

Spirulina- small but a spectacular species

Ms. Hemamalini Balaji

BDS, Saveetha Dental College and Hospitals

Corresponding Authors:

Ms. Hemamalini Balaji

Saveetha Dental College and Hospitals,

162, Poonamalle High Road, Chennai, Tamil Nadu, India.

Email:b.hemamalini27@gmail.com

Abstract:

Spirulina is a marine blue green algae which is being extensively studied as the biomass of these microalgae and the compounds they produce have been shown to possess several biological applications with numerous health benefits. Apart from being used as nutraceutical food supplement worldwide, it shows therapeutic benefits on an array of diseased conditions including hypercholesterolemia, hyperglycerolemia, cardiovascular diseases, inflammatory diseases, cancer and viral infections. *Spirulina* is also incorporated as a functional ingredient in food products and beverages.

The people in Africa have been known for consuming as *Arthrospira* (formerly, *Spirulina*) as principle food for past 100 years. But it became famous after it was successfully used by NASA as a dietary supplement for astronauts on space missions. There have been numerous studies investigating the efficiency and current clinical applications of *Spirulina* in treating several diseases in the recent years.

Keywords: Spirulina, micro algae, Anti oxidant, Anti cancer, Anti Inflammatory, Hypo lipidemic activity.

Introduction:

Spirulina is referred to Marine microalgae with spiral characteristics of its filaments. It is formally called *Arthrospira*, belonging to the class of cyanobacteria with characteristic photosynthetic capability. [1,2].

Spirulina naturally grows in high-salt alkaline water reservoirs in subtropical and tropical areas including America, Mexico, Asian and Central Africa [3,4]. There are many known species of *Spirulina*, of those *Spirulina platensis* (*Arthrospira platensis*), *Spirulina maxima* (*Arthrospira maxima*) and *Spirulina fusiformis* (*Arthrospira fusiformis*) are the most intensively described species as having high degree of medicinal values.

Composition:

Spirulina contains the high (up to 70%) content of protein, and also vitamins, especially B₁₂ and

provitamin A (β -carotenes), and minerals, especially iron. It is also rich in phenolic acids, tocopherols and γ -linolenic acid [5]. *Spirulina* lacks cellulose cell walls and therefore it can be easily digested [5].

Microalgae/cyanobacteria produce besides being one of the richest sources of proteins other value-added compounds, such as polyunsaturated fatty acids (PUFAs), carotenoids, phycobiliproteins, polysaccharides, vitamins, or sterol. Some of the produced PUFAs are essential ω -3 and ω -6 that can be included in functional, or nutraceutical foods, (eg. *Spirulina*) or as feed for chickens and cows, these, in turn, supplying eggs and milk enriched in those PUFAs. Other microalgae, or their derived-products, are used in the pharmaceutical industry, cosmetics, thalassotherapy, as biofertilizers, or as agents to fix soil particles, on golf-greens, as feed for animals, in aquaculture, or even in effluent treatments.

Arthrospira, is a promising cyanobacterium as it can be used in applications to lower hyperlipidaemia, hyperglycaemia, and hypertension, to protect against renal failure, and to promote growth of intestinal *Lactobacillus* [6 - 8].

Many toxicological studies have proven *Spirulina*'s safety. *Spirulina* now belongs to the substances that are listed by the US Food and Drug Administration under the category Generally Recognized as Safe (GRAS) [9-13]

This review provides emphasis on presenting the up to date developments of the clinical application of *Spirulina* or its derivatives for various therapeutic processes and whether this has side effects on long term usage and further describes the methods of preventing contamination.

Clinical Trials & Therapeutic Applications:

❖ Spirulina and Chronic Fatigue:

Spirulina has been promoted as "the food of the future" with "exceptional constituents" that contribute to high energy levels. A few of these constituents such as polysaccharides (Rhamnose and Glycogen) and essential fat (GLA) are absorbed easily by human cells and help in energy release. *Spirulina* increases 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 day⁻¹ did not ameliorate fatigue more than the placebo in any of the four subjects and possibly it has no effect on chronic fatigue [14].

❖ Prevents Cell death:

Spirulina prevents cell death induced by free radicals. Aqueous extract of *Spirulina* has a protective effect against apoptotic cell death due to free radicals.[15]

❖ Anti Inflammatory Activity:

It has been well documented that *Spirulina* exhibits anti-inflammatory properties by inhibiting the release of histamine from mast cells [16,17]

In Human Subjects:

In addition to being a disorder of lipid metabolism, atherosclerosis is now recognized as a chronic inflammatory disease [18, 19]. Excessive inflammation within the arterial wall may increase the risk factor for cardiovascular diseases. Antiinflammatory activity present in spirulina may prove to be beneficial in combating cardiovascular diseases.

