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A Review Article on Application of Spirulina in Medical Practises

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ABSTRACT

Spirulina is a safe, useful food that has been used for a very long time. It is a tiny, filamentous cyanobacterium. It is generated under regulated conditions in big outdoor ponds for commercial use. Here, we've included the information currently known on the therapeutic potential and uses of Spirulina in humans, as well as clinical data on the supplement's safety and adverse effects. Spirulina's chemical makeup, which includes proteins, carbs, vital amino acids, minerals (particularly iron), necessary fatty acids, vitamins, and colours, may have health benefits. Regarding this, it appears that the three main bioactive components of spirulina—sulfated polysaccharides, γ-linoleic acid (GLA), and the protein phycocyanine—have a substantial impact on enhancing bodily processes. Additionally, empirical data bolsters the immunomodulation and antiviral.

Keyword:- γ-linoleic acid (GLA), immunomodulation, phycocyanine

Introduction

The two most studied cyanobacterium species in pharmaceutical applications and the food business are Arthrospira platensis and Arthrospira maxima, which are members of the Microcoleaceae family and are more commonly referred to as Spirulina due to their spiral or helical structure [1-4] Because of the phycocyanin pigment that these microorganisms produce, they are categorised as blue-green algae because of their hue. On soils, rocks, under extreme physicochemical conditions, and in freshwater and oceanic settings, cyanobacteria have been identified in a variety of biological niches[5]. The obligatory photoautotrophic organism spirulina A filamentous species with a recognisable helical form. Its cyanobacterium possesses a Prokaryotic structure with many inclusions, ribosomes, and a multilayered cell wall With a lamellar photosynthetic system. Naturally occurring in alkaline waters with high mineral content, cyanobacteria flourish at temperatures Between 35 and 40◦C. Its filaments have a maximum length of 0.5 mm. The spiral The filament forms floating mats due to its structure and the gasvacuoles that are present inside the cells. Although there are several species of Spirulina in the wild, Spirulina platensis (S. Platensis) and Spirulina maximum (S. Maxima) are the most researched and utilised species. [6] Because spirulina contains a high concentration of both macro- and micronutrients, it has been regarded as a rich dietary source since the 1970s. Indeed, it is a great source of minerals, fatty acids, proteins, vitamins, pigments involved in photosynthetic reactions, and a number of secondary metabolites.[7] Different lipophilic pigments with varying bioactive qualities can be found in spirulina. The most prevalent ones are β-carotene and chlorophyll-a, which make up 9–12% of the lipid components. Other terpenoids found in Spirulina include zeaxanthin, canthaxanthin, β-cryptoxanthin, oscillaxanthina, echinenone, myxoxanthophyll, and xan-thophylls[8] . Provitamin A (β-carotene), vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B3 (nicotinamide), vitamin B6 (pyridoxine), vitamin B9 (folic acid), vitamin B12 (cyanocobalamin), vitamin C, vitamin D, and vitamin E (tocopherol) are all found in spirulina.

A number of minerals, including as iron, zinc, potassium, copper, manganese, magnesium, phosphorus, and calcium, can also be found in spirulina. [7,9,10,11]

Fig no.1 spiral filaments under microscope.

■*Anti-cancer function of spirulina:-*

There is strong evidence that S. platensis possesses antitumor and anticancer properties as well. In this context, it was found that intravenous injection of Radachlorin, a novel chlorine photosensitizer produced from S. platensis, resulted in considerable to full tumor Shrinkage[13] . Research indicates that PC exhibits a strong anti-tumor effect both in vitro And in vivo on a variety of cancer types, including breast cancer[14,15] , liver cancer[16], lung cancer[17,18] , colon cancer[19] leukemia[20], and bonemarrow cancer[21], However, in animal trials, even high-dose PC therapy did not result in substantial toxic effects or animal death[22], Significant morphological alterations were seen following the addition of PC to the tumor cell supernatant. These included the production of membrane blebs, nuclear and cytoplasmic condensation, apoptotic bodies, endolytic cleavage of DNA into minute oligo-nucleosomal fragments, and micronuclei that are indicative of apoptosis. These findings are consistent with past research where anti-cancer drug-treated cancer cells displayed characteristic apoptotic morphological indicators such shrinkage and membrane bleb development[23,24,25] ,The regulation of the cell cycle is crucial for the proper proliferation, differentiation, and death of cells.Dysfunction in this regard is directly linked to the development of tumors[26]. Tumor cells may multiply endlessly, whereas the normal cell cycle is tightly controlled. The G1/S checkpoint, the G2/M checkpoint, and the spindle checkpoint are the three main checkpoints in the cell cycle that must be successfully passed through for cell division. Cell cycle arrest and ultimately apoptosis result from failing one or more of these checkpoints. When PC was added to the cell culture medium, the colorectal tumor cells HT-29 and the lung cancer cells A549 entered the G0/G1 phase and stopped growing. This halted the manufacture of DNA and reduced the growth of tumor cells[27] .

