A comprehensive review on chlorella- its composition, health benefits, market and regulatory scenario

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Abstract
Microalgae are an assorted group of both single-celled and multiple-celled microorganisms which have survived all sorts of harsh environmental conditions to become the oldest surviving organisms on earth. They have been used to provide nutrition to humans and animals for centuries. Chlorella is one such single-celled algae which have huge nutritional value as it is enriched with proteins, minerals, lipids, etc. The focus on Chlorella as a nutritional source has increased just a few decades back as research proved that chlorella has a range of health benefits-ranging from hypertension to fibromyalgia. The market of chlorella is in billions of dollars right now and is bound to increase in the years to come as more and more people become aware of its health benefits. The current review focuses on the Composition of Chlorella, its Health Benefits, Current and Future Market and its current regulatory status in USA and EU.

Keywords: Chlorella, Health Benefits, Market Scenario, Regulatory status

1. Introduction
The oceans constitute about 70% of the earth and are hosts to immense biodiversity which includes the aquatic animals, plants and microalgae. Of these, the Microalgae are worth mentioning as they comprise the lowest level of the aquatic food chain and provide oxygen for many species in the aquatic environment. They are also the oldest surviving species on earth as is evident from the fact that Cyanobacteria are the first producers of earth’s oxygenous atmosphere [1,2]. Many microalgae have been utilised for CO2 bio-fixation [3,4]. CO2 fixation by microalgal species is more sustainable and eco-friendly as compared to other methods of CO2 removal [5]. These microorganisms are also a rich and valuable source of supply for molecules such as proteins, PUFA, polysaccharides and photosynthetic pigments. Microalgae have been an important part of the early civilizations [6]. The first use was reported way back in 2000y to the Chinese who used the microalgae Nostoc to survive the famine [7]. Chlorella is a freshwater, unicellular, green algae belonging to the family Chlorellaceae, whose name is derived from two words, ‘Chloros’ meaning green and Latin suffix ‘ella’ meaning small. Each cell of chlorella is 2-8 microns thick and doesn't has flagella. Chlorella consists of green photosynthetic pigments chlorophyll-a and chlorophyll b courtesy to which it is the richest source of chlorophyll available. Chlorella consists of 55-60% protein, 1-4% chlorophyll, 9-18% dietary fiber, vitamins and minerals [8]. Among the various species discovered – Chlorella vulgaris is the most researched until now. The first reported scientifically pure algal culture was of Chlorella vulgaris which was grown by a Dutch microbiologist, M.J. Beijerinck in 1890 [9]. By 1919, Otto Warburg published articles on his use of chlorella in the study of plant physiology. After years of extensive research on microalgae, scientists around the world speculated the fact that since microalgae have such high nutritive value, their production on a large scale can revolutionize agriculture for many more years to come. During the 1940s, two researchers named Jorgensen and Convit fed concentrated Chlorella soup to 80 patients in a leper treatment colony in Venezuela. The improvement in the physical condition of the patients was the first documented evidence of the potential of microalgae as a health supplement [9].

In the early 1950s, the research into chlorella as source of food was spearheaded by the Japanese. As a result of this the use of chlorella as a supplement rose in Japan exponentially.

Composition of Chlorella
1. Proteins
One of the most noteworthy nutritional characteristics of Chlorella is its high content of...
Protein i.e., 60% which includes most of the essential amino acids. This amount is three times more than that available in beef which is considered to be one of the most concentrated forms of protein available. Since microalgal protein has low molecular weight, it can be easily digested provided that the cells have been disrupted. Peptides extracted from *Chlorella vulgaris* have an important preventive impact on cellular damage [10].

2. Lipids
Some of the major lipidic components of *Chlorella vulgaris* are oleic, palmitic and linolenic acid [11]. *Chlorella emersonii*, *Chlorella vulgaris*, *Dunaliella* sp., *Nannochloris* sp. and *Phaeodactylum tricornutum* can have up to more than 50% lipid content with different productivity [12].

3. Polysaccharides
β-1,3-glucan found as a major component in chlorella can act as an antioxidant, immunostimulator and acts effectively in reducing the blood lipid levels [7]. Complexes found in *Chlorella pyrenoidosa*, and *Chlorella ellipsoidea* contain glucose along with combinations of galactose, mannose, rhamnose, N-acetylglucosamine, and N-acetylgalactosamine. These complexes have been proved to have immunostimulating properties [13, 14] and inhibitory action against pathogen *Listeria monocytogenes* and the fungus *Candida albicans* [15, 16].

