



# REVIEW ON REPORTED ACTIVITIES OF SPIRULINA

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**Abstract:** Spirulina is free-floating filamentous microalgae growing in alkaline water bodies. With its high nutritional value, Spirulina has been consumed as food for centuries in Central Africa. It is now widely used as nutraceutical food supplement worldwide. Recently, great attention and extensive studies 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 hypolipidemic, antioxidant, and antiinflammatory activities. Data from preclinical studies with various animal models consistently demonstrate the hypolipidemic activity of Spirulina. Although differences in study design, sample size, and patient conditions resulting in minor inconsistency in response to Spirulina supplementation, the findings from human clinical trials are largely consistent with the hypolipidemic effects of Spirulina observed in the preclinical studies. However, most of the human clinical trials are suffered with limited sample size and some with poor experimental design. The antioxidant and/or antiinflammatory activities of Spirulina were demonstrated in a large number of preclinical studies. However, a limited number of clinical trials have been carried out so far to confirm such activities in human. Currently, our understanding on the underlying mechanisms for Spirulina's activities, especially the hypolipidemic effect, is limited. Spirulina is generally considered safe for human consumption supported by its long history of use as food source and its favorable safety profile in animal studies. However, rare cases of side-effects in human have been reported. Quality control in the growth and process of Spirulina to avoid contamination is mandatory to guarantee the safety of Spirulina products.[1]

**Keywords:** Spirulina Platensis , Spirulina Asieh ,Spirulina Microalgae,6OHDA,ATC.

## **The Antioxidant, Immunomodulatory, and Anti-inflammatory Activities of Spirulina**

Spirulina is a species of filamentous cyanobacteria that has long been used as a food supplement. In particular, Spirulina platensis and Spirulina maxima are the most important. Thanks to a high protein and vitamin content, Spirulina is used as a nutraceutical food supplement, although its other potential health benefits have attracted much attention. Oxidative stress and dysfunctional immunity cause many diseases in humans, including atherosclerosis, cardiac hypertrophy, heart failure, and hypertension. Thus, the antioxidant, immunomodulatory, and anti-inflammatory activities of these microalgae may play an important role in human health. Here, we discuss the antioxidant, immunomodulatory, and anti-inflammatory activities of Spirulina in both animals and humans, along with the underlying mechanisms. In addition, its commercial and regulatory status in different countries is discussed as well. Spirulina activates cellular antioxidant enzymes, inhibits lipid peroxidation and DNA damage, scavenges free radicals, and increases the activity of superoxide dismutase and catalase. Notably, there appears to be a threshold level above which Spirulina will taper off the antioxidant activity. Clinical trials show that Spirulina prevents skeletal muscle damage under conditions of exercise-induced oxidative stress and can stimulate the production of antibodies and up- or downregulate the expression of cytokine-encoding genes to induce immunomodulatory and anti-inflammatory responses. The molecular mechanism(s) by which Spirulina

induces these activities is unclear, but phycocyanin and  $\beta$ -carotene are important molecules. Moreover, Spirulina effectively regulates the ERK1/2, JNK, p38, and I $\kappa$ B pathways. This review provides new insight into the potential therapeutic applications of Spirulina and may provide new ideas for future studies.[2]

### **Antioxidant and Antiproliferative Activities of Spirulina and Chlorella Water Extracts**

Liver fibrosis is a chronic liver disease that will further develop to cirrhosis if severe damage continues to form. A potential treatment for liver fibrosis is to inhibit activated hepatic stellate cell (HSC) proliferation and, subsequently, to induce HSC apoptosis. It has been reported that antioxidants are able to inhibit the proliferation of HSCs. In this study, the aqueous extract of spirulina was chosen as the source of antioxidant to investigate the inhibitory effect on the proliferation of HSC. The growth inhibitory effects of aqueous spirulina and chlorella extract on human liver cancer cells, HepG2, were also studied and compared in pairs. Results indicated that the total phenol content of spirulina was almost five times greater than that of chlorella ( $6.86 \pm 0.58$  vs  $1.44 \pm 0.04$  mg tannic acid equivalent/g of algae powder, respectively). The antioxidant activity of spirulina determined by the ABTS $\bullet$ + method was higher than chlorella (EC50:  $72.44 \pm 0.24$   $\mu$ mol of trolox equivalent/g of spirulina extract vs  $56.09 \pm 1.99$   $\mu$ mol of trolox equivalent/g of chlorella extract). Results of DPPH $\bullet$  assay also showed a similar trend as the ABTS $\bullet$ + assay (EC50:  $19.39 \pm 0.65$   $\mu$ mol of ascorbic acid equivalent/g of spirulina extract vs  $14.04 \pm 1.06$   $\mu$ mol of ascorbic acid equivalent/g of chlorella extract). The aqueous extracts of these two algae both showed antiproliferative effects on HSC and HepG2, but spirulina was a stronger inhibitor than chlorella. Annexin-V staining showed that aqueous extract of spirulina induced apoptosis of HSC after 12 h of treatment. In addition, the aqueous extract of spirulina triggered a cell cycle arrest of HSC at the G2/M phase. [3]