■*Anti-toxic effect of spirulina:-*

Lead, iron, arsenic (metalloid), cadmium, mercury, and mercury are the metals that are commonly linked to health issues[28]. The most frequent harmful effects of these substances are teratogenesis, cancer, immune system suppression, harm to the liver and kidney, damage to the neurological and respiratory systems, endothelial dysfunction, hypertension, vascular disease, and intestinal mucosal damage[29]. Complexation and chelation therapy are frequently used in treatment.The most often used chelating compounds include N-acetylcysteine, deferoxamine, diethyldithiocarbamate (DTC), penicillamine, 2,3dimercaptopropanol (BAL), 2,3-dimercaptosuccinicacid, ethylenediaminetetraacetic acid (EDTA), and diethylenetriaminepentaacetic acid (DTPA)[28]. Regardless of the dose, manner of administration, or animal type, spirulina demonstrated a protective effect against carbon tetrachloride, hexachlorohexane, and arsenic. Spirulina's antioxidant ability, as shown by HgCl2, has been linked to this beneficial impact[30] .A reduction of up to 65% in lipid peroxidation has been demonstrated by spirulina's antioxidant ability, which has been demonstrated in both in vitro and in vivo experimental settings. This is significantly more than the effects of a-tocopherol, butylated hydroxyanisole (45%), or beta-carotene[31]. Also, studies have demonstrated that algae possess a higher antioxidant potential than both gallic and chlorogenic acids[32]. Its carotene, tocopherol, phenolic compounds, and C-phycocyanin concentration have all been linked to this feature. These compounds are thought to serve an antioxidant role either alone or in combination, producing synergistic benefits. C-phycocyanin, a primary biliprotein comprising 20% of Spirulina's dry weight, demonstrates potent antioxidant activity by scavenging hydroxyl, alkoxy, and peroxyl free radicals implicated in lipoperoxidation and cytotoxicity[33]. Spirulina itself is not toxic, unlike current antidotes, as demonstrated by various preclinical studies of acute toxicity tests, subchronic toxicity, chronic toxicity, fertility and reproduction assessments, teratogenicity, multigenerational tests, and in vivo mutagenesis assays that used doses significantly higher than those humans can consume on a daily basis[34].

If one episode of anaphylaxis to spirulina occurs, C-phycocyanin has been identified as the potentially allergenic protein[35,36].

