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

1 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, P. 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 6.8 to 7% as on May 5, 2020 (WHO Situation Report-106; Max, R 2020). 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. (MOHFW, 2020). 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, A., 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, A., 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, M.G. and Normal, A.I., 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, H. 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, O.,1985; Sánchez, M., et.al., 2003; Habib, M.A.B., 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 E.I.D., 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, P., 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.

2 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 M. et.al., 2011). Later, Dangeard befell upon the anembu tribe which had been harvesting the filamentous algae from Lake Chad in Africa (Abdulqader, G., 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, C., 1966; Vonshak. A., 1997; Siva Kiran, R.R., 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 trichrome in an open left-handed helix. Naurally, 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 C., 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).

3 Nutritional and Therapeutic Properties of *Spirulina*

Spirulina is blue green microalgae, which is one of the oldest life forms on Earth (Ciferri, O.,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, R..,1994; Belay, A., 1997; Patel A., et.al.,2006; Parry E.I.D., 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, C. and Baicus, A., 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, W. and Sıed, H., 2005; Chew, B.P. and Park, J.S., 2004). Being a natural appetite suppressant it also improves digestive system. Babadzhanov et.al., in their study reported Spirulina having strong antioxidant as well as anti-inflammatory properties (Babadzhanov, A.S.et.al.,2004). It helps in maintaining the pH balance of the body, thereby reducing inflammation throughout the body without any side effects (Stahl, W. and Sıed, H.,2005; Chew, B.P. and Park, J.S., 2004; Rabadiya, B. and Patel, P., 2010). Therapeutic compounds present in *Spirulina* and their proven beneficial effects on human health have been presented in table 1.

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

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

3.1 Antiviral Properties

In many research studies, *Spirulina* has been reported to have strong antiviral activities. It is established in various reports that at low dosages *Spirulina* results in inhibition in viral replication however, at higher concentrations it completely results in blocking replication (Hayashi, K., et.al.,1993; Hayashi, K., et.al.,1996a). In case of herpes simplex virus Type-1 (HSV-1), a water based extract of *Spirulina* has been found effective in inhibiting viral cell-penetration and replication in a dose-dependent manner (Hayashi, K., et.al.,1993; Hayashi, K., et.al.,1996b, Hernández-Corona, A., et.al., 2002). The *Spirulina* extract, without suppressing host cell functions, inhibits viral protein synthesis. The antiviral activity of *Spirulina* is attributed

to calcium –spirulan (Ca-Sp), which has been shown to inhibit replication of many viruses by inhibition of viral penetration into target cells without host toxicity (Deng et. al., 2011; Deng and Chow, 2010; Falquet, 1997; Rhoades et. al., 1992). 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, T., 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 K., 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 (HVMV), mumps virus, measles virus and human immunodeficiency virus type 1 (HIV-1, HIV-2, and other series of enveloped viruses (Hayashi K., et. al., 1996; Simpore 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).

3.2 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, G., 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).

3.3 Immunomodulatory and Anti-allergic

Spirulina exhibits 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.

3.4 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).

3.5 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-phycocyanin (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, M.C., et.al.,2003). It is also known to have anti-inflammatory and anticancer properties (Hayashi K, et. al., 1993). Though, till date, there are no in vivo studies been done on human beings to understand the antioxidant effects of *Spirulina.*

3.6 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-phycocyanin 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).

4 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 pretty 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

5 Declarations

5.1 Acknowledgments

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5.2 Authors Contribution

All authors equally contributed in the work which is reported in the present manuscript. Before publication of this manuscript all the authors sincerely agreed with the terms and conditions of *AIJR Preprints*.

5.3 Competing Interests

The authors declared that there is no conflict of interest exist in the publication.

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