Current and Prospective Insights on Food and Pharmaceutical Applications of Spirulina

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Abstract
The blue green algae spirulina has been used by mankind as food and drug since ages. However, the last few decades have witnessed the unprecedented momentum in research on nutritional and medicinal potency of this unicellular alga. It has emerged as an undisputed medical food with the discovery and validation of a litany of health benefits ranging from antioxidant, anti-inflammatory, hypolipemic, antithrombotic, anti-diabetic, anticancer, immunostimulatory, antimicrobial, cardio-protective, hepatoprotective, anaemia protective, tissue engineering to aquaculture and livestock feed. Many hitherto unknown pharmacological properties are coming forth and myriad research projects are revolving around this miraculous cyanobacterium. Safety regulations recommend its inclusion in nutritional regimen for proofing body against ailments and augmenting vitality. Advances in effective cultivation, drying, extraction and purification techniques have been summarized. This review outlines the recent progresses and therapeutic possibilities of this spirulina.

Keywords: Spirulina, antioxidant, anticancer, immunomodulation, antidiabetic, neuroprotection

Introduction
Spirulina is a free-floating, microscopic, filamentous blue-green alga, thriving in alkaline fresh as well as salt water bodies (1) (Fig. 1). This cyanobacteria, belonging to the class cyanophyceae and order oscillatoriales is a storehouse of bioactive molecules viz. proteins (60-65% dry weight) with essential amino acids, polyunsaturated fatty acids, such as α-linoleic acid, vitamins (B12 and E), polysaccharides (calcium spirulan, immulan), minerals (Na, K, Ca, Fe, Mn and Se), pigments (chlorophyll, c-phycocyanin, allophycocyanin, β-carotene, lutein, zeaxanthin etc.). The c-phycocyanin content was determined to be 12.6% in dried spirulina (2). High content of dietary zeaxanthin was reported in its biomass (3). Also, an appreciable quantity of vitamin E was estimated in S. platensis (4). Gallic, chlorogenic, cinnamic, pinostrobin and hydroxybenzoic acids have been found to be the key constituents in various extracts of S. maxima (5). The importance of its high-molecular weight polysaccharides in mitigating several maladies has been well documented (6, 7, 8, 9).

Fig. 1. (A) Spirulina harvested on a filter (B) The biomass after squeezing out water (Pictures courtesy: http://www.spirulina-vera.com)
Several species of spirulina have attracted commercial importance viz. *Spirulina platensis*, *Spirulina maxima* and *Spirulina fusiformis*. It has been consumed since centuries in various parts of the globes, ranging from Aztec civilization in Latin America to tribes inhabiting Central Africa’s Lake Chad. At the United Nations World Food Conference in 1974, this alga was decorated with the epithet of ‘best food for the future’. Spirulina is deemed safe for human consumption evident by its long history of food use and contemporary scientific findings (1). Now, it has become a major ingredient in many nutraceutical formulations. Current times have seen rigorous investigation on its biological effects against many health problems. Findings have reported the functional food, antioxidant, immunostimulatory, anticancer, antiinflamamatory, hypolipemic, cardioprotective, antidiabetic, hepatoprotective, neuroprotective and antimicrobial potentials of this novel alga. Also, it has made strides into aquaculture and poultry feed.

A slew of spirulina-based herbal, vitamin and mineral supplements have been released to the market. These nutraceuticals marketed as tablets, capsules, dry flakes or in powder form have garnered enormous consumer interest. ‘Spirulina Pacifica’ is the trademark of a Hawaiian strain manufactured by Cyanotech Inc. ‘Earthrise Spirulina’ is the most popular brand in the USA. For a growing number of customers spirulina products have assumed panacea status. These products have secured good market in South America, Eastern Europe, large parts of Asia and Africa. In light of the recent surge in demonstrated clinical properties of spirulina, this review attempts to furnish the scattered data as a holistically informative piece.

