

Review

View Article Online

 Check for updates

Received 19 December 2023

Revised 03 April 2024

Accepted 27 April 2024

Available online 21 June 2024

Edited by Barbara Sawicka

KEYWORDS:

Spirulina
Chemical composition
Pharmacological action
Immunomodulator
Antioxidant

Natr Resour Human Health 2024; 4 (3): 277-286
<https://doi.org/10.53365/nrfhh/188021>
eISSN: 2583-1194
Copyright © 2024 Visagaa Publishing House

Exploring the Nutritional and Medicinal potential of Spirulina

Khushboo Gaur^{1,*}, Ankita Wal^{1,a}, Preeti Sharma¹, Amana Parveen¹, Prerna Singh¹, Prashant Mishra¹, Pranay Wal¹, N T Pramathesh Mishra²

¹Department of Pharmacy, PSIT-Pranveer Singh Institute of Technology (Pharmacy), Kanpur, UP- 209305, India

²Department of Pharmacology, Hygia College of Pharmacy, Lucknow, UP- 226020, India

ABSTRACT: Spirulina, a polyphyletic group of algae, is known for its economically significant products and is widely used as a dietary supplement. It is rich in essential elements and compounds, including proteins, antioxidants, vitamins, and minerals, making it a valuable nutritional resource. *Spirulina platensis*, in particular, has been extensively studied for its nutritional richness and antioxidant properties. This article reviews Spirulina's biochemical composition from 2005 to 2023, using data from databases like Medline and PubMed. It focuses on keywords such as spirulina, habitat, species, pharmacological action, toxicities, and medicinal uses. Spirulina stands out for its exceptional protein content, amino acid composition, and unique status as a plant-based source of vitamin B12 and essential fatty acids. It also contains a comprehensive micronutrient profile, including easily absorbable minerals like iron, calcium, phosphorus, and magnesium. Spirulina has various health benefits, including anti-diabetic, cardio-protective, hepatoprotective, anti-viral, antioxidant, anti-inflammatory, and anti-cancer activities. The research on spirulina highlights its potential as a valuable dietary supplement with diverse health benefits. Its rich nutritional composition and pharmacological actions make it a promising candidate for managing various ailments and enhancing overall health. Further studies are warranted to explore its full therapeutic potential and mechanisms of action.

1. INTRODUCTION

Algae, characterized by their chlorophyll and often existing in multicellular colonies with loose connections, exhibit a polyphyletic nature. These organisms are known for their economically significant products, widely utilized as dietary supplements in numerous countries (Diaz et al., 2023). Algae are renowned for their nutritional richness, providing a wide array of essential elements including fiber, minerals, proteins, antioxidants, pigments, lectins, polysaccharides, polyunsaturated fatty acids, lipids, halogenated compounds, and vitamins (Singh et al., 2023).

Research highlights the widespread use of algae-derived natural products, not only as dietary supplements but also for medicinal purposes. Algae are notable for their wide range of nutraceuticals and naturally occurring pharmacologically active compounds, which contribute to the high market value of these products (Ruzik, 2023; J. Zhang et al., 2021). Spirulina, a prominent member of the algae family, stands out in the food industry due to its remarkable therapeutic attributes, including high protein content, essential minerals, vitamins, amino acids, and fatty acids (Ali & Saleh, 2012). Spirulina, a

photosynthetic multicellular cyanobacterium (blue-green algae) categorized in the family Oscillatoraceae, thrives in robust sunlight, high temperatures, and alkaline environments. Rapid growth characterizes its development, making it well-suited to such conditions (Gogna et al., 2023). This photosynthesizing cyanophyte, is widely embraced as a dietary supplement powerhouse. Abundant in essential fatty acids, proteins, carotenoids, vitamin B complex, vitamin E, and minerals such as copper, manganese, magnesium, iron, selenium, and zinc, it serves as a nutrient-rich resource (Chandrasekara & Kumar, 2016).

Beyond its roles in food and pharmaceuticals, spirulina presents diverse potential applications. Recent research has unveiled that metabolites from spirulina can be utilized as valuable raw materials for biofuels and biomaterials, offering economic benefits. Moreover, studies indicate its efficacy in purifying wastewater, soil, and air, addressing environmental pollution concerns (Khavari et al., 2021). Over the past two decades, substantial strides have been made in comprehending the nutritional value and applications of spirulina. Researchers have delved into its nutritional components,

* Corresponding author.

E-mail address: dkhushi0515@gmail.com (Khushboo Gaur)

^a Equal contribution as a first author.

cultivation methods, extraction techniques, and various aspects, revealing significant progress. Numerous studies underscore the considerable potential of spirulina in enhancing health and treating various ailments. (Jara et al., 2018)

S. platensis, *S. maxima*, and *S. fusiformis*, among various spirulina species, have garnered extensive investigation and are recognized as edible sources with significant nutritional and therapeutic value. *S. platensis*, notably, stands out as the most widely used and accessible species, undergoing extensive research in fields such as the food industry and medicine (Liesianty et al., 2019). Its nutritional richness is complemented by potent antioxidant properties attributed to spirulins sulphated polysaccharides, phenolic compounds, C-phycocyanin, allophycocyanin, and selenocompounds (Beheshtipour et al., 2012). Widely utilized in dietary supplementation, *S. platensis* extracts are employed for treating and preventing conditions like diabetes and cancer, as well as reducing blood cholesterol and atherosclerosis. Despite cultivation under controlled conditions, some harmful cyanobacteria can still contaminate it (Gogna et al., 2023).

Microalgae Spirulina's chemical analysis reveals its remarkable composition of macro and micronutrients, contributing to various health benefits such as immunomodulation, anticancer, antioxidant, antiviral, and antibacterial activities. It serves as protection against malnutrition, inflammatory allergic reactions, hyperlipidemias, obesity, anemia, toxicity caused by heavy metals and chemicals, and radiation damage (Rutar et al., 2022)

Initially harvested and consumed from the lakes of Mexico and Africa, spirulina has transformed into a significant dietary supplement, even finding application for astronauts on space missions. According to NASA, spirulina is deemed equivalent to 1000 kg of vegetables and fruits, emphasizing its nutritional density and potential for space exploration (Balkrishna et al., 2023).

Table 1
General Composition
of Spirulina..

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

Source: Seghiri et al. (2019)

2. CHEMICAL COMPOSITION

Spirulina stands out as an exceptional natural source, boasting five times the protein content of meat, making it one of the richest protein sources available. This algae contains a comprehensive array of necessary and optional amino acids, offering a well-balanced amino acid composition. The general composition of spirulina is shown in Table 1. Notably, it presents an abundant concentration of β -carotene,

a precursor to vitamin A, further contributing to its nutritional profile (Alfadhly et al., 2022; Jung et al., 2019).

A distinctive attribute of spirulina is its status as the sole plant-based source of vitamin B12, surpassing liver content by 2.5 times. Additionally, it serves as a significant source of linolenic acid, an essential fatty acid crucial for hormone regulation and overall bodily processes. It is reported that 50-70% of spirulina comprises substantial protein, amino acids, minerals, fatty acids, polysaccharides, B vitamins (including vitamin B12), β -carotene, and iron. This makes spirulina a well-rounded and nutrient-dense dietary supplement (Lupatini et al., 2017).

