The nutritional value of Spirulina and utilization research

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Author contributions

Yuan-Yuan Wang conceived the structure of this article and wrote the paper. Bao-Liang Xu collected data and analyzed relevant studies. Chun-Ming Dong and Yan-Yan Sun directed the drawing and critically reviewed the article. All authors read and approved the final manuscript.

Competing interests

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Abbreviations

ACE, angiotensin-converting enzyme.

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Abstract

With the development of modern society, the demand for nutrition, health, and food safety among people is also increasing. More and more consumers are connecting their diet to a healthy lifestyle in order to reduce the occurrence of chronic diseases. Spirulina, known as green ginseng, is one of the most productive microalgae with high output value. It is considered as one of the most ideal dietary supplements due to its unique nutritional and health benefits. The main components of spirulina include protein, fat, vitamins, chlorophyll, and minerals. The protein content is particularly high, ranging from 60–70%. Spirulina can be used as a natural nutritional supplement, providing various essential nutrients needed by the body. Apart from being a nutritional supplement, spirulina is also widely utilized in the food, medicine, and cosmetics industries. Spirulina powder can be added to various foods such as bread, cakes, and biscuits to enhance their nutritional value. Spirulina extract can also be used in the production of healthcare and beauty products. Furthermore, the antioxidant and immune-boosting effects of spirulina make it a promising natural medicine for research in the treatment of cancer and liver disease. This paper aims to provide comprehensive information on the nutritional composition, secondary metabolites, and biological activities of spirulina, thereby contributing to the spirulina industry.

Keywords: Spirulina; Nutrition facts; Bioactive substances

Introduction

Spirulina is a freshwater algae that originates from the natural environment and is filled with wonders, mysteries, and value. It has been considered a valuable food and medicine by various civilizations throughout history and was widely consumed by Native Americans, for instance. With the advancements in modern science and technology and the growing focus on health and nutrition, spirulina has also gained prominence as a high-profile nutritional supplement and pharmaceutical raw material. Spirulina is abundant in a variety of nutrients, including high-quality protein, various vitamins, and minerals, and plays a crucial role in human health and the prevention of various diseases. Additionally, spirulina finds extensive applications in the food, medicine, cosmetics, and other industries, indicating its broad prospects [1]. To meet the demand for spirulina, there are various cultivation methods available, such as natural culture, artificial culture, and continuous culture. Among these, continuous culture is a commonly used method that enhances the yield and growth rate of spirulina. Furthermore, methods like ultrasonic cell wall breaking and enzymatic hydrolysis are often employed to extract the active components in spirulina [2]. Research has demonstrated that ultrasonic breaking of cell walls is an effective extraction method that preserves the nutrients and antioxidant components in algal cells [3–5]. Apart from its use as food and pharmaceutical ingredients, spirulina has several potential applications. In recent years, researchers have discovered that spirulina metabolites can serve as raw materials for biofuels and biomaterials, offering high economic value [6, 7]. Additionally, studies have shown that spirulina can be utilized for purifying wastewater, soil, and air to address environmental pollution concerns. Over the past two decades, significant progress has been made in understanding the nutritional value and applications of spirulina, with researchers extensively exploring its nutritional components, cultivation methods, extraction techniques, and other aspects. Numerous studies have highlighted the immense potential of spirulina in promoting health and treating ailments [8]. In recent years, there has been a growing focus on using spirulina as a raw material for biofuels and biomaterials, with researchers striving to maximize its value, thereby catalyzing a surge in green industries centered around microalgae. In this context, this article aims to delve into the nutritional value of spirulina and its research applications in fields like food, medicine, cosmetics, treatment, biofuels, etc., providing an overview of the current research status and future prospects of spirulina [9, 10]. In an era where significant advancements have been made in this research field, examining the future development and application of spirulina not only deepens our understanding of its nutritional value and potential applications but also emphasizes the need for more healthy, green, and sustainable natural resources like spirulina in terms of health, medicine, and energy.

Analysis of nutritional components of spirulina

Protein

Phycobilin is the primary protein found in spirulina, consisting of three proteins: phycocyanin, allophycocyanin, and phycoglobin. Leonard and Compere determined that the protein content in spirulina was approximately 50% of its dry weight [11]. Phycocyanin, the fundamental building block of phycobilin, is composed of α and β chain globulin subunit monomers that polymerize to form various structures, including trimers and hexamers. It exhibits light absorption capabilities within the range of 550–630 nm, with a maximum absorption wavelength of 610–620 nm and a molecular mass of 44–260 kDa. The α subunit of phycocyanin contains 2 cysteine and 2 methionine residues, with a molecular weight of 12-19 KDa. On the other hand, the β subunit contains 3 cysteine and 5 methionine residues, with a molecular mass of 14–21 KDa. Each subunit consists of 160–180 amino acid sequences. The phycocyanin molecule (Figure 1) possesses three chromophore groups attached to

