A REVIEW OF BOTANY, PHYTOCHEMISTRY, AND PHARMACOLOGY OF ARTHROSPIRA PLATENSIS (SPIRULINA)

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Abstract

Traditional medicine has relied solely on plants and plant-based natural products. Phytomedicines are a class of drugs that derive their therapeutic effects from plant-based sources. Humans have used plants for centuries as a source of medicine, and even today, there is a tremendous interest in developing natural compounds for medicinal purposes. The development of botanical drugs provides a viable alternative to traditional synthetic drugs and promises a safer alternative to drugs derived from animals or bacteria. Today there are many botanical drugs in clinical use, some of which have become generic drugs. Arthrospira platensis is the scientific name for Spirulina. It is a photosynthetic, filamentous, helical-shaped, multicellular, green-blue microalga. Arthrospira maxima and Arthrospira platensis are the two most important species. Binary fission is the mode of cell division for these type of microorganism. Botanists classify as microalga belonging to the Cyanophyceae class because it contains chlorophyll, but bacteriologists classify it as a bacteria due to its prokaryotic structure. In freshwater lakes or artificial habitats created especially for them, these group of microscopic organisms can be found living. Traditional healers have been using parts and extracts of algae to manage a range of health ailments, such as circulatory system problems, vision loss, and arthritis. Carbohydrates (15-25%), proteins (55-70%), essential fatty acids (18%), vitamins, minerals, and pigments such as carotenes, chlorophyll a, and phycocyanin make up its chemical composition and several new metabolites that have displayed notable pharmacological effects. The current review attempts to collect and organize data from academic publications, journals, and databases on the taxonomy, botany, phytoconstituents, and pharmacological qualities of Arthrospira platensis that have been previously described. These results can serve as a reliable foundation for the suggested usage of this Arthrospira in conventional and alternative therapy.

Keywords: Arthrospira platensis, Spirulina, Antidiabetic, Antimicrobial, Phytomedicine.

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1. Introduction

The thing that distinguishes algae from other plants is that they all use an autotrophic method of nourishment. They have developed into a remarkable variety of physiologically active substances. Algae have inspired innovative therapeutic molecules that have significantly improved human health and well-being. According to the fossil record, cyanobacteria (BGA) are among the planet's earliest living things and date back nearly 3.5 billion years. Algal compounds have considerable promise as a source of antibacterial substances that are either safer or more efficient than synthetic antimicrobial substances. Arthrospira platensis, this genus of tiny creatures, thrives in freshwater lakes and other artificial habitats with favourable environmental conditions, including high levels of sunlight and moderate temperatures. By leveraging their capacity to adapt in settings where other species could not, they spread from the African and tropical American lakes where they first appeared to other warm regions. Due to its low toxicity and great nutritional content, it is believed that the Aztecs and other prehistoric societies used it as a food source.

Arthrospira platensis was commonly referred to as "spirulina" during this century, but it has recently been renamed to fit a better taxonomic structure. Spirulina is an organism that belongs to the cyanobacteria group. They are made up of a single cell that can photosynthesise to create organic materials. Even though they are bacteria, they are assembled in filaments that give them the appearance of algae (hence the name blue algae).
Since many families have chosen to include a supplement in their diets and have prioritized nutrition and health, this cyanobacterium has taken on more significance in the twenty-first century. It is more reasonable to refer to "spirulina" as a whole when addressing the market since. However, A. platensis is popular Arthrospira branches can also be discovered and are all referred to as "spirulina." Millions of people using this supplement daily have caused an astonishing increase in the "spirulina" market, which is anticipated to reach $779 million USD by 2026. This increase in trade has boosted many countries' economies, which are now attempting to promote and develop their "spirulina" products. Arthrospira platensis is a more widely distributed species that has been used by traditional healers to treat a variety of medical complications. The species, like other Arthrospira, has been discovered to contain novel compounds, many of which are pharmacologically significant. Since no such review could be found, an attempt was made to compile up-to-date information about the phytochemical and pharmacological investigations on this Arthrospira platensis to highlight its therapeutic potential.[1-7]