**Uses of spirulina:** Spirulina has demonstrated a bewildering array of food and therapeutic properties. The key implications backed by scientific findings are as functional food and additives, antioxidant, anti-inflammatory, hypolipemic and antihypertensive, antidiabetic, anticancer, immunestimulant, antimicrobial, hepatoprotective, neuroprotection, antianaemic and antileucopenic and tissue engineering. *Spirulina biomass has also proved suitable as a nutritive aquaculture feed*. The food applications and health benefits are illustrated in Fig. 2.

![Fig 2. The food and pharmaceutical applications of spirulina](image-url)
As functional food, additive and prebiotic:

Spirulina has earned scientific validation regarding its role as healthy food component. This nutritious and easily digestible food can be consumed in several forms. It was demonstrated that the whole spirulina or its phycocyanin-rich fraction could be a suitable functional ingredient in soy milk, fruit juices and whole fruits (10). It was suggested that the ingestion of cocoa and spirulina powder mix can promote antioxidant status and vascular health (11). The flavonol-rich cocoa and phycocyanin-rich spirulina are assumed to work in synergy to increase the endothelial production of nitric oxide and act as a potent inhibitor of NADPH oxidase.

Spirulina is expected to enhance the nutritional content of conventional foods when incorporated as colorant, texturizing agent, gelling agent and prebiotic. The pigments phycocyanin and allophycocyanin are used in the food and beverage industry as a natural colorant. This blue colorant finds use in ice cream, sweets, chewing gum, candy, jelly, cake decorations as well as soft drinks, alcoholic drinks (12). It was observed that the incorporation of *S. platensis* increases raw pasta firmness and imparts it a stable color. Sensory analysis also showed better acceptance scores (13). The effect of *S. platensis* enrichment in semolina was observed. Addition of 2g spirulina in 100g semolina resulted in higher swelling index, lower cooking loss and increase in pasta firmness (14). It was discovered that date and spirulina powder-based food tablets are suitable for consumption by those having dysphagia (difficulty in swallowing food), to fulfill the nutritional requirement. Also, these tablets are expected to act as natural and cheap drug delivery carriers (15). It was observed that at lower heating or cooling rates, *S. maxima* gel exerted viscoelastic functions akin to that of pea protein, κ-carrageenan and starch. This finding may lead to the use of spirulina as thickener in food industry like the above hydrocolloids (16). It was observed that *S. platensis* stimulates proliferation of probiotic lactic acid bacteria. The addition of dry algal biomass at 10 mg/ml promoted growth of *Lactobacillus acidophilus* to 186%, suggesting the prebiotic potential of the microalga (17). A protective medium with spirulina as an ingredient was optimized for enhancing viability of *Lactobacillus rhamnosus* during lyophilisation. It was observed that the algal additive at 1.3%, along with lactulose and sucrose promotes viability of the microbe (18). The dermoprotective potential of raw spirulina and its lactic acid bacteria-fermented product was compared. The results showed that though both forms exert skin ameliorative functions; the fermented product performed better in terms of radical scavenging, anti-inflammation and UV protection. It was inferred that the fermentation process, released unidentified polyphenols and converted phycocyanin to phycocyanobilin. Based on the results, it was suggested that fermented spirulina can be a potent supplement for skin health (19).

Spirulina is an incredibly rich source of proteins that could efficiently fight against food deficiency in developing countries (20). The safety profile of spirulina was investigated and its microcystin toxin-free status was suggested. So, it is clear that the long-term dietary supplementation of this alga does not pose any health risks if consumed in moderation (21).

Antioxidant:

Lipid peroxidation is the degradation of lipids due to free radicals, generated by toxins. If not checked, the oxidative stress causes membrane rupture and mutagenic end-product malondialdehyde (MDA) are produced. The efficacy of spirulina in eliminating mercuric chloride-induced oxidative stress was investigated in mice. Its oral supplementation (800 mg/kg body weight, in olive oil, along with the toxin) for 40 days led to decline in lipid peroxidation and the activities of antioxidants enzymes viz. superoxide dismutase (SOD), catalase (CAT) and glutathione-S-transferase (GSH) were restored to normalcy (22). The supercritical fluid-extracted fraction of *S. platensis* was subjected to β-carotene bleaching method and DPPH assay to determine the optimal extraction conditions for antioxidants. The

