



Therapeutic and Nutritional Potential of Spirulina in Combating Covid-19 Infection

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Abstract

Human history has witnessed various pandemics throughout, and these cause disastrous effects on human health and country's economy. Once again, after SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome), the world is observing a very tough time fighting an invisible enemy, the novel COVID-19 coronavirus. Initially observed in the Wuhan province of China, now, it has spread across 210 countries. Number of corona affected confirmed cases have reached > 3 million globally and death toll has reached to 258,481 as on 6th May, 2020. Researchers are working round the clock, forming collaborative efforts and sharing their data to come up with a cure for this disease. The new coronavirus genome was quickly sequenced, and clinical and epidemiological data are continuously being collected and analyzed. This data is crucial for forming better public health policies and developing antiviral drugs and vaccines. As there is no vaccine available in market against COVID-19, personal health, immunity, social distancing and basic protection measures are extremely important. It is critical to avoid the virus infection and to strengthen the immune system as the coronavirus can be fatal for those with weak immunity. This article reviews the nutritional and therapeutic potential of *Spirulina*, which is considered as superfood and a natural supplement to strengthen the immune system. *Spirulina* is highly nutritious and has hypolipidemic, hypoglycemic and antihypertensive properties. *Spirulina* contains several bioactive compounds, such as phenols, phycobiliproteins and sulphated polysaccharides and many more with proven antioxidant, anti-inflammatory and immunostimulant/ immunomodulatory effects.

Keywords: anti-inflammatory, antioxidant, antiviral, COVID -19, polysaccharides, *Spirulina*

Introduction

Currently, SARS-CoV-2 or COVID-19, the causative pathogen of Coronavirus Disease is rapidly spreading across the world. The virus is zoonotic in origin and was transmitted to humans through yet unknown intermediary animals (Zhou et al. 2020). Coronavirus disease spreads primarily through contact with an infected person when they cough or sneeze (WHO 2020). It also spreads when a person touches a contaminated surface or object and subsequently touches eyes, nose, or mouth. The disease causes respiratory illness with flu like symptoms such as a cough, cold, fever and difficulty in breathing. Many people can be asymptomatic carrier of this disease spreading infections in the society. Globally, the reported fatality rate is in range of 3.8 to 4% as on 30th July, 2020 (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>). Most common diagnostics methods at present are RT-PCR test and antibody testing. However, for early detection serological tests kits are also being developed. To date, there is no fool proof vaccine have been developed against this disease. Therefore, alternate approaches are in practice to prevent transmission of COVID 19 such as, hand sanitization using alcohol-based hand rubs, washing hands with soap at least for 20 seconds, use of face masks and face shields by health workers, social distancing, home quarantine etc. As there is no vaccine and definitive treatment available so far, many experts recommend alternative protection measures in form of strengthening the immune system by consuming immunity boosting food/drinks and taking essential vitamins such as Vitamin A, B, C to improve general health (<https://www.mohfw.gov.in/pdf/ImmunityBoostingAYUSHAdvisory.pdf>). Amongst various immunity boosters prescribed by experts, *Spirulina*, which is a type of seaweed, is the most mentioned as an effective natural immunity enhancer for prevention of any potential infections (Belay 2002). This filamentous alga occurs naturally in tropical and subtropical lakes with high pH (Habib et al. 2008). *Spirulina* is currently being produced in more than 22 countries and used in over 77 countries (Sasson 1997). Its nutritional relevance is underlined by its adoption by the UN as the food of the future and by its use by NASA as part of its Astronauts' diet. *Spirulina* is described as a "Super food" (Tadros and Normal 1988; Kelly et al. 2011). This filamentous alga has been used as a source of protein and vitamin supplement in humans without any significant side-effects since long time (Admassu et al. 2015; FDA, 2003). *Spirulina* has a high protein content ranging up to 70%, it also contains several vitamins, like B12, provitamin A (β -carotenes), and minerals such as iron (Ciferri 1985; Sánchez et al. 2003; Habib et al. 2008). It is also rich in phenolic acids, tocopherols and γ -linolenic acid (Dillon et al. 1995). As *Spirulina* lacks cellulose in their cell walls, it can be easily digested (Dillon et al. 1995). Parry's *Spirulina* is the only organic *Spirulina* in the world awarded with GRAS (Generally Recognized as Safe) status by United States Food and Drug

Administration (USFDA) (Tarantino 2003; Salazar et al. 1996; Chamorro et al. 1997; Salazar et al. 1998; Belay 2002; Parry 2014). This blue-green filamentous alga is relatively easy to cultivate but flourishes mainly in large outdoor ponds under optimum sunlight, pH and nutrient conditions. Currently, *Spirulina* can be found in health food stores and is sold mainly as a dietary supplement in the form of health drinks, protein bars, capsules and tablets (Spolaore et al.2006). The aim of this review is to summarize the potential nutritional and therapeutic applications of *Spirulina* on human health in the context with current pandemic situation globally.

