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Nutritional and Medical Applications of Spirulina Microalgae

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Abstract: *Spirulina spp.* and its processing products are employed in agriculture, food industry, pharmaceutics, perfumery and medicine. Spirulina has several pharmacological activities such as antimicrobial (including antiviral and antibacterial), anticancer, metalloprotective (prevention of heavy-metal poisoning against Cd, Pb, Fe, Hg), as well as immunostimulant and antioxidant effects due to its rich content of protein, polysaccharide, lipid, essential amino and fatty acids, dietary minerals and vitamins. This article serves as an overview, introducing the basic biochemical composition of this algae and moves to its medical applications. For each application the basic description of disease, mechanism of damage, particular content of *Spirulina spp.* for treatment, *in vivo* and/or *in vitro* usage, factors associated with therapeutic role, problems encountered and advantages are given.

Keywords: anticancer, antimicrobial, antioxidant, chemical composition, immunostimulant, metalloprotective, Spirulina.

INTRODUCTION

Spirulina is the general name of filamentous, multicellular, blue-green microalgae belonging to two genera, namely Spirulina and Arthrospira, which consist of 15 species. *Spirulina platensis* is the most commonly available and widely used genus, which has been extensively studied in different fields specially food industry and medicine [1]. Chemical analysis of microalgae Spirulina indicates that it is an excellent source of some macro and micronutrients. This rich content of protein, vitamins, essential amino acids, dietary minerals, and essential fatty acids provide Spirulina with several health beneficial properties. Potential health effects include immunomodulation, anticancer, antioxidant, antiviral and antibacterial activities, as well as positive effects against malnutrition, hyperlipidemia, obesity, diabetes, heavy metal/ chemical-induced toxicity, inflammatory allergic reactions, radiation damage and anemia [2-5]. A coherent collection of medical benefits of some algae and micro algae classes has been presented elsewhere [6].

This entry focuses on some biological properties of Spirulina including anticancer, antimicrobial, metalloprotective, antioxidant and immunostimulant effects. The biochemical composition of this microalga has been reviewed. Recent data concerning clinical potential of Spirulina, not covered previously in the literature, as well as information related to the safety and side effects of Spirulina are also provided.

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CHEMICAL COMPOSITION OF SPIRULINA

Basically, Spirulina consists of 55-70% protein and 5-6% lipid (w/w dried cell). Polyunsaturated fatty acids (PUFAs) constitute 1.5-2% of the total lipid content of this alga. In fact, *Spirulina spp.* is rich in γ-linolenic acid (36% of the total PUFAs), vitamins (B_1, B_2, B_3, B_6, B_9, B_{12}, vitamin C, D and E), minerals (K, Ca, Cr, Cu, Fe, Mg, Mn, P, Se, Na and Zn), pigments (chlorophyll a, xanthophyll, betacarotene, echinenone, myxoxanthophyll, zeaxanthin, canthaxanthin, diatoxanthin, 3-hydroxyechinenone, beta-cryptoxanthin, oscillaxanthin, phycobiliproteins, C-phycocyanin, and allophycocyanin) and enzymes (e.g. lipase) [7-9]. Therefore, the biomass of this rich source of elements is employed as feed and food additives in many industries (e.g. agriculture, food, pharmaceutics, and perfumery). In general, the chemical characteristics of two species belonging to the same microalgal category differ according to specific source, culture condition, harvest time and extraction method, even if their appearance is similar. General composition can be summarized as follows (% of dry weight): Proteins: 50-70%; carbohydrates: 15-25%; lipids: 6-13%; nucleic acids: 4.2-6% and minerals: 2.2-4.8% [2,3,10,11].

CARBOHYDRATES

The major polymeric component in *S. platensis* is a branched polysaccharide, structurally similar to glycogen. High molecular weight anionic polysaccharides with antiviral and immunomodulating activities have been isolated from Spirulina [12]. The antiviral and immunomodulating

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activities of polysaccharides of Spirulina will be discussed in the related sections. A sulphated polysaccharide fraction with antiviral property (calcium spirulan) has been extensively purified and shown to be composed of rhamnose, 3-*O*-methylrhamnose (acofriose), 2,3-di-*O*-methylrhamnose, 3-*O*-methylxylose, uronic acids and sulfate [4,13].

