Spirulina in Health Care Management

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Abstract: *Spirulina* is a photosynthetic, filamentous, spiral-shaped and multicellular edible microbe. It is the nature's richest and most complete source of nutrition. *Spirulina* has a unique blend of nutrients that no single source can offer. The alga contains a wide spectrum of prophylactic and therapeutic nutrients that include B-complex vitamins, minerals, proteins, γ-linolenic acid and the super anti-oxidants such as β-carotene, vitamin E, trace elements and a number of unexplored bioactive compounds. Because of its apparent ability to stimulate whole human physiology, *Spirulina* exhibits therapeutic functions such as antioxidant, anti-bacterial, antiviral, anticancer, anti-inflammatory, anti-allergic and anti-diabetic and plethora of beneficial functions. Spirulina consumption appears to promote the growth of intestinal micro flora as well. The review discusses the potential of Spirulina in health care management.

Keywords: Spirulina, Health Care, Oxidative stress, Diabetes, Immunomodulation, Neutraceutical.

INTRODUCTION

Spirulina is a microscopic and filamentous cyanobacterium that belongs to family Oscillatoriaceae and has a long history of use as food and food supplement. Its name derives from the spiral or helical nature of its filaments. It was used as food in Mexico during the Aztec civilization some 400 years ago. It is still being used as food by the Kanembu tribe in the lake Chad area of the Republic of Chad where it is sold as dried bread called "dihe" [1]. *Spirulina* has been produced commercially for the last 20 years for food and specially feeds [5, 6, 7]. Habitats for *Spirulina* include the Pacific Ocean near Japan and Hawaii, and large freshwater lakes, including Lake Chad in Africa, Klamath Lake in North America, Lake Texcoco in Mexico, and Lake Titikaka in South America. The current use of this resource has three precedents: tradition, scientific and technological development, and the so-called, "green tendency" [32]. From 1970, the nutritional and medicinal studies on *Spirulina* have proliferated [25]. In 1970, the German Federal Republic supported investigations on human consumption of *Spirulina* in India, Thailand and Peru. In the Asian countries, the production was focussed on nutritious support for the undernourished population. The supplementation of meals with *Spirulina* could be a solid and cost-effective option to provide to the most vulnerable populations a solid basis of physical and mental health. Although this ancient alga has been consumed for centuries by traditional people, it was only rediscovered by scientists 30 years ago.

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The fame of this cyanobacterium is a result of its nutritional potential and economic significance, which arises from the unique characteristics of the cultivated species like *S. fusiformis, S. laxissima, S. subsalsa, S. lonar, S. labyrinthiformis, S. maxima* and *S. platensis*. Among these, *S. maxima* and *S. platensis* are widely exploited for the nutritional and therapeutic aspects. *Spirulina* is eaten as a nourishing food concentrate as it is highly rich in protein (60-70%) [16], vitamins (4%) [5], essential fatty acids and antioxidants. *Spirulina* serves as source of essential fatty acids such as linoleic acid (LA), γ-linolenic acid (GLA), [56], phycobiliproteins [8, 19, 20, 72], the most important being phycocyanin and allophycocyanin [12, 13], amino acids; the highest values are leucine (10.9% of total amino acids), valine (7.5%) and isoleucine (6.8%) [16] and minerals like iron. Groups of undernourished children and adults have responded well to *Spirulina* administration [69]. Treatment of the victims of nuclear disaster at Chernobyl, especially children whose bone marrow had been damaged from radiation exposure boosted the immune system [55]. Recent research has proven its high nutritive value and has lent credence to the claim of *Spirulina* as a high-energy super food and possible appetite suppressant [55]. Several studies have outlined the biochemical composition, immuno-stimulatory and therapeutic potential of *Spirulina* [33]. The World Health Organization described *Spirulina* as one of the greatest super foods on earth and NASA considers it as an excellent compact food for space travel, as small amount can provide a wide range of nutrients [40]. Toxicological studies of several *Spirulina* species have not revealed any toxic effect on kidney, liver, reproductive system and body physiology in general during and after acute or chronic doses [14, 44, 67, 82]. *Spirulina* lacks cellulose cell walls and therefore does not require chemical or physical processing in order to become digestible [18]. Moreover, *Spirulina* is relatively easy to cultivate, thereby sparking the early interest in it as a

