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SPIRULINA: AN EXCEPTIONAL SUPPLEMENT FOR CANCER SUPPORT

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ABSTRACT: Spirulina is a filamentous, spiral-shaped blue-green algae that contains a wide variety of bioactive compounds, making it a valuable nutraceutical. It boasts a unique combination of approximately seventy biologically active compounds, which enhances its therapeutic significance. Its potential role in combating carcinogenesis can be attributed to its antioxidant and anti-inflammatory properties, recognitions to components such as β-Carotene, C-Phycocyanin, Calcium Spirulan, and Linoleic and Linolenic acids. Investigation has shown that Spirulina extracts can enhance endonuclease activity, promote DNA repair, and induce apoptosis in cells. Some studies have also reported effects such as myelosuppression and improved immune function. Commercially available Spirulina is often used as an adjunct to chemotherapy. However, the evidence supporting its effectiveness in cancer treatment is quite limited, particularly in terms of clinical trials. This current work aims to consolidate contemporary data and create a systematic review of the findings.

INTRODUCTION: In recent years, Spirulina (Arthrospira) has gained significant attention from both the scientific and medical communities due to its properties as a nutraceutical and its potential as a source of pharmaceutical drugs [1]. The FDA and WHO have referred to it as a "super food" or a "miracle from the sea." Spirulina is rich in a variety of bioactive compounds and has emerged as an important nutraceutical due to its unique combination of therapeutic ingredients [2]. Its ability to prevent carcinogenesis is linked to its various antioxidant components. Cancer remains one of the leading causes of death worldwide [3].

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Typically, surgical resection is the first line of treatment for early-stage cancers, while chemotherapy is used for more advanced cases. Despite significant advancements in cancer treatment, the effectiveness of chemotherapeutic drugs is often limited by issues such as multidrug resistance and drug-induced side effects. Conventional chemotherapeutic agents frequently target a non-specific cell which means they can harm healthy cells in addition to cancerous ones [4].

In contrast, treatments derived from natural sources, such as plants and microalgae, may produce fewer side effects compared to traditional chemotherapies. Although the antioxidant properties of these organisms have been well studied, data on their anticancer effects remain limited. Complementary and alternative medicine (CAM) encompasses lifestyle choices, including the use of plant-based therapies for cancer remission, which often result in fewer or even no

side effects [5-7]. Spirulina is an unbranched, helicoidal, filamentous blue-green algae, or cyanobacterium, that belongs to the *Oscillatoriaceae* family **Fig. 1** [8]. It naturally thrives in a variety of aquatic environments, including fresh, alkaline, and saline waters, even those with extremely high pH levels. Spirulina is relatively easy to cultivate. The most extensively studied species of Spirulina are *Spirulina platensis*, *S. maxima*, and *S. fusiformis*, all of which are edible and offer high nutritional and potential therapeutic value. These species are commercially available under various brand names, such as SBGA (Spirulina BGA), Spiralyne, and Spiruline. Spirulina can be consumed orally in various forms, including capsules, tablets, powder, or flakes, whether dried or freeze-dried product [9-10].

Historically, Spirulina has been used as human food for centuries, including during the Aztec civilization. It has served as a protein-rich food source in various cultures across Mexico, Africa, Europe, and North America. However, its nutritional potential has only recently been fully understood, thanks to advancements in modern scientific technology. Spirulina gained particular notoriety when it was endorsed by NASA and the European Space Agency for cultivation and consumption by astronauts on long-term space missions [11-13].

FIG. 1: REPRESENTATION OF SPIRULINA

It has been utilized as a food supplement for the last 25 years without any undesirable side effects [14]. Spirulina is easily digestible because it lacks cellulose cell walls. Despite its simple structure, it has a complex composition rich in nutrients [15].

Nutritional Profile -Chemical Composition of Spirulina: The phytochemicals in Spirulina include essential amino acids (such as methionine and cysteine), lipophilic vitamins (A, E), hydrophilic vitamins (B1, B2, B3, B5, B6, B8, B9, and C), polyunsaturated fatty acids like eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and minerals (calcium, iron, copper, zinc, potassium, magnesium, manganese, and selenium) **Fig. 2** [16].