PROTEINS

Protein content of Spirulina (50-70% of dried weight), which exceeds that of meat, eggs, dried milk, grains and soybeans, contains all the essential amino acids specially leucine, valine and isoleucine. However, it somewhat seems deficient in methionine, cysteine, and lysine in comparison to standard alimentary proteins (meat, eggs or milk), while it is superior to all plant proteins including proteins from legumes [2,14]. As alternative protein source, two important nutritional values are estimated for Spirulina, the protein efficiency ratio (PER) (weight gain of an experimental animal, divided by the weight of proteins ingested using reference proteins) and net protein utilization (NPU) (percentage of nitrogen retained, when the source of proteins is the only limiting nutritional factor). Protein contents of Spirulina show very high digestibility (83-90% as compared to 95.1% for pure casein) due to lack of cellulose walls. Hence, cooking is not necessary for increasing the proteins availability. The NPU and PER values of Spirulina are calculated to be between 53-92% and 1.8-2.6, respectively. This is while the PER values of pure casein, maize, rice and wheat are 2.5, 1.23, 2.2 and 1.15 respectively [2, 3]. The major protein constituents with significant beneficial health effects are the phycobiliproteins phycocyanin C and allophycocyanin (at approximately 10:1 ratio), which have linear tetrapyrrole prosthetic groups (phycocyanobilin) covalently linked to specific cysteine residues of the proteins. Phycocyanins constitute about 15-25% of the dry weight of the microalgae [15,16]. Phycocyanins can be considered as a safe natural food colorant in non-acidic foodstuffs such as chewing gum, confectionaries and dairy products [16,17].

The chromophore phycocyanobilin (PCB) of Spirulina, which represents about 4.7% of the dried mass of phycocyanin significantly decreases Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity by being reduced to phycocyanorubin. This close homolog of bilirubin inhibits the activity of the enzyme complex. PCB supplementation may be employed for the prevention and therapy of various diseases mediated by NADPH oxidase hyperactivity e.g. cardiovascular diseases, diabetic complications, metabolic syndrome, allergic reactions, rheumatoid arthritis, cancer, Parkinson's and Alzheimer's disease. Oral uptake is possible via whole Spirulina, phycocyanin protein or isolated tetrapyrrole chromophore [18].

LIPIDS

Lipids, contents of Spirulina, are separated into a saponifiable fraction (83%) and a non-saponifiable fraction (17%), containing essential pigments, paraffin, sterols and terpene alcohol. Half of the total lipids are fatty acids (mostly ω-6 [12,14]) and Cholesterol (< 0.1 mg/100 g of Spirulina dry mass) [14], which is a component of Spirulina sterol fraction [19]. *S. maxima* and *S. platensis* contain γ-linolenic acid (GLA) , which comprise 10-20% and 49% of their fatty acids, respectively. Therefore, after human milk and some vegetable oils such as evening primrose, borage, blackcurrant seed and hemp oil, Spirulina can be considered as a good source of GLA *S. maxima* also contains unsaturated oleic and linoleic acids as well as saturated palmitic acid, which constitute more than 60% of its lipids. Monogalactosyl- and sulfoquinovosyl-diacylglycerol as well as phosphatidylglycerol are the major Spirulina lipids (20-25% each) [20].

MINERALS AND VITAMINS

Spirulina is claimed to be the richest whole-food source of vitamin B_{12} (and even its corrinoid forms, analogs and pseudovitamin B_{12}) and provitamin A (β carotene). Only 20g of this microalgae fulfils body requirements of vitamins B_1 (thiamine), B_2 (riboflavin) and B_3 (niacin) [2,3,14,21]. Although Spirulina does not fulfill the specific functional roles of vitamin B_{12} for humans [22] but its intake does not interfere with mammalian B_{12} metabolism [23]. A very sensitive microbiological test shows that 36% of vitamin B_{12} molecules present in *Spirulina spp.* are active in humans [5]. *S. platensis* consists of biologically active form of vitamin B_{12}, methylcobalamin, at concentration of 35-38 μg/100 g of dry Spirulina biomass [24].

The high levels of several micronutrients - especially minerals (iron 0.58-1.8, calcium 1.3-14, phosphorus 6.7-9.0 and potassium 6.4-15.4 g/kg) - in Spirulina, which have made it suitable nutritional supplement for vegetarians, are due to absorption of these elements while growing. Consequently, mineral content of Spirulina depends on source and culture conditions. Calcium, phosphorus and magnesium are present in quantities comparable to those found in milk. Spirulina is considered to be an iron rich food, with an iron content of ten times higher than common iron rich foods. Absorption of Spirulina iron is 60% more than ferrous sulphate (present in iron supplements) [2,3].

