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Spirulina: A Miraculous alga with Pharmaco-nutraceutical Potential as Future Food

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Abstract

Current projections indicate that the world is not on track to accomplish the global nutrition targets, because the Global Nutrition Report says malnutrition in every country on earth. In order to address this malnutrition issue, spirulina can be a better choice as a supplement diet that also fulfills India's protein consumption gap. Spirulina is microalgae that thrive in saline water and gained popularity as one of the "superfoods" due to a range of nutrient content such as proteins, minerals, carbohydrates, and many phytopigments. Medicinal use of the algae has been also mentioned in some ancient texts and formulations of Ayurveda. It is highly sought after in the food industry for coloration and food fortification purposes. The current review aims to provide a pharmaco-nutraceutical approach with all the information on its various characteristics such as nutraceuticals, cosmeceuticals, and pharmacological importance including possible advantages of Spirulina's potential to enhance healthcare.

Keywords: (a18) Algae; Microalgae; Bioactivity; Nutritional; Pharmacological activity; Spirulina; Superfood

Key Messages: As befits a Journal devoted to food, nutrition & dietetics information, for well being and is committed to improving quality of life. This article provides a bag of information for researchers & Health professionals, about Spirulina's high content of macro-micronutrients, and active compounds with their pharmacological properties. As proven by its long history of food uses and recent scientific findings, spirulina is considered safe for human consumption and also considered a future meal to combat malnutrition.

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INTRODUCTION

Nutritional deficiency is increasing in the world becomes a major challenge for mankind. This concern has led to an increase in the popularity of alternative, unconventional aquaculture diets, which include spirulina as a source of protein, vitamins, and minerals supplements. Spirulina is multicellular, photosynthetic prokaryote, filamentous blue-green algae, that prefers to grow in an alkaline aquatic ecosystem. It is one of the first photosynthetic creatures in nature, able to use light

directly for intricate metabolic processes.[1] It has a long history as a dietary supplement. As more and more health conscious consumers and researchers consistently appreciate its exceptional nutritional features and pharmacological characteristics, its popularity is growing on a global scale today. Interestingly, the UF/IFAS from NASA Settles an experiment for the suitability to grow Spirulina in space in 2021 as a bountiful and nutritious food crop for astronauts on long-term space missions and they found that Spirulina behaves in space exactly as it does on Earth.[2]

History of Spirulina

The nutrition from diet plays a major part in Ayurveda since it nourishes the mind, body, and spirit. Therefore, Ayurveda texts (Sanhitas & Nighantu) have been found about to uses of algae, mentioned as Jalmastu or Shaivaal (type spirulina). It is also used in ancient formulations by owing astringent, bitter, sweet, antipyretic, and digestive characteristics (Bhavprash & Dhanvantari Nighantu). Thus, Spirulina has been consumed as food for ages by various populations and has only recently been rediscovered. It was eaten by the Mayas, Toltecs, and Kanembu in Mexico during the Aztec civilization as early as over 400 years ago. Spirulina from Lake Texcoco was collected, dried, and made into a cake for consumption called "Diha" or "Die".[3] In Central Africa, the Chadians (Chad residents) have been consuming spirulina for millennia. When spirulina from Lake Kossorom (Chat) is harvested, it is also sold on the market and used to produce cakes or broths for meals. Moreover, it was also found by French researchers in Lake, trait within the 1960s, it is used as a daily food source after the 16th century. Early in the 1970s, the first large scale production was facilitated, garnering interest on a global scale. Millions of people across the world consume it today, and exploring more in addition to its nutritional worth. Surprisingly, it appears to have discovered a niche in Indian cuisine.[4,5]

