

Review Article**Spirulina-The Nature's Wonder: A Review**Arpita Mohan^{1*}, Neeta Misra², Deepak Srivastav³, Deepak Umopathy⁴, Shiva Kumar⁴¹MDS Student, Department of Oral Medicine & Radiology, Babu Banarasi Das College of Dental Sciences, Lucknow, India²Professor & Head, Department of Oral Medicine & Radiology, Babu Banarasi Das College of Dental Sciences, Lucknow, India³Assistant Professor, Department of Orthopedics, Hind Institute of Medical Sciences, Lucknow, India⁴Professor, Department of Oral Medicine & Radiology, Babu Banarasi Das College of Dental Sciences, Lucknow, India***Corresponding author**

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Abstract: Spirulina is a fresh water microalgae which has been used as a food supplement since many years. This alga contains a diverse concentration of nutrients and has emerged as a wonder drug because of its varied uses. It boosts the immunity and increases resistance to various infections. The antioxidant properties of spirulina are well known and anticancer action has also been reported. Spirulina plays an important role in metabolic diseases like diabetes, hypertension, anemia & others. Thus this multi beneficiary action of spirulina makes it an important natural product for the improvement of health of humans.**Keywords:** Spirulina, Health, Immunity, Antioxidant, Anticancer

INTRODUCTION

Spirulina is a cyanobacterium, (Oscillatoraceae family) which acquired the ability for photosynthesis before any other organism and is considered to be the ancestor from which the higher plants evolved [1]. Spirulina refers to various species of blue-green algae found naturally in lakes and grown commercially. *Arthrospira platensis* earlier known as 'Spirulina' *platensis* is a ubiquitous spiral-shaped blue-green unicellular microalgae which grows in fresh water, in salt water, as well as in brackish bodies of water. It is so named because of the fact that the filaments are spiral. It grows best in a highly alkaline environment of pH 10-12. Such conditions currently exist in certain lakes in Sub-Saharan Africa and formerly in Mexico and Central America. Spirulina has been used as a food source for centuries. In Africa, Spirulina has served as the sole source of nutrition in certain communities in times of famine, and the entire native populations have existed eating only Spirulina for over a month at a time [2]. Spirulina was originally harvested from lakes in parts of Africa and Mexico, dried and used as a food but it gained prominence more recently after it was used as a dietary supplement for astronauts on space missions. NASA has stated that the nutritional value of 1000 kg of fruits and vegetables equals one kg of spirulina [3].

Species

Various spirulina species are *Spirulina maxima*; *Spirulina platensis*, *Spirulina pacifica* (also known as *Arthrospira platensis*, *Arthrospira maxima*). *Arthrospira platensis* is the predominant species and commercially cultivated worldwide though *Arthrospira maxima* is produced in the South and Central American regions [4].

Spirulina: Nutrient Value

Spirulina is one of the natural sources containing the highest amount of protein — five times that of meat. Spirulina provides the majority of essential and non-essential amino acids. It has a fairly well-balanced amino acid pattern and contains the highest amount of beta-carotene, a precursor of vitamin A. It is the only vegetable source of vitamin B₁₂ having two and half times the amount in liver. It is also the source of the essential fatty acid γ -linolenic acid which is the precursor of hormones involved in regulation of body functions. ¹ The constituents of spirulina include protein (50-70%) including all essential amino-acids, essential fatty acids, polysaccharides, B vitamins particularly vitamin B₁₂, beta-carotene and minerals particularly iron [5].

Spirulina has been demonstrated to be an effective dietary source of vitamin A. An investigation in India on preschool children with vitamin A deficiency demonstrated that the bioavailability of carotenes from

spirulina was comparable to that from other sources such as carrots and green leafy vegetables thereby suggesting the potential use of spirulina as a dietary source of vitamin A [6].

Spirulina has a positive impact on weight and other parameters like arm circumference, height, albumin, prealbumin, protein and haemoglobin improved after spirulina supplementation [7].

Improvement in nutritional status of malnourished HIV-infected patients has also been shown by supplementing the diet with spirulina.

Moreover spirulina can be safely administered to children without any risk and is considered a very suitable food (United Nations World Health Organization, Geneva, Switzerland June 8th, 1993).

