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The Health Benefits Of Spirulina; With An Emphasis On Its Pharmacological Properties - A Review

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ABSTRACT:

Spirulina, a nutrient-rich single-cell protein, is gaining attention as a functional food source. With its composition comprising 55-70% protein, 25-30% carbohydrates, essential fatty acids, vitamins, and bioactive pigments like carotene and phycocyanin, it presents a promising alternative to synthetic food additives, which are linked to health risks such as cancer. As the food industry seeks safer, natural antioxidants, Spirulina emerges as a significant contender. Its bioactive properties not only hold medicinal potential but also inspire the development of synthetic analogs. This review examines the nutritional benefits, bioactive properties, and immunological applications of Spirulina, highlighting its recognition as a safe dietary supplement worldwide, its diverse biological activities and nutritional benefits, attributed to its high concentration of natural nutrients with bio-modulatory and immuno-modulatory functions. Various Spirulina preparations enhance immune responses by increasing the phagocytic activity of macrophages, stimulating antibody and cytokine production, and promoting the accumulation and activation of NK, T, and B cells. Additionally, Spirulina plays a regulatory role in lipid and carbohydrate metabolism, demonstrating effects on glucose and lipid profiles in both experimental models and diabetic patients. Its preparations have shown antiviral activity against enveloped viruses, including herpes, cytomegalovirus, influenza, and HIV, and possess antioxidant properties that may inhibit carcinogenesis and reduce organ toxicity, particularly in the liver, kidneys, and testes.

KEYWORDS: Dietary supplement, Carotene, Phycocyanin, Bio-modulatory, Immunomodulatory, Antioxidant, Antiviral.

INTRODUCTION:

Spirulina, a blue-green alga, has gained popularity as a health food globally due to its exceptional nutritional profile. As a microscopic, filamentous cyanobacterium in the class Cyanophyta, Spirulina is highly valued for its rich protein content, which ranges from 50% to 70% of its dry weight—significantly higher than other single-cell proteins and surpassing the protein content of many vegetable sources, such as soya flour, which contains about 35% protein. Adaptable to diverse habitats including alkaline saline waters, soils, and thermal springs, Spirulina is noted for its ease of cultivation and digestibility. The United Nations World Food Conference has praised Spirulina as "The best for tomorrow" due to its remarkable nutritional and practical benefits. [1-2]

In contrast to many foods, spirulina doesn't need to be cooked or treated in any way to increase the availability of protein, which makes production easier and preserves important elements like vitamins and polyunsaturated fatty acids. In addition to its potential applications as food and feed, spirulina is also being investigated for usage in fuels [3]. The nutritional value and possible pharmacological uses of Spirulina platensis in particular are being studied. It is being researched for its therapeutic qualities, such as antibacterial activity and suppression of viruses like Influenza A virus, human cytomegalovirus, measles virus, and Herpes simplex virus (HSV-1), and it shows promise in curing conditions like anaemia, tumour growth, and malnutrition. [4]

A variety of advantageous biological characteristics are displayed by Spirulina platensis and its preparations. According to reports, they can prevent cancer, lower blood cholesterol, boost immunity, lessen nephrotoxicity from toxic metals and medications, and protect against radiation damage [5]. Compounds such phenolic, phycobiliproteins, carotenoids, organic acids, sulphated polysaccharides (spirulas), and polyunsaturated fatty acids are thought to be responsible for these effects. Additionally, spirulina is added to a variety of food items to improve their nutritional profiles, which may help in the treatment of long-term illnesses like diabetes, high blood pressure, and heart disease. Due in significant part to its increased phenolic component content, spirulina extract has been observed to have stronger antioxidant activity when compared to chlorella. [6]

As potential biocontrol agents against plant pathogenic bacteria and fungi, spirulina and other cyanobacteria species have the capacity to produce a broad variety of antimicrobial compounds. Many medicinal compounds have historically been found in nature, and many contemporary medications have been made from natural sources, frequently with inspiration from traditional medicine. The screening of cyanobacteria for antibiotics and other pharmacologically active substances has become a more prominent focus of recent studies. Novel and physiologically active metabolites, both primary and secondary, are abundant in these algae species and have potential uses in medicine. Although the nutritional benefits of spirulina are widely recognised, little research has been done in India on its antibacterial qualities, especially those related to C-phycocyanin.

Various bacteriocins, polyphenols, fatty acids, glycolipids, terpenoids, and alkaloids are among the antimicrobial substances found in cyanobacterial exudates. In addition to having antibacterial, hormonal, poisonous, and antineoplastic actions, these secondary metabolites can affect both prokaryotic and eukaryotic microbes. A viable option towards creating novel medicines is investigating the antibacterial potential of spirulina, given the growing usage of antibiotics and the emergence of drug-resistant microorganisms. Though they are thought to have evolutionary relevance and to be vital in determining how organisms interact with one another, the characteristics of secondary metabolites in nature are still mostly unknown. Bioassays employing specific microorganisms are used to evaluate the antibacterial properties of cyanobacterial extracts. The agar diffusion method is frequently used in these experiments, including pour-plate and spread plate (seeded plate) approaches. Visible inhibition halos or zones of inhibition surrounding the extract application sites show the presence of antimicrobial properties. Escherichia coli, Bacillus cereus, Bacillus subtilis, and Micrococcus luteus are among the target bacteria commonly used in bacterial bioassays. The antibacterial qualities of cyanobacterial extracts are assessed and antibiotic residues in food are found using these bacteria. [7]

HISTORY:

Since the beginning of time, algae have been used as food and are important to many cultures, particularly in Asia. Microalgae consumption is a relatively new phenomenon. Like macroalgae, microalgae have been used traditionally across four continents, according to Jasby, however the majority of these uses are from Asia. In 1521, Arthrospira, also referred to as Spirulina, was first used as a meal. Hernan Cortez's expedition member Bernal Diaz del Castillo noted that Spirulina maxima was collected from Lake Texcoco, dried, and marketed in Tenochtitlan's (present-day Mexico City) marketplaces. "Small cakes made from some sort of ooze from the great lake," as he put it, were transformed into a cheese-like substance that resembled bread. [8–9]

The Aztec cuisine Tecuitlatl was described by Franciscan friar Bernardino da Sahagún as being "like hay" and "of clear blue colour," rather than "neither grass nor earth." Despite this early reference, Tecuitlatl lost popularity after the sixteenth century. The contemporary equivalent of Tecuitlatl, Spirulina, did not start commercial production in Lake Texcoco until the 1970s. The historical importance of Spirulina in Aztec civilisation is fascinatingly described by Farrar. [10]