Taxonomical and Botanical Description

A total of 533 natural products derived from marine cyanobacteria have been reported up to date. These secondary metabolites have a highly unequal taxonomic distribution. First off, just 13 distinct genera in all are identified as the source of these 533 natural compounds. Second, only five genera account for more than 90% of all these compounds. When you consider the innovative sampling techniques employed to collect these cyanobacteria from geographically and environmentally diverse settings, this uneven taxonomic distribution is quite surprising. [8,9] Arthrospira platensis, also known as Spirulina, is a prokaryotic bacterium from the phylum Cyanobacteria, which means it uses photosynthesis but lacks chloroplasts. It is a long, coiled cylinder with granulated cross walls. It develops trichomes, which are chains of vegetative cells surrounded by a slimy sheet that allows it to reproduce via binary fission. This cyanobacterium is a preadolescent trichome cell, which means it produces hairs with nearly cylindrical or disc-like shapes that branch out and give the cells the appearance of trees. Since these photosynthetic creatures were initially categorised as algae, there has been disagreement over the systematic place of cyanobacteria. The difference between prokaryotes and eukaryotes was identified in 1962. In eukaryotes, the main distinction is the presence of cell organelles surrounded by a phospholipidic membrane. Stanier and Van Neil (1962) proposed naming these microorganisms cyanobacteria after incorporating green-blue algae into the prokaryote kingdom. Bergey's Manual of Determinative Categorization recognised and initially published this classification.. [10,11] This planktonic bacterium thrives in tropical and subtropical water bodies with high carbonate and bicarbonate levels and a high pH. Three subspecies of the genus Arthrospira exist: A. platensis, A. fusiformis, and A. maxima. A. platensis has a broader diameter and typically longer trichomes than the other genus variations, allowing it to have multiple health benefits as well as survive in various climates. Each subspecies differs from one another in terms of helix diameter. Arthrospira platensis and Arthrospira maxima have different vacuoles, exterior covers, and capsule regularity. Its helical filaments can change into atypical morphologies, including irregularly curved and even linear shapes under specific temperature and pressure circumstances, which is regarded to be a permanent degeneration that cannot be reversed. [12-14]

Taxonomy of *Arthrospira platensis*:
- Kingdom: Monera
- Phylum: Cyanobacteria
- Class: Cyanophyceae
- Order: Nostocales
- Family: Oscillatoriaceae
- Genus: Arthrospira
- Species: platensis

Habitat and ecology
Spirulina can be grown in a variety of culture media, including Zarrouk, SSM (Sea Saltpeter Medium), Zarrouk medium, BG11 medium, Conway medium, F/2 medium, and Sea Water. They were initially organisms from African and tropical American lakes that spread to other warm regions of the world by utilizing their ability to adapt to places other organisms could not. (Lakes that are extremely salty or alkaline, volcanic cones, and so on)

Geographical distribution
A.platensis, the most common species, is found chiefly in Africa, Asia and South America. Central America is where you can find A. maxima . Until recently, this species made up most of the phytoplankton in Lake Texcoco's solar evaporation channels, while alkaline saline lakes in the semi-arid Sudan-Sahel region (Chad) and the Rift Valleys were dominated by A. fusiformis (mainly Kenya). There is a popular, but the probably false, idea that the saline, alkaline, tropical, and subtropical habitats are typical for the entire genus because A. fusiformis and A. maxima are regularly found there. The countries that produce the most Spirulina commercially include the US, Thailand, India, Taiwan, China, Pakistan, and Myanmar.[15-17]

Phytochemical Studies
Spirulina has undergone chemical testing. It as prominent source of vitamins, mineral and protein.

Components of *Arthrospira platensis*
- Proteins (until 70%)
- Carbohydrates (50-70%). Mainly glucose, galactose, mannose, and ribose.
- Pigments: Betacarotene (provitamin A) xanthophylls, zeaxanthin, beta-cryptoxanthin.
- Vitamins: (10%) Mainly vitamin D, vitamin C and vitamins of group B (Vitamin B12, folic acid, niacin, riboflavin)
- Fibre (59%), mainly mucilage.
- Nucleic Acids
- Fats. Mainly essential fatty acids. (Gamma-linolenic acid - Omega 6)
- Minerals: Especially iron and iodine, along with calcium, phosphorus, magnesium, manganese, copper, zinc, and selenium.

Proteins: Spirulina contains a lot of Protein (60%-70% of its dry weight). Because of the high quality and quantity of Protein in Spirulina, it is helpful in human nutrition. A protein's nutritional value is determined by its amino acid quality, digestibility coefficient, and biological value.
Spirulina contains essential amino acids, with leucine accounting for 10.9% of total amino acids, valine accounting for 7.5%, and isoleucine accounting for 6.8%. Denaturation of Spirulina protein is observed when algae is heated above 67 °C.[18]

Carbohydrates: About 13.6% of spirulina platensis are made up of glucose, rhamnose, mannose, xylose, and galactose. Because Spirulina's cell walls do not contain cellulose, it is a crucial diet for elderly patients and others who struggle with poor intestinal absorption. A novel high molecular weight polysaccharide called "Immulina" was discovered from Spirulina and had immunostimulatory properties. In dry microalgae, this highly water-soluble polysaccharide makes up 0.5% to 2.0% (w/w) of the total. [19]

Pigments: Spirulina contains some natural pigments. The distinctive colors of certain flamingo species is due to the pigments present in the algae in African Valley that consume these cyanobacteria. This understanding has led to the need of this microorganism as a source of pigmentation in fish, eggs, and chickens. Due to the accumulation of zeaxanthin, Spirulina also enhances the yellowness and redness of broiler chickens. Spirulina contains an essential group of pigments called phycocyanin, chlorophyll, and carotenoid. Carotenoid acts as a lipophilic antioxidant and as anticancer agent.[20]

Vitamins Spirulina has a relatively high provitamin A content when compared to other diets. Carotene can be harmful in large amounts, but when consumed through Spirulina or another vegetable, the body only converts the required amount into vitamin A, making it generally safe to consume. Because Spirulina is a very rich source of vitamin B12, these cyanobacteria are very beneficial for patients who require supplements to treat pernicious anaemia.[21]

