agronomy

Review

Algae as Crop Plants Being a Source of Bioactive Ingredients of Pharmaceutical and Dietary Importance

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Abstract: Algae are currently used in many areas, including dietetics, pharmacy, cosmetology and to increase the nutritional value of food and animal feed due to their chemical composition. They are a source of extremely valuable molecules, including polyunsaturated fatty acids and pigments. Algae are also a valuable source of protein and almost all essential vitamins. They are rich in pigments such as chlorophyll, carotenoids and phycobiliproteins. These substances have a wide range of commercial applications. Due to its very intensive use, the demand for this plant raw material is constantly growing. Therefore, the methods of growing and harvesting algae are constantly improved in order to maximize the cultivation effect while minimizing costs and energy inputs. Future research should focus on improving algae cultivation and harvesting systems, with an emphasis on the possibility of genetic modifications that would allow even more efficient algae cultivation. This review summarizes methods of micro- and macroalgae cultivation, the chemical composition of selected algae species, which are important from the pharmaceutical, dietary and cosmetic points of view and therapeutic and dietary applications of compounds derived from different algae species. The key conclusion drawn from this article is that algae are an extremely valuable raw material, rich in numerous macro- and micronutrients necessary for humans, the acquisition of which is part of the currently important strategy of ecological policy for obtaining raw materials for various industries.

Keywords: algae; algae cultivation; biomass; harvesting

Citation: Jabłońska-Trypuć, A. Algae as Crop Plants Being a Source of Bioactive Ingredients of Pharmaceutical and Dietary Importance. *Agronomy* **2024**, *14*, 895. https://doi.org/10.3390/agronomy14050895

Academic Editor: Da-Cheng Hao

Received: 29 March 2024
Revised: 20 April 2024
Accepted: 22 April 2024
Published: 25 April 2024

1. Introduction

Algae are the most common spore-bearing plants, with a very diverse morphological structure. Taking into account their structure, we can distinguish in this group both single-celled organisms and colony-forming organisms. Many species have the structure of multicellular thalli reaching several meters in size and forming the so-called "underwater meadows." Their main place of occurrence is the aquatic environment, although some species of algae live on solid substrates with high humidity [1,2]. The vast majority of algae are photoautotrophic plants with high photosynthetic activity. They are responsible for producing approximately 70% of the organic matter and oxygen on Earth as a result of photosynthesis. Taxonomically, algae include: cyanobacteria, dinoflagellates, diatoms, green algae, brown algae, red algae and stone algae [3–5].

In the countries of Africa, America, and especially Asia, the practical use of algae for medicinal, cosmetic and nutritional purposes has been known for millennia. The most exploited were and still are sea algae belonging to brown algae, red algae and green algae [6,7]. They are of key importance when it comes to obtaining new dietary, cosmetic and therapeutic products. In some countries, raw, cooked or dried algae are used as food or culinary seasoning for humans or as complete food for farm animals. Algae rich in chemical ingredients with medicinal and cosmetic properties are very popular [8]. Nowadays, marine algae containing biologically and pharmacologically active substances characterized by good digestibility and the comprehensive and gentle effects of the active ingredients contained in them are increasingly used [9,10].

This work will present methods of cultivating various species of algae, both microalgae and macroalgae, along with their advantages and disadvantages. In addition, the chemical compositions of selected species that have wide and important uses in dietetics, therapy and cosmetology will be reported. The species presented were selected due to their high dietary, therapeutic and cosmetic value. They belong to both the groups of microalgae and macroalgae. Selected species rich in specific, dietary and/or therapeutically important ingredients will be highlighted and described in particular detail. Selected types of genetic modifications undergone by various species of algae in order to obtain potentially better biomass growth or better quality of nutrients will also be presented.

Although numerous reports present numerous possibilities of using algae as a source of essential nutrients, such as fatty acids, minerals and dietary fiber, this review aims to critically assess the usefulness of algae as not only dietary but also therapeutic and cosmetic ingredients and methods of algae cultivation and harvesting. A completely new approach in this review is to combine and compile information regarding algae cultivation, including the advantages and disadvantages of various systems, as well as information regarding the chemical composition of selected species and the possibility of their use in pharmacy, dietetics and cosmetology. This work focuses on selected species of macroalgae and microalgae and considers their chemical composition, nutrient bioavailability and associated health effects based on clinical evidence. The work will also present algae cultivation methods along with their key advantages and disadvantages, as well as directions for genetic modifications of selected microalgae strains. Finally, future research directions that need to be undertaken to address the identified challenges and prioritize further advances in the use of algae in various industries will be discussed. To achieve the above-mentioned goals, the literature from the last 20 years was reviewed, with particular emphasis on recent research.

2. Algae Cultivation

Algae are a diverse group of polyphyletic, photosynthetic species that live in aquatic habitats, including lakes, rivers, oceans, and even sewage. Algae are generally classified as *Rhodophyta* (red algae), *Phaeophyta* (brown algae), and *Chlorophyta* (green algae). They are also classified by size into two groups: macroalgae and microalgae. Macroalgae, also known as seaweed, are large, multicellular algae visible to the naked eye, while microalgae are microscopic single cells that can be prokaryotic, such as cyanobacteria (*Chloroxybacteria*), or eukaryotic, such as green algae (*Chlorophyta*).

Algae cultivation for cosmetic, pharmaceutical and dietary purposes must take place in sterile conditions [11]. Algae biomass, which efficiently accumulates biogenic elements and light metals, can be managed, artificially enriched and used in various industries. Macroalgae are easy to separate from the culture medium or their living environment. Macroalgae biomass can be easily and mechanically collected using simple tools. However, microalgae must be centrifuged and/or filtered from the medium. These processes are more time-consuming and cost-intensive [12–14]. Taking into account the presented data, it seems necessary to focus scientists' attention mainly on developing algae cultivation methods that would be effective, as fast as possible and as little costly as possible.

