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SPIRULINA IN MODERN MEDICAL THERAPY: CURRENT KNOWLEDGE

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ABSTRACT

Spirulina, a Blue-Green Alga (BGA) that are the most primitive life forms on earth and have been consumed as food or medicine by humans for centuries. *Spirulina* contain various bioactive components, such as phycocyanin, carotenoids, essential amino acids, γ-linolenic acid, fibers, and plant like sterols, B vitamins, calcium, phosphorous, iron, pigments such as β-carotene, xanthophylls, and chlorophyll, and other bioactive compounds which can promote optimal health in humans. Studies have demonstrated that *Spirulina* species or their active components have plasma total cholesterol and triglyceride-lowering properties due to their modulation of intestinal cholesterol absorption and hepatic lipogenic gene expression. Furthermore, *Spirulina* is known to inhibit lipid peroxidation and have free radical scavenging activity, which can be beneficial for the protection against oxidative stress. The aforementioned effects of *Spirulina* can contribute to the prevention of many metabolic and inflammatory diseases. This review provides an overview of the current knowledge of the health-promoting functions of *Spirulina* against major diseases and health threats that prevail today and the protective effects of *Spirulina* against these diseases.

KEYWORDS

Spirulina, Bioactive Compounds, Health promoting effects.

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INTRODUCTION

Spirulina is a spiral blue green alga found ubiquitously in nature from a wide variety of ecological niches and environmental conditions. This alga is relatively easy to cultivate but flourishes only in alkaline lakes with an extremely high pH and in large outdoor ponds under controlled conditions. Typically there are few geographic areas that have enough sunlight to support growth of algae in open ponds naturally. However there are many reports now of this

organism from fresh water lakes and other water bodies[1]. It is widely known for its very high protein content and as a popular protein substitute to fight malnutrition. *Spirulina* is a "Super food". This alga is a very nutritious, concentrated whole food known to humankind. This spiral cyanobacterium has vibrant history, and occupies an intriguing biological and ecological niche in the plant kingdom. *Spirulina* is truly an amazing food, full of nutritional wonders[2].

Spirulina, contains large amounts of protein (70% dry weight), carotenoid (4000mg/kg), (omega-3 and omega-6 polyunsaturated fatty acids, Gamma Linolenic Acid (GLA), sulfolipids, glycolipids, polysaccharides, provitamins; vitamin A, vitamin E, various B vitamins; and minerals, including calcium, iron, magnesium, manganese, potassium, zinc, and selenium[3]. It is, therefore, a potential therapeutic agent for treating oxidative stress-induced diseases[4]. Apart from proteins, it also contains vitamins, especially B12 and provitamin A (β-carotenes), and minerals, especially iron. It is known to be rich in phenolic acids, tocopherols and γ-linolenic acid[5]. Lack of cellulose containing cell walls makes it easy to be digested[5]. Many studies and toxicological research has shown that *Spirulina* is safe for consumption. *Spirulina* is widely found in health food stores and is sold mainly as a dietary supplement in the form of health drinks or tablets. Nowadays, this organism is used as a food supplement and is marketed in the form of pills, capsules and powder or incorporated into various categories of food products like cakes, biscuits, noodles, health drinks, etc. Many countries world-wide are developing strategic programs for the production and use of *S. platensis*. This microalga has been used for many years now as dietary supplements without significant side-effects[6]. Because of the rich presence of many other bioactive compounds in *Spirulina* it is plausible that it has many more important applications especially in the medical field. This review attempts to highlight this aspect of *Spirulina*. This review article is an attempt to summarize the plausible available information concerning the applications of *Spirulina*, human clinical potential results and clinical data related to the safety and side effects of *Spirulina*.