The desiccated cell weight of spirulina comprises a notable 55-70% protein and 5-6% lipid content. Within this algae, the proportion of polyunsaturated fatty acids (PUFAs) to total lipids falls within the range of 1.5 to 2%. Spirulina supplements are predominantly rich in linolenic acid, constituting 36% of the total PUFAs (Seghiri et al., 2019). The comprehensive nutritional profile of spirulina includes an array of vitamins (B1, B2, B3, B6, B9, B12, C, D, and E), minerals (potassium, calcium, chromium, copper, iron, manganese, magnesium, phosphorus, selenium, and zinc), pigments (chlorophyll a, echinenone, allophycocyanin, xanthophyll, canthaxanthin, beta-carotene, phycobiliproteins, myxoxanthophyll, zeaxanthin, diatoxanthin, 3-hydroxyechinenone, beta-cryptoxanthin, oscillaxanthin, and C-phycocyanin), and enzymes such as lipase (Janda-Milczarek et al., 2023). This comprehensive composition underscores spirulina's role as a valuable and multifaceted dietary supplement. Spirulina composition may vary according to the culturing conditions and the methods of analysis (Priyanka et al., 2023).

3. NUTRITIONAL COMPOSITION

3.1. Protein and amino acid

Constituting 60 to 70 percent of spirulina's dry weight, protein stands out as a significant component. This ratio is particularly notable when compared to the roughly 35% found in many plant-based foods, even those acknowledged as "good protein sources." Notably, C-phycocyanin, a compound comprising approximately 20% of the algae's dry weight and featuring phycocyanobilin, a biliverdin homolog, stands out as one of the primary proteins in spirulina. This emphasizes spirulina's exceptional protein content, surpassing typical levels found in various plant-based sources (Pawar et al., 2020; Wild et al., 2018). Spirulina boasts high-quality protein (59–65%), surpassing soybeans, peanuts, and grains. Its cellulose-free cell walls aid digestion, with over 85% protein assimilation in 18 hours. Commercial spirulina powder is 60% protein, 20% carbs, 5% fats, 7% minerals, and 3–6% moisture, offering a low-fat, low-calorie, cholesterol-free protein source. Its amino acid composition, resembling casein, depends on the culture media used (Rahim et al., 2021). Spirulina sp. harbors 10 essential and 8 non-essential amino acids, with glutamic acid leading, followed by leucine and aspartic acid. Leucine is the highest essential amino acid, while glutamic acid tops the non-essential ones. With a protein content of 60.96%

of dry weight, *Spirulina* sp. is not only rich in protein but also encompasses all essential and non-essential amino acids, showcasing a remarkably high biological value for its proteins (Rosario et al., 2015).

3.2. Lipids and Fatty acids

Lipid and fatty acid composition in microalgae, including *Spirulina*, varies among strains and with culture conditions. Lipid accumulation often rises during environmental stress, particularly under nutrient deficiency. Microalgae show a decrease in saturated fatty acids and an increase in highly unsaturated fatty acids with higher NaCl concentrations (Ahda et al., 2023). Salt-induced stress prompts morphological, developmental, physiological, and biochemical changes in cells, impacting respiration, mineral distribution, ion toxicity, photosynthetic rate, and cell membrane permeability. This stress also influences lipid content both quantitatively and qualitatively (Bhakar et al., 2013).

Comprising approximately 5–10% of spirulina's dry weight, the lipid portion holds significance. Notably, the majority of fats in this fraction are essential lipids for humans. This includes notable amounts of gamma-linolenic, linoleic, and oleic acids, with particular attention on gamma-linolenic acid due to its scarcity in many foods. In fact, spirulina is regarded as the vegetable source with the highest quantity of gamma-linolenic acid, constituting around 20% of its total fatty acid content. This underscores the nutritional value of spirulina in providing essential lipids that are beneficial for human health (Can et al., 2017; Neag et al., 2022).

4. MICRONUTRIENT PROFILE

4.1. Vitamins

Spirulina stands out for its exceptional abundance of vitamin B12, a nutrient primarily found in foods of animal origin. This attribute makes spirulina particularly valuable for vegans, who typically exclude animal-derived foods. It emerges as a useful source of vitamin B12 for individuals following a vegan diet as depicted in Table 3 (Ismail et al., 2015; Salmeán et al., 2015). Furthermore, it is recognized as the most enriched complete-food source of provitamin A (carotene) and vitamin B12, encompassing corrinoid forms, analogues, and pseudo vitamin B12. Notably, a modest intake of just 20g of these microalgae provides the body with all the needed vitamin B1 (thiamine), B2 (riboflavin), and B3 (niacin), emphasizing spirulina's nutritional density (Hoseini et al., 2013; Kumar et al., 2018; Michael et al., 2019).

While spirulina doesn't replicate the precise functional roles of vitamin B12 in humans, it doesn't interfere with B12 metabolism in mammals (Jung et al., 2019). According to a susceptible microbiological test, 36% of the vitamin B12 molecules in *Spirulina* spp. are functional in humans (Alfadhly et al., 2022). Notably, *S. platensis* contains methylcobalamin, a physiologically active form of vitamin B12, at concentrations ranging from 35 to 38 g per 100 g of dry spirulina biomass. This

Table 2

Vitamins (mg) / 100g (Anvar & Nowruzi, 2021).

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

underscores the potential contribution of spirulina as a source of functional vitamin B12 for certain aspects of human nutrition (Sow & Ranjan, 2021).

4.2. Minerals

In contrast to cereals, commonly recognized as substantial iron sources, blue-green algae exhibit a notably higher iron concentration, ranging from 580 to 1800 mg/kg. The absence of a pericardium in algae eliminates phytates or oxalates that might impede iron absorption, a characteristic absent in grains. Notably, spirulina stands out for its elevated micronutrient content, particularly minerals, making it an ideal dietary supplement for vegetarians as depicted in Table 2 (Soni et al., 2017).

Table 3

Mineral component of spirulina (g/kg) (Janda-Milczarek et al., 2023).

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

The mineral composition of spirulina is contingent upon its source and the environment in which it is cultivated. Notably, spirulina exhibits levels of calcium, phosphorus, and magnesium comparable to those found in milk. A noteworthy distinction is its recognition as the most iron-rich food when compared to traditional iron supplements (Michael et al., 2019). Importantly, iron derived from spirulina demonstrates a remarkable 60% higher absorption rate than iron from ferrous sulfate, a common component in iron supplements. This highlights the nutritional significance of spirulina as a natural source of essential minerals, emphasizing calcium, phosphorus, magnesium, and notably, highly absorbable iron (Saraswathi & Kavitha, 2023). Spirulina encompasses a spectrum of essential minerals and trace elements in forms readily absorbed by the body. Potassium plays a pivotal role in regulating

electrolyte balance, and its deficiency can lead to issues such as heart problems and muscular collapse. Calcium, crucial for bone and dental health, is found in Spirulina in quantities equivalent to that in milk (Suliburska et al., 2016). Magnesium contributes to muscle function, aids in vitamin assimilation, and facilitates protein absorption. Manganese activates enzyme systems, supports neurotransmitters, and assists in stabilizing blood sugar levels. Iron, crucial for hemoglobin formation and oxygen transport in red blood cells, is abundantly present in Spirulina. Phosphorus, being the second most abundant mineral in the human body, helps maintain bone density and aids in the digestion of carbohydrates and B vitamins (Fithriani & Sinurat, 2019).