Naturally occurring algae can be an excellent and low-cost source of bioactive raw materials, but climatic conditions are often a limiting factor in obtaining algae growing in open reservoirs. The moderate climate and low average insolation of the northern hemisphere related to the meteorological conditions in this area make the use of algal (both micro- and macroalgae) biomass from open waters very limited. Micro- and macroalgae obtained in this way are insufficient in quantity to constitute a source of biomass for the pharmaceutical or cosmetic industry. Therefore, the focus is currently on developing systems for their efficient breeding. Algae cultivation in closed systems such as photobioreactors allows for control of the cultivation conditions, higher and faster biomass growth and maintaining the purity of the culture [15–17].

Generally, microalgae culture systems can be divided into two groups: open systems and closed systems. Open systems are tanks and ponds (circular, large and shallow, race track type), while closed systems are various types of photobioreactors, including plate, tubular, ring and air-lift plates [18–22]. Both of the presented systems have their advantages and disadvantages; however, the choice mainly depends on the cultured species and key applications of algal bioproducts.

Open breeding tanks are usually equipped with turbines that prevent the sedimentation of microalgal biomass. Such a microalgae cultivation system generates relatively low costs of both installation and maintenance, which is why it produces the largest quantity of biomass on a global scale [23]. Closed systems require the use of artificial lighting, which generates additional costs but allows for breeding a larger number of different species and gives higher biomass increases per unit of time. Moreover, in such a system, the problem of evaporation can be practically completely eliminated, and contamination of the culture can be prevented. The ability to create optimal conditions for microalgae growth allows for the maximization of biomass production [24–26]. However, when preparing breeding, at the stage of selecting the system, one should take into account not only climatic factors, energy costs, and the biology of the species being bred, but also the possibility of controlling conditions such as pH and temperature, the use of solar energy, expenditures related to the supply of water and nutrients, and the possibility of transferring culture from laboratory conditions to an industrial scale. The possibility of transferring breeding from laboratory conditions to industrial-scale breeding conditions is crucial if we are thinking about obtaining bioactive ingredients for the pharmaceutical and agri-food industries. This very important factor, which actually determines the success of algae cultivation, is often omitted in the literature. Cultures carried out in laboratory conditions are much easier to control because there are fewer factors at work and those that can be controlled. In open-pond conditions, there are definitely more factors that we cannot control or influence. The key factor in microalgae cultivation is light, which has the greatest impact on the efficiency of the photosynthesis process and thus the growth of biomass. Not only the type of light is important, but also the so-called photoperiod, i.e., the ratio of the length of periods of light and darkness during the day and the intensity of radiation. Too high a radiation intensity in the PAR range inhibits photosynthesis and may lead to damage to the photosynthetic apparatus. In a properly designed photobioreactor, light is the only factor influencing biomass growth [27–30].

Procedures for collecting microalgae, separating microalgal biomass from water and thickening it are the stages that generate the highest costs of microalgal biomass production [31,32]. Therefore, significant attention by the scientists should be paid to this stage of obtaining bioproducts from microalgae. Microalgae collection, which involves separating them from the substrate and dehydrating them, may constitute up to 30% of the total cost of obtaining biomass [33]. Currently, biological, chemical, mechanical and electrical harvesting techniques are used (Figure 1). Harvesting macroalgae is usually a fairly simple procedure that is limited to raking using simple tools or mechanical equipment, unlike microalgae, which require advanced methods. The literature data indicate that the most reliable methods are mechanical methods, especially extraction techniques. However, cost reductions and efficiency gains have been noted with the implementation of coagulation and flocculation. Biomass concentration is also achieved using centrifugation, filtration, flotation or a combination of the above. One of the factors that makes it difficult to harvest algae is the excess oxygen produced as a result of photosynthesis. It may promote the autoflotation of microalgae agglomerated in the coagulation process. Solving this problem has also not received enough attention, and it is a factor that reduces the efficiency of biomass extraction, which translates into lower efficiency in the production of bioactive ingredients from algae. An effective method that has been used for quite a long time is the collection of algae in micro-sieves, which require small surfaces [34–36].