There is also historical evidence of the usage of spirulina as food in the Republic of Chad, which is in Africa and about 10,000 kilometres from Lake Texcoco. The exact historical frame is unknown ; however, it seems that Spirulina has been ingested there for generations. In 1940, the French phycologist Dangeard published a study on "dihe," a cake from Arthrospira platensis (Spirulina). His description of dihe as a "true filamentous, spiral shaped blue alga" was mainly ignored until it was found in 1966 by J. Leonard. Leonard recognised the dried mats of S. Platensis as dihe and verified that it was collected from alkaline lakes in the Kanem region, which is close to Lake Chad [11–12]. Spirulina still plays a major role in the Kanembu tribe's local economy and is a vital source of protein. Simultaneously, the French Petroleum Institute started analysing Lake Texcoco Spirulina samples. As a result of these investigations, the first commercial Spirulina production was established in the 1970s. [13–14]

MORPHOLOGY:

The multicellular, filamentous, blue-green microalga known as spirulina contains symbiotic bacteria that have the ability to fix nitrogen from the atmosphere. It may have a disk-like or rod-like appearance. It contains carotenoids and chlorophyll a, as well as phycocyanin, its main photosynthetic pigment, which gives it its blue hue. Some species of Spirulina are red or pink because of phycoythrin. Spirulina are autotrophic organisms that reproduce by binary fission and carry out photosynthesis. The trichomes, which are helical-shaped filaments that only hold their shape in liquid environments or culture mediums, are what define the genus. Because of gas-filled vacuoles inside the cells, these filaments create floating mats. Trichomes range in size from 3 to 4 µm in width and 50 to 500 µm in length. In addition to other lysozyme-insensitive components, the cell wall of spirulina is similar to that of Gram-negative bacteria in that it contains peptidoglycan, a lysozyme-sensitive heteropolymer that offers structural integrity and osmotic protection. [15]

CULTIVATION AND PRODUCTION:

1.NATURAL PRODUCTION:

Studies of Spirulina's natural habitats, especially lakes with harsh conditions like high pH and alkalinity where other algae cannot flourish, are frequently the source of information regarding Spirulina farming. Notable examples are the lakes in the Great African Rift Valley, where flamingo numbers are sustained by thick colonies of Spirulina. According to estimates, these flamingos devour between 50 and 94 percent of the lake's daily primary production, or between 0.4 and 0.6% of the algal biomass, which is a substantial quantity of Spirulina [16]. Shallow raceways are used in the majority of commercial spirulina production systems, where paddle wheels mix cultures. Some spirulina is still being harvested from populations that occur naturally, though. After research was done in 1967 in partnership with the French Oil Institute, Sosa-Texcoco Ltd. started harvesting Spirulina maxima from Lake Texcoco in Mexico. Spirulina production has been a major activity at Lake Texcoco, which is 2,200 meters above sea level and has an average yearly temperature of 18°C. Since 1936 the same business had been mining the lake resources for soda. The largest single plant for producing spirulina biomass is this one.

During the "semi-natural" cultivation procedure, the algal biomass doubles every three to four days, and harvesting is done continuously. The biomass passes through pasteurisation, homogenisation, and spray drying after filtering (Origin, 1986). The initial prototype plant, which began operations in 1973, generated 150 tonnes of dry spirulina biomass annually. Later, it was expanded to produce 300 tonnes annually from 12 hectares of natural ponds instead. In order to overcome engineering obstacles and carry out the required toxicological testing before to launching the product, Sosa-Texcoco Ltd has spent almost US$5 million since 1977 (Origin, 1986). The company made a third of its revenue from the production of sodas from the cultivation of spirulina. Sosa-Texcoco, however, stopped producing spirulina in 1995.

Spirulina has also been grown in another semi-natural lake in Myanmar. Studies on four volcanic lakes with spirulina blooms have been conducted since 1984. By 1998, Twin Tang Lake's annual production had grown to 100 tonnes. About 40 percent of the spirulina is cultivated in outdoor ponds next to the lake, and the remaining 60 percent is collected from boats on the lake's surface. Boats gather buckets of spirulina during the summer blooming season, when it forms thick mats on the lake. After that, the spirulina is collected using parallel inclined filters, cleaned with fresh water, dewatered, and compressed. The noodle-like filaments created by extruding this paste are then sun-dried on sheets of clear plastic. After that, the dried spirulina chips are delivered to a pharmaceutical facility in Yangon, where they undergo pasteurisation and are formed into tablets.

2.LARGE-SCALE COMMERCIAL PRODUCTION:

Chlorella was first cultivated on a commercial scale in Japan in the early 1960s, and Spirulina was first cultivated on a big scale in Lake Texcoco, Mexico, in the early 1970s. There are currently at least 22 nations that produce spirulina, including the United States, Vietnam, Benin, Brazil, Burkina Faso, Chad, Chile, China, Costa Rica, Côte d'Ivoire, Cuba, Ecuador, France, India, Madagascar, Mexico, Myanmar, Peru, Israel, Spain, Thailand, and Togo. Shimamatsu (2004) estimates that 3,000 tonnes of spirulina are produced annually in the industrial sector. The four main steps in the commercial manufacturing of spirulina are culture, harvesting, drying, and packing. In order to satisfy the strict quality and safety requirements set by the food and supplement sector, careful monitoring is necessary at each stage as it has a significant impact on the ultimate yield and quality of the product.

With evaporation as the main loss factor, the production process uses a closed-loop system in which material is continuously recycled. Utilising a semi-continuous culture technique, the system harvests pond every day in accordance with 24-hour growth cycles. To maximise growth and guarantee traceability, the medium is recycled back into the original pond. Daily laboratory testing and the regular supply of make-up nutrients are necessary to ensure uniformity and ideal circumstances.

The culture is harvested by pumping it via PVC pipes to a processing facility, where a vacuum belt is used to rinse, concentrate, and further dehydrate it. The biomass paste is then turned into a fine, free-flowing powder by spray drying it. From pond to powder, the entire process takes less than fifteen minutes. In the Quality Control Laboratory, final product samples are examined, data is recorded, and the product is only released for packaging if it satisfies all safety and quality requirements.