There is no risk for the consumer in taking in of excessive iodine by Spirulina consumption (3 μg in 10g of dried biomass) [25,26], since the upper safe levels for total daily intake of iodine established by European Food Safety Authority (EFSA) and Scientific Committee on Food (SCF) is reported to be 600μg for a 60kg bodyweight adult.

ANTICANCER EFFECT OF SPIRULINA

The potential cancer chemopreventive effect of Spirulina has been reported [27, 28]. Carcinogenic steps can be inhibited or reversed by some specific agents (natural or synthetic) before the onset of cancer [27]. Grawish reported a tumor suppressive effect in hamster cheek pouch mucosa by Spirulina extract due to repair of the damaged DNA. Repair of DNA damage is due to endonuclease activity, which can be stimulated by the unique polysaccharide contents of Spirulina [28].

Studies suggest a relation between cancer and high level of prostaglandins (PGs) [29]. Cyclooxygenase (Cox, PGs H synthase) is a bifunctional enzyme, which catalyzes

biosynthesis of PGs from arachidonic acid as a substrate. Cyclooxygenase-1 (Cox-1) and cyclooxygenase-2 (Cox-2) are the two observed forms of this bifunctional enzyme. Cox-1 (as a constitutive enzyme) is responsible for maintaining normal physiologic function and the produced PGs play a protective role. Cox-2 (as an inducible form whose stimulators are mitogens, oncogenes, tumor promoters, and growth factors) is responsible for the production of PGs at inflammation sites [30]. It was shown that activity of Cox-2 (and not Cox-1) increases in malignant tissues of the colorectal cancer as well as human gastric and breast tumors [31]. *S.platensis* produces C-phycocyanin as a selective inhibitor of Cox-2. This inhibition is due to the conformation and big structure of phycocyanin (Fig. **1**), which facilitates the proper binding to the active site of Cox-2 [29]. It has recently been shown that selenium enriched *S. platensis* inhibited the growth of MCF-7 human breast cancer cells [32].

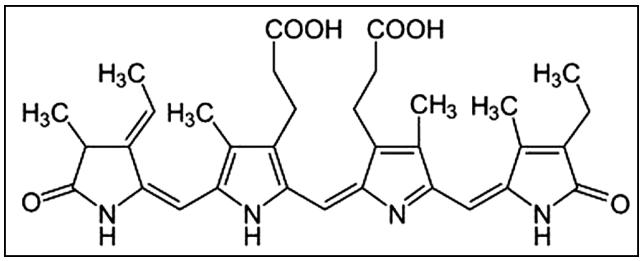

Fig. (1). Chemical structure of C-phycocyanin.

ANTIVIRAL ACTIVITY OF SPIRULINA

The major polymer in *S. platensis* is a branched polysaccharide, with a structure similar to glycogen. High molecular weight anionic polysaccharides isolated from Spirulina [33] possess antiviral and immunomodulating activities. A sulphated polysaccharide fraction with antiviral action (calcium spirulan) has extensively been purified and shown to be composed of rhamnose, 3-*O*-methylrhamnose (acofriose), 3-*O*-methylxylose, 2,3-di-*O*-methylrhamnose, uronic acids and sulphate [34]. An acidic polysaccharide fraction isolated from *S. platensis* has also been reported which induces the synthesis of Tumor Necrosis Factor-*alpha* (TNF-α) in macrophages [33].

The most promising active constituents of Spirulina are the protein phycocyanin [13], sulfated polysaccharide fractions [33], GLA [25] and certain sulfolipids [26]. Sulfated polysaccharide of Spirulina exerts its antiviral effect by inhibiting the replication of herpes simplex, human cytomegalovirus, influenza A, measles, mumps, human immunodeficiency and white spot syndrome viruses [2]. The effective concentration of calcium spirulan that can reduce viral replication by 50% is 11.4-2600 μg/ml [35]. It is known that Spirulina contains 2–5% of sulfolipids, which are effective against human immunodeficiency virus by selectively acting against DNA polymerase. For 50% inhibition of the virus, a minimum concentration of 24nM is required. Both the sulfonic acid moiety and the fatty acid ester side chain have a significant effect in potentiating the extent of inhibition [36]. A protein-bound pigment (i.e. allophycocyanin) purified from *S. platensis*, has shown an antiviral activity against enterovirus 71 [14]. This pigment inhibits 50% of enterovirus 71-induced cytopathic effect, viral plaque formation and viral-induced apoptosis at concentrations of 0.056–0.101 μM. Kaushik *et al.* [37] showed that addition of allophycocyanin to the cells before viral infection has a great impact on preventing enterovirus infection due to interfering with adsorption and penetration of the virus.