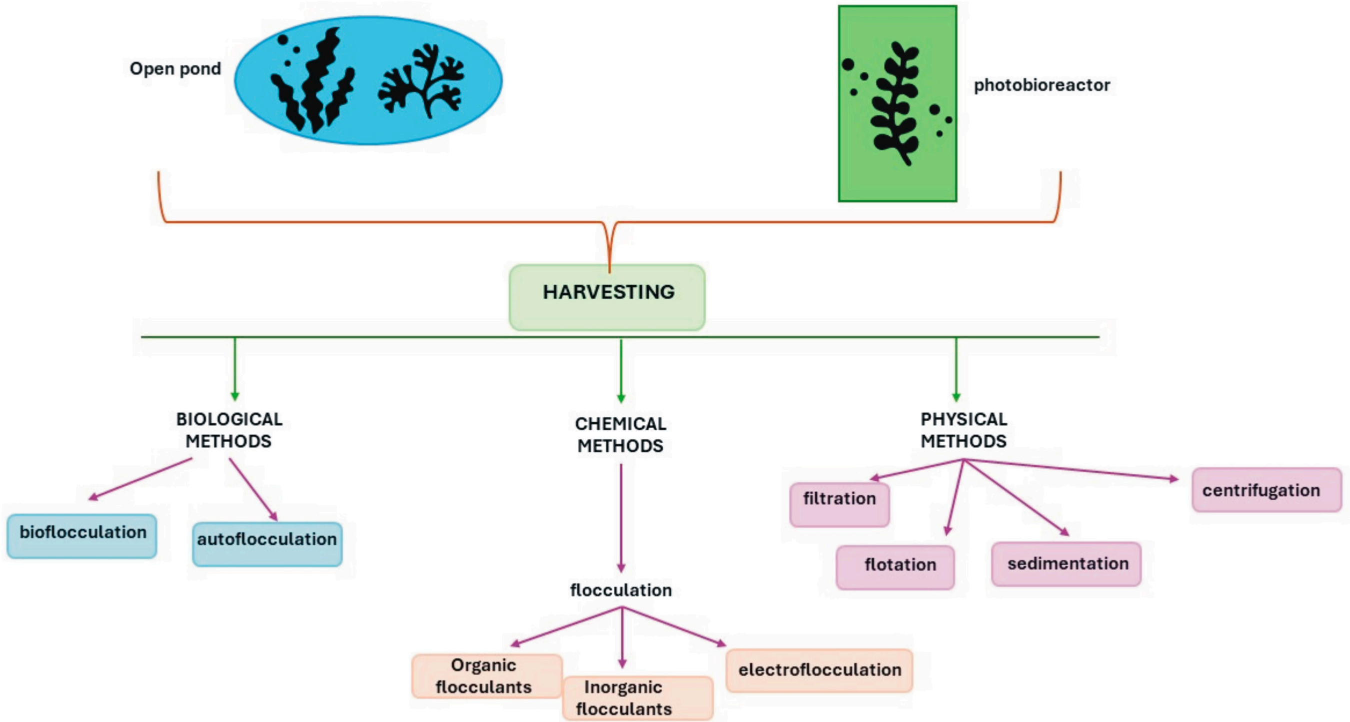

Figure 1. Microalgae harvesting methods.

The procedures implemented for harvesting both microalgae and macroalgae are constantly changing in order to improve their efficiency and effectiveness while maintaining an approach that is economically viable, ecologically sustainable and has broad commercial applicability. New trends emerging in the cultivation of microalgae should be emphasized [37]. The breeding methodologies presented so far, regardless of technical parameters or biological and chemical properties, are focused on monoculture breeding. The latest literature data indicate the possibility of growing microalgae in the form of co-cultures. The above-mentioned open microalgae cultivation systems pose a risk of contamination of the culture with other microorganisms, such as bacteria, fungi, yeasts or other microalgae species. Such disruptions in culture result in loss of biomass, depletion of nutrients, low productivity and, ultimately, culture failure. Due to these problems, the concept of co-culture based on specific consortiums of microorganisms emerged. Microalgae are characterized by their ability to adapt to changing environmental conditions, which allows them to survive even highly unfavorable environmental changes. It turns out that growing them together with selected microorganisms allows them to bypass the limitations of monocultures in open systems. It seems that creating more complex algae cultivation systems facilitates their better and more effective cultivation. Most likely, such systems in which algae are cultivated with other companion species more closely reflect their lives in natural ecosystems, where different species coexist and exert a positive or negative influence on each other. It may also be related to the secretion of various bioactive substances that stimulate or inhibit the proliferation of microalgae cells. Therefore, microalgae cultivation systems have been developed in consortiums on a laboratory and industrial scale, intended for various industries and various applications [38–40] (Figure 2).

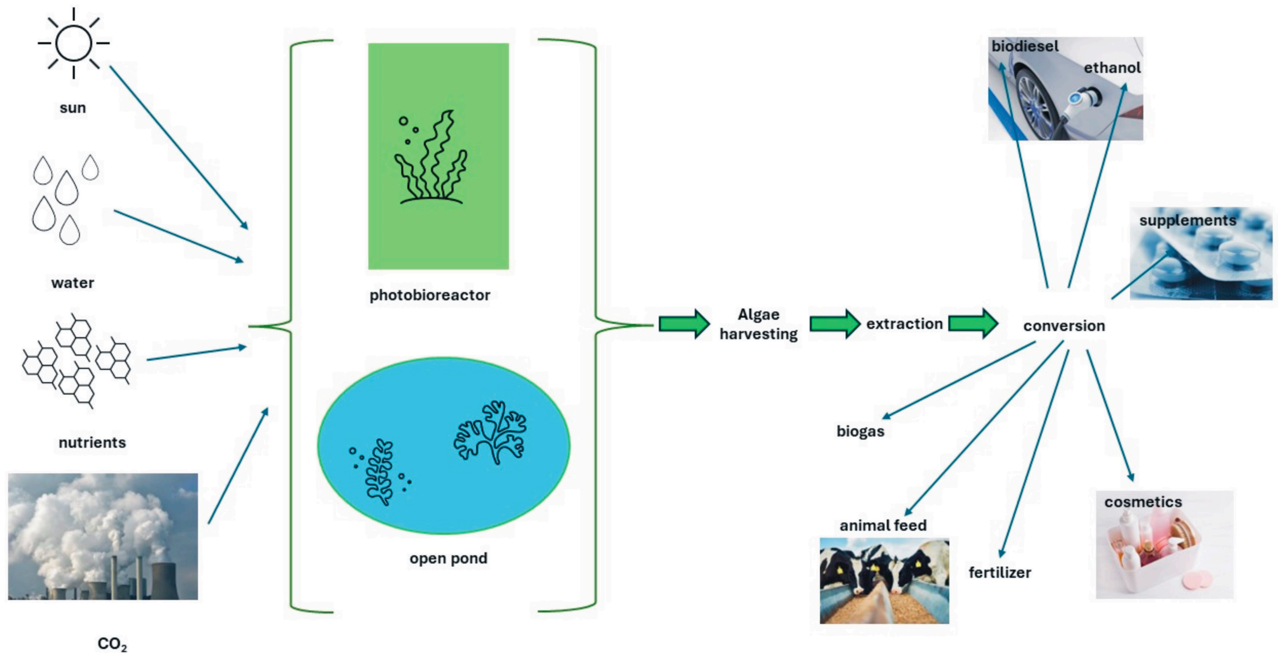

Figure 2. Microalgae and macroalgae cultivation systems and their potential applications.