### **Effect of pH on Phytochemical and Antibacterial Activities of Spirulina Platensis**

This study presents the effect of pH changes on productivity of Spirulina platensis. The highest content of its dry weight (0.0853 g/20 ml), chlorophylla (2.8  $\mu$ g/ml), carotenoids (2.6  $\mu$ g/ml), protein and carbohydrates are recorded at pH 10 (425 mg/g and 97 mg/g) respectively. As its phenolic content was maximized with acetone extract (0.52 mg/g) while flavonoids were detected with ethanol extract (7.6 mg/g). Antimicrobial activity of S. platensis was prepared in 70% (methanol, ethanol and acetone) at different pH values, and tested against some pathogenic bacterial. Its highest antibacterial activities were reported with 70% acetone extract. The maximum inhibition of Staphylococcus aureus NCTC-7447 was observed in acetone extract at pH 8.0 and 10, while it was recorded at pH 8.0 for E. coli NCTC-10418.[4]

### **Antioxidant Properties of Spirulina Asieh**

Spirulina is free-floating filamentous microalgae growing in alkaline water bodies. As early as over 400 years ago, Spirulina was eaten as food by the Mayas, Toltec's and Kanembu in Mexico during the Aztec civilization. Spirulina is a well-known source of valuable food supplements, such as proteins, vitamins, amino acids, minerals, fatty acids, etc. It is widely used in human and animal nutrition, as well as in the cosmetic industry. Both in vivo and in vitro trials have shown effective and promising results in the treatment of certain cancers and allergies, anemia, hepatotoxicity, viral infection, vascular diseases, radiation protection, and obesity. The antioxidant activities of Spirulina were demonstrated in a large number of preclinical studies. Antioxidants in preventing many human diseases. Findings of this study showed Spirulina can be used as a source of antioxidants.[5]

### **Antioxidant and Phytonutrient Activities of Spirulina Platensis**

Increasing the consumption of natural substances has increased the demand for biological sources such as Spirulina platensis. The study quantitatively investigates the antioxidant potential and phytonutrient contents in aqueous and ethanol extracts of spirulina. The spirulina was collected from a local farm of Pondicherry and mass cultured in our research laboratory. The spirulina biomass was evaluated for antioxidant potential viz. catalase, SOD, GPx, Vitamin C, Vitamin E, and reduced GSH; phytonutrients contents like total phenol, flavonoid, tannin, carbohydrates, and proteins in both aqueous and ethanolic extracts of spirulina. Significant enzymatic antioxidant activity was observed for ethanolic extract. However, aqueous extracts were higher for catalase, SOD, and GPx activity. The same trend was observed for non-enzymatic activities. Total phenol, flavonoid, and tannin content were observed and high in aqueous extract. However, protein and carbohydrate content were higher in ethanolic extract. We observed a significant change in antioxidant activity and phytonutrient content in ethanolic extract than in aqueous extracts. The strong antioxidant property and higher phytonutrient contents of spirulina can play a vital role in the dietary supplement and combating malnutrition.[6]