Fibre content in the single spirulina variety ranges from 3.6 g to 3.6 g per 100g. Spirulina had a high total, soluble, and insoluble dietary fibre content. The total, soluble, and insoluble dietary fibre contents were 14.98, 5.52, and 9.46%, respectively.[22]

Nucleic acids DNA and RNA. the nucleic acid content. The high concentration of nucleic acids

found in microbes, which can result in illnesses like gout, is one of the main issues with consuming them. RNA and DNA make up 2.2% to 3.5% and 0.6% to 1%, respectively, of Spirulina's dry weight, or less than 5% of these acids.[23]

Lipids There are 4-7% lipids in Spirulina. Linoleic acid (LA) and y-linolenic acid (GLA), Myristic, heptadecanoic, stearic, oleic, palmitoleic, omega-3, and omega-6 fatty acids are among the important fatty acids found in Spirulina. The two fatty acids with the lowest and highest contents are myristic and palmitic, respectively. The latter is necessary for the production of prostaglandins and arachidonic acid and is thought to have therapeutic effects. Compared to LA, GLA has a 170-fold greater ability to lower LDL cholesterol.[24-28]

Minerals Iron in Spirulina is 60% more absorbable than iron sulfate and other supplements. As a result, it may be an sufficient source of iron in anemic pregnant women. Iron can aid in the treatment of anemia and hypertension. Potassium, magnesium, calcium, zinc, phosphorous, and iron are the most important inorganic micronutrients in Spirulina. They are essential for human body nutrition. Calcium and phosphorus levels are comparable to those found in milk. This micronutrient's proportion (Ca:P) is adaptable with bone health and helps to reduce decalcification. Spirulina contains 1.7, 15, and 10 mg of iron, calcium, and phosphorous, respectively.[29-31]

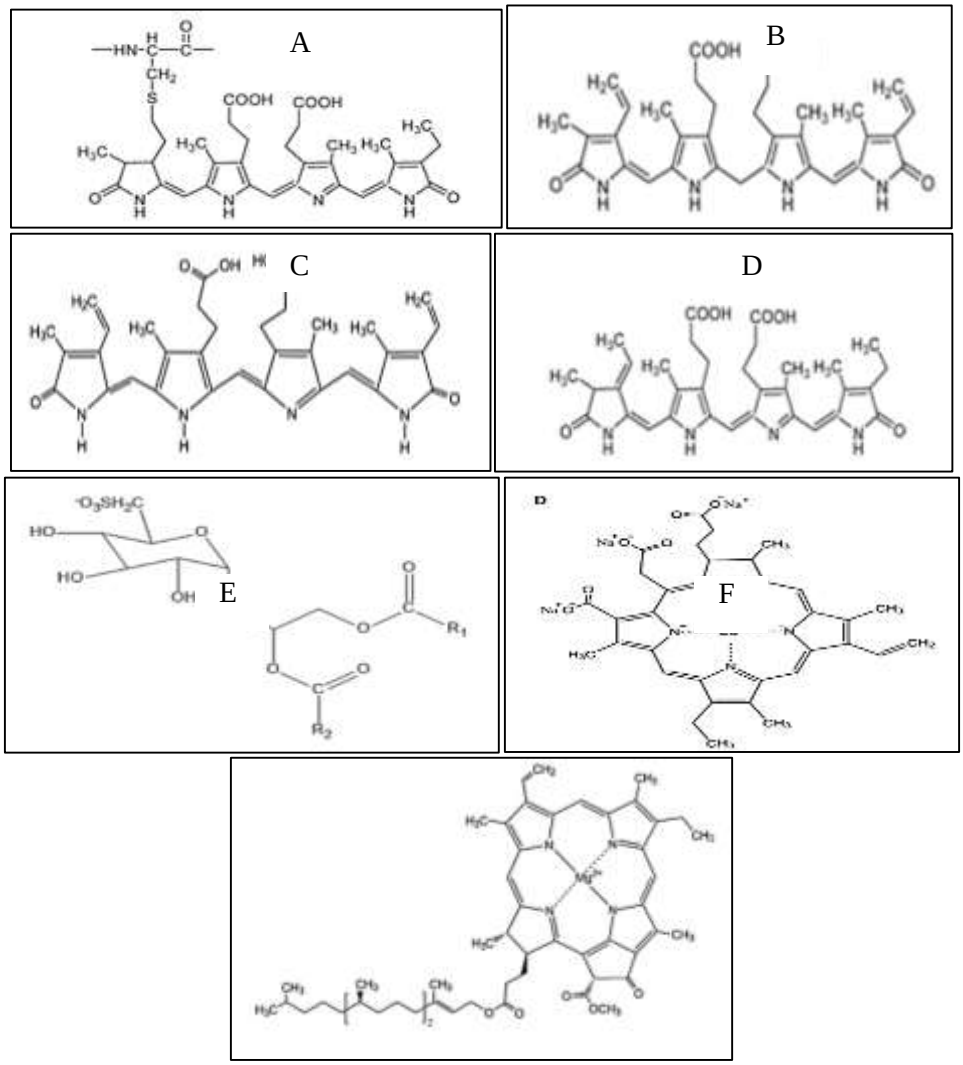

Figure 1 Compounds structure extracted from Arthrospira platensis Origin A)Bilirubin B)Phycocyanobilin C)Phycocyanin D)Biliverdin E)Chlorophyllin F)Chlorophyll A G)Sulfolipidssulfoquinovosyl diacylglycerol (SQDG)