Influence of *Spirulina* on IgA levels in human saliva demonstrated that it enhances IgA production, suggesting a pivotal role of microalga in mucosal immunity. [20]

In a recent *in vitro* study, the antioxidant and antiinflammatory properties of four different *Spirulina* preparations were evaluated with a cell-free as well as a cell-based assay. It was found that *Spirulina* dose-dependently inactivated free superoxide radicals generated during an oxidative burst. Equally significant, *Spirulina* dose-dependently reduced the metabolic activity of functional neutrophils, indicating the antiinflammatory activity[21].

Animal Studies:

A number of animal studies have been carried out to evaluate the antioxidant and/or antiinflammatory activities of *Spirulina*. In one study with aged male rats, *Spirulina* reversed age-related increase in proinflammatory cytokines in

cerebellum, such as tumor necrosis factor-alpha (TNF α) and TNF β . *Spirulina* supplementation also significantly decreased the oxidative marker MDA whereas increased the cerebellar beta-adrenergic receptor function which was reduced by aging. The observation thus demonstrated the antioxidant and antiinflammatory activities of *Spirulina* in aged rats. [22]

❖ Hypo lipidemic Activity-combating Cholesterol:

Cardiovascular disease remains the number one cause of death in developed countries, despite increased awareness, and high cholesterol is one of the most important risk factors in atherosclerosis. 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. [23]. A clinical study showed a significant reduction in LDL : HDL ratio in 15 diabetic patients who were given *Spirulina*. [24].

In the mouse study, supplementation of 16% *Spirulina* in a high fat and cholesterol diet resulted in a significant reduction in total serum cholesterol, LDL, VLDL cholesterol and phospholipids whereas serum HDL cholesterol was concurrently increased. In addition, high hepatic lipids induced by the high fat and cholesterol diet were markedly reduced by *Spirulina* consumption [25]. The mechanism behind the Hypolipidemic activity of spirulina is not yet brought to light. But there is a hypothesis suggesting Phycocyanin is a water soluble protein and enriched in *Spirulina*.

Ingestion of phycocyanin preparation made from SPC resulted in a significant decrease in serum total cholesterol and atherogenic index whereas serum HDL cholesterol was concurrently increased. It was thus suggested that phycocyanin might be the active ingredient in *Spirulina* responsible for the hypolipidemic activity [26].

❖ Anti Cancer Effect:

Cancer is one of the most threatening disease in the present day scenario. There are Anti cancer drugs in use but despite their great antitumoral activity in human, they produce unwanted side-effects. It has been argued that the combined antioxidant and immune modulation characteristics of *Spirulina* may have a possible mechanism of tumor destruction and hence play a role in cancer prevention.

Recent study showed that when the *Spirulina* was enriched with Selenium and combined with the anticancer drugs, a significant decrease of the proliferation rate and an increase of apoptosis rate were observed. [27].

Thus Se-enriched *Spirulina* as a vector for anticancer drug delivery enables to associate any anticancer drug with Se (Patent FR1257009). This process allows high drug delivery and produce significant anti-proliferative effect. The functionalization of selenium nanoparticles (SeNPs) with *Spirulina* polysaccharides (SPS) has been developed in a study [28]. Results suggest that the strategy to use SPS as a surface decorator could be an effective way to enhance the cellular uptake and anticancer efficacy of nanomaterials. SPS-SeNPs may be a potential candidate for further evaluation as a chemopreventive and chemotherapeutic agent against human cancers.

❖ **Anti oxidant activity:**

A study showed that supplementation of *Spirulina* with a daily dose of 8g for 4 weeks significantly prolonged the time to fatigue, reduced TBARS induced by excise, and increased the plasma glutathione, protein carbonyls, catalase, and total antioxidant capacity levels. [29]

C-phycocyanin (C-PC) is one of the major biliproteins of *Spirulina* with antioxidant and radical scavenging properties. C-PC, a selective cyclooxygenase-2 inhibitor, induces apoptosis in lipopolysaccharide-stimulated RAW 264.7 macrophages. It is also known to exhibit anti-inflammatory and anticancer properties [30].

Phycocyanin has the ability to scavenge free radicals, including alkoxyl, hydroxyl and peroxy radicals. It also decreases nitrite production, suppresses inducible nitric oxide synthase (iNOS) expression, and inhibits liver microsomal lipid peroxidation [31,32-42].

Consumption of spirulina:Safety or Harmful:

As even a coin has two sides there are both advantages and some disadvantages in consuming Spirulina as a food. There are reports from many studies which suggests the safety as well as harm in its long term usage.