3. Chemical Components of Algae of Biological Importance

Algae, both micro- and macroalgae, are of great biological importance in nature because, in the aquatic environment, as the main producers of organic matter, they are the basic food and supplier of oxygen for animals. First of all, they are a rich source of various metabolites of trophic and dietary importance for humans and animals, as well as pharmacologically and cosmetically active substances (Table 1) [41]. Therefore, they are increasingly used by humans for food purposes but also for industrial purposes in the production of feed, food, medicines, cosmetics and culinary spices. Algae are a rich source of easily digestible proteins, carbohydrates, lipids, vitamins and mineral salts. They contain significant amounts of exogenous amino acids and unsaturated fatty acids (EFAs), including gamma-linolenic acid (GLA), eicosapentenoic acid (EPA) and docosahexanoic acid (DHA), which are essential for humans and animals [42,43].

Table 1. Examples of algae and their biologically active ingredients used in dietetics, cosmetics or therapy.

Species Name	The Most Important Biologically Active Ingredients	Dietary, Cosmetic or Therapeutic Use	References
Chondrus crispus (macroalgae) *Gigartina mamillosa* (macroalage)	10% of d.m.—proteins, 15%—iodine, bromine, sulfur compounds 55%—phytocolloids, β-carotene, vitamins: B1, B2, B5, C, PP and acidic polysaccharides, mainly carrageenan	Carrageenan gel—it regulates the viscosity of cosmetic, therapeutic preparations, emulsion stabilizer, anti-inflammatory, protective coating, moisturizer, an inhibitor of herpes simplex virus (HSV), human cytomegalovirus, vesicular stomatitis virus, bactericidal agent, against cracking of the skin, food additive	[44,45]
Eisenia bicyclis (macroalgae)	Mannite, alginic acid, iodine	Sweet taste, removing poisonous substances and heavy metals, stimulation of metabolism, regulation of thyroid function, reduction of hypertension, prevention of calcification of arteries, healing effect in rheumatism, gout, and arthritis	[46,47]

Table 1. *Cont.*

Species Name	The Most Important Biologically Active Ingredients	Dietary, Cosmetic or Therapeutic Use	References
Laminaria ochroleuca Laminaria digitata Laminaria saccharina Laminaria hyperborea Chorda filum Phylophora nervosa (macroalgae)	Alginic acid, laminarin, mineral salts, algin (in the form of sodium-potassium salt), mannitol	Poisonous substances and heavy metals removing, food additive, protect against photosensitivity, soothing effect on excessive tan, regulate seborrhea and restore normal functioning of oily skin, lipolytic properties, cellulite treatment	[48,49]
Fucus vesiculosus Fucus serratus Fucus spiralis (macroalgae)	Iodine, bromine and other trace elements, vitamin C, fucoidin, algin, laminarin, alginic acid, mannitol	Metabolism stimulation, in hypothyroidism, strengthen the immune system, inhibit the development of cancer, clean teeth and periodontium, and protect against the harmful effects of UV radiation, slimming preparations that have a beneficial effect on hair, nails and skin, activate a long-lasting mechanism of slow release of fat deposits, cellulite and skin stretch marks treatment, moisturizing, regenerating, nourishing, cleansing and firming effect on the skin.	[50–53]
Ulva lactuca Ulva pertusa (macroalgae)	Vitamin C, provitamin A (β-carotene), proteins, potassium, iron, iodine	Influence immune system, eyesight, skin moisturizing cosmetics, collagen I and elastin protection, collagen III biosynthesis stimulation, epidermis condition improvement, cellular metabolism activation, amino acid composition similar to human elastin, food additive for humans and animals: cats, dogs, horses, cattle, poultry, aquarium fish, ornamental birds.	[54,55]
Porphyra sp. Nori (Japanese name) (macroalgae)	Protein rich in exogenous amino acids, potassium, phosphorus, magnesium, iodine, B vitamins, vitamin C	Food additive, source of protein, vitamins and mineral salts, lowering cholesterol levels and inhibiting of intestinal infections, food additive for animals: cats, dogs, aquarium fish, ornamental birds, horses, cattle and poultry.	[56–58]
Undaria pinnatifida Himanthalia lorea Himanthalia elongata (macroalage)	Alginic acid and its salts—alginates, magnesium, calcium, potassium, sulfur, phosphorus, selenium, iron, B vitamins, vitamin C, fucoidin, exogenous amino acids	Removing of toxic substances and heavy metals, skin moisturizer increasing its ability to store water, source of minerals for the human body, necessary for the proper functioning of metabolic processes. It inhibits the development of tumors, e.g., breast and bronchial cancer, and is effective in rheumatic diseases, gout, arthritis, etc.	[59–61]
Corallina officinalis Corallina mediterranea (macroalgae)	Sulfated polysaccharides, steroidal compounds, high polyunsaturated fatty acids	Skin revitalizer, vehicle for active substances. Remineralizes and acts as an insulator for the skin in extreme temperature conditions, antioxidant properties.	[62,63]
Pelvetia canaliculate (macroalgae)	A rich source of acidic polysaccharides used in the form of extracts or macerates	Improves hair density, elasticity, volume and tensile strength h.	[64,65]