2.1 REMEDIAL PONDS:

Spirulina is usually cultivated in enormous raceway ponds, which are usually constructed of concrete or lined with reinforced plastic that is appropriate for drinking water. This design was created in the 1950s and is still in use today. As the depth varies from 15 to 40 cm, the ponds can range in size from about 2,000 m² to 5,000 m², with water contents varying from 400 to 1,000 m³. Depending on the season, the desired algal density, and the final product's biochemical makeup, the depth is changed. The culture must be mixed in order to maintain consistent temperature and nutrient diffusion, avoid self-shading, and guarantee even light dispersion. Paddle wheels are frequently used to mix the culture, which also helps to avoid scum development, which is sometimes misinterpreted as the accumulation of algal biomass. Continuous mixing is maintained during controlled outdoor production to prevent scum, which occurs when there is insufficient mixing in natural environments. [17]

2.2 THE CULTURE MEDIA'S COMPOSITION:

The culture media used in the cultivation of spirulina is made to closely mimic its natural habitat. It usually makes use of a modified form of Zarouk's original medium, which is made up of water, sodium bicarbonate or carbonate, and supplies of iron, phosphorus, nitrogen, and more trace minerals. In an alkaline environment, this medium promotes the growth of Arthrospira platensis, which inhibits the growth of undesirable impurities and guarantees a near-monoculture of the target algae. Reputable vendors that guarantee that their goods fulfil requirements for heavy metals and other pollutants provide the nutrients. Importantly, neither the manufacturing nor the cultivation procedures involve any harmful compounds, pesticides, herbicides, or solvents. [18–19]

2.3 HARVESTING THE BIOMASS:

Spirulina harvesting frequency is determined by the daily growth rate, which is reliant on temperature and light levels. At the height of the season, for example, the Earthrise plant can harvest around 3 metric tonnes of Spirulina every day. The harvested culture is transported to a processing facility via PVC pipes, where it is filtered through stainless steel screens to remove impurities and concentrate the biomass. A fine, free-flowing powder is created by processing the concentrated paste in a spray drier to eliminate moisture, while the filtrate is put back into the pond.

2.4 DESICCATION AND PACKAGING:

The production of high-quality spirulina depends on timely and proper drying. The cost-effectiveness of spray drying makes it the method of choice for large-scale production, even though freeze drying produces better results overall. Spirulina droplets are added to a chamber where water is rapidly evaporated in order to perform spray drying. No stabilisers, additives, or preservatives are added; the powder is heated for a short time before sinking to the bottom. Rapid drying helps protect pigments, enzymes, and nutrients that are susceptible to heat.

Maintaining ideal moisture levels is essential for controlling the drying temperature, which influences the growth of bacteria and mould. After drying, the powdered spirulina is weighed, vacuum-sealed in oxygen-barrier bags to prevent oxidation and air exposure, and then packaged in cardboard boxes. These boxes are handled carefully to avoid contamination, sealed, and labelled with lot numbers and weight. For up to four years, the product can retain its nutritional qualities and biochemical makeup under these circumstances.

GROWTH FACTORS:

Spirulina requires suitable climate conditions, particularly year-round sunshine, to be grown in large quantities. It can be difficult to achieve ideal growth because of a variety of environmental conditions, including temperature variations, wind, rainfall, and sun radiation.

1.NUTRIENT MEDIUM:

Spirulina needs more salt and nutrients than Scenedesmus and Chlorella. The fact that Spirulina is only found naturally in salt lakes is probably due to its requirement for high salt levels [20]. The media utilised in contemporary Spirulina manufacturing facilities are variants of Zarrouk's initial recipe. For Spirulina to thrive as best it can, these media are made especially to maintain high alkalinity and a consistent supply of bicarbonate ions. [21]

2.CARBON SOURCE:

Spirulina does not thrive when organic molecules are the only carbon source, according to Ogawa and Terui. The production of cyanobacteria in mass culture was improved by adding extracts from different organic manures to a minimum medium devoid of sodium chloride. Using this technique, Spirulina platensis and Spirulina subsalsa produced 5–30% more dry matter. [22–23]

The effects of elevated ambient CO_2 on Spirulina photosynthesis and growth were investigated by Gordillo et al. Because of its effect on the pigment content of the algae, they discovered that greater CO_2 levels reduced the maximum biomass production, but they had no effect on the maximum growth rate. [24]

The impact of nutrient supplementation on the biomass production of Spirulina platensis in open raceway ponds was investigated by Vieira Costa et al. [58]. They added carbon in the form of sodium bicarbonate, nitrogen in the form of urea, phosphate, sulphate, ferric iron, magnesium, and potassium, as well as nitrogen on the growth rate of the cyanobacteria Spirulina plantensis. The biomass output in supplemented lagoon water was 0.78 ± 0.01 g/L (dry weight), they discovered. The biomass, however, rose to 0.82 ± 0.01 g/L after 40 hours of culture when 2.88 g/L of sodium bicarbonate was added. [25]

3.TEMPERATURE:

For optimal Spirulina yield, the culture temperature should be kept between 30 and 35°C, even when the outside temperature reaches 38°C. Temperatures above 35°C can harm the cultures and result in bleaching. Even in situations where the temperature outside is high, partial shadowing can successfully reduce the culture temperature to about 30°C .[26]

Spirulina species exhibit maximum specific growth rates at varying temperatures: 0.144 for Spirulina fusiformis at 37°C and 0.141 for Spirulina platensis at 32°C. Additionally, Spirulina platensis produces the most biomass (2.4 g/L) and chlorophyll a (16.6 mg/L) at 32°C temperatures. Peak biomass production for Spirulina fusiformis is 2.3 g/L and peak chlorophyll a production is 14.2 mg/L at 37°C [27]

4.LIGHT:

Certain light intensities are necessary for the best growth of cyanobacteria called spirulina. The light intensity should be between 20 and 30 kilolux (K lux) during its growing phase. Spirulina can flourish and reach its full potential for growth within this range because it offers the perfect conditions for photosynthesis [28]

The photosynthetic productivity of the filamentous cyanobacterium Spirulina platensis was investigated using a cone-shaped helical tubular photobioreactor. Compact fluorescent cool white lights were used to illuminate this 0.255 m² photobioreactor. The daily input radiation energy was 1249 kJ. A maximum photosynthetic efficiency of 6.83% was attained, translating into a daily production rate of 15.9 g of dry biomass per square metre. [29]

5. pH:

The physiological characteristics of algae and the availability of nutrients are greatly influenced by pH levels. The ideal pH range for spirulina growth is between 9 and 11. Because bicarbonate and salt ions are used during mass cultivation, the ideal pH of the nutritional medium changes from 8.4 to 9.5. The solubility of minerals and carbon sources is impacted by this pH range, which impacts nutrient availability and general growth. [30]