4. Chlorophyll
Chlorella is considered as one of the major sources of Chlorophyll. It contains more chlorophyll than most of the processed chlorophyll containing supplements available [9]. Some of the health benefits of Chlorophyll include healing of sores, ulcers, haemorrhoids, regulation of menstruation, helpful in haemophilia, improves diabetes and asthma, etc. Since the structure of chlorophyll closely resembles heme which combines with proteins to form haemoglobin, chlorophyll has been proven to be useful in increasing the red blood cells. Due to its high chlorophyll content it is also called “supreme whole food concentrate” [17].

5. Vitamins and minerals
Chlorella is a very rich source of vitamins and minerals and it can be easily be taken by both adults and children for the fulfilment of their daily dietary intake of vitamins. Some of the vitamins found in major quantities in chlorella are: Alpha-carotene, beta-carotene, Vitamin B1, B2, B3, B5, B6, E and vitamin K. Vitamins found in minor quantities are Folic acid, biotin, inositol, choline and Vitamin B12 [17]. The following figure adapted from chlorella-echlorial website summarises the components found in Chlorella.

Chlorella and Its Benefits

- **Health benefits**
  *Chlorella* produces a molecule called lutein, which has been proved to prevent and treat macular degeneration and has anti-cataract properties [18]. Extracts of *Chlorella* have been acknowledged for having activity against tumours [19, 20], antioxidant [21], anti-inflammatory [22], and antimicrobial activities [23]. *Chlorella* has been shown to lower blood pressure and cholesterol levels, speed up wound healing, and augment the immune system [9]. It also has the capability to relieve symptoms and improve the lifestyle of people with fibromyalgia, hypertension and ulcerative colitis [24, 25]. Chlorella inhibited the aortic atheromatous lesions and caused great suppression of the low-density lipoprotein (LDL) cholesterol levels [26].

- **Chlorella as an ingredient for cosmetic products**
  Microalgal extracts are an abundant source of bioactive proteins, vitamins, minerals, and carotenoid pigments such as astaxanthin. Spirulina and Chlorella are some of the microalgal species which are established in the skin care market [27]. One such product on market containing *Chlorella vulgaris* is Dermochlorella® which stimulates collagen synthesis in the skin and hence helps in combating wrinkles [28].

- **Chlorella in food products**
  Spaghetti enriched with Chlorella vulgaris has been formulated and compared to standard spaghetti made with semolina by Fradique *et al*. The authors compared the cooking time, chemical composition, swelling index, etc and concluded that the presence of Chlorella increased the nutritional profile of pasta. Also, it was noted that there were no significant changes in the cooking time and texture of the pasta [29].
• **Chlorella In animal nutrition**

Microalgae may also be used for animal nutrition, wherein ≥30% of algae produced worldwide is currently used in animal nutrients [30]. The addition of Chlorella in the diet of egg-laying hens was studied by Grigorova et al., 2006. The authors observed that on addition of 2% and 10% algal biomass to the diet of laying hens, the total cholesterol level decreased in the yolk whereas quantity of linoleic acid and palmitic acid increased significantly [31].

• **Chlorella in Fish feed**

The effect of dietary Chlorella on the growth performance and physiological parameters such as blood parameters and digestive enzyme of Gibel carp (Carassius auratus gibelio) has been evaluated by Xu et al., 2014. The addition of 0.8-1.2% of Chlorella resulted in better growth, higher contents of lysozyme that has an effect on the protein/lipid metabolism and immunity of gibel carp and additionally higher amount of digestive proteins (amylase, lipase and protease) was found in comparison to the control group without Chlorella supplementation. Moreover, the cholesterol of fish fed with Chlorella was lower than that found in the control group [32]. The consequences of Chlorella vulgaris (supplement meals) on blood and immunological parameters of Caspian salmon exposed to Viral nervous Necrosis virus and it was observed that the presence of Chlorella in fish fed food can act as a herbal immunostimulant [33].