■*Beneficial Effects of spirulina in neurodegenartive disease:-*

•Spirulina in parkinson's disease:-

The etiology of Parkinson's disease (PD), a neurological illness that progresses over time and is chronic, is multifactorial. The majority of those affected are older; the onset of PD rises with age, peaking at 1-2% around 60–65 years of age[37]. Gene variants that encode α-Synuclein (α-Syn), including the A53T mutation, GBA (glucosylceramidase β), LRRK2 (leucinerich repeated kinase 2, encoding LRRK2 protein), and MAPT (microtubule associated protein Tau) have been identified as potentially predisposing individuals to Parkinson's disease (PD)[38] .Parkinson's disease (PD) is characterized by non-motor symptoms such depression, constipation, sleep difficulties, and dementia that can occur earlier and have a major impact on quality of life[39]. as well as motor symptoms like bradykinesia, stiffness, tremors, and postural instability[40]. Brain inflammation has long been recognized as a major factor in neurodegenerative diseases like Parkinson's disease (PD). High concentrations of pro-inflammatory chemicals have been found in both the CSF fluid and the brains of PD patients, according to post-mortem clinical investigations[41,42]. Also, it has been demonstrated that α-Syn increases COX-2 expression [43]and activates microglial NADPH oxidase through CD11b[44] Remarkably, A53Tα-Syn and Aβ40/42 fibril production were effectively inhibited by CPC.Stable connections between C-PC and α-Syn suggest that transitory contacts might prevent fibril formation[45] This neuroinflammation can be reduced by diets high in foods that have anti-inflammatory and antioxidant properties, and spirulina has been demonstrated to have neuroprotective properties . Studies conducted in vitro and in vivo have demonstrated that the antioxidant components of spirulina, such as phycocyanin, can prevent or delay oxidative damage by reducing ROS accumulation[46], activating the CAT, SOD, and GPx antioxidant enzyme systems[47], and reducing ROS generation. Based on recent data, neuronal cells express CX3CL1, which interacts to the G protein-coupled receptor CX3CR1 found in microglia. This process regulates the activation of microglia and reduces the amounts of TNF-α, IL-6, and IL-1β[48,49]. One intriguing feature is that oral C-PC therapy crosses the blood-brain barrier and exhibits effects in the hippocampal regions.[50] After a 6-hydroxydopamine (6-OHDA) lesion, rats given an enhanced diet containing Spirulina showed improved recovery of striatal dopamine-positive TH nerve fibers and SNpc-positive TH neurons one month post-loss. Major Histocompatibility Complex II (MHC II) expression, a biomarker linked to the activation of M1 microglia, also showed a decrease in the quantity

of activated microglia (M1 phenotype, pro-inflammatory)[51]. By seeing a significant increase in TH+ and NeuN+ cells and a decrease in activated microglial cells as measured by MHC II expression, the scientists demonstrated that Spirulina was neuroprotective in this α-Syn model of Parkinson's disease. Spirulina has the ability toincrease the expression of the fractalkin receptor (CX3CR1) on microglia,which is in a 6-OHDA model of Parkinson's disease[52] figure no.2 [82]

Fig no.2 Effects of spirulina in Parkinson's disease

■***Anti-hypertensive effect of spirulina:-***

Oxidative stress and inflammation are major contributors to cardiovascular disorders, including hypertension, atherosclerosis, cardiac hypertrophy, and heart failure. It has been shown that oxidative stress causes an excess of ROS to be produced in situations related to cardiovascular disease[53] .The impact of silicon-enriched spirulina (SpSi) dietary supplementation on the structure and function of the vascular system in hypertension has been assessed. Decreases in extracellular matrix breakdown were correlated with increases in collagen and elastin levels. The positive benefits of SpSi supplementation that have been demonstrated here may be related to Spirulina enrichment and present intriguing chances to reduce cardiovascular risks[54]. By raising endothelial nitric oxide synthase (eNOS), blocking ACE, regulating the renin-angiotensin system, vasoconstricting metabolites, and preventing platelet aggregation, spirulina can be useful as a blood pressure-lowering drug[55]. Spirulina consumption may have significant long-term effects on hypotensive treatments in cardiology[56].

Role	Effect	Dose or concentration	Analysis Methodology	Ref
Cardiovascular Protection	Atheroclerosis disease reduction	200 µM	HMOX-1, P22, VCAM, eNOS	[83]
	Preventing the oxidative stress, inflammation, and cardiac damage brought on by AMI	50 mg/kg administered subcutaneously	Lipid peroxidation, pro-inflammatory and proapoptotic cytokines, CK, AST, ALT, ROS, nitrites, and oxidized glutathione	[84]

	Preventing the development of atherosclerosis and cardiovascular illnesses	0.25 %and 1.25 %(oral)	MDA, GOT, GPT, catalase, SOD, GSH-Px, HMG CoA, and cholesterol	[85]

Table 1. The biological roles of the recovered phycocyanin from Spirulina, together with an explanation of its primary activities, dose, or concentration, and the analytical techniques employed, are presented.