5. PHARMACOLOGICAL ACTIONS OF SPIRULINA

5.1. Anti-diabetic effect

Spirulina demonstrates potential benefits in managing type-2 diabetes mellitus. Lympaki et al. (2022), reported that it can reduce fasting, postprandial blood glucose, and glycosylated hemoglobin (HbA-1c) levels in diabetic individuals. In diabetic rats, spirulina enhances the activity of hexokinase and glucose-6-phosphatase enzymes, leading to improved plasma insulin and C-peptide levels (Okechukwu et al., 2019).

Spirulina Platensis from Turkey has potent antidiabetic effects, as noted by Guldaz et al. (2020). It lowers blood sugar and oxidative stress in diabetic rats, increasing antioxidant enzyme levels (GSH-Px and SOD) by 19% to 59%. Moreover, it reduces glucose, triglyceride, total cholesterol levels, and malondialdehyde content by up to 56%, indicating significant anti-hyperglycemic, anti-hyperlipidemic, and antioxidative properties.

Rabeh et al. (2021), studied Spirulina (*S. platensis*) for its effect on STZ-induced hyperglycemia and kidney impairment in rats. Rats receiving varied Spirulina supplements showed increased final body weight, feed efficiency, and body weight gain compared to controls. Diabetic rats exhibited improved insulin concentration, lower glucose levels, and better kidney function. Spirulina also reduced serum lipid profile and increased glutathione peroxidase, suggesting its potential in managing diabetic neuropathy.

Furthermore, a study by He et al. (2022), showed that the combination of Spirulina, *Grifola frondosa*, and *Chlorella* powders had hypoglycemic effects in type 2 diabetic mice. This combination improved biochemical indicators, reduced inflammation, repaired liver and intestinal damage, and regulated intestinal flora. Additionally, it increased the expression of the PI3K/AKT pathway, enhancing glucose uptake by liver cells, potentially through SCFAs.

5.2. Cardio-protective effect

Short-term dietary supplementation with spirulina for just 10 days has been shown to have a cardioprotective effect during ischemic events. This effect is achieved through antioxidative, anti-inflammatory, and anti-apoptotic mechanisms, leading to

a reduction in infarction size and improved cardiac function. Spirulina supplementation appears to be safe and may offer a straightforward approach to counteracting detrimental mechanisms triggered during ST-elevation myocardial infarction (STEMI), potentially enhancing myocardial salvage in the setting of myocardial infarction (MI) (Vilahur et al., 2022). In a study, two lyophilized peptides from Spirulina digestion were orally administered to SHR rats. The peptides were found to reduce blood pressure for up to 8 hours after supplementation, outperforming captopril. This suggests that these peptides have a longer-lasting ACE-inhibiting effect compared to captopril (Suo et al., 2022). Spirulina supplementation with high-intensity interval training reduced adipokine levels, improved body weight/BMI, and enhanced lipid profiles, suggesting a synergistic strategy for obesity management in males (Supriya et al., 2023). Furthermore, recent research has indicated that prolonged spirulina supplementation can alter the gut microbiota, which in turn affects lipid metabolism and body weight (Dinicolantonio et al., 2020)

5.3. Hepatoprotective activity

Spirulina platensis (SP) supplementation alleviated hematological abnormalities, serum liver markers, hepatic necrosis, and inflammation, as well as dyslipidemia in rats intoxicated with carbon tetrachloride (CCl₄). Analysis revealed that SP countered the CCl₄-induced elevation in hepatic levels of Ki-67 (a marker of cell proliferation), interleukin-6, and tumor necrosis factor-alpha, along with the expression of cyclooxygenase-2 messenger RNA. Importantly, SP supplementation restored the decreased levels of the proapoptotic protein p53 in the liver of rats treated with CCl₄ (Mohamed et al., 2021). In a wistar rat study, Spirulina extract at 9% concentration showed significant hepatoprotective effects against d-GalN-induced liver damage. It reversed negative effects on antioxidant enzymes, reduced inflammatory markers, and decreased lipid peroxidation. Histological analysis confirmed its efficacy, comparable to BHT, in protecting the liver (Al-Qahtani & Binobead, 2019). Another study showed Spirulina's effects on hyperlipidemia and liver function in rats and humans over two weeks. Rats were fed diets with 25% soybean oil and 25% butter to induce hyperlipidemia, with butter causing more severe hyperlipidemia. Spirulina reduced hyperlipidemia in rats in a dose-dependent manner. In humans, 4 gm/day of Spirulina reduced hyperlipidemia, with effects depending on dosage and frequency (Al-Hussaniy et al., 2023)

5.4. Anti-viral activity

Several recent studies have highlighted the potential of natural compounds as antiviral agents against a range of viruses. Joseph et al. (2020) found that green tea and spirulina extracts effectively blocked the entry of SARS-, MERS-, and SARS-CoV-2 pseudotyped viruses, suggesting their potential against emerging coronaviruses. Garcia-Ruiz et al. (2022) demonstrated that Spirulina powder inhibited SARS-CoV-2 infection, even at higher viral inoculum levels, indicating its

potency as a therapeutic candidate for COVID-19.

5.5. Antioxidant activity

Spirulina demonstrates robust antioxidant activity both in vitro and in vivo, as evidenced by multiple studies. In Swiss albino mice, *S. fusiform* protects against oxidative stress induced by mercuric chloride. The presence of mercuric chloride (4.5 mg/kg body weight IV) in spirulina has been shown to enhance lipid peroxidation by reducing glutathione and other antioxidant enzymes in the liver. Spirulina supplementation has been reported to effectively reduce oxidative stress (Ebid et al., 2022; Guldass et al., 2020).

Recent studies have explored the antioxidant potential of fresh spirulina-containing products, revealing synergistic interactions with other ingredients that enhance antioxidant activity and prolong shelf life (Stunda-Zujeva et al., 2023). Incorporating Spirulina into food products, such as probiotic labneh, not only improves nutritional content but also increases antioxidant activity and probiotic viability, offering a promising functional food option (Chlorophyll a, carotenoids) (Bortolini et al., 2022).

5.6. Anti-bacterial activity

Several studies have explored the antimicrobial and antioxidant potential of *Spirulina platensis* extracts. Abdel-Moneim et al. (2022) assessed the extract's efficacy against various pathogens, with *Klebsiella pneumoniae* exhibiting the highest sensitivity. Conversely, *Proteus vulgaris* displayed the lowest susceptibility.

