycocyanin	15000 –19000

Table 3: Vitamins (mg / 100g) (Sharma et al., 2019; Babadzhanov et al., 2004**)**

B1 (Thiamine)	0.1.5 – 0.30
B2 (Riboflavin)	4.0 – 7.0
B3 (Niacin)	10.0 – 25.0
B6 (Pyridoxine)	0.5 – 1.5
B12 (Analogue)	0.10 – 0.30

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Folic acid	0.05 – 0.30
Inositol	70 – 90
Vitamin K	0.90 – 1.05

5. Pharmacological actions of *spirulina*

5.1 Anti-diabetic

spirulina can lower the levels of fasting, postprandial blood glucose, glycosylated haemoglobin (HbA-1c), in type-2 diabetes mellitus people **(**Layam et al., 2006**)**. In diabetic rats, *spirulina* can boost the activity of the enzyme's hexokinase and glucose-6-phosphatase. Plasma insulin and C-peptide are improved by *spirulina* **(**Okechukwu et al., 2019**)**. *S maxima* reduced dyslipidemia brought on by carbon tetrachloride **(**Joventino IP et al.2012**)** and showed hypolipidemic effects, particularly on triacylglycerols (TAG) and LDL cholesterol.

Clinical studies have revealed that *spirulina* supplementation is effective in the management of cholesterol and glucose levels in type 2 diabetes at the dose of 2g/day for two months. It was successful in enhancing the lipid profiles and glycosylated haemoglobin (HbA(1c)) levels of the diabetic individuals. These results point to the positive effects of *spirulina* supplementation in lowering participants lipid profiles and regulating their blood glucose levels **(**Oriquat et al., 2019**)**. Additionally, it was found that *S. maxima* can stop the development of fatty liver in CD-1 male and female mice with experimental diabetes. Because of this, diabetic patients have a higher quality of life and live longer **(**Metwally et al., 2015**)**. Another study found that adding *spirulina* to a diet higher in chromium helped type 2 diabetes patients with hyperglycemia, lipid profiles, blood pressure, and weight control **(**Parikh P,2001**)**

5.2 Cardio-protective activity

Spirulina has been found to lower cholesterol levels in people with hyperlipidemic nephrotic syndrome. Lipoprotein levels rise in the nephrotic syndrome as a result of increased lipoprotein production, which results in secondary hyperlipidemia. *Spirulina* contains a sizable quantity of γ-linolenic acid (GLA), a vital fatty acid that can inhibit the buildup of cholesterol in the body. Spray-dried capsules form of *spirulina* are widely used in hypercholesterolemic nephrotic syndrome due to presence of higher

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content of antioxidants, GLA, amino acids, and fatty acids (Rodrıguez-Hernández et al., 2001**).**

Doxorubicin (DOX) use during cancer therapy results in cardiotoxicity. *Spirulina* was found to have a protective effect against the doxorubicin cardiotoxicity. In a mouse model, the blue-green algae *spirulina* has the potential to act as a cardioprotective agent, by preventing the production of free radicals **(**Deng et al.2008**)**. *Spirulina* has a high concentration of Phycobiliprotein C-phycocyanin, which inhibits atheroma and reduces oxidative stress and NADPH oxidase production in hamsters fed an atherogenic diet **(**Samuels et al.,2008**)** Additionally, it was demonstrated that *S. platensis* was effective in treating hyperlipidemia and could reduce plasma lipoprotein lipase in hyperlipidemic rats.

In liver the hepatoprotective effect is shown by *spirulina* by lowering the lipid profile and lipoperoxidation products. It has a hypolipidemic impact, particularly on triacylglycerol concentrations (LDL) as well as indirectly on cholesterol (HDL). Additionally, it is reported that *spirulina,* decreases both systolic and diastolic blood pressure when administered orally at the dose of 4.5 g/kg for 6 weeks **(**Khan et al.,2005**)**. The C-phycocyanin molecule in *spirulina* has been given credit for its ability to reduce fat levels. Systolic and diastolic blood pressure lowering is another benefit of taking *spirulina* orally **(**Agrawal et al., 2013**)**.

Spirulina's high potassium and low sodium concentrations have a beneficial impact on blood pressure **(**Layam et al., 2006**)**.

According to one theory, C-phycocyanin prevents platelet aggregation by preventing calcium from being mobilised and by mediating free radicals that are generated by platelets **(**Duran et al., 2007**)**. *Spirulina* has also been found to have atherosclerosis-inhibiting properties **(**Nagaoka S. Et al., 2005**)**.

