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A Prominent Superfood: Spirulina platensis

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Abstract

Our planet's resources have been declining, as you know. The life qualities of humans have also changed a little because of their economy, nutrition, sports, and family life. Therefore, more alternative resources are being sought after by humans. Also, in the food supply for animals, scientists have been researching different and alternative supplements for growth performance, immunity, reproduction, and metabolism. Spirulina platensis and its contents have been linked to a nutritional component in both human and animal health and welfare. Growth and immunomodulation properties of this supplement have been widely studied in animals and humans, recently. Nowadays, nutritional specifics of S. platensis are a main focus for researchers. S. platensis is a singlecell protein due to its rich components, such as protein, essential amino acids, fatty acids, antioxidant pigments, carotenoids, beta-carotene, and phycocyanin. Today, researchers study the nutritional quality and investigate the effects of S. platensis on growth, immunity, antioxidant, antitoxicologic, anticancerogenic, cholesterol and glucose metabolism, and fertility. For these reasons, S. platensis may be acceptable as an alternative and/or superfood for the next generation. So, we review this information regarding S. platensis using historical background, literature reviews, qualitative studies, and microscopic appearances in this chapter.

Keywords: super food, Spirulina platensis, microalgae

1. Introduction

Population growth, depletion of food resources, and balanced diets require the usage of new food sources. For many years, there have been antibiotics, hormones, or drugs used for improving health and immunity, and to fight against disease. Today, antibiotic resistance has become a reality, and using a more natural approach to additives in both humans and animals has become a more acceptable alternative. The natural additives are using a protein source to

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© 2017 The Author(s). Licensee InTech. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. replace the use of the antibiotics, hormones, and drugs. Natural additives are contained in a big scientific family, but mostly they come from plant derivatives and extracts. The nutritional status of these supplements is important for use as a food additive. Among these additives, microalgae are prevalent throughout history. The utilization of these algae as a protein source has been observed by researchers for many years. There are several types of microalgae, but especially Spirulina, namely *S. platensis*, has been studied more than others due to its rich components, positive effects, and being a supplement that is nontoxic.

S. platensis is a filamentous cyanobacterium known as blue-green algae, which is often used as a single cell protein. This microalgae contain essential amino acids, proteins, fatty acids, antioxidant pigments, carotenoids, beta-carotene, and phycocyanin. It has been designated as a health food by the World Health Organization (WHO), and it has the potential to become one of the best alternative treatments in the twenty-first century. Also, according to the National Institutes of Health (NIH), *S. platensis* can be used as a treatment for the nervous system and metabolism, including weight loss, diabetes, and high cholesterol. And today, well-known scientific sources say that Spirulina is a "superfood" and a "miracle from the sea."

1.1. Classification

S. platensis is a member of Phormidiaceae family. It is a filamentous and multicellular cyanobacterium which is figured like a cylindrical filament [1]. Also, it is a photosynthetic bacterium, and according to Bergey's Manual of Determinative Bacteriology (1974) it is considered to be in eukaryotic organisms [2]. Actually, there have only been one more algae in this family, named Arthrospira, which was confirmed by Gomont in 1989 [3]. He explained that Spirulina and Arthrospira are different due to their features such as helix type, cell wall, visibility under microscopy, diameters, and filaments (**Figure 1**). According to Botanics, the name of *S. platensis* was called *Arthrospira platensis* [4] at first because of its oxygenic photosynthetic feature, but today, the worldwide researchers use the term "Spirulina" for this microalgae.

1.2. Historical perspective

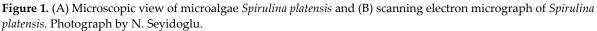
S. platensis was first isolated from Lake Texcoco by the Aztecs in the sixteenth century and they called it "tecuitlatl" [5]. Later, Dangeard happened upon the Kanembu tribe which had been harvesting these excellent microalgae from Lake Chad in Africa [6]. He then coined the name "dihe" for *S. platensis* which had been used for bread, meals, and cakes in the 1940s. *S. platensis* was analyzed chemically and it quickly prompted research in 1964 [7]. During that year, studies began on this microalgae by botanists, microbiologists, and scientists, and also reviewed by some researchers [8, 9].

Early in the 1990s, NASA studied the cultivation of *S. platensis* as a food source for long-term outer-space programs. They modified the growth process using environmental factors and suggested that this microalgae could be used as palatable diet [10]. Also, in 1967, *S. platensis* was touted as a "wonderful future food source" by the International Association of Applied Microbiology [11].

The World Health Organization reported that *S. platensis* has no risk and is a good food supplement for health [12]. Included in this issue, in 2003, the Intergovernmental Institution studied this microalgae for malnutrition (IIMSAM) and developed a charter with the United Nations Economic and Social Council (UNECOSOC). They agreed that Spirulina should be used against malnutrition for humans, especially in developing countries.

In 2011, the National Institutes of Health proposed that *S. platensis* could be used in human research, but they requested further studies on the effects of Spirulina [13]. *S. platensis* was suggested as a safe dietary supplement by The Food and Drug Administration (FDA) in 2012 [14]. They recommended a 3–10-g daily dose of this microalgae for human health. Notably, according to the European Food Safety Authority (EFSA), *S. platensis* also helps to control the blood sugar level for glycemic health [15].





1.3. Nutritional composition

The superfood *S. platensis* includes bioactive components such as proteins, amino acids, minerals, vitamins, pigments, nucleic acids, carbohydrates, and lipids, shown in **Tables 1–6**.

Food protein origin	Protein (%)
Spirulina powder	60–70
Whole dried egg	47
Beer yeast	45
Skimmed powdered milk	36
Whole soybean flour	36
Parmesan cheese	36
Wheat germ	27
Peanuts	26
Chicken	19–24
Fish	19.2–20.6
Beef meat	17.4

Table 1. Quantity of Spirulina platensis proteins and other foods [33].

Protein and amino acids	g/100 g
Protein	57.47
Tryptophan	0.929
Threonine	2.97
Isoleucine	3.209
Leucine	4.947
Lysine	3.025
Methionine	1.149
Cystine	0.662
Phenylalanine	2.777
Tyrosine	2.584
Valine	3.512
Arginine	4.147
Histidine	1.085
Alanine	4.515
Aspartic acid	5.793
Glutamic acid	8.386
Glycine	3.099
Proline	2.382
Serine	2.998

National Nutrient Database for Standard Reference, Release 28 slightly revised May, 2016. Available from: https://ndb.nal.usda.gov/ndb/foods/show/3306?

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Table 2. Protein and amino acids in Spirulina platensis powder (nutritional value per 100 g).

Vitamins	mg/100g
Provitamin A equiv.	2.330 × 103 IU/kg
Vitamin E d-a-tocopherol	5
Thiamin B1	3.5
Riboflavin B2	4.0
Niacin B3	14.0
Vitamin B6 pyridoxine	0.8
Vitamin B12 cobalamin	0.32
Folic acid	0.01
Biotin	0.005
Phantothenic acid	0.1
Vitamin K	2.2

Table 3. Vitamins in *Spirulina platensis* powder [133].

Fatty acids	(%)
Myristic acid	0.23
Palmitic acid	46.07
Palmitoleic acid	1.26
Oleic acid	5.26
Linoleic acid	17.43
Gamma-Linolenic acid	8.87
Others	20.88

Table 4. Fatty acid composition of Spirulina platensis powder [134].

Mineral	mg/100g
Calcium	700
Chromium	0.28
Copper	1.2
Iron	100
Magnesium	400
Manganese	5.0
Phosphorus	800
Potassium	1400
Sodium	900
Zinc	3.0

 Table 5. Minerals in Spirulina platensis powder [133].

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Pigments	mg/100g
Carotenoids	370
Chlorophyll a	1000
C-Phycocyanin	14,000

Table 6. Pigments in Spirulina platensis powder [133].

1.3.1. Protein and amino acids

S. platensis is the most useful microalgae for nutrition due to its components, especially protein. The nutritional level of protein is almost 70% of its dry weight and also has a high quantity and quality belonging to amino acids [1]. *S. platensis* contains all of the essential amino acids, as shown in **Table 2**. Researchers reported that although methionine and cysteine are found in a lower value, albumin and casein are found in a higher value, of animal proteins, respectively, in eggs and milk [8, 16]. *S. platensis* contains biliproteins, especially C-phycocyanin which is 20% of all protein fractions. C-Phycocyanin molecule has an antioxidant feature, which regulates immunity and protects the organism against diseases [17].

1.3.2. Vitamins

S. platensis has the richest vitamin source of vitamin A (beta-carotene), vitamin E, thiamin (vitamin B1), biotin (vitamin B7), and inositol (vitamin B8) in food. Beta-carotene is in a biotransformed state which can be absorbed by humans, and is also important for antioxidant processes in organisms [18]. On the other hand, there is a conflict of cobalamin (vitamin B12) content in *S. platensis*. Some researchers reported that *S. platensis* has no reliable vitamin B12. They explain that it is a pseudovitamin B12 which is inactive and in a form that the human organism cannot uptake at a cellular level [19, 20]. However, other researchers claimed that *S. platensis* has a great amount of B12 compared to other sea algae and they indicated that vitamin B12 in this microalgae is important for vegetable nutrition, especially for humans who do not eat meat [21, 22].

