

# **Neutraceutical Value of Spirulina (Arthrospiral)**

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### **ABSTRACT:**

Spirulina is a multicellular, free floating, microscopic filamentous cyanobacterium. Spirulina now named arthrosporic is used as food in Mexico, central Africa from prolonged period. It was still being used as a food into the native population of Chad area obtained from the small lakes. It's collected and sun dried and further cut into small pieces and utilized in dried form known as dihe Spirulina is a ubiquitous organism found in variety of environments like soil, sand, brackish water, seawater, fresh water etc. Spirulina possesses high contents of proteins, Gamma linolenic acid, vitamins, lipids and minerals showing functional biological activities hence it may be promising drugs treatment and prevention of many diseases. The present review has focused on the different bioactive compounds which are present in spirulina namely, proteins, carbohydrates, lipids, vitamins, minerals, nucleic acids, antioxidants, pigments and enzymes for pharmaceutical and healthcare purposes.

**KEYWORDS:** Spirulina, Bioactive molecules, pharmaceutical applications.

# I. INTRODUCTION:



FIG:1 SPIRULINA

Under nutrition is the result of insufficient, improper food intake, resulting in a decadent

\_\_\_\_\_ nutritional status characterized by lower height and/or weight that those expected for one's age.<sup>[1]</sup> Such condition, being frequently related to protein, vitamin, mineral deficiency, constitutes a public health problem all over the world, but particularly in developingcountries.<sup>[2]</sup> There is well-known, well-founded, enormous potential for a higher variety of microalgal species to be utilized in human nutrition. A myriad of microalgae Spirulinacontain protein of large quality for humans.<sup>[3]</sup> Several of the most common microalgalspirulina pigments (chlorophyll, β-carotene and lutein) are beneficial as well as important tohuman health, possessing cancer prevention activity and functioning as antioxidants, Neuroprotectant and antiinflammatory.<sup>[4]</sup> In the interest of developing source effectiveprotein sources more for preventing/reversing malnutrition, increasing attention has been turned tomicroalgae Spirulina. Single cell protein, i.e., crude or refined sources of protein thatoriginates from microorganisms such as bacteria, yeasts, fungi or algae,<sup>[5]</sup> represent a beneficial offer to many industries (e.g., fuel, cosmetic, therapeutic), including the feed, food and nutritional ones.<sup>[6,7]</sup>The important utilization or use of algae as a non-conventional protein source was suggested some decades ago.<sup>[8]</sup> Since then, several types of algae and their protein content have been tested for this purpose and, although toxicity problems have been reported for some species, promising results have been demonstrated for others. Among the latter. we have Spirulina.<sup>[9]</sup>Initially Spirulina was classified in the plant kingdom because of its richness in plant pigments as well as its property/ability of photosynthesis. It was latterly included in the bacteria kingdom based on new understanding on its genetics, biochemical and physiology properties.<sup>[10]</sup>Spirulina is accepted as free-floating filamentous microalgae with spiral characteristics of its filaments. It is formally called arthrosporic, belonging to the class of cyanobacteria with



characteristic photosynthetic as well as anticancerous capability. <sup>[11,12]</sup>.

### **BOTANICAL DISCRIPTION:**



Fig No:1 Spirulina plant

- **Botanical Name**: Arthrospiral platensis
- **Kingdom**: Monera
- **Class**: Cyanophyceae
- Order: Spirulinales
- **Family**: Spirulinaceae
- Species: Spirulina platensis and Spirulina maxima.
- Biological source: Blue green algae, spirulina platensis and Spirulina maxima, it is naturally grown in alkaline and warm media in the sea and fresh water.

#### **Chemical constituents:**

- Proteins (55-70%).
- Carbohydrates (15-25%).
- Amino acids.
- Essential fatty acids (18%).

- Vitamins(E,B1,D1,B12,)
- Pigments like carotenes, chlorophyll and phycocyanin.

#### Ethnobotanical Uses of Spirulina

1. External use of Spirulina can speed up hair growth. Moreover consumption, this algae is used as a component in shampoos and conditioning treatments.

2. It also helps in hair re-growth. The bioactive potential of Spirulina is still being evaluated in preclinical studies using animal models.

3. On the other hand, these studies seem to indicate Spirulina's strong anti-oxidant, anti-cancer, and anti-viral properties as well as its capacity to fight diabetes, obesity, and inflammatory allergic responses.