5.3 Anti-viral activity

S. platensis aqueous extract can inhibit HIV-1 replication in peripheral blood mononuclear cells (PBMC), human T cell lines and Langerhans cells **(**Hsiao et al.,2005**)**. *S. platensis*, a marine alga, has produced a sulphated polysaccharide known as calcium *spirulina* (Ca-SP), which exhibits anti-herpes and anti-human immunodeficiency virus activity both in vitro and ex vivo **(**Cheong et al., 2010**)**. Commercial preparation of hot

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water extract of *Spirulina maxima* showed the antiviral activity performed by microplate inhibition assay over several viruses. It impedes the infection of human cytomegalovirus (HCMV), pseudorabies virus (PRV), herpes simplex virus type 2 (HSV-2) and HSV-1 respectively **(**Hernández-Corona et al., 2002**)**.

5.4 Anti-oxidant activity

Spirulina appears to have high antioxidant activity both in vitro and in vivo, according to a number of studies**.** In Swiss albino mice, *S. fusiform* is protects against oxidative stress brought on by mercuric chloride. Presence of Mercuric chloride (4.5 mg/kg body weight IV) in *spirulina* has been demonstrated to promote lipid peroxidation by decreasing glutathione and other antioxidant enzymes in the liver. *Spirulina* supplementation has also reported to reduce oxidative stress **(**Zhou et al.,2005**)**.

C-phycocyanin, a powerful in vivo and in vitro peroxyl radical scavenger, is abundant in *S. platensis*. Additionally, C-Phycocyanin (from *S. platensis*) was found to successfully reduce CCl(4)-induced lipid peroxidation in rat liver **(**Wang L, et al., 2007**)**. Chlorella water extract shown anti-inflammatory and antioxidant activity in chronic liver fibrosis. Antioxidants have been shown to have the ability to stop hepatic stellate cells' (HSCs) growth **(**Estrada et al., 2001**)**.

5.5 Anti-bacterial activity

Spirulina extracts prepared using various solvents have been examined for their antimicrobial properties. The methanolic extract of *S. platensis* has a high quantity of linolenic acid, which is responsible for the alga's antibacterial action (Thamilmaraiselvi et al., 2018; Bhat et al., 2000). The antibacterial effects of *spirulina* extract shown on gram-positive and gram negative bacteria such as *Candida albicans*, *Staphylococcus aureus*, *Escherichia coli* and *Aspergillus niger*. According to the findings, all *Spirulina* fractions obtained through supercritical fluid extraction were most toxic to *C. albicans*. The synergistic action of fatty acids may be responsible for this antibacterial activity **(**Wu et al., 2005**)**.

Over the different kind of human pathogenic bacteria the aqueous extract of *S.Platensis* showed antibacterial activity done by agar diffusion method. *Klebsiella pneumoniae* and *Proteus vulgaris* showed the water extract's maximum and lowest levels of

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antibacterial activity, respectively. The strongest biological activity against *Klebsiella pneumonia* was likewise demonstrated by acetone extract of *S. platensis* **(**Patel et al., 2006**)**.

5.6 Anti-cancer activity

Spirulina may have a chemopreventive effect on cancer, according to reports. Before the development of cancer, several specific medicines (natural or synthetic) can stop or reverse carcinogenic pathways. *Spirulina* extract, according to Grawish, has a tumor-suppressing impact on the mucosa in the cheek pouch of hamsters as a result of DNA repair. (Chamorro-Cevallos et al., 2008).

Endonuclease activity, which is necessary for DNA damage repair, can be enhanced by the special polysaccharide composition of spirulina **(**Mendiola et al., 2007**)**.

Prostaglandin (PG) levels have been linked in studies of cancer **(**Mala et al., 2009**)**. A dual-purpose enzyme called cyclooxygenase (Cox) catalyses the manufacture of PGs using arachidonic acid as a substrate. Both Cox-1 and Cox-2 are known variants of this enzyme with dual functions. 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 **(**O'Shaughnessy et al., 2002**)**. It is reported that the activity of COX 2 increases in malignant tissues of colorectal cancer as well as in human gastric and breast tumours. **(**Grawish et al., 2008**)**. C-phycocyanin is a specialised inhibitor of Cox-2 produced by *S. platensis*. The shape and substantial structure of phycocyanin, which promotes appropriate binding to the active site of Cox-2, are to blame for this inhibition **(**Mala et al., 2009). Selenium-enriched *S. platensis* has recently been demonstrated to suppress the development of MCF-7 human breast cancer cells **(**Reddy et al., 2000**)**.