Pharmacological Activities

S. No	Phenolic compounds	Pharmacological uses
1	Gallic acid	antioxidant, anti-inflammatory, and antineoplastic properties

2	p–OH benzoic acid	antimicrobial, antialgal, antimutagenic, antiestrogenic, hypoglycemic, anti-inflammatory, anti-platelet aggregating, nematicidal, antiviral, antioxidant
3	Vanillic acid	Treatment for cancer, diabetes, obesity, neurodegenerative, cardiovascular, and hepatic diseases
4	Syringic acid	prevention of diabetes, CVDs, cancer, cerebral ischemia
5	p-coumaric acid	antioxidant, anti-inflammatory, antidiabetic, anti-ulcer, anti-platelet, anticancer activities
6	Quercetin	Treatment for conditions of the heart and blood vessels and to prevent cancer.
7	Cinnamic acid	To reduce inflammation, lower blood sugar and cholesterol levels, improve memory, and the increased growth of "good" gut bacteria.
8	Caffeic acid	antioxidant and anti-inflammatory effects.
9	Ferulic acid	anti-inflammatory, antimicrobial, anticancer (for instance, lung, breast, colon, and skin cancer), anti-arrhythmic, and antithrombotic activity

Table 1: Phenolic compounds present in Arthrospira platensis and their pharmacological uses

Anticancer activity

According to some theories, the combination of antioxidant and immune-modulating abilities of Spirulina may have a mechanism for destroying tumours and so aid in the prevention of cancer. There has only ever been one human Study, despite a large number of animal and in vitro investigations. The effects of Spirulina on oral carcinogenesis, specifically leucoplakia, were the focus of this investigation. Due to peptide components that have varied inhibitory effects on tumour cells, c-phycocyanin has demonstrated active anti-tumor activities. By blocking the cycle at either the S or M phase and preventing tumor cells from entering G1, C-PC treatment in tumor cells can slow down cell proliferation. Damage to gene regulation, which prevents cell apoptosis and allows malignant cells to proliferate, makes C-PC-induced apoptosis excellent for treating cancer in the body. Since Bcl-2 controls this induced apoptosis, it can effectively stop the spread of tumours throughout the body without damaging healthy cells. It is not unexpected that there have been few human studies performed to date because most malignancies make it logistically hard to conduct cancer prevention trials with lower cancer incidence as an endpoint. Based on earlier studies on hamsters that demonstrated tumour shrinkage after topical application or consumption of Spirulina extract, Mathew et al. Carried out research on 77 patients.[32-35] They stated that 45% of their study cohort showed complete remission of leucoplakia after consuming Spirulina pills for a year. The fact that the serum concentrations of retinal carotene did not rise despite supplementation led the investigators to believe that other Spirulina ingredients may have capability for the anticancer effects. Despite the fact that their results seem encouraging, the unblinded, non-randomized experiment they used cannot be regarded as proof of a beneficial outcome.[36,37,41-43]

Antimicrobial activity

The qualities of algae include antiviral, antifungal, antibacterial, anticancer, and antiplasmodial. More research on animals and people is required to ascertain these chemicals' effectiveness in whole-organism systems. In preliminary activity screening, other methods of preventing and treating fungal skin infections should also be taken into account. A new chemotherapeutic therapy for skin infections and other disorders using antimicrobials generated from algae may begin if these challenges are given the attention they deserve. Research into the characteristics of algae is being done all around the world.[38] A major microalga with antibacterial activity against numerous harmful bacteria and fungi is spirulina platensis. Due to their significance as feeds for humans and their functional qualities in vitro or in vivo, Spirulina is one of numerous algae genera that have drawn particular attention. One of these genera, S. platensis, has undergone significant cultivation in order to create a protein-rich substance for use in nutrition or industry (blue pigment).[39,40] It provides a wide range of therapeutic benefits. As a result, it is also utilized in preventative and social medicine. Medical experts have advised against it for better health.[41-44]

Antioxidant and Antiproliferative activity

Liver fibrosis is a chronic liver disease that, if not treated, can progress to cirrhosis. To treat liver fibrosis, inhibiting activated hepatic stellate cell (HSC) proliferation or inducing HSC apoptosis could be used. The antioxidant activity of Spirulina has been shown to inhibit HSC proliferation during the G2/M phase. Spirulina's primary antioxidant component is C-phycocyanin. HepG2 cells were used in this Study. (Cancer cells derived from the human liver).[45-48]