Table 1. *Cont.*

Species Name	The Most Important Biologically Active Ingredients	Dietary, Cosmetic or Therapeutic Use	References
Hypnea musciformis *Digenea simplex* *Chondria* sp. *Rhodymenia* sp. (macroalgae)	Sugar acids, minerals and peptides	Improving hair surface, adding shine and strength to dry, damaged hair.	[66–68]
Ceramium rubrum (macroalage)	Contains a keratin-like substance	For the care of hands, feet and nails.	[69]
Codium tomantosum *Codium Müllerii* *Enteromorpha compressa* *Enteromorpha flexuosa* *Enteromorpha intestinalis* (macroalgae)	Rich in exogenous amino acids, peptides, sugars, mineral salts and vitamins	It causes deep and long-lasting hydration of the skin and epidermis and their biological regeneration. Soothing and desensitizing skin sensitive to allergens. Nourishing effect on the entire body and its skin.	[70,71]
Macrocystis pyrifera (macroalgae)	Alginic acid and its salts—alginates, mineral salts	It controls excessive activity of enzymes associated with skin aging, protects and repairs the intercellular matrix of connective tissue, especially the layer connecting the dermis with the epidermis.	[72,73]
Monostroma sp. (macroalgae)	Phytosterols and acidic polysaccharides, aqueous extracts	It moisturizes and elasticizes the skin and has a positive effect on collagen biosynthesis, food additive.	[74,75]
Chlorella vulgaris (microalgae)	microelements, protein, amino acids, fatty acids, vitamins and chlorophylls	Cosmetics, detoxification, delaying cellular oxidation processes, prevention of premature aging, elimination of free radicals, acceleration of wound healing, protection against harmful radiation, elimination of unpleasant odors, food for humans, in the form of tablets, capsules and liquid, addition to animal feed. Used in the pharmaceutical, cosmetic and food industries.	[76–78]
Spirulina maxima *Spirulina platensis* (microalgae)	Proteins rich in exogenous amino acids, a rich source of iron, potassium, iodine, selenium and vitamins, a source of essential unsaturated fatty acids, including gamma-linolenic acid.	diet ingredient in the form of tablets, capsules and extracts for anemia, fatigue and detoxification. Food additive for humans and farm animals.	[79–81]
Hizikia fusiformis (macroalgae)	Vitamins, minerals, essential unsaturated and saturated fatty acids	Food additive and extract for the production of cosmetic preparations.	[82,83]
Caulerpa sp. (macroalgae)	Vitamins, minerals, essential unsaturated and saturated fatty acids, aromatic compounds	Food additive, cosmetic additive	[84,85]
Alaria esculenta *Palmaria palmata* *Callophyllis variegata* (macroalgae)	Vitamins, minerals, essential unsaturated and saturated fatty acids	Food additive for humans and animal feed.	[86–88]
Gracilaria sp. (macroalgae)	Agar, vitamins, minerals, essential unsaturated and saturated fatty acids	Food and animal feed additive. Source of agar used in microbiology, molecular biology and medical laboratories, food, pharmaceutical, brewing industries and other industries for fermentation processes.	[89,90]

Table 1. *Cont.*

Species Name	The Most Important Biologically Active Ingredients	Dietary, Cosmetic or Therapeutic Use	References
Cladosiphon okamuranus (macroalgae) *Crypthecodinium conii* (microalgae)	Vitamins, minerals, unsaturated fatty acids, mainly gamma-linolenic acid	Additive to food and dietary or cosmetic preparations.	[91,92]
Porphyridium cruentum (microalgae)	A rich source of arachidonic acid, polysaccharides, phycobilin, phycoerythrin and phycocyanin and vitamin B12	Used in the pharmaceutical, cosmetic and food industries. Phycobilins are used not only as dyes, but also have health-promoting properties	[93,94]
Nannochloropsis sp. *Phaeodactylum tricornutum* *Nitzschia* sp. (microalgae)	Eicosapentaenoic acid (EPA)	A source of essential unsaturated fatty acids led by EPA. In biotechnology for the production of dietary and cosmetic preparations. Food additive	[95–97]
Odontella aurita *Isochrysis galbana* (microalgae)	Fatty acids and other lipids	Used in the pharmaceutical and cosmetic industries and for the production of dietary preparations for children	[98,99]
Gelidium sp. *Gelidiella* sp. *Ahnfeltia* sp. (macroalgae)	Acidic polysaccharides, mainly agar	A source of agar for microbiology, molecular biology, medical laboratories, food, pharmaceutical, brewing and other industries, mainly fermentation.	[100–102]
Kappaphycus sp. *Euchema* sp. *Betaphycus gelatinum* (macroalgae)	Various varieties of carrageenan	A source of carrageenan, used as a gelling agent, stabilizer and substance giving structure to food products.	[103–105]
Ascophyllum nodosum *Macrocystis* sp. (macroalgae)	Alginic acid, laminarin, fucoidin	Stabilizer, emulsifier, gelling agent, alginates are used in the textile industry to produce dyes for printing on clothes, production of paper, clothing and slimming products. Calcium alginates used in the medical industry in burn dressings, which facilitate healing and can be removed painlessly, and in dentistry and prosthetics to create molds, used in cosmetics, mainly in skin protective and moisturizing creams.	[106–108]
Lyngbya majuscula (macroalgae)	Peptides and other compounds with immunomodulatory and cytostatic properties	In the pharmaceutical and food industries used to produce immunomodulatory preparations and cytostatics.	[109]
Dunaliella salina, *Dunaliella bardowil* (microalgae)	A rich source of carotenoids, mainly beta-carotene and tocopherols	Biological antioxidants that protect cells and tissues against damage caused by free radicals. Used by the pharmaceutical, food and cosmetics industries.	[110,111]
Haematococcus pluvialis (microalgae)	Xanthophylls dominate: astaxanthin, lutein, canthaxanthin and zeaxanthin	Used by the pharmaceutical, food and cosmetics industries as antioxidants and dyes for pharmaceutical, cosmetic and food products.	[112–114]
Gymnodinium sp. (microalgae)	Phytosterols and unsaturated fatty acids, mainly docosahexanoic acid (DHA)	Regenerative and rejuvenating effect on the skin and its products, and activates collagen biosynthesis.	[115]
Spirogyra sp. *Oedogonium* sp. (microalgae)	Peptides and sulfolipids	Antibiotic, anthelmintic and antiviral activity, e.g., against Herpes simplex	[116–118]

Table 1. *Cont.*

Species Name	The Most Important Biologically Active Ingredients	Dietary, Cosmetic or Therapeutic Use	References
Sargassum pallidum (macroalgae)	Alginic acid and other acidic polysaccharides, polypeptides, mannitol	Antithrombotic properties and lowers cholesterol and lipid levels in the human body.	[119,120]
Lithothamnion calcareum (macroalgae)	A rich source of minerals and vitamins	It has a detoxifying effect, activating the metabolism and firming the skin.	[121]
Nostoc commune *Nostoc flagelliforme* *Nostoc pruniforme* (microalgae)	A gelatinous mucus rich in acidic polysaccharides and proteoglycans	It is used in the form of compresses in allergic and inflammatory skin conditions. It has an antiseptic effect.	[122,123]
Diatoma sp. *Fragilaria* sp. *Gomphonema* sp. *Melosira* sp. *Navicula* sp. *Pinnularia* sp. *Synedra* sp. (microalgae)	Silicon compounds, mainly silica	Bioindicators of water pollution and a source of diatomaceous earth used for refining purposes, making toothpastes and scrubs.	[124–127]