Studies reporting safety of Spirulina:

Supplementation of *Spirulina* in the diet at the doses much higher than any anticipated human consumption did not cause any signs of embryotoxic effects.

Spirulina had no detectable adverse effects on reproductive performance, embryo and fetus development and growth [43].

Intake of diet containing *Spirulina* significantly increased litter size whereas birth weights of pups were comparable to those from other groups. Finally, a study with pregnant rats to assess the

general reproductive performance showed that *Spirulina* feeding did not change body weight of male and female rats with no signs of toxicity and was not associated with any adverse effects on any measures of reproductive performance including fertility, gestation and abnormal pups [44].

Study reporting Spirulina as Harmful:

Finally, an association of *Spirulina* consumption and development of a mixed immunoblasting disorder with characteristic features of bullous pemphigoid and pemphigus foliaceus was reported in an 82-year-old healthy woman [44].

Despite of favorable safety profile in rodents, there were reports raising the concerns of the safety of *Spirulina* consumption. A low level of mercury and other heavy metals were reported in *Spirulina* grown in open water source [45]. Consumption of such *Spirulina* preparation could lead to increased deposit of mercury and other heavy metals causing toxic effects. However, with controlled water sources for growing *Spirulina*, commercial *Spirulina* products tested contained mercury or lead at the levels much lower than the guidelines for daily intake of those elements by the WHO's Food and Agriculture Organization (FAO) [46]

Conclusion:

Spirulina is a micro algae which has an amazing potential to play a major role in Therapeutics. A little of its usage in medicine has been established by numerous studies still more of its hidden properties are yet to be explored. Some of its properties such as Anti oxidant, Anti inflammatory, Anti cancer, Anti aging (prevents cell death), Drug delivery System, etc. Along with these actions in Humans has been described briefly in this Review.

Hope this review will serve the purpose of aiding in future Research work to unleash the further components present in Spirulina. Spirulina has a promising role to be played in the upcoming developments of Modern Medicine.

References:

- 1) Sapp J. The Prokaryote-Eukaryote Dichotomy: Meanings and Mythology. *Microbiol and Mol Biol Rev.* 2005; 69:292–305.
- 2) Komárek J, Hauer T. Worldwide electronic publication. Univ. of South Bohemia and Inst of Botany AS CR; 2009. CyanoDB.cz - On-line database of cyanobacterial genera. <http://www.cyanodb.cz>.
- 3) Vonshak A, editor. *Spirulina platensis (Arthrospira): Physiology, Cell-biology and Biotechnology.* London: Taylor & Francis; 1997.
- 4) Gershwin ME, Belay A, editors. *Spirulina in human nutrition and health.* Boca Raton: CRC Press; 2008.
- 5) Dillon JC, Phuc AP, Dubacq JP. Nutritional value of the alga Spirulina. *World Review of Nutrition and Dietetics.* 1995; 77:32–46.
- 6) Yamagushi K. Recent advances in microalgal bioscience in Japan, with special reference to utilization of biomass and metabolites: A review. *J. Appl. Phycol.* 1997;8:487–502. doi: 10.1007/BF02186327.
- 7) Liang S., Xueming L., Chen F., Chen Z. Current microalgal health food R & D activities in China. *Hydrobiologia.* 2004;512:45–48. doi: 10.1023/B:HYDR.0000020366.65760.98.
- 8) Vilchez C., Garbayo I., Lobato M.V., Vega J.M. Microalgae-Mediated chemicals production and wastes removal. *Enzyme Microb. Technol.* 1997;20:562–572. doi: 10.1016/S0141-0229(96)00208-6.
- 9) Tarantino LM. Agency Response Letter GRAS Notice No. GRN000127. FDA Home page, October 2003.
- 10) Salazar M, Chamorro G, Salazar S, Steele C. Effect of *Spirulina maxima* consumption on reproductive and peri- and postnatal development in rats. *Food and Chemical Toxicology.* 1996:353–359
- 11) Chamorro G, Salazar S, Favila-Castillo L, Steele C, Salazar M. Reproductive and peri-and postnatal evaluation of *Spirulina maxima* in mice. *Journal of Applied Phycology.* 1997;9(2):107–112.
- 12) Salazar M, Martínez E, Madrigal E, Ruiz LE, Chamorro GA. Subchronic toxicity study in mice fed *Spirulina*. *Journal of Ethnopharmacology.* 1998;62(3):235–241. [PubMed]
- 13) Belay A. The potential application of *Spirulina (Arthrospira)* as a nutritional and therapeutic supplement in Health management. *Journal of the American Nutraceutical Association.* 2002;5:27–48.
- 14) Baicus C, Baicus A. Spirulina did not ameliorate idiopathic chronic fatigue in four N-of-1 randomized controlled trials. *Phytotherapy Research.* 2007;21(6):570–573. [PubMed]
- 15) Wan-Loy Chu^{1†}, Yen-Wei Lim, Ammu K Radhakrishnan and Phaik-Eem Lim -Protective effect of aqueous extract from *Spirulina platensis* against cell death induced by free radicals- *BMC Complementary and Alternative Medicine* 2010, 10:53 doi:10.1186/1472-6882-10-53
- 16) Yang H-N, Lee E-H, Kim H-M. *Spirulina platensis* inhibits anaphylactic reaction. *Life Sciences.* 1997;61(13):1237–1244. [PubMed]
- 17) Kim H-M, Lee E-H, Cho H-H, Moon Y-H. Inhibitory effect of mast cell-mediated immediate-type allergic reactions in rats by *Spirulina*. *Biochemical Pharmacology.* 1998;55(7):1071–1076. [PubMed]
- 18) Lusis AJ. Atherosclerosis. *Nature.* 2000;407:233–241. [PMC free article] [PubMed]
- 19) Glass CK, Witztum JL. Atherosclerosis. the road ahead. *Cell.* 2001;104:503–516. [PubMed]
- 20) Ishii K, Katoch T, Okuwaki Y, Hayashi O. Influence of dietary *Spirulina platensis* on IgA level in human saliva. *Journal of Kagawa Nutrition University.* 1999;30:27–33.)