Table 1: General Composition of Spirulina [4]

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

Table 2: Phytopigments (mg / 100g) [4]

Total Carotenoids	400 – 650
Beta Carotene	150 – 250
Xanthophylls	250 – 470
Zeaxanthin	125 – 200
Chlorophyll	1300 – 1700
Phycocyanin	15000 –19000

Table 3: Vitamins (mg / 100g) [4]

Vitamin B1 (Thiamine)	0.1.5 – 0.30
Vitamin B2 (Riboflavin)	4.0 – 7.0
Vitamin B3 (Niacin)	10.0 – 25.0
Vitamin B6(Pyridoxine)	0.5 – 1.5
Vitamin B12 (Analogue)	0.10 – 0.30
Folic acid	0.05 – 0.30
Inositol	70 – 90
Vitamin K	0.90 – 1.05

Nutrient profile of Spirulina vs other foods

- 180% more calcium than whole milk
- 670% more protein than tofu
- 3100% more beta carotene than carrots
- 5100% more iron than spinach
- more antioxidant and anti-inflammatory activity in 3 g of Spiurlina than in five servings of fruits and vegetables [8]

Mechanism of Action

Spirulina can be used simply as a protein supplement but it is also considered to have specific effects on the immune system. Preliminary studies in

healthy humans suggest that spirulina increases the production of the cytokines, tumour necrosis factor, interleukin (IL)-2, and interferon, and causes CD4+ T-helper cell proliferation [9, 10]. It also appears to increase the activity and cytotoxicity of natural killer cells [11]. Animal studies have demonstrated chemoprotective effects when spirulina is given with various cytotoxic drugs [12-14]. Several animal studies have investigated the potential of spirulina to have a protective effect against toxicity related to various cytotoxic agents such as cardiotoxicity, nephrotoxicity & hepatotoxicity [13].

Health benefits of Spirulina

Research on Spirulina’s health benefits has been far-ranging. In addition to antioxidant and anti-inflammatory effects other potential health applications are:

- Protection of the liver and kidneys
- Improvement of blood quality and prevention of anaemia
- Benefits for diabetes
- Reduction in Blood Pressure
- Removal of heavy metals from the body
- Radioprotection
- Prevention of liver and renal toxicity
- Antioxidant action
- Immune protection
- Relief in allergic reactions [2]

Spirulina as Antioxidant

One of most important characteristics of Spirulina is its antioxidant property. Antioxidants are the substances which neutralize the free radicals generated due to oxidative stress. Free radicals are not only nuisance molecules in the atmosphere but can cause havoc inside the body. They are the unstable products of normal cell processes. Free radicals can damage the concerned cell & lead to the death of these cells. Oxidative stress directly or indirectly leads to various disorders like diabetes, atherosclerosis, rheumatoid arthritis, recurrent aphthous stomatitis, cancer, etc. [1]. Very high amounts of beta-carotene, tocopherol and combined form of these antioxidants make Spirulina a very good source of natural antioxidant along with high protein. These antioxidants can become pro-oxidants and protect the body from oxidative stress [1].

The iron chelating properties of spirulina was discovered when human neuroblastoma cells *in vitro* were exposed to toxic amounts of iron and then to spirulina, which revealed that the iron induced oxidative stress was reduced [10]. Geriatric patients administered spirulina for 16 weeks showed a remarkable improvement in the antioxidant potential, as measured by the increased levels of antioxidant status in plasma of these individuals [15]. A double-blinded, placebo controlled study performed on individuals after exercise, showed decreased amount of creatine kinase, (an indicator of muscular breakdown) when they were

supplemented with spirulina. Moreover their exhaustion time in the treadmill exercise increased by 52 seconds. This could be explained by the antioxidant potential of spirulina [16].

Anticancer Effects of Spirulina

As early as 1987, researchers at Harvard University's School of Dental Medicine published evidence that a combination of Spirulina and Dunaliella microalgae extracts induced the regression of tumors in the mouths of rodents. Total tumor regression was found in 30% of the animals receiving the Spirulina and Dunaliella extracts, while partial tumor regression was found in all of the remaining 70% of the animals; meanwhile, in the control group, no tumor regression was found [17].

Various animal studies have demonstrated the anti cancer effect of spirulina [18, 19]. Chemoprevention of cancer & reduced incidence of liver tumors has also been documented [20]. The chemopreventive capacity to reverse precancerous lesions of spirulina is attributed to the antioxidant property with high amount of beta carotene and superoxide dismutase [21, 23].