6.AGITATION:

The uniform distribution of CO_2 and the avoidance of temperature stratification are two advantages of agitating algae cultures. Numerous agitation technologies, such as motor-driven paddles, pumps, air lift systems, gravity flow systems, and human agitation techniques, have been documented. Each of these methods contributes to optimal growth and stable cultural conditions. [31]

LIFE CYCLE:

There are three basic phases in the trichomes formation process:

1. Trichome Fragmentation: The growth process is started when trichomes split into smaller pieces.
2. Hormogonia Cell Enlargement and Maturation: To get ready for additional development, these fragments known as hormogonia go through enlargement and maturation.
3. Elongation of Trichomes: When trichomes reach maturity, they might split into filaments or more hormogonia. Through binary fission, the cells in these hormogonia proliferate, lengthen, and take on a helical shape.[41]

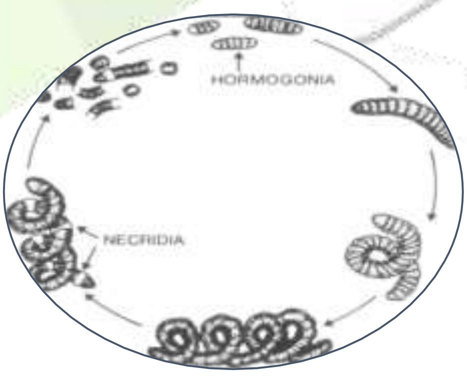

Figure.1. Life Cycle Of Spirulina.

BIOCHEMICAL COMPOSITION OF SPIRULINA PLATENSIS:

Arthrospira sp., another name for Spirulina sp., is a multicellular, spiral-shaped, photosynthetic, blue-green microalga that grows best in warm regions. Spirulina platensis and Spirulina maxima are the two species that are most frequently used. According to biochemical tests of several strains of Spirulina, this algae has a lot of promise for use in human nutrition and health. Proteins, minerals, vitamins, important amino acids, fatty acids (including γ-linolenic acid), glycolipids, sulfolipids, and phycobilins (including phycocyanin) are all abundant in it. The high nutritional value of Spirulina has been shown in rat studies using repletion testing, protein efficiency ratio, and net protein utilisation. [32–33]

Table 1. Therapeutically important compounds of spirulina and its effects.

Sr.No	Compounds	Effect
1.	Ca-Sp	Immuno-enhancing, Anticancer, Antiviral, Induce haematopoiesis
2.	Sulpholipid	Antiviral
3.	B-Carotene	Anticancer, Antioxidant, Source of Vit-A
4.	Cyanovirin-N	Antiviral
5.	Vitamin E	Antioxidant, Anticancer
6.	Phycocyanin	Reduce toxicity, Immuno-enhancing
7.	GLA	Precursor of Prostaglandin, In Arthritis, Heart disease, Obesity, Manic depression

Table 2. The major components of Spirulina with importance making it an ideal dietary supplement

Sr.No.	Nutrient	% Composition	Details	Reference
1.	Protein	55 to 70	All 8 essential amino acids: isoleucine, lysine, methionine, phenylalanine, threonine, tryptophane and valine 10 nonessential amino acids: alanine, arginine, aspartic acid, cystine, glutamic acid, glycine, histidine, proline, serine, and tyrosine	[34]
2.	Lipids	6	Gamma-linolenic acid(GLA), alpha-linolenic acid (ALA), linolenic acid(LA)stearidonic(SDA), eicosapentaenoic acid(EPA) docosahexaenoic acid(DHA), arachidonic acid(AA)	[35-36]
3.	Vitamins	0.75	Thiamine(B1), riboflavin(B2), niacin(B3), pyridoxine(B6), folic acid(B9), cyanocobalamin(B12), biotin(B7), vitamin D, pantothenic acid (B5), vitamin E (tocopherol),inositol	[37-38]
4.	Minerals	8	Potassium, calcium, chromium, copper, iron, magnesium, manganese, phosphorus, selenium, sodium, and zinc.	[39]
5.	Photosynthetic Pigments	346mg/100g (variation) notice according to the processing method	Alpha-carotene, beta-carotene, xanthophylis, cryptoxanthin, echinenone, zeaxanthin, lutein, chlorophyll, phycocyanin	[39-40]

ANTI-VIRAL STUDIES OF SPIRULINA:

The blue-green algae Spirulina's antiviral qualities were initially studied in 1993 by Hayashi et al. A hot water-soluble extract from S. platensis was shown in their study to efficiently and dose-dependently block the multiplication of herpes simplex virus type 1 (HSV-1) in HeLa cells, with concentrations ranging from 0.08 to 50 mg/mL. It is noteworthy that the extract exhibited antiviral action due to interference with the viral penetration process, rather than a virucidal effect.[42]

The 1993 findings by Hayashi et al. marked the beginning of a new phase in antiviral research. By fractionating the hot water extract from S. platensis using a bioactivity-directed method in 1996, Hayashi and Hayashi were able to isolate calcium spirulan (Ca–SP), a new sulfated polysaccharide that chelates calcium ions and has antiviral properties. Ca–SP was purified by DEAE cellulose chromatography and gel filtration on Sepharose 6B subsequent to 10% trichloroacetic acid treatment.

Ca–SP had remarkable therapeutic indices and shown strong antiviral action against enveloped viruses such as HIV-1, HSV-1, human cytomegalovirus (HCMV), measles, mumps, influenza A virus, and coxsackievirus, but no antiviral activity against non-enveloped viruses like poliovirus and coxsackievirus. In accordance with the effects shown with the aqueous extract of Spirulina, the antiviral action of Ca–SP was ascribed to its capacity to specifically prevent HSV-1 from penetrating host cells.[43]

Ca–SP has shown strong anticancer effects in addition to antiviral action, especially in preventing experimental lung metastases. Its capacity to attach to cell surface rhamnose receptors is probably what causes this anticancer action. One of the main ingredients of Ca-SP, rhamnose, interacts with particular receptors on lung-metastasizing tumour cells that come from different initial tumours.[44]