Historical Background of *Spirulina*

The term *Spirulina* remains in use is because of historical reasons (Vonshak 1997). In sixteenth century, *S. platensis* was first isolated from Lake Texcoco by the Aztecs and they devised the term “tecuitlatl” for *Spirulina* (Habib et al. 2011). Later, Dangeard befell upon the anembu tribe which had been harvesting the filamentous algae from Lake Chad in Africa (Abdulqader 2000). In 1940s he coined the name “dihe” for *S. platensis* which had been used extensively in many food products such as bread, meals, and cakes. In 1964, *Spirulina* was analyzed chemically and taken up for research studies by botanists, microbiologists, and scientists to explore its biotechnological potential (Zarrouk 1966; Vonshak 1997; Siva Kiran 2015). *Spirulina*, a blue green alga refers to the dried biomass of *Arthrospira platensis* (Gershwin, and Belay 2007). The two species of *Arthrospira* were classified as *A. maxima* and *A. platensis* in the genus *Spirulina*. It belongs to photosynthetic bacteria that cover the groups Cyanobacteria and Prochlorophyta. Scientifically, there is a distinction exists between *Spirulina* and the genus *Arthrospira*. *Arthrospira* species are free-floating, autotrophic, filamentous cyanobacteria characterized by multicellular and cylindrical trichome in an open left-handed helix. Naturally, these are habitants of tropical and subtropical lakes, show proliferative growth in in presence of high pH and high carbonate and bicarbonate concentrations (Habib et al. 2008; Sili et al. 2012). *A. platensis* is generally found in Africa, Asia, and South America, whereas *A. maxima* is confined to Central America (Vonshak, 1997). Mostly, open raceway ponds with paddle wheels are being used for commercial production of *Spirulina* (Habib et al. 2008).

Nutritional and Therapeutic Properties of *Spirulina*

Spirulina is blue green microalgae, which is one of the oldest life forms on Earth (Ciferri 1985). It is partly responsible for producing the oxygen in the planet's atmosphere billions of years ago and supported origin of life on earth. *Spirulina* is declared world's first superfood, which has a diverse nutritional composition (Kelly et al. 2011). The protein content of *Spirulina* is in range of 55 to 70% protein which is more than or equivalent to beef, chicken, and soybeans. It is also found to be a rich source of essential and non-essential amino acids, gamma-linolenic acid (GLA), carotenoids, linoleic acid, arachidonic acid, vitamins, iron, calcium, phosphorus, nucleic acids RNA & DNA, chlorophyll, and phycocyanin (Henrikson 1994; Belay 1997; Patel et al. 2006; Parry 2014). *Spirulina* offers a wide range of health benefits almost immediately upon ingestion as it lacks cellulose in cell wall. It offers an instantaneous boost to one's energy and helps in improving the endurance and in reducing fatigue (Baicus and Baicus 2007). It is a natural immunity booster, and provides excellent support for the heart, liver, and kidneys. *Spirulina* is a natural detoxifier, oxygenates blood, and help in removal of body toxins, thus reducing the chances of illness (Stahl and Sied 2005; Chew and Park 2004). Being a natural appetite suppressant, it also improves digestive system. Babadzhanov et al. (2004) in their study reported *Spirulina* having strong antioxidant as well as anti-inflammatory properties (Babadzhanov et al. 2004). It helps in maintaining the pH balance of the body, thereby reducing inflammation throughout the body without any side effects (Stahl and Sied 2005; Chew and Park 2004; Rabadiya and Patel 2010). Therapeutic compounds present in *Spirulina* and their proven beneficial effects on human health have been presented in table 1.