One of the first studies on the use of spirulina in treatment of Oral Leukoplakia was conducted in India and it showed promising results. In the clinical trial 1g/day of Spirulina fusiformis for chemoprevention of oral cancer was given to 44 subjects with oral Leukoplakia. Complete regression of lesions was observed in 45% (20 of 44 subjects) whose diet was supplemented with spirulina. This compared favourably with those receiving placebo: only 3 of 43 (7%) showed a complete regression in lesions ($p < 0.0001$). The response appeared to be greater in those with homogeneous lesions. Increased serum concentrations of retinol or beta-carotene were not observed nor was toxicity reported. Sixty people received the spirulina. Assessment of response was carried out by a physician and a dentist who were unaware of the allocated treatment group but it is unclear to what extent the spirulina and placebo capsules were well-matched. Muscular pain and headaches were reported by 7 and 5 patients taking spirulina and no adverse events were reported by those in the placebo group [23].

In a novel recent clinical trial Spirulina was used in the treatment of Oral Submucous Fibrosis and statistically significant results were obtained in mouth opening, burning sensation and tongue protrusion. No side effects were observed with spirulina [24].

Significant Clinical improvement in Oral Submucous Fibrosis disease indicators like mouth opening, burning sensation, blanching & painful oral ulcerations was also observed proving Spirulina as a safe and reliable modality in the management of oral submucous fibrosis [25].

Antidiabetic Property of Spirulina

Diabetes mellitus, a metabolic disorder, is becoming a major health problem. Long time use of various drugs can lead to various side effects. The antihyperglycemic effect of spirulina may be due to the down-regulation of NADPH and NADH, a cofactor in the fat metabolism. The higher activity of glucose-6-phosphatase provides H^+ , which binds with $NADP^+$ in the form of NADPH and is helpful in the synthesis of fats from carbohydrates. Spirulina may be capable of oxidizing NADPH. In one of the animal studies it was shown that the activity of hexokinase in the liver decreased markedly, while the activity of glucose-6-phosphatase increased significantly in diabetic control rats. Treatment with spirulina in diabetic rats increased the hexokinase activity and decreased the glucose-6-phosphatase activity. The enhanced hexokinase activity in spirulina treated rats suggested a greater uptake of glucose from blood by liver cells. Thereby showing that Spirulina may produce high $NADP^+$, which results in down regulation of lipogenesis and lower risk of the tissues for oxidation stress and high resistance for diabetes [26].

Antidiabetic effect was also seen by supplementing spirulina 2 g/day doses for two months on blood glucose levels, glycosylated hemoglobin and lipid profile. The lowering of fasting and postprandial blood glucose levels and in the HbA1c level showed the antidiabetic property of spirulina [27].

Spirulina in Hypertension & Hyperlipidemia

Spirulina has hepatoprotective properties by decreasing liver lipid profile and lipoperoxidation products. Spirulina has a hypolipemic effect, especially on the concentrations of triacylglycerols and the cholesterol associated to low density lipoprotein and indirectly on total cholesterol and cholesterol associated to high density lipoprotein values. It was also shown that spirulina reduced systolic and diastolic blood pressure when given by oral route (4.5 g/day, for 6 weeks) [28]. This lipid lowering property has been attributed to the C-phycoerythrin molecule in spirulina [29]. Oral administration of spirulina is also associated with reduction in systolic and diastolic blood pressure [28]. The high potassium, and low sodium contents of Spirulina, have positive effects on blood pressure [30]. It has been proposed that C-phycoerythrin inhibits platelet aggregation through inhibition of calcium mobilization and mediation of free radicals released by platelet [31]. Inhibitory effects of Spirulina on atherosclerosis have also been reported [32].

Spirulina in Anaemia

Spirulina possibly enhances red cell production and function [33]. Over a 12-week study period, there was a steady increase in average values of mean corpuscular haemoglobin with spirulina intake. Older women benefitted more rapidly from Spirulina supplements [34]. Levels of anaemia also decreased in children when their diet was supplemented with spirulina [35].

Role of Spirulina in Immunity

Spirulina helps in building immunity and improving resistance to viral infections. Spirulina can enhance components of the mucosal and systemic immune system as it activates the cells of innate immune system. Several pre-clinical animal studies have shown good immune stimulatory effects in a variety of species. In humans, mammals, chicken and fish Spirulina produces an immune stimulating effect by enhancing the resistance to infections, the capacity of influencing haemopoieses, and stimulating the production of antibodies and cytokines. Spirulina has also been shown to activate macrophages, T and B cells [36]. Sulfolipids derived from spirulina have also proved effective against HIV. Extracts from Spirulina biomass have also been found active against herpes virus, cytomegalovirus, influenza virus, etc. Spirulina extracts have also been shown capable of inhibiting carcinogenesis [37].