■*Anti-oxidant and Anti-inflammatory Effect of spirulina:-*

Phycocyanin and β-carotene, two of the active ingredients found in spirulina, have strong anti-inflammatory and antioxidant properties[57]. The protective role of spirulina against toxicity caused by carbon tetrachloride (CCl_4)[58], metals (arsenic, mercuric chloride, chromium, cadmium, and fluoride)[59,60,61,62,63]. Natural killer cell activity appears to be stimulated by supplements, which appear to impact innate immunity more so than acquired immunity. There are many applications for this ability, which raises CD4+ counts in HIV+ patients and improves oxidative stress and NK activity markers in healthy participants. Spirulina's ability to protect the liver from methotrexate's hepatotoxicity has been investigated in the context of chemotherapy treatments. Malondialdehyde and tumor necrosis factor α were decreased when a high dose of Spirulina was administered for 21 days before starting methotrexate treatment[64]. Figure no.3 [65]

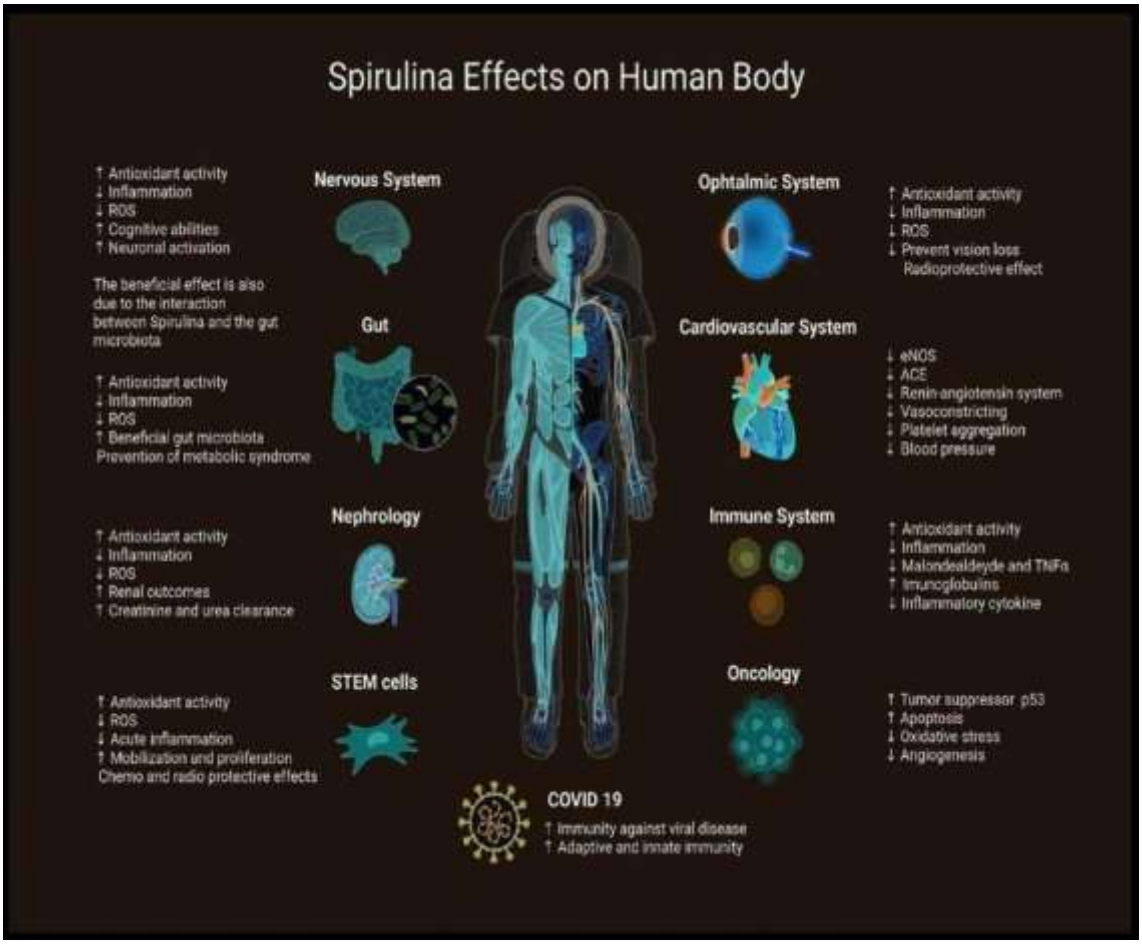

Fig 3. An summary of Spirulina's Impact on the body's different region

■*Spirulina for Astronauts' Healthcare:-*

Astronauts are subjected to a range of stressors during their mission that may have long-term detrimental effects on their health. Using the abbreviation "RIDGE" (radiation from space, confinement and isolation, distance from Earth, gravitational fields, and hostile and NASA highlights the primary risks associated with space travel in restricted environments. For example, it has been well demonstrated that exposure to microgravity has multiple detrimental impacts on human health, especially since the development of space stations, which are livable for extended periods of time. These impacts might even have long-term repercussions on gastrointestinal disorders, with implications for astronauts' microbiota make up[66-75]. The human body's physiological functions include respiratory system, muscular tone, heart rate, and thermos-regulation[76]. Astronauts in a microgravity environment face several major

health hazards, such as musculoskeletal alterations like decreased muscular strength and increased bone fragility, vision impairment, endothelium dysfunction, metabolic abnormalities, and behavioural changes brought on by weariness or tension, as well as consequences for mental health. High levels of cosmic radiation are experienced by astronauts in space, and this radiation can harm DNA, cause mutations, oxidative stress, acute radiation syndromes, injure the central nervous system, cause tissue illnesses like cardiovascular disease, and alter the microbiota in the gut. More precisely, the development of oxidative stress, which damages DNA and mitochondria, is one of the primary impacts of space travel at the molecular and intracellular level[77,78].

■ ***Effects of Spirulina platensis on productive performance:-***