Promising results are found in studies on Spirulina platensis's antiviral capabilities against HIV-1 replication. In their 1996 study, Ayehunie et al. examined how an aqueous extract of S. platensis affected T cell lines and HIV-1-infected peripheral blood mononuclear cells (PBMCs), among other human cell types. They discovered that at 5–10 µg/mL, the extract cut down on syncytium development and viral production by 50%. Spirulina platensis extract doses ranging from 9 to 30 µg/mL shown notable inhibitory effects against Rauscher murine leukaemia virus (RLV), according to similar findings. The strong antiviral effects of the extract were demonstrated by the clear correlation between this inhibition and the inactivation of HIV-1 virions. [45]

The 2–5% sulfolipids found in spirulina have been shown to be effective against HIV. A 50% reduction of HIV reverse transcriptase's DNA polymerase activity is achieved by these sulfolipids at a dose of 24 nM. Significantly enhancing this inhibitory impact are the fatty acid ester side chain and the sulfonic acid moiety. [46]

The protein-bound pigment allophycocyanin, which was isolated from Spirulina platensis, has demonstrated antiviral action against enterovirus 71 in the kidney cells of African green monkeys and rhabdomyosarcoma. It suppresses 50% of viral plaque formation, viral-induced apoptosis, and the enterovirus-induced cytopathic impact at doses ranging from 0.056 to 0.101 µM. Allophycocyanin is particularly effective when given prior to viral infection, suggesting that it may disrupt early phases of viral replication, including virus adsorption and penetration.[47]

Other Spirulina species, like Spirulina maxima, have shown antiviral efficacy against said herpesvirus 1 (SuHV-1), HCMV, and HSV-2, among other human and animal herpesviruses. Nevertheless, similar activity was not seen against several enveloped viruses, including the vesicular stomatitis virus (VSV) and two measles strains. Instead of having a virucidal impact on herpesviruses, as S. platensis does, S. maxima extracts prevent infection by obstructing the viral reproduction cycle's adsorption and penetration phases. High polarity chemicals are associated to the antiviral efficacy of S. maxima extracts, which is affected by varying solvent polarities. Extracts from spirulina may therefore develop into effective medicines that could prolong the normal lives of AIDS patients. [48]

HYPOGLYCEMIC ACTIVITY OF SPIRULINA:

Diabetes is a long-term illness that interferes with the body's capacity to control blood sugar. Type 1 and type 2 are its two main manifestations. Insulin-producing cells in the pancreas are attacked by the immune system in type 1 diabetes, an autoimmune disease that results in little or no insulin production. Insulin pumps or injections are necessary for people with type 1 diabetes to control their blood glucose levels. Conversely, insulin resistance or inadequate insulin production are associated with type 2 diabetes. Although lifestyle modifications including diet and exercise can frequently manage it, some people may need insulin therapy or medication. Other types include prediabetes, which is defined by high blood sugar levels that are not yet high enough to be categorised as type 2 diabetes, and gestational diabetes, which develops during pregnancy. One characteristic of diabetes mellitus is chronic hyperglycemia, which is characterised by persistently elevated blood sugar levels brought on by problems with insulin secretion or sensitivity. Increased oxidative stress is linked to this illness, which may make complications from diabetes worse.[49]

A number of problems are frequently brought on by hyperglycemia, a feature of diabetes mellitus. These include a higher risk of cardiovascular disease, obesity, atherosclerosis, hyperlipidaemia, and hypertension. These disorders can be exacerbated by chronically elevated blood sugar levels, which can have a major negative influence on general health and raise the risk of major health problems.[50]

In mice with alloxan-induced diabetes, spirulina has been demonstrated to lower blood glucose, triglycerides, and total cholesterol. After only five days of treatment, Spirulina platensis showed notable antidiabetic benefits, indicating that it may be used as a medicinal agent to manage diabetes.[51]Spirulina maxima showed hypoglycemia characteristics in experiments with male rats that were streptozotocin-induced diabetics. In the hippocampus tissue of obese rats, treatment with glycyrrhizin and spirulina decreased acetylcholinesterase activity as well as blood glucose, cholesterol, and leptin levels. Spirulina, which is high in antioxidants and nutrients, may be a useful dietary addition to help avoid issues from diabetes, particularly when paired with kefir. [52] The microalga Spirulina platensis exhibits a variety of biological roles and is abundant in proteins, minerals, vitamins, and γ-linolenic acid. As a therapeutic agent, it may be used to treat diseases including diabetes mellitus. Spirulina also has anti-lipidemic and anti-hyperglycemia qualities, which help to improve insulin sensitivity, reduce blood sugar, and regulate cholesterol and triglycerides. [53]

Spirulina's abundance of antioxidant bioactive components, including beta-carotene and phycocyanin, is thought to have antihyperglycemic properties. These substances may improve blood sugar management by increasing the pancreatic beta cells' ability to secrete insulin and by making it easier for blood glucose to reach peripheral tissues. [54]

Streptozotocin-induced diabetic rats' blood glucose levels have been demonstrated to return to normal when given spirulina, and no pancreatic insulitis symptoms were seen after therapy. Reduced hexokinase activity in the liver and elevated glucose 6-phosphatase activity in muscle tissue are thought to be the causes of its hypoglycemic effects. Insulin's impact may also include decreased hepatic glucose synthesis, increase peripheral glucose elimination, and decrease intestinal glucose absorption. [55,56]

Arthrospira has been demonstrated to lower blood glucose levels by reducing free radicals and correcting antioxidant imbalances due to its high amount of γ-linolenic acid and (ω-6) polyunsaturated fatty acids. Glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) levels were markedly elevated by 240% and 60% in healthy mice and by 19% and 59% in diabetic animals, respectively, after receiving spirulina treatment. Furthermore, in diabetic rats, Arthrospira ingestion decreased levels of malondialdehyde, triglycerides, total cholesterol, and blood glucose by 20%, 31%, 22%, and up to 56%, respectively. Studies have shown that spirulina has anti-oxidative, anti-hyperglycemic, and anti-hyperlipidemic effects both in vitro and in vivo. [57]

Spirulina platensis extract has strong antioxidant activity in addition to its antidiabetic benefits, as evidenced by its total antioxidant capacity and DPPH-reducing ability. Across all experiments, the methanolic extract exhibited the highest antioxidant activity and had considerable inhibitory effects on α-amylase (96.46%) and α-glucosidase (97.42%), two important enzymes linked to diabetes. The extract was analysed using gas chromatography-mass spectrometry (GC-MS), which revealed a number of bioactive substances, such as phytol, cholestan-3-ol, 1-monolinoleoylglycerol trimethylsilyl ether, and different fatty acids. These elements might complement one another to improve the extract's antidiabetic and antioxidant qualities. [58]

