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Spirulina: A Promising Natural Aid in Diabetes Management

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ABSTRACT:

Diabetes mellitus is a widespread metabolic disorder marked by chronic hyperglycemia due to defects in insulin secretion, insulin action, or both. The incidence of diabetes mellitus is rising at an alarming rate. Type 2 diabetes mellitus, in particular, is driven by lifestyle factors and genetic predispositions. Management strategies emphasize lifestyle modifications, including diet and exercise, as well as pharmacological treatments. Recently, the potential of functional foods and natural supplements, such as Spirulina, has garnered significant interest. Spirulina, a nutrient-dense cyanobacterium, has been consumed for centuries as it is high in protein and vitamin. It exhibits multiple health benefits, including immune modulation and anti-inflammatory properties. Recent studies have explored Spirulina's potential in managing diabetes mellitus. Spirulina’s bioactive compounds, such as phycocyanin, and gamma-linolenic acid, contribute to these therapeutic effects. Additionally, Spirulina may aid in weight loss and mitigate diabetes-related complications, such as neuropathy, nephropathy, and cardiovascular disease. This review highlights the historical use, nutritional profile, and emerging evidence on Spirulina's role in diabetes mellitus management. It discusses how Spirulina can be incorporated into the diet and emphasizes precautions for its use. While promising, Spirulina should complement rather than replace conventional diabetes mellitus treatments. Further research is necessary to fully understand its mechanisms and long-term benefits in diabetes mellitus management.

Keyword Spirulina, T2DM, Diabetes mellitus, Nutraceutical

1. Introduction

A collection of metabolic illnesses often referred to as diabetes mellitus (DM) are characterized by consistently elevated blood sugar levels. Diabetes has grown increasingly prevalent; by 2040, the World Health Organization predicts that there will be 642 million instances of the disease worldwide, up from 422 million in 2014 [1, 2]. A number of variables, such as sedentary lifestyles, poor eating habits, and genetic susceptibility, are contributing to this epidemic [3]. The primary cause of it is disturbances in the feedback loops that link the action and secretion of insulin [4]. Normal glucose levels in the body are disrupted by β-cell dysfunction and reduced insulin production. Excess FFAs (Free fatty acids) and high blood sugar cause endoplasmic reticulum (ER) stress, which triggers the unfolded protein response (UPR) pathways that cause β-cell failure [5, 6]. Stress brought on by elevated saturated fat acids stimulates the UPR pathway by various pathways, such as blocking the sarco/endoplasmic reticulum Ca2+ ATPase (SERCA), which is in charge of ER Ca2+ mobilization, activating IP3 receptors, or directly impairing ER homeostasis [7, 8]. Moreover, chronically high glucose elevates proinsulin production and islet amyloid polypeptides (IAPP) in β-cells, leading to a buildup of misfolded insulin and IAPP and an increase in ROS produced by oxidative protein folding [9]. Insulin-sensitive cells' impaired metabolic response to insulin is known as insulin resistance (IR) or, on a broader scale, a diminished or impaired ability of blood glucose levels to respond to circulating insulin [10]. Insulin deficiency, or IR, can be divided into three major categories: (i) Decreased release of insulin from β-cells; (ii) Insulin antagonists in plasma can harm insulin receptors or signaling pathways; they can be from non-hormonal origins or counter-regulatory hormones; and (iii) decreased target tissue insulin response. The combination of β-cell failure and IR leads to severe hyperglycemia and the progression of T2DM (Type 2 diabetes mellitus) [11]. Despite not being contagious, type 2 diabetes is becoming more common, so different approaches to managing and treating it are being developed. The primary classes of oral antidiabetic medications include biguanides, sulfonylureas, TZD (thiazolidinedione), meglitinide, DPP-4 (dipeptidylpeptidase 4) blokers, α-glucosidase inhibitors, SGLT2 (sodium-glucose cotransporter) inhibitors, and. If the HbA1C level is 7.5% while taking medication or if the baseline HbA1C is ≥9%, a combination regimen with two oral drugs or insulin may be advised [12]. Modern approaches prioritize lifestyle changes, such as dietary adjustments and increasing physical activity, as the first line of treatment. Additionally, the potential of functional foods and natural medicines as complementary therapies alongside pharmacological treatments is gaining significant interest among researchers.