### **Enhancement of Immune Activation Activities of Spirulina Maxima Grown in Deep-Sea Water**

In this study, the immuno-modulatory and anticancer activities of marine algae, *Spirulina maxima* grown in deep-sea water (DSW), were investigated. It was found that the extract of *S. maxima*, cultured in DSW, effectively suppressed the expression of Bcl2 in A549 cells as well as inhibiting various human cancer cells with concentration dependency, which possibly implies that the extracts may play more important roles in controlling cancer cell growth. The secretion of cytokines IL-6 and TNF- $\alpha$  from human B cells was also greatly increased, compared to those of the extract grown in conventional sea-water. The growth of Human Natural Killer (NK) cells in the presence of the extracts from DSW was significantly higher ( $12.2 \times 10^4$  viable cells/mL) when compared to the control ( $1.1 \times 10^4$  viable cells/mL). Based on HPLC analysis, the increase in the biological activities of the extracts from DSW was caused by considerably high amounts of  $\beta$ -carotene and ascorbic acid because the DSW contained high concentrations and good ratios of several key minerals for biosynthesizing  $\beta$ -carotene and ascorbic acid, as well as maintaining high cell growth.[7]

### **Antiviral and Antimicrobial Activities of Spirulina**

PLATENSIS The total crude (70%) methanol extract and five successive extracts of *Spirulina platensis* were tested against four types of viruses using cell viability assay and nine strains of Gram (+ve) and Gram (-ve) bacteria as well as *Candida albicans* using disc diffusion method. The results revealed that the total methanol and n-hexane extracts were significantly active against all tested viruses showing mean % inhibition of 56.7% and 66.7% against rotavirus Wa strain; 60% and 63.3% against adenovirus type 7; 53.3% and 50% against adenovirus type 40 respectively and 50% for both extracts against Coxsackievirus B4. The ethyl acetate extractive was active only against rotavirus Wa strain with 53.3% inhibition. Normal hexane extract was most potent against *Salmonella senftenberg* with 58.5% inhibition. GC-MS analysis of the saponifiable and unsaponifiable fractions of the n-hexane extract besides the total carbohydrate, phenolic, flavonoid and tannin contents of the crude methanol extract were carried out.[8]

### **Evaluation of Anticandidal Activities of Spirulina Metabolite Against Candida Albicans**

In this pilot study, Zarrouk media was optimized in terms of biomass production and metabolites for the culture growth of, *Spirulina* species; *Spirulina maxima* and *Spirulina platensis* and their extract were tested against a nosocomial fungal species *Candida albicans* (*C. albicans*) to explore anticandidal activity. The corresponding growth and metabolite was measured in terms of turbidity, chlorophyll, carotenoid and protein content. The culture was harvested by centrifugation and extracted with 75% methanol by freeze thaw method. Supernatant was collected, evaporated to dryness and stored at -20 °C. Anticandidal activities were assessed based on the agar-well diffusion method. The lawn of *C. albicans* was maintained at  $1.5 \times 10^5$  CFU/ml on Sarbourn dextrose (SD) agar plates under sterile conditions. The plates were dried at 37 °C for 30 minutes. Wells of 6mm diameter were created by using sterile agar borer. The dried supernatants were dissolved in normal saline (0.8% NaCl) and poured in each well (100  $\mu$ l) control well carried 100 $\mu$ l normal saline. Poured wells were incubated for 18 hours at 37 °C and after that measured the zone of growth inhibition. Anticandidal activity was found to be maximum in the dissolve of late stationary phase of *S. maxima* where in *S. platensis* dissolve were less effective. The study concludes that antifungal activity of *Spirulina* species should be explored on the basis of their metabolite structure and function is needed to develop an effective edible fungicide in near future[9]

### **Antioxidant, Immunomodulating, and Microbial-Modulating Activities of the Sustainable and Ecofriendly Spirulina Alberto Finamore**

The highly nutritional and ecofriendly *Spirulina* (*Arthrospira platensis*) has hypolipidemic, hypoglycemic, and antihypertensive properties. *Spirulina* contains functional compounds, such as phenolics, phycocyanins, and polysaccharides, with antioxidant, anti-inflammatory, and immunostimulating effects. Studies conducted on *Spirulina* suggest that it is safe in healthy subjects, but attitude to eating probably affects the acceptability of *Spirulina* containing foods. Although the antioxidant effect of *Spirulina* is confirmed by the intervention studies, the concerted modulation of antioxidant and inflammatory responses, suggested by in vitro and animal studies, requires more confirmation in humans. *Spirulina* supplements seem to affect more effectively the innate immunity, promoting the activity of natural killer cells. The effects on cytokines and on lymphocytes' proliferation depend on age, gender, and body weight differences. In this context, ageing and obesity are both associated with chronic low grade inflammation, immune impairment, and intestinal dysbiosis. Microbial-modulating activities have been reported in vitro, suggesting that the association of *Spirulina* and probiotics could represent a new strategy to improve the growth of beneficial intestinal microbiota. Although *Spirulina* might represent a functional food with potential

beneficial effects on human health, the human interventions used only supplements. Therefore, the effect of food containing Spirulina should be evaluated in the future.[10]