- 21) Dartsch PC. Antioxidant potential of selected *Spirulina platensis* preparations. *Phytother Res.* 2008; 22:627–633. [PubMed]
- 22) Gemma C, Mesches MH, Sepesi B, Choo K, Holmes DB, Bickford PC. Diets enriched in foods with high antioxidant activity reverse age-induced decreases in cerebellar beta-adrenergic function and increases in proinflammatory cytokines. *J Neurosci.* 2002;22:6114–6120. [PubMed].
- 23) Ramamoorthy A, Premakumari S. Effect of supplementation of *Spirulina* on hypercholesterolemic patients. *Journal of Food Science and Technology.* 1996;33(2):124–128.
- 24) Mani UV, Desai S, Iyer U. Studies on the long-term effect of *Spirulina* supplementation on serum lipid profile and glycated proteins in NIDDM patients. *Journal of Nutraceuticals, Functional and Medical Foods.* 2000; 2(3):25–32.
- 25) Kato T, Takemoto K, Katayama H, Kuwabara Y. Effects of *Spirulina (Spirulina platensis)* on dietary hypercholesterolemia in rats. *J Jap Soc Nutr Food Sci.* 1984;37:323–332.
- 26) Nagaoka S, Shimizu K, Kaneko H, Shibayama F, Morikawa K, Kanamaru Y, Otsuka A, Hirahashi T, Kato T. A novel protein C-phycocyanin plays a crucial role in the hypocholesterolemic action of *Spirulina platensis* concentrate in rats. *J Nutr.* 2005;135:2425–2430. [PubMed]
- 27) P.Riva1 and P.Oreal1-P03.17
ANTICANCER DRUG AND SELENIUM-ENRICHED SPIRULINA PLATENSIS: A NEW CONCEPT FOR DRUG DELIVERY AND HIGH ANTI-PROLIFERATIVE ACTIVITYM. © European Society for Medical Oncology 2013.
- 28) "Surface decoration by *Spirulina* polysaccharide enhances the cellular uptake and anticancer efficacy of selenium nanoparticles"-Fang Yang, Quanming Tang, Xueyun Zhong, Yan Bai, Tianfeng Chen, Yibo Zhang, Yinghua Li, and Wenjie Zheng *Int J Nanomedicine.* 2012; 7: 835–844. Published online 2012 February 17. doi: 10.2147/IJN.S28278 PMID: PMC3284226
- 29) Kalafati M, Jamurtas A, Nikolaidis MG, Paschalis V, Theodorou A, Sakellariou G, Koutedakis Y, Kouretas D. Ergogenic and Antioxidant Effects of *Spirulina* Supplementation in Humans. *Medicine & Science in Sports & Exercise.* 2010;42:142–151. [PubMed]
- 30) Reddy MC, Subhashini J, Mahipal SVK, et al. C-Phycocyanin, a selective cyclooxygenase-2 inhibitor, induces apoptosis in lipopolysaccharide-stimulated RAW 264.7 macrophages. *Biochemical and Biophysical Research Communications.* 2003;304(2):385–392. [PubMed]
- 31) Riss J, Décordé K, Sutra T, Delage M, Baccou JC, Jouy N, Brune JP, Oréal H, Cristol JP, Rouanet JM. Phycobiliprotein C-phycocyanin from *Spirulina platensis* is powerfully responsible for reducing oxidative stress and NADPH oxidase expression induced by an atherogenic diet in hamsters. *J Agric Food Chem.* 2007;55:7962–7967. [PubMed]
- 32) González R, Rodríguez S, Romay C, Ancheta O, González A, Armesto J, Remirez D, Merino N. Anti-inflammatory activity of phycocyanin extract in acetic acid-induced colitis in rats. *Pharmacol Res.* 1999; 39:55–59. [PubMed]
- 33) Romay C, Delgado R, Remirez D, González R, Rojas A. Effects of phycocyanin extract on tumor necrosis factor-alpha and nitrite levels in serum of mice treated with endotoxin. *Arzneimittelforschung.* 2001; 51:733–736. [PubMed]
- 34) Remirez D, Ledón N, González R. Role of histamine in the inhibitory effects of phycocyanin in experimental models of allergic inflammatory response. *Mediators Inflamm.* 2002;11:81–85. [PMC free article] [PubMed]
- 35) Remirez D, Fernández V, Tapia G, González R, Videla LA. Influence of C-phycocyanin on hepatocellular parameters related to liver oxidative stress and Kupffer cell functioning. *Inflamm Res.* 2002; 51:351–356. [PubMed]
- 36) Romay Ch, González R, Ledón N, Remirez D, Rimbau V. C-phycocyanin: a biliprotein with

