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Review Article

Spirulina Rising: A Foundation in Microalgal Phyconutrients

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Abstract

Microalgae are an abundant and available source of phycochemical antioxidants. They demonstrate anti-inflammatory properties and may help ameliorate autoimmune disorders. Certain microalgae can be sourced for omega-3 fatty acid DHA [1-4]. Microalgae may help prevent specific diseases and promote health. Since they constitute two-thirds of the earth's biomass, microalgae could or should play an essential role in preventive medicine and a fundamental role in human nutrition globally [5]. In this paper, microalgae as food are noted historically unto the current era, from the ancient Aztec culture, to Lake Chad in central Africa, to commercial cultivation in Calexico, California, and to the Big Island of Hawaii, among other locations around the globe. Microalgae, in particular spirulina, hold promise as a nutritious food source for countries with limited resources, in which the population may be undernourished or malnourished. The reasons for microalgae's status as a potential "phyconutrient savior" are described herein.

Keywords: Astaxanthin; Omega-3 Fatty Acid DHA; Oxidative Stress; Phycocyanobilin; Phyconutrients; Treg Cells

Abbreviations

AST: Astaxanthin; DHA: Docosahexaenoic Acid; O_2: Oxygen; PhyCB: Phycocyanobilin

Introduction

During the past sixty years, profound changes have taken place in the food industry and the dietary habits of people in developed and emerging countries. Mass farming has led to the progressive decline of soil fertility. Widespread use of fertilizers to restore essential elements, such as nitrogen, phosphorus, and potassium, and the use of herbicides and pesticides are designed to achieve maximum crop yield at the expense of nutritional quality. This pervasive exploitation results in toxic residues and buildups that inhibit soil microorganisms and deplete soil micronutrients. Insufficient organic matter and trace minerals in the soil are responsible for nutritionally-poor crops that, over time, lead to pathological conditions in animals and humans that feed on these deficient foods. Also, food transformation processes, medium- and long-term preservation, storage, distribution, and the pathways that deliver raw sources to finished goods on the shelf adversely impact the quality and quantity of nutrients contained in most foods.

The system of production and transportation of foods can result in the depletion of natural enzymes that are necessary for digestion. The majority of processed foods lack natural enzymes due to large scale agricultural practices, soil impoverishment, transformation processes, foods preservation techniques, storage methods, and cooking at high temperatures.

The human body is under undue stress due to inadequate and, at times, toxic food that has been adversely affected by faulty food supply standardization, transportation, and processing. The United States and Europe are in the throes of an obesity epidemic as well as experiencing extremely high rates of diabetes and cardiovascular disease, yet they are affluent countries. Their readily-available food and sedentary lifestyles are major contributors to many health conditions and diseases. Also, the healthcare systems of many countries have failed to offer natural alternatives for preventing disease and improving the health of patients with chronic disease.

Personalized medicine has arrived with the advancement of molecular diagnostics and the advent of the Internet. Once nutritional and nutraceutical companies fully realize the value of integrating dietary supplements with companion diagnostics, the adoption of such diagnostics by doctors will accelerate the development of specialized dietary supplements.

In order to develop a new generation of health-promoting and disease-curing products, and thus a new paradigm in healing and prevention, researchers must further study the interactions between foods and the body, and how foods effects the disease and healthy states. By developing novel nutritional supplements with combinations of whole foods and supplements, researchers may be able to alleviate chronic diseases, thereby improving the quality of life for nearly every person on the planet. The following discussion examines the potential of cultivated microalgae as a source of potentially protective and curative nutraceuticals.

Discussion

Microalgae are the richest, natural sources of two of the most promising phycochemical antioxidants known, phycocyanobilin (PhyCB) and astaxanthin (AST) [6-9], which target two primary sources of oxidative stress. Moreover, PhyCB has anti-inflammatory potential owing to its impact on Treg cells, which help to prevent and control autoimmune disorders. The cell wall polysaccharides of many microalgae exert immunostimulant effects, stemming from their ability to vitalize receptors on dendritic cells. These polysaccharides have potential as adjuvants in the management of cancer or infection [10-16].