4. It also shows great benefit in Hypercholesterolemia, hyperglycemia, cardiovascular disease, and cancer treatments using nutraceuticals.

5. Spirulina is additionally used to prepare food with alternative ingredients. For example, nutritious blocks, stylish noodles, instant noodles, cookies and beverages.

6. Spirulina is one of the extraordinary quality natural feed additives that can be used in animal and poultry nutrition.

7. It has the capability to strengthen the immune system, release anxiety and help the body to cleanse. Thus, Spirulina effectively release IBS by detoxifying the intestine and stop constipation.

#### Spirulina quality specification :

The end product will fetch about 600 to 650 per kg .the following quality specification are met.

S. No	Particulars	Quality %
1	Moisture	3%
2	Protein	65%
3	Fat	7%
4	Crude Fiber	9%
5	Carbohydrates	16%
6	Energy (100 gms)	346 KCal
7	Mold & Fungus	Nil
8	Coliforms, Salmonella, streptococci bacteria, and fermented odor	NII

#### Table No:1 Percentage [%] Quality of spirulina in particulars.

#### Nutritional composition of spirulina :

Spirulina composition may vary according to the culture condion and the methods of analysis.table one shows the results uodated by third party laboratory and by earth raise nutritional LLC in terms of macro nutrients, vitamins, meanerals, and phytonutrients.



#### Nutritional value of spirulina :

Spirulina is found as an excellent source of proteins ,vitamins,dietary minerals,and pigments revealed by chemical analysis.specific arthrospira source ,cuiture conditions and season of production regulates its biochemical composition.

Lipids:

Spirulina presents a lipid fraction of approximately 5-10% of its dry weight. The important thing to this respect is that fats that make up such fraction are -mainly- essential lipids to human. Hence, Spirulina is considered a good source of gamma-linolenic, linoleic and oleic acids. The first one has received much attention since there are not many food sources that contain a significant amount; in fact, Spirulina is considered the vegetable source with the highest quantity (Ramirez 2006). The importance of gammalinolenic acid relies on the fact that it is the precursor of prostaglandins, leukotrienes and thromboxane's; thus, as they are mediators in inflammation and immune processes, they participate in the course of conditions such as arthritis, diabetes, cardiovascular disease, and cellular aging (Sankar Narayanan et al., 1995) (13.14).

#### Proteins and enzymes:

Proteins are biopolymers of amino acids, are essential for human beings, as they cannot be obtained without feeding, because of some deficiency in synthesizing them in enough amount. In addition, besides nutritional benefits some proteins, smaller peptides and amino acids have functions that contribute to a few health benefits. As microalgal species Arthrosporic and Chlorella are rich in protein and amino acid they may be used as nutraceuticals or be included in functional foods to prevent tissue damage and diseases. The total protein was 50-65% of which nearly 9.9% was non-protein nitrogen. Total protein was extracted by three successive extractions methods using water as a solvent. The isoelectric point was found to be 3.0. The polyacrylamide gel electrophoretic pattern showed seven bands. The in vitro digestibility was found to be 85% when assayed with a pepsin pancreatic system. Khan also reported the biochemistry and industrial potential of Spirulina (Sankaranarayanan et al.1995). It's consumption by human populations indicated a lack of toxic effects on human bodies. It could be used as a source of chemical and other basic commodities like enzymes, vitamins, lubricants, pigments, etc. Many species of microalgae and blue green algae under suitable conditions grew fastly

and produced large biomass with high protein content (Shklar and Swartz,1988)<sup>[14-16]</sup>