Spirulina is a microscopic, spiral-shaped cyanobacterium, specifically the dried biomass of *Arthrospira platensis*, an oxygen consuming bacteria present in both fresh and marine waters globally [13]. Historically, it has been consumed as food, dating back to the Aztec civilization [14]. This alga is a significant dietary staple for humans, known for being a rich source of protein and vitamins, and is generally well-tolerated without notable side effects [15]. The species *Arthrospira platensis* and *Arthrospira maxima* are particularly valued for their nutritional and therapeutic benefits [16]. Spirulina is widely available in health food stores, typically marketed as a nutritional product in the form of tablets and health beverages. It is known for its ability to regulate immunological responses and its anti-inflammatory properties, which include suppressing histamine production from mast cells [17]. Numerous studies have explored Spirulina's effectiveness and possible therapeutic management of several medical conditions. Some randomized controlled trials and systematic reviews indicate that Spirulina may alleviate several symptoms and possess anticancer, antiviral, and antiallergic properties [18]. Recent research has also noted its effects on lipid and glucose metabolism [19], although the exact mechanisms remain unclear. This review will focus on Spirulina's potential as a nutritional supplement or treatment for managing diabetes mellitus.

2. History of Spirulina

Spirulina, one of the oldest known foods, dates back over three billion years. It originally thrived in Lake Texcoco in Mexico and Lake Chad in north-central Africa. The earliest reliable historical records of its use come from the Spanish conquistadors, notably Cortes, who reported during the conquest of the Aztecs (1519-1525) that the Aztecs consumed a green food, referred to as the “Food of the Gods,” in pie form [20]. In 1965, spirulina was rediscovered by French botanist Jean Leonard during a trans-Saharan Belgian expedition. He observed women of the Kanembu people in Chad preparing and selling edible green cakes made from the algae [21]. Later, in the late 1960s and early 1970s, the Institut Franscais du Petrole collaborated with a Mexican company, SOSA-TEXCOCO, to study the algae blooms in Lake Texcoco. This led to the establishment of the first large-scale spirulina production plant on the shores of Lake Texcoco in the late 1970s [22]. Today, spirulina is cultivated globally in aquaculture farms, particularly in Australia, Central America, Southeast Asia, and Africa. Recognized for its high protein content and rich nutritional profile, NASA has considered spirulina as a potential food source for astronauts on long-term space missions [13, 23].

3. Nutritional profile of spirulina

This cyanobacterium consists of 55–70% protein, 6–13% nucleic acids, 15–25% carbohydrates, 5–6% lipids, and 2.2–4.8% minerals. This alga contains essential fatty acids (γ-linolenic acid, arachidonic acid, stearidonic acid, α-linolenic acid, docosahexaenoic acid, and eicosapentaenoic acid), fat soluble vitamins and minerals (lead, calcium, magnesium, potassium, iron, zinc, nickel, chromium, selenium, manganese, copper, and sodium), and carotenoids [24, 25]. Spirulina has a high content of pigments like beta-carotene and chlorophyll. It also contains phycobilins, specifically phycocyanin and allophycocyanin, which are structurally similar to bile pigments such as bilirubin. These phycobilins are bound to proteins in Spirulina cells, forming phycobiliproteins [26]. Furthermore, spirulina contains all of the key amino acids needed by the human body, making it the greatest organic source of digestible protein. Its high digestibility is attributed to the absence of cellulose in its cell wall, which is made up of 86% digestible carbohydrates [27]. These qualities have led to Spirulina’s widespread acceptance and recognition in numerous nations. It is approved for use as food or a nutritional product by the FDA in the United States and the Brazilian Health Regulatory Agency (ANVISA) in Brazil, having been granted GRAS (Generally Recognized as Safe) designation [24, 28].

4. Spirulina and Diabetes Management

The tiny filamentous cyanobacterium Spirulina platensis, somewhere known as "blue-green alga,” has drawn a lot of interest as a functional food because of its links to antioxidant and anti-inflammatory qualities as well as cholesterol regulation [29]. It is a great source of minerals, phycocyanin, carotenoids, protein, and vitamins, particularly B12. There is growing clinical and scientific data supporting its ability to manage a number of chronic illnesses, including diabetes [30, 31] (Figure 1).