Effects on Diabetes and Cholesterol Lowering

One of the most significant risk factors for atherosclerosis is High cholesterol, and yet, despite improved knowledge, cardiovascular disease continues that may lead to cause of death in developed regions. Nakeya et al. (1988) found a significant decrease in low-density lipoprotein (LDL) cholesterol after 8 weeks of treatment, despite the fact that the initial human trial did not show a significant increase in high-density lipoprotein (HDL) levels. As well, the atherogenic effect was diminished. In a more recent study, Rama Moorthy and Rajkumari (1996) found a significant decrease in blood cholesterol, triglycerides, and LDL cholesterol as well as an improve in HDL cholesterol in ischemic heart disease patients who received Spirulina pills. Therefore, there is enough data to indicate the therapeutic effects of Spirulina in allergic rhinitis, although larger studies are required.[49] The antioxidant -carotene in Spirulina may have anticancer properties, although the relationship between -carotene levels and carcinogenesis cannot be regarded as a cause of carcinoma.[50] There have been some promising studies on the cholesterol-lowering properties of Spirulina, but more extensive research is required before any firm conclusions can be made. Finally, there are no high-quality data trials on Spirulina's use as an antiviral or treatment for chronic fatigue. The evidence points to Spirulina as a safe food supplement with minimal adverse effects at this time, but its potential as a medication is still up in the air.[51-53]

Anti-inflammatory activity of Spirulina

Spirulina has been shown to have anti-inflammatory activity in both in vivo and in vitro studies due to C-phycocyanin (C-PC), a Bili protein. C-Pc exerts anti-inflammatory activity by inhibiting the formation of proinflammatory cytokines. Furthermore, it was demonstrated that for Spirulina's anti-inflammatory activity, not only proinflammatory cytokine expression but also inducible nitric oxide synthase (ins) and cyclooxygenase-2 (COX-2) expression must be inhibited.[54] The dose level of *Arthrosporic platensis*, which gives the body enough C-phycocyanin to regulate cyclooxygenase-2 and nitric oxide in the body, directly affects the efficacy of its anti-inflammatory actions. Suppressing the production of the two inflammatory molecules mentioned earlier is essential for the de-inflammatory process.[55]

Antiviral Applications

Due to the antiretroviral action included in the extracts, which stops viral reproduction, an aqueous extract of *Arthrosporic platensis* reduces plaque formation in a variety of viral strains. In one investigation, an A. platensis extract was used to incubate influenza strains for 72 hours, and the results showed that the A. platensis was able to block 70-94% of the tested virus yields (Chen et al., 2016).[45] Due to the cyanobacteria's safety and toleration when the algae are given in high doses, the utilization of this organism could be turned into a remedy for viral treatments. The possible antiviral effects of Spirulina are not strongly supported by any in vivo investigations. S. platensis water extract contains calcium spirulina, a sulphated polysaccharide that is the active ingredient (Ca-Spa). Ca-Spa (calcium spirulina) Several enveloped viruses, including Herpes simplex type I, human cytomegalovirus, measles and mumps virus, influenza A virus, and human immunodeficiency virus-1, are said to be inhibited by in vitro replication according to Hayashi et al (HIV-1).[56] An aqueous extract of S. platensis was shown to prevent HIV-1 replication in human T-cells, peripheral blood mononuclear cells, and Langerhans cells in vitro by K. Ishii et al. (1999). It is advantageous to employ herbs and algae products with known antiviral capabilities to combat particular viruses since immune modulation allows for their usage even after the infection has taken hold.[57]

Chronic fatigue

The "future food" Spirulina has been promoted as having "extraordinary ingredients" that help people feel energized. Some of these components, including vital fat (GLA) and polysaccharides (Rhamnose and Glycogen), are readily absorbed by human cells and help with energy release. Vitamin B6 is produced by the healthy lactobacillus that Spirulina increases in the colon, helping to release energy. Despite this advertising, the one known placebo-controlled randomized trial demonstrated no discernible difference between Spirulina and placebo in terms of fatigue levels. In any of the four patients, Spirulina at a dose of 3g per day had no more effect on fatigue than a placebo, and it might not affect chronic fatigue.[58]

Treatment for arsenic poisoning

Millions of people are at risk of suffering chronic arsenic poisoning, which has no known treatment. These countries also have significant levels of arsenic in their drinking water. To determine the effectiveness of Spirulina extract mixed with zinc in the treatment of chronic arsenic poisoning, a placebo-controlled, double-blind trial was conducted.[59] A placebo (17 patients) or spirulina extract (210 mg with 2 mg of zinc) was given twice daily for 16 weeks to 41 patients with chronic arsenic poisoning. Each patient was given access to arsenic-free drinking water by installing a locally

built water filter at the household level. Comparing changes in skin symptoms (clinical ratings) and arsenic levels in urine and hair between the placebo and Spirulina extract with zinc groups allowed researchers to assess the effectiveness of the treatment. Chronic arsenic poisoning with melanosis and keratosis was successfully treated with spirulina extract and zinc twice daily for 16 weeks.[60]