ANTIBACTERIAL ACTIVITY OF SPIRULINA

Antimicrobial activity of Spirulina extracts obtained using different solvents has been studied. Demule *et al.* [38] reported that the antimicrobial activity of the methanolic extract of *S. platensis* is due to the presence of γ-linolenic acid, an antibiotically-active fatty acid present in a high concentration in this alga. Mendiola *et al.* [39] studied the antimicrobial activities of Spirulina extract against *Staphylococcus aureus* (gram positive bacterium), *Escherichia coli* (gram negative bacterium), *Candida albicans* (yeast) and *Aspergillus niger* (fungus). Results showed that *C. albicans* were the most sensitive microorganism to all Spirulina fractions, which were obtained by the supercritical fluid extraction. This antimicrobial activity could be related to a synergic effect of fatty acids. Mala *et al.* [40] studied the antibacterial activities of various organic and aqueous extracts of *S. platensis* against different species of human pathogenic bacteria by the agar-solid diffusion method. Maximum and minimum antimicrobial activity of water extract was observed against *Klebsiella pneumoniae* and *Proteus vulgaris,* respectively. Acetone extract also showed the highest biological activity against *Klebsiella pneumonia* [40].

HEAVY-METAL POISONING ACTIVITY OF SPIRULINA

Different metals damage certain tissues by causing oxidative stress. Aerobic organisms can be protected against free radicals by antioxidants, which are endogenously synthesized compounds such as reduced glutathione (GSH), superoxide dismutase (SOD) and nitric oxide (NO) [41]. Some examples of the protection effects of Spirulina against metal poisoning are given in the following sections.

CADMIUM INDUCED POISONING

Cadmium induces cellular thiol depletion that may cause an imbalance between the pro-oxidant and antioxidant systems. Cadmium increases the production of reactive oxygen species (ROS) in tissues and inhibits the activity of some enzymes of the antioxidative defense system. ROS (e.g. H_2O_2, O_2^- and OH radical), which are formed and degraded by all aerobic organisms, can readily react with some biomolecules including lipids, proteins, lipoproteins and DNA. The protective effect of *S. platensis* against cadmium-induced oxidative stress could be either indirect through the enhancement of the activity of GSH peroxidase and superoxide dismutase (free radical scavengers) or direct by inhibiting peroxidation of lipid and scavenging of free radicals. These characteristics are due to the high concentration of antioxidant components of *S. platensis* [41].

LEAD INDUCED POISONING

Lead poisoning causes morphological changes in bone marrow cells, pathophysiological changes in tissues and necrosis in proximal tubular cells. Furthermore, it causes dysfunction in kidney, alters glomerular filtration rate, decreases sperm count and causes changes in the composition of proteins and lipids of the red blood cell membrane. The later inhibits hemoglobin (Hb) synthesis and leads to insufficient erythrocyte production and reduced red cell survival. Spirulina showed a protective effect against cadmium and lead induced alteration in the counts of T lymphocyte, reticulocyte, red and white blood cells in rats [19]. Spirulina may improve the metabolism of iron and Hb in rats with Pb, Cd, Zn, and Hg induced poisoning [41, 42]. This phenomenon is attributed to the metal-binding capacities of the blue-green algae [21].

IRON INDUCED TOXICITY

One of the most important agents that cause oxidative stress and decline of neuronal functions is iron. Oxidative stress and formation of the reactive oxygen species (ROS) are caused by iron interactions with many cellular processes. Iron toxicity also induces a significant elevation in lactate dehydrogenase (LDH) release due to cellular necrosis. Spirulina extract (especially phycocyanin) increases the cellular antioxidant enzymes (glutathione reductase and glutathione peroxidase), which are known to protect the body against the deleterious effects of ROS [20].