Algae, both microalgae and macroalgae, contain many different carbohydrates (up to 60% of dry weight), most of which are acidic polysaccharides of great cosmetic and therapeutic importance [128]. The most common polysaccharides include alginic acid and its potassium, sodium and magnesium salts called algines, agar, laminarin, carrageenan, fucoidin and mannitol [129,130]. Also common in algae are sugar alcohols such as mannitol, erythritol, ribitol and sorbitol, as well as cyclitols, mainly meso-inositol, laminitol and scylitol [131]. Algae contain a lot of vitamins, especially from the B group, carotenoids, especially β-carotene (provitamin A) and various xanthophylls, vitamin C (ascorbic acid) and vitamin E (tocopherols) [132,133]. Among the algae, green algae and dinoflagellates, especially golden algae, are very rich in carotenoids, the content of which is several times higher than in vascular plants [134,135]. Moreover, algae (both micro- and macroalgae) are a rich source of many other metabolites, e.g., porphyrins, such as chlorophylls, cytochromes, phycocyanins and phycoerythrins; polyamines, mainly putrescine and spermidine; and quinones, especially benzo- and naphthoquinone-derivatives [136,137]. There are also many different steroid compounds in algae, especially phytosterols, such as cycloartenol, brassinosterol, fucosterol, ergosterol, lanosterol, lophenol, sitosterol and stigmasterol, which have great cosmetic and therapeutic importance [138,139]. Also, algae, mainly brown algae, red algae and green algae, are rich in various terpenoids, especially from the group of mono- and sesquiterpenes [140]. Some brown algae and green algae from the group of zycophytes contain significant amounts of polycyclic polyphenols: fucols, floretols and fucofloretols, which have antibiotic, anti-inflammatory, anticancer and metal ion chelating properties [141]. Some algae produce a large variety of chemically unsaturated aliphatic and cyclic hydrocarbons that function as phytoncides, pheromones, and sometimes as factors involved in sexual chemotaxis. In addition, algae are very rich in minerals, the content of which is almost ten times higher than in vascular plants. The dominant macroelements include phosphorus, sodium, potassium, calcium, chlorine and magnesium, and the microelements include iodine, iron, zinc, manganese and copper [142]. The abundance of bioactive substances makes algae one of the most desirable raw materials for the pharmaceutical, cosmetic and agri-food industries. Many of these compounds have not yet been thoroughly tested and the molecular mechanisms of their action in human cells are not yet known, which opens the way to learning about many potential drugs, supplements, cosmetics and food ingredients. The chemical structures of many of these compounds are also yet to be described. The possibility of the simultaneous presence of potentially toxic ingredients, such as microplastics, heavy metals, pesticides, cancerogenic compounds, EDC compounds and others, alongside those with a beneficial effect on the human body, should also be taken into account (Figure 3). Some species of algae, especially those from the group of cyanobacteria, produce highly poisonous toxins, especially for humans and animals, as well as competing algae species [143,144].

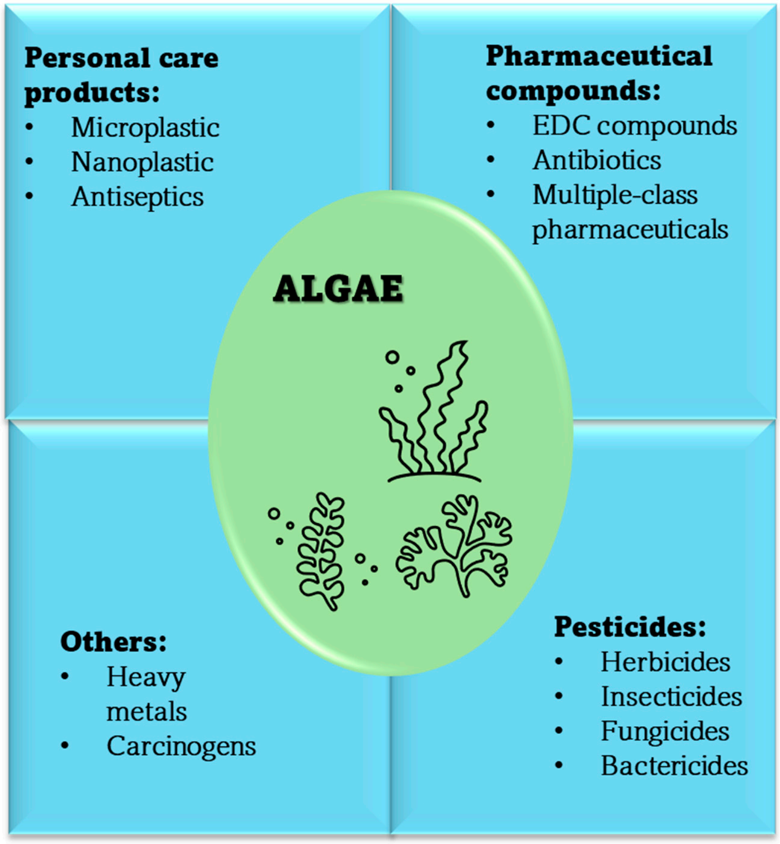

Figure 3. Presence of selected environmental, hazardous contaminants in algae.