Scientific Description

A genus of blue-green algae in the Oscillatoriaceae family is called Spirulina. Blue-green algae are among the most primitive life forms on earth with their cellular structure as a simple prokaryote and have the ability to do photosynthesis like a plant. However, they share features with primitive bacteria because they lack a plant cell wall. Spirulina, the name comes from a Latin word meaning tiny spiral. It is microscopic, spiral shaped, which belongs to photosynthetic bacteria that cover the groups Cyanobacteria and Prochlorophyta. Spirulina as a cyanobacteria typically carries out oxygenic photosynthesis with water as an electron donor and uses carbon dioxide as a carbon source. Spirulina is filamentous, helicoidal trichomes, performs oxygenic photosynthesis, and reproduces by binary fission. It is especially found in tropical and subtropical areas, which have warm bodies of water with high carbonate/bicarbonate concentration, increased pH, and salinity, that are ideal for its growth. Additionally, it can be found in soil, brackish water, freshwater, lakes, marshes, ponds, seawater, and thermal springs.[1] Spirulina grows best in water that is alkaline, salty (>30 g/L), high in pH (8.5-11.0), and temperature between 30 to 35°C, where there is a lot of solar radiation at altitude. Since spirulina is an obligate photoautotroph, it cannot thrive on substrates containing organic carbon molecules in the dark. It mostly assimilates nitrates and decreases carbon dioxide in the presence of light. Spirulina is an obligate photoautotroph thus it cannot grow in the dark on media containing organic carbon compounds. Among the different species of Spirulina genus, mainly two species i.e. *Spirulina platensis (Arthrospira platensis), Spirulina maxima (Arthrospira maxima),* are the most intensively investigated as edible with high nutritional as well as potential therapeutic values. Spirulina refers to the dried biomass of *S. platensis*, occurs in Africa, Asia, and South America, whereas *Arthrospira maxima* are confined to Central America.[6,5] In India, Spirulina cultivation is now being most popular.

Spirulina as a Food Source

The diet or "Aahar" has a specific significance in human health as a way of the good life, health, and well being, according to Ayurveda doctrine. As per Ayurveda texts, the diet known as Mahabhaisjaya, this Sanskrit term that merits consideration for "medicine," refers to the substances that have the ability to have healthy effects on the body, therefore a diet is believed to have health effects beyond just satisfying hunger. Acharya Charak argued that a diet should be followed in order to prevent sickness from developing and to provide the body with the essential nutrients it needs.[7] That's why the idea that prevention is preferable to cure has long been promoted in India. The conclusion is "*Tat cha nityam prayunjeet svasthyam yen anuvartate, Ajaatanam vikaranam anuttpattikaram cha yat.*" (5th Sutra Sthana in Charaka Samhita). This scripture also supported the above Acharya Charaka theory. Another verse reads, "*Pathye sati gadaartasya*

kim aushadh nishevane." Gadaartasya pathye kim aushadh nishevane, which emphasizes the value of a healthy diet. According to this phrase, if whole some food is consumed in a planned manner, there is no need to administer medications. because, in the absence of a healthy diet, this will not be able to cure the sickness.[8]

Based on these principles, a promising nutritional supplement for improving meals is spirulina due to its great supply of proteins, vitamins, minerals, -carotene, fatty acids, and other essential nutrients, making it an ideal food & fodder.[9] It has also an advantage for food security because it can generate protein and energy with less land and water than animals. Spirulina's body has a weak cell wall and a smooth texture, which facilitates easy digestion. Moreover, a protein known as Phycocyanin is a pigment binding, light harvesting pigment obtained from the *S. platensis*, and used extensively as a colorant, food additive, fluorescent dye, cosmetics, and medication.[10,11] Spirulina is consumed in tablet and powder form, and it tastes like grass. Its powder is an extremely adaptable ingredient that may be used in anything that can think of, such as smoothies, baked goods, omelets, and muffins.[12] Likewise, to fortify green tea powder qualities, a mixture of tea and microalgae provide all the essential nutrients.

According to NASA, one kilogram of Spirulina has an equivalent nutritional value to 1,000 kilograms of fruits and vegetables. Scientists in Spain & Japan demonstrated that spirulina extract contains this phycocyanin is a potent water soluble antioxidant. Because of its ecologically sustainable and nutrient rich dietary supplement qualities, spirulina rose to fame after NASA utilized it effectively as a food supplement for astronauts on space missions. Spirulina is being researched as a possible solution for long duration space missions as well as food security and hunger issues. Additionally, it is successfully employed in the fight against malnutrition by WHO, UNICEF, and many African governments. Spirulina has recently been included in the Odisha State Government's Child Nutrition Program in India. Because it is nutrient dense and associated with numerous health advantages, it is regarded as a superfood.