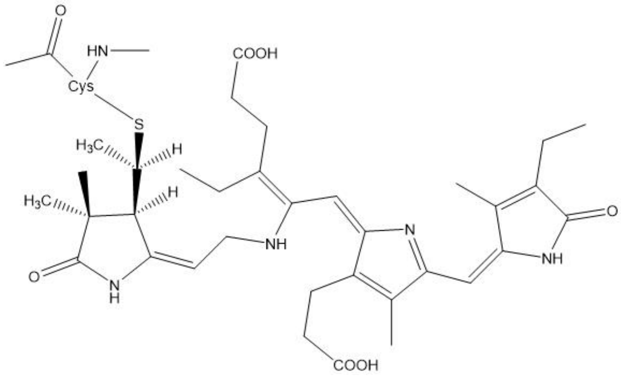

Figure 1 The molecular structure of phycocyanin

the alpha-84, beta-84, and beta-155 positions, respectively. Phycocyanin has a molecular weight of 44 kDa, an isoelectric point of 4.3, and a maximum absorption wavelength of 620 nm. Furthermore, studies have demonstrated that the amino acid sequences of α subunits (or β subunits) of phycocyanin from different species exhibit high homology, and their crystal structures are also remarkably similar [12]. Phycocyanin is a protein with diverse physiological activities, primarily promoting protein absorption and exhibiting antioxidant, anti-tumor, and anti-inflammatory properties. Additionally, phycocyanin effectively dissipates heat and can be utilized as a natural pigment in food and cosmetics [13, 14].

Polysaccharides

The polysaccharide of Spirulina platensis is a complex heteropoly sugar, with a sulfate content of about 6%. It is primarily composed of D-mannose, D-glucose, D-galactose, L-rhamnose, and glucuronic acid, among others [15]. These components make up approximately 14% to 16% of the dry weight of Spirulina. Additionally, it contains small amounts of xylose, arabinose, galactose, ribose, fucose, galacturonic acid, and other monosaccharides. Spirulina polysaccharides have the ability to balance the antioxidant system and eliminate free radicals [16]. As a result, they can inhibit oxidative damage in the body, increase serum insulin levels, enhance the activity of superoxide dismutase (SOD), and reduce the levels of MDA, thereby achieving the desired effect of lowering blood sugar [17].

Lipids

Spirulina is a type of low-fat algae, with a fat content of approximately 6% to 9%. It contains almost all the essential amino acids and many important unsaturated fatty acids that are necessary for the human body. These unsaturated fatty acids include gamma-linolenic acid, docosahexaenoic acid, and eicosapentaenoic acid. Notably, Spirulina is the only plant known to be rich in gamma-linolenic acid among autotrophs [18]. Research has shown that gamma-linolenic acid has various functions, such as reducing blood lipid levels, regulating blood pressure, and lowering cholesterol. It plays a significant role in the prevention and treatment of cardiovascular diseases, which has garnered global attention [19, 20]. Additionally, gamma-linolenic acid possesses antioxidant properties and can contribute to skin whitening and delaying the effects of skin aging.

Chlorophyll

The chlorophyll content of Marine Spirulina surpasses that of terrestrial plants. Chlorophyll is a natural bioactive substance that serves not only as a pigment and deodorant but also as a treatment for various medical conditions [21]. It is even utilized in the production of different types of toothpaste [22]. Chlorophyll a, typically appearing as a dark green or dark green oily or paste, consists of a magnesium and nitrogen on four pyrrole rings. It is the general term for green pigments with porphyrins as their structure [23]. While insoluble in water, it easily dissolves in ethanol, acetone, and dimethyl sulphone, making it a natural and non-toxic fat-soluble pigment [24, 25]. Due to its structure, chlorophyll a is unstable and sensitive to light, heat, acids, and bases. The content of chlorophyll a in Spirulina is approximately 1% to 2%, which can serve as an indicator for evaluating the biomass and yield of algae. Moreover, similar to heme, chlorophyll possesses remarkable physiological functions and holds promising applications in medicine, food, cosmetics, and other industries [26–28].

Function of bioactive substances in Spirulina

Spirulina is a nutrient-rich algae that serves as a natural superfood and synthesizes numerous biologically active secondary metabolites during its growth. These secondary metabolites exhibit various effects, including antioxidation, anti-inflammatory properties, immune regulation, and anti-tumor activity. As a result, they hold significant potential for applications in medicine, healthcare products, cosmetics, and other industries. Table 1 presents the identified secondary metabolites of spirulina thus far.

Spirulina, a green algae known for its remarkably high protein content, is regarded as a promising "cell factory" due to its potential as a nutrient source for organisms and as a producer of bioactive peptides with therapeutic properties. In recent years, numerous studies have demonstrated that certain peptides released through hydrolysis exhibit significant biological activities, including blood pressure reduction, antioxidation, anti-inflammation, anti-cancer effects, and immune regulation. The biological activity and mechanisms of spirulina proteolytic peptides have been extensively documented in various literature sources, as outlined in Table 2.