MERCURIC CHOLORIDE INDUCED POISONING

Mercury causes many adverse health effects (renal, neurological, respiratory, dermatologic, immune, reproductive and developmental sequel). Mercuric chloride causes significant increase in lipid peroxidation level, serum glutamic oxloacetic transminase (SGOT) and serum glutamic pyruvic transminase (SGPT) activity and significant decrease in the activity of reduced glutathione, superoxide dismutase, catalase and glutathione-S-transferase activity in liver. Spirulina significantly increases liver glutathione (GSH) level, superoxide dismutase (SOD), catalase (CAT) and glutathione S- transferase (GST) activity as antioxidant potential and thereby decreases the level of lipid peroxidation, which in turn reduces the transaminases (SGOT & SGPT) activity in serum [43]. The metalloprotective role of Spirulina may be related to its contents of vitamins E and C, beta-carotene, as well as enzyme superoxide dismutase, selenium and brilliant blue polypeptide pigment phycocyanin [43, 44].

ANTIOXIDANT ACTIVITY OF SPIRULINA

Spirulina has antioxidant properties as indicated by the *in vitro* and *in vivo* studies [38, 45-47]. The protective effects of Spirulina against CCl_4-induced liver toxicity are due to free radical scavenging. This observation is attributed to its high contents of proteins, lipids, minerals (zinc, manganese, magnesium and selenium), and some vitamins (beta carotene, riboflavin, cyanocobalamin, alfa-tocopherol, and alfa-lipoic acid).

For evaluating the antioxidant activity of different natural products, metal-chelating activity is widely used. Bermejo *et al.* [4] demonstrated that *S. platensis* protein extract possessed an excellent antioxidant activity. Results showed that the protein extract of *S. platensis* scavenged hydroxyl and peroxyl radicals and also had inhibitory activity against lipid peroxidation. Scavenging of these free radicals by *S. platensis* can be an effective prevention for a living organism against oxidative stress. An antioxidant can function either by inhibiting the processes that activate free radical formation (by intercepting the formation of the reactive radical species), or inhibiting free radical action (by scavenging the radical) or suppressing amplification of the radical damage (by further intercepting the attack of secondary-derived radicals on their biological components) or reducing iron ions which are known to catalyze many processes leading to the appearance of free radicals (by iron-chelating properties) [45]. Gad *et al.* [46] reported that the chelating activity of Spirulina exhibited a strong inhibition of errozine–Fe^{2+} complex formation due to its antioxidant compounds as electron donors.

IMMUNOSTIMULANT EFFECTS OF SPIRULINA

Spirulina facilitates production of antibody, increases activated peritoneal macrophages, and induces growth of spleen cells in response to Concavalin A (Con A). Production of IL-1 and antibody was enhanced by the addition of the Spirulina extract to the cultured spleen cells [48]. The initial target cells for Spirulina are macrophages. In myeloid cells, Spirulina exhibits an additive effect on Toll-like receptor (TLR)-mediated cytokine production pathways. Spirulina glycolipids serve as Toll ligands for stimulation of TLR2 & 4 together with bacillus calmette-guerin (BCG) cell wall skeleton [49].

Watanuki *et al.* [50] studied the immunostimulant effects of the dietary *S. plantensis* in carp, Cyprinus carpio. Fish were fed with Spirulina and the parameters of non-specific defense mechanisms (phagocytosis and superoxide anion production) were performed on the 1^{st}, 3^{rd} and 5^{th} day. Spirulina enhances responses of phagocytic activity and superoxide anion production in kidney phagocytic cells (for at least 5 days). The expression of interleukin (IL)-1β and tumor necrosis factor (TNF)-α genes also increased in fish treated with Spirulina. The expression of IL-10 gene was decreased. Furthermore, the numbers of *Aeromonas hydrophila* were decreased in the liver and kidney of Spirulina-treated fish [50]. Antimicrobial (including antiviral and antibacterial), metalloprotective and immunostimulant effects as well as antitumor and antioxidant activities of Spirulina are summarized in Table **1**.

In general, Spirulina is considered a generally recognized as safe (GRAS) nontoxic dietary supplement [14] at normal levels of consumption. However, information on the possible interactions with pharmaceutical compounds or other dietary supplements is lacking. Few side effects have been reported from the ingestion of Spirulina including headache, stomach ache, flushing of the face and muscle pain [51]. A few cases of severe side-effects of hepatotoxicity [52] and rabdomyolysis [51] are also reported. *Spirulina spp.* should be avoided by phenylketonuria patients [51] and patients with autoimmune diseases [53,54] (due to its immunomodulatory activity). It has been reported that Spirulina caused diarrhea and

Table 1. Summary of some Studied Biological Effects of Spirulina Microalgae.

