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Spirulina: Properties, Benefits and Health-Nutrition Relationship

Spirulina: Özellikleri, Faydaları ve Sağlık-Besin İlişkisi

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ABSTRACT

Spirulina is a natural product that is scientifically used in many fields due to its many beneficial contents such as antioxidants, essential amino acids, high-quality proteins and essential unsaturated fats. Spirulina is known as a nutriment-dense food as it has vitamins A, C, E and B and many minerals including calcium, zinc, magnesium and selenium. In particular, selenium and vitamin C are vitamins with antioxidant properties and protect our cells and tissues against potential damage. Due to these properties, Spirulina is used in food, cosmetics and medical fields. Since it contains antioxidant properties, it is used in several diseases such as arthritis, diabetes, anemia, cancer and cardiovascular diseases. In many studies, the properties of Spirulina have been investigated and positive results have been obtained. Also, the significance of Spirulina has improved with its use in fields such as pharmacology, cosmetics, medicine and food. In this study, the importance of this microalgae, which has numerous benefits, has been tried to be emphasized with today's approach and studies in the fields of biochemistry, biotechnology and medicine.

Keywords: Antioxidant, Cancer, Health, Natural Product, Spirulina

ÖZ

Spirulina, antioksidanlar, esansiyel amino asitler, yüksek kaliteli proteinler ve esansiyel doymamış yağlar gibi birçok faydalı içeriği nedeniyle bilimsel olarak birçok alanda kullanılan doğal bir üründür. Spirulina, A, C, E ve B vitaminleri ve kalsiyum, çinko, magnezyum ve selenyum gibi birçok mineral içeriğine sahip olduğu için besleyiciliği yoğun bir gıda olarak bilinir. Özellikle selenyum ve C vitamini antioksidan özelliklere sahip vitaminlerdir ve hücrelerimizi ve dokularımızı olası hasarlara karşı korurlar. Bu özelliklerinden dolayı Spirulina gıda, kozmetik ve tıp alanlarında kullanılmaktadır. Antioksidan özellikler içerdiğinden artrit, diyabet, anemi, kanser ve kardiyovasküler hastalıklar gibi çeşitli hastalıklarda kullanılır. Birçok çalışmada Spirulina'nın özellikleri araştırılmış ve olumlu sonuçlar elde edilmiştir. Ayrıca, Spirulina'nın farmakoloji, kozmetik, tıp ve gıda gibi alanlarda kullanımıyla da önemi artmıştır. Bu çalışmada, sayısız faydası bulunan bu mikroalglerin önemi günümüz yaklaşımlarıyla ve biyokimya, biyoteknoloji ve tıp alanlarında yapılan çalışmalarla vurgulanmaya çalışılmıştır.

Anahtar Kelimeler: Antioksidan, Kanser, Sağlık, Doğal Ürünler, Spirulina

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INTRODUCTION

Spirulina (Arthrospira) is a spiral blue green microalgae and a enrollee of cyanobacterium sub-assembly. Spirulina fusiformis (SF), Spirulina platensis (SP) and Spirulina maxima (SM) are the main eatable species.[1]

Spirulina plantensis is an gram negative prokaryote, which includes chlorophyll a making oxygenic photosynthesis. Also, It is accepted as an drug spring and ideal food, owing to its rich protein, lipid and polysaccharide.[2] The amounts of biomolecule of species are given in Table 1.

Table 1. Biochemical Mass Composition of Algae Stated on a Dry Matter Form [3-4]

Species	Protein %	Carbohydrates %	Nucleic acid %	Lipid %
Spirulina maxima	70	15	4	6
Spirulina fusiformis	58	10	2	7
Spirulina platensis	63	14	5	9
Chlorella vulgaris	58	18	4	14
Scenedesmus quadricauda	47	22	-	28
Chlorella pyrenoidosa	57	26	-	2
Scenedesmus obliquus	56	17	6	14
Dunaliella salina	57	32	-	6
Synechoccus sp.	63	15	5	11