Antioxidant activity

Oxidative stress refers to an imbalance between oxidation and anti-oxidation within the body. This condition arises from the excessive accumulation of reactive oxygen species, including superoxide anion ($\cdot O^{2-}$), hydrogen peroxide (H_2O_2), hydroxyl group (-OH), and others. Cell peroxidation leads to the formation of malondialdehyde (MDA), which alters cell membrane permeability and causes cellular damage. Oxidative stress serves as a primary contributor to metabolic disorders, cardiovascular diseases, inflammation, liver injury, and various other ailments. Many chronic and age-related diseases, such as hypertension, hyperlipidemia, diabetes, Parkinson's disease, and Alzheimer's disease, stem from oxidative stress. Spirulina, due to its abundance of bioactive ingredients like phycocyanin, carotenoids, and algal polysaccharides, can enhance the body's antioxidant capacity [72, 73]. It aids in preventing lipid peroxidation, DNA damage, and the removal of free radicals.

At present, numerous studies have focused on the antioxidant effect of spirulina. Spirulina exhibits robust antioxidant enzyme activity, which effectively inhibits intracellular lipid peroxidation and DNA damage, while also efficiently eliminating free radicals [74]. Furthermore, spirulina demonstrates specific protective effects on the nervous system and kidneys of animals by reducing oxidative stress [75]. Given its high antioxidant activity, spirulina is considered a promising agent for the prevention and treatment of cardiovascular diseases [76, 77]. Despite limited clinical studies in humans, spirulina's potent antioxidant capacity enables it to effectively treat chronic obstructive pulmonary disease and skeletal muscle damage caused by intense exercise [78, 79].

However, there are various methods available for detecting antioxidant systems, with the DPPH free radical clearance assay being the most commonly used. Ding Xiaomei et al. extracted polysaccharide from Spirulina platensis using conditions of pH = 8, temperature of 90°C, solid-liquid ratio of 1:40, and an extraction time of 2 hours [80]. The resulting IC50 value of 0.463 g/L confirmed the DPPH free radical scavenging ability. Yu Chengming et al. conducted a study that demonstrated a significant scavenging effect of DPPH free radicals when the phycocyanin concentration was 8 g/L, reaching a scavenging rate of 89.95%, which was superior to VC and indicated the excellent antioxidant capacity of phycocyanin [81]. Zhang Yifang et al. purified spirulina algal protein and through antioxidant experiments, proved its superior scavenging ability compared to VC [82]. The results highlighted the strong antioxidant ability of Spirulina spirulina's algin. Li Ling et al. conducted in vitro experiments to determine the scavenging effects of polysaccharides from Spirulina and Spirulina on -OH and $\cdot O^{2-}$ [83]. They also used a lipid peroxidation model induced by FeSO4 and thiobarbituric acid spectrophotometry to study the anti-lipid peroxidation and oxidative damage properties of these polysaccharides. The findings revealed that a concentration of 0.15 $mg \cdot mL^{-1}$ of polysaccharides from Spirulina platensis effectively removed oxygen free radicals and inhibited DNA oxidation and oxidative damage.

Table 1 Secondary metabolites of Spirulina and their effects

Secondary metabolite	Effect	Reference
Spirulina phycocyanin	A blue protein with antioxidant and anti-inflammatory effects.	[29–31]
Spirulina phycocyanin	A red pigment with strong antioxidant effects that helps protect cells from free radical damage.	[32–33]
Polysaccharide	Spirulina contains a variety of polysaccharides, such as glycans, glycoproteins and peptides, which have immunomodulatory, antiviral and anti-tumor effects.	[34–36]
Spirulinamidase	A colored protein that plays an important role in the immune system.	[37]
Spirulina flavonoids	It has strong antioxidant and anti-inflammatory effects.	[38–39]
Lithium ion	Spirulina contains a small amount of lithium ions, which have anti-depressant and nerve calming effects.	[40]
Spirulina protein peptide	A protein containing a variety of amino acids that has antibacterial, antiviral and anti-tumor effects.	[41–42]
Docosahexaenoic acid	It is a kind of polyunsaturated fatty acid with many effects such as anti-cardiovascular disease, anti-cancer, anti-diabetes and lowering cholesterol.	[43]
Carotenoid	Carotenoids such as beta-carotene, xanthin, and orangetin, which are found in spirulina, can improve the function of the human immune system through their antioxidant and anti-inflammatory effects.	[44]
Spirulina sheath amine alcohol	It has various bioactive functions such as antioxidant, immune regulation, hypoglycemic, lipid-lowering, anti-inflammatory, etc.	[45]

Table 2 Biological activity of Spirulina-derived peptides and possible mechanism of action