1.3.3. Minerals

S. platensis contains many minerals such as potassium, calcium, chromium, copper, iron, magnesium, manganese, phosphorus, selenium, sodium, and zinc. This microalgae is a good component due to its iron, calcium, and phosphorus contents. The ferrous component in this microalgae can be easily digested and bioactive in an organism easily which is important for pregnant adult females [23]. The utilization of calcium and phosphorus contents of *S. platensis* has an important impact on bone calcification and improves bone health [24].

1.3.4. Lipids

Lipid contents of *S. platensis* are only 4–7%, but it has important essential fatty acids for humans: gamma-linolenic acid and linolenic acid. These components are also mediators of immune and cardiovascular system due to their precursor effects of prostaglandins and leukotrienes [25].

The *S. platensis*' other lipids are stearidonic acid, eicosapentaenoic acid, docosahexaenoic acid, and arachidonic acid, respectively.

1.3.5. Carbohydrates

S. platensis contains 13.6% carbohydrates, which are glucose, mannose, galactose, and xylose. Nevertheless, it does not contain cellulose, which cannot be absorbed by humans and thereby this feature makes *S. platensis* easily digestible and a safe nutrient for human consumption. It is significant for people who have intestinal malabsorption and for the elderly [24]. Likewise, there is also a polysaccharide molecule, isolated from *S. platensis*, which has a huge molecular weight. This polysaccharide has an immunomodulator effect called "immulina" by scientific authorities [26, 27].

1.3.6. Nucleic acids

Nucleic acids play a role in uric acid metabolism. They catabolize the uric acid to adenine and guanine which causes gout and cardiovascular diseases [28]. So, the World Health Organization recommends about 80-g daily dosage of *S. platensis*.

1.3.7. Pigments

S. platensis has some natural pigments which color this microalgae, such as c-phycocyanin, chlorophyll, xanthophyle, beta-carotene, zeaxanthin, and allophycocyanin. The most important are phycocyanin, chlorophyll, and beta-carotene. C-Phycocyanin is the most important pigment, which includes iron, and contains 14% of its dry weight. Also, *S. platensis* is one of the best nutrients that contains the highest chlorophyll value (1%). Chlorophyll is known as a detoxifier and purifier phyto-nutrient. It improves the carbohydrate, protein, and lipid metabolism and affects reproduction positively. Carotenes constitute half of this microalgae, especially beta-carotene. The carotenes and xanthophyle in *S. platensis* are demonstrated in different metabolism pathways in the body, and also better influence the function of vitamins and minerals in an organism [29]. Nowadays, diets rich in carotenes are found to be important for human health due to its effects in reducing the risk of diseases [30, 31] (**Table 6**).

2. Utilization of S. platensis worldwide

2.1. Usage as food

Plants and plant extracts have been the focus for improved health in recent years. *S. platensis* is one of the most sought after natural alternatives for nutrition in both human and animal. *S. platensis* is a microalgae that has been consumed for centuries due to its high nutritional value and supposed health benefits. Apart from its easy production, *S. platensis* has a high nutritional ability. Its affects on growth, antioxidants and antiviral features, immunomodulator activity, and hypocholesterolemic influence have been proposed by researchers over the years. Likewise, it is indicated as a nontoxic supplement, and the World Health Organization has

supported it as a health nutrient [32]. *S. platensis* is used in many countries, such as Mexico, United States, Japan, Taiwan, India, Singapore, Germany, Spain, Switzerland, Holland, and many others. It is added in food marketing such as candies, chewing gums, appetizers, sports tablets, and bread. As well as its many uses in food, it is a component in some cosmetics such as creams, masks, tonics, and shampoos [33].

Natural additives have also been added to animal feed for healthy animal growth in recent years. At the same time, in the farming sector, it is preferred as it is a natural and economical product, as well as healthy, and it is shown to have rapid growth performance. *S. platensis* is one of the most sought after ingredients for animal feed as compared to other nutrients due to its high protein contents and nourishing features. Its growth, antiviral, antidiaretic, antioxidant, probiotic, hypocholesterolemic, antiallergic, analgesic, anthelmintic, anticarcinogenic, antiparasitic, immune system activator, and cardiovascular protective effects for animals have been reported by researchers [34–39].

S. platensis grows naturally in shallow bodies of water and in the presence of an alkaline medium of high salinity [40, 41]. The primary component for growing this microalgae is sodium bicarbonate. The production systems for this microalgae are found in Thailand, United States, Africa, China, and Chile, mostly where the Pacific Ocean, fresh water, and deep oceans exist. On the other hand, in Turkey and Bulgaria, *S. platensis* has been cultivated experimentally and recently.

Clinical and experimental trials have shown that *S. platensis* can be utilized for both human and animal safety. There have also been many studies that can help explain the benefits of this interesting microalgae. Its high biological components are an interest for scientists in recent centuries. Although it has been reported as a nontoxic supplement, current studies have continued to test its safety.

S. platensis can be used for immune enhancement, growth, as a nutritional food source, protector of metabolism, and many other important benefits for both humans and animals. It is amazing that all of these different features exist in this one specific microalgae. This is why scientific evidences call this microalgae a "super food." Nevertheless, in that respect there is always a need for continued studies regarding natural additives such as *S. platensis* to explain the study of their effects on humans and animals.

2.2. Effect of S. platensis on the growth of bacteria and animals

S. platensis does not contain cellulose on its cell wall. Therefore, this microalgae can be absorbed in the intestinal mucosa and improve the intestinal function and mucosal digestion. Although *S. platensis* can repress the harmful microorganism such as Candida, it can help to increase the good microorganism such as *Lactobacillus* and *Bifidobacteria*. So, this increase of *Lactobacillus* population helps the absorption and digestion of food [42–44]. At the same time, the biological components in *S. platensis*, such as phycocyanin, polysaccharide, and gamma-linolenic acid, have an important role for improving overall body function. The Scientific Committee on Food (SCF) and the European Food Safety Authority (EFSA) also recommend 10 g of *S. platensis* as

a supplement for daily intake in order to protect the health of humans, and research indicates that there is no risk with this microalgae use as a food [14].

The focus on S. platensis is due to its protein bioavailability, and that is the reason for this important microalgae to be compared to others. Its high protein content can improve growth performances of both humans and animals. The application of S. platensis for protein malnutrition has resulted in good weight gain, hematological responses, and positive nitrogen balance in metabolism with no side effects. Foods containing high protein are especially useful for malnutrition in humans, as malnutrition is a global problem. Studies, which estimate the effects, were performed in Africa, where malnutrition is prevalent, especially in children. The children and older people were separated according to their protein malnutrition first, and then rehabilitated with S. platensis for these studies [45–49]. The studies resulted in positive weight gain, normalized blood values, and optimized the health of human immunodeficiency virus (HIV)-negative children. The study of Simpore et al. [47] compared HIV-negative and positive children, and showed a positive weight gain between 15 and 25 g/day with children given S. platensis. They reported that S. platensis is a good food source for malnutrition. On the other hand, Azabji Kenfazk et al. [49] studied HIV-infected and malnourished adults, using S. platensis for 12 weeks. At the end of that study, positive improvement in body composition and body weight was concluded.

There are many different studies that point out the growth performance of *S. platensis* in animals [50–57]. For example, Moreira et al. [50] studied the Wistar rat using *S. platensis* as an added nutrient at 8.8, 17.6, and 26.4% doses of forage. They reported that there was a significant increase in weight in the 17.6% group. Heidarpour [35] used 0-, 2-, 6-, and 25-g *S. platensis* for cattle, and noted weight gain every 15 days. He observed no statistical differences in growth performances when comparing all groups. On the other hand, although some researchers found positive effects of *S. platensis* as a supplement with fish [52], some of them reported no significant changes in growth performances in fish [53, 54]. Seyidoglu and Galip [51] tried to elucidate the effects of *S. platensis* on growth performance in rabbits. They indicated that there was a positive effect of supplementing *S. platensis* on growth performance due to dose, animals, and environmental changes.

When comparing all these studies, there were different results about the supplementing dose and effects of the *S. platensis*. So, there continues to be more studies which are necessary to determine dietary concentration and the effects of this interesting microalgae.

3. Utilization of *S. platensis* for health

3.1. Immune system and allergy

Hematopoietic system is important for repairing tissues, generating important body cells, and protecting healthy regulation. The immune system is one of the most important systems within the hematopoietic system. Together, they are all responsible for protecting the host. The immune system of the organism is classified as an innate immune system and adaptive

immune system. The innate immune system is the first barrier to protect the organism against infections. This system includes macrophages, neutrophiles, natural killer cells, and lectins. On the other hand, providing a more specialized and active defense against diseases is called an adaptive immune system, in which there are antibodies, lymphocytes, and cytokines. These two immune systems are in a sensitive balance with each other.