Also, it is a wealthy source of vitamins, minerals and antioxidants comprising phenolic compounds. Spirulina moreover includes about 4–8% lipid that is mainly consisted of polyunsaturated essential fatty acids as α-linoleic acid, gamma linolenic acid, Eicosapentaenoicacid (EPA), Docosahexaenoicacid (DHA).[1]

Table 2. Fatty Acid Profile of S. maxima and S. platensis (g/kg dwt)

	Fatty acid							
Species	14:0	16:0	16:1	18:0	18:1	18:2	18:3	Reference
Spirulina plantensis	0,17	49	2,5	2,4	11	16,5	18,6	**Babadzhanov et al.[5]; Lugara et al.[6]**
Spirulina maxima	-	57	2,2	2,1	6	16	13,8	**Paula da Silva et al.[7]**

The amounts of fatty acids of Spirulina species are showed in Table 2. The amounts of trace elements of Spirulina species are given in Table 3.

Table 3. Macromineral Content of Three Batches The Algal Species (g/100g dwt)

	Trace element				
Species	Calcium	Magnesium	Sodium	Potassium	Reference
Spirulina plantensis	% 0,207	% 0,486	% 2,033	% 1,675	**Ramirez-Rodrigues et al.[8]**
Spirulina maxima	% 0,520	% 0,285	% 1,763	% 2,379	**Paula da Silva et al.[7]**
Spirulina fusiformis	% 0,901	% 0,426	% 0,88	% 1,1	**Dubey [4]**

Spirulina platensis involves two characteristic rich pigmented antioxidants like phycocyanin and carotenoids.[9] Spirulina contains about 2,000 IU/g of dry beta-carotene.[10] Carotenoids are very pigments found in plants and beta carotene. Also, carotenoids is one construction of carotenoids in microorganisms that substantial weld of vitamin A. Besides, carotenoids be able to used as natural immunostimulants for healing the alives immune status and antioxidant capacity.[9]

Phycocyanin is located on the outer surface of the thylakoid membrane.[11] C-Phycocyanin are microalgae/cyanobacteria proteins situated in the granules which grap light and transplant energy, the phycobilissomas; these are similar to light-convening complexes of green plants including chlorophyll a and chlorophyll b.[12] Phycocyanin absorbs at 610-620 nm. This

colorant is fairly stable in the pH gap of 5–8 and displays a very powerful red fluorescence when offer in its naturel form.[13]

Spirulina has been successfully grown on a commercial scale for many years around the world, since it can be grown in excessive instances such as high salinity, temperature and alkalinity. It grows decent betwen the temperature of 37°C and 35°C. Also, ıt grows up the best at a high bicarbonate concentrations and high pH (9-11).[14] This durableness allows Spirulina to outperform different contaminating microalgae or scrapers.[15]

Spirulina has been used to cure several diseases like as anemia, arthritis, cancer, cardiovascular disease and diabetes is known to generate compounds that have high neuroprotective activity.[16] There are numerous reports of the protective impacts of Spirulina on various damaged tissues outside the nervous system. Spirulina improves nephrotoxicity excited by amikacin through its antiinflammatory and antioxidant particulars.[17] Also, It has been reported that tissue toxicity and oxidative stress excited by deltamethrin will be repressed pursueing administration of Spirulinain mice.[18] On the respects, Spirulina effectually improves renal biomarkers, hepatic and hematologic of toxicity owing to diazinon in the male rats through its antiinflammatory and antioxidant activities.[17]

Besides, Spirulina arranges the extracellular signal arranged kinase (ERK1/2), p38, IκB and c-Jun NH2- terminal kinase (JNK) signaling paths, resulting in anti inflammatory, anticancer and antioxidant effects.[19]

In addition to these, Spirulina is a strong premonitory for the immune system, as indicate in animal experiments, by accelerating the natural killer and phagocytic activities. Also, hypocholesterolemic impacts have been rendered in many animal studies. In some studies, Spirulina has a preserve impact against many toxicants comprising mercury, acetaminophen, D-galactosamine and coppertoxicity.[20] Spirulina activates prevents lipid peroxidation, cellular antioxidant enzymes and prevents free radicals, DNA damage, and enhances the activity of catalase and superoxide dismutase.[19]