Industrial Application of Spirulina

By industrial application, different varieties of this microalgae (spirulina) are commercially utilized in a variety of industries, including nutraceuticals, food & beverage production, animal feed, cosmetics, perfumery, and agriculture. Moreover, Spirulina is formulated as pharmaceutical products like powder, tablet, capsules, liquid, granules, and gelling agents, etc. Likewise, it is extensively used in the food, beverage, and cosmetic or personal care industries, because it is a huge source of natural edible dye (pigments) that give products their blue colour and can be blended with other colours to create unique new hues. For the production of finished goods, carotenoids, lipids, algal proteins, hydrocolloids, and others are beneficial and in great demand. Therefore, the main factors driving market expansion are a surge in demand for natural ingredients and R & D investments in commercial spirulina products. The government's promotion of spirulina production also promotes market expansion. The initiatives/programs of the Government and/or NGOs to combat malnutrition in undeveloped areas. Further, the global Spirulina market was estimated to be valued at $393.6 million in 2019 and is expected to grow to $897.61 million by 2027 at a CAGR of 10.5%. The major market players by geography are the nations of North America, Europe, Asia-Pacific, and LAMEA. According to Data Bridge Market Research, in the projection period of 2022–2028, the spirulina powder market is projected to increase at a CAGR of 7.90%, from a value of USD 1024.91 million in 2021 to reach USD 1883.03 million by 2029.[13,4,14]

Nutritional value of Spirulina

Nutraceuticals are edibles or food additives that provide supplements to regulate biological functions of living, categorized into nutrients, herbals, dietary supplements, and dietary fibers. Spirulina is nature’s gift as a superfood to mankind and is long held as a highly nutritious food for some decades. The World Health Organization referred to spirulina as "a very suitable food" in 1974 and described it as an interesting food for multiple reasons, is high in protein & iron, and can be given to children without any harm. *Spirulina platensis* has received increasing attention due to its rich source of macro and micronutrients including high quality protein demonstrated by its 70% content and the inclusion of minerals, vitamins, amino acids, and important fatty acids, among other nutrients.[9] So, this rich biomass as well as its primary or secondary metabolites produced by it can be employed as feed and food additives in many industries, science, and medicine.[15] Further, *Spirulina platensis* is the ultimate source for the production of SCP (Single cell protein) and plant based protein. Dried spirulina comprises (see Fig. 1 & Table 1) 60-76% protein, 6-24% carbs, and 4-24% fat, according to the USDA Food Composition Database.[9] It’s a complete

protein source meaning it has all the essential & non-essential amino acids, and essential fatty acids like Alpha-linoleic acid, Gamma-linoleic acid, stearidonic acid, eicosapentaenoic acid arachidonic acid In accordance with the Recommended Dietary Allowance (RDA) one tablespoon of spirulina has Omega-3 and Omega-6 fatty acids, vitamins B1 (thiamin, 11% of RDA), copper (21% RDA), B2 (riboflavin, 15% of RDA), and B3 (niacin, 4% of RDA), iron (11% of RDA), manganese (Mn), potassium (K), and magnesium (Mg). Moreover, simple sugars like glucose, fructose, and sucrose are also minutely present, along with polyols like glycerol, mannitol, and sorbitol.[16]