Diabetes mellitus causes a significant decrease in the liver's plasma concentrations of antioxidant enzymes and trace minerals, while increasing levels of malondialdehyde, glucose, lipid profiles, alanine transaminase (ALT), aspartate aminotransferase (AST), tumour necrosis factor-α (TNF-α), and interleukin-6 (IL-6). TNF-α, IL-6, glucose, AST, ALT, malondialdehyde, and other lipid markers were all decreased when S. platensis was administered orally at doses of 20 and 30 mg/kg BW. At the same time, trace mineral plasma concentrations rose, including those of iron, copper, zinc, and selenium, and antioxidant enzyme activity increased. Spirulina platensis may therefore provide vital trace minerals that aid in the production of antioxidant enzymes, which in turn may lower blood sugar, lessen inflammation, and enhance lipid profiles. [59]

The preventive effects of Spirulina fusiformis in streptozotocin-induced diabetic rats are thought to be attributed in part to its antioxidant activity. Because it keeps renal function markers like urea, creatinine, and uric acid within normal limits, this microalga efficiently protects kidney injury. Reduced HbA1C readings further demonstrate that Spirulina fusiformis improves glycaemic management and lowers hyperlipidaemia. Histopathological analyses show that it shields tissues from oxidative damage, reducing pancreatic and liver problems. Important bioactive substances found in S. fusiformis, including phycocyanin and voronikhin, have antidiabetic and antihyperglycemic effects. [60]

Spirulina has been demonstrated to lessen oxidative stress linked to hyperglycemia by lowering the generation of reactive oxygen species and free radicals. The effects of streptozocin on the liver, kidneys, and levels of antioxidant enzymes at the cellular level are lessened by its inhibition of DPP-IV, alpha-amylase, and alpha-glucosidase activities. In rats given streptozocin, spirulina can reduce markers of lipid, liver, and kidney disorders, suggesting that it could be a promising supplement for diabetics. Although certain bioactive components may also play a role, its overall antioxidant qualities may be the source of its antidiabetic effects. [61]

MECHANISM OF ANTIDIABETIC COMPOUND:

The antidiabetic effects of Spirulina-derived compounds are thought to involve several mechanisms, including.

1.Insulin sensitization. Spirulina extracts have been shown to enhance insulin sensitivity in both animal models and human studies. This improvement is likely due to polysaccharides and phycocyanin, which facilitate better glucose uptake and utilization by cells.[62]

2. Spirulina's antidiabetic properties also include inhibiting gluconeogenesis, the liver's process of producing glucose from non-carbohydrate sources. Compounds that assist control glucose metabolism, such gamma-linolenic acid and other fatty acids found in spirulina, may be responsible for this suppression. [63]

3. Antioxidant activity: Phycocyanin, carotenoids, and vitamin E are among the many antioxidants found in spirulina extracts. These substances efficiently scavenge free radicals and lessen oxidative stress, which is a major cause of diabetes-related problems.

4. The protein composition of spirulina is noteworthy; it makes about 60–70% of its dry weight and contains bioactive peptides that are produced from this protein. Spirulina's antidiabetic properties may be largely attributed to these peptides, which also enhance glucose metabolism and promote general metabolic health.

5. Anti-inflammatory activity: Type 2 diabetes and insulin resistance are significantly influenced by chronic inflammation. Because of their anti-inflammatory qualities, spirulina extracts can promote improved metabolic health and insulin sensitivity by reducing inflammation in adipose tissue.[64]

6. Insulin Receptor Activation: A chromium-binding peptide that activates insulin receptors has been linked to the hypoglycemic effects of Spirulina phycocyanin. Improved blood sugar management is a result of this activation, which also increases insulin signalling and glucose absorption.

7. There is growing evidence that the gut microbiota has a major impact on insulin resistance and glucose metabolism. Spirulina extracts have been demonstrated to alter the gut microbiota's composition, which may improve glucose homeostasis in animal models and improve metabolic health. [65]

ANTI-CANCER ACTIVITY OF SPIRULINA:

Spirulina is an alga that is high in nutrients and contains phycocyanin and β-carotene, both of which have been found to have anticancer effects. Spirulina has been shown in numerous tests on lab animals to have immune-stimulating and antioxidant properties that can stop the growth of some types of cancer. These characteristics help explain why it is regarded as a potent phytonutrient that fights cancer. [66]

Rich in carotenoids and carotenes, spirulina extracts are frequently employed as natural colouring agents. They are powerful antioxidants, and studies indicate that eating a lot of foods high in carotenoid-rich foods may lower your chance of developing several types of cancer. [67] Significant antioxidant activity is displayed by carotenoids, especially when exposed tolight. In both humans and animals, they provide vital metabolic functions include scavenging free radicals to prevent diseases like cancer, boosting immunological function, and converting to vitamin A. Up to 2,000 IU of β-carotene per gramme of dry weight is found in spirulina, the main carotenoid that is known to have potential antioxidant, anti-carcinogenic, and radioprotective qualities. [68–69] Antioxidant-rich foods, such as those containing carotenoids, phycocyanin, superoxide dismutase, and vitamins C and E, are a good way to prevent cancer. These substances promote general health by reducing oxidative stress. [70]

Beta-carotene is found in a naturally chelated matrix in the whole food spirulina, which increases its bioavailability. Important carotenoids like zeaxanthin and beta-cryptoxanthin, as well as less well-known ones like myxoxanthophyll and echinenone, are present in addition to beta-carotene. Extracts from spirulina have shown promise in preventing the development of cancer.[71]

According to one study, spirulina can stabilise liver disease and stop it from developing into cirrhosis. Spirulina dramatically decreased the size and incidence of stomach and skin tumours in another animal trial. The researchers came to the conclusion that diets high in fruits and vegetables that contain carotenoid may provide protection against prostate cancer. Consuming carotenoid-rich foods has been linked in numerous previous studies to a lower risk of developing a number of malignancies. Beta-carotene is especially well-known for its ability to shield the skin from the harmful effects of sunlight and for its potential to prevent skin cancer.[72]

Spirulina extract has been shown in numerous trials to either prevent or suppress cancer in people and animals. Evaluations conducted in vitro indicate that the polysaccharides included in spirulina improve DNA repair production and enzyme activity in the cell nucleus. The growth of human colon and hepatocellular cancer cells has been demonstrated to be inhibited by water extracts of Spirulina platensis. Moreover, Spirulina platensis and Chlorella vulgaris chloroform extracts decrease breast cancer cell viability.