MEDICAL APPLICATIONS

From ancient times *Spirulina* was used as a food component and it has been thoroughly investigated using *in vitro* and *in vivo* experiments, including cell and tissue culture, animal testing and human clinical trials, to establish its role in human health management. There has been a surge and rapid rise in the number of publications in peer reviewed scientific journals and book chapters covering health aspects of *Spirulina* that have appeared during the last three decades. These articles described experimental approaches involving whole cell *Spirulina* preparations, various cell extracts and purified biomolecules, aiming at elucidating the potential health benefits of the consumption of this microalga, so far with exciting results. Potential health effects included: immunomodulation, antioxidant, anticancer, antiviral and antibacterial activities, as well as positive effects against malnutrition, hyperlipidemia, diabetes, obesity, inflammatory allergic reactions, heavy metal/chemical-induced toxicity, radiation damage and anemias[5,7-12].

ANTI-CANCER AND IMMUNE SYSTEM EFFECTS

Chemotherapy is one of the principle treatment methods used to cure cancer. Another approach is to use a group of drugs that kill or inhibit the growth of cancer cells[13]. These drugs have serious life threatening side effects, like hair loss, mouth sores, diarrhea, and nausea and vomiting, loss of appetite and fatigue[13]. These conditions make it imperative to search for new anticancer agents from various resources. *Spirulina* has many properties that make it a very attractive alternative in cancer treatment. Properties of *Spirulina* increase phagocytic activity of macrophages and stimulate antibodies and cytokines production. It may also help in lipid and carbohydrate metabolism. Studies also demonstrate its benefits as an antiviral agent

against HIV and other cancers[13]. There are no *in vivo* studies providing strong evidence supporting the possible antiviral properties of *Spirulina*. Water extract of *S. platensis* produced an active component that is a sulfated polysaccharide, calcium spirulan (Ca-Sp). According to Hayashi *et al*[14], Ca-Sp inhibits the *in vitro* replication of several enveloped viruses including *Herpes simplex* type I, human cytomegalovirus, measles and mumps virus, influenza A virus and human immunodeficiency virus-1 (HIV-1).Another more recent study showed *in vitro* that HIV-1 replication in human T-cells, peripheral blood mononuclear cells and Langerhan were inhibited with an aqueous extract of *S. platensis*[15]. NK activation by *Spirulina* has some advantage in combinational use with BCG-cell wall skeleton for developing adjuvant-based antitumor immunotherapy[16]. The molecular mechanism of the human immune potentiating capacity of *Spirulina* has been evaluated by analyzing blood cells of volunteers with pre and post oral administration of hot water extract of *Spirulina*. As a result, in humans *Spirulina* acts directly on myeloid lineages and either directly or indirectly on NK cells[17].

USE OF *SPIRULINA* IN CHRONIC FATIGUE

Spirulina an alga with unique constituents has been highlighted as the food of the future that contribute to high energy levels in people who consume it. Polysaccharides like Rhamnose and Glycogen and essential fat like GLA are absorbed easily by human cells and help in energy release. *Spirulina* supports healthy *Lactobacillus* in the intestine, enabling the production of Vitamin B6, that also helps in energy release. Despite this promotion, the only available placebo-controlled randomized trial showed that the scores of fatigue were not significantly different between *Spirulina* and placebo. *Spirulina* administered at a dose of 3 g per day did not ameliorate fatigue more than the placebo in any of the four subjects and possibly it has no effect on chronic fatigue[18].

Role of *Spirulina* in Immunomodulation

In a clinical trial 40 male and female volunteers between the age group of 50 years or older took a *Spirulina* supplement of 3 g per day for 12 weeks. A marked increase in values of the mean corpuscular hemoglobin in volunteers of both sexes was recorded. A rapid increase in indoleamine 2, 3-dioxygenase enzyme activity that is a sign of immune function and white blood cell count were also observed for the majority of the volunteers[19]. In a recent clinical trial involving two studies, a pilot study with 11 individuals and a double-blind placebo controlled study with 12 individuals, healthy volunteers supplemented their diet with 200 or 400 mg per day, respectively, for seven days with Immulina® an extract of *A platensis*. An increase of natural killer cell activity following administration of Immulina® was observed. Evidence was presented that Braun-type lipoproteins of the *Spirulina* commercial extract were responsible for the major portion of the *in vitro* monocyte activation[20]. HIV-infected and under nourished patients in a randomized study were studied to compare the effect of *A. platensis* vs. soybean as food supplements on insulin-resistant HIV-infected patients[21]. 19 g of supplement (*Spirulina* or soybean) were administered to patients daily for 8 weeks. It was concluded that the insulin sensitivity in HIV patients improved more when *Spirulina* rather than soybean was used as nutritional supplement[22]. Furthermore, when HIV-infected or HIV-negative undernourished children and HIV-infected adults were treated with *Spirulina* supplementation, clinical improvement was always observed, including weight increase, improvement of hematological parameters and decrease in the HIV viral load[23-26].