### **In Vitro Antiviral and Antimicrobial Activities of Spirulina Platensis Extract**

Spirulina platensis are filamentous, undifferentiated, non-toxigenic cyanobacteria that have been used as food since ancient times. There have been numerous studies on its antioxidant and antimicrobial actions. In this study antibacterial and antiviral effect of ethanol extract of Spirulina platensis were tested. The reduction of infectious viral units after treatment with ethanol extract of Spirulina platensis was tested. Non toxic doses of Spirulina platensis revealed 53.3%, 66.7%, 76.7%, 56.7%, and 50% reductions in vitro for infectious units of adenovirus type 7, Coxsackievirus B4, astrovirus type 1, rotavirus Wa strain, and adenovirus type 40 respectively. Using disc diffusion method to show the antibacterial effect of ethanol extract of Spirulina platensis against different bacterial strains (Escherichia coli, Staphylococcus aureus, Salmonella typhi, and Enterococcus faecalis) in addition to Candida albicans, inhibition zones were observed with Enterococcus faecalis and Candida albicans.[11]

### **Nutritional and Medical Applications of Spirulina Microalgae**

Spirulina spp. and its processing products are employed in agriculture, food industry, pharmaceuticals, perfumery and medicine. Spirulina has several pharmacological activities such as antimicrobial (including antiviral and antibacterial), anticancer, metalloprotective (prevention of heavy-metal poisoning against Cd, Pb, Fe, Hg), as well as immunostimulant and antioxidant effects due to its rich content of protein, polysaccharide, lipid, essential amino and fatty acids, dietary minerals and vitamins. This article serves as an overview, introducing the basic biochemical composition of this algae and moves to its medical applications. For each application the basic description of disease, mechanism of damage, particular content of Spirulina spp. for treatment, in vivo and/or in vitro usage, factors associated with therapeutic role, problems encountered and advantages are given.[12]

### **Antioxidant and Antimicrobial Activities of Spirulina Platensis Extracts and Biogenic Selenium Nanoparticles Against Selected Pathogenic Bacteria and Fungi**

This study investigated the antimicrobial and antioxidant activity of three Spirulina extracts (methanol, acetone, and hexane) and the biological selenium nanoparticles (SeNPs) fabricated by Bacillus subtilis AL43. The results showed that Spirulina extracts exhibited antimicrobial activity against tested pathogens. Besides, Spirulina extracts significantly scavenged ABTS and DPPH radicals in a dose-dependent manner. The methanolic extract had higher total phenolic content, antimicrobial activity, and antioxidant activity than other extracts. The selenium nanoparticles were synthesized by Bacillus subtilis AL43 under aerobic conditions and were characterized as spherical, crystalline with a size of 65.23 nm and a net negative charge of -22.7. We evidenced that SeNPs possess considerable antimicrobial activity against three gram-positive, three gram-negative bacteria, and three strains from both Candida sp. and Aspergillus sp. Moreover, SeNPs were able to scavenge ABTS and DPPH radicals in a dose-dependent manner. An association was found between the total phenolic content of Spirulina and SeNPs and their biological activities. Our results indicate that Spirulina and SeNPs with significant antimicrobial and antioxidant activities seem to be successful candidates for safe and reliable medical applications.[13]