Allergy, Rhinitis, and Immunomodulation

Spirulina has been demonstrated to possess anti-inflammatory effects by preventing mast cell histamine release. In a randomized, double-blind, placebo-controlled trial, people with allergic rhinitis were given either a placebo or Spirulina daily for 12 weeks. Peripheral blood mononuclear cells were extracted before and after Spirulina feeding, and the levels of cytokines (interleukin-4 (IL-4), interferon- (IFN-), and interleukin-2 (IL-2) that are crucial for controlling Ige-mediated allergy were evaluated. The findings revealed that a high dose of Spirulina significantly decreased IL-4 levels by 32%, highlighting the microalga's anti-allergic rhinitis benefits. Spirulina has been demonstrated to boost IgA synthesis and affect level of IgA in human saliva, suggesting that microalga are crucial for mucosal immunity.[61] To identify the molecular basis for Spirulina's ability to stimulate the human immune system, a Japanese research team examined blood cells taken from volunteers before and after receiving a hot water extract of Spirulina platensis. When given to male volunteers, microalga extracts boosted IFN- production and Natural Killer (NK) cell destruction. Spirulina consumption significantly reduced symptoms and physical findings, such as nasal discharge, sneezing, congestion, and itching, compared to placebo, in a recent double-blind, placebo-controlled research from Turkey. The Study evaluated the effectiveness and tolerability of Spirulina for treating patients with allergic rhinitis. A few examples of how immunity may alter as a result of dietary inadequacies include the production of T cells, the response of secretory IgA antibodies, cytokines, and NK cell activity. [62-64]

2. Conclusion

This review clearly demonstrates Arthrospira platensis pharmacological and therapeutic potential. The presence of various phytoconstituents and secondary metabolites has been linked to a wide range of bioactivity. It is recommended that crude extracts be purified in order to isolate bioactive principles. New medications could be created by fusing the active components extracted from this mangrove with synthetic counterparts. To learn more about how traditional healers use this plant to treat wounds and skin conditions, animal studies are required. Before using the extracts or components from this plant for therapeutic purposes, toxicology research should be done. Superfood status is accorded to Arthrospira platensis due to its high nutritious content. Arthrospira platensis has a wide range of nutrients, including Protein, vitamins, vital fatty acids, amino acids, minerals, and phytonutrients. Arthrospira platensis can be used as a substitute for vitamin supplements due to its high phytonutrient content.

3. References

Tacia G. The Medical Research of Spirulina. Journal of Medical Research. 2004; 13(11): 691-9.

Belay A. The potential application of Spirulina (Arthrospira) as a nutritional and therapeutic supplement in health management J. Am. Nutraceutical Assoc. 2002; 5 27-48.

Ciferri O. Spirulina, the edible microorganism Microbiol. Rev. 1983; 47 4 551.

Chamorro G, Salazar M, Favila L, et al. Pharmacology and toxicology of Spirulina alga Rev. Invest. Clin. 1996; 48 5 389-99.

Bloor, S England, R.R.Antibiotic production by the cyanobacteria Nostoc muscorum. J. Appl. Microbiol. and Biotech. 1989; 1(4):367-372.

Boussiba S, Affalo C. An insight into the future of microalgal biotechnology. Innov Food Technol. 2005; 28:37–39

Colla L M, Furlong E B And Costa J A V. Antioxidant properties of Spirulina (Arthospira) platensis cultivated under different temperatures and nitrogen regimes Braz. Arch. Biol. Technol. 2007; 50 1 161-7

Jeeji Bai N. A taxonomic appraisal of the genera Spirulina and Arthrospira In Mahato AK, Vidyavati (eds) Recent trends in algal taxonomy, vol I, Taxonomical issues. APC Publications PVT LTD, New Delhi, 1999; pp 253

Clement G. A new type of food algae. In: Mateles RJ, Tannenbaum SR (eds) Single-cell protein. Massachusetts Institute of Technology Press, Cambridge. 1968.

Dadheech Pk, Ballot A, Casper P, et al. Phylogenetic relationship and divergence among planktonic strains of Arthrospira (Oscillatoriales, Cyanobacteria) of African, Asian and America origin deduced by16S-23S ITS and phycocyanin operon sequences. Phycologia. 2010; 49(4):361–372

Desikachary Tv, Jeeji Bai N. Taxonomic studies in Spirulina. In: Seshradi CV, Jeeji Bai N (eds) Spirulina ETTA national symposium. MCRC, Madras.1992; pp 12–21

Desikachary Tv, Jeeji Bai N. Taxonomic studies in Spirulina II. The identification of Arthrospira ("Spirulina") strains and natural samples of different geographical origins. Arch Hydrobiol Suppl 116 Algol Stud. 1996; 83:163–168

Ferreira Ls, Rodrigues Ms, ConvertiA, et al. Arthrospira (Spirulina) platensis cultivation in tubular photobiore- actor: use of no-cost CO2 from ethanol fermentation. Appl Energy. 2012; 92:379–385

Fox RD. Spirulina the alga that can end malnutrition. Futurist. 1985; 19:30–35

Gao K, Li P, Watanabe T, HelblingEw. Combined effects of ultraviolet radiation and temperature on morphology, photosynthesis, and DNA of Arthrospira (Spirulina) platensis (Cyanophyta). J Phycol. 2008; 44:777–786

Gershwin Me, Belay A. In: Gershwin ME, Belay A (eds) Spirulina in human nutrition and health. CRC Press/Taylor & Francis Group, Boca Raton. 2018.