**Adverse Effects of Chlorella**

Consumption of Chlorella as a nutraceutical has initiated investigations to find any possible side effects that it may cause. Some Customers have shown side effects such as nausea, vomiting and gastric issues with some brands of chlorella tablets. Chlorella if not processed efficiently is poorly digestible and may lead to gastrointestinal issues [34]. Chlorella tablets have been shown to cause acute tubulointerstitial nephritis which may ultimately lead to renal failure [35]. It has also been labelled as a weak allergen and can be of clinical significance to certain types of people [34].

**Market Scenario of Chlorella and Its Products**

In the last few years, there is a growing curiosity among customers on ‘healthy food’ or nutrition rich food. Health conscious consumers are driving the call for products which promote better health, increase longevity and prevent chronic diseases [36]. Therefore, the use of microalgal biomass and its derived metabolites has become a pioneering approach for the production of healthier food products [37].

Looking at the current microalgae-based products in the market, Dried whole spirulina is the largest with more than 12,000 tonnes of spirulina biomass being produced every year; of which 70 per cent is produced in China, India and Taiwan. Following Spirulina is the production of Chlorella which is around 5000 tonnes per year.

As consistent with Transparency Market Research, the global nutraceutical market (which includes functional food and beverages ingredients, dietary supplements, and personal care and pharmaceuticals), which was earlier valued at US$ 182.60 Bn in 2015, will rise to US$ 278.96 Bn by 2021, exhibiting a CAGR of 7.3% for this period [38]. On the basis of revenues, functional food ingredients are the leading product segment with a share of over 31% in 2014. As the functional food industry continues to grow, food firms worldwide are focused on developing new functional food and beverages with added ingredients [39]. For instance, the Chlorella ingredients market is poised to register a CAGR of 25.4%, to reach US$ 700 M by 2022. According to another report the global algae product market is projected to reach US$3,318.1 million by 2022, with a CAGR of 6.7% from 2017 to 2022 [40].

In this study, the marketplace is divided into five major divisions according to geographies, namely North America, Europe, Asia-Pacific, Latin America, and the Middle East & Africa. North America was found to dominate the global algae products market in 2016. This large share of North America is mainly credited to the growing nutraceutical market. The growth of this industry is primarily due to factors such as an increase in the ageing population, ever-increasing healthcare awareness, and higher frequency of allergies and intolerance.

The market drivers, restraints and opportunities in the algal product market according to the research by research and market. com is presented in table 1 below:

<table>
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<th>Table 1: Drivers, Restraints and Opportunities in global algal product market [40]</th>
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<td><strong>Drivers</strong></td>
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<td>- Growing Demand for Algae Products from the Pharmaceutical and Nutraceuticals Industries</td>
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<tr>
<td>- Increasing Utilization of Pigments from Microalgae Due to Strict Regulations Regarding the Inclusion of Synthetic Colours and Flavours</td>
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<tr>
<td>- Increasing Preference to Algae Sourced Products, especially Omega-3 Fatty Acids</td>
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At the present, the demand for Spirulina and Chlorella based products is high and anticipated to increase at a CAGR of 7.1% from 2017 to 2022 (USD 238.3 million). This is motivated by the rise in demand for natural food colours, increasing vegetarianism, strict regulations regarding inclusion of colours and flavours, and growing undernourishment across the globe [41]. The predominant driver which is fuelling the boost of global chlorella powder ingredient market is the ability of chlorella to get rid of heavy metal content and ash content like mercury from the body. Air pollution is the major source of numerous toxic metals that gain access into our body via mouth, nose, skin and digestive tract. Chlorella acts as an ion exchange resin and binds to these toxic metals in the gastrointestinal tract and removes the toxins from the body. The growing number of health-conscious customers and constant growth in population are some of the other drivers for worldwide Chlorella powder market. The lack of knowledge regarding the health benefits of chlorella is one of the major restraints which is hampering the growth of Chlorella market. Since chlorella requires carbonated water and artificial light/shade for its optimum growth, the cost of chlorella increases. These additional costs add up to increase the price of the final product and this high pricing also plays as a major challenge in the growth of chlorella’s market.
Regulatory Perspective of Chlorella Eu

There are three regulations which are applicable for the marketing of microalgae and its components \(^{43}\):

- **Regulation on food safety**
  This is the European Community Regulation on Food Safety (EC 178/2002) published in 2002 in the Official Journal of the European Communities (1.2.2002 EN L 31/1). It applies to food products using whole microalgae organisms or products which include microalgae. This regulation is applicable in case of Chlorella as it is used as a whole microorganism or its contents are used in combination with other ingredients.). This regulation provides detailed regulations covering all the stages of production, processing and distribution of food and feed. Food safety is an important issue and requires due attention when the algae are produced in open air systems as it may lead to contamination with other microorganisms.