Bioactive Compounds in <i>Spirulina</i>			
Sr. No.	Name of compound	Properties	References
1	Ca-Sp (Calcium-Spirulan)	Immunity enhancer, Anticancer	Cheng-Wu et al. 1994; Hayashi et al. 1996a; Hayashi et al. 1996b
		Antiviral Induces haematopoiesis	
2	Sulpholipids	Antiviral	Gustafson 1989
3	Beta-carotene	Source of Vitamin A, Anticancer, Antioxidant	Kapoor and Mehta 1993
4	Cyanovirin-N	Antiviral	Ozdemir et al. 2004
5	GLA (Gamma Linolenic Acid)	Treatment of Arthritis, Anticancer, Fat-metabolism	Nichols and Wood 1986
6	Vitamin-E	Antioxidant	Khan et al. 2005
7	Phycocyanin	Antioxidant, Anticancer	Reddy et al. 2003
		Immunity booster, Detoxifier	Cheng-Wu et al. 1994; Patel 2006; Chen et al. 2012
		Antiviral, Induces Haematopoiesis	

Table 1: Therapeutically important compounds in *Spirulina* and their applications

Antiviral Properties

Researchers from National Cancer Institute (NCI), USA studied potential antiviral compounds extracts from blue green algae, including *Spirulina platensis*. The NCI research group found 60 various cyanobacteria culture to have the bioactive substances that caused significant antiviral effect by reducing cytopathic effects induced by viral infections (Patterson et al. 1993). Acidic polysaccharides from *Spirulina* such as calcium spirulan (Ca-SP) are the potent virus inhibitors against several enveloped viruses (Hayashi et al. 1996). Highest antiviral activity was detected in *S. maxima* extracts prepared from methanol-water (3:1) (Hernández-Corona et al. 2002). The extracts of cyanobacteria in methanol contain sulfated polysaccharides which significantly prevents virus attachment to host cell. The inhibition of the fusion between uninfected CD4+ lymphocytes greatly enhances antiviral activity as this makes virus unable to take over host machinery. This stops the viral reproduction and multiplication (Feldmann et al. 1999; Singh et al. 2011). The extract does not kill the virus but interferes with the virus entry into host cells (Hayashi et al. 1993). However, methanol (MeOH) and water extracts of *Spirulina plantensis* were significantly effective against adenovirus type 40 and reduces the infection 50% and 23% respectively. The nontoxic concentrations for all the extracts were 2 mg/ml (Sayda et al. 2012). The calcium spirulan (Ca-Sp) a sulfated polysaccharide isolated from *Spirulina platensis* inhibits many virus replications and exhibits broad-spectrum antiviral activity against the HSV-1, influenza virus, Human cytomegalovirus (HCMV), mumps virus, measles virus and human immunodeficiency virus type 1 (HIV-1, HIV-2, and other series of enveloped viruses (Hayashi et al. 1996; Simpure et al. 2005; Feldmann et al. 1999; Singh et al. 2011). The inhibition of entry of Dengue virus by carbohydrate inhibitors was studied by Kazuya et al. (2013). The study made by Gorobets et al. (2002) showed that the addition of *S. platensis* on bacteriophage T4 (bacterial virus) produced an inhibiting effect on the reproduction of the bacteriophage in *Escherichia coli* B cells. The purified pigment allophycocyanin of *Spirulina platensis* also exhibits antiviral activity and it neutralizes the cytopathic effects induced by *Enterovirus 71*. The allophycocyanin pigment protein basically delays viral RNA synthesis and activates apoptosis in both human rhabdomyosarcoma cells and Afrin green monkey kidney cells (Shih et al. 2003).

Immunostimulant

S. platensis which is primarily used as a dietary supplement, now had been reported to exhibit several therapeutic properties such as immune-stimulating and antiviral activities. It had been found to activate macrophages, NK cells, T-cells, B-cells, and to induce the production of interferon gamma and other cytokines (Khan et.al.,2005; Simpore et al. 2005; Theodore et al. 2013). Natural substances isolated from *S. platensis* had been found to be effective inhibitors against several enveloped viruses by blocking viral absorption penetration and some replication stages of progeny viruses after penetration into cells (Weid, 2000).