Safari et al. (2020) isolated and purified C-Phycocyanin (C-PC) from *Spirulina platensis* using lysozyme and ammonium sulfate precipitation. They evaluated its antioxidant properties using DPPH radical-scavenging activity, FRAP, and Fe²⁺-chelating activity, and found significant antioxidant activity. Antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Streptococcus iniae*, and *Yersinia ruckeri* was also demonstrated, with *L. monocytogenes* being most sensitive and *S. iniae* the most resistant. MIC and MBC values indicated moderate antibacterial activity of C-PC (Bellahcen et al., 2019). These findings underscore the potential of *Spirulina platensis* extracts and C-PC as natural antimicrobial and antioxidant agents.

5.7. Anti-cancer activity

A water extract of commercial Spirulina exhibited significant anticancer effects on A549 lung carcinoma cells, inducing apoptosis, inhibiting cell cycle progression, and modulating key proteins involved in cell proliferation and survival. Importantly, the extract showed no cytotoxicity to normal human skin fibroblasts (Silva et al., 2021).

Phycocyanin isolated from *Spirulina platensis* showed anti-cancer activity against HepG-2 cell lines, with dose-dependent inhibition of α -amylase and β -glucosidase enzymes. Additionally, it exhibited anti-inflammatory effects, suggesting its potential as a natural therapeutic agent (Prabakaran et al.,

2020). *Spirulina platensis* extracts demonstrated significant cytotoxic effects against L20B and MCF7 human cancer cell lines, with the presence of various bioactive compounds suggesting its potential as a source of anticancer agents (Tajvidi et al., 2021). A combination of gamma-tocotrienol (γ T3) and Spirulina showed a significant reduction in tumor volume in a mouse model of breast cancer. While both γ T3 and Spirulina individually modulated immune cell populations, the combination treatment did not show synergistic anticancer effects (Subramaiam et al., 2021).

Spirulina offers antioxidant, anti-inflammatory, and immune-boosting effects. It also shows promising effect in fighting infections, managing diabetes, and reducing cholesterol. Additionally, It aids in detoxification, making it a valuable dietary supplement as tabulated in Table 4.

6. TOXICITY PROFILE OF SPIRULINA

6.1. Heavy metal

Various metals induce oxidative stress, resulting in tissue damage. To counteract the detrimental effects of free radicals in aerobic organisms, both endogenous and synthetic antioxidants play a crucial role. Endogenous substances such as nitric oxide (NO), reduced glutathione (GSH), and superoxide dismutase (SOD) function as protective mechanisms (F. Zhang et al., 2020).

In the subsequent sections, we delve into specific examples illustrating how spirulina demonstrates protective properties against metal poisoning. Through its antioxidant mechanisms, spirulina showcases its potential in mitigating the harmful impact of metals on biological tissues, offering a promising avenue for addressing oxidative stress-related damage.

6.1.1 Lead

Spirulina supplement demonstrates protective, antioxidant, and anti-apoptotic effects against lead acetate-induced hepatic damage in rats. Both low and high doses of Spirulina effectively improve biochemical parameters and prevent lead-induced changes in plasma and liver antioxidant status (El-Tantawy, 2016). Spirulina emerges as a protective agent against lead and cadmium toxicity, exhibiting its efficacy in various cell types, including T lymphocytes, RBCs, WBCs, and reticulocytes. Notably, its metal-binding capabilities prove instrumental in improving iron and hemoglobin metabolism in rats subjected to lead toxicity (Al-Dhabi, 2013). These findings suggest that Spirulina could be a valuable dietary supplement for mitigating the harmful effects of lead toxicity on the liver.

6.1.2 Cadmium

Cadmium instigates an imbalance in the antioxidant-peroxidant system by depleting thiol groups, initiating the generation of reactive oxygen species (ROS) in tissues. This disruption ultimately leads to the inhibition of antioxidant defense enzymes. ROS, encompassing hydrogen peroxide, hydroxyl radical, and peroxy radical, are produced and

Table 4
Biological Response of Spirulina.

Biological Activity	Specific Effects	Bioactive Compounds	References
Anti- Cancer	Damaged DNA repairing Induction of G1 cell cycle arrest, mitochondria-mediated apoptosis in MCF-7 human breast carcinoma	Se-enriched Spirulina	Subramaiam et al. (2021)
Antiviral	It can inhibit HIV-1 replication. Exhibits anti-herpes and anti-human immunodeficiency virus activity both in vitro and ex vivo.	sulphated polysaccharide calcium spirulina	Mader et al. (2016); Sibiya et al. (2022)
Anti- Bacterial	supercritical fluid extraction	linolenic acid	B and F (2018)
Antioxidant	Reduce CCl(4)-induced lipid peroxidation It has ability to stop hepatic stellate cells' (HSCs) growth	C-Phycocyanin (from <i>S. platensis</i>)	Grover et al. (2021)
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	Bannu et al. (2019); Blas-Valdivia et al. (2022)
Anti- Diabetic	Enhance the lipid profiles and glycosylated haemoglobin (HbA1c).	Spirulina supplementation (2 g/day for 2 months)	Oriquat et al. (2019)

eliminated by aerobic organisms, posing susceptibility to proteins, lipids, lipoproteins, and DNA. *S. Platensis*, abundant in antioxidant compounds, emerges as a potential defender against cadmium-induced oxidative stress. Its capacity to enhance antioxidant enzyme activity, including superoxide dismutase and GSH peroxidase, is noteworthy. Additionally, it is reported to possess actions that counter lipid peroxidation and scavenge free radicals (Bhattacharya, 2020; Pérez-Alvarez et al., 2021).

6.1.3 Iron

Iron emerges as a prominent contributor to oxidative stress, triggering the deterioration of brain cells and impeding their functions. Its interaction with various intermittent processes induces oxidative stress, marked by the production of reactive oxygen species. Iron poisoning, characterized by cellular necrosis, significantly elevates the release of lactate dehydrogenase (LDH). The phycocyanin content in spirulina extract demonstrates a stimulatory effect against antioxidant enzymes crucial in safeguarding humans from the detrimental impact of reactive oxygen species. Notably, this includes glutathione peroxidase and reductase (Mohanty & Samanta, 2018; Sagara et al., 2015).

7. CONCLUSION

In conclusion, spirulina, a cyanobacterium belonging to the family Oscillatoraceae, has established itself as a nutritional powerhouse with diverse applications. Its rich composition of essential elements, including proteins, vitamins, minerals, and antioxidants, positions it as a valuable dietary supplement with potential therapeutic benefits. Spirulina's unique attributes, such as being a plant-based source of vitamin B12 and possessing substantial protein content, make it particularly

beneficial for individuals following vegan diets (Wang et al., 2023).