Spirulina methanolic extracts also stop human breast cancer cell lines and L20B cancer cells from growing after a brief incubation period. Moreover, the extract stops the development of intestinal cancer cell lines in mice. Human cell lines for acute leukaemia (Kasumi-1) and chronic myelogenous leukaemia (K-562) show notable cytotoxic responses to a 70% ethanolic extract. In addition, spirulina extracts prevent lung cancer in mice, liver cancer, hepatoma, oral squamous cell carcinoma in humans and hamsters, and tumours in the buccal pouches of the hamster's mouth.[73]

Biologically active phycobiliproteins that are essential to phycobilisomes, including C-phycocyanin (C-PC), allophycocyanin (APC), and phycoerythrin (PE), are found in Spirulina platensis. Mice with live tumour cells have been demonstrated to have higher survival rates when given C-PC orally. Spirulina platensis's isolated phycocyanin showed antitumor properties against squamous cell carcinoma. Spirulina and Dunaliella extracts have been shown in studies by Schwartz and Shklar (1987) to cause tumours produced by dimethylbenz(a)anthracene (DMBA) in hamsters to regress. Because of an increased immune response that targets malignant cells while protecting normal cells, oral treatment of these extracts inhibited the formation of tumours. Furthermore, it has been demonstrated that C-phycocyanin inhibits human leukaemia K562 cells' growth and viability via a number of different pathways. [74–75]

C-phycocyanin (C-PC), a significant biliprotein found in Spirulina platensis, has antioxidant and radical scavenging qualities. By inhibiting cyclooxygenase-2 (COX-2) and causing apoptosis in vitro, it exhibits anti-inflammatory and anti-cancer properties. Elevated C-PC in Spirulina causes HeLa cells to undergo apoptosis by activating different caspases and upregulating CD59 proteins (2, 3, 4, 6, 8, 9, and 10). [77–76]

Cell shrinkage, membrane blebbing, and chromatin condensation are common apoptotic symptoms that result from the release of cytochrome c from mitochondria into the cytoplasm. Furthermore, human melanoma A375 and breast adenocarcinoma MCF-7 cells have demonstrated strong antiproliferative activity against purified selenium-containing phycocyanin (Se-PC) from selenium-enriched Spirulina, causing apoptosis marked by sub-G1 cell accumulation, nuclear condensation, and DNA fragmentation. [78]

The haematopoietic action of spirulina is crucial for its anticancer properties, which include increasing immune cell populations and promoting innate resistance to cancer and other illnesses. It stimulates the innate immune system by increasing the production of natural killer (NK) cells, interferon, and tumour necrosis factor alpha (TNF-α), especially when S. platensis hot water extracts are ingested. Studies on animals have shown that spirulina extracts can be injected directly into malignant tumours to halt their growth. Oral consumption of spirulina over an extended period of time slowed the progression of cancer in 45% of participants in a human trial involving individuals with oral leukoplakia, an early-stage disorder that can result in cancer. In order to validate and clarify the anticancer benefits of spirulina in people, additional clinical research is required. [79]

SPIRULINA'S ANTI-INFLAMMATORY PROPERTIES:

The enzyme cyclooxygenase-2 (COX-2) is essential for converting arachidonic acid into prostaglandins and other eicosanoids, which are significant pain and inflammatory mediators. Because COX-2 is usually activated during inflammatory responses, it is a prime target for anti-inflammatory medications, in contrast to COX-1, which is constitutively produced in numerous tissues. For the development of treatments for inflammatory disorders like arthritis, it is crucial to comprehend how COX-2 is regulated and functions. [80]

COX-2 overexpression is associated with increased prostaglandin E2 (PGE2) levels, which are commonly seen in a number of cancers, such as those of the colon, breast, lung, prostate, skin, cervix, pancreas, and bladder. Given this link, COX-2 may be a target for therapeutic intervention in the treatment of cancer since it may be important in carcinogenesis and the advancement of cancer. Developing successful techniques to limit COX-2's activity and lessen its effects on tumour growth requires an understanding of the processes by which it contributes to cancer biology. [81]

Prostaglandin overproduction can mediate immunological suppression, impact cell proliferation, and cause inflammation. Cancer and chronic inflammatory disorders are among the pathological ailments that are exacerbated by these behaviours. It is crucial to control these mediators in therapeutic settings since high prostaglandin levels can promote inflammatory responses and change immunological function, which can aid in the growth and progression of tumours. Developing focused therapies to address inflammation-related illnesses and cancers can be made easier with better understanding of their functions. [82-83]

Numerous studies have shown that colon cancer cell lines and converted fibroblasts can undergo apoptosis when exposed to nonsteroidal anti-inflammatory medications (NSAIDs) and selective COX-2 inhibitors. The apoptotic effect implies that focussing on COX-2 could be a viable approach to cancer treatment, since these substances not only reduce inflammation but also encourage the death of cancer cells. Knowing the fundamental processes behind this induction might help one better understand how they might be used as oncology treatment agents. [85–84]A pigment called phycocyanin, which is present in spirulina, is known to selectively inhibit COX-2, functioning as a natural inhibitor of COX-2. Because of this characteristic, it can control inflammation linked to COX-2 activity. Scholars have examined how phycocyanin triggers apoptosis in tumour cells and the processes that underlie this action. By comprehending these impacts, new approaches to cancer treatment using natural substances may become apparent. [86]

Phycocyanin triggers the production of reactive oxygen species (ROS) in tumour cells and activates caspases involved in the apoptotic process, which results in apoptosis. Furthermore, Bcl-2, a crucial apoptosis regulator, is down-regulated by phycocyanin. The unique anti-inflammatory qualities of spirulina are attributed to its high phycocyanin content. Additionally, spirulina has around ten times the amount of carotenoids (such β-carotene, lycopene, and lutein) as carrots, which increases its antioxidant ability. By squelching ROS, these antioxidants have inherent anti-inflammatory properties. Blue-green algae contain the photo harvesting pigment phycocyanin, which is categorised as a phycobiliprotein. In contrast to membrane-bound carotenoids, phycobiliproteins are soluble in water and aggregate to form membrane-adhering aggregates known as phycobilisomes. Up to 20% of the dry weight of blue-green algae is typically made up of phycocyanin, demonstrating the substance's important function and existence in these organisms. [87]