Biological activity	Mechanism of action	Reference
Antioxidant activity	Scavenging free radicals; It can obviously reduce the oxidative hemolysis of erythrocyte caused by azodiisobuamidine hydrochloride, protect erythrocytes, reduce the production of malondialdehyde in erythrocytes, and improve the enzyme activity of superoxide dismutase, catalase and glutathione peroxidase.	[46–47]
Anti-inflammatory activity	Inhibition of endothelial cell inflammation and anti-atherosclerosis activity, inhibition of reactive oxygen species (ROS), interleukin-8 (IL-8), interleukin-6 (IL-6). And resistance to inflammation of different tissues (hepatitis, arthritis, colitis, brain damage).	[48–53]
Improve lipid metabolism disorders	It can reduce the levels of triglyceride (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in serum and liver, increase the levels of medium and high density lipoprotein cholesterol in serum and liver, and thus regulate the expression of genes related to lipid metabolism.	[54]
Cholesterol-lowering activity	Lower serum cholesterol.	[55]
Cholesterol-lowering and antioxidant activity	Lower serum cholesterol, triglycerides, low density lipoprotein cholesterol, alanine aminotransferase and aspartate aminotransferase.	[56]
Anti-obesity activity	The expression of genes involved in regulating lipid metabolism.	[57]
Hypoglycemic activity	Activation of insulin signaling pathway and glucokinase expression. Improve tissue sensitivity to insulin regulation. Relieve diabetic nephropathy and reduce oxidative stress in urine and kidneys.	[58–60]
Antidiabetic activity	Inhibition of dipeptidyl peptidase IV (DPP-IV) activity.	[61]
Hypotensive activity	Inhibit angiotensin converting enzyme activity.	[62–68]
Anti-photoaging activity of skin	Reduce malondialdehvde (MDA) content, improve the activity of SOD, superoxide dismutase (CAT) and glutathione peroxidaseGSH-Px. Reduce the expression of MMP-I and MMP-3.	[69]
Antiallergic activity	Inhibition of mast cell degranulation, inhibition of antigen-stimulated RBL-2H3 cell amino hexatase release and cytokine production.	[70]
Anticancer activity	Remove superoxide anion and hydroxyl radical, improve cell oxidative pressure. It showed strong inhibitory effect on tumor cells (HepG-2, MCF-7, SGC-7901, A549, HT-29).	[71]

Anti-inflammatory activity

The inflammatory response is a defensive reaction that occurs following tissue injury or the invasion of foreign substances. It serves as the foundation for the development of numerous diseases. Chronic inflammation, often referred to as the "precursor" of cancer, is found to be present in 25% of tumors during their formation and progression, according to epidemiological investigations. Prolonged inflammation poses a threat to cardiovascular health, leading to conditions such as atherosclerosis and thrombosis, ultimately resulting in heart disease [84]. Additionally, it damages nerve tissue, increasing the risk of Alzheimer's disease. Severe inflammatory reactions can spread from localized inflammatory sites, causing infections that may progress to sepsis and eventually lead to death. Currently, commonly used clinical anti-inflammatory drugs often come with significant side effects, including damage to human tissues and organs, as well as immunosuppression. Therefore, the development of effective anti-inflammatory drugs with minimal toxic side effects is of utmost importance [85]. Spirulina is abundant in bioactive substances such as phycocyanin, spirulina polysaccharide, eicosapentaenoic acid, SOD, vitamins, and flavonoids. It has become a prominent research focus in the medical field worldwide. The therapeutic potential of spirulina proteolytic peptides in treating inflammation and related diseases has been extensively reported. Peptides derived from macrospirulina, such as LDAVNR, MMLDF, and phycocyanin, have demonstrated anti-inflammatory effects in vitro or in animal models [86]. Phycocyanin peptides exhibit diverse anti-inflammatory effects, including scavenging various oxygen free radicals, inhibiting lipid peroxidation, suppressing amino acid metabolism, inhibiting histamine release in mast cells, and reducing TNF-α release [87–90].

LEDON et al. investigated the anti-inflammatory response of phycocyanin, an extract derived from spirulina, and observed changes in the concentration of prostaglandin E2 (PGE2) and the activity of phospholipase A2 (PLA2) in the presence of phycocyanin [91]. The results demonstrated that phycocyanin exhibited a certain degree of anti-inflammatory activity due to its inhibitory effect on PGE2 production and PLA2 activity. Guzman S et al. discovered that extracts of two crude polysaccharides extracted from spirulina exhibited superior anti-inflammatory activity compared to indomethacin [92]. Matsui MS et al. conducted in vitro tests and found that polysaccharide from Spirulina algina could inhibit the formation of erythema caused by strong stimulation [93]. In vitro experiments revealed that the polysaccharide could inhibit the aggregation and adhesion of haemophilic lymphocytes. Therefore, it is considered a topical anti-inflammatory drug. Chen Zhongwei et al. established an inflammation model in rats by inducing ear swelling using xylene [94]. Dexamethasone was used as a control, and ear swelling in mice served as an experimental indicator. The results showed that the ear swelling inhibition rate of the 0.3% spirulina group was better than that of the positive control drugs, and dexamethasone could cause atrophy of the liver, spleen, and thymus in rats. Spirulina exhibited a better anti-inflammatory effect than dexamethasone and had no adverse effects on liver, kidney, thymus, or spleen indices.