Macroeutricata		Vitamin	100
Calories	373	Vitamin A (as (I-contene)b	352.000 B
Total fet (g)	4.3	Vitamis K.	1990 mcg
Saturated fat	1.95	Thiaming HCL (Vitamin B1)	0.5 mg
Polystruturated fat	1.93	Riveflavin (Vitamin B2)	433 mg
Monoutstaturated fat	0.26	Niscis (Vitamine 33)	14.9 mg
Chalesterol	< 0.3	Vitamin B6 (Pyridex, HCL)	0.96 mg
Tonal carbohydraue (g)	17.8	Vitamin B12	162 mcg
Dietary fiber	2,7	Minerals	
Sugara	1.3	Calcium	468 mg
Lactose	< 0.1	Irun	87.4 mg
Protein B	63	Piosphorus	961 mg
Excepted awine acids (mg)		lodine	142 mg
Histidian	1000	Magnesium	319 mg
Insleurine	3300	Zied	1.45 mg
Leocine	5380	Selenism	25.5 mcg
Lysine	2960	Cooper	0.47 mg.
Methionine	1170	Manganese	3.26 mg
Phenylalanine	2750	Chromium	<400 mg
Throusine	2860	Potassion	1,660 mg
Tryptophan	1090	Sodium	641 mg
Valine	3940		
Non-essential amino acids (mg)		<b>Phylosutrients</b>	
Alanine	4590	Phycocyanis (mean)h	37.2%
Arginine	4310	Chiorophyll (muss)b	1.2%
Aspartic acid	5990	Superoxide dismutase (SOO)	531,000 f
Cystine	590	Gamma feedenic acid (GLA)	1080 mg
Glutanic acid	9130	Total caretensids (neurith	504 mg
Glycine	3130	B-carotene (mean)h	211 mg
Proline	2380	Zeasanhin	101 mg
Serine	2760		
Tyronian	2508		
Source: Salmain et al., 2015			

#### Table No:2 Nutritional profile of spirulina powder [composition by 100g]

#### Nucleic acids:

This fraction refers to the DNA and RNA content in Spirulina. Nucleic acids' catabolism yields uric acid, since purines-adenine and guanine are being degraded. High levels of uric acid are correlated to the development of gout, kidney stones and, more recently, cardiovascular disease Spirulina's content of nucleic acids is about 4-6% of its dry weight; these values are -for muchlower than that of other single-cell protein sources (e.g., yeast contains about 20% of its dry matter) and other microalgae like Chlorella. The World Health Organization recommends that the daily total nucleic acid consumption should not exceed 4 g; to get such quantity from the blue-green algae, one would have to consume up to 80 g. (Yu and Gutman, 1967; Seegmiller et al., 1967).[17]

#### Vitamins:

Of all the vitamins, vitamin B12 is the largest and most complex; it represents all of the biologically active cobalamins. The fact that Spirulina has an exceptionally high content of vitamin B12 –as other sea weed do– is of great importance because such vitamin is usually contained only in animal origin foods. Thus, this



alga might be considered as a good source for vegans, since they do not consume any animalorigin foods. Spirulina is also a good source of beta-carotene, containing about 700-1700 mg/kg, which once absorbed will be bio transformed into vitamin A. Human requirements of vitamin A are of approximately 1g hence 1-2 g of algae will be enough to assure this need. Moreover, opposite to the use of commercial supplements, an overdose would be nonprobable because beta-carotene (vs. retinol) is not cumulatively-toxic and its bioavailability has been verified in preclinical and clinical studies (Mitchell et al., 1990; Gireeshet al., 2004; Watanabe, 2007 and Annapurna et al., 2007).[18].

#### Minerals:

The inorganic nutrients of most relevance in Spirulina are iron, calcium and phosphorous. Populations that consume little animal foods -because of their own beliefs, preferences, or accessibility- are at a higher risk of developing iron deficiency; this disease is clinically manifested as microcytic and hypochromic anemia since hemoglobin is not present in sufficient quantities in erythrocytes (koury and ponka,2014;denic and Agarwal,2007). Additionally, those same people tend to consume a great amount of fiber which contains phytates and oxalates which, in turn, lower the bioavailability of iron in vegetable sources. Finally, plant foods contain only non-heme iron, which is more prone to be affected by absorption inhibitors (i.e., phytates). Spirulina could be able to counteract these two aspects:

a) its iron content is substantially high: comparatively, cereals –which are usually considered good sources of iron contain between 150-250 mg/kg; blue-green algae contain about 580-1800 mg/kg;

b) algae don't have pericardium (as cereals do)hence it does not present phytates/oxalates that could chelate iron and lower its absorption (Walter, 1997; WHO, 2007). For its side, calcium and phosphorous contents are comparable to those of the milk. The relative proportion (Ca:P) of these micronutrients is compatible with the preservation of bone health since it reduces decalcification risk. Moreover, as it was previously stated, the cyanobacteria of interest an oxalate-free plant food, thus as with iron, it provides calcium with high availability, thus it improves its absorption. (craig and mangels,2009)<sup>[19-21].</sup>

Among the varied products in which dried, flaked, or powdered Spirulina is now incorporated are: baked desserts, beer, breakfast cereals, confectionary, corn chips, crackers, doughnuts, food bars, frozen desserts, juice smoothies, muffins, pasta, popcorn, salad dressing, snack foods, and soups. Several cookbooks dedicated to Spirulina have been published.