The pigment that gives spirulina its rich bluish hue, C-phycocyanin, has been demonstrated to have strong hepatoprotective properties and to efficiently scavenge free radicals. In addition to contributing to the antioxidant qualities of spirulina, this indicates that C-phycocyanin is essential for maintaining liver health. The substantial amount of omega-3 α-linolenic acid found in blue-green algae has been shown in an in vivo investigation to reduce plasma levels of arachidonic acid. This connection implies that eating blue-green algae may help control the inflammatory processes linked to the metabolism of arachidonic acid. [88]

ANTI-NEPHROTOXICITY AND ANTI GENOTOXICITY OF SPIRULINA:

Spirulina has shown promising effects in reducing urea and creatinine levels in rats experiencing nephrotoxicity induced by cisplatin. Studies suggest that it provides protective benefits against nephrotoxicity and neurotoxicity in various models, including those induced by cyclophosphamide and cadmium in albino rats, as well as chromium-induced nephrotoxicity in Wistar rats. These findings indicate that Spirulina may have potential as a therapeutic agent in mitigating renal and neurotoxic damage in these experimental models.

Further research is needed to elucidate the mechanisms involved and the clinical implications of these effects. Polysaccharides derived from Spirulina have demonstrated the ability to protect DNA from radiation-induced damage, primarily through excision repair mechanisms. Research indicates that Spirulina can reduce the recurrence of micronuclei in polychromatic erythrocytes of mice exposed to gamma radiation. Additionally, its polysaccharides initiate the repair processes of nuclear enzymes and enhance DNA repair activities. Spirulina also offers protective effects against the harmful impacts of various toxicants, such as cyclophosphamide, cisplatin, and urethane, by reducing lipid peroxidation and chromosomal damage. It significantly decreases DNA fragmentation in the liver and lowers the incidence of micronuclei in erythrocytes in animals fed a diet contaminated with aflatoxin. These findings suggest that Spirulina may play a valuable role in cellular protection and DNA repair in the context of toxic exposures. [89]

SPIRULINA'S IMPACT ON INNATE IMMUNIITY:

Spirulina has demonstrated positive effects on innate immune functions and can enhance nonspecific immunity through various mechanisms. Notably, novel sulfated polysaccharides, referred to as calcium-spirulan (Ca-Sp), have been isolated from its water extract. These compounds exhibit immunomodulatory and antiviral activities, suggesting their potential role in supporting immune health. Research indicates that Ca-Sp may enhance the activity of immune cells and improve the body's response to viral infections, highlighting the therapeutic potential of Spirulina in immunological applications. [90-91]

Spirulina's polysaccharides and phycocyanin have been demonstrated to increase immunity in mice by encouraging the development of the spleen, thymus, and bone marrow. According to research, even when exposed to environmental pollutants and diseases, spirulina improves the performance of important immune cells and organs. [92-93] By activating erythropoietin (EPO), phycocyanin specifically promotes haematopoiesis, especially erythropoiesis. Research indicates that in a variety of animal models, such as cats, mice, and chickens, phycocyanin and polysaccharides both boost the formation of white blood cells and improve the phagocytic activity of macrophages. Additionally, the water-soluble extract of S. platensis increases the activity of natural killer (NK) cells and induces macrophages to secrete interleukins like IL-1, which increases tumoricidal action. [94-95]

SPIRULINA'S IMPACT ON A SPECIFIC IMMUNITY:

Spirulina compounds have been shown in experiments to improve the immune system's humoral and cellular components. After consuming spirulina, lymphocytes—important immunological components—are released into the bloodstream. Studies reveal that giving mice spirulina greatly boosts the splenic cells' ability to produce IgM antibodies. Spirulina water extract also increases the production of particular antibody classes, such as IgA and IgE, and encourages the growth of spleen cells in culture. [96–97]

Spirulina has been demonstrated to suppress mast cell activity and to produce IgA against food allergens, which gives it anti-allergic qualities. [98]. Another ingredient in spirulina, phycocyanin, improves mucosal immunity by reducing inflammation and preventing the production of histamine. Spirulina can, however, aggravate autoimmune illnesses that already exist or cause them in people who are genetically prone to them. Spirulina has been shown to stimulate the expression of the anti-apoptotic gene bcl-2 in haematopoietic cells in mice, which may prevent apoptosis. [100–99]

It is well known that spirulina promotes haematopoiesis, which raises the formation of white blood cells (WBCs) and red blood cells (RBCs). It enhances T-cell activation, increases antibody production, and activates natural killer (NK) cells and macrophages, all of which have an impact on both innate and adaptive immunity. Because of its many functions, spirulina is a useful supplement for boosting blood synthesis and immune function.

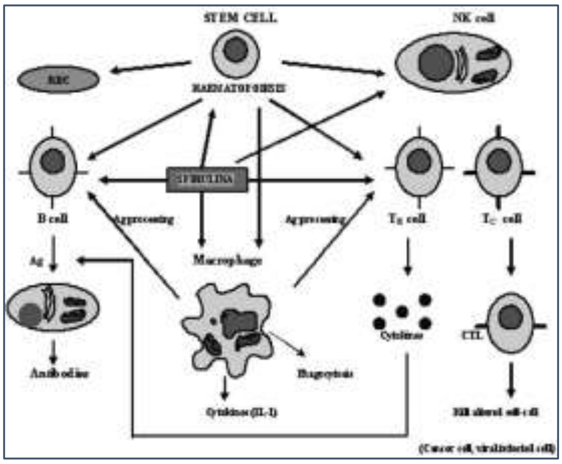

Figure.2. Effect of Spirulina on Immune System

Spirulina is known to enhance hematopoiesis, leading to increased production of red blood cells (RBCs) and white blood cells (WBCs). Its effects extend to both innate and adaptive immunity, as it activates macrophages and natural killer (NK) cells, boosts antibody production, and stimulates T-cell activation. This multifaceted role makes Spirulina a valuable supplement for supporting immune health and overall blood production.

CONCLUSION:

This review highlights the potential of Spirulina as a valuable health food in human diets and the food sectors. Recognized as a superfood, it serves as an effective dietary supplement for combating malnutrition. Spirulina has been shown to lower cholesterol, reduce fatty liver accumulation, prevent tumor formation, enhance immune function, and protect kidney health. Notably, S. platensis is rich in essential nutrients, including minerals like calcium and potassium, proteins, carbohydrates, essential fatty acids, vitamins, carotenes, chlorophyll a, and phycocyanin. Consequently, Spirulina may serve both as a medicinal resource for various diseases and a daily source of nutrition.

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