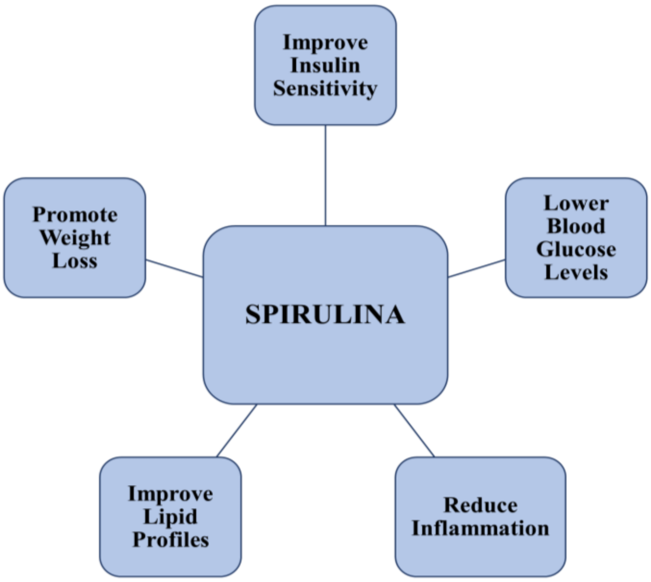

Figure 1 Pathways through which Spirulina Manages Diabetes. Spirulina aids in diabetes management by enhancing insulin sensitivity, lowering blood glucose levels, reducing inflammation, improving lipid profiles, and promoting weight loss.

4.1 Improving Insulin Sensitivity

Studies have been conducted on the potential health benefits of Spirulina platensis, including the potential to enhance insulin sensitivity. It includes omega-3 and omega-6 fatty acids, which are critical for preserving the integrity of cell membranes and enhancing the sensitivity of insulin receptors [32]. The precise chemical pathway that spirulina works to raise insulin sensitivity is unknown. However, recent research has shown that its mechanism likely involves an elevation of the hepatic mitochondrial content, as shown by the significant dose-dependent rise in hepatic PGC-1α, TFAM (Mitochondrial transcription factor A) expression, and mt-DNA copy number, as well as the positive correlation. Based on Spirulina's altering impacts on nuclear and mitochondrial parameters, polysaccharides from Spirulina platensis improve nuclear enzyme performance and DNA damage surveillance and repair processes [33, 34]. Furthermore, Spirulina extract has been shown to have a protective effect in vitro against mitochondrial malfunction and degeneration in horses with Equine Metabolic Syndrome [35].

4.2 Lowering Blood Glucose Levels

Spirulina has been shown to have blood sugar-lowering effects. It enhances the response to insulin and the metabolism of glucose. It enhances lipid metabolism, which can lower high cholesterol and triglycerides, lower blood glucose levels, and enhance general metabolic health [29, 36]. Supplementing with spirulina has been demonstrated in clinical investigations to substantially reduce fasting blood glucose levels. Spirulina consumption, for instance, was shown to enhance long-term glucose control in a trial including individuals with type 2 diabetes by lowering fasting glucose and glycosylated hemoglobin (HbA1c) levels [37]. A two-month period of daily consumption of 2 grams of spirulina significantly improved HbA1c and fasting plasma glucose levels in another trial including 25 individuals with type 2 diabetes [38]. Further research with diabetic animal models confirmed Spirulina's potential in lowering blood glucose levels, supporting its use in diabetes management.

4.3 Reducing Inflammation

Spirulina has demonstrated significant anti-inflammatory properties through various mechanisms. Spirulina contains phycocyanin, which is a potent antioxidant. It scavenges free radicals and prevents oxidative damage to cells [19, 39]. Spirulina has been shown to lower the production of pro-inflammatory cytokines such as TNF-α (Tumor necrosis factor- α), IL-1β (Interleukin- 1β), and IL-6 [40]. Reducing these cytokines can result in less inflammation overall because they are important components of the inflammatory process. Enzymes implicated in the inflammatory response, such as COX-2 (cyclooxygenase-2) and iNOS (inducible nitric oxide synthase), are inhibited by spirulina [41]. By inhibiting these enzymes, spirulina can effectively reduce inflammation and associated pain. Research indicates that spirulina supplementation can improve insulin sensitivity and lower levels of IL-6, a marker of inflammation [42]. This is particularly beneficial for individuals with metabolic disorders, as inflammation is a common component of these conditions.