TABLE 4: Biological Response of Spirulina

BIOLOGICAL ACTIVITY	SPECIFIC EFFECTS	BIOACTIVE COMPONENT	REFRENCES
Anti- Cancer	Damaged DNA repairing Induction of G1 cell cycle arrest, mitochondria mediated apoptosis in MCF-7 human breast carcinoma	Se-enriched Spirulina	**(**Fournier et al.,2000**)**

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Anti- viral	Can inhibit HIV-1 replication. exhibits anti-herpes and anti-human immunodeficiency virus activity both in vitro and ex vivo.	sulphated polysaccharide calcium spirulina	**(**Hsiao et al., 2005**;** Hernández-Corona et al., 2002**)**
Anti- Bacterial	supercritical fluid extraction	linolenic acid	**(**Patel et al., 2006**)**
Anti- Oxidant	Reduce CCl(4)-induced lipid peroxidation It has ability to stop hepatic stellate cells' (HSCs) growth	C-Phycocyanin (from S. platensis)	**(**Zhou et al., 2005**)**
Cardio-protective	an essential fatty acid that can inhibit the build-up of cholesterol inhibits atheroma and reduces oxidative stress and NADPH oxidase prevents platelet aggregation by preventing calcium from being mobilised	gamma-linolenic acid (GLA) Phycobiliprotein C-phycocyanin C-phycocyanin	**(**Rodrıguez-Hernández et al., 2001**;** Khan et al., 2005**]**
Anti- Diabetic	Enhance the lipid profiles and glycosylated haemoglobin (HbA(1c).	spirulina supplementation (2 g/day for 2 months)	**(**Oriquat et al., 2019**)**

6. Toxicity profile of *spirulina*

6.1 Heavy metal

Different metals causes oxidative stress, leads to particular tissue damage. Antioxidants, which are endogenous substances that protect against free radicals in aerobic organisms, synthetic substances such nitric oxide (NO), reduced glutathione (GSH), and superoxide dismutase (SOD) **(**Zhang et al., 2020**).**

The following sections provide some illustrations of how *spirulina* can protect against metal poisoning.

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6.2 Lead

Lead poisoning is the major cause of morphological changes in red bone marrow cells, tissue etiological changes and tubular cell necrosis. It also causes kidney damage, alters glomerular filtration rate, swaps the proteins and lipid composition, reduces sperm count and pregnancy risk. These alterations results in decreased Hb synthesis, insufficient erythropoiesis and less cell viability. *Spirulina* is reported to show protective action against lead and cadmium toxicity in various body cells such as T lymphocytes, RBC, WBC, Reticulocyte etc. Due to the metal binding ability of this algae it is proved to improve Fe and Hb metabolism in rats exposed to lead toxicity (Chen et al., 2009; El-Tantawy, 2016).

6.3 Cadmium

Cadmium causes imbalance between the antioxidants and peroxidants system due to its thiol depletion action, leads to inception of reactive oxygen species (ROS) in tissues finally results in inhibition of antioxidant defence enzymes. ROS like hydrogen peroxide, hydroxyl radical, peroxyl radical are generated and destroyed by all aerobic organisms, they are most susceptible to proteins, lipids, lipoproteins, DNA etc. *S.Platensis* is rich in antioxidant compounds which may defend against cadmium induced oxidative stress, it can enhance the activity of antioxidant enzymes like superoxide dismutase and GSH peroxidase. It is reported that it posses lipid peroxidation and free radical scavenging action **(**Kulshreshtha et al., 2008**;** Bhattacharya et al., 2020**)**

6.4 Iron

Amoung other metals iron is the major substance that develop oxidative stress leading to declination of brain cell and its functions. It interrelates with the various intermittent process that causes oxidative stress including production of reactive oxygen species. Because of cellular necrosis, iron poisoning causes a large increase in lactate dehydrogenase (LDH) release. Phycocyanin content of *spirulina* extract showed the stimulatory activity against the antioxidants enzymes which defends the human from

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detrimental effect of ROS particularly glutathione peroxidase and reductase (Mohanty et al., 2018**;** Sagara et al., 2015**).**

7. Conclusion

Spirulina natural and synthetic products are widely used in the agriculture, food supplement, aroma industry and medicine. It posses various pharmacological action such as anticancer , antimicrobial, antibacterial, immunostimulant, metalloprotective and antioxidant action due to the presence of micro and macronutrient like proteins, minerals, lipids, amino acids, essential fatty acids, polysaccharides and vitamins. Presence of endonucleases that restores damaged DNA, fatty acid specifically linolenic acid and calcium sulphated polysaccharide are responsible for spirulina's antiviral, antibacterial and anticancer activity. In the twenty-first century, a scarcity of natural food products generates a vitamin and mineral deficiency in the general population. Because of its high protein, polyunsaturated fatty acid (-linolenic acid), vitamin, mineral, colour, and enzyme content, *S. platensis*, a blue-green microalga, is manufactured and used as a substitute for other feed and food additives. This article discusses the biochemical profile of algae along with its potent medical application. Each application includes a description of the fundamentals of the disease, the toxicity profile, the specific *Spirulina* species content for therapy, in vivo and/or in vitro usage, aspects associated to the therapeutic role, and advantages.

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