Many studies indicate that Spirulina or its extracts can prohibit cancer in animals and human. In vitro studies propose that polysaccharides of Spirulina increase DNA repair synthesis and cell nucleus enzyme activity. Apart from, Spirulina is a strong bracer for the immune system. Nutrition studies indicate that even small quantity of Spirulina tone up both the cellular mechanism and humoral of the immune.[21]

Components of Spirulina has been reported to exhibit antitumor activities in many cancer cells, including breast cancer, colon, pancreatic, liver, prostate, and gastric cancer.[22] Ravi et al. (2015) explored the role of components of Spirulina as an antineoplastic agent in triple negative breast cancer cells and emerged the molecular mechanism behind its anti-cancer activity. Similarities and functions of elements such as phycocyanin in the structure of Spirulina are given in Table 4[23]

Table 4. Outline of The Biological Specialities and Specific Impacts of The Major Base Lines of Spirulina

Ingredient	Biological specialities	Specific impacts	Reference
β-Carotene	Antioxidant, anticancer, immunomodulatory, anti inflammatory	(İnactivate single oxygen, That can damage DNA molecules and lipids) (can warn divers stem cells, including differ-entiate into progenitor cells)	**Mohammadi et al.[24]; Haghighat et al.[25]**
Phycocyanin	Antioxidant, anticancer, antifungal	(Immuno stimulants and hepatoprotective), (is anticancer functions in multiple cancer cells inclusive melanoma, chronic myeloid leukemia, cervical cancer, lung cancer and colon cancer)	**Hao et al.[9]; Hassaan et al.[26]**
γ-Linolenic acid (GLA)	Antibacterial, antiinflammatory, anticancer	Has proven to suppress BACE1 activity	**Youn et al.[27]**

Table 4 (Continued). Outline of The Biological Specialities and Specific Impacts of The Major Base Lines of Spirulina

Ingredient	Biological specialities	Specific impacts	Reference
Eicosapentaenoic acid (EPA), Dokosaheksaenoik asit (DHA)	Antibacterial, antiinflammatory, antioxidant, antimicrobial	Very Facilitating neurotransmitter oscillation, acting like a neurothophic factors), there are quite inhibitory effects on manifold Gram-positive bacteria and Gram-negative bacteria	**Sun et al.[28]; De Oliveria Souza et al.[29]**

In this table, Spirulina species having antioxidant activity and phenolic compounds different fields of use and their purposed use are laboured to be explained.

The use of Spirulina in studies

Studies on the antioxidant and anti-inflammatory activity with Spirulina

Antioxidants are compound derivatives which neutralize reactive oxygen species (ROS) and free radicals in the cell. These antioxidants ensure protection toward injury caused by free radicals effectively played very substantial roles in the evolvement of many different chronic disease comprising cancer, anaemie, aging, cardiovasculer diseases, inflammation.[30-31]

Al-Qahtani and Binobead (2019) conducted a study to helpful dietary impact toward liver sores reasoned by galactosamine was researched ensuring trust to human health using different animal model. Non chronic (acute) hepatotoxicity was excited in Wister rats with D-galactosamine (D-GalN) dogged by cure with BHT (butylated hydroxytoluene) and with Spirulina aqueous extractat several concentrations. Also, The impact of Spirulina at divergent concentrations were tested and compared with BHT remedy. Spirulina watery extract at about 9% resulted in a essential reduce in the levels of inflammatory determiners TNFa, IL1 and IL6 band and alkaline phosphatase besides decline TBARS, whereas it showed effective an increase in the oxidative stress determiner like as GST, GR, SOD, GSH, CAT and GPX total protein when contrasted to the levels saved with that group processed with D-GalN. Results besides signified that Spirulina watery extract at about 9% concentration was evenly efficient inprotecting liver injury as it was seed with BHT. The results acquired in the present study very openly showned the positive helpful protective impact of Spirulina, when used as diet, on the security and useful protection of liver from damages caused by toxicants.[32]