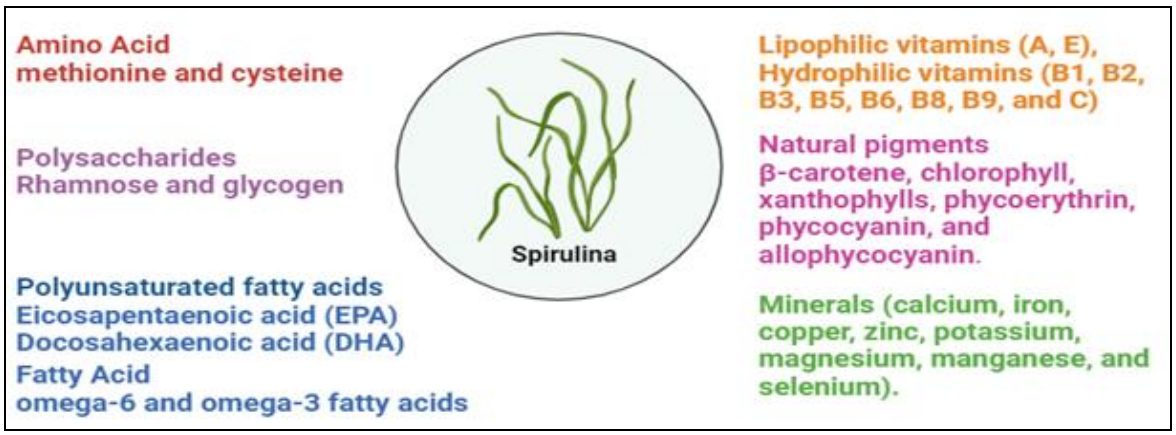

FIG. 2: CHEMICAL COMPOSITION OF SPIRULINA

The protein content of Spirulina is well-known, comprising about 70% of its dry weight, and its amino acid profile is comparable to that of an egg, containing almost all essential amino acids. According to a report from healthline.com, the omega-6 and omega-3 fatty acids in Spirulina are present in an approximately 1.5:1 ratio. Spirulina is particularly rich in a unique sulfated polysaccharide called calcium spirulan (Ca-SP), which has been reported to enhance DNA repair and inhibit the *in-vitro* replication of several enveloped viruses [17]. Other polysaccharides in Spirulina, such as rhamnose and glycogen, are easily absorbed by human cells, facilitating energy release [18]. Spirulina may also support the growth of probiotics like Lactobacilli in the intestine, which contribute to the production of vitamin B6. While it is often claimed that Spirulina contains vitamin B12, this is a

misconception; it contains pseudovitamin B12, which has not been proven to be effective in humans [19]. As a comprehensive health booster, Spirulina's free-radical scavenging properties can be attributed to natural pigments such as β-carotene, chlorophyll, xanthophylls, phycoerythrin, phycocyanin, and allophycocyanin. These compounds may work individually or synergistically. Spirulina is an excellent source of phycocyanin, a tetrapyrrolic compound that gives Spirulina its blue-green color and may protect against oxidative damage. It has been reported to lower total cholesterol, "bad" LDL cholesterol, and triglycerides while increasing "good" HDL cholesterol, as noted by healthline.com. Additionally, beta-carotene, a precursor of vitamin A, has been associated with anticancer effects. Recently, there has been a surge of interest in the biological antioxidants found in Spirulina [20-23].

Therapeutic Properties of Spirulina: Beyond its rich nutritional profile, Spirulina has been reported to possess a wide range of therapeutic properties, including alleviating inflammation, oxidative and immune stress, allergies, rhinitis, diabetes, diabetic nephropathy, hepatopathy, nephrotoxicity, hypercholesterolemia, hyperglycerolemia, drug-induced toxicities, viral and bacterial infections, cardiovascular diseases [24-44] and certain types of cancer [45-47]. Spirulina appears to enhance immunity and provide protection against toxic metals and harmful radiation. It may also reduce lipid peroxidation, a key driver of many serious diseases, by mitigating oxidative damage to fatty structures. However, evidence for the effectiveness of Spirulina in cancer treatment is limited. Most studies investigating its efficacy against cancer have been conducted on human cell lines or rodent models [48]. It has been strongly suggested that the antioxidant and immune-modulating properties of Spirulina might work together to induce apoptosis, disrupt tumors, and potentially prevent cancer [49].