- **On novel food and novel food ingredients**
  This regulation applies to those foods and food ingredients that were not on the European market before May 15, 1997. For example, the EPA- and DHA-rich microalgal oils have only recently been introduced to the market and thus fall under this regulation, despite EPA and DHA have a significant history of consumption before May 15, 1997. According to this regulations, companies have to provide the proof of the safety of the food product (which includes animal studies) to the EFSA before the commercialization of the product. Important ideology applied in this regulation is that novel foods and food ingredients must be safe for consumers (should not be dangerous or nutritionally disadvantageous) and should be properly labelled so as not to mislead the consumer. Specific requirements concerning the labelling of novel food and food ingredients which are additional to the general European requirements on food labelling have been provided by this regulation \(^{44}\). The application ought to mention any characteristics (such as composition, nutritional value and intended use) and the presence of materials that can affect the health of individuals or that give rise to ethical concerns.

- **On nutrition and health claims for food:**
  The European Regulation on Nutrition and Health Claims made on Foods was introduced In 2006 \(^{45}\). This regulation states that health claims on food/feed products shall be based on and substantiated by generally accepted scientific evidence. EFSA Panel on Dietetic Products Nutrition and Allergies (NDA) provides the scientific opinions on all health claims made in food/feed products. The regulation states that scientific corroboration should be the main feature to be taken into consideration for the use of nutrition and health claims and the applicant should justify the same using claims.

USA

The two laws applicable to microalgal products after they are in the market in the USA are:

- the Federal Food, Drug and Cosmetic Act (FD&C) introduced in 1938 \(^{46}\), which regulates all foods and food additives
- the Dietary Supplement Health and Education Act (DSHEA) introduced in 1994, which amended the FD&C Act to cover dietary ingredients and supplements.

Both these acts are regulated by the USFDA. The FDA Center for Food Safety and Applied Nutrition (CFSAN) is responsible for regulating food ingredients and ensuring that those ingredients are safe and lawful. The authorisation of feed products falls under the FDA Center for Veterinary Medicine (CVM). The official status of a food substance depends on whether it is used in a conventional food, a dietary supplement or as a component of a dietary supplement product. For the FDA, any substance which has been added intentionally to food is a food additive and is subject to premarket review and approval by FDA, except when the substance is generally recognised, among qualified experts, as safe (GRAS) under the conditions of its intended use. In case dried Spirulina biomass is approved, it does not mean that an extract from Spirulina biomass is automatically approved.

According to the classification of the Center for Food Safety and Applied Nutrition, algal biomass such as Spirulina, Chlorella, Dunaliella, Haematococcus, Schizochytrium, P. cruentum are classified as food sources falling into the GRAS (Generally Recognized As Safe) category. Some other products which have been granted the GRAS status are oils obtained from Schyzochitrium and Ulenia, as well as a whole microalgal protein powder and a lipid ingredient derived from Chlorella \(^{47}\).

Conclusion

As the population is on a boom, day by day the need and demand of nutritive food and health products are also increasing concomitantly. Algae have survived on the surface of the earth from last billions of years, Chlorella is also once such alga which was although present for years on this earth but its nutrition profile and other health benefits have been studied only recently. Chlorella has been shown to have a plethora of nutrients ranging from proteins to lipids to
carbohydrates, etc. It also has been proved to be useful in diseases like hyperlipidemia, hypertension, ulcerative colitis, etc., Chlorella also has proven anti-inflammatory, anti-oxidant and anti-tumour properties. Even though it has some reported side effects associated with some population, the market value of chlorella has been on the rise mainly due to its ability to bind different heavy metals. Considering the fact that it is a product with second largest market volume in algal products globally, Chlorella is surely a super food of the future. The future market potential is estimated to be of billions of dollars but the market is slowed down by challenges such as the high production costs and lack of awareness among the general public. Hence, more research is required to reduce the production costs associated with Chlorella and people must be enlightened on the properties of this spectacular microorganism called-Chlorella.

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