S. platensis can produce high protein, amino acids, vitamins, beta-carotene, pigments, and polysaccharides as a bioactive agent. All these components have an enhanced effect on the production of antibodies and cytokines. Especially polysaccharide, in this microalgae, has an effect on macrophages and T- and B-cell proliferations, and so it is said that S. platensis can improve the resistance of the organism. However, the effects of S. platensis on the immune system have not yet been precisely determined. The first experimental study was performed on mice in 1994, and it investigated at the effects of supporting antibody production [58]. In that study, it was reported that C-phycocyanin and polysaccharide in S. platensis activated the proliferation of monocytes, erythrocytes, granulocytes, and fibroblastosis in the bone marrow, and thereby the hematopoietic and immune systems were activated. In the University of Mississippi, a polysaccharide that is called "Immulina" was extracted from S. platensis by researchers [26]. They measured the immunostimulatory activity on human monocyte cells in vitro, and reported positive monocyte activation due to the effect of polysaccharide. Some researchers demonstrated that S. platensis plays an important role in the balance of immune system cells [59-65]. All these researchers reported that polysaccharides and phycocyanin have a positive role in erythropoietin activity, which is based on improved T-lymphocytes, and triggered leukocytes and bone marrow growth. Moreover, Løbner et al. [60] observed the increased CD4+ cell proliferation in humans using Immulina. There are two studies which also used S. platensis supplement (Immulina) with healthy humans. They reported that hemoglobin levels, natural killer cell activity, and monocytes were increased [27, 61]. Although some of the studies did showed the immune stimulatory effect of this microalgae on adaptive immune system [62-64], some of the studies [65] found no effect on the immune system, which can be explained by mutation in protocols and strains, and also the ratio of *S. platensis*.

An allergic response is a reaction of the immune system against a harmless substance such as pollen, nutrition, house mites, or other substances. Today, it is an increasing problem in the world. The protection and treatment process of allergies is aided by natural foods, especially *S. platensis*. According to researchers [66], *S. platensis* can regulate T-helper cells (Th) in allergic rhinitis. In that study, which was the first human study investigating at allergies, the role of T-helper 2 cells (Th2) and IL-4, which induced the production of IgE, was inhibited by this microalgae. According to the results, *S. platensis* supplements had a positive effect on allergic patients. In another study about food allergies, the researchers investigated the immunoglobulins role (IgA, E, G1) in the protective effects of *S. platensis*. They suggested that *S. platensis* may enhance the IgA antibody, which worked as a blocking antibody toward IgE, and thereby had protective effects against allergic reactions [67].

The supplementing of *S. platensis* was also used for adolescent animals, which have an immature immune system, which has been shown to improve the immune system and living ratio [62, 68]. Some researchers studied this concept with poultry and reported that there was

a positive immunomodulator effect of *S. platensis* through the decreasing of the nutrients in macrophages [69]. According to other studies in animals, there have been increases in hemoglobin, erythrocytes, natural killer value, T–lymphocytes, and cytokine activity with this microalgae [70–72]. Prompya and Chitmanat [53] studied fish over a 60-day duration using this microalgae and found a statistically significant increase in white and red blood cells. There was another research which studied newborn pigs, and the results found a significant increase in cytokines and interleukins [72].

For many years, *S. platensis* has been used as a food additive for both humans and animals. According to scientific findings, the components are sufficient for healthy nutrition, the protective activity of the body and disease therapies. Also, according to the Food and Drug Administration, *S. platensis* has been designated as a "safe food" [14] due to its natural properties for health therapies.

3.2. Anemia

Anemia refers to a decreased number of circulating red blood cells and is the most common blood disorder. Insufficient nutritional intake, toxic metals, and environmental contamination cause there to be a disruption in the red blood cell production pathways, and thereby anemia is the result. Also, iron deficiency is the most common cause of anemia in pregnant women, older people, and children [61]. In literature reviews, several studies have shown that several types of anemia have been treated by *S. platensis* due to its phycocyanin content [73–75]. The mechanism of C-phycocyanin is explained through the stimulation of the hematopoiesis and the endogenous erythropoietin (Epo). The Epo is known as an indicator for the proliferation and differentiation of erythrocytes. Along with this result, some research have also demonstrated that *S. platensis* has a positive impact on different types of anemia due to its rich components such as essential amino acids, folic acids, vitamin B12, and high iron which have an important role in erythropoiesis [48, 76, 77]. There are also some animal studies regarding anemia that have shown the beneficial effects of *S. platensis* on hemoglobin and serum iron levels [47, 86, 88].

3.3. Obesity

S. platensis has a hypocholesterolemic effect due to its C-phycocyanin component. It was reported that C-phycocyanin inhibits the reabsorption of bile acids in the ileum and also cholesterol in the jejunum [78–80]. In some studies, humans using *S. platensis* supplements showed lower results in cholesterol and triacylglycerol levels, and an increase in high-density lipoprotein levels. All of these effects indirectly reduced both diastolic and systolic blood pressure and gave a protective effect on the cardiovascular system [51, 81–83]. In another study [84], researchers treated hyperlipidemia nephrotic syndrome with *S. platensis* by applying 1-g *S. platensis* per day for 2 months and observed whether *S. platensis* consumption decreases lipid profile and helps to reduce the hyperlipidemia nephrotic syndrome. Also, all these researchers suggested that *S. platensis* is important to maintain a healthy cardiovascular system including blood lipid profile as well as treating precardiovascular disease. In vascular

lesions such as coronary artery disease, the proteoglycan metabolism protecting cardiovascular cells is associated with exogen polysaccharides that are present in *S. platensis*. This pathway was studied by Sato et al. [85] and has been found to be an important element in coronary artery disease.

Cardiovascular diseases, obesity, and diabetes are linked with each other. The risk of cancer development is enhanced by these diseases in both humans and animals. On that point, some researchers point out the effects of *S. platensis* on obesity and diabetes [86–89]. During a 4-week study, *S. platensis* supplement (2.8 g) was taken by obese people, and the total body weight and biochemical values were determined. A reduction in body weight and lower cholesterol levels in obese humans was observed, in the lower significant level. Also, the other researchers observed the positive effects on diabetics using supplements of *S. platensis* [86, 89]. In these studies, obese humans with high blood sugar and lipid profiles were studied to determine the antidiabetic mechanism of this microalgae and have suggested that the gamma-linolenic acid in *S. platensis* may be attributed to the reduction in hyperglycemia.

S. platensis has been applied to animal feed and it has been reported that *S. platensis* plays a substantial part in lipid metabolism in animals, such as a decreased effect on total cholesterol, lipid profile, and glucose [5, 35, 90, 91]. They suggested that *S. platensis* could reduce serum cholesterol, and thereby have positive effects on lipid metabolism. In fact, cholesterol metabolism is significant in these creatures, especially in the milk production during lactation. The fatty acid profile of this microalgae is a prominent source and may stimulate milk production. The application of *S. platensis* to both humans and animals has been reviewed by The Dietary Supplements Information Expert Committee (DSI-EC) with experimental researches of animals, human clinical, and animal studies, and has reported that *S. platensis* does not have any risk for nutritional consumption. However, as there are quite limited studies in animals, especially in ruminants shown by researchers, more animal studies will be necessary to study this functional microalgae.

3.4. Healing and antibiotic effects

Wound healing is a process of repairing skin or tissue, and this process is also important for regulating hemostasis. During the healing process, bacteria and other pathogens are present at damaged areas where the pyretic situation occurs as a result of the inflammation. Natural pharmaceutical compounds are generally used to heal such wound areas. In addition, *S. platensis* or its extracts have been widely used in creams, solutions, raw juices, and ointments for skin health in recent times. Collagen fibrils, which is the plant constituent contained in microalgae, have attributes that have positive effects on wound closure during the healing process [92]. Rabadiya et al. [93] suggested that the antibiotic effects of *S. platensis* had inhibitive effects of bacteria and promoted skin healing, during the scarring process. Also, another study suggested that aqueous extract of *S. platensis* has a healing activity and it is an economical method for promoting skin, especially for diabetic wounds [94].

The anti-inflammatory effect of *S. platensis* is explained as an inhibitive effect of gamma-linolenic acid [95–97]. Gamma-linolenic acid is important to control inflammation and cell proliferation. The high value of gamma-linolenic acid inhibits the work of prostaglandin and

the progression of inflammation. On the other hand, some researchers reported that *S. platensis* and its extract C-phycocyanin, can regulate the cytotoxicity and inflammation-associated factors such as ions, COX-2, tumor necrosis factor (TNF)- α , and IL-6 with BV-2 microglial cell during the inflammatory process [98].

Antibacterial activity of *S. platensis* is also caused by the activation of phagocytosis in mononuclear cells and this bacterial clearance is associated with liver health. The increase in T-cell and mononuclear phagocytes in liver by *S. platensis* has been reported [99].