The antioxidant activity in the plant extracts necessitates powerful proof of the physiological functions of antioxidants in the cellular level. In respect to evaluate the antioxidant strength of the a bilberry extract (phytocomplex) functionalized on Spirulina, conventional chemical methods (ABTS and DPPH) were compared to in vitro cellular responses by use of HepG2 human hepatocyte carcinoma cell lines. OxiCyan® (phytocomplex) was determined to affect on HepG2 cells in a dual mode: as a cytoprotective agent by induction of Nrf2/ARE pathway and with a direct effect on ROS scavenging. Directly ROS sweeping activity of OxiCyan® depended on the anthocyanin part ensured by bilberry, while the gene activation of the Nrf2/ARE pathway was induced by Spirulina chemical components. OxiCyan® have indicated a very high antioxidant activity in the cellular degree by both scavenging ROS and stimulating the gene expression of inherent antioxidant cell defense.[33]

In another study, was make to assess the toxic impacts of imidacloprid (IMI) insecticide on the upgrowth performance, immune response, and oxidative status of Oreochromis niloticus, Nile tilapia and the preserver role of nutritional supplementation of Spirulina platensis (SP). Nile tilapia fish were exposed to a mixture of imidacloprid (IMI) and Spirulina. A total of six studies were performed with Spirulina as control group (0g/kg), 20g/kg and 40g/kg, and 0,0 (IMI) and 0,05 µg/kg (IMI). The toxicity of imidacloprid in fish and the effect of Spirulina against this toxicity were

investigated. Fish were nourished on the concerned diets up to distinct satiation thrice a day for 8 weeks in every treatment. Two-way ANOVA revealed a important decline in growth indices, hepatic SOD (superoxide dismutase), glutathione peroxidase and catalase activities in the IMI-exposed fish. The dietary supplementation of SP indicated stimulating impacts in the growth performance, immune biomarkers, antioxidants and haemato biochemical of Nile tilapia with optimum level of about 20 g SP/kg diet.[34]

Studies on the effect of cancer with Spirulina

Cancer is a complex disease that arises with the uncontrolled cleavage and proliferation of many cells and is under the imfact of environmental conditions and genetic. More than 100 types of cancer are known.[35] Cancer treatment is a long and difficult process. The side effects of the drugs used are quite high. For this reason, treatments with natural active substances have gained importance today. One of these is Spirulana.

Kepekçi et al. (2013) conducted a study to aimed to investigate the hepatoprotective potential of biomass structure of Spirulina platensis very prospered in phenolic compounds. The preservative impacts of the biomass of Spirulina platensis with low quantity of phenolics (SP1) and with highamounts of phenolics (SP2) toward CCl4 excited acute hepatotoxicity were commentated in rats. The enhanced levels of MDA, AST and ALT along with reduced activities of CAT and SOD were importantly ($p< 0,01$) cured by SP2. Histological researchs exhibited that SP2 was more potent than phenolics SP1 inprotecting the liver from toxic damage of CCl_4 and conservating the hepatocyte ultrastructure. Besides, The lesions inclusive lymphocyte infiltration, necrosis and hepatocyte damage like dilations in endoplasmic reticulums, irregular lamellar organisation and the presence of large number of cytoplasmic vacuolization were ameliorated by phenolics SP2.[36]