4.4 Enhancing Lipid Profiles

Glycolipid H-b2, which is found in spirulina, suppresses pancreatic lipase function in a dose-related manner, lowering postprandial triglyceride (TG) levels. Phycocyanin may exert similar effects [43]. Furthermore, gamma-linolenic acid (GLA), which is mostly produced from linoleic acid (LA) by the enzyme delta-6-desaturase, is abundant in spirulina. Mineral deficiencies, alcohol and tobacco addiction, aging, and serious medical disorders can all limit the functioning of this enzyme, which can result in GLA deficits that exacerbate arterial thickness, high blood pressure, and dyslipidemia [44]. Spirulina also contains vitamin B3, known to improve dyslipidemia [29]. A meta-analysis of 20 studies involving over 1,000 participants found that spirulina significantly improved HDL-C levels, reduced LDL-C, TG levels, and total cholesterol (TC). This improved lipid profile is associated with enhanced insulin sensitivity, particularly in individuals with metabolic disorders [45].

4.5 Supporting Weight Loss

Phenylalanine, an amino acid found in spirulina, promotes the release of cholecystokinin, a hormone that controls energy intake, reduces hunger, and slows stomach emptying. This may result in less food consumption and less appetite, which can help with weight loss [46, 47]. Spirulina has been associated in clinical research with lower body weight, BMI, and waist circumference. In contrast to a placebo group, those using spirulina dropped an average of 3.22 kg over the course of 12 weeks, according to one study [48]. B vitamins and antioxidants, two important vitamins and minerals that support general health and metabolic activities, are abundant in spirulina [49]. Its anti-inflammatory qualities could aid in lowering inflammation, which is frequently linked to weight gain and metabolic problems. Some studies have shown that spirulina supplementation can significantly reduce body fat and improve cholesterol levels, further supporting weight loss efforts.

5. Spirulina and Diabetes Related Complications

5.1 Diabetic Neuropathy

Spirulina platensis has demonstrated potential in managing diabetic neuropathy through several mechanisms. Spirulina is rich in antioxidants, particularly C-phycocyanin, which helps scavenge ROS and protect neuronal cells [19, 50]. It mitigates inflammatory responses by lowering pro-inflammatory cytokines, which can exacerbate nerve damage. Spirulina exhibits antinociceptive effects, reducing pain sensitivity. Animal studies showed that rats treated with Spirulina had lower pain responses in formalin tests [51]. In diabetic rats, oral administration of Spirulina at 500 mg/kg for one month significantly reduced pain scores and hyperglycemia compared to untreated diabetic controls [52]. Another study found that

Spirulina reversed neuropathic pain induced by chronic constriction injury, highlighting its therapeutic potential in managing diabetic neuropathy [53].

5.2 Diabetic Nephropathy

Spirulina influences several specific pathways to manage diabetic nephropathy primarily through its bioactive compounds and their effects on oxidative stress, inflammation, and metabolic regulation. Spirulina has been shown to activate the NRF2 (Nuclear factor erythroid 2-related factor 2) pathway, which plays a crucial role in cellular defense against oxidative stress. An antioxidant enzyme, such as HO-1 (heme oxygenase-1), is upregulated when NRF2 is activated. These enzymes shield renal cells from oxidative stress and elevated glucose levels, which are linked to diabetic nephropathy [54-56]. Spirulina also modulates the NF-kB (Nuclear factor k-B) pathway, which is involved in inflammatory responses. By inhibiting NF-kB activation, spirulina can reduce the indication of inflammatory mediators that contribute to the progression of diabetic nephropathy, thus alleviating inflammation in renal tissues [57, 58].

5.3 Cardiovascular Disease

The antioxidant and anti-inflammatory effects of spirulina protect the cardiovascular system by reducing oxidative damage to blood vessels and improving endothelial function. Spirulina's ability to improve lipid profiles and glycemic control can indirectly contribute to better cardiovascular health by reducing the risk factors associated with diabetes-related heart disease [59]. Spirulina can improve lipid profile by increasing HDL and lowering LDL and VLDL levels. These changes are crucial for reducing the risk of atherosclerosis and other cardiovascular diseases [60]. Studies indicate that spirulina can decrease cholesterol absorption in the intestines and enhance the antioxidant capacity of the blood, leading to improved lipid metabolism [61]. Spirulina may promote vasodilation and improve blood flow by enhancing NO release, which can lead to lower blood pressure [62]. Research has shown that spirulina supplementation can significantly reduce blood pressure in individuals with hypertension, a common issue in diabetic patients [63].