The algae's remarkable capacity to thrive in robust sunlight, high temperatures, and alkaline environments contributes to its rapid growth, making it a versatile and sustainable resource. Beyond its roles in food and pharmaceuticals, spirulina exhibits promising applications in biofuel and biomaterial production, as well as environmental remediation, showcasing its multifaceted utility. *S. platensis*, *S. maxima*, and *S. fusiformis*, among various spirulina species, have been extensively studied for their nutritional and therapeutic value. Notably, *S. platensis*, the most widely used species, is recognized for its nutritional richness and potent antioxidant properties attributed to various compounds such as C-phycocyanin, polysaccharides, and phenolic compounds (Mutanda et al., 2020). The comprehensive nutritional profile of spirulina, encompassing macro and micronutrients, underscores its role in addressing various health concerns, including immunomodulation, anticancer, antioxidant, antiviral, and antibacterial activities (Silva et al., 2021). Spirulina has demonstrated promising pharmacological actions, contributing to its potential in managing conditions such as diabetes, cardiovascular diseases, and liver-related issues.

Moreover, spirulina's ability to protect against heavy metal toxicity, including lead and cadmium, further highlights its significance in combating environmental pollutants. Its antioxidant mechanisms play a crucial role in mitigating oxidative stress induced by iron, showcasing its potential in preserving brain cell functions.

Despite the promising attributes of spirulina, it is essential to consider potential variations in its composition based on cultivation conditions and analysis methods. Additionally, ongoing research continues to unravel new dimensions of spirulina's applications and benefits, emphasizing the need for

sustained exploration into its diverse therapeutic potentials. Overall, spirulina stands as a resilient, nutrient-dense, and environmentally valuable resource with substantial implications for human health and well-being.

CONFLICTS OF INTEREST

None

ORCID

Khushboo Gaur	0000-0002-6758-8000
Ankita Wal	0000-0002-5563-1382
Preeti Sharma	0000-0003-2081-5007
Amana Parveen	0009-0007-0550-1719
Prerna Singh	0009-0000-2872-3487
Prashant Mishra	0009-0002-1367-1703
Pranay Wal	0000-0002-6342-6290
N T Pramathesh Mishra	0000-0001-9268-841X

AUTHOR CONTRIBUTIONS

KG, AW, PW, PS- Layout and concept of the paper; AW, PW- design review study and formatted manuscript; PS, AP, PS, PM, NTPM- helped prepare the manuscript and data collection; KG, AW, NTPM- Final review.

REFERENCES

- Abdel-Moneim, A.M.E., El-Saadony, M.T., Shehata, A.M., Saad, A.M., Aldhumri, S.A., Ouda, S.M., Mesalam, N.M., 2022. Antioxidant and antimicrobial activities of *Spirulina platensis* extracts and biogenic selenium nanoparticles against selected pathogenic bacteria and fungi. *Saudi Journal of Biological Sciences*. 29(2), 1197–1209. <https://doi.org/10.1016/j.sjbs.2021.09.046>
- Ahda, M., Suhendra, Permadi, A., 2023. *Spirulina Platensis* Microalgae as High Protein-Based Products for Diabetes Treatment. *Food Reviews International*, 1–9. <https://doi.org/10.1080/87559129.2023.2238050>
- Al-Dhabi, N.A., 2013. Heavy metal analysis in commercial *Spirulina* products for human consumption. *Saudi Journal of Biological Sciences*. 20(4), 383–388. <https://doi.org/10.1016/j.sjbs.2013.04.006>
- Alfadhly, N., Alhelfi, N., Altemimi, A.B., Verma, D.K., Cacciola, F., Narayanankutty, A., 2022. Trends and Technological Advancements in the Possible Food Applications of *Spirulina* and Their Health Benefits: A Review. *Molecules*. 27(17), 5584. <https://doi.org/10.3390/molecules27175584>
- Al-Hussaniy, H.A., Al-Tameemi, Z.S., Al-Zubaidi, B.A., Oraibi, A.I., Naji, F.A., Kilani, S., 2023. Pharmacological properties of *Spirulina* species: Hepatoprotective, antioxidant and anticancer effects. *Farmacia*. 71(4), 670–678. <https://doi.org/10.31925/farmacia.2023.4.2>
- Ali, S.K., Saleh, A.M., 2012. *Spirulina*-an overview. *International journal of Pharmacy and Pharmaceutical sciences*. 4(3), 9–15.
- Al-Qahtani, W.H., Binobead, M.A., 2019. Anti-inflammatory, antioxidant and antihepatotoxic effects of *Spirulina platensis* against D-galactosamine induced hepatotoxicity in rats. *Saudi Journal of Biological Sciences*. 26, 647–652. <https://doi.org/10.1016/j.sjbs.2018.01.003>
- Anvar, A.A., Nowruzi, B., 2021. Bioactive properties of spirulina: A review. *Microbial Bioactives*. 4, 134–142. <http://dx.doi.org/10.25163/microbioacts.412117B0719110521>
- B, T., F, S.P., 2018. Investigation of phytochemical constituents in *Spirulina fusiformis* for antibacterial activity. *National Journal of Physiology, Pharmacy and Pharmacology*. 8(11), 1491–1495. <https://doi.org/10.5455/njppp.2018.8.0417030072018>
- Balkrishna, A., Dev, S.N.C., Joshi, B., Mishra, R.K., 2023. *Spirulina*: A Miraculous alga with Pharmaco-nutraceutical Potential as Future Food. *International Journal of Food*. 11(3), 128–136. <http://dx.doi.org/10.21088/ijfnd.2322.0775.11323.7>
- Bannu, S.M., Lomada, D., Gulla, S., Chandrasekhar, T., Reddanna, P., Reddy, M.C., 2019. Potential therapeutic applications of C-phycoerythrin. *Current Drug Metabolism*. 20, 967. <https://doi.org/10.2174/1389200220666191127110857>
- Beheshtipour, H., Mortazavian, A.M., Haratian, P., Darani, K.K., 2012. Effects of *Chlorella vulgaris* and *Arthrospira platensis* addition on viability of probiotic bacteria in yogurt and its biochemical properties. *European Food Research and Technology*. 235, 719–728. <https://doi.org/10.1007/s00217-012-1798-4>
- Bellahcen, T.O., Cherki, M., Sánchez, J.A.C., Cherif, A., Amrani, A.E., 2019. Chemical composition and antibacterial activity of the essential oil of *Spirulina platensis* from Morocco. *Journal of Essential Oil Bearing Plants*. 22(5), 1265–1276. <https://doi.org/10.1080/0972060X.2019.1669492>
- Bhakar, R.N., Kumar, R., Pabbi, S., 2013. Total lipids and fatty acid profile of different *Spirulina* strains as affected by salinity and incubation time. *International Journal of Plant Research*. 26, 148–54. <https://doi.org/10.5958/j.2229-4473.26.2s.133>
- Bhattacharya, S., 2020. The role of *Spirulina* (*Arthrospira*) in the mitigation of heavy-metal toxicity: an appraisal. *Journal of Environmental Pathology*. 39(2), 149–157. <https://doi.org/10.1615/jenvironpatholtoxiconcol.2020034375>
- Blas-Valdivia, V., Moran-Dorantes, D.N., Rojas-Franco, P., Franco-Colin, M., Mirhosseini, N., Davarnejad, R., Halajisani, A., Tavakoli, O., Cano-Europa, E., 2022. C-Phycocyanin prevents acute myocardial infarction-induced oxidative stress, inflammation and cardiac damage. *Pharmaceutical Biology*. 60(1), 755–763. <https://doi.org/10.1080/13880209.2022.2055089>
- Bortolini, D.G., Maciel, G.M., Fernandes, I., Pedro, A.C., Rubio, F., Branco, I.G., Haminiuk, C., 2022. Functional properties of bioactive compounds from *Spirulina* spp.: Current status and future trends. *Food Chemistry: Molecular sciences*. 5, 100134. <https://doi.org/10.1016/j.fochms.2022.100134>
- Can, S.S., Koru, E., Cirik, S., 2017. Effect of temperature and nitrogen concentration on the growth and lipid content of *Spirulina platensis* and biodiesel production. *Aquaculture International*. 25, 1485–1493. <https://doi.org/10.1007/s10499-017-0121-6>
- Chandrasekara, A., Kumar, T., 2016. Roots and tuber crops as functional foods: A review on phytochemical constituents and their potential health benefits. *International Journal of Food Science*. 2016, 3631647. <https://doi.org/10.1155/2016/3631647>
- Diaz, C.J., Douglas, K.J., Kang, K., Kolarik, A.L., Malinowski, R., Torres-Tiji, Y., Molino, J.V., Badary, A., Mayfield, S.P., 2023. Developing algae as a sustainable food source. *Frontiers in Nutrition*. 9, 3147. <https://doi.org/10.3389/fnut.2022.1029841>
- Dinicolaantonio, J.J., Bhat, A.G., Okeefe, J., 2020. Effects of spirulina on weight loss and blood lipids: a review. *Open Heart*. 7(1), 1003. <https://doi.org/10.1136/openhrt-2018-001003>
- Ebid, W.M., Ali, G.S., Elewa, N.A., 2022. Impact of *Spirulina platensis* on physicochemical, antioxidant, microbiological and sensory properties