S. platensis and its extracts, especially calcium, do not allow the viruses to attack and infect the cells. On that point, there are some written reports about the inhibition effect of viral replication and natural defenses [100]. Referring to the animal studies, *S. platensis* has been shown to be beneficial as an antiviral agent and lead to a limitation of foot and mouth disease [101]. The researchers studied the calcium extract of this microalgae in vitro, and indicated that the replication of viruses, such as herpes, measles, or mumps, was interfered by this extract. In some other studies, aqueous extracts of *S. platensis* diminished the HIV-1 virus and enterovirus replication in T-cells, Langerhans, and peripheral blood mononuclear cells due to the polysaccharides activity of this microalgae [102, 103].

Helminth infections contribute to diseases such as anemia, eosinophilia, and malnutrition. Studies about marine natural products, which are used for anthelmintic situation, were reviewed by Mayer et al. [104]; however, sufficient anthelmintic effect by *S. platensis* on the parasites was not observed.

3.5. Fertility

There are many factors that affect infertility in female humans and animals such as age, size and physical condition, reproductive history, and nutrition [105]. *S. platensis* is an amazing food for supporting fertility and pregnancy due to its contents. It was reported that high protein and essential amino acid components of *S. platensis* may have improved fertility by enhancing the gonad weight and gonadosomatic index, and thereby had positive effects on reproductive function [106]. Granaci et al. [107] studied with boars and found that *S. platensis* can increase the fertilizing ability of sperms. Some researchers suggested that *S. platensis* improves the sperm motility and tone due to lactate dehydrogenase (LDH) in spermatozoa, which is increased by this microalgae [108, 109]. Also, it is known that thyroid hormones (T3 and T4) are associated with increased testosterone stimulation [110], which in turn helps spermatogenesis, which were studied in rats supplemented with *S. platensis*. It was also described that these thyroid hormones regulated by this microalgae can show an improvement in rats, which have a testicular injury and dysfunction, due to its antioxidant components [111, 112].

3.6. Antioxidant, anticancer and antitoxicity effects

The natural antioxidants are vitamins (B1, B5, B6, and E6), minerals (zinc, manganese, and copper), amino acid (methionine), beta-carotene, and trace elements (selenium). *S. platensis*, which contains phenolic acids, beta-carotene, and tocopherols, is a very important natural source for the intake of antioxidants. The antioxidant effect has been examined in vivo and in

vitro [113, 114]. *S. platensis* has antioxidant and immunomodulatory properties which appear in the mechanism of tumor destruction and also in cancer prevention [115]. Some researchers studied liver cancer and reported that lymphocyte activity and survival rate in cancer-stricken organisms can be increased by the supply of *S. platensis* [17] through C-phycocyanin activating the immune system and playing an important role to prevent the progress of local and oral cancer [116].

Beta-carotene contained in *S. platensis* at a high value protects the free radicals and tumors induced by chemicals and enhances the immunologic resistance of the body, also decreasing lung cancer [117, 118]. The inhibitory effects of *S. platensis* and its extracts on carcinogenesis for both humans and animals were reported in some studies [119–121]. Grawish et al. [119] showed the inhibition of dysplastic tumoral changes in cheek pouch mucosa in hamsters. In another study, the protective phyto-antioxidant functions of liver tumors were determined, by an increase of the Bax/Bcl-2 ratio, which is associated in the apoptosis mechanism of hepatocellular carcinoma cell line HepG2 [120]. Additionally, *S. platensis* and its contents have protective effects against drugs, chemicals, and xenobiotics on liver tissue [120, 122, 123]. Abdel Daim et al. [124] reported that the protective mechanism of *S. platensis* against Deltamethrin induced oxidative stress through the inhibition of lipid peroxidation and releasing of free radicals or enhancing of the activity superoxide dismutase. Related to all these studies, it has been suggested that *S. platensis* may have a positive effect on anticancerogenic and oxidative situations.

S. platensis consists of proteins, lipids, carbohydrates, elements, and vitamins such as β carotene, riboflavin, cyanocobalamin, α -tocopherol, and α -lipoic acid [125]. As discussed, with all these substances, S. platensis has beneficial effects against nephrotoxicity and cardiotoxicity [125–127]. Mohan et al. [126] showed that S. platensis may protect against cisplatin-induced nephrotoxicity in rats. Also, Khan et al. [127] described the protective effect of S. platensis against doxorubicin-induced cardiotoxicity. In the world, there are some threats which are spreading dangerously such as arsenic and radiation in the water. The millions of people living in Bangladesh, India, Taiwan, and Chile are consuming high concentrations of arseniccontaminated drinking water and thousands of them are exposed to chronic arsenic poisoning [128]. Specific treatment for this situation is unavailable. Misbahuddin et al. [128] showed that S. platensis extract plus zinc could be beneficial for the treatment of chronic arsenic poisoning with melanosis and keratosis. Likewise, in another study it was determined that S. platensis could protect the testes against mercury chloride-induced testicular damage by its rich antioxidants and antitoxicity activity [129]. An important example of radiation and S. platensis effects is the Chernobyl disaster. In Ukraine and Belarus, people live with radiation, which is in contaminated water, land, and nutrients. Due to this effect, poisoning, leukemia, cancer, birth defects, anemia, and thyroid disease have appeared. On that point, there is some unpublished work which talks about the effects of S. platensis on these symptoms and diseases [130]. Also, the protective effects of this microalgae and its extract polysaccharides and phycocyanin were shown by Belookaya et al., Wu et al., and Qishen et al [130-132]. They reported that S. platensis and its extracts decrease the radioactivities, and improve the bone marrow reproduction and immune system.

4. Conclusions

A prominent super food, *S. platensis*, has been known for its importance for health instead of medicine for centuries. Many studies have been performed on the effects of this interesting microalgae on both humans and animals. Today, studies observe at the nutritional quality and investigate the medicinal aspects of *S. platensis* on growth, hematopoietic system, immune system, allergy, anemia, cholesterol, obesity, diabetes, wound healing, fertility, viral and bacterial diseases, parasites, and helminth diseases. Besides these effects, anti-inflammatory, antibiotic, antipyretic, antioxidant, anticancer, and antitoxicity effects have also been determined by researchers. The potential effects have been addressed with in vivo and in vitro experiments, and contribute to the literature.

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References

- Ciferri O. Spirulina, the edible microorganism. Microbiology Reviews. 1983. PMCID: PMC283708
- [2] Sánchez M, Bernal-Castillo J, Rozo C, Rodríguez I. Spirulina (arthrospira): an edible microorganism: a review. Universitas Scientiarum. 2003;8(1):7–24. PMC283708
- [3] Castenholz RW, Waterbury JB. Oxygenic photosynthetic bacteria. In: Staley JT, Bryant MP, Pfenning N, Holt JG., editors. Bergey's Manual of Systematic Bacteriology. Williams and Wilkins Co; Baltimore, 1989. p. 1710–1806. ISBN:0683041088 9780683041088 0683011189 9780683011180

- [4] Gershwin ME, Belay A. Spirulina in Human Nutrition and Health. CRC Press; USA, 2007. DOI: 10.1007/s10811-009-9467-0.
- [5] Habib M, Ahsan B, Parvin M, Huntington TC, Hasan MR. A review on culture, production and use of spirulina as food for humans and feeds for domestic animals and fish. Food and Agriculture Organization of The United Nations; 2008. Retrieved 2011. Available from: ftp://ftp.fao.org/docrep/fao/011/i0424e/i0424e00.pdf [Accessed 2016/08/18].
- [6] Abdulqader G, Barsanti L, Tredici M. Harvest of *Arthrospira platensis* from Lake Kossorom (Chad) and its household usage among the Kanembu. Journal of Applied Phycology. 2000;12:493–498. DOI: 10.1023/A:1008177925799
- [7] Zarrouk C. Contribution to the cyanophyceae study: influence various physical and chemical factors on growth and photosynthesis of *Spirulina maxima*. [thesis]. Faculty of Science, University of Paris; 1966.
- [8] Vonshak A. *Spirulina platensis* (Arthrospira): Physiology, Cell-Biology and Biotechnology. Taylor & Francis; London, 1997. DOI: 10.1023/A:1008177925799
- [9] Siva Kiran RR, Madhu GM, Satyanarayana SV. Spirulina in combating protein energy malnutrition (PEM) and protein energy wasting (PEW)—A review. Journal of Nutrition Research. 2015;3(1):62–79. DOI: 10.13140/RG.2.1.3149.0325
- [10] Tadros MG. Normal, Al. Characterization of Spirulina biomass for CELSS diet potential. NASA Technical Reports Server. 1988; DOI: 19940009624
- [11] Sasson A. Micro Biotechnologies: Recent Developments and Prospects for Developing Countries. Place de Fontenoy, Paris. France: United Nations Educational, Scientific and Cultural Organization (UNESCO), BIOTEC Publication 1/2542; 1997. p. 11–31.
- [12] Intergovernmental Institution for the use of Micro-algae Spirulina Against Malnutrition. Preamble-Introductory Note [Internet]. 5 March 2003. [Updated: 2 July 2014]. Available from: www.iimsam.org/http://www.iimsam.org/images/IIMSAM-CHAR-TER.pdf [Accessed: 2016/08/18]
- [13] Natural Medicines Comprehensive Database Consumer Version. "Blue-green algae" [Internet]. November 18, 2010. [Updated: Retrieved April 15, 2011]. Available from: https://medlineplus.gov/druginfo/natural/923.htlm [Accessed: 2016/08/18]
- [14] Food Drug Administration. FDA Agency Response Letter GRAS Notice No. GRN 000127 [Internet]. 2003. Available from: http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/GRAS Listings/ucm153944.htm [Accessed: 2012/12/7]
- [15] EFSA European Food Safety Authority (EFSA). Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) claiming maintenance of normal blood glucose concentrations. In: EFSA, editor. EFSA Panel on Dietetic Prod-

ucts, Nutrition and Allergies; Parma, Italy. EFSA Journal; 2010. p. 1490. DOI: 10.2903/ j.efsa.2010.1490