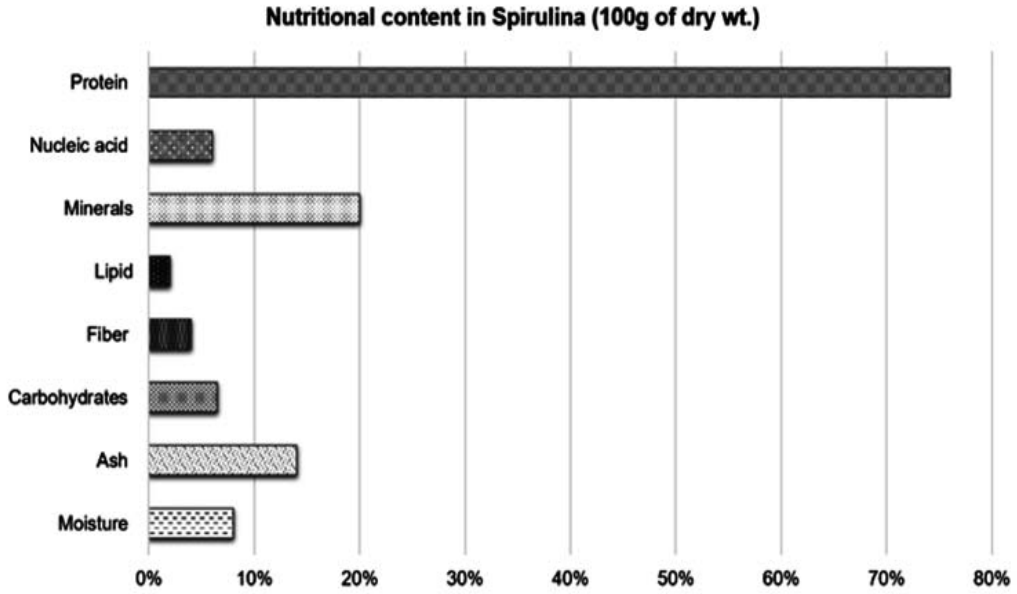

Fig. 1: Chemical composition of Spirulina (100g of dry wt.).

Table 1: Nutritional composition of Spirulina (powder dried weight)

Vitamins Component Content (per 1g dry wt.)		**Minerals Content (per 1g dry wt.)**	
Vitamin B1 (Thiamine)	48 µg	Phycocyanin	180 mg
Vitamin B2 (riboflavin)	55 µg	Chlorophyll	11 mg
Vitamin B3 (Niacin)	0.15 mg	Carotenoids	6 mg
Vitamin B6 (Pyridoxine)	8 µg	Zeaxanthin	1.01 mg
Vitamin B12 (Cyanocobalamin)	2 µg	**Pigments**	
Tocopherol (Vitamin E)	0.41 mg	Phycocyanin	180 mg
Vitamin A (***source*** Beta-carotene)	55 µg	Chlorophyll	11 mg
Pantothenic acid	0.71 mg	Carotenoids	6 mg
Biotin, Folic acid	0.55 mg	**Total carbohydrate content per 100g**	
Inositol acid	0.7mg	Dietary fiber	7.7 gram
Bioflavonoids	10 mg	Sugars	1.3 gram
Vitamin K	2.2 µg	Lactose	< 0.1 gram
Minerals (per 1g dry wt.)		**Essential amino acids (mg/100 g)**	
Potassium (K)	16 mg	Histidine	1000
Calcium (Ca)	15 mg	Isoleucine	3500

table cont...

Phosphorus (P)	10 mg	Leucine	5380
Manganese (Mn)	3 mg	Lysine	2960
Zinc (Zn)	70 mg	Methionine	1170
Magnesium (Mg)	3.7 mg	Phenylalanine	2750
Sodium (Na)	2.5 mg	Threonine	2860
Iron (Fe)	1.7 mg	Tryptophan	1090
Iodine	3.9 mg	Valine	3940

Abbreviations: µg-Micro gram; mg-Milligram; wt.-Weight

Health benefits

As a super food due to its nutrient rich profile, it improves muscle strength & endurance and boosts brain energy as it increases Ribonucleic acid. Scientific studies revealed its capacity of lowering blood sugar levels. Spirulina improves digestive system health. It is good for the heart as it can lower LDL and triglyceride levels as well as inhibition of LDL cholesterol levels in serum.[17,18] Spirulina contains β-carotene as a vitamin A source, important in preventing eye diseases, while iron and vitamin B12 of this useful in treating hypoferric anemia and pernicious anemia. It is effective in the treatment of atopic child eczema therapy because it contains γ-linolenic acid, additionally used in premenstrual syndrome and in immune system stimulation as well as anti-allergic effects by inhibiting the release of histamine.[19] Spirulina was found to be beneficial for eyesight by increasing the serum zeaxanthin level and inhibiting corneal neovascularization. Thus spirulina is a reservoir of active secondary metabolites revealing positive effects against different ailments such as diabetes, hyperlipidemia, inflammatory allergic reactions, metal/chemical induced toxicity, malnutrition, obesity, and anemia. Moreover, a paste of Spirulina is utilized as a face pack, due to its anti-aging characteristics.[20,15]