### CAROTENOID AND C- PHYCOCYANINS CONTENT IN SPIRULINA POWDER

Calibration curves was constructed by analysing a mixture containing total five carotenoids at different concentration levels and plotting peak area against the concentration of each reference standard. The curves showed good linearity and the correlation coefficients were between 0.997 and 0.999 for all of the compounds over the concentration ranges of the quantification. The recovery of four carotenoids excepting diatoxanthin was assessed by spiking samples with higher and lower concentrations of each reference compound, 1000 and 30 ng, respectively. Spiking with 19.2 and 2.8 ng was done for fifth carotenoids i.e., diatoxanthin. The average recoveries were between 85.6% and 107.4% (n = 3). The limits of detection (LOD) were determined by serial dilution method based on a signal-to-noise. The peak purity was determined by the photodiode array detector and the corresponding computer software that confirmed the singularity of each peak. All-trans- $\beta$ carotene, all-trans-zeaxanthin, 9-cis- $\beta$ -carotene and diatoxanthin were found to be the major carotenoids present in spirulina.13-cis-β-Carotene was also detected. The content of Altran's-βcarotene was highest among the remaining four major carotenoids in AP-1, C1, C2 and C5 while that of all-trans-zeaxanthin was highest in the remaining samples. AP-1, C1 and C2 contained more than 1.6 mg/g dry weight of total carotenoids while the other samples contained less than 0.8 mg/g total carotenoid content. AP-1 showed highest total carotenoid content of  $4.43 \pm 0.03$ mg/g. The green photosynthetic pigment chlorophyll a which is essential for the photosynthesis in cyanobacteria as primary electron donor was also determined at the same LC conditions used for carotenoid analysis with a different wavelength. AP-1 showed the highest level of C-PC, chlorophyll a, a major bile protein of spirulina, was extracted by grinding the sample powder with sea sand and sonication at 4 °C. The extraction efficiency observed at pH 7 was higher than at pH 4 and 10. Among the three major pigments spirulina, the content of in

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CPHYCOCYANINS (C-PC) was highest with a value of 10–25% (w/w). The average percentages of carotenoids and chlorophyll a and were 0.03–0.38% and 0.26–1.1%, respectively. The total carotenoid content varied by up to eight-fold among the commercial samples, while the content variations of C-PC and chlorophyll a were 1.6 and 1.8-fold, respectively.<sup>[22][23]</sup>

#### MECHANISM OF ACTION: Antioxidant and Anti-inflammatory Effects

Spirulina contains several active ingredients, notably *B*-carotene and phycocyanin that have potent anti-inflammatory and antioxidant activities. The antioxidant and anti-inflammatory properties of phycocyanin were first reported in 1998and confirmed by various studies there after Phycocyanin has the ability to scavenge free radicals, including hydroxyl, alkoxyl, and peroxyl radicals. It also decreases nitrite production, decreases inducible nitric oxide synthase (INOS) expression and inhibits liver microsomal lipid peroxidation, using recombinant technology. phycocyanin protein has been obtained and the antioxidant activity is also shown with the recombinant phycocyanin protein.As antiinflammatory activities, phycocyanin inhibits cytokine formation, pro inflammatory such as TNFα, suppresses cyclooxygeanase-2 (COX-2) expression and lowers prostaglandin production. In addition, phycocyanin has been reported to suppress the activation of nuclear factor-kB (NFκB) through preventing degradation of cytosolic  $I\kappa B-\alpha$  and modulate the mitogen-activated protein kinase (MAPK) activation pathways, including the p38, c-Jun N-terminal kinase (JNK), and extracellular-signal-regulated kinase pathways.<sup>[24-40]</sup> (ERK1/2)