### **Functional Composition, Nutritional Properties, and Biological Activities of Moroccan Spirulina Microalga**

The present study aimed to characterize the nutraceutical properties and the antimicrobial effect of Moroccan Spirulina (Arthrospira platensis). The nutritional composition was evaluated, including water content, crude protein, total carbohydrates, lipids, phenolic composition, macro- and micromineral content, fiber content, and energy value. Then, the microbiological analysis and antioxidant activity were measured. The antimicrobial activity was evaluated using the minimum inhibitory concentration method on bacteria and fungi. Moroccan Spirulina contained a large amount of protein ( $76.65 \pm 0.15\%$ ), followed by carbohydrates ( $6.46 \pm 0.32\%$ ), minerals ( $20.91 \pm 0.88\%$ ), crude fiber ( $4.07 \pm 1.42\%$ ), lipids ( $2.45 \pm 0.82\%$ ), ash ( $14.56 \pm 0.74$ ), and twenty phenolic acids being identified and quantified. Moreover, flavonoid and phenolic contents were present at  $15.60 \pm 2.74$  mg RE/g dw and  $4.19 \pm 0.21$  mg GAE/g dw, respectively. Microbiological risk assessment indicated that this product is safe to be consumed as a human food product. The antioxidant activity was higher in the methanolic fraction ( $23$  mg TE/g dw) (DPPH).[14]

### **Identification of Anti-diabetes Peptides from Spirulina Platensis**

In this study, ultrasound coupled with subcritical water (USW) technology was employed to extract *S. platensis* protein, and its inhibitory effect on three enzymes ( $\alpha$ -amylase,  $\alpha$ -glucosidase and dipeptidyl peptidase-4 (DPP-IV)) was evaluated. Subsequently, using insulin resistant-HepG2 cell model, the data presented that the USW-extracted protein significantly ( $p < 0.01$ ) increased glycogen content, hexokinase and pyruvate kinase activities. Then, 11 peptides were identified from intact protein or the HPLC-separated protein fractions by LC-MS/MS. After in silico prediction, 3 peptides (GVPMPNK, RNPFFVAPLLTVAAR and LRSELAAWSR) were synthesized, and their  $\alpha$ -amylase,  $\alpha$ -glucosidase and DPP-IV inhibition activities were validated. Among them, LRSELAAWSR displayed the medium activity on  $\alpha$ -amylase ( $IC_{50} = 313.6 \mu\text{g/mL}$ ), but the best activities on  $\alpha$ -glucosidase ( $IC_{50} = 134.2 \mu\text{g/mL}$ ) and DPP-IV ( $IC_{50} = 167.3 \mu\text{g/mL}$ ). In summary, for the first time, anti-diabetes peptides were identified from *Spirulina platensis*, which are useful for functional food additives and pharmaceuticals against type 2 diabetes.[15]

### **United States Pharmacopeia Safety Evaluation of Spirulina**

The Dietary Supplements Information Expert Committee (DSI-EC) of the United States Pharmacopeial Convention (USP) reviews the safety of dietary supplements and dietary supplement ingredients for the purpose of determining whether they should be admitted as quality monographs into the United States Pharmacopeia and National Formulary (USP-NF). The United States Food and Drug Administration (FDA) has enforcement authority to pursue a misbranding action in those instances where a dietary supplement product indicates that it conforms to USP standards but fails to so conform. Recently DSI-EC undertook a safety evaluation of spirulina, a widely used dietary ingredient. DSI-EC reviewed information from human clinical trials, animal studies, and regulatory and pharmacopeial sources and analyzed 31 adverse event reports regarding spirulina to assess potential health concerns. At the conclusion of this review, DSI-EC assigned a Class A safety rating for *Spirulina maxima* and *S. platensis*, thereby permitting the admission of quality monographs for these dietary supplement ingredients in USP-NF. DSI-EC continually monitors reports concerning the safety of dietary supplements and dietary supplement ingredients for which USP dietary supplement monographs are developed. The DSI-EC may revisit the safety classification of spirulina as new information on this dietary ingredient becomes available.[16]

### **Antioxidant Activities of Phycocyanobilin Prepared from Spirulina Platensis**

The antioxidative activity of phycocyanobilin from *Spirulina platensis* was evaluated against oxidation of methyl linoleate in a hydrophobic system or with phosphatidylcholine liposomes. Phycocyanobilin as well as phytochemicals including  $\alpha$ -tocopherol, caffeic acid and zeaxanthin, effectively inhibited the peroxidation of methyl linoleate and produced a prolonged induction period. Oxidation of phosphatidylcholine liposomes was also controlled markedly by adding phycocyanobilin or  $\alpha$ -tocopherol. Phycocyanobilin was distributed outside in the liposomes to scavenge radicals from AAPH and to prevent initiation of radical chain reactions. When the concentrations of phycocyanin and phycocyanobilin in the reaction mixture were adjusted equally on a phycocyanobilin basis, the activity of phycocyanobilin was almost the same as that of phycocyanin in the AAPH-containing reaction mixture. The antioxidizing action of phycocyanin prepared from spray-dried *Spirulina* almost agreed with that from fresh *Spirulina* in the AAPH-containing reaction mixture. These results suggest that phycocyanobilin is responsible for the majority of the antioxidative activity of phycocyanin and may act as an effective antioxidant in a living human body.[17]