- [16] Fujisawa T, Narikawa R, Okamoto S, Ehira S, Yoshimura H, Suzuki I, Masuda T, Mochimaru M, Takaichi S, Awai K, Sekine M, Horikawa H, Yashiro I, Omata S, Takarada H, Katano Y, Kosugi H, Tanikawa S, Ohmori K, Sato N, Ikeuchi M, Fujita N, Ohmori M. Genomic structure of an economically important cyanobacterium, *Arthrospira* (*Spirulina*) platensis NIES-39. DNA Researches. 2010;17:85–103. DOI: 10.1093/dnares/ dsq004
- [17] Iijima N, Fugii I, Shimamatsu H, Katoh S. Anti-tumor agent and method of treatment therewith. U.S. Patent Pending. 1982;1150. Available from: https://docs.google.com/ viewer?url=patentimages.storage.googleapis.com/pdfs/US8404650.pdf [Accessed: 2013/08/06].
- [18] Kapoor R, Mehta U. Utilization of beta-carotene from *Spirulina platensis* by rats. Plants Foods for Human Nutrition. 1993;43(1):1–7. DOI: 8464841.
- [19] Watanabe F. Vitamin B12 sources and bioavailability. Experimental Biological Medicine (Maywood). 2007;232(10):1266–1274. DOI: 10.3181/0703-MR-67.
- [20] American Dietetic Association; Dietitians of Canada. Position of the American Dietetic Association and Dietitians of Canada: Vegetarian Diets. Journal of the American Dietetic Association. 2003;103(6):748–765. DOI: 10.1053/jada.2003.50142
- [21] Khan Z, Bhadouria P, Bisen PS. Nutritional and therapeutic potential of Spirulina. Current Pharmaceutical Biotechnology. 2005;6:373–379. DOI: 16248810
- [22] Becker EW. Handbook of microalgal mass culture. In: Richmond A, editor. Nutritional Properties of Microalgae: Potentials and Constraints. Boca Raton, Florida: CRC Press; 1986. p. 339–419. ISBN-10: 0849332400 ISBN-13: 978-0849332401
- [23] Puyfoulhoux G, Rouanet JM, Besancon P, Baroux B, Baccou JC, Caporiccio B. Iron availability from iron-fortified Spirulina by an in vitro digestion/Caco-2 cell culture model. Journal of Agriculture and Food Chemistry. 2001;49:1625–1629. DOI: 11312906
- [24] Walter P. Effects of vegetarian diets on aging and longevity. Nutrition Reviews. 1997;55(1):61–68. DOI: 10.1111/j.1753-4887.1997.tb06106.x
- [25] Kulshreshtha A, Zacharia AJ, Jarouliya U, Bhadauriya P, Prasad GB, Bisen PS. Spirulina in health care management. Current Pharmaceutical Biotechnology. 2008;9:400–405. DOI: 18855693
- [26] Pugh N, Ross SA, Elsohly HN, Elsohly MA, Pasco DS. Isolation of three weight polysaccharide preparations with potent immunostimulatory activity from *Spirulina platensis*, Aphanizomenon flos-aguae and Chlorella pyrenoidosa. Planta Medica. 2001;67:737–742. DOI: 10.1055/s-2001-18358
- [27] Nielsen CH, Balachandran P, Christensen O, Pugh ND, Tamta H, Sufka KJ, Wu X, Walsted A, Schjørring-Thyssen M, Enevold C, Pasco DS. Enhancement of natural killer

cell activity in healthy subjects by Immulina®, a Spirulina extract enriched for Brauntype lipoproteins. Planta Medica. 2010;76(16):1802–1808. DOI: 10.1055/s-0030-1250043.

- [28] Seegmiller JE, Laster L, Howell RR. Biochemistry of uric acid and its relation to gout. The New England Journal of Medicine. 1963;268:764–773. DOI: 10.1056/ NEJM196304042681406
- [29] Babadzhanov AS, Abdusamatova N, Yusupova FM, Faizullaeva N, Mezhlumyan L. G, Malikova M KH. Chemical composition of *Spirulina platensis* cultivated in Uzbekistan. Chemistry of Natural Compounds. 2004;40:3. DOI: 10.1023/B:CONC. 0000039141.98247.e8
- [30] Stahl W, Sied H. Bioactivity and protective effects of natural carotenoids. Biochimica et Biophysica Acta. 2005;1740(2):101–107. DOI: 10.1016/j.bbadis.2004.12.006
- [31] Chew BP, Park JS. Carotenoid action on the immune response. Journal of Nutrition. 2004;134(1):257–261. DOI: 14704330
- [32] Hasler C. Functional foods: Benefits, concerns and challenges A position paper from the American Council on Science and Health. Journal of Nutrition. 2002;132:3772–3781. DOI: 12468622
- [33] Henrikson R. "Superfood Spirulina microalgae future", Microalgae Spirulina, superalimento del futuro. 2nd ed. Ronore Enterprises; 1994. 222 p. Available from: http:// es.slideshare.net/maguifley/microalga-spirulina-robert-henrikson-50-mb
- [34] Armstrong DG. Gut-active growth promoters, control and manipulation of animal growth. In: Buttery PJ, LIndsay D, Haynes NB, editors. Control and Manipulation of Animal Growth. London: Butterworths; 1986. p. 21–37. Available from: https:// books.google.com.tr/books?id=ha_YBAAAQBAJ&pg=PA21&lpg=PA21&dq=armstrong,+gut+active+growth&source=bl&ots=nI5Z8CbU0R&sig=herW-RY_CWIG8o7luNFj115FHB_I&hl=tr&sa=X&ved=0ahUKEwiPkbH7q9_OAhULshQK HXHTCSIQ6AEIHTAA#v=onepage&q=armstrong%2C%20gut%20active %20growth&f=false
- [35] Heidarpour A, Fourouzandeh-Shahraki AD, Eghbalsaied S. Effects of *Spirulina platensis* on performance, digestibility and serum biochemical parameters of Holstein calves. African Journal of Agricultural Research. 2011;6(22):5061–5065. DOI: 10.5897/ AJAR11.1076
- [36] Kay RA. Microalgae as food supplement. Critical Reviews in Food Science and Nutrition. 1991;30:555–573. DOI: 10.1080/10408399109527556
- [37] Kahraman Z. "Herbal Feed Additive and Their Usage in Laying Hen Diets", Bitkisel yem katkı maddelerinin yumurta tavuğu yemlerinde kullanımı (in Turkish). Tavukçuluk Araştırma Dergisi. 2009;8(1):34–41. Available from: http://arastirma.tarim.gov.tr/ tavukculuk/Belgeler/web%20English%20Doc/journal%20(Dergimiz)/Dergimiz %20Cilt%208%20Sayi%201/Cilt%208%20Sayi%201%20Makale%207%20Bitkisel

%20Yem%20Katk%C4%B1%20Maddelerinin%20Yumurta%20Tavu%C4%9Fu %20Yemlerinde%20Kullan%C4%B1m%C4%B1.pdf