Spirulina use leads to higher levels of natural killer cells, interferon gamma and more potent production of interleukins [38].

It has also been seen to have an inhibitory effect on the release of histamine from mast cells during an allergic inflammatory response.

Ingestion of spirulina contributes to the functional preservation of the intestinal epithelium which acts as a first line of mucosal barrier against infections [39]. Inhibition of humoral immune response, cell mediated immune response (delayed type hypersensitivity) and TNF-alpha was noticed in a dose-dependent manner in mice [40].

Spirulina has also been found to protect against hay fever [41]. In allergic rhinitis patients, a more recent double-blind, placebo-controlled study showed marked reduction in the secretion of pro-inflammatory IL-4 [42].

It was also seen to reduce inflammation in arthritis patients and this reduction was due to the stimulation to secrete IL-2 which regulates inflammatory response [43].

Radio-protective role of Spirulina

Spirulina has a protective role in Protection against Radiation and its Effects. Feeding children subjected to low level of radiation over a long period of time with 5 grams of Spirulina a day resulted in the reduction of Cesium-137 in urine by 50% [43]. The c-phycoyanin and polysaccharide extracts of Spirulina stimulate recovery of white blood cells and bone marrow cell counts. The anaemic condition induced by irradiation was also reduced [45].

Spirulina modulates the immune system favourably and it has strong anti-oxidant and anti-inflammatory effects. Some of the beneficial aspects of Spirulina in radiation effects may be due to its ability to bind to heavy metals and radioisotopes.

CONCLUSION

Spirulina has emerged as the wonder food supplement. Several leading organizations are utilizing this beneficial action. Very few adverse effects have been reported with the use of spirulina which include headache, muscle pain, flushing of the face, sweating, and difficulty in concentrating. Skin reactions have also been reported in some individuals. The highly diverse nutritive nature of spirulina together with its antioxidant and protective health benefits have been utilized in various health related problems. The effectiveness of spirulina is being very rapidly recognized and being made use of in the treatment and management of various life threatening diseases. The potential health benefits of spirulina must be adequately recognized and implemented thus making full use of this nature's gift.

REFERENCES

1. Desai K, Sivakami S; Spirulina the wonder food of the 21st century. Asia Pacific Biotech News, 2004; 8(23):1298-1302
2. Capelli B, Cysewski GR; Potential Health Benefits of spirulina microalgae:A review of existing literature. Nutra Foods, 2010, 9(2)19-26
3. Ravi M, De SL, Azharuddin S, Paul SFD; The beneficial effects of spirulina focusing on its immunomodulatory and antioxidant properties. Nutrition and Dietary Supplements, 2002; 2: 73-83.
4. Thomas SS; The role of parry organic spirulina in health management. 2010.
5. Khan Z, Bhadouria P and Bisen PS; Nutritional and therapeutic potential of spirulina. Curr Pharm Biotechnol., 2005; 6(5): 373-379.
6. Annapurna V, Shah N, Bhaskaram P, Bamji M, Reddy V; Bioavailability of spirulina carotenes in pre-school children. J Clin Biochem Nutr., 1991; 10:145-151
7. Azabji-Kenfack M, Edie Dikosso S, Loni EG, Onana EA, Sobngwi E, Gbaguidi E *et al.*; Potential of *Spirulina platensis* as a nutritional supplement in malnourished hiv-infected adults in sub-Saharan Africa: A randomised, single-blind study. Nutr Metab Insights., 2011; 4: 29-37
8. Moorhead K, Capelli B, Cysewski G; Nature's Superfood: Spirulina. 2005.
9. Hirahashi T, Matsumoto M, Hazeki K, Saeki Y, Ui M, Seya T; Activation of the human innate immune system by Spirulina: augmentation of interferon production and NK cytotoxicity by oral administration of hot water extract of *Spirulina platensis*. Int Immunopharmacol., 2002 2(4): 423-434.