### **The Role of Gamma Irradiation on Growth and Some Metabolic Activities of Spirulina Platensis.**

*Spirulina platensis* cells were exposed to different doses of gamma irradiation 0.0; (control), 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0 Kilo Gray (kGy) using Co60 as a gamma source at the Cyclotron Unit, Nuclear Research Center, Egyptian Atomic Energy Authority. After which, the cells were cultivated on Zarrouk medium for 14 days (the exponential phase of growth). The optimum growth of *Spirulina platensis* was recorded at 2.0 kGy as compared to the control after the 14th day of incubation. All of the following analyses were done after 10 days of growth. The results of pigments analysis revealed that the chlorophyll a and carotenoid contents of *Spirulina platensis* were reached their maximum rate at a dose of 2.0 kGy, which induces the same trend for phycobiliprotein fractions. The photosynthetic activity and total carbohydrate content of the irradiated *Spirulina* cells increased with elevating the doses of gamma irradiation and reached a maximum value at a dose of 2.0 kGy as compared to the control. The activity of ribulose-1,5-bisphosphate-carboxylase/ oxygenase (RUBISCO) was increased up to irradiation dose of 2.0 kGy. whereas, the maximum activity of the phosphoenol pyruvate carboxylase (PEPCASE) was recorded at the irradiation dose of 1.0 kGy.[18]

### **Hyperglycemia, Oxidative Stress, Liver Damage and Dysfunction in Alloxan-Induced Diabetic Rat are Prevented by Spirulina Supplementation**

Medicinal plants have long been used against life-threatening diseases including diabetes, with more or less success. Some of these plants have been shown to possess antioxidant activities, which could help improving diabetes inconveniences. In that context, we investigated the effects of spirulina supplementation on alloxan-induced diabetic rats, hypothesizing that co-administration of spirulina with rat diet could ameliorate diabetes complications and provide as benefits as the common antidiabetic insulin. Following alloxan treatment, male Wistar rats were fed daily with 5% spirulina-enriched diet or treated with insulin (0.5 IU/rat) for 21 days. Both spirulina and insulin treatments of diabetic rats resulted in a significant reduction in fasting blood glucose and an increase of glycogen level. Spirulina supplementation also impeded loss of body weight and ameliorated hepatic toxicity indices, i.e. alkaline phosphatases and transaminases activities, bilirubin levels and lipid peroxidation. Besides, triglycerides, total cholesterol, and low-density lipoprotein cholesterol levels decreased in the serum. Moreover, diabetic rats fed with spirulina exhibited sig changes in antioxidant enzyme activities in the liver (ie, decrease in superoxide dismutase and increase in catalase and glutathione peroxidase activities). The beneficial effects of spirulina or insulin were confirmed by histological study of the liver of diabetic rats. Overall, this study indicates that treatment with spirulina decreased hyperglycemia and oxidative stress in diabetic rats, this amelioration being even more pronounced than that provided by insulin injection. Therefore, administration of this alga would be very helpful in the prevention of diabetic complications.[19]

### **In Vitro Antioxidant and Antiproliferative Activities of Selenium-Containing Phycocyanin from Selenium-Enriched Spirulina Platensis**