EFFECTS AGAINST HYPERLIPIDEMIA

In a study the antioxidant activity of *Spirulina maxima* was evaluated against lead acetate-induced hyperlipidemia and oxidative damage in the liver and kidney of male rats. The study showed that *Spirulina maxima* was able to ameliorate the

negative effects of the lead acetate-induced changes on plasma and liver lipid levels and on the antioxidant status of the liver and kidney. *S.maxima* brought about great improvement in the biochemical parameters of the liver and kidney compared the normal values of the Control group[27]. Blood pressure and plasma lipid concentrations decreases, especially triacylglycerols and low density lipoprotein-cholesterol have been demonstrated as a result of oral consumption of *Spirulina*. It has also been shown to indirectly modify the total cholesterol and high density lipoprotein cholesterol values. A water extract from *Spirulina* may inhibit the intestinal absorption of dietary fat by inhibiting pancreatic lipase activity[2].

ROLE OF *SPIRULINA* IN ALLERGY AND RHINITIS

It has been well documented that *Spirulina* has anti-inflammatory properties by inhibiting the release of histamine from mast cells[28,29]. In a recent randomized, double-blind placebo-controlled trial[30], individuals with allergic rhinitis were given daily, either placebo or *Spirulina* for 12 weeks. Peripheral blood mononuclear cells were isolated before and after the *Spirulina* feeding and levels of cytokines (interleukin-4 (IL-4), interferon-γ (IFN-γ) and interleukin-2), which are important in regulating immunoglobulin (Ig) E-mediated allergy, were measured. The study showed that high dose of *Spirulina* significantly reduced IL-4 levels demonstrating the protective effects of this microalga toward allergic rhinitis. Ishii *et al*[31] studied the influence of *Spirulina* on IgA levels in human saliva and demonstrated that it enhances IgA production, suggesting a pivotal role of microalga inmucosalimmunity. A Japanese team identified the molecular mechanism of the human immune capacity of *Spirulina* by analyzing blood cells of volunteers with pre- and post-oral administration of hot water extract of *Spirulina platensis*. IFN-γ production and Natural Killer (NK) cell damage were increased after administration of the microalga extracts to male volunteers[32]. In a recent double-blind, placebo-controlled study evaluating the influence of *Spirulina* for treating patients with allergic rhinitis, the algal consumption significantly improved the symptoms and physical findings compared with placebo, including nasal discharge, sneezing, nasal congestion anditching[33].

EFFECTS AGAINST DIABETES, OBESITY AND HYPERTENSION

Water-soluble fraction of *Spirulina* was found effective in lowering the serum glucose level at fasting while the water-insoluble fraction suppressed glucose level at glucose loading[34]. Similar results were found in many other studies. In a human clinical study involving 15 diabetics, a significant decrease in the fasting blood sugar level of patients was observed after 21 days of 2 g/day *Spirulina* consumption. In a double-blind-crossover (study versus placebo,) Eun *et al,* (2008)[35] have found that a supplementary diet of 2.8g of *Spirulina* 3 times a day over 4 weeks resulted in a statistically significant reduction of body weight in obese outpatients[36]. *Spirulina* has also been found to suppress high blood pressure in rats. A vasodilating property of rat aortic rings by *Spirulina* possibly dependent upon a cyclooxygenase dependent product of arachidonic acid and nitric oxide has been reported by Paredes-Carbajal *et al*, (1991)[37] did a preliminary study on the effect of polysaccharides and phycocyanin on peripheral blood and hematopoietic system of bone marrow in mice[38-40]. Their studies showed that C-phycocyanin and polysaccharides from *Spirulina* had a high erythropoetin (EPO) activity[5].