Hypoglycemic activity

Under normal circumstances, the blood sugar level in the human body is maintained at a dynamic balance between 80–120 mg/dL. Hyperglycemia can lead to various chronic complications, including cerebral infarction, myocardial infarction, blindness, kidney failure, and diabetes. Compared to conventional hypoglycemic drugs, spirulina, as a natural plant, has a better hypoglycemic effect and lower toxicity [95]. Researchers have discovered that spirulina primarily affects glucose glycogen, mainly by promoting liver glycogen synthesis or inhibiting its degradation. Through the observation of spirulina's hypoglycemic effect on diabetic rats, Hozayen WG et al. found that spirulina can inhibit hexokinase activity in liver cells, enhance glucose-6-phosphatase activity in muscles, and reduce glucose absorption in the intestine [96]. This improves insulin's hypoglycemic activity and reduces liver glycogen synthesis, promoting glucose utilization by peripheral tissues. OU et al. studied the effect of phycocyanin in spirulina on diabetes induced by tetrafluoracil and discussed its related molecular mechanism [97]. It was demonstrated that phycocyanin may activate the insulin signaling pathway and protein kinase in the pancreas, liver, and pancreas, promoting liver glycogen degradation and reducing blood glucose levels. Setyaningsih et al. measured the anti-hyperglycemic activity of rats by feeding them biological substances containing spirulina and phycocyanin [98]. The results showed that these substances reduced blood sugar levels in mice. Qi Qinghua et al. used hydrochloric acid precipitation technology to separate and purify polysaccharides and proteins from spirulina [99]. They found that the isolated polysaccharide from Spirulina had a significant effect on hyperglycemia symptoms in diabetic mice induced by alloxouracil, suggesting its potential as a new type of functional food.

In addition, for sprinters, spirulina polysaccharides can be appropriately consumed to reduce blood sugar and blood lipids, improve the body's antioxidant capacity, and enhance its anti-inflammatory capacity, thereby reducing exercise fatigue. The results have demonstrated that the administration of polysaccharide derived from spirulina platensis significantly improves hyperglycemia in rats, effectively counteracts liver glycogenolysis caused by adrenaline, and inhibits glucose absorption in the intestines of mice. Moreover, spirulina polysaccharides have been found to significantly alleviate hyperglycemia symptoms in mice with alloxouracil-induced diabetes and elevate their antioxidant levels. It is crucial for sprinters to closely monitor their blood sugar and blood lipid levels. Based on the analysis of experimental findings, polysaccharide from Spirulina algina can enhance the body's sugar absorption, increase insulin sensitivity, and consequently reduce the rate of glucose absorption in muscle and adipose tissue. Additionally, polysaccharide from Spirulina platensis can regulate serum fat composition, decrease the expression of sterol regulatory element binding protein in liver tissue, and promote the synthesis of damaged liver mitochondria, thereby effectively enhancing cell regeneration and exerting an anti-fatigue effect.

Hypotensive activity

Hypertension is a systemic condition characterized by elevated arterial pressure and accompanied by functional or organic changes in the heart, blood vessels, brain, and kidneys, all of which are caused by persistent high blood pressure. The most commonly used synthetic antihypertensive drugs, such as captopril, enalapril, acapril, and Lisinopril, primarily work by inhibiting the angiotensin-converting enzyme (ACE). Inhibiting ACE leads to a decrease in angiotensin II and an increase in bradykinin, a vasodilator, which ultimately lowers blood pressure. However, while these synthetic drugs effectively lower blood pressure, they also come with certain adverse reactions, such as dry cough, taste disturbance, rash, and so on [100, 101]. Therefore, the development of safe and effective antihypertensive drugs holds great significance for the prevention and treatment of hypertension. Blood pressure-lowering peptides derived from dietary proteins are considered safer alternatives to synthetic antihypertensive drugs. For instance, the antihypertensive effect of active peptides from seaweed may be attributed to the inhibition of ACE and renin. The renin-angiotensin system plays a crucial role in regulating blood pressure. One mechanism involves inhibiting angiotensin I, which is produced from angiotensinogen, by using renin. The other mechanism involves competitively binding the active site of ACE to prevent the conversion of angiotensin I to angiotensin II, thereby inhibiting kinin hydrolysis and preventing vasoconstriction [102]. ROJAS V et al. demonstrated that active peptides with a molecular weight less than 2 ku exhibited the highest ACE inhibitory activity [103]. Liu Lichuang et al. found that pepsin hydrolysate, trypsin hydrolysate, and a complex hydrolysate of spirulina protein significantly inhibited the increase in blood pressure in essential hypertensive rats (SHR) [104]. Additionally, trypsin and the complex enzyme hydrolysate showed promising therapeutic effects on hypertension. However, the administration of spirulina protein alone did not have a significant impact on SHR hypertension, indicating that the peptides obtained under the three hydrolysis conditions had notable antihypertensive effects.