- of functional labneh. *Discover Food*. 2(1), 29. <http://dx.doi.org/10.1007/s44187-022-00031-7>
- El-Tantawy, W.H., 2016. Antioxidant effects of Spirulina supplement against lead acetate-induced hepatic injury in rats. *Journal of Traditional and Complementary Medicine*. 6(4), 327–331. <https://doi.org/10.1016/j.jtcme.2015.02.001>
- Fithriani, D., Sinurat, E., 2019. Utilization of spirulina as functional food: Phytosterol and amino acid profiles study. *IOP Conference Series: Earth and Environmental Science*. 278, 012028. <https://doi.org/10.1088/1755-1315/278/1/012028>
- García-Ruiz, D., Villalobos-Sánchez, E., Alam-Escamilla, D., Elizondo-Quiroga, D., 2022. In vitro inhibition of SARS-CoV-2 Infection by dry algae powders. *Scientific Reports*. 12(1), 17101. <https://doi.org/10.21203/rs.3.rs-1416575/v1>
- Gogna, S., Kaur, J., Sharma, K., Prasad, R., Singh, J., Bhadariya, V., Kumar, P., Jarial, S., 2023. Spirulina- An Edible Cyanobacterium with Potential Therapeutic Health Benefits and Toxicological Consequence. *Journal of the American nutrition association*. 42(6), 559–572. <https://doi.org/10.1080/27697061.2022.2103852>
- Grover, P., Bhatnagar, A., Kumari, N., Bhatt, A.N., Nishad, D.K., Purkayastha, J., 2021. C-Phycocyanin-a novel protein from *Spirulina platensis* In vivo toxicity, antioxidant and immunomodulatory studies. *Saudi Journal of Biological Sciences*. 28(3), 1853–1859. <https://doi.org/10.1016/j.sjbs.2020.12.037>
- Guldas, M., Ziyank-Demirtas, S., Sahan, Y., Yildiz, E., Gurbuz, O., 2020. Antioxidant and anti-diabetic properties of Spirulina platensis produced in Turkey. *Food Science and Technology*. 41, 615–625. <https://doi.org/10.1590/fst.23920>
- He, X., Zhu, Y., Jiang, X., Qiu, Y., Yin, F., Xiong, W., Liu, B., Huang, Y., 2022. Spirulina compounds show hypoglycemic activity and intestinal flora regulation in type 2 diabetes mellitus mice. *Algal Research*. 66, 102791. <https://doi.org/10.1016/j.algal.2022.102791>
- Hoseini, S.M., Khosravi-Darani, K., Mozafari, M.R., 2013. Nutritional and medical applications of spirulina microalgae. *Mini reviews in Medicinal Chemistry*. 13, 1231–1237. <https://doi.org/10.2174/1389557511313080009>
- Ismail, M., Hossain, M.F., Tanu, A.R., Shekhar, H.U., 2015. Effect of spirulina intervention on oxidative stress, antioxidant status, and lipid profile in chronic obstructive pulmonary disease patients. *BioMed research International*. 2015, 486120. <https://doi.org/10.1155/2015/486120>
- Janda-Milczarek, K., Szymczykowska, K., Jakubczyk, K., Kupnicka, P., Skonieczna-Żydecka, K., Pilarczyk, B., Tomza-Marciniak, A., Ligenza, A., Stachowska, E., Dalewski, B., 2023. Spirulina supplements as a source of mineral nutrients in the daily diet. *Applied Sciences*. 13(2), 1011. <https://doi.org/10.3390/app13021011>
- Jara, A.D.L., Ruano-Rodríguez, C., Polifrone, M., Assunção, P., Brito-Casillas, Y., Wägner, A.M., Serra-Majem, L., 2018. Impact of dietary Arthrospira (Spirulina) biomass consumption on human health: main health targets and systematic review. *Journal of Applied Phycology*. 30, 2403–2423. <https://doi.org/10.1007/s10811-018-1468-4>
- Joseph, J., Ajay, A., Das, V.A., Raj, V.S., 2020. Green tea and Spirulina extracts inhibit SARS, MERS, and SARS-2 spike pseudotyped virus entry in vitro. *BioRxiv*, 2020–2026. <https://doi.org/10.1101/2020.06.20.162701>
- Jung, F., Krüger-Genge, A., Waldeck, P., Küpper, J.H., 2019. Spirulina platensis, a super food? *Journal of Cellular Biotechnology*. 5(1), 43–54. <https://doi.org/10.3233/JCB-189012>
- Khavari, F., Saidijam, M., Taheri, M., Nouri, F., 2021. Microalgae: Therapeutic potentials and applications. *Molecular Biology Reports*. 48(5), 4757–4765. <https://doi.org/10.1007/s11033-021-06422-w>
- Kumar, A., Mohanty, V., Yashaswini, P., 2018. Development of high protein nutrition bar enriched with *Spirulina platensis* for under-nourished children. *Current Research in Nutrition and Food Science Journal*. 6(3), 835–844. <http://dx.doi.org/10.12944/CRNFSJ.6.3.26>
- Liestianty, D., Rodianawati, I., Arfah, R.A., Assa, A., Patimah, S., Muliadi., 2019. Nutritional analysis of spirulina sp to promote as superfood candidate. *IOP Conference Series: Materials Science and Engineering*. 509, 12031–12031. <https://doi.org/10.1088/1757-899X/509/1/012031>
- Lupatini, A.L., Colla, L.M., Canan, C., Colla, E., 2017. Potential application of microalga *Spirulina platensis* as a protein source. *Journal of the Science of Food and Agriculture*. 97(3), 724–732. <https://doi.org/10.1002/jsfa.7987>
- Lympaki, F., Giannoglou, M., Magriplis, E., Bothou, D.L., Andreou, V., Dimitriadis, G.D., Markou, G., Zampelas, A., Theodorou, G., Katsaros, G., Papakonstantinou, E., 2022. Short-Term Effects of Spirulina Consumption on Glycemic Responses and Blood Pressure in Healthy Young Adults: Results from Two Randomized Clinical Trials. *Metabolites*. 12(12), 1180. <https://doi.org/10.3390/metabo12121180>
- Mader, J., Gallo, A., Schommartz, T., Handke, W., Nagel, C.H., Günther, P., Brune, W., Reich, K., 2016. Calcium spirulan derived from *Spirulina platensis* inhibits herpes simplex virus 1 attachment to human keratinocytes and protects against herpes labialis. *Journal of Allergy and Clinical Immunology*. 137(1), 197–203. <https://doi.org/10.1016/j.jaci.2015.07.027>
- Michael, A., Kyewalyanga, M.S., Lugomela, C.V., 2019. Biomass and nutritive value of Spirulina (*Arthrospira fusiformis*) cultivated in a cost-effective medium. *Annals of Microbiology*. 69, 1387–1395. <https://doi.org/10.1007/s13213-019-01520-4>
- Mohamed, N.A., Hashem, M., Alzahrani, A.M., Abdel-Moneim, A.M., Abdou, H.M., 2021. Hepatoprotective effect of *Spirulina platensis* against carbon tetrachloride-induced liver injury in male rats. *The Journal of Pharmacy and Pharmacology*. 73(11), 1562–1570. <https://doi.org/10.1016/j.intimp.2014.05.014>
- Mohanty, D., Samanta, L., 2018. Dietary supplementation of Spirulina ameliorates iron-induced oxidative stress in Indian knife fish *Notopterus Notopterus*. *Environmental Toxicology and Pharmacology*. 61, 71–78. <https://doi.org/10.1016/j.etap.2018.05.007>
- Mutanda, T., Naidoo, D., Bwapwa, J.K., Anandraj, A., 2020. Biotechnological applications of microalgal oleaginous compounds: current trends on microalgal bioprocessing of products. *Frontiers in Energy Research*. 8, 598803. <https://doi.org/10.3389/fenrg.2020.598803>
- Neag, E., Stupar, Z., Varaticeanu, C., Senila, M., Roman, C., 2022. Optimization of Lipid Extraction from *Spirulina spp.* by Ultrasound Application and Mechanical Stirring Using the Taguchi Method of Experimental Design. *Molecules*. 27(20), 6794. <https://doi.org/10.3390/molecules27206794>
- Okechukwu, P.N., Ekeuku, S.O., Sharma, M., Nee, C.P., Chan, H.K., Mohamed, N., Froemming, G.R.A., 2019. In vivo and in vitro antidiabetic and antioxidant activity of spirulina. *Pharmacognosy Magazine*. 15(1), 17–29. http://dx.doi.org/10.4103/pm.pm_431_18
- Oriquat, G.A., Ali, M.A., Mahmoud, S.A., Eid, R.M., Hassan, R., Kamel, M.A., 2019. Improving hepatic mitochondrial biogenesis as a postulated mechanism for the antidiabetic effect of *Spirulina platensis* in comparison with metformin. *Nutrition, and Metabolism*. 44(4), 357–364. <https://doi.org/10.1139/apnm-2018-0354>
- Pawar, A.R., Rao, P.S., Jadhav, R.S., 2020. Nutraceutical value of spirulina (arthrospira): a review. *World Journal of Pharmaceutical Research*. 9(5), 315–328. <https://doi.org/10.20959/wjpr20205-17256>
- Pérez-Alvarez, I., Islas-Flores, H., Gómez-Oliván, L.M., Sánchez-Aceves, L.M., Chamorro-Cevallos, G., 2021. Protective effects of