Spirulina has been shown in numerous research to support its growth-promoting properties. Spirulina can be added to poultry diets from the embryonic stage until the egg is laid. Spirulina platensis intraperitoneally increased the expression of genes in quail chicks linked to immunity, antioxidants, and hatchability [79]. According to Ibrahim et al., spirulina added to drinking water for four weeks at concentrations of 0.5, 1 and 2 g/liter considerably raised the average body weight. growth, health, greatest significant feed conversion ratio (FCR), feed efficiency, European Production Efficiency scores, and a notable decrease in abdominal fat were all present, along with an increase in the relative weights of the carcass and internal organs. The growth performance of Japanese quails fed diets containing both animal and vegetable protein was enhanced by adding spirulina (1 or 2 g/kg diet) without compromising the quality of the meat or the gut flora of the quails fed the vegetable protein source; no effect was shown in the quails provided the animal protein diet[80,81].

Conclusion:-

Limited consumption of natural food stuff in the 21st century leads to insufficiency of vitamins and main minerals in the mortal population. product of blue green microalgaeS. platensis, serves as an indispensable approach as feed and food complements due to their rich contents of protein, poly-unsaturated adipose acids(- linolenic acid), vitamins as well as minerals, colors and enzymes. Spirulina has several pharmacological conditioning similar as anticancer, antiviral, antibacterial, metalloprotective, antioxidant and immunostimulant goods. Mechanisms of anticancer, antiviral and antimicrobial goods of Spirulina are due to its content of endonuclease(which form damaged DNA), calcium sulfated polysaccharide(which inhibits in vitro replication of contagions) and adipose acids(especially high content of- linolenic acid), independently. In addition, the metalloprotective part of Spirulina may be attributed to the presence of beta- carotene, vitamins C and E, enzyme superoxide dismutase, selenium and brilliant blue polypeptide color phycocyanin. Research has also concentrated on the immunostimulant goods of Spirulina. Some experimental compliances indicate that phycocyanin, sulfated polysaccharide fragments, GLA and certain sulfolipids are the most promising active ingredients of Spirulina. nonetheless, further exploration is demanded to rate the effectiveness of Spirulina as a source of implicit medicinals and nutraceuticals. Different chemical composition and colorful pharmacological conditioning have been reported for the microalgae. These antithetical results may be related to differences in the geographical origin, harvesting period, waterless medium characteristics as well as inheritable variations,post-harvest processing conditions, the system of birth and type of detergents used. likewise, commerce of microalgae with natural or foreign parcels of the consumed foode.g. pH, fat, protein, water content, antioxidants, oxygen attention and preservative, needs further disquisition

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