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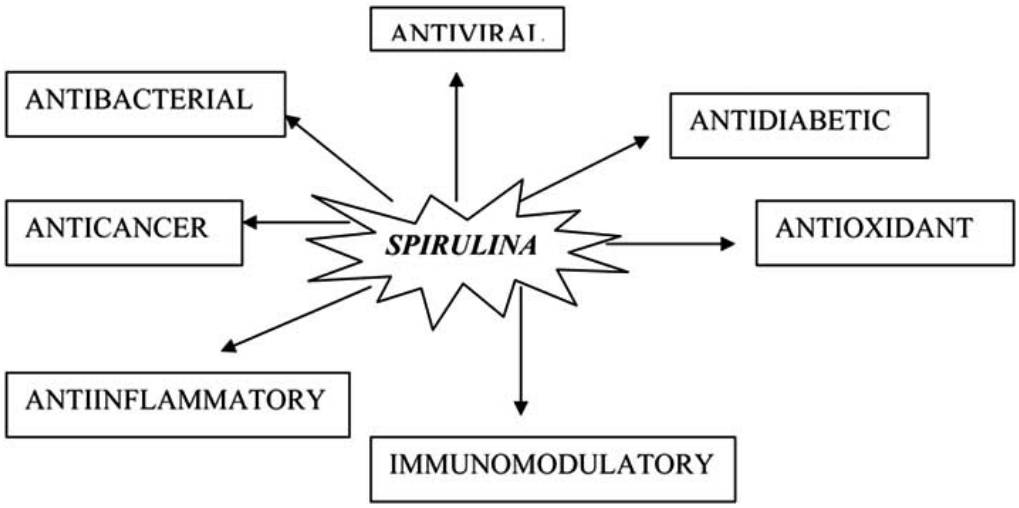

Fig. (1). Applications of *spirulina* in health care.

commercial food supplement with potential therapeutic health benefits. *Spirulina* is gaining more attention in recent times from medical scientists as a neutraceutical and source of potential pharmaceuticals (Fig. **1**).

ANTI-OXIDANT PROPERTIES OF *SPIRULINA*

Several studies have demonstrated that *Spirulina* possess significant antioxidant activity both *in vitro* and *in vivo*. Miranda *et al.* [51] studied the antioxidant activity of carotenoids, phenolics and tocopherols extracted from *S. maxima* and found that the phenolic compounds responsible for the antioxidant properties of the *S. maxima* extracts were organic acids (caffeic, chlorogenic, quimic, salicylic, synaptic and trans-cinnnamic) which acted individually and synergistically while Estrada *et al.* [21] demonstrated the antioxidant activity of the phycobiliproteins, phycocyanin and allophycocyanin present in *Spirulina* biomass. Manoj *et al* [49] reported that the alcohol extract of *Spirulina* inhibited lipid peroxidation more significantly (65%) than the chemical antioxidants like α-tocopherol (35%), butylated hydroxy anisol (45%) and β-carotene (48%). The water extract of *Spirulina* is also shown to have more antioxidant effect (76%) than gallic acid (54%) and chlorogenic acid (56%). Phycocyanin also inhibited liver microsomal lipid peroxidation. Zhi-gang *et al.* [84] studied the antioxidant effects of two fractions of a hot water extract of *Spirulina* using three systems that generate superoxide, lipid, and hydroxyl radicals. Both fractions showed significant capacity to scavenge hydroxyl radicals (the most highly reactive oxygen radical) but no effect on superoxide radicals. One fraction had significant activity in scavenging lipid radicals at low concentrations.

