

## NUTRACEUTICAL VALUE OF *SPIRULINA* (*ARTHROSPIRA*): A REVIEW

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Article Received on  
22 Feb. 2020,

Revised on 12 March 2020,  
Accepted on 02 April 2020,

DOI: 10.20959/wjpr20205-17256

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### ABSTRACT

Under nutrition constitutes all public health problem particularly in developing countries. The utilization of algae such as *Spirulina*, as a functional food was suggested decades ago due to the fact that it is not only a protein-dense food source, but because its amino acid profile is considered as of large biologic-value protein content. *Arthrospira platensis* is the widely available source of spirulina that contains distinctive natural pigments, including C-phycocyanin (C-PC) and carotenoids. *Spirulina* is most widely accepted free-floating filamentous microalgae growing in alkaline water bodies. With its higher nutritional value, *Spirulina* has been consumed as food for

centuries in Central Africa. This alga is a rich source of vitamins, proteins, minerals, amino acids and other nutrients. Its main use is as a food supplement. It is now largely used as nutraceutical food supplement worldwide. Recently, extensive studies and great attention have been devoted to evaluate its therapeutic benefits on an array of diseased conditions including hypercholesterolemia, hyperglycerolemia, cardiovascular diseases, inflammatory diseases, cancer and viral infections. The cardiovascular benefits of *Spirulina* are primarily resulted from its antioxidant, hypolipidemic and anti-inflammatory activities. This article serves as an overview, introducing the basic biochemical composition of this algae and moves to nutraceutical applications. In addition to that article shows mechanism of action of spirulina.

**KEYWORDS:** Spirulina, nutritional composition, Carotenoid, anti-inflammatory, antioxidant, Hypolipidemic Activity, *Arthrospira platensis*.

## INTRODUCTION

Under nutrition is the result of insufficient, improper food intake, resulting in a decadent nutritional status characterized by lower height and/or weight than 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 developing countries.<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 *Spirulina* contain protein of large quality for humans.<sup>[3]</sup> Several of the most common microalgal spirulina pigments (chlorophyll,  $\beta$ -carotene and lutein) are beneficial as well as important to human health, possessing cancer prevention activity and functioning as antioxidants, Neuroprotectant and anti-inflammatory.<sup>[4]</sup> In the interest of developing source more effective protein sources for preventing/reversing malnutrition, increasing attention has been turned to microalgae *Spirulina*. Single cell protein, i.e., crude or refined sources of protein that originates from microorganisms such as bacteria, yeasts, fungi or algae,<sup>[5]</sup> represent an 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 *Arthrospira*, belonging to the class of cyanobacteria with characteristic photosynthetic as well as anti-cancerous capability.<sup>[11,12]</sup>

Among all number of *Spirulina* species, three species of *Spirulina*, including *Spirulina maxima* (*Arthrospira maxima*), *Spirulina platensis* (*Arthrospira platensis*) and *Spirulina fusiformis* (*Arthrospira fusiformis*) are most intensively investigated as those *Spirulina* species are edible with high potential as well as nutritional therapeutic values.<sup>[10, 13-15]</sup> In terms of nutrition, *Spirulina* is a rich food source of micro and macronutrients including high quality gamma-linolenic, protein, iron, acid, minerals, vitamins, sulfated polysaccharides and

phycocyanin.<sup>[16,17]</sup> Hence *Spirulina* is of great interest as it offers the possibility of being used as a *functional food* as well as nutritional food.<sup>[18]</sup> *Spirulina* is well recognized in its nutritional value because of its unusual high protein content (60–70% by dry weight) and its richness in essential fatty acids, vitamins, minerals and other nutrients.<sup>[10,13]</sup> Because of its unusual high nutritional values, high protein content the Intergovernmental Institution for the use of Micro-Algae *Spirulina* Against Malnutrition (IIMSAM) was launched in the middle 1970s to promote *Spirulina* as high nutritional food to work against starvation and malnutrition in all over the world.<sup>[19]</sup>

In this review, emphasis is given to the potential, nutritional and toxicological beneficial effects properties of *Spirulina*, since information has been reported, although some pharmacological activities –mainly those related to the algae's antioxidant and enzyme inhibitor capacity with highlights on *Spirulina*'s anti-inflammatory, hypolipidemic and antioxidant activities in preclinical and clinical studies. In addition, our current understanding on the mechanisms of action and the potential side-effects of *Spirulina* consumption are briefly summarized.