Uses of spirulina in healthcare
pressure of 220-320 bar, temperature 55°C with 10% ethanol-blended CO₂ or 320 bar pressure at 75°C temperature with pure CO₂, proved optimal for the extraction (23). The protective effect of S. platensis on gentamicin sulphate-induced changes in the levels of lipid peroxidation and antioxidants in the kidney was investigated in murine models. The algae when consumed at a dose of 1g/kg, elicited significant nephroprotective activity by decreasing lipid peroxidation and elevating the levels of GSH, SOD, GPX, NO, creatinine and urea. Biochemical as well as histological results corroborated the findings (24).

From a battery of in vitro tests, it was concluded that S. platensis and phycocyanin have radical-scavenging and metal chelation properties. The inhibition of hydroxyl and peroxyl radicals and the lipid peroxidation were attributed to the antioxidants (25). The possible anti-teratogenic effect (prevention of congenital abnormalities) of S. maxima aqueous extract against hydroxyurea abuse in mouse embryos was determined. The phycobiliprotein-rich extract showed a protective effect in a dose-dependent manner without any side effects. (26). Valproic acid is a teratogen causing neural tube defects in mammals. The effect of S. plattenisis was investigated in counteracting the oxidative stress imposed by valproic acid. On the gestation day 8, sodium valproate was injected, while spirulina was orally administered at 125, 250, and 500 mg/kg daily from day 0 to 18. Spirulina decreased the incidence exencephaly and other genetic aberrations. Increased level of SOD, CAT and GPx was determined (27). It was reported that spirulina can decrease the frequency of cadmium-induced teratogenicity as exencephaly (a condition in which brain is located outside the skull), micrognathia (a condition when the jaw is undersized) and skeletal abnormalities. At a dose of 500mg/kg, the algal antioxidants could attenuate the toxicity of cadmium on mice foetus (28). Also, the aqueous extracts of spirulina showed protection against t-butyl hydroperoxide-induced cytotoxicity and reactive oxygen species in cultured C₆ glial cells (29). The antioxidant activity of the aqueous extract of S. platensis was assessed using both chemical and cell-based assays. In the cell-based assay, mouse fibroblast cells (3T3) cells were incubated for 1 h in a medium containing the algal aqueous extract or positive controls vitamin C and E prior to the addition of 50 μM DPPH or ABTS. After 24 h incubation, DPPH and ABTS assays were conducted. The extract did not elicit any cytotoxicity and reduced significantly apoptotic cell death due to by 4 to 5-fold. The radical scavenging activity of the extract was measured about 50% of vitamin C and E (30).

Spirulina has emerged as a novel and affordable source of antioxidant ergothioneine (a naturally occurring aminoacid) (31). The antioxidant, radical scavenging, and metal-chelating activities of spirulina were evaluated alone and in combination with whey protein concentrate. The in vitro results showed the dose-dependent activity of spirulina; whereas the in vivo study revealed its protection against CCl₄-induced liver damage. The free radical scavenging properties and antioxidant activity effect were more pronounced in rats receiving the combination of spirulina and whey protein concentrate (32).

Anti-inflammatory and antiarthritic effect:
The anti-inflammatory effect of spirulina was studied in zymosan-induced arthritis in mice (33). After 8 days of administration, the abnormal level of β-glucuronidase in synovial fluid was measured to have fallen down. Inhibition of the inflammatory reaction, without any damage to the chondrocytes was observed. Phycocyanin was assumed to be the component exerting the antiarthritic effect. The effect of polysaccharide extract from S. platensis was assessed on corneal neovascularisation both in vivo and in vitro. Topical application of the polysaccharide significantly inhibited the new vessel formation in alkali burn model of cornea. The results suggested that the polysaccharide may be effective in the therapy of corneal opacities involving neovascularization and inflammation (33).