Both selenium and phycocyanin have been reported to show potent cancer chemopreventive activities. In this study, we investigated the in vitro antioxidant and antiproliferative activities of selenium-containing phycocyanin (Se-PC) purified from selenium-enriched *Spirulina platensis*. The antioxidant activity of Se-PC was evaluated by using four different free radical scavenging assays, namely, the 2,2'-azinobis-3-ethylbenzothiazolin-6-sulfonic acid (ABTS) assay, 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay, superoxide anion scavenging assay, and erythrocyte hemolysis assay. The results indicated that Se-PC exhibited stronger antioxidant activity than phycocyanin by scavenging ABTS, DPPH, superoxide anion, and 2,2'-azobis-(2-amidinopropane)dihydrochloride free radicals. Se-PC also showed dose-dependent protective effects on erythrocytes against H<sub>2</sub>O<sub>2</sub>-induced oxidative DNA damage as evaluated by the Comet assay. Moreover, Se-PC was identified as a potent antiproliferative agent against human melanoma A375 cells and human breast adenocarcinoma MCF-7 cells. Induction of apoptosis in both A375 and MCF-7 cells by Se-PC was evidenced by accumulation of sub-G1 cell populations, DNA fragmentation, and nuclear condensation. Further investigation on intracellular mechanisms indicated that depletion of mitochondrial membrane potential ( $\Delta\Psi_m$ ) was involved in Se-PC-induced cell apoptosis. Our findings suggest that Se-PC is a promising organic Se species with potential applications in cancer chemoprevention.[20]

### **Growth Response of Spirulina Platensis in Papaya Skin Extract and Antimicrobial Activities of Spirulina Extracts in Different Culture Media**

Growth response of *Spirulina platensis* in papaya skin extract media and their antimicrobial activity were studied. Five different concentrations e.g. 10gm/L, 8gm/L, 6 gm/L, 4 gm/L and 2gm/L of Papaya (*Carica papaya*) skin extract media and BD1 (control) medium were used in this study. After 8 days of cultivation, the optical density (0.33) was recorded in BD1 medium and among the five different concentrations of papaya skin extract media the maximum was found (0.31) in 6gm/L. Antimicrobial activity of *Spirulina platensis* grown in three media namely Zarrouk, BD1 media and media made from papaya skin extract was also studied. Only freeze dried *Spirulina platensis* powder extract showed inhibitory effect against bacteria and no antifungal activity was observed.[21]

### **Biochemical Composition and Antioxidant Activities of Arthrospira (Spirulina) Platensis in Response to Gamma Irradiation**

*Arthrospira (Spirulina) platensis* is a blue-green alga, rich with bioactive components and nutrients. To evaluate effect of gamma irradiation, *A. platensis* was exposed to different doses of 0.0, 0.5, 1.0, 1.5, 2.0 and 2.5 kGy. The data showed that the phenolic and proline contents significantly increased with the increase of gamma irradiation doses up to 2.0 kGy, above which a reduction was observed. The soluble proteins and malondialdehyde (MDA) contents were stimulated by all tested irradiation doses. Furthermore, the vitamins (A, K and B group) and mineral contents (N, P, Na, K, Ca, Mg and Fe) were stimulated by the

irradiation doses compared with the control. The activities of some N-assimilating and antioxidant enzymes were significantly increased with the irradiation doses up to 2.0 kGy. This study suggests the possible use of gamma irradiation as a stimulatory agent to raise the nutritive value and antioxidant activity of *A. platensis*. [22]

### **Antimicrobial Activity of Spirulina Platensis Extracts Against Certain Pathogenic Bacteria and Fungi**

Ethanol, methanol and aqueous extracts of the algal plant *Spirulina platensis* were evaluated for their antimicrobial activity against four types of Gram positive bacteria namely *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Bacillus cereus* and *Enterococcus faecalis*. Six types of Gram negative bacteria were also tested. They were *Pseudomonas aureginosa*, *Proteus vulgaris*, *Salmonella typhi*, *Enterobacter cloacae*, *Klebsiella pneumoniae* and *Escherichia coli*. Four species of *Candida sp.* were also bioassayed their response when the extracts were used. All of these algal extracts irrespective of their types inhibited the growth of all microbes to varying degrees. Methanol extract showed strong and superior antibacterial activity against all bacterial strains especially with regard to Gram positive bacteria (*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Bacillus cereus* and *Enterococcus faecalis*) as compared to ethanol or aqueous extracts. Less or no activity was observed against *Penicillium sp.* ( $5 \pm 0.41$ ) and *Candida parapsilosis* ( $08 \pm 0.44$ ) in aqueous extract with 50mg/mL concentration. The minimum inhibitory concentration value of ethanol and methanol extract ranged between 5-100mg/mL for different strains tested. It was clearly noticed that *Spirulina* had a broad spectrum activity against bacteria and fungi in all the extracts tested. These findings support the traditional use of *Spirulina* as probiotic agent or in the treatment of different infections in area. [23]