10. Lobner M, Walsted A, Larsen R, Bendtzen K, Nielsen CH; Enhancement of human adaptive immune responses by administration of a high-molecular-weight polysaccharide extract from the cyanobacterium *Arthrospira platensis*. *J Med Food.*, 2008; 11(2): 313-322.
11. Nielsen CH, Balachandran P, Christensen O, Pugh ND, Tamta H, Sufka KJ *et al.*; Enhancement of natural killer cell activity in healthy subjects by Immulina(R), a *Spirulina* extract enriched for Braun-type lipoproteins. *Planta Med.*, 2010; 76(16): 1802-1808.
12. Bhattacharyya S, Mehta P; The hepatoprotective potential of *Spirulina* and vitamin C supplementation in cisplatin toxicity. *Food Funct.*, 2012; 3(2): 164-169.
13. Khan M, Shobha JC, Mohan IK, Naidu MU, Sundaram C, Singh S *et al.*; Protective effect of *Spirulina* against doxorubicin-induced cardiotoxicity. *Phytother Res.*, 2005;19(12): 1030-1037.
14. Mohan IK, Khan M, Shobha JC, Naidu MU, Prayag A, Kuppusamy P *et al.*; Protection against cisplatin-induced nephrotoxicity by *Spirulina* in rats. *Cancer Chemother Pharmacol.*, 2006; 58(6): 802-808.
15. Mittal A, Kumar PV, Banerjee S, Rao AR, Kumar A; Modulatory potential of *Spirulina fusiformis* on carcinogen metabolizing enzymes in Swiss albino mice. *Phytother Res.*, 1999; 13(2): 111-114.
16. Trushina EN, Gladkikh O, Gadzhieva ZM, Mustafina OK, Pozdniakov AL; The influence of spirulina and selen-spirulina on some indexes of rat's immune status (Article in Russian). *Vopr Pitan.*, 2007;76(2): 21-25.
17. Schwartz J, Shklar G; Regression of experimental hamster cancer by beta carotene and algae extracts. *J Oral Maxillofacial Surg.*, 1987; 45(6): 510-515.
18. Akao Y, Ebihara T, Masuda H, Saeki Y, Akazawa T, Hazeki K *et al.*; Enhancement of antitumor natural killer cell activation by orally administered *Spirulina* extract in mice. *Cancer Sci.*, 2009; 100(8):1494-1501.
19. Grawish ME, Zaher AR, Gaafar AI, Nasif WA; Long-term effect of *Spirulina platensis* extract on DMBA-induced hamster buccal pouch carcinogenesis (immunohistochemical study). *Med Oncol.*, 2010; 27(1): 20-28.
20. Hamidah A, Rustam ZA, Tamil AM, Zarina LA, Zulkifli ZS, Jamal R; Prevalence and parental perceptions of complementary and alternative medicine use by children with cancer in a multi-ethnic Southeast Asian population. *Pediatr Blood Cancer.*, 2009;52(1):70-74
21. Pinazani M, Marra F, Caliquiri A, Franco R, Gentilline A, Failli P *et al.*; Inhibition of pentoxifylline of extracellular signal regulated kinase activation by platelet derived growth factor in hepatic stellate cells. *Br J Pharmacol.*, 1996; 119(6): 1117-1124.
22. Wataru M, Katsumiy, Shojik; Carotenoid composition of *Spirulina maxima*. *Bulletin of Japanese society of scientific fisheries* 1986; 52(7): 1225-1227.
23. Mathew B, Sankaranarayan R, Nair PP, Varghese C, Somanathan T, Amma BP *et al.*; Evaluation of chemoprevention of oral cancer with *Spirulina fusiformis*. *Nutr Cancer*, 1995; 24(2):197-202
24. Mulk BS, Deshpande P, Velpula N, Chappidi V, Chintamaneni RL, Goyal S; *Spirulina* and pentoxifylline- a novel approach for treatment of oral submucous fibrosis. *J Clin Diagn Res.*, 2013; 7(12): 3048-3050.
25. Chole R, Patil RK; Clinical improvement in oral submucous fibrosis with *Spirulina*, a newer drug. *Journal of Oral Sign*, 2013; 5(2): 61-64.
26. Layam A, Reddy CLK; Antidiabetic Property of *Spirulina*. *Diabetologia Croatica*, 2006; 35(2): 29-33.
27. Parikh P, Mani U, Iver U; Role of *Spirulina* in the control of gli- cemia and lipidemia in type 2 Diabetes Mellitus. *J Med Food.*, 2001; 4(4):193-199.
28. Duran PVT, Hermosillo AF, Oropeza MAJ; Antihyperlipemic and antihypertensive effects of *Spirulina maxima* in an open sample of mexican population: a preliminary report. *Lipids in Health and Disease*, 2007; 6: 33.
29. Nagaoka S, Shimizu K, Kaneko H, Shibayama F, Morikawa K, Kanamaru Y *et al.*; A novel protein C-phycoyanin plays a crucial role in the hypocholesterolemic action of *Spirulina platensis* concentrate in rats. *J Nutr.*, 2005, 135(10): 2425-2430.
30. Guan Y, Zhao HY, Ding XF, Zhu YY; Analysis of the contents of elements in *Spirulina* from different producing areas. *Guang Pu Xue Yu Guang Pu Fen Xi*, 2007; 27(5): 1029-1031.
31. Hsiao G, Chou PH, Shen MY, Chou DS, Lin CH, Sheu JR; C-phycoyanin, a very potent and novel platelet aggregation inhibitor from *Spirulina platensis*. *J AgricFood Chem.*, 2005; 53(20): 7734-7740.
32. Cheong SH, Kim MY, Sok DE, Hwang SY, Kim JH, Kim HR *et al.*; *Spirulina* prevents atherosclerosis by reducing hypercholesterolemia in rabbits fed a high-cholesterol diet. *J Nutr Sci Vitaminol. (Tokyo)*, 2010; 56(1): 34-40.
33. Carmel R; Nutritional anemias and the elderly. *Semin Hematol.*, 2008; 45(4): 225-234.
34. Selmi C, Leung PS, Fischer L, German B, Yang CY, Kenny TP *et al.*; The effects of *Spirulina* on anemia and immune function in senior citizens. *Cellular & Molecular Immunology*, 2011; 8(3): 248-254.
35. Branger B, Cadudal JL, Delobel M, Ouoba H, Yameogo P, Ouedraogo D *et al.*; *Spiruline* as a food supplement in case of infant malnutrition in