Antihyperlipemic, antithrombotic and antihypertensive:
The modern sedentary...
lifestyle and greasy food habits have resulted in the overwhelming surge in deadly maladies like atherosclerosis and hypertension. To counteract the cholesterol deposition and to protect the heart, spirulina has been studied vigorously. The fibrinolytic effect of c-phycocyanin from *S. fusiformis* was investigated against vascular endothelial cells. The pigment showed increased clot dissolving activity in dose- and time-dependent manners by inducing urokinase-type plasminogen activator in the cells (34). The effect of oral administration of *S. maxima* was evaluated on serum lipids and blood pressure (35). When consumed at a dose of 4.5 g/day for 6 weeks, a pronounced hypolipemic effect was observed. Further, the potency of *S. platensis* diet at a dose of 0.5 g/day, in treating high fat diet-induced hypercholesterolemia in rabbits was evaluated. Results showed that levels of serum cholesterol decreased in the spirulina-fed rabbits and high-density lipoprotein content measured higher than control (36).

**Amelioration of diabetes drug side effects:**

The drugs prescribed to treat diabetes often lead to many side effects. Common issues as nausea, headache, weight gain, bloating, constipation, diarrhoea may arise or serious problems as liver damage, heart complication, pancreatitis, tumour, bone loss, erectile dysfunction, psychosis and muscle spasm are encountered. The protective effects of *S. fusiformis* extract against rosiglitazone (a standard type II diabetes drug)-induced osteoporosis was assessed in insulin resistant rats. After 45 days, the integrity of the bone surface as well as the bone strength improved. The bone restoration was assumed to be due to the high content of calcium and phosphorous in spirulina. The chromium and α-linoleic acid content was held responsible for decline in the fasting serum glucose, HDL, LDL and triglycerides levels. These findings suggested that synergistic therapy of rosiglitazone and spirulina can be recommended for attenuating the risk of osteoporosis (37). The intake of *S. maxima* extracts, 2 weeks prior to and 4 weeks during streptozotocin administration was reported to reverse the detrimental effects of the drug on male reproductive organ. The extract significantly increased the body and testis weight, metabolic parameters, normal seminiferous tubules, Leydig cell number, testosterone levels and mRNAs for steroidogenic enzymes (38). Clinical prospects of spirulina in alleviating other side effects are worth-exploring.

**Antimutagenic and anticancer effects:**

Several studies testify that spirulina extracts are promising chemopreventive agents. Its antimutagenic effect on mice was investigated using cyclophosphamide as a mutagen (39). The subjects were fed with spirulina, 2 weeks prior to mutagen injection. Improvement in semen quality and prevention of post-implantation losses were observed in spirulina-treated group. It was inferred that the alga offers protection to the germ cells against cyclophosphamide abuse. The selenium-enriched *S. platensis* extract inhibited the growth of human breast cancer MCF-7 cells through induction of G1 cell cycle arrest and mitochondria-mediated apoptosis. Induction of apoptosis was evident from the accumulation of sub-G1 cell population, DNA fragmentation and nuclear condensation. The up-regulation of Bax and Bad expression and down-regulation of Bcl-xl expression accounted for the mitochondrial dysfunction, leading to cancer cell death (40). The oral administration of hot-water extract of *S. platensis* was reported to enhance NK cytotoxicity in humans. Through complex immunological and molecular studies, it was inferred that spirulina can be implicated with BCG-cell wall skeleton for synergistic development of adjuvant-based antitumor immunotherapy (41). Doxorubicin is a well-established anticancer drug, but is riddled with many side effects, including reproductive aberrations. The possible role of spirulina in alleviating its testicular toxicity was investigated in albino rats (42). Rats administered with intra peritoneal doxorubicin at a dose of 3 mg/kg once in a week for 35 days, suffered a significant decrease in sperm count and body weight. Biochemical and histopathological studies showed spirulina at a dose of 250 mg/kg,
administered daily prior to doxorubicin administration restored semen quality, sperm count and body weight. The combination treatment restored testicular impairment to normalcy. The use of spirulina as complementary and alternative medicine (CAM) by breast cancer survivors in Malay was reported (43). The functionalization of selenium nanoparticles with spirulina polysaccharides could be successfully carried out. As a surface decorator, the polysaccharide enhanced the cellular uptake of the assembly and resultant cytotoxicity towards several human cancers. The chemotherapeutic potency of the assembly towards human melanoma A375 cells was mediated through apoptosis (9).