Neuroprotectant: Phenotypic outcomes are generally governed by epigenetic processes suggesting a possible connection between neurological disorders and food quality. Neuroprotective effects of Spirulina are well proof in ischemic brain damage with progressive suppressed in TUNEL positive cells and caspase3 activity in the ischemic hemisphere. Cerebral ischemia and Brain ischemia are a condition marked by the cerebral hypoxia that leads to the generation of free radicals, nitrogen species or reactive oxygen and energy crisis. Phycocyanobilin and Phycocyanin present in the Spirulina have anti-oxidant activities strong and anticyclooxygenase-2 that reduce peroxynitrite induced oxidative damage to DNA. Further advancement and intervention studies in omics

technology may provide important information in understanding the action of microglia mediated neuro-inflammation and the possible ability of nutritional approaches in regulating microglia aging. Dietary supplementation with Spirulina in rat model of Parkinson's disease results in significant decrease in lesion volume and reduces microglial activation<sup>[41]-[44]</sup>

# Hypolipidemic Activity

Although the hypolipidemic effect of Spirulina has been demonstrated in clinical and preclinical studies, our understanding on its mode of action is almost totally lacking. The active ingredients in Spirulina responsible for the hypolipidemic activity remain to be identified. In a study with S. platensis concentrate (SPC), it was shown that SPC could bind cholesterol metabolites bile acids and lowers the cholesterol solubility. Feeding rats with SPC significantly increased fecal excretion of cholesterol and bile acid. It was thus proposed that inhibition in intestinal cholesterol and bile acid absorption following SPC feeding mav represent а mechanism for the hypercholesteraemic action of SPC.<sup>[45]</sup>

# Health beanefits of spirulina :

# 1.Spirulina Is Extremely High in Many Nutrients

Spirulina is an organism that grows in both fresh and salt water.It is a type of cyanobacteria, which is a family of single-celled microbes that are often referred to as blue-green algae.Just like plants, cyanobacteria can produce energy from sunlight via a process called photosynthesis.Spirulina was consumed by the ancient Aztecs but became popular again when NASA proposed that it could be grown in space for use by astronauts.A standard daily dose of spirulina is 1–3 grams, but doses of up to 10 grams per day have been used effectively.This tiny alga is packed with nutrients. A single tablespoon (7 grams) of dried spirulina powder contains (2Trusted Source):

- **Protein:** 4 grams
- Vitamin B1 (thiamine): 11% of the RDA
- Vitamin B2 (riboflavin): 15% of the RDA
- Vitamin B3 (niacin): 4% of the RDA
- **Copper:** 21% of the RDA
- **Iron**: 11% of the RDA

It also contains decent amounts of magnesium, potassium and manganese and small amounts of almost every other nutrient that you need. In addition, the same amount holds only 20 calories and 1.7 grams of digestible carbs. Gram for gram, spirulina may be the single most nutritious



food on the planet. A tablespoon (7 grams) of spirulina provides a small amount of fat around 1 gram including both omega-6 and omega-3 fatty acids in an approximately 1.5–1.0 ratio. The quality of the protein in spirulina is considered excellent comparable to eggs. It gives all the essential amino acids that you need. It is often claimed that spirulina contains vitamin B12, but this is false. It has pseudovitamin B12, which has not been shown to be effective in humans (3Trusted Source, 4Trusted Source

# 2.powerful anti oxidants and anti inflamatory properties

oxidative damage can harm your DNA and cells.This damage can drive chronic inflammation, which contributes to cancer and other diseases.Phycocyanin can fight free radicals and inhibit production of inflammatory signaling molecules, providing impressive antioxidant and anti-inflammatory effects (6Trusted Source, 7Trusted Source, 8Trusted Source).

# 3. Can Lower "Bad" LDL and Triglyceride Levels

Heart disease is the world's leading cause of death.Many risk factors are linked to an increased risk of heart disease.As it turns out, spirulina positively impacts many of these factors. For example, it can lower total cholesterol, "bad" LDL cholesterol and triglycerides, while raising "good" HDL cholesterol.

# 4. Protects "Bad" LDL Cholesterol From Oxidation

Fatty structures in your body are susceptible to oxidative damage.This is known as lipid peroxidation, a key driver of many serious diseases (13Trusted Source, 14Trusted Source).For example, one of the key steps in the development of heart disease is the oxidation of "bad" LDL cholesterol (15Trusted Source).Interestingly, the antioxidants in spirulina appear to be particularly effective at reducing lipid peroxidation in both humans and animals

# 5. Moringa Can Lower Cholesterol

Having high cholesterol has been linked to an increased risk of heart disease.Fortunately, many plant foods can effectively reduce cholesterol. These include flaxseeds, oats and almonds.