Spirulina in Cardiovascular Diseases

Cardiovascular disease is one of the major causes of death in developed countries, despite increased awareness, and high cholesterol is one of the most important risk factors in atherosclerosis. Nakaya *et al*[41], in the first human study, gave 4.2 g day^{-1} of *Spirulina* to 15 male volunteers and, although there was no significant increase in high-density lipoprotein (HDL) levels, the authors observed a significant reduction of high-density lipoprotein (LDL) cholesterol after 8 weeks of treatment. The

atherogenic effect also declined significantly in the above group[43]. Ramamoorthy and Premakumari[42] in a more recent study administered *Spirulina* supplements in ischemic heart disease patients and found a significant reduction in blood cholesterol, triglycerides and LDL cholesterol and an increase in HDL cholesterol. More research is needed before *Spirulina* can be recommended to lower cholesterol levels but its role as a natural food supplement in combating hyperlipidaemia, in combination with other therapeutic options, should not be overlooked. Finally, Mani *et al*,[43] in a clinical study, found a significant reduction in LDL: HDL ratio in 15 diabetic patients who were given *Spirulina*. This alga also has been found to reduce high blood pressure in rats.

ANTI-INFLAMMATORY EFFECTS

Free bilirubin, in recent research's show, that it functions physiologically as a potent inhibitor of NADPH oxidase activity. Blue green algal chromophore phycocyanobilin (PCB), such as *Spirulina*, also has been found to be a potent inhibitor of this enzyme complex, likely because in mammalian cells it is rapidly reduced to phycocyanorubin, a close homolog of bilirubin[44]. The significance of the protean roles of NADPH oxidase activation in pathology is well known, it thus appears likely that PCB supplementation may have versatile potential in prevention and therapy particularly in light of rodent studies demonstrating that orally administered *Spirulina* or phycocyanin can exert a wide range of anti-inflammatory effects. Until PCB-enriched Spirulina extracts or synthetically produced PCB are commercially available, the most feasible and least expensive way to administer PCB is by ingestion of whole *Spirulina*[44].

CHRONIC ARSENIC POISONING: A RANDOMIZED TRIAL

Arsenic toxicity has affected millions of people in Bangladesh, India, Taiwan and Chile who consume high concentration of arsenic through drinking water that are released into the waters from industrial effluents. So all these people are at risk of chronic arsenic poisoning for which there is no specific treatment. A placebo-controlled, double-blind study was conducted to evaluate the effectiveness of *Spirulina* extract plus zinc in the treatment of chronic arsenic poisoning[45]. Forty-one patients with chronic arsenic poisoning were randomly treated by either placebo (17 patients) or *Spirulina* extract (250 mg) plus zinc (2 mg) (24patients) twice daily for 16 weeks. Each patient was supplied with arsenic-safe drinking water by installing a locally made water filter at household level. Effectiveness of *Spirulina* extract plus zinc was evaluated by comparing changes in skin manifestations (clinical scores) and arsenic contents in urine and hair, between the placebo- and S*pirulina* extract plus zinc-treated groups. Results showed that *Spirulina* extract plus zinc twice daily for 16 weeks may be useful for the treatment of chronic arsenic poisoning with melanosis and keratosis[45]. More randomized trials are required but the results are promising.

PROBIOTIC EFFECTS

Live microbes are consumed as human food supplement for centuries which has a beneficially effect on the host because of its well-known nutritional value. The probiotic efficiency of *S. platensis* is its positive influence on lactic acid bacteria and also its potent antibacterial activity against human pathogenic bacteria[46]. Phenolic acids, tocopherols and ß-carotene present in *Spirulina* that are known to exhibit antioxidant properties. Miranda *et al,* (1998)[2] evaluated the antioxidant capacity of a *Spirulina* extract[47]. A methanolic extract of *Spirulina* was determined *in vitro* and *in viv*o to elucidate antioxidant properties. Due to its high antioxidant properties and high levels of other potent bioactive compounds *Spirulina* has been shown to prevent cataract[48], acute allergic rhinitis[49], cerebral ischemia[3] and vascular reactivity[50] and has also been shown to be effective against cadmium[51] and arsenic induced-toxicities[52]. Some of these properties have been confirmed through studies while additional

pharmacological properties need to be proved. *Spirulina platensis* is effectively suppressed peripheral sensitization via modulation of glial activation, improved motor recovery in collagen-induced arthritic rats[53].