**Immunestimulatory** : It was reported that immulina, a high-molecular-weight polysaccharide from spirulina was a potent activator of nuclear factor kappa B (NF-kB) and induced both IL-1α and TNF-β mRNAs in THP-1 human monocytes (6). Mice fed with immulina-enriched chow for a period of for 4-5 days, exhibited changes in several immune parameters. The ex vivo production of IgA and IL-6 from Peyer’s patch cells was enhanced 2-fold and interferon-α production from spleen cells was increased 4-fold. The enhanced production of these immune indicate that immulina bolsters innate immunity by stimulating both mucosal and systemic immune systems. It was demonstrated that immulina activates human acute monocytic leukemia (THP-1) cells at a dose dependent manner, stimulating leukocytes response to inflammatory and infectious signals (44). The immunomodulatory effect of hot-water extract, phycocyanin and cell-wall component extract of spirulina was evaluated in mice models. The spirulina extracts enhanced proliferation of bone-marrow cells and induced colony-forming activity in the spleen-cell culture supernatant. Granulocyte macrophage-colony stimulating factor and interleukin-3 were detected in the culture supernatant (45). The immune response elicited on consumption of immulina was investigated. As a measure of the adaptive immunity, the changes in leukocyte responsiveness to Candida albicans and tetanus toxoid were evaluated in vitro (46). Intake of immulina caused an immediate but temporary increase of Candida-induced CD4+ T-helper cell proliferation; whereas toxoid-induced T-helper cell proliferation was increased in individuals over 50 years of age. The Candida-elicated production of the Th1 cytokines TNF-α, IL-2 and IFN-γ was increased after immulina administration for 3 days, and the increased IL-2 production lasted up to 56 days. The immune-suppressive effect of S. fusiformis in mice was studied (47). The in vivo effect of spirulina on humoral immune response, cell-mediated immune response and tumour necrosis TNF-α was investigated in mice. When administered at a dose of 400-800mg/kg body wt, it significantly inhibited the humoral as well as cell-mediated immune response and TNF-α in a dose-dependent manner. In vitro tests showed that, S. fusiformis at dose range of 50-100μg/ml decreases the mitogen-induced T lymphocyte proliferation. The above-discussed studies are testimony to the immune-modulatory aspects of spirulina.

**Antimicrobial** : The antimicrobial activity of S. platensis was studied against various Gram-positive, Gram-negative bacteria and fungal species. The methanol extract showed maximum antimicrobial potency. GC-MS analysis identified the volatile components of S. platensis to be heptadecane and tetradecane (48). The supercritical fluid extraction and ethanol fractionation of S. platensis demonstrated some degree of activity towards Staphylococcus aureus, Escherichia coli, Candida albicans and Aspergillus niger (23). S. platensis was tested for its probiotic efficacy and inhibitory effect against several pathogens (17). The doses of 5 and 10 mg/ml promoted growth of Lactobacillus acidophilus up to 171.67% and 185.84%, respectively. Maximum inhibition was reported against Proteus vulgaris, the pathogen notorious for urinary tract and wound infections. The water extract of S. platensis demonstrated significant antimicrobial activity against Klebsiella.
pneumoniae and Proteus vulgaris (NCIM2027); whereas, the acetone extract shows pronounced biological activity against Klebsiella pneumoniae followed by Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli and Staphylococcus aureus (49). The effect of spirulina supplement in combating HIV patients was assessed in a six month follow-up. The patients administered with spirulina at a dose of 10 g/day showed significant improvement in weight, arm girth, number of infectious episodes, CD4 count and protidemia (protein level in blood) (50). HIV-infected patients develop abnormalities of glucose metabolism due to the virus and antiretroviral drugs. The normalizing effect of S. platensis was assessed in HIV-infected patients. The results of the two-month long study suggested that, the insulin sensitivity in HIV patients improves significantly (about 225%) when spirulina supplement (19 g/day) is taken. Further study is needed to evaluate efficacy of spirulina in combating HIV symptoms (51).