Pharmacological Activity & their Mechanism

A range of Spirulina derived natural compounds have been shown to portray crucial biological functions, revealed from numerous *in vitro and in vivo* studies. This has been accomplished through the use of phytochemical compounds and their bioactivity in drug discovery. The different pharmacological properties of *S. platensis* are critically summarized (see Table 2), which are adapted from a number of cited Scientific Journals.

Table 2: Pharmacological potential & mechanism of Spirulina

Properties	Study Type	Mechanism
Anti-anemic activity	*In vivo* *Clinical*	By elevating Hb level and RBC count in Pb and Cd induced anemia of rats.[21] Moreover, by raising the level of mean capsular hemoglobin (MCH), corpuscular volume (MCV), and MCHC) in rabbits. It ameliorates anemia in subjects.[22]
Antibacterial activity	*In vitro*	A predominant fatty acid compound from the extract inhibited Staphylococcus aureus MTCC-96, and Salmonella *typhimurium* MTCC-98.[23] Similar activity was observed against human food borne pathogens.[24]
Anti-cancer effects	*In vivo*	The C-phycocyanin pigment from Spirulina was found to be a selective inhibitor against cyclooxygenase-2 (Cox-1), Cox-2, and MCF-7 human breast cancer cells.[15]
	In vitro	Additionally, it enhanced the cell nucleus enzyme activity, apoptosis enzymes, DNA repair synthesis, and inhibited the growth of human colon & hepatocellular carcinoma cells (HCC), proliferations etc.[20]
Anti-diabetic/ Hypoglycemic properties	*In vivo* *Clinical*	It increased in concentrations of active cretin hormones, glucagon like peptide1, and glucose dependent insulinotropic polypeptide against streptozocin induced diabetic rats.[25] Similarly, it enhances insulin resistance to reduce blood glucose levels. [26] Spirulina polysaccharides inhibited α-glucosidase for activity.[27] An oral supplementation to 45-60 Yrs. old male diabetic patients showed a significant reduction (P<0.001) in pre-post glucose levels.[18]

table cont...