REDUCES RADIATION SICKNESS

In Ukraine and Belarus, *Spirulina* has been used as a "medicine food" for treating radiation sickness. There have been reports of children from Chernobyl who suffered radiation poisoning from eating food grown on radioactive soil. Their bone marrow was damaged, rendering them immune-deficient. Bone marrows of such children cannot produce normal red or white blood cells. Also these children were anemic and suffered from terrible allergic reactions. These sick children when fed with five grams of *Spirulina* each day made dramatic recoveries within six weeks. Research continuing through 1999 in Belarus showed immune building, normalization of peroxide lipid oxidation and detoxifying effects of *Spirulina* supplements in children and teenagers. *Spirulina* produced a polysaccharide that showed both chemo-protective and radio-protective properties in laboratory animals *Spirulina* extract provided a radio-protective effect in mouse bone marrow cells. An extract of *Spirulina* combined with vitamin complex led to a correcting effect in rats exposed to radiation[54].

ANTI-AGING AND NEUROPROTECTIVE EFFECTS

Significant number of studies suggest *Spirulina* should be considered therapeutic intervention for the aging brain. Some of the outstanding properties of *Spirulina* could be linked to the activation of the innate immune system, first line of defense in our bodies. The inflammation seen with normal aging can be down regulated with spirulina, as seen by the benefits of *Spirulina* administration in arthritis. *Spirulina* seem to have certain effects on the central nervous system to counteract oxidative stress and inflammation that occur as a consequence of aging and to aid regeneration of the brain following injury or neurodegenerative disease[55].

***SPIRULINA* REDUCES KIDNEY AND LIVER TOXICITY CAUSED FROM MERCURY, DRUGS AND CHEMICAL POLLUTANTS**

Detoxification of the body is an essential role played by the kidney in cleansing the body of toxins. There has been a keen interest to search for substances that can help cleanse the kidneys of toxic side effects from heavy metal poisoning or from high intake of medicines or pharmaceutical drugs. In Japan, studies with rats suggest *Spirulina* phycocyanin extract may have a beneficial effect for humans suffering from heavy metal poisoning. Phycocyanin enhances the immune system. Phycocyanin raises lymphocyte activity and acts by strengthening the body's resistance through the lymph system is suggested by research in Japan. Prevention degenerative organ diseases by boosting immunity can be caused by Phycocyanin. Intake of small dosages of phycocyanin daily maintains or accelerates normal control cell functions that prevents generation of malignancy such as cancer or inhibits its growth or recurrence as suggested by a Japanese patent[56-58].

CONCLUSION

Spirulina has potential for being a wonder food supplement and several leading organizations have praised its beneficial effects. In fact, it is among the most nutritious, concentrated whole food sources found in nature, contributing to its being known as a super food. In this review, we have compared a volume of research showing the potential of this microalga as a food supplement and the range of health benefits and the role of its bioactive compounds to combat major diseases. Studies on this spiral blue-green algae began in the 1970's, and since there have a significant increase in the interest in this micro-algal research.

From this review it may be concluded that *Spirulina* shows potent immune stimulating effects; anti-viral activity against a variety of harmful viruses; promise as a cancer preventative agent and in the treatment of tumors. *Spirulina* shows far ranging cardiovascular benefits including improvement of blood lipid profiles, prevention of atherosclerosis,

and control of hypertension. The potential of *Spirulina* and its constituent pigment C-phycocyanin in reducing the toxic effects of heavy metals, drugs and toxic chemicals on kidney and liver, its role in reducing radiation effects and neurotoxicity has been reviewed and it encourages further research for considering daily supplementation with *Spirulina*.

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CONFLICT OF INTEREST
I declare that I have no conflict of interest.

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