In a different study, the anticancer and antimutant potential of a liquid aqua extract of Spirulina product (SE) toward the non small cell human lung cancer A549 cell line was examined. After qualitative analysis, ıt is researched the impact of SE on cell viability, morphology and proliferation. Also, the influence of Spirulina product on organise of the cell cycle, expression of cell cycle/apoptosis relevant proteins and induction of apoptosis in lung cancer cells has evaluated. In addition, their research the cytotoxic impact of Spirulina product on normal human skin fibroblasts (HSF). Their studies proved that SE dramatically decreased cancer cell proliferation and viability, which was with by cell cycle inhibition in the phase G1, prominent morphological changes and induction of apoptosis. Besides, their determined no cytotoxic effect of the examined Spirulina extract on normal skin fibroblasts. Their molecular labours demonstrated that SE decreased the phosphorylation of Rb and Akt proteins, decreased the expression of CDK4, cyclin D1, and enhanced the Bcl2 to Bax ratioin the A549 cells. As a result, the results acquired ensure evidence of the anticancer activity of the Spirulina product toward lung cancer cells and vigorously support the information of the chemopreventive particulars of Spirulina.[37]

In another study on cancer, Shokri et al. (2014) was to research the immunomodulatory impacts of Spirulina platensis by gauging the levels of serum interleukin IL-17, IL-10, IL-4, interferon (IFN)-|gama| and tumor necrosis factor (TNF)-α in mice suffered from systemic candidiasis and breast cancer. C/Balb female mice were vaccinat with Candida albicans and SMMT (spontaneous mouse mammary tumor). 5 days after Candida albicans vaccination, the serum levels of texture preventer of metalloproteinase-1 were appreciated by Enzyme- linked immunosorbent assay (ELISA). The animals were remedied daily with Spirulina platensis solution (about 0,2 mL, 800 mg/kg, orally) for 3 days afore IV defiance with Candida albicans, and SMMT challenge with SC and

sustained for 10 days. The survival ability rate and so tumor size of animals in the experiment were specified. ELISA designated the levels of IFN-γIFN Tγ-4, TNF-α, IL-17 and IL-10 cytokines in supernatants. The results indicated which S.platensis reduced the secretum of IL-4 (about 45 pg/mL) and IL-10 (about 208 pg/ml) in tumor carrying mice get infected with C.albicans, while the levels of IFN-γ, IL-17 and TNF-α enhanced to nearly about (93, 137 and 316 pg/mL) and in this group. These results openly offer that S. platensis has a extraordinary immunomodulatory impact, which provides a scientific verification for the very popular use of this inherent item, and reinforced in the appendix research of their full mechanism of action.[38]

Synergic studies on cancer, antioxidant and anti-inflammatory effects of food ingredients with Spirulina

There are many studies related to active ingredients in Spirulina. These studies indicate how changes active ingredients of Spirulina in metabolism. In respect to define this, the change of Spirulina compound in different living organisms was researched Table 5.