Immunomodulatory and Anti-allergic

In several research studies, *Spirulina* has been reported to exhibit anti-inflammatory properties by preventing the release of histamine from mast cells (Chirasuwan et al. 2007 & 2009). In a recent randomized, clinical, double-blind placebo-controlled trial (Cleaveland et al. 2001), individuals diagnosed with allergic rhinitis were fed daily basis, either with placebo or *Spirulina* for 12 weeks. Samples of peripheral blood mononuclear cells were isolated before and after the *Spirulina* feeding and levels of cytokines (interleukin-4 (IL-4), interferon- γ (IFN- γ) and interleukin-2), which are important in regulating immunoglobulin (Ig)E-mediated allergy, were measured. The study reported that an optimum dose of *Spirulina* considerably reduced IL-4 levels by 32%, demonstrating the protective effects of this microalga toward allergic rhinitis. Ishii et al. (1999) studied the influence of *Spirulina* on immunoglobulins IgA levels in human saliva and confirmed that it enhances IgA production, suggesting a pivotal role of microalga in mucosal immunity. It is well understood and proven with many research studies that deficiency of nutrients is responsible for many significant changes in immunity, which establishes as changes in production of T-cells, secretory IgA antibody response, cytokines and NK-cell activity. The studies also suggest that nutritional properties *Spirulina* may modulate the immune system by covering nutritional deficiencies.

Anti-Inflammatory

Various research studies reported that free bilirubin functions physiologically as a potent inhibitor of NADPH oxidase activity. Similarly, phycocyanin (PC), a blue green pigment protein found in *Spirulina*, also reported to be a potent inhibitor of this enzyme complex. This protein has been observed to reduce rapidly in phycocyanorubin, in mammals which is a close homolog of bilirubin (Helliwell 2011). Phycocyanin extracted from *Spirulina* can be administered orally as an anti-inflammatory agent. The easiest and most economical way to administer phycocyanin is intake of whole *Spirulina* in either in form of tablets or capsules. (McCarty 2007).

Antioxidant

Antioxidants are compounds that help to fight cell and DNA damage that leads to cancer, heart disease and other chronic diseases. Some antioxidants are synthesised by body and others are present in form of different foods whose intake is through diet. C-phycoyanin (C-PC) is one of the most important biliproteins of *Spirulina* with antioxidant and free radical scavenging properties. C-PC, a selective cyclooxygenase-2 inhibitor, induces apoptosis in lipopolysaccharide-stimulated RAW 264.7 macrophages (Reddy et al. 2003). It is also known to have anti-inflammatory and anticancer properties (Hayashi et al. 1993). Though, till date, there are no in vivo studies been done on human beings to understand the antioxidant effects of *Spirulina*.

Hepatoprotective

Spirulina has a great hepatoprotective potential due to its composition. The natural antioxidant compounds present in *Spirulina* like vitamins (E and C), minerals, phenolic compounds and some fatty acids may act individually or together provide protection and strengthen the liver functions (Garcia-Martinez et al. 2007). Intraperitoneal administration of C-phycoyanin of *Spirulina platensis* was found successful in reduction of lipid peroxidation in the liver microsomes in CCl₄-intoxicated rats (Bhat and Madyastha, 2000). Role of *Spirulina* in preventing the chronic hepatitis from being transformed to hepatic cirrhosis was well described by Gorban et al. (2000). In histopathological studies, the efficacy of *Spirulina fusiformis* was found very promising. Upon administration of optimised dosages of *Spirulina* extracts regeneration of hepatocytes was reported. The hepatoprotective property of the extract may be attributed to the presence of various bioactive constituents which are present in *Spirulina fusiformis* (Mathew et al. 1995). To get a clear understanding on mechanism of action of *Spirulina* in liver protection extensive research is required (Sharma and Dunkwal, 2012).

Conclusions

Several research studies recommended that *Spirulina* can be a potential and ideal candidate for conjugative or alternate therapy against disease treatments due to possible synergetic effect of many bioactive compounds present in the whole cell. It has been demonstrated that the use of *Spirulina* and its extracts may significantly reduce cancer and viral diseases. Though, more research is needed to determine the usefulness of *Spirulina* against COVID 19 like killer diseases. Scientists across the world and primarily in India, China, Japan, USA are studying this extraordinary superfood to unlock its full potential. However, it is clear from published research and in vivo clinical

studies that *Spirulina* is safe natural superfood to be consumed for ideal health and wellness. The multifunctional role of *Spirulina* components makes it an ideal natural remedy with massive prophylactic and therapeutic properties.

“Let your food be your medicine”. Hippocrates

Acknowledgments

Sincere thanks to Reliance Industries Limited for funding and fellow colleagues for their valuable inputs and help in writing the manuscript.

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