## NUTRITIONAL COMPOSITION OF SPIRULINA

Food supplements are increasingly popular all over the world, including those based on microalgae.<sup>[20]</sup> Most often, such products contain biomass of cyanobacteria belonging to the genera of *Arthrospira* (sold as 'Spirulina') and are marketed for their potential, biological and nutritional value activity.<sup>[21]</sup> *Spirulina* is one of the most important/valuable sources of nutrition. The protein content of *Spirulina* is between 60 and 70% of its dry weight. In addition to that it also contains vitamins (beta carotene, vitamin B-12, vitamin E), essential fatty acids (gamma-linoleic acid, palmitic acid, linoleic acid, oleic acid, etc.), various mineral substances (iron, calcium, phosphorus, magnesium, and trace minerals), polysaccharides (rhamnose and glycogen), enzymes (SOD responsible for quenching free radicals) glycolipids and sulfolipids, and various pigments like carotenoids, phycocyanin, chlorophyll as represented in.<sup>[22-27]</sup>

Carotenoids are a class of natural lipid-soluble pigments that are valuable for the red, yellow, and orange colors found in various microorganisms and plants. They primarily function as photosynthesis aids and are used in the various photo protection process.<sup>[28]</sup> The health benefits of carotenoids to animals and humans are becoming increasingly day by day. For example, there is evidence that these pigments may protect humans from serious disorders

associated with inflammatory and oxidative stress including skin degeneration and aging, certain types of cancer, cardiovascular disease, and age-related diseases of the eye, such as macular degeneration or cataracts.<sup>[29-31]</sup>

Phycocyanins from *Spirulina* are mostly consumed as functional colorants and natural edible due to their brilliant blue color with excellent anti-cancer, antioxidant and anti-inflammatory activities. In addition to C- phycocyanins, APC possesses strong antioxidant activity, in terms of scavenging peroxy radicals, whereas CPC is better at scavenging hydroxyl radicals.<sup>[32]</sup>

### Protein and Amino Acids

*Spirulina*'s high protein content ranges between 60 to 70% of its dry weight. This is an exceptional proportion since the vast majority of plant-based foods contain only about 35%.<sup>[33]</sup> In fact, C-phycocyanin, a molecule which contains a homolog of biliverdin (phycocyanobilin),<sup>[34]</sup> is one of the major proteins present in *Spirulina*, accounting for about 20% of algae's dry weight.<sup>[35]</sup>

*Spirulina* protein exhibits other characteristics that increase its nutritional value as well as its nutraceutical value. For example, its biologic value (BV) –i.e., a measure of the nitrogen retained within the body in relation to the nitrogen absorbed– its net protein utilization (NPU), which represents the percent content of nitrogen ingested that remains within the organism. Moreover, *Spirulina* has a relatively more digestibility coefficient (DC), which is the proportion of nitrogen contained in foods that is mainly absorbed.<sup>[36]</sup> The algae also having a good protein efficiency ratio (PER), the simplest and most common method used to evaluate proteins by animal feeding tests.<sup>[37]</sup>

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

Calibration curves was constructed by analyzing 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 (S/N)

ratio of 3:1.<sup>[38,39]</sup> 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.<sup>[39]</sup> 13-*cis*- $\beta$ -Carotene was also detected. The content of all-*trans*- $\beta$ -carotene 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.<sup>[39]</sup>

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 biliprotein 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 in spirulina, the content of C-PHYCOCYANINS (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>[39]</sup>

## MECHANISM OF ACTION

### Antioxidant and Anti-inflammatory Effects

*Spirulina* contains several active ingredients, notably  $\beta$ -carotene and phycocyanin that have potent anti-inflammatory and antioxidant activities. The antioxidant and anti-inflammatory properties of phycocyanin were first reported in 1998<sup>[40,41]</sup> and confirmed by various studies thereafter.<sup>[42,53]</sup> Phycocyanin has the ability to scavenge free radicals, including hydroxyl, alkoxyl, and peroxy radicals. It also decreases nitrite production, decreases inducible nitric oxide synthase (INOS) expression and inhibits liver microsomal lipid peroxidation.<sup>[40-53]</sup> Using recombinant technology, phycocyanin protein has been obtained and the antioxidant activity is also shown with the recombinant phycocyanin protein.<sup>[54,55]</sup>

As anti-inflammatory activities, phycocyanin inhibits cytokine formation, pro inflammatory such as TNF $\alpha$ , suppresses cyclooxygenase-2 (COX-2) expression and lowers prostaglandin

E (2) production.<sup>[44,46, 49-51]</sup> In addition, phycocyanin has been reported to suppress the activation of nuclear factor- $\kappa$ B (NF- $\kappa$ B) through preventing degradation of cytosolic I $\kappa$ B- $\alpha$ <sup>[50]</sup> and modulate the mitogen-activated protein kinase (MAPK) activation pathways, including the p38, c-Jun N-terminal kinase (JNK), and extracellular-signal-regulated kinase (ERK1/2) pathways.<sup>[56,57]</sup>

### 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.<sup>[58]</sup> 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 strong anti-oxidant activities and anti-cyclooxygenase-2 that reduce peroxynitrite induced oxidative damage to DNA.<sup>[59]</sup> Further advancement and intervention studies in omics technology may provide important information in understanding the action of microglia mediated neuro-inflammation<sup>[60]</sup> and the possible ability of nutritional approaches in regulating microglia aging.<sup>[61]</sup>