#### 6. May Have Anti-Cancer Properties

Some evidence suggests that spirulina has anti-cancer properties.Research in animals indicates that it can reduce cancer occurrence and tumor size (19Trusted Source, 20Trusted Source).Spirulina's effects on oral cancer — or cancer of the mouth — have been particularly well studied.Spirulina Is Extremely High in Many Nutrients.Spirulina is an organism that grows in both fresh and salt water.It is a type of cyanobacteria, which is a family of single-celled microbes that are often referred to as blue-green algae.Just like plants, cyanobacteria can produce energy from sunlight via a process called photosynthesis.Spirulina was consumed by the ancient Aztecs but became popular again when NASA proposed that it could be grown in space for use by astronauts.A standard daily dose of spirulina is 1–3 grams, but doses of up to 10 grams per day have been used effectively.This tiny alga is packed with nutrients. A single tablespoon (7 grams) of dried spirulina powder contains (2Trusted Source):

# 7. May Reduce Blood Pressure

High blood pressure is a main driver of many serious diseases, including heart attacks, strokes and chronic kidney disease.

While 1 gram of spirulina is ineffective, a dose of 4.5 grams per day has been shown to reduce blood pressure in individuals with normal levels.

# 8. May Improve Muscle Strength and Endurance

Exercise-induced oxidative damage is a major contributor to muscle fatigue.Certain plant foods have antioxidant properties that can help athletes and physically active individuals minimize this damage.

# **II.** CONCLUSION :

Nutritional supplements may be consumed for different reasons e.g., compensating an insufficient energy, macronutrient (carbohydrates, lipids, proteins) or micronutrient (vitamins and minerals) intake with the objective of preventing or reversing an illness. The cardiovascular benefits of Spirulina are primarily resulted from its hypolipidemic, antioxidant, and anti-inflammatory activities Total carotenoid and C-PC content exhibited positive significant correlations with antioxidant activities. These results provide a strong scientific foundation for the establishment of standards for the commercial distribution of quality spirulina products. These aspects are important to take into account at the production sites as well as throughout the commercialization of spirulina products to preserve the quantity and quality of natural substances unaltered with nutritional and health benefits. In this context different species of Spirulina, possibly having different biological



effects, showed different acceptability. Therefore, the study of the relationship between liking and markers of antioxidant and immune status should be considered in human studies.

# REFERENCE

- [1]. UNICEF. Undernutrition. [On line] 2006 May [cited 2011 Dec 9]; Available at: URL:http://www.unicef.org/progressforch ildren/2006n4/index\_undernutrition.html
- [2]. Simpore J, Zongo F, Kabore F, et al. Nutrition rehabilitation of HIV-infected and HIV negative undernourished children utilizing Spirulina. Ann Nutr Metab, 2005; 49: 373-380.
- [3]. Becker EW. Micro-algae as a source of protein. Biotechnol Adv., 2007; 25: 207– 210. PMID: 17196357
- [4]. Pangestuti R, Kim S-K. Biological activities and health benefit effects of natural pigments derived from marine algae. J Funct Foods., 2011; 3: 255–266.
- [5]. Becker EW, Venkataraman LV. Production and utilization of the bluegreen alga Spirulina in India. 1984 Biomass, 4: 105125.
- [6]. Apt KE, Behrens PW. Commercial developments in microalgal biotechnology. J Phycol, 1999; 35: 215-26.
- [7]. Olaizola M. Commercial development on microalgal biotechnology: from the test tube to marketplace. Biomolecular Engineering, 2003; 20: 459-66.
- [8]. Belay A, Kato T, Ota Y. Spirulina (Arthospiral): potential application as an animal feed supplement. J App Phycol, 1996; 8: 303-11.
- [9]. Hwang JH, Lee T, Jeng KC, et al. Spirulina prevents memory dysfunction, reducesoxidation vestressdamage and augments antioxidant activity in senescence-accelerated mice. JNut Vitaminol, 2011; 57: 186-91.
- [10]. Vonshak A. (editor). Spirulina platensis (Arthrospira): Physiology, cell-biology and biotechnology. London: Taylor & Francis, 1997.
- [11]. Sapp J. The prokaryote-eukaryote dichotomy: Meanings and mythology. Microbiol Mol Biol Rev., 2005; 69: 292–305.