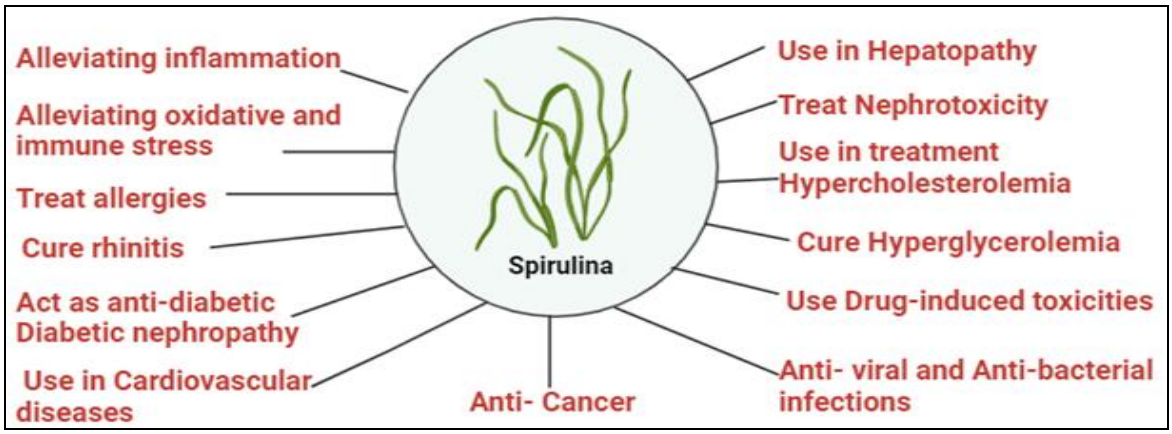

FIG. 3: THERAPEUTIC POTENTIAL OF SPIRULINA

Cancer encompasses a group of diseases marked by uncontrolled cell growth and the spread of abnormal cells, resulting in a mass known as a neoplasm or tumor [50]. If this unchecked spread continues, it can ultimately lead to death. One key characteristic of cancer is the rapid proliferation of abnormal cells that grow beyond their normal boundaries, invade other parts of the body, and can eventually spread to other organs. This process, known as metastasis, is the leading cause of death in cancer patients [51]. Esophageal cancer is among the top causes of cancer-related deaths worldwide. It arises in the lining of the esophagus. Adenocarcinoma is a specific type of cancer that develops in the cells responsible for producing and secreting mucus and other fluids [52]. Phenolic extracts play a significant role in cancer prevention. These include simple phenols, flavonoids, lignins, lignans, tannins, xanthones, and coumarins, which have been identified from algal sources. Research has demonstrated that these phenolic compounds possess strong anti-cancer properties and can effectively combat several disorders related to oxidative stress. Numerous studies indicate that the protective benefits of dietary phenols on health stem from their anti-inflammatory and antioxidant properties [53]. The primary mechanism through which phenolic compounds exert anti-carcinogenic effects is their ability to induce cell cycle arrest and inhibit oncogenic signaling pathways that regulate

cell proliferation, angiogenesis, and apoptosis [54]. Additional mechanisms include modulating reactive oxygen species (ROS) levels, promoting tumor-suppressor proteins like p53, and facilitating the differentiation and normalization of cells [55].

Recent research has highlighted the promising role of natural products in cancer treatment, particularly in enhancing traditional therapies [56]. Notably, scientific advancements have led to the discovery of several new anticancer drugs derived from both synthetic and natural compounds, particularly those from marine organisms. The remarkable antitumor capabilities of Spirulina platensis stem from its dual action: immune modulation and potent antioxidant activity [57]. This remarkable algae species, known as Arthrospira, produces powerful compounds called phycobiliproteins such as c-phycocyanin (C-PC), phycocyanobilin, and allophycocyanin (APC) which not only exhibit compelling antitumor and anticancer activities but also offer antimicrobial properties against bacteria, fungi, and viruses. Embracing the potential of natural products like Spirulina could revolutionize cancer treatment, offering hope for a healthier future. Following are the main nutrients fight against cancer [58].

β- Carotene: Beta carotene is a well-known antioxidant and one of the most significant natural compounds for combating cancer. Spirulina contains a high level of beta carotene. Research indicates that beta carotene dramatically prevents the development of squamous cell carcinoma [59]. Additionally, Spirulina, along with other herbs, has been shown to inhibit tumor growth. Studies involving animals demonstrate a marginally significant decrease in both the size and number of tumors associated with the use of beta carotene [60].

Polysaccharides: The remarkable water-soluble polysaccharides extracted from Spirulina have been shown to greatly enhance endonuclease activity, playing a crucial role in the effective repair of radiation-damaged DNA through excision repair and unscheduled synthesis [61]. When it comes to combating human malignancies, the powerful combination of polysaccharides and phycocyanin derived from Porphyra yezoensis proves to be highly effective [62]. Moreover, acidic polysaccharides from *A. platensis* demonstrate a potent tumor necrosis factor (TNF)-dependent tumoricidal effect in macrophages, showcasing their potential in cancer therapies [63]. Spirulina's complex polysaccharides also stand out for their ability to inhibit the proliferation of glioma cells (murine RSV-M), achieving this by downregulating angiogenesis and partially modulating interleukin-17 production [64]. Furthermore, the innovative SPS-SeNPs, which are selenium nanoparticles (SeNPs) fused with Spirulina polysaccharides, offer exciting possibilities for future treatments [65].