- [38] Halidou Doudou M, Degbey H, Daouda H, Leveque A, Donnen P, Hennart P, Dramaix-Wilmet M. The effect of spiruline during nutritional rehabilitation: systematic review. Revue d Épidémiologie et de Santé Publique. 2008;56(6):425–431. DOI: 10.1016/j.respe. 2008.08.004.
- [39] Kocaoğlu Güçlü B, Kara K. "Use of Alternative Feed Additives in Ruminant Nutrition: 1. Probiotic, Prebiotic, and Enzyme", Ruminant Beslemede Alternatif Yem Katkı Maddelerinin Kullanımı: 1. Probiyotik, Prebiyotik ve Enzim. (In Turkish). Journal of Veterinary Faculty of University of Erciyes. 2009;6(1):65–75.
- [40] Saxena PN, Ahmad MR, Shyan R, Amla DV. Cultivation of Spirulina in sewage for poultry feed. Experientia. 1983;39:1077–1083. DOI: 10.1007/BF01943117
- [41] Vonshak A, Tomaselli L. Arthrospira (Spirulina): systematics and ecophysiology. In: Whitton BA, Potts M, editors. Ecology of Cyanobacteria. Kluwer Academic Publishing; The Netherlands, 2000. p. 505–523. DOI: 10.1007/0-306-46855-7_18
- [42] Fox RD. Spirulina production & potential. Aix-en-Provence: Edisud; 1996. p. 89. ISBN: 285744883X, 9782857448839
- [43] Richmond A. Mass culture of cyanobacteria. In: Mann N, Carr N, editors. Photosynthetic Prokaryotes. 2nd ed. Plenum Press; New York, 1992. p. 181–2010. DOI: 10.1007/978-1-4757-1332-9_6
- [44] Pulz O, Gross W. Valuable products from biotechnology of microalgae. Applied Microbiology and Biotechnology. 2004;65:635–48. DOI: 10.1007/s00253-004-1647-x
- [45] Dogan M. "The Effect Mechanisms of Probiotic Bacteria in Gastrointestinal System", Probiyotik Bakterilerin Gastrointestinal Sistemdeki Etki Mekanizması. Electronic Journal of Food Technologies. 2012;7(1):20–27. e-ISSN:1306-7648.
- [46] Belay A. The potential application of Spirulina (Arthrospira) as a nutritional and therapeutic supplement in health management. The Journal of the American Nutraceutical Association. 2002;5:27–48. Available from: http://www.macoc.fr/resources/The +Journal+of+the+American+Nutraceutical+Association+vol+5+spring+2002+Spiruline.pdf
- [47] Simpore J, Zongo F, Kabore F, Dansou D, Bere A, Nikiema JB, Pignatelli S, Biondi DM, Ruberto G, Musumeci S. Nutrition rehabilitation of HIV-infected and HIV-negative undernourished children utilizing spirulina. Annals of Nutrition & Metabolism. 2005;49(6):373–380. DOI: 10.1159/000088889
- [48] Yamani E, Kaba-Mebri J, Mouala C, Gresenguet G, Rey JL. Use of spirulina supplement for nutritional management of HIV-infected patients: Study in Bangui, Central African Republic. Medecine Tropicale. 2009;69(1):66–70. DOI: 19499738

- [49] Azabji Kenfack M, Edie Dikosso S, Loni G, Onana A, Sobngwi E, Gbaguidi E, Ngougni Kana AL, Nguefack T, Von der Weid D, Njoya O, Ngogang J. Potential of *Spirulina platensis* as a nutritional supplement in malnourished HIV-infected adults in Sub-Saharan Africa: a randomised, single-blind study. Nutrition and Metabolic Insights. 2011;4:29–37. DOI: 10.4137/NMI.S5862
- [50] Moreira LM, Rocha ASR, Ribeiro CLG, Rodrigues RS, Soares LS. Nutritional evaluation of single-cell protein produced by *Spirulina platensis*. African Journal of Food Science. 2011;5(15):799–805. DOI: 10.5897/AJFS11.184
- [51] Seyidoglu N, Galip N. Effects of Saccharomyces cerevisiae and Spirulina platensis on Growth performances and biochemical parameters in rabbits. Journal of Kafkas Veterinary Faculty. 2014;20(3):331–336. DOI: 10.9775/kvfd.2013.9988
- [52] Derkenbaşı S, Ünal H, Karayücel I, Aral O. Effect of dietary supplementation of different rates of Spirulina (*Spirulina platensis*) on growth and feed conversion in guppy (Poecilia reticulara Peters, 1860). Journal of Animal and Veterinary Advances. 2010;9(9):1395–1399. DOI: 10.3923/javaa.2010.1395.1399
- [53] Promya, J, Chitmanat C. The effects of *Spirulina platensis* and *Cladophora* algae on the growth performance, meat quality and immunity stimulating capacity of the African sharptooth catfish (*Clarias gariepinus*). International Journal of Agriculture and Biology. 2011;13:77–82. ISSN Online: 1814–9596 10–272/DJZ/ 2011/13–1–77–82
- [54] Ungsethaphand T, Peerapornpisal Y, Whangchai N and Sardsud U. Effect of feeding *Spirulina platensis* on growth and carcass composition of hybrid red tilapia (Oreochromis mossambicus × O. niloticus). Maejo International Journal of Science and Technology. 2010;4(02):331–336. Available online at www.mijst.mju.ac.th
- [55] Peiretti PG, Meineri G. Effects of diets with increasing levels of *Spirulina platensis* on the performance and apparent digestibility in growing rabbits. Livestock Science. 2008;118:173–177. DOI: 10.1016/j.livsci.2008.04.017
- [56] Grinstead GS, Tokach MD, Dritz SS, Goodband RD, Nelssen JL. Effects of *Spirulina platensis* on growth performance of weanling pigs. Animal Feed Science and Technology. 2000;83:237–247. DOI: 10.1016/S0377-8401(99)00130-3
- [57] Araújo KGL, Facchinetti AD, Santos CP. Influence of intake of Spirulina biomass on body weight and feed intake in rats. Food Science and Technology. 2003;3(1): 6–9. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0101-20612003000100003 (Accessed 1999/07/06).
- [58] Cheng-Wu Z, Chao-Tsi T, Zhen ZTY. The effects of polysaccharide and phycocyanin from *Spirulina platensis* on peripheral blood and hematopoietic system of bone marrow in mice. Proceedings of the Second Asia-Pacific Conference on Algal Biotechnology. National University of Singapore. 1994. p. 58.

- [59] Mao TK, Van de Water J, Gershwin ME. Effect of Spirulina on the secretion of cytokines from peripheral blood mononuclear cells. Journal of Medicinal Food. 2000;13:135–140. DOI: 10.1089/jmf.2000.3.135
- [60] Løbner M, Walsted A, Larsen R, Bendtzen K, Nielsen CH. Enhancement of human adaptive immune responses by administration of a high-molecular-weight polysaccharide extract from the cyanobacterium *Arthrospira platensis*. Journal of Medicinal Food. 2008;11(2):313–322. DOI: 10.1089/jmf.2007.564
- [61] Selmi C, Leung PS, Fischer L, German B, Yang CY, Kenny TP, Cysewski GR, Gershwin ME. The effects of Spirulina on anemia and immune function in senior citizens. Cellular and Molecular Immunology. 2011;8:248–254. DOI: 10.1038/cmi.2010.76
- [62] Qureshi MA, Garlich JD, Kidd MT. Dietary *Spirulina platensis* enhances humoral and cell-mediated immune functions in chickens. Immunopharmacology and Immunotoxicology. 1996;18:465–476. DOI: 10.3109/08923979609052748
- [63] Baojiang G. Study on effect and mechanism of polysaccharides of *Spirulina platensis* on body immune functions improvement. Proceedings of 2nd Asia Pacific Conference on Algal Biotechnology, Garland Publishers; 1994. p. 24.
- [64] Watanuki H, Ota K, Tassakka AC, Kato T, Sakai M. Immunostimulant effects of dietary Spirulina platensis on carp. Aquaculture. 2008;258:157–163. DOI:10.1016/j.aquaculture. 2006.05.003
- [65] Hirahashi T, Matsumoto M, Hazeki K, Saeki Y, Ui M, Seya T. Activation of the human innate immune system by Spirulina augmentation of interferon production and NK cytotoxicity by oral administration of hot water of *Spirulina platensis*. International Immunopharmacology. 2002;2:423–434. DOI: 11962722
- [66] Mao TK, Van de Water J, Gershwin ME. Effects of a Spirulina based dietary supplement on cytokine production from allergic rhinitis patients. Journal of Medicinal Food. 2005;8(1):27–30. DOI: 10.1089/jmf.2005.8.27
- [67] Hayashi O, Hirahashi T, Katih T, Miyajima H, Hirani T, Okuwaki Y. Class specific influence of dietary *Spirulina platensis* on antibody production in mice. Journal of Nutritional Science and Vitaminology. 1998;44 (6):841–845. DOI: 10197315
- [68] Belay A, Toshimitsu K, Yoshimichi O. Spirulina (Arthrospira): Potential application as an animal feed supplement. Journal of Applied Phycology. 1996;8:303–311. DOI: 10.1007/BF02178573
- [69] Hamad AA, Saud IA, Ali A, Qureshi MA. Enhancement of chicken macrophage phagocytic function and nitrite production by dietary *Spirulina platensis*. Immunopharmacology and Immunotoxicology. 2001;23(2):281–289. DOI: 10.1081/IPH-100103866
- [70] Simsek N, Karadeniz A, Karaca T. Effects of the *Spirulina platensis* and Panaxginseng oral supplementation on peripheral blood cells in rats. Revue de Médecine

Vétérinaire. 2007;158(10):483–488. Available from: http://www.revmedvet.com/2007/ RMV158_483_488.pdf