6. How to Incorporate Spirulina into Your Diet

Spirulina is a versatile and nutrient-rich supplement that can be added to various foods and drinks. It comes in powder, tablets or capsules, and flakes, which can be sprinkled on food. Spirulina can be used in smoothies, juices, water, salad dressings, soups, energy bars, and snacks. To make smoothies, combine one banana, one cup spinach, one cup frozen berries, one teaspoon spirulina powder, and one cup almond milk with one or two teaspoons of spirulina powder added. For juices, mix Spirulina powder into fresh vegetable or fruit juices, starting with a small amount (1/2 teaspoon) and gradually increasing to your taste preference. Stir Spirulina powder into a glass of water for a quick and simple option. For salad dressings, add 1-2 teaspoons of Spirulina powder to homemade dressings, stir it into soups after cooking to preserve its nutrients, and use it in energy bars or protein balls. For baked goods, add Spirulina powder to the batter of muffins, pancakes, or bread, using a small amount to avoid altering the taste too much. Mix 1 teaspoon of Spirulina powder into a cup of Greek yogurt and top with honey and granola. To incorporate Spirulina into your diet, start slowly, balance flavours with sweet or citrusy flavours, stay hydrated by drinking plenty of water throughout the day, and maintain consistency. To ensure safety and quality, purchase Spirulina from reputable suppliers, store it in a cool, dark place, and consult a healthcare provider if you have any health conditions or are taking medications [64, 65].

7. Precautions and Considerations

Spirulina platensis is a supplement that has potential benefits for managing diabetes mellitus. But before taking Spirulina, it is imperative to speak with a healthcare professional, particularly if you are suffering from diabetes, as they may offer tailored guidance based on your medical history and current prescriptions. Regular monitoring of blood glucose levels is crucial to ensure the supplement does not adversely affect your diabetes management. Some individuals may be allergic to Spirulina or other blue-green algae, which can cause symptoms like itching, rash, or breathing difficulties. It also contains iodine, which can be problematic for people with iodine sensitivity or thyroid issues [66]. Autoimmune conditions may be affected by Spirulina’s stimulation of the immune system, which may be harmful to those with autoimmune diseases like lupus, multiple sclerosis, or rheumatoid arthritis. Phenylketonuria (PKU) individuals should avoid Spirulina due to its phenylalanine content, which they cannot metabolize properly [67]. Spirulina can also interact with antidiabetic medications, potentially leading to hypoglycemia. To ensure the safety and effectiveness of Spirulina, it is recommended to start with a low dose and gradually increase it, monitoring for any adverse effects. Common doses range from 1 to 8 grams per day. In terms of diet and lifestyle, it is important to use Spirulina as a supplement rather than a substitute for a balanced diet and to drink plenty of water to avoid dehydration [68]. Pregnant or breastfeeding women should consult their healthcare provider before using Spirulina. Potential side effects include digestive issues, and an adjustment period may occur as the body adjusts to the supplement [69].

8. Conclusion

Spirulina platensis offers a promising complementary approach to managing DM. Its rich nutritional profile, including vitamins, essential fatty acids, proteins, and minerals positions it as a potent functional food with various health benefits. Research highlights that it lowers blood glucose level, improves insulin sensitivity, reduces inflammation, enhances lipid profiles, supports weight loss, and mitigates diabetes-related complications such as neuropathy, nephropathy, and cardiovascular disease. These multifaceted benefits are primarily attributed to its antioxidant, anti-inflammatory, and metabolic regulatory properties. Incorporating Spirulina into the diet can be easily achieved through various forms, such as powders, tablets, or flakes, and can be added to smoothies, juices, soups, and baked goods. However, it is crucial to approach its use with caution, especially for individuals with specific health conditions. While Spirulina shows significant promise, it should be used as a supplement to, rather than a replacement for, conventional diabetes treatments and a balanced diet. Ongoing research and clinical studies will further elucidate its mechanisms and long-term benefits, solidifying its role in the comprehensive management of DM.

Conflict of interest

There is no conflict of interest.

Author’s Contribution

Concept and execution Sumit Dutta, Cinon Borah
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