- Burkina-Faso. Archives de pédiatrie, 2003; 10(5): 424-431.
36. Schwartz J, Shklar G; Regression of experimental hamster cancer by beta carotene and algae extracts. J Oral Maxillofac Surg., 1987; 45(6): 510-515.
 37. Blinkova LP, Gorobets OB, Baturo AP; Biological activity of Spirulina. Zh Mikrobiol Epidemiol Immunobiol., 2001; 2: 114-118.
 38. Hirahashi T, Matsumoto M, Hazeki K, Saeki Y, Ui M, Seya T; Activation of the human innate immune system by Spirulina: augmentation of interferon production and NK cytotoxicity by oral administration of hot water extract of *Spirulina platensis*. Internat Immunopharmacol., 2002; 2(4): 423-434.
 39. Shklar G, Schwartz J; Tumor necrosis factor in experimental cancer regression with alphotocopherol, beta-carotene, canthaxanthin and algae extract. Eur J Cancer Clin Oncol., 1988; 24(5): 839-850.
 40. Sheahan S, Bellamy CO, Harland SN, Harrison DJ, Prost S; TGF beta induces apoptosis and EMT in primary mouse hepatocytes independently of p53, p21Cip1 or Rb status. BMC Cancer, 2008; 8:191-201.
 41. Simporo J, Zongo F, Kabore F, Dansou D, Bere A, Nikiema JB; Nutrition Rehabilitation of HIV-Infected and HIV-Negative Undernourished Children Utilizing Spirulina. Annal Nut Metabolism., 2005; 49(6): 373-380.
 42. Hosoyamada Y, Takai T, Kato T; Effects of water-soluble and insoluble fractions of Spirulina on serum lipid components and glucose tolerance in rats. Journal of Japanese Soc Nutr Food Sci., 1991; 44(4): 273-277.
 43. Hayashi T, Hayashi K, Maeda M, Kojima I; Calcium spirulan, an inhibitor of enveloped virus replication, from a blue-green alga *Spirulina platensis*. J Nat Prod., 1996; 59(1): 83-87.
 44. Loseva LP, Dardynskaya IV; Spirulina natural sorbent of radionucleides. Research Institute of Radiation Medicine, Minsk, Belarus. Paper presented at the 6th International Congress of Applied Algology, Czech Republic, 1993.
 45. Cheng-Wu Z, Chao-Tsi T, Zhen ZY; The effect of polysaccharide and phycocyanin from *Spirulina platensis* var. on peripheral blood and hematopoietic system of bone marrow in mice. Paper presented at the 2nd Asia-Pacific Conference on Algal Biotechnology. Malaysia, 1994.