Cardio, hepato and pulmo protective:
Doxorubicin used for chemotherapy leads to cardiac toxicity characterized by decrease in myocardial contractility, mediated by reactive oxygen species-induced apoptosis. The cardioprotective efficacy of spirulina was assessed in doxorubicin administered mice (52). The animals treated with 4 mg/kg of the drug, once a week for a month were fed with the algal extract 3 days twice daily for 7 weeks. The spirulina-fed group demonstrated lower mortality (26%), less ascites (peritoneal cavity fluid), lower levels of lipid peroxidation and restoration of antioxidant enzymes.

Several studies have shown that spirulina possesses ameliorative property against stress-induced liver injuries. The hepatoprotective effect of S. platensis on cadmium toxicity was evaluated on rats (53). After a month-long experimental period, the liver samples of the subjects were tested for determination of MDA and cellular antioxidants. S. platensis treatment showed marked decrease in lipid peroxidation (lower MDA) and increase of the GSH, SOD, NO levels. The curative effect S. maxima on patients with non-alcoholic fatty liver diseases were reported (54). Ultrasonography and the aminotransferase data proved the hepatic amelioration by the oral supplementation of the alga. The protective power of c-phycocyanin on H2O2-induced liver damage was investigated (55). Viability of human hepatocyte L02 cell was determined by MTT and alanine aminotransferase (ALT) tests. It was observed that the hepatocytes incubated with c-phycocyanin were able to resist morphological changes, decrease in metabolic enzyme levels and chromatic condensation. The ameliorative effect of spirulina was investigated on non-alcoholic steatohepatitis (fatty liver disease) models of rats. Analyses of blood ans liver samples showed the increase in plasma liver enzymes and liver fibrosis, increases in productions of reactive oxygen species from liver mitochondria and from leukocytes, activation of NK-kB and change in the lymphocyte surface antigen ratio. Spirulina administration reversed these adverse changes to a significant degree. The mechanisms of action were deduced to be due to anti-oxidative and anti-inflammatory actions (56).

The effect of c-phycocyanin extracted from S. platensis was investigated on paraquat-induced pulmonary fibrosis in rats. The animals orally administered with c-phycocyanin (50 mg/kg) daily were subjected to histological assays on days 1, 3, 7, 14, and 28. The homogenized lung sample was measured for hydroxyproline and MDA, which showed significant decrease in c-phycocyanin-treated group. The observation showed that c-phycocyanin could alleviate pulmonary alveolitis and fibrosis in rats with paraquat poisoning (57).

Antianaemic and antileucopenic:
The effect of S. platensis in alleviating toxic impacts of heavy metal-adulterated diet was investigated (58). The results suggested that the algal supplementation may be useful in treatment of leukaemia and anaemia caused by lead and cadmium. Based on experimental outcome, it was inferred that 12 week supplementation of spirulina may
ameliorate anaemia in senior citizens. Steady increase in the corpuscular haemoglobin content in the blood samples of the subjects was recorded (59).

**Neuroprotection and tissue engineering**: The effect of *S. platensis* extract and its phycocyanin was investigated on the activities of the antioxidant enzymes SOD, CAT, GPx and GR, lipid peroxidation inhibitory activity and glutathione in iron-subjected SH-SY5Y neuroblastoma cells (60). The bioactive compounds exerted antioxidant activity evident from its protection of glutathione peroxidise and glutathione reductase against oxidative stress. These results suggested that *S. platensis* extract can be implicated for therapy of iron-mediated neurodegenerative disorders as Alzheimer’s or Parkinson diseases. The protective effect of spirulina in transient middle cerebral artery occlusion (MCAO)-induced focal cerebral ischemia-reperfusion injury was evaluated in rats (61). Male albino rats administered with spirulina at a dose of 180 mg/kg, per day for 7 days were subjected to arterial blockage. Spirulina pretreatment significantly reduced the histological changes and neurological deficits. Significant reversal in the elevated brain MDA content and restoration of the decreased enzymes were observed. The possible protective potential of spirulina on hippocampal progenitor cells against lipopolysaccharide (LPS) abuse was determined (62). Rats fed with 0.1% spirulina-supplemented diet were given single intra peritoneal injections of LPS (1 mg/kg). It’s followed by injection of the rats with thymidine analog BrdU (50 mg/kg), in order to detect the proliferating cells. Quantification of the BrdU positive cells showed that the spirulina-enriched diet could partially check the LPS-induced decrease in progenitor cell proliferation. Spirulina showed more pronounced effect in combination with other natural antioxidants as blueberry, green tea, vitamin D and camosine.