Dietary supplementation with Spirulina in rat model of Parkinson's disease results in significant decrease in lesion volume and reduces microglial activation.<sup>[62]</sup> Anti-inflammatory effects of Spirulina have also been investigated/searched against LPS-induced inflammation in rodent model. LPS insult causes increased astrogliosis with activation of GFAP in existing cells and decreased proliferation of neural progenitor cells (NPCs). However, diet supplemented with 0.2% Spirulina for 30 days before LPS administration prevents the LPS induced decrease in NPC proliferation.<sup>[63]</sup> Researchers at University of Yaounda<sup>[64]</sup> found that food nutrition with Spirulina for 84 days in malnourished children's infected with HIV stimulates weight gain and increase fat free mass as compared to soya beans. In addition, antiretroviral treatment (ART) along with Spirulina showed more beneficial effects than ART joined to soybeans (increased CD4 cell counts and reduces viral load in Spirulina group). Spirulina platensis was also seen to suppress the peripheral sensitization, improve motor coordination and restore motor activity in collagen-induced arthritic rats by reducing NF-200 accumulation in spinal cord neurons suggesting a possible neuroprotective role of Spirulina for treating of rheumatoid arthritis.<sup>[65]</sup> Spirulina also helps the viability of astrocytes.<sup>[66]</sup>



Interestingly, polycaprolactone Spirulina nanofiber mat (composite nanomedicine) was proved to be effective against CNS injury as it decreases the astrocyte activation which in turn, could reduce inflammation induced by astrogliosis. Neuroprotective ability of Spirulina is also marked in alpha-synuclein model of Parkinson's disease, where increased expression of tyrosine hydroxylase (TH) positive and NeuN positive cells was observed. Like that, reduced number of activated microglia was also reported as determined by the reduced OX6 (MHC-II) immunostaining.<sup>[67]</sup>

### Microbial modulating activities

It has been recently concluded that, in the majority of commercially available *Spirulina* food supplements, *Arthrospira platensis* was the predominant taxon (81.2–100.0%) among the cyanobacteria.<sup>[68]</sup>

*Spirulina* (*Arthrospira*) *platensis* is able to decrease the ability of growth of some Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus vulgaris*) and Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus subtilis*, and *Bacillus cumuli*'s.<sup>[69]</sup> In fact, *Spirulina* produces in-vitro metabolites with antibacterial activity (Figure 1).<sup>[70-73]</sup> The methanol extract from grown culture medium of *Spirulina* showed a higher antimicrobial activity than hexane,<sup>[70]</sup> dichloromethane,<sup>[69,70]</sup> petroleum ether,<sup>[71]</sup> ethyl acetate<sup>[71,72]</sup> extracts, and volatile components (heptadecane and tetradecane).<sup>[71]</sup> especially against *Streptococcus faecali*,<sup>[71]</sup> *Staphylococcus epidermidi*<sup>[71]</sup> and *Candida albicans*,<sup>[71]</sup> Gram-positive bacterium *Staphylococcus aureus*,<sup>[72]</sup> and Gram-negative bacterium *Escherichia coli*.<sup>[72]</sup>

On the contrary, low (minimum inhibitory concentrations, MIC  $\geq$  512  $\mu$ g/ml) or no inhibitory effect was found against other bacteria (*Pseudomonas aeruginosa*, *Salmonella typhirium*, and *Klebsiella pneumoniae*).<sup>[72]</sup> El-Sheekh et al.<sup>[70]</sup> purified an antimicrobial substance (molecular formula C<sub>15</sub>H<sub>18</sub>NO<sub>8</sub>) from *Spirulina platensis* in addition to no characteristic odor and yellowish green color. This extract (soluble in methanol, diethyl ether, chloroform, and dimethyl sulfoxide, but sparingly soluble in water and acetone) was active against the unicellular fungus *Candida albicans* (MIC = 30  $\mu$ g/ml) and the Gram-positive *Bacillus subtilis* (MIC = 60  $\mu$ g/ml) at low concentrations in comparison to the action against the Gram-negative bacterium *Pseudomonas aeruginosa* (MIC = 85  $\mu$ g/ml).<sup>[70]</sup> Besides, *Spirulina* has been recently used in the bio functionalized gold nanoparticles synthesis with antibacterial activity against Gram-positive organisms (*Bacillus subtilis* and *Staphylococcus aureus*).<sup>[72]</sup>

Therefore, the research on advanced medical applications of *Spirulina* derived products in the diagnosis of infectious diseases caused by Gram-positive organisms is growing.<sup>[74]</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 may represent a mechanism for the hypocholesterolemic action of SPC.<sup>[75]</sup>

### 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's studies.

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