Antifungal activity	*In vitro*	The different solvent extract inhibited the growth of skin disease-causing pathogens like *Candida albicans, trichophyton rubrum, and Malassezia furfur*.[28]
Anti-genotoxicity	*In vivo*	Spirulina extract was effective against arsenic-induced genotoxicity in *Orechromis niloticus*.[29] Also, accelerated the DNA repair, reduced DNA fragmentation, and had protective effects against cyclophosphamide, cisplatin & urethane.[20]
Anti-inflammatory property	*In vivo*	Reduced beta-glucuronidase activity and increased anti-oxidant enzyme activity in rheumatoid arthritis model of mice.[30] Moreover, it suppressed inflammatory cytokines, by decreasing IL-6, TNF-α, MDA and IL-1β relative to the LPS group.[31]
Anti-oxidant property	*In vitro*	Its C-phycocyanin showed DPPH radical-scavenging activities, similarly in FRAP & Fe2+ chelating potential.[32] Polysaccharides and different products from spirulina showed same capacity.[33]
Antiviral activity	*In vitro*	A pigment allophycocyanin and a sulfated polysaccharide inhibited the replication of numerous viruses such as enterovirus 71, HIV-1, HSV-1, HSV-2, HCMV, 20 and influenza, human cytomegalovirus, herpes simplex, influenza A, measles, mumps respectively.[15, 34]
Anti-nephrotoxicity	*In vivo*	Provide protection against Cd & Cr-induced renal toxicity in Wistar rats.[35] Similarly, against nephrotoxicity induced by cyclosporine A/gamma radiation in rats, on blood markers as and histopathological observations.[36]
Anti-obesity and Weight loss effects	*Clinical*	Inhibited NADPH oxidase and induces insulin resistance, suppresses adipocyte oxidative stress in clinical and preclinical trials.[37, 38]
Heavy Metal Removal potential	*In vivo*	An oral administration of the extract with zinc in patients of chronic arsenic poisoning protected from lead toxicity, and lipid peroxidation serve as an endogenous antioxidant in rats.[39]
Hypolipidemic effects	*In vivo* *Clinical*	The extract regulated the cholesterol and triglyceride levels in rat models.[40] Phycocyanins from this algae showed similar effects.[26] Oral supplementation to 45-60 yrs. old male diabetic patients, increased HDL level.[18]
Hepatoprotective property	*In vivo*	Phycocyanin-rich extract revealed significant protection against paracetamol-induced toxicity in rats.[18] Similar results showed against d-galactosamine-induced model of rats.[42]
Immunomodulatory effects	*In vivo*	Gamma-linolenic acid and phycocyanin from spirulina modulated the immune system, Inhibiting the release of histamine and modulating CD3 & CD20.[43] Moreover, in response to Con A, increased spleen cell development as well as IL-1 and antibody production.[44]
Cytotoxicity	*In vitro*	Spirulina extract had strong cytotoxicity against the HepG2 cell line (IC50 20.56 ± 1.7 µg/mL) followed by MCF7 & Hela cell in a MTT assay.[28]
Neuroprotective property	*In vivo*	Decreases the level of ROS, nitric oxide and lipid peroxidation Improves locomotor activity.[45] Moreover, in an AlCl3-induced Alzheimer's disease rat model, it significantly increased AchE genes, restored the reduced brain neurotransmitters, and improved brain oxidative status.[46]
Probiotic property	*In vitro*	Spirulina promotes the growth of lactic acid-producing bacteria such as Lactococcus lactis, L. casei, L. bulgaricus, L. acidophilusand Streptococcus thermophilus, as well as the extension of vitamin B1.[47, 48]
Wound healing activity	*In vitro*	The extract incorporated in a skin cream, exhibited wound healing effects on the HS2 keratinocyte cell line with the highest cell viability and significant proliferation.[49]

ABBREVIATIONS

HDL - high density lipoprotein; **AchE** - Acetylcholinesterase; **Cd** - Cadmium; **Cox** - Cyclooxygenase; **Cr** - Chromium; DPPH; 2,2-diphenyl-1-picrylhydrazyl; **Hb** - Hemoglobin; **HIV** - human immunodeficiency virus, **HSV** - Herpes Simplex Virus; **HS2** - Hepatic Stem cell type 2; IL-1β- Interleukin-1β; INF-α- interferon alpha; **LPS** - Lipopolysaccharide; **MCF** - Michigan Cancer Foundation-7; **MCH** - Mean Corpuscular Volume; **MCV** - Mean Corpuscular Hemoglobin; **MDA** - Mass Drug Administration; **MTCC** - Microbial Type Culture Collection & Gene Bank; **MTT** - 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide; **NADPH** - Nicotinamide Adenine Dinucleotide Phosphate; **Pb** - Lead; **RBC** - Red Blood Cell; **ROS** - Reactive Oxygen Species.