Specific microalgae can be utilized as commercial sources of the omega-3 fatty acid DHA, which appears to replicate most of the various health benefits of fish oil and natural beta-carotene [1-4]. The abundant 9-cis form may prove to have health-promoting effects distinct from those of the synthetic all-trans form. Algal DHA has an appeal to vegetarians; however, among many consumers, the odor is a deterrent in its consumption. If the flavor and odor of spirulina can be improved, by innovative cultivation techniques, spirulina could be used in a wide range of functional foods as a protein-rich source of PhyCB, zeaxanthin, iron, vitamin K, and immunostimulant polysaccharides [17].

The development of cost-effective commercial techniques for preparing PhyCB-enriched spirulina extracts would make it feasible to administer optimal clinical doses of PhyCB in pill form and potentially give rise to topical or injectible preparations of PhyCB, which could be helpful for various medical applications. Also, such extracts might prove to be more effective than whole spirulina in the treatment of autoimmune disorders [17].

Microalgae-derived nutraceuticals seem poised to play a central role in future strategies for preserving and restoring health, lessening the infirmities of aging, and optimizing physiological processes.

Microalgae as food

Algae are a class of photosynthetic organisms that harvest the energy of sunlight to convert carbon dioxide to the range of organic compounds required for life, generating oxygen (O_2) in the process. Remarkably, they constitute two-thirds of the earth's biomass. There may be over 25,000 distinct species of algae. They occur as microscopic single-cell forms (microalgae) as well as large multicellular forms (macroalgae), such as ocean kelp. The microalgae include the most ancient organisms to have evolved on earth: the blue-green algae, known as cyanobacteria. These microalgae have existed for at least 3.6 billion years. They are original bacteria (prokaryotes) because, unlike the types of cells found in animals or plants, they do not contain a nucleus or other membranous intracellular structures (such as chloroplasts or mitochondria). Spirulina, *Arthrospira platensis*, is a type of blue-green algae [17].

Over the eons, blue-green algae contributed to boosting the O_2 content of the earth's atmosphere; so much so that, about 2.3 billion years ago, another type of microalgae arose, commonly known as green microalgae. These relatively newer organisms are more like plant and animal cells (eukaryotes) as they contain a nucleus and various intracellular structures, notably chloroplasts that harvest light nergy and generate O_2. Also, unlike blue-green algae, green microalgae have a sturdy cell wall [17]. Chlorella *(Chlorella pyrenoidosa)* is a type of green microalga that has achieved some commercial significance.

Humans have been harvesting wild-growing microalgae from lakes for hundreds, perhaps thousands of years, for use as food. When the Spaniards first encountered the Aztecs, they found the Aztecs using fine nets to dredge spirulina (called "techuitlatl") from the surface of Lake Texcoco, a large lake surrounding their capital city Tenochtitlan (now Mexico City). They dried and used it in a variety of foods. This resultant food was reported to be popular among the messenger runners, who needed enhanced endurance. This Aztec practice of harvesting and consuming techuitlatl died out soon after the Spanish conquest. However, consumption of spirulina still flourishes among the Kanembu people, who live along the shores of Lake Chad in Central Africa. Spirulina grows well in the warm alkaline waters of this lake. The Kanembu people collect it in clay pots, drain the water through cloth bags, lay it in the sun to dry, and fashion it into small squares, known as dihé. This dihé is crumbled, mixed with a sauce of tomatoes and peppers, and added to a wide range of their food dishes. They also apply it as a poultice to treat certain skin disorders.

These traditional practices now appear to be quite practical, as spirulina and other microalgae are remarkably nutritious. At least 60% of spirulina's caloric content comes from protein, making it the most protein-rich natural food known [17]. Since spirulina lacks a thick cell wall, the protein is highly digestible. Also, it is exceptionally rich in a wide range of essential micronutrients (although it lacks vitamin C). Spirulina is especially rich in a highly-bioavailable form of iron. It is an excellent source of vitamin K, essential not only for blood clotting function but also for bone health. The carotenoids, beta-carotene and zeaxanthin, play vital roles in visual function [18]. Like all photosynthetic organisms, spirulina contains chlorophyll; but it also contains another light-harvesting molecule, phycocyanobilin (PhyCB) that is responsible for the "blue" color in blue-green algae [5]. PhyCB has shown potential as an antioxidant nutraceutical [8].