- [71] Qureshi MA, Ali RA. Spirulina platensis exposure enhances macrophage phagocytic function in cats. Immunopharmacology and Immunotoxicology. 1996;18(3):457–463. DOI: 10.3109/08923979609052747
- [72] Shen YB, Piao XS, Kim SW, Wang L, Liu P, Yoon I, Zhen YG. Effects of yeast culture supplementation on growth performance, intestinal health, and immune response of nursery pigs. Journal of Animal Science. 2000;87:2614–2624. DOI: 10.2527/jas.2008-1512
- [73] Simsek N, Karadeniz A, Keles ON, Unal B. Spirulina platensis feeding inhibited the anemia- and leukopenia-induced lead and cadmium in rats. Journal of Hazardous Materials. 2009;164(2–3):1304–1309. DOI:10.1016/j.jhazmat.2008.09.041
- [74] Zikic V, Stajn AS, Ognjanovic BI, Pavlovic SZ, Saicic ZS. Activities of superoxide dismutase and catalase in erythrocytes and transaminases in the plasma of carps (*Cyprinus carpio* L.) exposed to cadmium. Physiological Research. 1997;46(5):391–396. DOI: 9728486
- [75] Kostic MM, Ognjanovic B, Dimitrijevic S, Zikic RV, Stajn A, Rosic GL, Zivkovic RV. Cadmium-induced changes of antioxidant and metabolic status in red blood cells of rats: in vivo effects. European Journal of Haematology. 1993;51(2):86–92. DOI: 10.1111/ j.1600-0609.1993.tb01598.x
- [76] Hug C, Von der Weid D. Spirulina in the fight against malnutrition. Geneva (Switzerland) 15 Foundation Antenna Technologies. Rue de Neuchâte. 2011; No.: 29-1201. 16. Available from: http://www.antenna.ch/medias/Spirulina-Assessment-and-Prospects.pdf (Accessed Feb 2011).
- [77] Mani U, Sadliwala A, Iyer U, Parikh P. The effect of Spirulina supplementation on blood haemoglobin levels of anaemic adult girls. Journal of Food Science and Technology. 2000;37:642–644. ISSN 0022-1155
- [78] Yeganeh S, Teimouri M, Amirkolaie AK. Dietary effects of *Spirulina platensis* on hematological and serum biochemical parameters of rainbow trout (*Oncorhynchus* mykiss). Research in Veterinary Science. 2015;101:84–88. DOI: 10.1016/j.rvsc. 2015.06.002
- [79] Nagaoka S, Shimizu K, Kaneko H, Shibayama F, Morikawa K, Kanamaru Y. A novel protein C-phycocyanin plays a crucial role in the hypocholesterolemic action of *Spirulina platensis* concentrate in rats. Journal of Nutrition. 2005;135(10):2425–2430. DOI: 16177207
- [80] Bhat VB, Madyastha KM. Scavenging of peroxynitrite by phycocyanin and phycocyanobilin from *Spirulina platensis*: protection against oxidative damage to DNA. Biochemical and Biophysical Research Communication. 2001;285:262–266. DOI: 10.1006/ bbrc.2001.5195u

- [81] Juarez-Oropeza MA, Mascher D, Torres-Duran PV, Farias JM, Paredes-Carbajal MC. Effects of Spirulina on vascular reactivity. Journal of Medicinal Food. 2009;12(1):15–20. DOI: 10.1089/jmf.2007.0713
- [82] Torres-Duran PV, Ferreira-Hermosillo A, Juarez-Oropeza MA. Antihyperlipidemic and antihypertensive effects of *Spirulina maxima* in an open sample of Mexican population: a preliminary report. Lipids in Health and Disease. 2007;26:6–33. DOI: 10.1186/1476-511X-6-33
- [83] Samuels R, Mani UV, Iyer UM, Nayak US. Hypocholesterolemic effect of Spirulina in patients with hyperlipidemic nephrotic syndrome. Journal of Medicinal Food. 2002;5(2):91–96. DOI: 10.1089/109662002760178177
- [84] Park HJ, Lee YJ, Ryu HK, Kim MH, Chung HW, Kim WY. A randomized double-blind, placebo-controlled study to establish the effects of Spirulina in elderly Koreans. Annals of Nutritional and Metabolism. 2008;52(4):322–328. DOI: 10.1159/000151486
- [85] Sato T, Yamamoto C, Fujiwara Y, Kaji T. Biological activities of exogenous polysaccharides via controlling endogenous proteoglycan metabolism in vascular endothelial cells. Journal of Pharmaceutical Society of Japan (Yakugaku Zasshi). 2008;128(5):717–723. DOI: http://doi.org/10.1248/yakushi.128.717
- [86] Becker EW, Jakober B, Luft D, Schmulling RM. Clinical and biochemical evaluations of Spirulina with regard to its application in the treatment of obesity. Inst. Chem. Pfanz. Nutrition Reports International. 1986;33(4):565. ISSN: 0029-6635
- [87] Mani UV, Desai S, Iyer U. Studies on the long-term effect of Spirulina supplementation on serum lipid profile and glycated proteins in NIDDM patients. Journal of Nutraceuticals Functional & Medical Foods. 2000;2(3):25–32. DOI:10.1300/J133v02n03_03
- [88] Hosoyamada Y, Takai Y, Toshimitsu K. Effect of water soluble and insoluble fractions of Spirulina over serum lipids and glucose resistance of rats. Journal of Japan Society of Nutrition and Food Science. 1991;44:273–277. DOI: http://doi.org/10.4327/jsnfs.44.273
- [89] Parikh P, Mani U, Iyer U. Role of Spirulina in the control of glycemia and lipidemia in type 2 diabetes mellitus. Journal of Medicinal Food. 2001;4(4):193–199. DOI: 10.1089/10966200152744463
- [90] Iwata K, Inayama T, Katoh T. Effect of *Spirulina platensis* on plasma lipoprotein lipase activity in fructose induced hyperlipidemia in rats, Journal of Nutritional Science and Vitaminology. 1990;36:165–171. DOI: 10.3177/jnsv.36.165.
- [91] Simkus A, Oberauskas V, Laugalis J, Zelvyte R, Monkevicience I, Sederevicius A, Simkiene A, Pauliukas K. The effect of weed *Spirulina platensis* on the milk production in cows. Abstract, Veterinarija ir Zootechnika. 2007;38:60. ISSN 1392-2130
- [92] Panigrahi BB, Panda PK, Patro VJ. Wound healing activity of spirulina extracts. International Journal of Pharmaceutical Sciences Review and Research. 2011;6(2):132– 135. DOI: 10.17179/excli2014-697

- [93] Rabadiya B, Patel P. Spirulina: Potential clinical therapeutic application (review). Journal of Pharmacy Research. 2010;3(8):1726–1732. ISSN: 0974-6943
- [94] Syarina P, Karthivashan G, Abas F, Arulselvan P, Fakurazi S. Wound healing potential of Spirulina platensis extracts on human dermal fibroblast cells. EXCLI Journal. 2015;14:385–393. DOI: 10.17877/DE290R-7598
- [95] Hudson BJ, Karlis IG. The lipids of the alga Spirulina. Journal of the Science of Food Agriculture. 1974;25:759–763. DOI: 10.1002/jsfa.2740250703
- [96] Nichols B, Wood B. The occurrence and biosynthesis of gamma linolenic acid in *Spirulina platensis*. Lipids. 1986;3(1):46–50. DOI: 10.1007/BF02530968
- [97] Remirez D, González R, Merino N, Rodriguez S, Ancheta O. Inhibitory effects of Spirulina in zymosan-induced arthritis in mice. Mediators of Inflammation. 2002;11(2): 75–79. DOI: 10.1080/09629350220131917
- [98] Chen JC, Liu KS, Yang TJ, Hwang JH, Chan YC, Lee IT. Spirulina and C-phycocyanin reduce cytotoxicity and inflammation-related genes expression of microglial cells. Nutritional Neuroscience. 2012;15(6):252–256. DOI: 10.1179/1476830512Y.000000020.
- [99] Qureshi M, Kidd MT, Ali RA. Spirulina extract enhances chicken macrophage functions after in vitro exposure. Journal of Nutritional Immunology, 1996;3(4):35–45. DOI: 10.1300/J053v03n04_04
- [100] Hayashi T, Hayashi K., Maeda M, Kojima I. Calcium Spirulan, an inhibitor of enveloped virus replication, from a blue-green alga *Spirulina platensis*. Journal of Natural Products. 1996; 59(1):83–87. DOI: 10.1021/np960017o
- [101] Daoud HM, Soliman EM. Evaluation of *Spirulina platensis* extract as natural antivirus against foot and mouth disease virus strains (A, O, SAT2). Veterinary World. 2015;8(10): 1260–1265. DOI: 10.14202/vetworld.2015.1260-1265.
- [102] Shih SR, Tsai KN, Li YS, Chueh CC, Chan EC. Inhibition of enterovirus 71-induced apoptosis by allophycocyanin isolated from a blue-green alga *Spirulina platensis*. Journal of Medical Virology. 2003;70(1):119–125. DOI: 10.1002/jmv.10363
- [103] Ozdemir G, Karabay NU, Dalay MC, Pazarbasi B. Antibacterial activity of volatile component and various extracts of *Spirulina platensis*. Phytotherapy Research. 2004;18(9):754–757. DOI: 10.1002/ptr.1541
- [104] Mayer AMS, Rodrigues AD, Berlinck RG, Hamann MT. Marine pharmacology in 2005– 6: Marine compounds with anthelmintic, antibacterial, anticoagulant, antifungal, antiinflammatory, antimalarial, antiprotozoal, anti tuberculosis, and antiviral activities; affecting the cardiovascular, immune and nervous systems, and other miscellaneous mechanisms of action. (review). Biochimica et Biophysica Acta. 2009;1790:283–308. DOI: 10.1016/j.bbagen.2009.03.011
- [105] Woodhead AD. Nutrition and reproductive capacity in fish. Symposium of Proceedings of Zoology Society. London. 1960;19:23-28. Available from: http://

journals.cambridge.org/download.php?file=%2FPNS %2FPNS19_01%2FS0029665160000104a.pdf&code=61907413b7b8bb1b8eb4aa14d4bda 045