Anticancer activity

The progression of cancer is a gradual process, making it suitable for the utilization of natural, synthetic, or biological substances to reverse, inhibit, or prevent tumor development and their transformation into malignant cancers, as well as to prevent the occurrence of invasive or metastatic diseases. Phycocyanin, an essential component of spirulina, is water-soluble, non-toxic, and exhibits a certain level of stability. It has been extensively studied and applied in various research studies. Bobbili et al. and Fan Min discovered that phycocyanin can eliminate free radicals and induce apoptosis in AK-5 tumor cells and human cervical cancer Hela cells, respectively [105, 106]. Additionally, it has been observed that polysaccharide derived from Spirulina platensis can inhibit the growth of S180 transplanted tumors in mice, delay the cell division cycle of tumor cells, and induce apoptosis [107, 108]. Furthermore, studies have demonstrated that high concentrations of phycocyanin can induce apoptosis in lung adenocarcinoma cells [109]. MAHMOUD et al. conducted research that showed spirulina to have significant tumor regression effects, improved survival rates, inhibition of A-fetoprotein tumor markers, improved liver biomarkers, and reduced hepatoma pathology in advanced hepatocellular carcinoma [110]. These findings suggest that spirulina holds promise as a potential treatment for hepatocellular carcinoma.

Immune regulation

The occurrence and development of diabetes, senile diseases, and malignant tumors are closely related to the immune disorder of the body. With the in-depth study of the immune mechanism and biological effect of spirulina, the application of spirulina in the prevention of immune disorder diseases has a promising future. Spirulina contains various active ingredients that can enhance the body's immune function, such as carotenoids, phycocyanin, spirulina polysaccharides, and gamma-linolenic acid, which can enhance immune function [111, 112]. Its mechanism primarily involves enhancing the proliferation of bone marrow cells and promoting the formation of immune effector cells like macrophages, T cells, and B cells. Additionally, phycocyanin can promote phytohemagglutinin to stimulate lymphocyte transformation and improve lymphocyte activity [113, 114]. Lv Xiaohua et al. reported that polysaccharide from Spirulina algina can enhance the proliferation ability of peripheral blood monocytes in patients with chronic hepatitis B and produce immunomodulatory effects [115]. According to the study conducted by Xu Jiaohong et al., polysaccharide from Spirulina platensis can significantly increase the number of antibody-producing cells and the activity of NK cells [116]. The results suggest that polysaccharide from Spirulina platensis can enhance the humoral immunity and NK cell activity of mice. Phycocyanin can enhance immune function by primarily enhancing the proliferation of bone marrow cells and promoting the formation of immune effector cells like macrophages, T cells, and B cells. Additionally, phycocyanin can promote phytohemagglutinin to stimulate lymphocyte transformation and improve lymphocyte activity [117].

Lose Weight

Algae is a beneficial option for weight loss due to its low fat, calorie, and fiber content. In the ancient "food therapy Materia Medica", kelp was noted to "reduce Qi and help slim down". Algae is rich in dietary fiber, which can reduce the intake of energy in the body, leading to a decline in the digestion and absorption of nutrients in the intestines. Additionally, it promotes gastrointestinal peristalsis, eliminating harmful substances from the body and maintaining intestinal health [118]. Spirulina is abundant in phenylamino acids, which can influence the brain to control appetite, balance cravings, effectively regulate body fat content, and alleviate hunger caused by other weight loss methods. Spirulina can reduce the infiltration of macrophages into visceral fat, prevent the accumulation of liver fat, decrease oxidative stress, improve insulin sensitivity, and promote satiety. Research has demonstrated that moderate supplementation of spirulina can enhance apolipoprotein A1 levels and reduce apolipoprotein B, aiding in weight loss and lowering Body Mass Index. Spirulina achieves weight loss by reducing the permeability of macrophages into visceral fat and preventing the accumulation of liver fat and oxidative stress [119].

Development, utilization and application prospect of spirulina

Application in dairy products

Phycocyanin, a water-soluble protein, has a positive impact on reducing water solubility and increasing the firmness of yogurt. When spirulina powder is added during the yogurt-making process, it results in a curd-like and firm yogurt with the distinct aroma of spirulina and frankincense, and a vibrant green color [120]. To make cheese, it is recommended to prepare the soft cheese beforehand, and then add 1% spirulina powder while freezing and adding salt. Stir the mixture and store it in the refrigerator. Spirulina can enhance the protein and beta-carotene content of soft cheese, reduce moisture, and prolong its shelf life.