ANTI-DIABETIC PROPERTIES OF *SPIRULINA*

Spirulina has been shown to possess antihyperglycemic and antihyperlipidemic properties in experimental models. In patients with type-2 diabetes mellitus, *Spirulina* diet lowered fasting blood glucose, postprandial glucose and reduction in the glycosylated haemoglobin (HbA-1c) [40]. The aqueous extract of *S. maxima* is very effective in alleviating the abnormalities of carbohydrate and lipid metabolisms induced by excess fructose in Wistar rats (Urmila *et al.,* Unpublished observations). Treatment with *Spirulina* in diabetic rats increased the hexokinase activity and decreased the glucose-6-phosphatase activity. *Spirulina* has a beneficial effect on plasma insulin and C-peptide [47]. In a study measuring the effect of blue green algae on glucose levels in diabetic rats & mice, the water soluble fraction is found to be effective in lowering the serum glucose level at fasting as well as on glucose loading [74, 65]. *S. maxima* exhibited hypolipidemic effects, especially on triacylglycerols (TAG) and the LDL-Cholesterol [78] and prevented dyslipidemia induced by carbon tetrachloride [77]. The elevation of total cholesterol, LDL and VLDL cholesterol and phospholipids in the serum was reduced significantly when the experimental high cholesterol diet was supplemented with 16% *Spirulina* [39]. The fall in HDL cholesterol caused by the high cholesterol diet is also prevented in mice fed with *Spirulina*. Adipohepatosis induced by a high fat and high cholesterol diet is also reduced rapidly when the mice are shifted from the high fat, high cholesterol diet to a basal medium supplemented with *Spirulina*. Liver levels of triglycerides and phospholipids responded significantly in rats fed a diet supplemented with 5% *Spirulina* and either 60% glucose or 60% fructose [17]. The biomodulatory effects of *Spirulina* on mammalian physiology are summerised in Table **1**.

IMMUNOMODULATRY EFFECTS OF *SPIRULINA*

Spirulina is a powerful tonic for the immune system. In studies on mice, hamsters, chickens, turkeys, cats and fish, *Spirulina* consistently improved immune system function. *Spirulina* not only stimulates the immune system, it actually enhances the body's ability to generate new blood cells. The spleen and thymus glands show enhanced function. Macrophages, T-cells and Natural killer (NK) cells exhibit enhanced activity following *Spirulina* administration. Feeding of even small amounts of *Spirulina* to mice resulted in following immuno-modulatory functions [48, 24].

[1] Mice fed *Spirulina* showed increased numbers of splenic antibody-producing cells in the primary immune response to sheep red blood cells,

Table 1. Biomodulatory Effects of *Spirulina* on Metabolism

Food supplemented with	Experimental model	Effects
S. platensis	Rat	Reduction of cholesterol [39]
S. platensis	Rat	Reduction of blood glucose [74]
S. platensis	Human	Reduction of body weight [4]
S. platensis	Rat	Increased activity of lipase [36]
S. platensis	Rat	Inhibition of maltase and sucrase [45]
S. fusiformis	Mouse	Modulation of carcinogen metabolic enzymes [53]
S. fusiformis	Mouse	Modulation of lead toxicity [71]
S. platensis	Rat	Increased iron status during pregnancy and lactation [38]

[2] The percentage of phagocytic cells in peritoneal macrophages from mice fed a *Spirulina diet* was significantly increased**,**

[3] The proliferation of spleen cells by either Concanavalin A (Con A) or phytohemagglutinin (PHA) was significantly increased,

[4] Addition of a hot water extract of *Spirulina* (SHW) to an *in vitro* culture of spleen cells significantly increased proliferation of these cells with no effect on thymus cells,

[5] The hot water extract of *Spirulina* also significantly enhanced interlukin-1 (IL-1) production from peritoneal macrophages, and

[6] Addition of the hot water extract of *Spirulina* to *in vitro* spleen culture and the supernatant of macrophages resulted in enhancement of antibody production.

Spirulina administration resulted in alleviation of allergic symptoms induced by shrimp extract. Co-administration of *Spirulina* with shrimp extract significantly enhanced the level of IgG1 & IgA in comparison to IgE [25]. Administration of *S. platensis* over a period of one year resulted in significant elevation in total secretory IgA levels in saliva [35].

ANTI-INFLAMMATORY PROPERTIES OF *SPIRULINA*

The phycocyanin extract of *Spirulina* exhibited anti-inflammatory activity in experimental models [22]. Phycocyanin is shown to inhibit inflammation in mouse ears [65]. The anti-inflammatory effect seemed to be a result of phycocyanin to inhibit the formation of leukotriene B4, an inflammatory metabolite of arachidonic acid [66]. C-phycocyanin is a free radical scavenger [9] and has significant hepatoprotective effects [79]. *S. fusiformis* has promising anti-inflammatory activity against adjuvant-induced arthritic animals [62]. Table **2** shows the immuno-modulatory and anti-inflammatory effects of *Spirulina.*