- [106] James R, Sampath K, Thangarathinam R, Vasudevan I. Effect of dietary Spirulina level on growth, fertility, coloration and leucocyte count in red swordtail, xiphophorus helleri. The Israeli Journal of Aquaculture. 2006;58(2):97–104. DOI: http:// hdl.handle.net/10524/19166
- [107] Granaci V. Achievements in the artificial insemination of swine. Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca. Animal Science and Biotechnologies. 2007;382–386. Available from: http://journals.usamvcluj.ro/ index.php/zootehnie/article/viewFile/2012/1937
- [108] Kistanova E, Marchev Y, Nedeva R, Kacheva D, Shumkov K, Georgiev B, Shimkus A. Effect of the *Spirulina platensis* included in the main diet on the boar sperm quality. Biotechnology in Animal Husbandry. 2009;25(5–6):547–557. Available from: http:// www.doiserbia.nb.rs/img/doi/1450-9156/2009/1450-91560906547K.pdf (Accessed 2009).
- [109] Belay A, Ota Y, Miyakawa K, Shimamatsu H. Current knowledge on potential health benefit of Spirulina. Journal of Applied Phycology. 1993;5(2). DOI: 10.1007/BF00004024
- [110] Dohle GR, Smit M, Weber RFA. Androgens and male fertility. World Journal of Urology. 2003;21(5):341–345. DOI: 10.1007/s00345-003-0365-9
- [111] Yousef MI, Abdallah GA, Kamel KI. Effect of ascorbic acid and vitamin E supplementation on semen quality and biochemical parameters of male rabbits. Animal Reproduction Science. 2003;76(1–2):99–111. DOI: http://dx.doi.org/10.1016/ S0378-4320(02)00226-9
- [112] Rezvanfar MA, Sadrkhanlou RA, Ahmadi A. Shojaei-Sadee H, Rezvanfar M, Mohammadirad A, Salehnia A, Abdollahi M. Protection of cyclophosphamide-induced toxicity in reproductive tract histology, sperm characteristics, and DNA damage by an herbal source; evidence for role of free-radical toxic stress. Human and Experimental Toxicology. 2008;27(12):901–910. DOI: 10.1177/0960327108102046
- [113] Falquet J. Nutritional Aspects of Spirulina. Antenna Technologies. Available from: http://www.antenna.ch/en/documents/AspectNut_UK.pdf
- [114] Pratt DE. Natural antioxidants from plant material. In: Huang MT, Ho CT, Lee CY, editors. Phenolic Compounds in Food and their Effects on Health. II. American Chemical Society, Washington, 1992; p. 54–71. Chapter DOI: 10.1021/ bk-1992-0507.ch005
- [115] Karkos PD, Leong SC, Karkos CD, Sivaji N, Assimakopoulos DA. Spirulina in clinical practice: evidence-based human applications. Evidence Based Complementary and Alternative Medicine: eCAM. 2011;2011:531053 DOI: 10.1093/ecam/nen058.

- [116] Li B, Zhang X, Gao M, Chu X. Effects of CD59 on antitumoral activities of phycocyanin from *Spirulina platensis*. Biomedicine & Pharmacotherapy. 2005;59(10):551–560. DOI: 10.1016/j.biopha.2005.06.012
- [117] Suda D, Schwartz J, Shklar G. Inhibition of experimental oral carcinogenesis by topical beta carotene. Harvard School of Dental Medicinal Carcinogenesis.1986;7(5):711–715.
 DOI: 10.1093/carcin/7.5.711
- [118] Schwartz J, Shklar G, Reid S, Trickler D. Prevention of experimental oral cancer by extracts of Spirulina-Dunaliella algae. Nutrition and Cancer. 1988;11(2):127–134. DOI: 10.1080/01635588809513979
- [119] Grawish ME. Effects of *Spirulina platensis* extract on Syrian hamster cheek pouch mucosa painted with 7,12-dimethylbenz[a]anthracene. Oral Oncology. 2008;44(10): 956–962. DOI: 10.1016/j.oraloncology.2007.11.0141.
- [120] Ismail MF, Ali DA, Fernando A, Abdraboh ME, Gaur RL, Ibrahim WM, Raj MH, Ouhtit A. Chemoprevention of rat liver toxicity and carcinogenesis by Spirulina. International Journal of Biological Science. 2009;2;5(4):377–387. PMID: 19521547 PMCID: PMC2695150.
- [121] Mishima T, Murata J, Toyoshima M, Fujii H, Nakajima M, Hayashi T, Kato T, Saiki I. Inhibition of tumor invasion and metastasis by calcium spirulan (Ca-SP), a novel sulfated polysaccharide derived from a blue-green alga, *Spirulina platensis*. Clinical & Experimental Metastasis. 1998;16(6):541–550. PMID: 9872601.
- [122] Karadeniz A, Cemek M, Simsek N. The effects of Panax ginseng and *Spirulina platensis* on hepatotoxicity induced by cadmium in rats. Ecotoxicology and Environmental Safety. 2009;72(1):231–235. DOI: 10.1016/j.ecoenv.2008.02.021.
- [123] Vadiraja BB, Gaikwad NW, Madyastha KM. Hepatoprotective effect of C-phycocyanin: protection for carbon tetrachloride and R-(+)-pulegone-mediated hepatotoxicity in rats. Biochemical and Biophysical Research Communications. 1998;19;249(2):428–431. DOI: 10.1006/bbrc.1998.9149.
- [124] Abdel-Daim MM, Abuzead SM, Halawa SM. Protective role of Spirulina platensis against acute deltamethrin-induced toxicity in rats. PLoS One. 2013;8(9):e72991. DOI: 10.1371/journal.pone.0072991
- [125] Karadeniz A, Yildirim A, Simsek N, Kalkan Y, Celebi F. Spirulina platensis protects against gentamicin-induced nephrotoxicity in rats. Phytotherapy Research. 2008;22(11):1506–1510. DOI: 10.1002/ptr.2522.
- [126] Mohan IK, Khan M, Shobha JC, Naidu MU, Prayag A, Kuppusamy P, Kutala VK. Protection against cisplatin-induced nephrotoxicity by Spirulina in rats. Cancer Chemotherapy and Pharmacology. 2006;58(6):802–808. DOI: 10.1007/ s00280-006-0231-8.

- [127] Khan M, Shobha JC, Mohan IK, Naidu MU, Sundaram C, Singh S, Kuppusamy P, Kutala VK. Protective effect of Spirulina against doxorubicin-induced cardiotoxicity. Phyto-therapy Research: PTR. 2005;19(12):1030–1037. DOI: 10.1002/ptr.1783.
- [128] Misbahuddin M, Islam AZ, Khandker S, Ifthaker-Al-Mahmud, Islam N, Anjumanara. Efficacy of spirulina extract plus zinc in patients of chronic arsenic poisoning: a randomized placebo-controlled study. Clinical Toxicology (Phila). 2006;44(2):135–141. PMID: 16615668.
- [129] El-Desoky GE, Bashandy SA, Alhazza IM, Al-Othman ZA, Aboul-Soud MA, Yusuf K. Improvement of mercuric chloride-induced testis injuries and sperm quality deteriorations by *Spirulina platensis* in rats. PLoS One. 2013;8(3) DOI:10.1371/journal.pone. 0059177.
- [130] Belookaya TC. From Chairman of Byelorussian Committee "Children of Chernobyl" May 31, 1991. Available from: http://www.naturalpharmainternational.com/1/upload/ reduces_effects_of_radiation_for_the_children_of_chernobyl.pdf
- [131] Wu LC, Ho JA, Shieh MC, Lu IW. Antioxidant and antiproliferative activities of Spirulina and Chlorella water extracts. Journal of Agriculture and Food Chemistry. 2005;53(10):4207–4212. DOI: 10.1021/jf0479517
- [132] Qishen P, Guo BJ, Kolman A. Radioprotective effect of extract from *Spirulina platensis* in mouse bone marrow cells studied by using the micronucleus test. Toxicology Letters. 1989;48(2):165–169. DOI: 2505406
- [133] Belay A. Mass culture of Spirulina outdoors. The Earthrise Farms experience. In: Vonshak, A., Ed. Spirulina platensis (Arthrospira): Physiology, Cell-biology and Biotechnology. Taylor and Francis. London. 1997. pp. 131–158.
- [134] Othes S, Pire R. Fatty acid composition of Chlorella and Spirulina microalgae species. Journal of AOAC International. 2001;84:1708–1714.





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