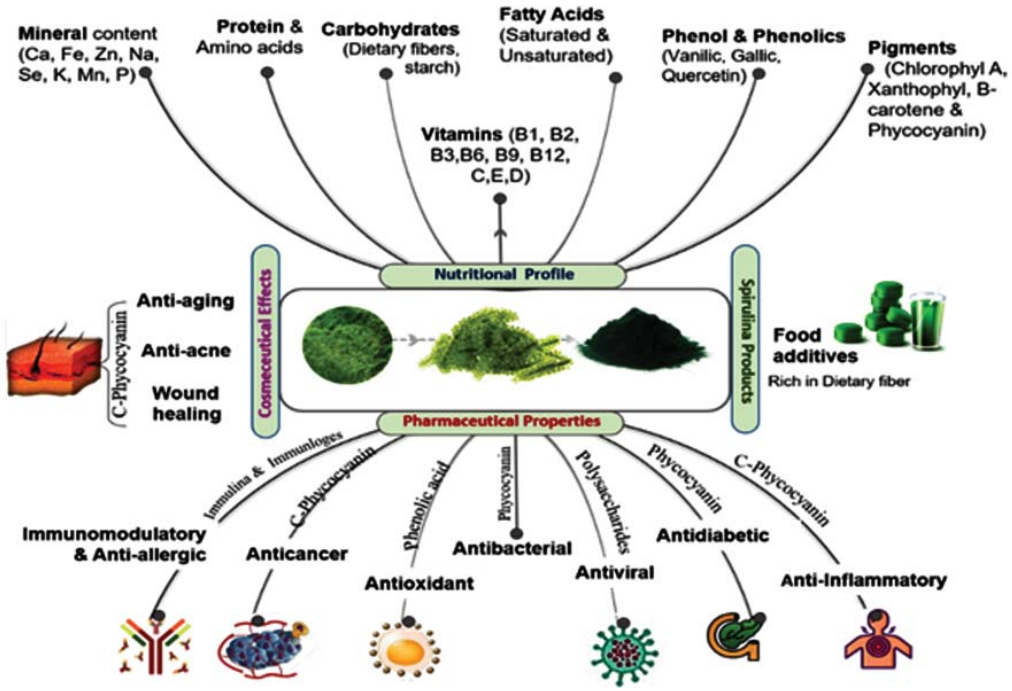

Fig. 2: Graphical illustration of nutraceutical profile & biological properties of Spirulina.

Cosmeceutical Importance

Uses of natural ingredients in the cosmetic industry have been noticed over the last years and similar trends were also observed for marine origin products like spirulina pigments and its metabolites enrich nutra-cosmetic formulations.[50] It is used to fortify the hair, nails, and skin in the form of cream, gel, and mask. Several reports and market claims supported the algae as an anti-aging product for antioxidant, brightening, and anti-acne properties, as well as the natural moisturizing capacity of the amino acids and proteins of algae, is used to the natural moisturizing ability which protects skin cells from drying out. Likewise, other by-products from the algae including terpenoids, pigments, phycobiliproteins (phycocyanin), and lipids (carotenoids, sterols), revealed antioxidant, wound healing, anti-inflammatory, and stabilizing properties in emollients. Moreover, Spirulina is enriched with vitamins that also aid in skin toning, healing dark circles, purifying skin, and encouraging hair growth by inhibiting dandruff.[51,52]

Toxicological Aspects

It is commonly recognized that any organisms or substance must be considered in the safety assessment. For this, it is revealed from *in vivo* experiments that when spirulina or phycocyanin compound was orally given to rats for 14 weeks at a concentration of up to 5% in the diet, the rats did not exhibit any harmful effects. Interestingly, Spirulina has not yet demonstrated any toxicity on the liver, kidney, reproductive system, and body physiology, during and after acute or chronic doses, at higher doses than any anticipated human consumption.[53,54] Although, even at high doses, it seems to be safe, so, it may be used as a source of single cell protein for humans without risk. However, it might also be contaminated through other chemical hazards or metals as per their source of origin. Therefore, it is important to have assurance about the spirulina source or marketed brands. Furthermore, women who are expecting or nursing should follow their doctor's recommendations about the same.

CONCLUSION

Spirulina is already a well known nutritional supplement to fulfill the nutritional requirement of the increasing population. This is supported by information on Spirulina's nutritional worth and biological processes, making it a healthy choice for diet planning, fighting malnutrition, and/or therapeutic uses. Preclinical and post-clinical research is continuously being conducted to determine the bioactive potentials of spirulina. However, these studies appear to show that Spirulina has potent pharmacological effects, which

has increased interest in it as a therapeutic diet. This review provides updated detailed information about the bioactive constituents and nutraceutical importance along with the scientifically claimed medicinal uses of Spirulina. Moreover, given everything stated above, can be concluded that Spirulina has a variety of benefits, including high biological importance, availability of nutrients, ease of cultivation due to minimal growth requirements, and safety in terms of consumption (no toxicities), to mention a few. More studies are hardly needed to support its claimed benefits. Additional prospects for the growth of the spirulina market will arise from the expansion of public and private efforts supporting aquaculture research and development as well as consumer well being awareness.

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