ANTI-VIRAL PROPERTIES OF *SPIRULINA*

Spirulina at lower concentration reduces viral replication while at higher concentration blocks replication. Importantly, with a therapeutic index of >100, *Spirulina* extract is non-toxic to human cells at concentrations stopping viral replication. Water soluble extract of *Spirulina* is shown to inhibit viral cell-penetration and replication of the Herpes Simplex Virus Type 1 (HSV-1) in cultured HeLa cells in a dose dependent manner. At just 1 mg/ml, the extract is shown to inhibit viral protein synthesis without suppressing host cell functions. *Spirulina* fed hamsters when challenged with the HSV-1, had prolonged survival times and higher survival rates [27]. The anti-viral activity is attributed to sulphated polysaccharide termed "Calcium Spirulan", which has been shown to inhibit replication of many enveloped viruses by inhibition of viral penetration into target cells without host toxicity. Presently, Calcium Spirulan (Ca-Sp) has been shown to exhibit activity against human cytomegalovirus, measles virus, mumps virus, influenza A virus, human immunodeficiency virus (HIV-1) as well as HSV-1 [28]. The active Ca-Sp could be a good candidate for therapeutic inter-

Table 2. Immunomodulatory and Anti-Inflammatory Effects of *Spirulina*

Food supplemented with	Experimental model	Effects
S. fusiformis	Human	Reversal of tobacco-induced oral cancer [50]
S. platensis	Mouse	Proportional reduction of IgE, increase of IgA [26]
S. platensis	Mouse	Increased phagocytic activity. Increased spleen cell proliferation. Increased antibody production [24]
S. platensis	Chicken	Increased phagocytic activity. Increased NK cell-mediated anti-tumor activity. Increased antibody production.[60]
S. platensis	Invitro, cat	Increased phagocytic activity [61]
S. platensis	Rat	Inhibition of mast cells. Decrease in local allergic reaction. Decrease in serum histamine levels. Reduced allergy induced mortality [41, 81]

vention against HIV-1 and other viruses because of its low anticoagulant activity, long half-life in the blood, and dose-dependent bioactivity [29, 30, 31].

ANTI-CANCER PROPERTIES OF *SPIRULINA*

Spirulina may offer some degree of protection against certain forms of cancer through its effect on the immune system, through a direct effect in the repair of DNA, and antioxidant protection from reactive oxygen species generated during normal or abnormal metabolism and from toxic substances in the environment. The only human study on the effect of *Spirulina* on chemoprevention of cancer is that by Mathew *et al* [50] who studied the effect of *Spirulina* on oral leukoplakia (a precancerous lesion) in pan tobacco chewers in Kerala, India. Discontinuation of *Spirulina* supplementation, resulted in recurrent lesions in almost half of the subjects. Ingestion of an extract of *Spirulina* and *Dunaliella* is shown to inhibit chemically induced carcinogenesis in hamster buccal pouches [69, 70]. Earlier studies often attributed the anti-cancer effect of algae to its carotenoids since β-carotene had been shown to have an effect similar to that of algal extract. A recent study, however, showed that the Ca-Sp, is responsible for inhibition of tumor invasion and metastasis [52]. Both the *in vivo* and *in vitro* effects of Ca-Sp suggest that the intra-venous administration of Ca-Sp reduces the lung metastasis of melanoma cells by inhibiting the tumor invasion of the basement membrane. Polysaccharide extract of *S. platensis* has chemo-protective and radio protective capability, and may be a potential adjunct to cancer therapy [83].

Of major interest to ongoing research in inflammation as well as breast cancer is the finding that C-phycocyanin selectively inhibits cyclooxygenase-2 (COX-2), but has no effect on COX-1 [63]. The COX enzymes which are involved in prostaglandin synthesis are over expressed in many breast cancer cells. Hence the inhibition of COX-2 by Spirulina resulted in reduced tumor growth and inhibition of angiogenesis. β-carotene may also help to protect skin against the damaging effects of sunlight and help to prevent skin cancer [43].

PROBIOTIC EFFECT OF *SPIRULINA*

Spirulina acts as a functional food feeding beneficial intestinal flora, especially *Lactobacillus* and *Bifidus*. Maintaining a healthy population of these bacteria in the intestine reduces potential problems from opportunistic pathogens like *E.coli* and *Candida albicans.* Feeding rats a diet supplemented with 5% *Spirulina* for 100 days resulted in the following:

[1] The weight of the caecum increased by 13%;

[2] *Lactobacillus* increased by 32.7%;

[3] Vitamin B1 inside the caecum increased by 43%.