antioxidant, anti-inflammatory and neuroprotective effects. *Curr Protein Pept Sci.* 2003; 4:207–216. [PubMed]

- 37) Khan M, Varadharaj S, Shobha JC, Naidu MU, Parinandi NL, Kutala VK, Kuppusamy P. C-phycocyanin ameliorates doxorubicin-induced oxidative stress and apoptosis in adult rat cardiomyocytes. *J Cardiovasc Pharmacol.* 2006; 47:9–20. [PubMed]
- 38) Patel A, Mishra S, Ghosh PK. Antioxidant potential of C-phycocyanin isolated from cyanobacterial species *Lyngbya*, *Phormidium* and *Spirulina* spp. *Indian J Biochem Biophys.* 2006; 43:25–31. [PubMed]
- 39) Riss J, Décordé K, Sutra T, Delage M, Baccou JC, Jouy N, Brune JP, Oréal H, Cristol JP, Rouanet JM. Phycobiliprotein C-phycocyanin from *Spirulina platensis* is powerfully responsible for reducing oxidative stress and NADPH oxidase expression induced by an atherogenic diet in hamsters. *J Agric Food Chem.* 2007; 55:7962–7967. [PubMed]
- 40) Cherng SC, Cheng SN, Tarn A, Chou TC. Anti-inflammatory activity of c-phycocyanin in lipopolysaccharide-stimulated RAW 264.7 macrophages. *Life Sci.* 2007;81:1431–1435. [PubMed]
- 41) Shih CM, Cheng SN, Wong CS, Kuo YL, Chou TC. Antiinflammatory and antihyperalgesic activity of C-phycocyanin. *Anesth Analg.* 2009; 108:1303–1310. [PubMed]
- 42) Manconia M, Pendás J, Ledón N, Moreira T, Sinico C, Saso L, Fadda AM. Phycocyanin liposomes for topical anti-inflammatory activity: in-vitro in-vivo studies. *J Pharm Pharmacol.* 2009;61:423–430. [PubMed]
- 43) Chamorro G, Salazar M, Favila L, Bourges H. Pharmacology and toxicology of *Spirulina* alga. *Rev Invest Clin.* 1996; 48:389–399. [PubMed]
- 44) Salazar M, Chamorro GA, Salazar S, Steele CE. Effect of *Spirulina maxima* consumption on reproduction and peri- and postnatal development in rats. *Food Chem Toxicol.* 1996; 34:353–359. [PubMed]
- 45) Johnson PE, Shubert LE. Accumulation of mercury and other elements by *Spirulina* (cyanophyceae) *Nutr Rep Int.* 1986; 34:1063–1070.
- 46) Slotton DG, Goldman CR, Franke A. Commercially grown *Spirulina* found to contain low levels of mercury and lead. *Nutr Rep Int.* 1989; 40:1165–1172.

Article History:-----

Date of Submission: 19-07-2013

Date of Acceptance: 29-08-2013

Conflict of Interest: NIL

Source of Support: NONE