- Spirulina (*Arthrospira maxima*) against toxicity induced by cadmium in *Xenopus laevis*. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*. 248, 109099. <https://doi.org/10.1016/j.cbpc.2021.109099>
- Prabakaran, G., Sampathkumar, P., Kavisri, M., Moovendhan, M., 2020. Extraction and characterization of phycocyanin from *Spirulina platensis* and evaluation of its anticancer, antidiabetic and antiinflammatory effect. *International Journal of Biological Macromolecules*. 153, 256–263. <https://doi.org/10.1016/j.ijbiomac.2020.03.009>
- Priyanka, S., Varsha, R., Verma, R., Ayenampudi, S.B., 2023. Spirulina: A Spotlight on Its Nutraceutical Properties and Food Processing Applications. *Journal of Microbiology, Biotechnology and Food Sciences*. 12(6), 4785. <https://doi.org/10.55251/jmbfs.4785>
- Rabeh, N.M., El-Banna, N.H., El-Kady, K.A., Ghonim, N.M., 2021. Effect of Spirulina (*Spirulina platensis*) on Blood Glucose Level and Renal Impairment in Diabetic Rats. *Egyptian Journal of Nutrition and Health*. 16(2), 53–69. <https://dx.doi.org/10.21608/ejnh.2021.239556>
- Rahim, A., Çakir, C., Ozturk, M., Şahin, B., Soulaïmani, A., Sibaoueih, M., Nasser, B., Eddoha, R., Essamadi, A., Amiri, B.E., 2021. Chemical characterization and nutritional value of *Spirulina platensis* cultivated in natural conditions of Chichaoua region (Morocco). *South African Journal of Botany*. 141, 235–242. <https://doi.org/10.1016/j.sajb.2021.05.006>
- Rosario, J.C., Josephine, M, R., 2015. Mineral profile of edible algae *Spirulina platensis*. *International Journal of Current Microbiology and Applied Science*. 4, 478–83.
- Rutar, J.M., Hudobivnik, M.J., Nečemer, M., Mikuš, K.V., Arčon, I., Ogrinc, N., 2022. Nutritional quality and safety of the spirulina dietary supplements sold on the Slovenian market. *Foods*. 11(6), 849. <https://doi.org/10.3390/foods11060849>
- Ruzik, L., 2023. Microalgae with active biological metal-nanoparticles as a novel food. Biosynthesis, characterization and bioavailability investigation-Review. *Trends in Food Science & Technology*. 104127. 139, 104127. <https://doi.org/10.1016/j.tifs.2023.104127>
- Safari, R., Amiri, Z.R., Kenari, R.E., 2020. Antioxidant and antibacterial activities of C-phycocyanin from common name *Spirulina platensis*. *Iranian Journal of Fisheries Sciences*. 19, 1911–1927. <https://doi.org/10.22092/ijfs.2019.118129>
- Sagara, T., Nishibori, N., Kishibuchi, R., Itoh, M., Morita, K., 2015. Non-protein components of *Arthrospira (Spirulina) platensis* protect PC12 cells against iron-evoked neurotoxic injury. *Journal of Applied Phycology*. 27, 849–855. <https://doi.org/10.1007/s10811-014-0388-1>
- Salmeán, G.G., Castillo, L.H., Chamorro-Cevallos, G., 2015. Nutritional and toxicological aspects of *Spirulina (Arthrospira)*. *Nutricion Hospitalaria*. 32(1), 34–40. <https://doi.org/10.3305/nh.2015.32.1.9001>
- Saraswathi, K., Kavitha, C.N., 2023. Spirulina: Pharmacological Activities and Health Benefits. *Journal of Young Pharmacists*. 15(3), 441–447. <https://doi.org/10.5530/jyp.2023.15.59>
- Seghiri, R., Kharbach, M., Essamri, A., 2019. Functional Composition, Nutritional Properties, and Biological Activities of Moroccan Spirulina Microalga. *Journal of Food Quality*. 2019, 3707219. <https://doi.org/10.1155/2019/3707219>
- Sibiya, T., Ghazi, T., 2022, C.A., 2022. The Potential of *Spirulina platensis* to Ameliorate the Adverse Effects of Highly Active Antiretroviral Therapy (HAART). *Nutrients*. 14(15), 3076. <https://doi.org/10.3390/nu14153076>
- Silva, M.R.O.D., Silva, M., Silva, G., Lima, A.L.D., Bezerra, L.R.D., Marques, R.P., A, D.D., 2021. Bioactive compounds of *Arthrospira spp.* (*Spirulina*) with potential anticancer activities: a systematic review. *ACS Chemical Biology*. 16(11), 2057–2067. <https://doi.org/10.1021/acscchembio.1c00568>