4. Therapeutic and Dietary Significance of Chemical Ingredients Obtained from Algae

Many species of algae, especially marine ones, mainly from the group of brown algae, red algae and green algae, contain chemically diverse organic compounds with a very wide range of biological and pharmacological activity. Such examples are algal metabolites with cytostatic properties, e.g., laxafycin, scytophycin, tantazoline, some sulfonated glycoproteins and other compounds with anticancer activity [145,146]. Some algae contain glycoproteins that have anti-inflammatory and antibiotic properties, activating immune processes, lowering blood pressure and cholesterol levels and lowering the freezing point of water, as well as mitigating the negative effects of excess ultraviolet radiation. These types of proteins are found not only in marine algae but also in freshwater algae of the following genera: *Chlorella*, *Scenedesmus* and *Spirulina* [147,148]. Algae, especially marine macroalgae, are used to obtain many preparations used in therapy or cosmetics with a broad spectrum of action, including eliminating swelling, pimples and inflammation, moisturizing dry skin, improving its elasticity and firmness, strengthening capillaries and regulating skin pH [149,150]. Extracts from some algae contain chemical ingredients with anti-allergic, anti-inflammatory, anti-stress, antibiotic, detoxifying, antithrombotic and regenerating properties for the skin and its products. Among the high content of various carbohydrates, the most noteworthy are acidic polysaccharides: agar, alginates, fucans and carrageenans. They are characterized by antiseptic properties and intensive water-binding properties. Therefore, they are used, among others, in the production of cosmetics that protect against excess UV radiation, moisturize, firm and regenerate the skin and hair [151,152]. Some of them, especially alginates and fucans, activate collagen biosynthesis and proliferation of skin fibroblasts, as well as skin blood supply and metabolism. They are used in massage preparations to remove cellulite and accelerate wound healing, regenerate the epidermis and damaged hair, and reduce the oiliness of the skin and hair. Algae are a rich source of various phytosterols, which are commonly used in cosmetic and therapeutic preparations [8,153,154]. They are characterized by high biological activity, usually stimulating many biochemical and physiological processes related to the functioning of the entire body as well as the skin. They have an activating, anti-inflammatory, anti-allergic, antioxidant effect, neutralize free radicals, have antithrombotic properties, lower cholesterol levels, and enhance the regeneration of muscle, connective tissue and epithelial tissue. Phytosterols easily accumulate in sebum and the intercellular cement of the skin, strengthening the lipid barrier of the epidermis and inhibiting water loss through the skin. They also activate the biosynthesis of collagen and elastin in the skin, which has a beneficial effect on its firmness and elasticity [155]. Algae are also rich in polyamines, which, in cooperation with phytohormones, interact with DNA and RNA, phospholipids and some acidic proteins, activating processes such as cell division, replication, transcription, translation, active transport across membranes and many others [156]. Among the very biologically active chemical components found in numerous species of algae are polyunsaturated fatty acids, especially arachidonic, gamma-linolenic (GLA), docosahexanoic (DHA) and eicosapentenoic (EPA). These acids in the human and animal body are converted into eicosanoids, i.e., prostaglandins, leukotrienes and thromboxanes acting locally in cells, with versatile physiological and metabolic functions mainly related to the processes of blood coagulation, inflammation, defense, immunity, muscle contraction and many others [157,158]. Some algae are a rich source of tocopherols as well as carotenoids, mainly β-carotene and xanthophylls with strong antioxidant properties, e.g., *Dunaliella salina* and *Haematococcus pluvialis*. These compounds have a beneficial effect not only on the entire human body but also on the skin because they inhibit the oxidative degeneration of the main proteins collagen and hyaluronic and chondroitinsulfuric acids. Chlorophyll, phycocyanin and cytochrome pigments, especially P-450, found in large amounts in algae, have cosmetic and therapeutic applications in the processes of hypoxia, detoxification, regeneration, antiseptics and the removal of unpleasant odors. Quinone compounds from the group of benzo- and naphthoquinones found in some algae also have antibacterial, antifungal, and antioxidant properties, protecting against excess ultraviolet and brightening the skin and hair, i.e., inhibiting the biosynthesis of melanin pigments [159–161].

Algae of dietary importance, used as food or culinary spices, include some species of the following genera: *Chlorella*, *Spirulina*, *Porphyra*, *Monostroma*, *Ulva*, *Laminaria*, *Undaria*, *Hizikia*, *Chondrus*, *Caulerpa*, *Alaria*, *Palmaria*, *Callophylis*, *Gracilaria* and *Cladosiphon*. The most commonly used algae for obtaining cosmetic products include the following species: *Chondrus crispus*, *Mastocarpus stellatus*, *Ulva lactuca*, *Ascophyllum nodosum*, *Alaria esculenta*, *Spirulina platensis*, *Chlorella vulgaris*, *Dunaliella salina*, *Nannochloropsis oculata*, *Laminaria* sp. and *Porphyra* sp. [112,162–164]

In turn, the following types or species of algae are currently used to produce various pharmaceutical or cosmetic preparations: *Spirulina*, *Porphyridium*, *Nannochloropsis*, *Phaeodactylum tricornutum*, *Nitzschia*, *Crypthecodinium cohnii*, *Gelidium*, *Gracilaria*, *Gelidiella*, *Odontella aurita*, *Isochrysis galbana*, *Ahnfeltia*, *Eucheuma*, *Chondrus crispus*, *Betaphycus gelatinum*, *Kappaphycus*, *Gigartina*, *Mazzaella*, *Sarcothalia*, *Laminaria*, *Macrocystis pyrifera*, *Ecklonia*, *Lessonia*, *Durvillaea*, *Ascophyllum nodosum*, *Chlorella*, *Porphyridium cruentum*, *Lyngbya majuscula*, *Dunaliella salina*, *Dunaliella bardwil*, *haematococus pluvialis*, *Phymatolithon*, *Ulva*, *Monostroma* and *Sargassum* [165–169].