Since *Spirulina* did not supply this additional B1, it must have improved overall B1 absorption. The study suggests eating *Spirulina* increases *lactobacillus* and may increase efficient absorption of Vitamin B1 and other vitamins from the entire diet [76]. More recently Parada *et al* [58] have reported a stimulatory effect of extracellular products from the alga on lactic acid bacteria including *Lactobacillus lactis, Streptococcus thermophilus, L. casei, L. acidophilus* and *L. bulgaricus*.

ANTI-BACTERIAL ACTIVITIES OF *SPIRULINA*

Spirulina exhibits potent antibacterial activities against pathogenic bacteria [57, 59]. Administration of 0.1% *Spirulina* group resulted in heightened bacterial clearance (*E.coli & S. aureus*) by 30 minutes post-injection and the bacterial counts were almost negligible in the blood. This heightened bacterial clearance is attributed to the immunopotentiating effects of *Spirulina* [59]. The methanol extract of *S. platensis* showed more potent antimicrobial activity than dichloromethane, petroleum ether, ethyl acetate extracts and volatile antibacterial components [57].

OTHER EFFCETS OF *SPIRULINA*

Spirulina is a rich source of γ-linolenic acid (10 gm of *Spirulina* contains over 100 mg of GLA) 40]. The dietary intake of GLA can help in arthritis, heart diseases, aging symptoms, manic depression, alcoholism and schizophrenia [34]. Free radicals are involved in neurodegenerative disorders such as ischemia and aging. Treatment of animals with *Spirulina* has been shown to reduce neurodegenerative changes in aged animals [80]. Oral administration of phycocyanin (*Spirulina* pigment) crosses blood brain barrier implicating its use in neurodegenerative diseases involving oxidative stress such as Parkinsonism and Alzheimer's disease [64]. S*pirulina*-enriched diets may prevent age-related declines in the cerebellar noradrenergic receptor function [10, 11]. *Spirulina* has an anti-aging effect due to the presence of tyrosine, vitamin E or tocopherol and selenium. Anti-aging foods such as *Spirulina* are ideal for older people who do not eat much, eat inappropriately or cannot absorb enough nutrients. Spiral *Spirulina* is the ideal anti-aging whole food and its high levels of natural β-carotene have been shown to be much more effective than the synthetic form found in many supplements. *Spirulina* is used as a dietary supplement on dyslipidemic and hypertensive patients [78]. *Spirulina* have biosorption capacity for cadmium and lead and hence used as bioremediation agent for removal of cadmium and lead from wastewater [2]. *Spirulina* was shown to be hepatoprotective against anti-tubercular drug induced hepatotoxicity in rats [23]. *Spirulina* supplementation significantly improved enzymatic and non-enzymatic antioxidants and decreased the tardive dyskinesia induced by haloperidol [75].

COMMERCIAL ASPECTS OF *SPIRULINA*

Spirulina is marketed and consumed in Germany, Brazil, Chile, Spain, France, Canada, Belgium, Egypt, United States, Ireland, Argentina, Philippines, India, Africa, and other countries, where public administration approved human consumption (Henrikson, 1994). Some of the best worldwide known *Spirulina* producing companies include: Earthrise Farms (USA), Cyanotech (USA), Hainan DIC Microalgae Co., Ltd (China), Marugappa Chettiar Research Center (India), Genix (Cuba) and Solarium Biotechnology (Chile).

CONCLUSION

Despite the few human studies done so far on the health benefits of *Spirulina*, the evidence for its potential therapeu-

tic application(s) is overwhelming in the areas of immunomodulation, viral and bacterial infections, diabetes and cardiovascular disorders and cancer. Traditional therapies always rely on the use of natural products and have been the source of information for the discovery of many drugs we have today. Currently, increased cost of health care has become a driving force in the shift towards interest in wellness, self-care, and alternative medicine, and a greater recognition between diet and health care. *Spirulina* is potent candidate in these new health care approaches. Large scale clinical research on primates will further solidify the health care merits of Spirulina for humankind.

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