The application in flour products

Algae can be ground into powder or made into a paste, serving as a raw material in food production to enhance nutritional value. Additionally, algae possesses strong water absorption, gelling, thickening, and film-forming abilities, which can improve the processing quality of flour-based products. In a study conducted by Mostolizadeh et al., 0.25% to 1% spirulina powder was added to pasta, resulting in a significant increase in essential amino acids and unsaturated fatty acids in the food [121]. Pasta with 0.25% spirulina powder exhibited favorable microbial characteristics and nutritional value. It enhances satiety and is considered a sustainable food option.

Application in animal feed

Incorporating spirulina into animal feed can enhance the nutritional value of food, meeting the dietary requirements of humans. Spirulina shows potential as a protein source in poultry, pork production, and aquaculture. According to the study conducted by ANDREWS et al., the addition of 1% to 4% spirulina powder to the diet of Labeo rohita resulted in a significant increase in the total number of red blood cells, hemoglobin, and white blood cells [122]. Furthermore, serum total protein, albumin, globulin, and respiratory burst activity were also significantly elevated.

A significant number of application studies on various aquaculture animals have demonstrated that spirulina powder not only showcases its high nutritional value but also possesses a range of functional effects on aquatic animals. Spirulina's phycocyanin, polysaccharide, and beta-carotene content can enhance the immunity of cultured animals, while the polysaccharides found in microalgae can bolster the immune response, making it suitable for aquatic feed. This, in turn, aids in enhancing the disease resistance of farmed animals.

Currently, a significant amount of spirulina powder has been utilized in food or aquatic feed in foreign countries. However, the application of spirulina powder in aquatic feed in China is still in a relatively early stage, and the potential of spirulina resources has not been fully realized. Therefore, it is necessary to conduct more comprehensive and in-depth systematic research and enhance the dissemination of research results. This will enable aquaculture operators to gain a better understanding of the superiority of spirulina.

The application of spirulina in medicine

Manufacturing drug carriers. Spirulina, being a natural porous carrier, has the potential to be utilized in the production of drug carriers [123]. Its cell surface contains a significant amount of cell wall proteins, polysaccharides, amino acids, fatty acids, and other substances, which contribute to its strong drug adsorption capacity. By altering parameters such as particle size, surface properties, and pore size, the drug carrier made from spirulina can effectively control the dissolution rate and release behavior of the drug [124]. Furthermore, as a drug carrier, spirulina can stabilize the biochemical and chemical properties of drugs, prolong their residence time in the body, and enhance the effectiveness of drug therapy.

For liver disease treatment. Spirulina is abundant in nutrients such as lutein and beta-carotene, which possess antioxidant and anti-inflammatory properties. These nutrients can mitigate the detrimental effects of oxidative damage and inflammation on liver cells, thus safeguarding their well-being [125]. Additionally, the diverse array of nutrients and bioactive substances found in spirulina can help prevent liver complications like hepatitis and cirrhosis, promoting overall liver health [126]. Studies have indicated that polysaccharides extracted from spirulina exhibit inhibitory effects on the replication of the hepatitis C virus, suggesting their potential as a treatment for hepatitis C.

The application of spirulina in cosmetics

Spirulina is enriched with a variety of antioxidant substances, including carotenoids and vitamin E, which effectively combat free radicals, safeguard the skin against environmental pollution and oxidative damage, and possess anti-aging properties. Furthermore, spirulina is abundant in natural moisturizing factors and polysaccharides, which aid in maintaining skin moisture and promoting a soft and supple complexion. The peptides present in spirulina stimulate collagen synthesis, resulting in firmer and more elastic skin. Additionally, the sulfides found in spirulina can alleviate skin inflammation and discomfort, exhibiting certain anti-inflammatory effects. Moreover, spirulina contains natural whitening ingredients like lutein and carotenoids, which effectively inhibit melanin synthesis, reducing the appearance of dark spots and dullness [127].

The moisturizing rate within 24 hours was nearly equivalent to that of the body lotion containing 2% polysaccharide mass fraction and 5% glycerol solution. The SPF of the moisturizing lotion, with a polysaccharide content ranging from 0.3% to 1.0%, was found to be 10 to 15 at the wavelength of 280 to 320 nm, indicating its effectiveness in providing protection against UV rays.

Application of spirulina in health care products

Enhance immunity. Spirulina comprises a diverse range of nutrients and antioxidants that can aid in boosting the body's immune system, strengthening its resilience, and safeguarding against infections and diseases.

Regulating blood lipids and blood sugar. The assortment of nutrients found in spirulina has the potential to lower blood lipids and blood sugar levels, thereby acting as a preventive measure against chronic conditions like cardiovascular disease and diabetes.