Hindek F. Morphology of trichomes in Spirulina fusiformis Voronichin from Lake Bogoria, Kenya. Arch Hydrobiol Suppl 71 Algol Stud. 1985; 38(39):209–218

Iltis A. Tolerance de salinite de Spirulina platensis (Gom.) Geitler, (Cyanophyta) dans les mares natronoes du Kanem (Tchad). Cash ORSTOM, Hydrobiol. 1968; 2:119–125

Carr Ng, Whitton Ba. The biology of cyanobacteria.Blackwell Scientific Publications, Oxford.1982; 688.

Jeeji Bai N, Seshadri Cv. On coiling and uncoiling of trichomes in the genus Spirulina. Arch Hydrobiol Suppl 60 Algol Stud. 1980; 26:32–47

Komærek J, Lund Jwg. What is "Spirulina platensis," in fact? Arch Hydrobiol Suppl 85 Algol Stud. 1990; 58:1–6

Melack JM. Photosynthesis and growth of Spirulina platensis (Cyanophyta). In an equatorial lake (Lake Simbi, Kenya). Limnol Oceanogr. 1979; 24:753–760

Mühling M, Somer Fi Eld Pj, Harris N et al. Phenotypic analysis of Arthrospira (Spirulina) strains (cyanobacteria). Phycologia. 2006; 45(2):148–157

Qiao C, Li Bs, Zeng Zq. Alkaline lakes and Spirulina (Arthrospira) resources in the sandy land of Erdos. J Arid Land Res Environ. 2001; 15(4):86–91

Tomaselli L. Systematic and ecology. In: Vonshak A (ed) Spirulina platensis (Arthrospira): physiology, cell-biology, and biotechnology. Taylor & Francis Ltd, London. 1997; 1–19, 233.

Tomaselli L, Torzillo G, Giovannetti L, et al. Recent research on Spirulina in Italy. Hydrobiologia. 1987; 151(152):79–82

Verma K, Mohanty P. Alterations in the structure of phycobilisomes of the cyanobacterium Spirulina platensis in response to enhanced Na + level. World J Microbiol Biotechnol. 2000; 16:795–798

Vonshak A. Spirulina platensis (Arthrospira): physiology, cell- biology and biotechnology. Taylor & Francis Ltd, London. 1997; 233.

Vonshak A. Spirulina: growth, physiology, and biochemistry. In: Vonshak A (ed) Spirulina platensis (Arthrospira): physiology, cell biology, and biotechnology. Taylor & Francis Ltd, London,1997; 43–65

Vonshak A, Tomaselli L. Arthrospira (Spirulina) Systematics and ecophysiology. In: Whitton BA, Potts M (eds) The ecology of cyanobacteria. Their diversity in time and space. Kluwer Academic Publishers, Dordrecht. 2000; 505–522, 669.

Yaacob, N. S.; Yankuzo, H. M.; Devaraj, S et al. Anti-Tumor Action, Clinical Biochemistry Profile and Phytochemical Constituents of a Pharmacologically Active Fraction of S. crispus in NMU-Induced Rat Mammary Tumour Model. PLoS One. 2015; 10 (5), e0126426

Diniz, A. F. A. De Oliveira Claudino, B. F. et al. Spirulina platensis Consumption Prevents Obesity and Improves the Deleterious Effects on Intestinal Reactivity in Rats Fed a Hypercaloric Diet. Oxid Med Cell Longev. 2021; 3260789.

Li, Y.The Bioactivities of Phycocyanobilin from Spirulina. J Immunol Res. 2022; 4008991.

Marzorati, S.; Schievano, A.; Idà, A et al. Carotenoids, chlorophylls and phycocyanin from Spirulina: supercritical CO2 and water extraction methods for added value products cascade. Green Chemistry. 2020; 22 (1), 187-196.

Li, T. T.; Liu, Y. Y.; Wan, X. Z et al. Regulatory Efficacy of the Polyunsaturated Fatty Acids from Microalgae Spirulina platensis on Lipid Metabolism and Gut Microbiota in High-Fat Diet Rats. Int J Mol Sci. 2018; 19 (10).

Nagaoka, S.; Shimizu, K.; Kaneko, H et al. A novel protein C-phycocyanin plays a crucial role in the hypocholesterolemic action of Spirulina platensis concentrate in rats. J Nutr. 2005; 135 (10), 2425-30.