Table 5. Combination of Spirulina with Other Ingredients and Effect

Other item	Source	Effect	Reference
Ferrous fumarate	Yellow River carp	Obtained results, demonstrated that Spirulina and ferrous fumarate drug supplementation can enhance intestinal health through both detraction tissue peroxidation and increment intestinal digestive enzyme activity	**Ren et al.[39]**
Cocoa powder	Microencapsulated microalgae (MM)	There was an increment of DPPH method and phenolic compounds augmenting 39 and 31% in the MM chocolate milk.	**Batista de Oliveria et al.[40]**
Pomegranate juice	Rats	Study openly shows that pomegranate juice and Spirulina platensis have hepatoprotective imfact on carbon tetrachloride (CCl4) reason hepatotoxicity in rats by means of antioxidant activity.	**Hossam El-Beltagi et al. [41]**
Vegan kefir	Milk	Increasing Spirulina platensis concentration enhanced applied to milk the counts of lactococci and lactobacilli the total phenolic content of kefir, while pH values of vegan kefir samples reduced.	**Sözeri Atik et al.[42]**
Linseed oil	Mullets (Mugil liza)	It is decided that a partial inclusion of Spirulina and linseed oil (about 50%) is possible, and ameliorate its growth performance, and that this rate can increment antioxidant responses, and so can arrange the mullets fillet attribute without effecting adversely fillet fatty acid content.	**Rosas et al. [43]**
Aloe vera and guar gum	Mango	It was obtained that the Spirulina, aloe vere and guar gum coatings decreased the weight loss and the respiration rate of the tropical mango fruits. Mango fruits coating with SPE + GG substantially indicated higher hardness in comparison with the control. The results besides showed that the total antioxidant activity and phenol were very much higher in the SPE + GG coated fruits, since compared to other ones.	**Ebrahimi and Rastegar [44]**
Sargassaum vulgar	Spodoptera littoralis	Study consequences revealed the impact of tested algae importantly S. platensis and Sargassaum vulgaras a potential source of inbred pesticides to check mentioned pest.	**Rashwan and Hammad [45]**
Thyme	Rabbit	Spirulina and thyme supplementation enhanced the gama linolenic acidcontent of rabbit meat, while Thyme meliorated the oxidative stability of freeze-dried meat and raw	**Dalle Zotte et al.[46]**
Glucomannan	Rats	The glucomannan prospered surimi diet excited antioxidant, pro-inflammatory and hypocholesterolemic effects, whereas the addition of about 3 g/kg Spirulina reserved those antioxidant and hypocholesterolemic impacts However, decreased the inflammation observed.	**Vazquez-Velasco et al. [47]**
Crab chitosan	Bacteria	The achieved crab chitosan eatable films unified with SE indicated excellent potential to be used foractive food packaging owing to its great antibacterial and antioxidant activities. Also, The mixture showed protection against bacteria.	**Balti et al. [48]**
Blueberry, spinach	Rats	The data obtained, suggest that blueberry, spinach and Spirulina supplements may have preservative effect versus neurodegeneration.	**Wang et al. [49]**
Thyme	Rabbit	Thyme and Spirulina supplemented diets had a substantial effect on yellowness and redness of Longissimus dorsi. Spırılina–Thyme and Thyme groups that also indicated the very utmost content of fatty acids and α-tocopherol content and the very lower lipid oxidation.	**Dal Bosco et al. [50]**
Panax ginsengon	Albino rats	Ginseng and S. platensis treatments indicated marked reduce lipid peroxidation and increment of the endogeny antioxidants levels. These results propose that P. ginseng and S. platensis may play a role in reduction the toxic impact of cadmium elements and its antioxidant particulars	**Karadeniz et al. [51]**

Table 5 (Continued). Combination of Spirulina with Other Ingredients and Effect

Other item	Source	Effect	Reference
Blueberry	Rat	In the study, increased striatal dopamine recovery seem in animals cured with Spirulina and blueberry diet flourished in antiinflammatory and antioxidants phytochemicals and intersected with an early, transient increment in OX-6-positive microglia	**Strömberg et al.** [52]

*Other item: food product used with Spirulina, Source: Animal cell or bacteria in which the food is used with Spirulina, Effect: Positive effect of Spirulina food on animal cells or bacteria

Table 5 shows the concomitant use of Spirulina and other metabolites. The combined use of Spirulina and other substances has shown a synergistic effect in the studies. The use of Spirulina had a positive impact on other substances. The combined use of Spirulina and food products had a positive effect on the cancer and antiocidants. The synergistic effect is also explained in the table 5.

CONCLUSION AND RECOMMENDATIONS

Compared to the raw materials taken into consideration in the food industry, due to its very rich protein, amino acid, essential fatty acid, carotenoid, mineral and vitamin content, Spirulina has been bring into focus of for many studies for many years. Besides, ıt has been used in many areas for many aim and continue to be used. It is reported that it has antioxidant, antimicrobial, anticancer, anti-inflammatory, hypoglycemic and hypolipidemic functions, besides its liver, nervous system and kidney protective effects. In addition, some types are widely used as food supplements. Spirulina, which contains many phytochemicals, is widely used as a food supplement or in the medical and pharmaceutical fields. As stated above, due to its numerous benefits for human health, we wanted to emphasize the importance of this microalgae by bringing together many studies on Spirulana with this study. We hope that one day, the products created with different formulations will take place more on the shelves in food markets and pharmacie.

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