### **Antioxidant Effects of Spirulina Supplement Against Lead Acetate-Induced Hepatic Injury in Rats**

Lead is a toxic metal that induces a wide range of behavioral, biochemical and physiological effects in humans. Oxidative damage has been proposed as a possible mechanism involved in lead toxicity. The current study was carried out to evaluate the antioxidant activities of *Spirulina* supplement against lead acetate -induced hepatic injury in rats. Five groups of rats were used in this study, Control, Lead acetate (100 mg/kg), Lead acetate (100 mg/kg) + 0.5 g/kg *Spirulina*, Lead acetate (100 mg/kg) + 1 g/kg *Spirulina* and Lead acetate + 25 mg/100 g Vitamin C (reference drug). All experimental groups received the oral treatment by stomach tube once daily for 4 weeks. Lead intoxication resulted in a significant increase in serum alanine transaminase (ALT), aspartate transaminase (AST) activities, liver homogenate tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), caspase-3, malondialdehyde (MDA), nitric oxide (NO) levels and a significant decline of total serum protein, liver homogenate reduced glutathione (GSH) level and superoxide dismutase (SOD) activity. Both doses of *Spirulina* supplement as well as Vitamin C succeeded to improve the biochemical parameters of serum and liver and prevented the lead acetate-induced significant changes on plasma and antioxidant status of the liver. Both doses of *Spirulina* supplement had the same anti-apoptotic activity and high dose exhibited more antioxidant activity than that of low dose. In conclusion, the results of the present work revealed that *Spirulina* supplement had protective, antioxidant and anti-apoptotic effects on lead acetate-induced hepatic damage. [24]

### **Antibacterial Activity of Volatile Component and Various Extracts of Spirulina Platensis**

The methanol, dichloromethane, petroleum ether, ethyl acetate extracts and volatile components of *Spirulina platensis* were tested in vitro for their antimicrobial activity (four Gram-positive, six Gram-negative bacteria and *Candida albicans* ATCC 10239). GC-MS analysis of the volatile components of *S. platensis* resulted in the identification of 15 compounds which constituted 96.45% of the total compounds. The volatile components of *S. platensis* consisted of heptadecane (39.70%) and tetradecane (34.61%) as major components. The methanol extract showed more potent antimicrobial activity than dichloromethane, petroleum ether, ethyl acetate extracts and volatile components. Copyright © 2004 John Wiley & Sons, Ltd. [25]

### **Neuroprotective Activities of Spirulina Platensis in the 6-OHDA Model of Parkinson's Disease Are Related to Its Anti-Inflammatory Effects**

*Spirulina platensis* (SPI) is a cyanobacterium, presenting anti-inflammatory and antioxidant actions. Considering the importance of inflammation and oxidative stress in Parkinson's disease (PD), SPI neuroprotective effects were evaluated in a model of PD. Male Wistar rats were divided into: sham-operated (SO), untreated 6-OHDA and 6-OHDA treated with SPI (25 and 50 mg/kg, p.o.). The 6-OHDA was injected into the right striata and SPI treatments started 24 h later for 2 weeks. The SO and untreated 6-OHDA-

lesioned groups were administered with distilled water, for the same period. Afterwards, the animals were subjected to the apomorphine-induced rotational test and euthanized for striatal measurements of DA and DOPAC, nitrite and TBARS and immunohistochemistry assays for TH, DAT, iNOS and COX-2. SPI reduced the apomorphine-induced rotational behavior, DA and DOPAC depletions and nitrite and TBARS increases, at its high dose. Furthermore, TH and DAT immunoreactivities in the lesioned striatum of the untreated 6-OHDA-lesioned group were attenuated by SPI. Similarly, immunoreactivities for iNOS and COX-2 were also decreased after SPI treatments. In conclusion, we showed that behavioral and neurochemical alterations in hemiparkinsonian rats were partly reversed by SPI, characterizing the neuroprotective potential of Spirulina and stimulating translational studies focusing on its use as an alternative treatment for PD.[26]

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