Like many other marine organisms, spirulina synthesizes inorganic nanoparticles and holds immense promise in nanomedicines. Recently, spirulina has made major strides in tissue engineering domains. A highly porous scaffold was fabricated by electrospinning its biomass. The nanofibers in the scaffold might act as extracellular matrices for stem cell culture (63). The electrospun polycaprolactone nanofiber containing spirulina was evaluated for its potential as extracellular matrix in the culture of glial cells (64). The extract was observed to increase growth and metabolic activity of the astrocytes. This result holds promise in treatment of central nervous system (CNS) injury. A hollow copper microspiral was synthesized using spirulina as a scaffold (65). It was suggested that an array of low cost and reproducible biomaterials could be manufactured using this filamentous alga.

**Aquaculture and livestock feed**: It was observed that white shrimp injected with the hot-water extract of *S. platensis* and immersed in the extract-fortified seawater could combat *Vibrio alginolyticus* *L. vannamei* better than the control. At the studied doses, increased phagocytic activity and the pathogen elimination was observed (66). It was observed that *S. platensis* or *S. maxima* supplementation in fish feed significantly enhanced the antioxidant ergothioneine content (31). The antimicrobial potency of ethanolic extracts of *S. platensis* was studied against fish and shellfish pathogens e.g. *Pseudomonas putida*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Aeromonas hydrophila*, *Vibrio alginolyticus*, *Vibrio anguillarum*, *Vibrio fluvialis*, *Vibrio parahaemolyticus*, *Vibrio harveyi*, *Vibrio fisheri*, *Edwardsiella tarda* and *Escherichia coli*. The promising result recommends the inclusion of the alga in aqua feed (67). Spirulina was evaluated as a substitute of soybean and alfalfa in the feed, on the basis of meat quality of growing rabbits (68). No significant changes in biochemical composition were observed apart from increased fatty acid content in the perirenal fat in spirulina-fed rabbits. The results of this study suggest that *S. platensis* could potentially be used in rabbit nutrition with consequent benefits on the nutritional quality of rabbit meat for consumers.

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**Advancement and bottlenecks in spirulina technology**: Spirulina needs multiple steps of processing before reaching to market (Fig. 3). So, appropriate technology can spare manual labour, energy and expenses. Current scenario in cultivation, dehydration, extraction and purification is explored below.

The amount of phenolic compounds could be enhanced approximately eight-fold by light treatment (69). The shift in high light intensity led to increase in total amounts of carbohydrate, phycocyanin, carotenoid, malondialdehyde and antioxidant activities. A trinuclear iron (III) furoate was developed for regulating the biochemical composition of *S. platensis* biomass, which when supplemented at 5-10 mg/l increased iron, amino acid, peptide and carbohydrate contents in the alga (70). The influence of several factors on growth and protein content of *S. platensis* was determined, which showed about 60% improved productivity at aerial sparging without any additional mechanical stirring, low salinity and 1% of CO$_2$. Under intermittent illumination, when light/dark frequency increased from 0.01-20 Hz, specific growth rate and light efficiency were enhanced (71). It was suggested that silver coated polyester film fixed in culture racks serves as a reflector of light intensity and stimulates chlorophyll production (72). These innovative strategies may be adopted for energy-efficient and cost-effective spirulina cultivation.