- Singh, S.K., Shukla, L., Yadav, N., Singh, P.K., Singh, S.M., Yadav, M.K., Kaushalendra, Kumar, A., 2023. Spirulina: From Ancient Food to Innovative Super Nutrition of the Future and Its Market Scenario as a Source of Nutraceutical, In: First (Eds.); B. Neilan, M. Passarini, P. Singh, A. Kumar, et al., (Eds.), *Cyanobacterial Biotechnology in the 21st Century*. Springer, Singapore, pp. 51–61. https://doi.org/10.1007/978-981-99-0181-4_4
- Soni, R.A., Sudhakar, K., Rana, R.S., 2017. Spirulina-From growth to nutritional product: A review. *Trends in Food Science & Technology*. 69, 157–171. <https://doi.org/10.1016/j.tifs.2017.09.010>
- Sow, S., Ranjan, S., 2021. Cultivation of Spirulina: An innovative approach to boost up agricultural productivity. *The Pharma Innovation*. 10, 799–813. <https://doi.org/10.22271/tpi.2021.v10.i3k.5889>
- Stunda-Zujeva, A., Berele, M., Lece, A., Šķesters, A., 2023. Comparison of antioxidant activity in various spirulina containing products and factors affecting it. *Scientific Reports*. 13(1), 4529. <https://doi.org/10.1038/s41598-023-31732-3>
- Subramaiam, H., Chu, W.-L., Radhakrishnan, A.K., Chakravarthi, S., Kanga, R., Selvaduray, Y.-Y., Kok, 2021. Evaluating Anticancer and Immunomodulatory Effects of Spirulina (*Arthrospira*) *platensis* and Gamma-Tocotrienol Supplementation in a Syngeneic Mouse Model of Breast Cancer. *Nutrients*. 13, 2320. <https://doi.org/10.3390/nu13072320>
- Suliburska, J., Szulińska, M., Tinkov, A.A., Bogdański, P., 2016. Effect of *Spirulina maxima* Supplementation on Calcium, Magnesium, Iron, and Zinc Status in Obese Patients with Treated Hypertension. *Biological Trace Element Research*. 173(1), 1–6. <https://doi.org/10.1007/s12011-016-0623-5>
- Suo, Q., Yue, Y., Wang, J., Wu, N., Geng, L., Zhang, Q., 2022. Isolation, identification and in vivo antihypertensive effect of novel angiotensin I-converting enzyme (ACE) inhibitory peptides from Spirulina protein hydrolysate. *Food & Function*. 13(17), 9108–9118. <https://doi.org/10.1039/D2FO01207C>
- Supriya, R., Delfan, M., Saeidi, A., Samaie, S.S., Kiyumi, M.H., Escobar, K.A., Laher, I., Heinrich, K.M., Weiss, K., Knechtle, B., Zouhal, H., 2023. Spirulina Supplementation with High-Intensity Interval Training Decreases Adipokines Levels and Cardiovascular Risk Factors in Men with Obesity. *Nutrients*. 15(23), 4891. <https://doi.org/10.3390/nu15234891>
- Tajvidi, E., Nahavandizadeh, N., Pournaderi, M., Pourrashid, A.Z., Bossaghzadeh, F., Khoshnood, Z., 2021. Study the antioxidant effects of blue-green algae Spirulina extract on ROS and MDA production in human lung cancer cells. *Biochemistry and Biophysics Reports*. 28, 101139. <https://doi.org/10.1016/j.bbrep.2021.101139>
- Vilalur, G., Sutelman, P., Ben-Aicha, S., Mendieta, G., Radiké, M., Schoch, L., Casaní, L., Borrell-Pagés, M., Padro, T., Badimon, L., 2022. Supplementation With Spirulina Reduces Infarct Size and Ameliorates Cardiac Function in a Pig Model of STEMI. *Frontiers in Pharmacology*. 13, 891801. <https://doi.org/10.3389/fphar.2022.891801>
- Wang, Y.Y., Xu, B.L., Dong, C.M., Sun, Y.Y., 2023. The nutritional value of Spirulina and Utilization Research. *Life Research*. 6(3), 15–15. <https://doi.org/10.53388/LR20230015>
- Wild, K.J., Steingäß, H., Rodehutschord, M., 2018. Variability in nutrient composition and in vitro crude protein digestibility of 16 microalgae products. *Journal of animal physiology and animal nutrition*. 102(5), 1306–1319. <https://doi.org/10.1111/jpn.12953>
- Zhang, F., Man, Y.B., Mo, W.Y., Wong, M.H., 2020. Application of Spirulina in aquaculture: a review on wastewater treatment and fish growth. *Reviews in Aquaculture*. 12(2), 582–599. <https://doi.org/>

[10.1111/raq.12341](https://doi.org/10.1111/raq.12341)

Zhang, J., Shi, J., Chang, X., 2021. A model of algal growth depending on nutrients and inorganic carbon in a poorly mixed water column.

Journal of Mathematical Biology. 83, 1–30. <https://doi.org/10.1007/s00285-021-01640-z>