Phycocyanin (PC): Phycobiliproteins, including C-phycocyanin (C-PC), allophycocyanin (APC), and phycoerythrin (PE), play a crucial role in the phycobilisomes of Spirulina platensis, showcasing their potential health benefits [66]. Research highlights that mice with live tumor cells experienced a significantly higher survival rate when C-PC from Spirulina was administered orally. Moreover, compelling studies conducted remarkable effects of Spirulina and Dunaliella extracts on oral tumors in hamsters. They discovered that the induction of squamous cell carcinoma in hamsters through DMBA (dimethylbenz(a) anthracene) resulted in tumor regression when these extracts were used. This suggests that the oral administration of Spirulina and Dunaliella extracts not only supports the immune system but also effectively halts tumor progression. Importantly, these natural extracts are nontoxic to healthy cells while actively inhibiting the proliferation of cancerous cells. C-phycocyanin, in particular, has been shown to hinder the growth and survival of human leukemia cells, demonstrating its multifaceted anti-cancer properties Represented in **Table 1**. Embracing the power of Spirulina could be a transformative step toward [67-70].

TABLE 1: ANTI-CANCER PROPERTIES OF SPIRULINA IN VARIOUS CANCERS

Sr. no.	Researchers and Year	Name of the Cancer	Mechanism	Experimental Organism	References
1	DIC, Japan, 1983	Liver	Anticancer	Mice	[71]
2	Schwarttz and Shklar¸	Oral –squamous cell	cytotoxic and	Human and	[72]

	1987	carcinoma	cytostatic activity	hamster	
3	Schwarttz and Shklar, 1987	Squamous cell carcinoma	Total tumor regression	Hamster	[73]
4	Schwarttz et al., 1988	Oral buccal pouches tumor	Immune response	Hamster	[74]
5	Lisheng et al., 1991	Hepatoma	Inhibited proliferation of abscitic hepatoma cells	Mice	[75]
6	Hayashi et al., 1994	HeLa cells	Cytotoxic	*In-vitro*	[76]
7	Chen and Zhang, 1995	Colon	The no. of aberrant crypts reduced significantly	Rats	[77]
8	Babu, et al., 1995; Mathew et al., 1995	oral leukoplakia	Combined antioxidant and immune modulation	Human	[78]
9	Mishima et al., 1998	Lung cancer	Marked decrease of lung cancer; antiheparanase activity inhibits metastasis and invasion	Mice	[79]
10	Liu et al., 2000	Leukemia	Inhibited growth of K562 leukemia cell	Mice	[80]
11	Chen and Wong, 2008	Human melanoma A375 cells and human breast adenocarcinoma MCF-7 cells	Apoptosis and antiproliferative agent	In vitro	[81]
12	Akao, et al., 2009	B16 melanoma	natural killer cells dependent tumoricidal actvity	Human and Mice	[82]
13	Grawish, et al., 2010	Squamous cell carcinoma induced by 0.5% of 7, 12-dimethylbenz[a]a nthracene (DMBA)	Tumor regression	Hamsters	[83]
14	Parages, et al., 2012	B16 melanoma cells - Indirectly helps in oral cancers	production of macrophage - tumor necrosis factor- (TNF)	*In-vitro*	[84]
15	Hernandez FY, et al., 2017	Human acute leukemia Kasumi-1 and chronic myelogenous leukemia K-562 cell lines	cytotoxicity in K562 and Kasumi-1 cell lines.	Cell culture	[85]
16	Elham Tajvidi , et al., 2021	Lung Cancer cell	Stop the cells in phase G_2, consequently, the cells won't enter phase M and it stops the proliferation of the cancer cells.	Cell culture	[86]

CONCLUSION: A healthy diet is essential for preventing and treating some of the most serious diseases affecting our world today. Spirulina, alongside other cyanobacteria, stands out for its remarkable benefits in sustainable food production and the nutraceutical industry. This not only supports a healthier planet but also presents a critical solution to the hunger crisis. Renowned for its extensive health advantages, spirulina is a nutritious and safe food that many consider a miracle supplement and an effective adjunct to treatment. However, it is important to acknowledge that spirulina harvesting can sometimes result in the presence of harmful substances that may pose risks to human health. For example, certain strains may contain microcystins, which accumulate in the liver and could lead to cancer and other serious liver issues. Fortunately, ongoing research on

spirulina is paving the way for the development of safe and health-promoting foods. Spirulina is packed with antioxidants and boasts a rich protein content characterized by a complete amino acid profile, inclusive of all essential amino acids. Its impressive spectrum of vitamins, including the B vitamin complex, Vitamin C, and Vitamin E, further enhances its appeal. The extensive body of research highlights the incredible health benefits tied to spirulina, showcasing its powerful blend of micro and macro nutrients. Furthermore, it is known for its anti-inflammatory and anticancer effects, providing an essential boost to the immune system and promoting a healthier gut microbiota when incorporated into a balanced diet. Embrace spirulina's potential and take a proactive step towards better health today.

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