Pre-dehydration treatment and drying are crucial steps for preservation of spirulina products. Antioxidants (á-tocopherol and tertiary-butyl hydroquinone or TBHQ) and two Blanching methods (microwave and water bath) were employed to inactivate enzymes prior to dehydration. TBHQ proved better than á-tocopherol in minimizing the lipid peroxidation of blanched samples; whereas á-tocopherol was more suited than TBHQ in unblanched samples. Microwave blanching exerted a greater stabilizing effect than water bath blanching. The combined effect of TBHQ and microwave blanching was found to be the most effective pre-dehydration treatment for minimizing lipid peroxidation in drying spirulina. Optimization of the low-cost sun-drying method produced a dried product with comparable stability to that of spray-dried product (73). Drying of *S. platensis* on convective hot air was optimized through response surface methodology (RSM). At the optimum condition of 55°C temperature and 3.7 mm sample thickness, least loss in bioactive lipids and pigments were observed (74). However, these drying techniques lead to the loss of a significant percentage of phycocyanin and carotenoid, warranting technological innovation.

The advent of effective extraction, purification, contaminant detection techniques and equipment has facilitated nutrients isolation from spirulina. The efficacy of supercritical carbon dioxide extraction and conventional solvent extraction was compared in recovery of α-linoleic acid from *S. platensis*. RSM optimization proved the suitability of the former over the latter in complete retrieval of α-linoleic acid (75). The supercritical CO$_2$ extraction of antioxidants from *S. platensis* was optimized using RSM. About 10.26 g/kg of extracts, containing flavonoids, α-carotene, vitamin A and α-tocopherol, palmitic acid, linolenic acid and linoleic acid was obtained under the optimum conditions of 48°C at 20 MPa over a period of 4h (76). The supercritical fluid extraction parameters were optimized by RSM to obtain appreciable yield of vitamin E from *S. platensis* (4). The optimal conditions enhanced the tocopherol content to 12-fold as compared to the initial concentration in the crude form. The effect of ultrasonic extraction on yields of anticancer polysaccharides from *S. maxima* was studied (8). At optimal extraction condition of 60 kHz frequency and 60°C temperature applied for 30 min, extraction yield of 19.3% was reported. Human stomach cancer cells showed about 89% susceptibility to the water-soluble polysaccharides-rich extract. Microfiltration and ultrafiltration conditions proved suitable for pure, food grade c-phycocyanin extraction (77). An aqueous two-phase multi-stage countercurrent distribution technology was suggested for...
effective and low cost separation of c-phycocyanin and allophycocyanin from *S. platensis* cell homogenate (12). The adulterant determining efficacy of least square support vector machines (LS-SVM) models under both full spectra and near infra red spectroscopy was advocated (78). For the optimum extraction of β-carotene from *S. platensis*, the processing parameters were optimized. The most favourable conditions were determined to be 1.5 spirulina in 50ml n-heptane at 30°C ultrasonicated for 8 min. Methanol preretreatment (2 min) raised the yield 12 times which measured 47.10% (79).

**Conclusion**

Being consumed since centuries, spirulina has well established itself as a superfood, an excellent weapon against an array of nutritional deficiencies. The above presented findings validate the potency of spirulina in thwarting several health issues. Moreover, there is a plethora of unexploited novel compounds and biological activities in this alga, worth-exploring. Innovative formulations are required to fortify conventional foods with spirulina. Economically feasible techniques of cultivation, drying and isolation of bioactive compounds are needed for maximum utilization. In recent years, spirulina has garnered enormous attention from research fraternity as well as industries as a thriving source of nutraceuticals and pharmaceuticals. Spirulina-based dietary habit must be promoted in the interest of the masses. This cheaply accessible functional food can sustainably combat malnutrition that eclipses the third world countries. However, quality control should be taken care of in order to ensure consumer safety. The clinical application of this microalga as complementary and alternative medicine (CAM) can reduce the cost of healthcare. This review is expected to convey contemporary scenario, kindle interest and help envision new implications of this abundantly available resource.

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