Biological Properties	Specific Effects	Bioactive Component	References
Anticancer	Repairing of damaged DNA	Polysaccharides	[5]
	Selective Inhibition of Cyclooxygenase-2	C-phycocyanin	[6]
	Induction of G1 cell cycle arrest, mitochondria mediated apoptosis in MCF-7 human breast carcinoma	Se-enriched Spirulina	[9]
Antiviral	Blocking virus adsorption and penetration into vero cells	Calcium spirulan (sulfated polysaccharide)	[10-12]
	Inhibition of the DNA polymerase activity	Sulfolipids	[13]
	Inhibition of enterovirus 71-induced cytophtic effect, viral plaque formation, and viral-induced apoptosis	Protein-bound pigment allophycocyanin	[14]
Antibacterial		Fatty acids e.g. GLA	[15-19]
Metalloprotective	Inhibiting lipid peroxidation, scavenging free radicals, enhancement of the activity of GSH peroxidase and superoxide dismutase	Antioxidant components	[20-24]
Antioxidant	Metal-chelating activity, free radical scavenging activity	Carotenoids, vitamin E, Phycocyanin, and chlorophyll	[25-27]
Immunostimulant			[28-30]

erythema after consumption of amounts corresponding to four Spirulina tablets over a 3-h period, in a 14-year old individual [55]. A study in a mouse model of Amytrophic Lateral Sclerosis (ALS) has revealed a neuroprotective effect of Spirulina consumption which is believed to be due to slowing down or stopping of motor neuron degeneration [55]. Until better efficacy and safety studies are published, the ALSUntangled Group does not support the use of Spirulina in patients with ALS [56].

CONCLUSION

Limited consumption of natural food stuff in the 21st century leads to deficiency of vitamins and main minerals in the human population. Production of blue green microalgae *S. platensis*, serves as an alternative approach as feed and food additives due to their rich contents of protein, poly-unsaturated fatty acids (γ-linolenic acid), vitamins as well as minerals, pigments and enzymes. Spirulina has several pharmacological activities such as anticancer, antiviral, antibacterial, metalloprotective, antioxidant and immunostimulant effects. Mechanisms of anticancer, antiviral and antimicrobial effects of Spirulina are due to its content of endonuclease (which repair damaged DNA), calcium sulfated polysaccharide (which inhibits *in vitro* replication of viruses) and fatty acids (specially high content of γ-linolenic acid), respectively. In addition, the metalloprotective role of Spirulina may be attributed to the presence of beta-carotene, vitamins C and E, enzyme superoxide dismutase, selenium and brilliant blue polypeptide pigment phycocyanin. Research has also focused on the immunostimulant effects of Spirulina. Some experimental observations indicate that phycocyanin, sulfated polysaccharide fractions, GLA and certain sulfolipids are the most promising active constituents of Spirulina. Nevertheless, more research is needed to rate the effectiveness of Spirulina as a source of potential pharmaceuticals and nutraceuticals.

Different chemical composition and various pharmacological activities have been reported for the microalgae. These contradictory results may be related to differences in the geographical origin, harvesting period, aqueous medium characteristics as well as genetic variations, post-harvest processing conditions, the method of extraction and type of solvents used. Furthermore, interaction of microalgae with intrinsic or extrinsic properties of the consumed food e.g. pH, fat, protein, water content, antioxidants, oxygen concentration and preservative, needs more investigation.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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ABBREVIATIONS

PER = Protein efficiency ratio:

NPU = Net protein utilization

PCB = Chromophore phycocyanobilin

NADPH = Nicotinamide adenine dinucleotide phosphate

GLA = γ-linolenic acid

EFSA = European Food Safety Authority

SCF = Scientific Committee on Food

PGs = Prostaglandins

Cox = Cyclooxygenase

TNF-α = Tumor necrosis factor-alpha

GSH = Glutathione

SOD = Superoxide dismutase

NO = Nitric oxide

ROS = Reactive oxygen species

Hb = Hemoglobin

LDH = lactate dehydrogenase

SGOT = Glutamic oxloacetic transminase

SGPT = Serum glutamic pyruvic transminase

GSH = Glutathione

SOD = Superoxide dismutase

CAT = Catalase

GST = Glutathione S- transferase:

TNF = Tumor necrosis factor

TLR = Toll-like receptor

BCG = Bacillus calmette-guerin

GRAS = Generally recognized as safe:

ALS = Amytrophic Lateral Sclerosis

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