- [12]. Komarek J, Hauer T. CyanoDB.cz—Online database of cyanobacterial genera. Worldwide electronic publication, Univ. of South Bohemia and Inst of Botany AS CR2009;<u>http://www.cyanodb.cz</u>.
- [13]. Ramírez-Moreno L, Olvera-Sánchez R. Uso tradicionaly actual de Spirulina sp. INCI, 2006; 31(9): 657-63.
- [14]. Sankaranarayanan R, Nair PP, Varhese C, 1995. Evaluation of chemoprevention of oral cancer with Spirulina fusiformis. NutrCancer, 24(2): 197-202
- [15]. Sankar Narayanan R, Nair PP, Varhese C, 1995. Evaluation of chemoprevention of oral cancerwithSpirulina fusiformis. NutrCancer, 24(2): 197-202.
- [16]. Shklar G, Swartz J. 1988. Tumor necrosis factor in experimental cancer regression with alpha-tocopherol, beta-carotene, cathaxanthin and algae extract. Eur Cancer Clin Oncol,24(5): 839-50
- [17]. Yu T, Gutman AB, 1967. Uric acid nephrolithiasis in gout. Ann Intern Med, 67(6):1133-48
- [18]. Mitchell GV, Grundel E, Jenkins M, 1990.Effects of graded dietary levels of Spirulina maxima on vitamins A and E in male rats. J Nutr, 120(10): 1235-40.
- [19]. Koury MJ, Ponka P, 2004. New insights into erythropoiesis: the roles of folate, vitamin B12 and iron. Annu Rev Nutr, 24: 105-31.
- [20]. Craig WJ, Mangels AR, 2009. American Dietetic Association. Position of the American Dietetic Association: vegetarian diets. J Am Diet Assoc, 109(7): 1266-82.
- [21]. Watanabe F, 2007.Vitamin B12 sources and bioavailability. Exp Biol Med, 232: 1266
- [22]. Shrstha Sinha, Nisha Patro and Ishan K. Patro, "Spirulina Supplementation in Neuroprotection," Frontiers in Neuroscience, 2018; 12: 966, 9.
- [23]. Woo Sung Park, Hye-Jin Kim, Min Li, Dong Hoon Lim, Jungmin Kim, Sang-Soo Kwak, Chang-Min Kang, Mario G. Ferruzzi and Mi-Jeong Ahn, —Two Classes of Pigments, Carotenoids and C-Phycocyanin, in Spirulina Powder and Their Antioxidant Activities, I molecules, 2018; 23: 2065, 4.
- [24]. Romay C, Armesto J, Remirez D, Gonzalez R, Ledon N, Garc´ 1a I. Antioxidant´ and anti-inflammatory



properties of C-phycocyanin from bluegreen algae. Inflamm Res., 1998; 47: 36– 41.

- [25]. Romay C, Ledon N, Gonz´alez R. Further studies on anti-inflammatory activity´ of phycocyanin in some animal models of inflammation. Inflamm Res., 1998; 47: 334–338.
- [26]. Riss J, Decord´ e K, Sutra T, et al. 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.
- [27]. Gonzalez R, Rodr' Iguez S, Romay C, et al. Anti-inflammatory activity of' phycocyanin extract in acetic acidinduced colitis in rats. Pharmacol Res., 1999; 39: 55–59.
- [28]. Romay C, Delgado R, Remirez D, Gonzalez R, Rojas A. Effects of phycocyanin' extract on tumours necrosis factor-alpha and nitrite levels in serum of mice treated with endotoxin. Arzneimittelforschung, 2001; 51: 733– 736.
- [29]. Remirez D, Ledon N, Gonz´ alez R. Role of histamine in the inhibitory effects of´ phycocyanin in experimental models of allergic inflammatory response. Mediat Inflamm, 2002; 11: 81–85.
- [30]. Remirez D, Fernandez V, Tapia G, Gonz´ alez R, Videla LA. Influence of´ Cphycocyanin on hepatocellular parameters related to liver oxidative stress and Kupffer cell functioning. Inflamm Res., 2002; 51: 351–356.
- [31]. Romay Ch, Gonzalez R, Led´ on N, Remirez D, Rimbau V. C-phycocyanin: A´ biliprotein with antioxidant, antiinflammatory and neuroprotective effects. Curr Protein Pept Sci., 2003; 4: 207–216.
- [32]. 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.
- [33]. Patel A, Mishra S, Ghosh PK. Antioxidant potential of C-phycocyanin isolatedfrom cyanobacterial species Lyngbya, Phormidium and Spirulina spp. Indian J Biochem Biophys, 2006; 43: 25–31.