5. Microalgae Genetic Engineering

In recent decades, the issues of microalgae biotechnology have attracted increasing interest. Scientists, often in cooperation with industry, have developed various technologies for growing microalgae, which are currently being implemented for biomass production [170]. However, it is still important to improve various microalgae cultivation technologies to minimize production costs. Growth rates vary between species and depend on cultivation methods and bioprocess conditions. Genetic modifications used in microalgae currently involve not only conventional techniques and processes in the field of genetic and molecular engineering but also the regulation of metabolic pathways. Genomics, transcriptomics, proteomics and metabolomics methods are used to define and study complex biological systems. It is now crucial to introduce a new and rapid biological implementation, for example, combining transcriptome analysis with genome sequencing, which in turn can be used to predict the strength and functionality of the promoter. Genome editing is intended to lead to high levels of production of the chemical [171–173].

An example of the use of genetically modified algae is the process of obtaining recombinant proteins for the pharmaceutical and food industries. Microalgae can be grown in bioreactors easily, quickly, relatively less expensive than human cell culture, and subjected to genetic manipulation. Proteins synthesized by microalgae can undergo post-translational modifications in a manner similar to that of human/animal cells. Additionally, the ability of microalgae to secrete proteins into the growth medium simplifies their further processing [174,175]. Recombinant proteins can be expressed in both the nucleus and chloroplasts. Expression of specific loci in the chloroplast genome leads to high levels and stable expression and allows for simple determination of the insertion site. Therapeutic proteins undergo post-transcriptional and post-translational modifications (such as splicing, proteolysis, protein folding, glycosylation, and the formation of disulfide bonds) that are crucial for their biological function. Examples of genetically engineered microalgae that are being used in the pharmaceutical industry are: *Chlamydomonas reinhardtii*, *Thalassiosira pseudonana*, *Chlorella vulgaris*, *Haematococcus pluviali*, *Fistulifera solaris* and *Schizochytrium* sp. [176,177]. Genetic engineering methods are also used to improve the qualitative and quantitative synthesis of various lipids by algae. The microalgae species most frequently subjected to genetic manipulation to improve the production of usable lipids are *Synechocystis* sp., Chlamydomonas reinhardtii, Nannochloropsis oceanica, Phaeodactylum tricornutum, Nannochloropsis salina and Scenedesmus obliqnus. Modifications related to lipid biosynthesis in microalgae include: insertion of the Escherichia coli acetyl-CoA synthetase gene, which increases the amount of synthesized fatty acids and biomass production; genetic improvement of the microalga *Phaeodactylum tricornutum* for improving neutral lipid accumulation through overexpression of malic enzyme; introduction of transgenic overexpression of thioesterases in order to modify the chain length of fatty acids; changes in the expression of the heterologous elongase causing an eight-fold increase in DHA content; and many others [178–180]. Also, other valuable biologically active substances, such as carotenoids, can be synthesized by genetically engineered algae. They are strong antioxidants used in the cosmetics, agri-food, aquaculture and pharmaceutical industries [181].

Although it is still somewhat of a challenge, we are increasingly using genetic engineering methods to improve transformation and expression systems. A key element in increasing the efficiency of microalgae cultivation is also adjusting the conditions of their cultivation. Only the combination of these two elements, genetic manipulation and effective breeding conditions, can give the expected results in the form of optimal productivity. The most important problems faced by microalgae cultures are primarily the high costs of infrastructure, operation and maintenance, as well as the production and extraction of bioproducts. The benefits of using genetic engineering methods to improve the efficiency of algae cultivation would enable the mass production of many bioactive substances of plant origin, crucial for, among others, the pharmaceutical industry. The most important factors that should be addressed as a priority are improving yields and product quality. Other problems include the low availability of high-performance genetic and molecular tools, the low stability of the genetic system and the low efficiency of manipulation outside the laboratory [182]. It should be remembered that environmental safety related to the cultivation of microalgae, especially genetically modified ones, is also a very important factor. The potential of GM microalgae should be assessed to ensure their commercialization, energy and food security and no risk to humans, animals or the environment. Since genetically modified algae can be grown on an industrial scale both in open ponds and in closed photobioreactors, the potential risk of releasing modified algae into the natural environment must be taken into account. To reduce the likelihood of such a situation occurring, genetic biological protection strategies are being developed. These are active strategies (killing escaped cells by expressing toxic proteins) and passive strategies (using knockouts of native genes to reduce fitness outside a controlled environment). As a result of experimental studies, it was shown that escape frequencies are below detection limits. However, in the natural environment, other mechanisms may appear related to the complexity of environmental matrices and the multitude of physical factors that do not occur in controlled experimental conditions. Therefore, it is crucial to choose a biological protection strategy that will allow the elimination of algae in the natural environment while maintaining maximum productivity in the laboratory and without the need to use chemicals [183].

6. Conclusions

In recent years, algae, especially marine brown algae, red algae and green algae, have been increasingly used in many branches of the pharmaceutical, cosmetic, chemical, food and feed and textile industries. An important feature is the good bioavailability and comprehensive pharmacological or cosmetic effects of the chemical ingredients contained in them. Algae extracts contain biologically active substances that easily penetrate the surface layer of the skin into its deeper layers, mainly blood vessels, and thus affect the physiological and metabolic processes of the entire body. Algae constitute a huge reservoir of food rich in trophic ingredients for humans and animals, as well as a rich source of various pharmacologically and cosmetically active chemical ingredients, which have so far been used by humans to a negligible extent. Recently, transgenic algae have been increasingly used in biotechnological processes to obtain various cosmetic, therapeutic and dietary products. There is hope that in the coming years, algae will be increasingly used by humans as a very valuable raw material for the production of medicines, cosmetics, food and feed, as well as for detoxification purposes and in plant sewage treatment plants.

Taking into account the above, it should be emphasized how important a raw material algae have now become, both from the point of view of the pharmaceutical and agri-food industries. They are a raw material that can be obtained using low-energy, ecological breeding methods supported by modern methods of genetic and molecular engineering.

Funding: This work was financially supported by the Ministry of Education and Science, Poland, under the research project number WZ/WB-IIŚ/6/2022.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The author declares no conflicts of interests.

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