Torres-Duran, P. V.; Ferreira-Hermosillo, A.; Juarez-Oropeza, M. A.Antihyperlipemic and antihypertensive effects of Spirulina maxima in an open sample of Mexican population: a preliminary report. Lipids Health Dis. 2007; 6, 33

Deng, R.; Chow, T. J. Hypolipidemic, antioxidant, and antiinflammatory activities of microalgae Spirulina. Cardiovasc Ther. 2010; 28 (4), e33-

45.
Li, B.; Chu, X. M.; Xu, Y. J et al. CD59 underlines the antiatherosclerotic effects of C-phycocyanin on mice. Biomed Res Int. 2013; 729413.
Coue, M.; Tesse, A.; Falewee, J et al. Spirulina Liquid Extract Protects against Fibrosis Related to Non-Alcoholic Steatohepatitis and Increases Ursodeoxycholic Acid. Nutrients 2019; 11 (1).
Borowitzka, M. A. Microalgae in Medicine and Human Health. In Microalgae in Health and Disease Prevention, 2018; 195-210.
Negi, H.Gupta, M. Walia, R et al. Medicinal Plants and Natural Products: More Effective and Safer Pharmacological Treatment for the Management of Obesity. Curr Drug Metab. 2021; 22 (12), 918-930.
Trickler D et al. Prevention of experimental oral cancer by extracts of Spirulina-Dunaliella algae. Journal of Nutrition and Cancer. 1988; 11(2): 127-134.
Wu Lc, Ho Ja, Shieh Mc, et al. Antioxidant and antiproliferative activities of Spirulina and Chlorella water extracts. J Agric Food Chem. 2005; 53(10):4207-12.
Shih Cm, Cheng Sn, Wong Cs, et al. Antiinflammatory and antihyperalgesic activity of C-phycocyanin Anesth Analg. 2009; 108(4):1303-10.
Mani UV et al. Studies on the long-term effect of Spirulina supplementation on serum lipid profile and glycated proteins in NIDDM patients. Journal of Nutraceuticals, Functional and Medical Foods. 2000; 2(3): 21–32.
Mathew B et al. Evaluation of chemoprevention of oral cancer with Spirulina fusiformis. Journal of Nutrition and Cancer. 1995; 24(2): 197-202
Newman, D. J. Cragg, G. M. Natural Products as Sources of New Drugs from 1981 to 2014. J Nat Prod. 2016; 79 (3), 629-61.
Ramamoorthy A, Premakumari S. Effect of supplementation of Spirulina on hypercholesterolemic patients. Journal of Food Science and Technology.1996; 33(2): 119–128.
Mao TK et al. Effects of a Spirulina-based dietary supplement on cytokine production from allergic rhinitis patients. Journal of Medicinal Food. 2005; 8(1): 27–30.
Kim HM. et al. Inhibitory effect of mast cell-mediated immediate-type allergic reactions in rats by Spirulina. Journal of Biochemical Pharmacology. 1998; 55(7): 1071-1076.
Yang H. N. et al. Spirulina platensis inhibits anaphylactic reaction. Journal of Life Sciences. 1997; 61(13): 1237-1194.
Dillon JC. et.al. Nutritional value of the alga Spirulina. Journal of Nutrition Diet. 1995; 77: 32-46
Dasgupta T et al. Chemomodulation of carcinogen metabolizing enzymes, antioxidant profiles, and skin and fore-stomach papilloma genesis by Spirulina platensis. Journal of Molecular cell Biochemistry. 2001; 220(1-2): 17-20.
Belay A et al. Current knowledge on potential health benefits of Spirulina. Journal of Applied Phycology. 1993; 5: 235-41.
Mazo VK. et al. Microalgae Spirulina in human nutrition. Journal of National Library of Medicine. 2004; 73(1): 45-53.
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; 131- 158.
Tokusoglu O, Unal Mk. Biomass Nutrient Profiles of Three Microalgae: Spirulina platensis, Chlorella vulgaris, and Isochrisis galbana. Journal of Food Science. 2003; 68 (4): 1144-1148.
Elfar Oa, Billa N, Lim Hr, et al. Advances in delivery methods of Arthrospira platensis (Spirulina) for enhanced therapeutic outcomes. Bioengineered. 2022;13(6):14681-718.
Jiang W, Miao L, Lin Y, Ci L et al. Spirulina (Arthrospira) platensis as a protein source could improve growth, feed utilization, and digestion and physiological status in juvenile blunt snout bream (Megalobrama amblycephala). Aquaculture Reports. 2022 Feb 1;22:100932.
Abdel-Latifah M, El-ashram S, et al. The effectiveness of Arthrospira platensis and microalgae in relieving stressful conditions affecting finfish and shellfish species: An overview. Aquaculture Reports. 2022;24:101135.
Zanolla V, Biondi N, Niccolai A, et al. Protein, phycocyanin, and polysaccharide production by Arthrospira platensis grown with LED light in annular photobioreactors. Journal of Applied Phycology. 2022;34(3):1189-99.
Ghanbarzadeh M, Moazami N, Shahavi MH, et al. Study of bioactive compounds in Arthrospira platensis MGH-1 fortified with iron and zinc micronutrients, and manganese. Journal of Applied Phycology. 2022; 2:1-4.
Chee kuankwei et al. Elucidation and isolation of specific bioactive compound in cyanobacteria isolates. 2012.