- [34]. Riss J, Decord´ e K, Sutra T, et al. 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.
- [35]. Cherng SC, Cheng SN, Tarn A, Chou TC. Anti-inflammatory activity ofcphycocyanin in lipopolysaccharidestimulated RAW 264.7 macrophages. Life Sci., 2007; 81: 1431–1435.
- [36]. Shih CM, Cheng SN, Wong CS, Kuo YL, Chou TC. Anti-inflammatory and antihyperalgesic activity of Cphycocyanin. Anesth Analg, 2009; 108: 1303-1310. 53. Manconia M, Pendas J, Led' on 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.
- [37]. Ge B, Qin S, Han L, Lin F, Ren Y. Antioxidant properties of recombinant allophycocyanin expressed in Escherichia coli. J Photochem Photobiol B., 2006; 84: 175–180.
- [38]. Guan XY, Zhang WJ, Zhang XW, et al. A potent anti-oxidant property: Fluorescent recombinant alpha- phycocyanin of Spirulina. J Appl Microbiol, 2009; 106: 1093–1100.
- [39]. Khan M, Varadharaj S, Ganesan LP, et al. C-phycocyanin protects againstischemiareperfusion injury of heart through involvement of p38 MAPK and ERK signaling. Am J Physiol Heart Circ Physiol, 2006; 290: H2136–H2145.
- [40]. Li XL, Xu G, Chen T, et al. Phycocyanin protects INS-1E pancreatic beta cellsagainst human islet amyloid polypeptide-induced apoptosis through oxidative attenuating stress and modulating JNK and p38 mitogenactivated protein kinase pathways. Int J Biochem Cell Biol., 2009; 41: 1526–1535.
- [41]. Wang, Y., Chang, C. F., Chou, J., Chen, H. L., Deng, X., and Harvey, B. K. (2005). Dietary supplementation with blueberries, spinach, or spirulina reduces ischemic brain damage. Exp. Neurol, 193: 75–84. doi: 10.1016/j.expneurol.2004.
- [42]. 40. Li XL, Xu G, Chen T, et al. Phycocyanin protects INS-1E pancreatic beta cellsagainst human islet amyloid



polypeptide-induced apoptosis through attenuating oxidative stress and modulating JNK and p38 mitogenactivated protein kinase pathways. Int J Biochem Cell Biol., 2009; 41: 1526–1535.

- [43]. Wang, Y., Chang, C. F., Chou, J., Chen, H. L., Deng, X., and Harvey, B. K. (2005). Dietary supplementation with blueberries, spinach, or spirulina reduces ischemic brain damage. Exp. Neurol, 193: 75–84. doi: 10.1016/j.expneurol.2004. 12.014
- [44]. Bhat, V. B., and Madyastha, K. M. (2001). Scavenging of peroxynitrite by phycocyanin and phycocyanobilin from Spirulina platensis: protection against oxidative damage to DNA. Biochem. Biophys. Res. Commun, 285: 262–266. doi: 10.1006/bbrc.2001.5195
- [45]. Patro, I., Nagayach, A., Sinha, S., and Patro, N. (2016). —General physiology and pathophysiology of microglia during neuroinflammation, in Inflammation: The Common Link in Brain Pathologies, 1st Edn, eds N. Jana, A. Basu, and P. N. Tandon (Singapore: Springer), 17–42. doi: 10.1007/978-981-10-1711-7\_2
- [46]. Wu, Z., Yu, J., Zhu, A., and Nakanishi, H. (2016). Nutrients, microglia aging, and brain aging. Oxid. Med. Cell Longev, 2016: 7498528. doi: 10.1155/2016/7498528 Xiao, X. M., and Li, L. P. (2005). Arginine treatment for asymmetric fetal growth restriction. Int. J. Gynaecol. Obstet, 88: 15–18. doi: 10.1016/j.ijgo.2004.09.017
- [47]. Nagaoka S, Shimizu K, Kaneko H, et al. A novel protein C-phycocyanin playsa crucial role in the hypocholesterolemic action of Spirulina platensis concentrate in rats. J Nutr, 2005; 135: 2425–2430.