The cell walls of many microalgae, including those of spirulina, contain complex polysaccharides that can boost immune function, as they mimic the cell wall structures of some pathogenic bacteria. Also, specific marine microalgae can make substantial amounts of docosahexaenoic acid (DHA), one of the two long-chain omega-3 fats [1-3], more commonly known for the protective properties of fish oil (Figure 1).

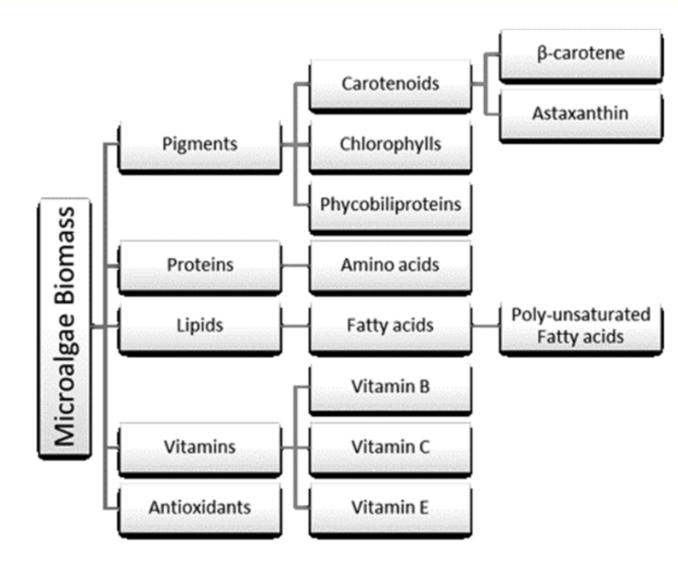

Figure 1: *Components of microalgal biomass. Note. Reproduced from Microalgae: A potential alternative to health supplements. Adapted from Apurav., et al. (2019). Note. Notwithstanding Spirulina, most microalgae contain vitamin C. Figure 1 details prominent components; however, there are others not listed herein. (See Supplemental Note 2 for a more complete list of microalgae components.)*

Commercial cultivation of microalgae

The discovery that microalgae, such as Spirulina and Chlorella, are nutritional powerhouses, particularly proficient in generating protein of adequate nutritional quality, spurred scientists and entrepreneurs to attempt to grow various microalgae commercially for food use, beginning in the 1960s. Although a blue-green alga, known as *Aphanizomenon flos-aquae,* has been harvested from natural lakes in Oregon, most efforts at commercial microalgae production have employed artificial open ponds or enclosed photobioreactors. The latter methods allow cultivation conditions to be carefully controlled, discouraging contamination of the cultures with other types of microalgae, some of which can be notably toxic. (Spirulina requires warm temperatures to grow efficiently.) Photobioreactors have further advantages in that they can operate year-round, and a higher density of algae can be achieved by using intense illumination. To date, cultivation in ponds has been cheaper and thus more commercially successful, but design innovations are expected to make photobioreactors more cost-competitive.

Chlorella was the first microalga to be produced successfully for commercial use in the 1960s. It is currently produced in open ponds in Thailand, Japan, and Indonesia, and has achieved popularity as a nutraceutical food in Japan. However, algae experts soon recognized that Spirulina had certain advantages, making it easier to produce. It thrives in alkaline conditions which discourage the growth of other microalgae; whereas, Chlorella lives best at a neutral pH favorable to the growth of competing algae. Spirulina can be easily harvested with screens; Chlorella is so minuscule that it requires expensive centrifuges to be harvested. Also, owing to their thick cell walls, the Chlorella cells need to be fragmented before Chlorella can be consumed as food; whereas, Spirulina is readily-digestible in its intact form. Thus, efforts to grow Spirulina in open ponds were introduced and achieved success in the late 1970s. Current major Spirulina growers include Earthrise Farms in Calexico, California, and Cyanotech of Hawaii. Other major Spirulina farms are found in China, India, Thailand, and Taiwan, and Spirulina is being grown commercially in several other countries in tropical or semi-tropical regions of the world. Cultivation of Spirulina in natural alkaline lakes is underway in Myanmar and Chad, but an effort to grow Spirulina in Lake Texcoco was abandoned owing to product contamination. Aphanizomenon is cultivated in Klamath Lake in Oregon. Other types of microalgae are being grown commercially; however, not as foods but as sources of nutraceuticals.