Improve the digestive system. Spirulina is abundant in dietary fiber, probiotics, and other substances that can stimulate intestinal motility, facilitate regular bowel movements, enhance abdominal comfort, and optimize the functioning of the digestive system.

Anti-fatigue. Spirulina encompasses a diverse array of vitamins and antioxidants that can supply the body with essential nutrients and energy, thereby assisting in the reduction of fatigue and stress levels.

Beauty. Spirulina comprises a range of beauty-enhancing nutrients, including lutein and beta-carotene, that contribute to the promotion of healthy skin, hair, and nails, ultimately enhancing their appearance and maintaining their overall well-being.

In general, spirulina has a range of effects in healthcare products, which can provide comprehensive protection and maintenance for people's health.

Spirulina can thrive in intense light and high-temperature environments, exhibiting a high growth rate, abundant oil yield, and remarkable adaptability. As a result, it is widely recognized as a promising biomass energy source.

Spirulina in the application of biofuels

Biodiesel production. Spirulina contains a significant amount of oil, with approximately 25 grams of oil extractable from every 100 grams of spirulina [128]. These oils are abundant in unsaturated fatty acids, which can be extracted and transformed into biodiesel for energy, making them promising raw materials for biodiesel production.

Production of biogas. When spirulina undergoes photosynthesis in the presence of light, it generates a substantial quantity of oxygen and hydrogen [129]. These gases can be harnessed and utilized as clean energy sources in various devices, including fuel cells. Additionally, under anaerobic conditions, spirulina can be converted into biogas, serving as a viable alternative to natural gas [130].

Reduce greenhouse gas emissions. Spirulina is a highly efficient absorber of carbon dioxide. It possesses the capability to utilize carbon sources for growth and effectively sequester a substantial amount of carbon for the production of biodiesel and biogas. These fuels exhibit lower carbon emissions and contribute to the reduction of environmental pollution and global climate change. In summary, spirulina holds a broad range of potential applications in biofuels and can effectively address energy and environmental challenges (Figure 2) .

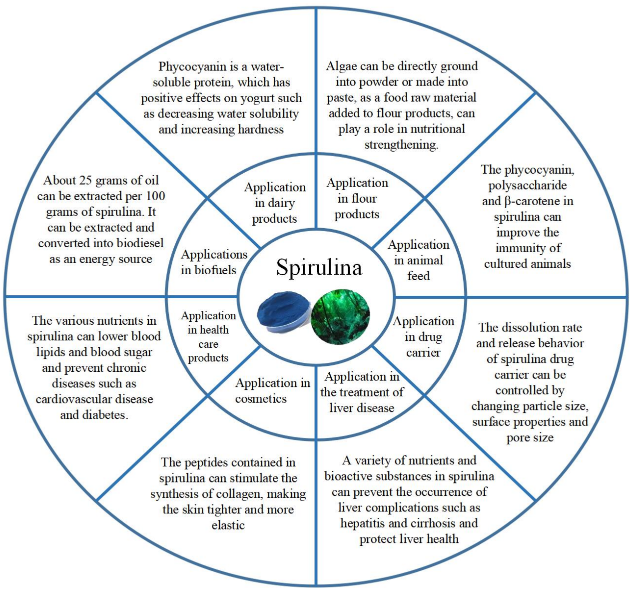

Figure 2 Bioactive substances and their applications

Prospect

As a 21st century "superfood", Spirulina is widely used as a natural food supplement worldwide. It has a long history of being safe and non-toxic to consume. It is a staple in the daily diets of African and Native American populations. Spirulina is abundant in nutrients and is highly safe. It is a protein source with low fat, low calories, and no cholesterol, which can enhance human immunity, combat viruses and oxidation, and aid in disease treatment. It is highly effective for human health and holds significant value in the fields of health food and beauty products. However, the extraction yield is generally low, limiting the further development of spirulina products and failing to fully meet consumer demand. Improving the extraction method, reducing production costs, increasing the extraction rate of spirulina's active substances, and enhancing clinical trials are the focal points and directions of future spirulina research. With the advancement and maturity of genetic engineering technology, applying genetic engineering to modify, breed, and mutate spirulina holds the potential to create greater benefits for humanity, warranting further investigation.

Currently, the mechanism of spirulina and its applications in other fields are being studied both domestically and internationally. Spirulina possesses strong antioxidant capabilities, making it suitable not only for the healthcare industry but also for the preservation of fruits, vegetables, and aquatic products. Its market potential is immeasurable. However, it is important to note that while spirulina and its products are gaining popularity among the public, it is necessary to fully understand the potential risks of spirulina as a nutritional supplement. This includes assessing whether it causes sensitization or has antagonistic effects when combined with certain substances. Relevant research institutions and scholars should conduct risk assessments on spirulina. Considering its safety, nutritional value, and functional characteristics, spirulina and its active substances have a promising future in the research and development of functional food and preservatives. They are expected to become a new star in the healthcare product and preservative industries, ultimately serving human health more effectively.

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