Due to their high protein content, microalgae were considered to be potentially useful for countries with limited resources, where malnutrition was common. However, this supplemental nutrition source in such countries did not come to pass as microalgae have proved to be expensive to cultivate, costing 10–12 USD per kilogram to produce high-quality Spirulina. Nonetheless, Spirulina as an additive to baby formulas or other foodstuffs has proven to be helpful in some countries. Due to exceptionally high beta-carotene content of Spirulina even modest intakes of this microalga, have helped prevent human blindness [18] in regions of India, where beta-carotene and vitamin A tend to be inadequate.

Since Spirulina and Chlorella never caught on as major foodstuffs in countries with limited resources. They are now marketed primarily as a type of nutraceutical food, mostly in wealthier countries. They can be added as powders to "smoothies" (a thick, blended drink) or specific rrecipes. However, they are consumed more commonly in the form of tablets or capsules, being due, in part, because many people find the flavor and smell unpleasant.

The consumption of these algae foods as rich sources of protein has underachieved. Other commonly-available foods, such as beans and eggs, are currently cost-effective to produce. Also, relatively few people consume Spirulina and Chlorella in adequate doses to achieve daily protein requirements. Nonetheless, there is good reason to anticipate that commercial microalgae can make a vital contribution to human health as some are potent sources of nutritional compounds (phyconutrients) that show potential as protective nutraceuticals. In particular, phycocyanobilin and astaxanthin are the richest, natural sources of phyconutrients, which are advantageous in the control of oxidative stress [19-24].

Conclusion

Microalgae are a natural and feasible source of phycochemical antioxidants. They have anti-inflammatory characteristics and may lessen the impact of autoimmune disorders. Certain microalgae can provide omega-3 fatty acid DHA. Microalgae could prevent specific diseases and be injested or applied to promote health and longevity. Microalgae constitute two-thirds of the earth's biomass. Thus, they should be considered for applications in medicine and preventive medicine as well as human nutrition, particularly in countries where people have insufficient food sources and suffer from malnutrition. Microalgae have a long history of cultivation and consumption and, historically, have been known for their health benefits and as a food source. However, to achieve their promise, several diverse but interconnected factors must come together. First and foremost, microalgae, particularly Spirulina must be successfully cultivated in diverse regions and climates around the world at an affordable end-user price, the taste must become ubiquitously palatable, and governments and people must be made aware of the life-sustaining properties of this elemental and promising phyconutrient and food source.

Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest, at the time of its research and writing. Subsequently, Dr. Mark F. McCarty has become co-inventor and co-owner of U.S. and E.U. patents on the use of PhyCB oligopeptides as nutraceuticals, and holds an E.U. patent on the use of PhyCB for the prevention and control of diabetic glomerulosclerosis.

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Supplementary Note 1

Parts of this paper were previously made available in a booklet entitled, *A Guide to Health-Protective Microalgal Phyconutrients*, posted on the Capitalife, Inc. (USA) website, and used with permission.

Supplementary Note 2

For a more complete list of microalgae components, refer the the following course: Galasso C, Gentile A, Orefice I, Ianora A, Bruno A, Noonan DM, Sansone C, Albini A, Brunet C. Microalgal Derivatives as Potential Nutraceutical and Food Supplements for Human Health: A Focus on Cancer Prevention and Interception. Nutrients. 2019 May 29;11(6):1226. doi: 10.3390/nu11061226. PMID: 31146462; PMCID: PMC6627306.

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