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Review

A Spotlight on the Potential of Microscopic Motile Algae as Novel Sources for Modern Cosmetic Products

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Abstract: The recognition and use of algae in the very trend-driven cosmetic industry is progressively increasing. Up to now, the main focus was on large seaweeds and a limited number of microalgae. However, motile microalgae, flagellates, remain underscored in this aspect, although some of them are utilized commercially. Flagellates from different taxonomic groups occupy various habitats and contain bioactive high-value multifunctional compounds, some of which are novel. Moreover, they may simultaneously produce different substances, which together with the development of downstream processing technologies, makes them a promising source for modern biotechnology. The present review covers data on 411 strains, 251 species from 110 genera from 6 phyla, and is oriented generally towards less explored flagellates. It demonstrates their great potential as bearers of interesting novel compounds that can be beneficially applied in modern cosmetics. Safety aspects of both sources and products are also discussed. Considering the gaps in the knowledge, the necessity to expand the research on both well-known and yet unexplored microalgae is shown, encouraging the development of upstreaming processes, including phycoprospecting. Last but not least, this paper outlines the role of living culture collections and of using good taxonomic expertise before running the biochemical tests, cultivation, and bioengineering experiments.

Keywords: bioactive compounds; cryptophytes; dinoflagellates; euglenophytes; extremophiles; flagellates; green algae; haptophytes; ochrophytes; pyrrhophytes

Citation: Stoyneva-Gärtner, M.; Uzunov, B.; Gärtner, G. A Spotlight on the Potential of Microscopic Motile Algae as Novel Sources for Modern Cosmetic Products. *Cosmetics* **2024**, *11*, 115. https://doi.org/10.3390/cosmetics11040115

Academic Editors: Se-Kwon Kim and Nikolaos Labrou

Received: 12 May 2024
Revised: 3 June 2024
Accepted: 25 June 2024
Published: 9 July 2024

1. Introduction

Following the trends of modern lifestyle, the cosmetics industry currently is oriented towards natural bioactive ingredients, which appear to be not only of high cosmetic efficacy but are also less harmful compared to chemicals-based products [1–7] and may reduce the negative impact on the environment caused by synthetic substances [8]. Moreover, currently, a considerable amount of evidence points to the negative effects of the environmental stress driven by ultraviolet (UV) radiation and air pollution on skin and hair conditions, thus further reinforcing the need for safe natural substances that are able to effectively prevent or mitigate their deleterious effects [9,10]. Additionally, environmentally concerned consumers demand such safe personal care or cosmetic commodities to be obtained in novel eco-friendly and cost-effective processes in order to avoid over-exploiting of wild biological resources [1,11,12].

Therefore, the ever-expanding market led to the advancement of green technologies with the progressive search and exploration of novel compounds derived from different organisms [8,13]. The significantly boosted current interest in algae, which produces a great palette of useful bioactive substances [14], is compliant with this trend [9,10,15]. Over 15,000 novel compounds have been chemically determined [16] and many of these natural substances with antimicrobial, antifungal, antiviral, anti-inflammatory, antiallergic, antioxidant, anti-melanogenic, anti-aging, hypoglycemic, and immunosuppressive properties [1–5,16–23] are highly marketable. Cosmetic formulations may incorporate the whole algal cells or only some of the algal biologically active substances in face-, body-, hair-, dental- and personal-care products. In them, algae and their metabolites act as sunscreens, constituents in after-sun products, anti-wrinkle agents, moisturizers, texture-enhancing or thickening agents, tanning agents, whitening agents, and anti-cellulite agents [9,12]. Although very few of these novelties have been applied commercially [12], the number of such formulations is significantly expanding. In addition, nowadays some algal compounds are in the research focus due to their innovative applications in nanoproducts for modern cosmetics [19] and in the nutricosmetic formulations of combined food supplements and cosmeceuticals for improving skin care and delaying aging [24–26].

The term "algae" has no taxonomic standing but in an operational way embraces a large group (estimated between 30,000 and 1 million species [27]) of micro- and macroscopic, prokaryotic, and eukaryotic unicellular and multicellular organisms, which perform oxygenic photosynthesis since ca. 2 billion years and include ancestors of land plants [28–30]. Algae are characterized by great diversity regarding their lifestyle in different habitats, such as all aquatic environments (including hot springs), ice and snow, caves, soils, and all types of hard substrates like tree barks, rocks, walls, etc. [12,19,31]. Considering this variety of substrates and ecological conditions, algae bear different reproductive, cytological, biochemical, and morphological features that allow their adaptation and successful evolution.

Although in modern classification systems algal morphology is not used among the main taxonomical features, phycologists continue to use specific terms to describe the level of morphological differentiation of their thalli according to the morphological system developed by A. Pascher [28,32–34]. The morphological types include two main groups. First is the group of unicellular algae, which are divided according to their motile abilities and relevant ultrastructural features into four types: (1) flagellate (or also monadoid, or motile), which includes algae that are capable of active motion based on specific organelles named flagella; (2) palmelloid (or also capsular, or hemi-motile), which embraces algae in a common mucilage capsule that have ultrastructural organization of flagellate algae but have no flagella or bear false flagella (pseudoflagella) which allow motion only in extremophilic conditions; (3) rhizopodial (or, amoeboid), which is kept for algae that move by specific cytoplasmic protrusions, named rhizopods; and (4) coccal, which covers non-motile algae that do not bear specific motion organelles and are equipped with a thick, well-developed cell wall (Figure 1).

Algae in all these four types can live separately, as single cells, or can aggregate in colonies, or in so-called coenobia (specific colonies formed from sister cells with fixed cell numbers and fixed shapes) (Figure 1). In the cases of rhizopodial type, the cell aggregations are called plasmodia (Figure 1). The second large morphological group that embraces diverse multicellular algae, all of which are immotile, is not discussed in the present paper

Current reviews of the application of algal naturally derived products revealed the highest utilization of multicellular red, brown, and green marine macroalgae (seaweeds) [1,21], which offer different unique products of high biological value and can be directly collected from natural habitats [1,11,21,23,35]. Over the years, the scientific community also recognized the extreme potential of cultivated microalgae as producers of multipurpose biologically active compounds [21–23,35]. However, there are substantial differences in the prices of natural and synthetic substances, thus encouraging the development of cost-effective technologies to meet this major challenge for the microalgal application in human affairs [36]. Up to now, most of the studies and industries utilize a few microalgal species, while many of the representatives of the algal fascinating realm remain unexploited [12,19]. Among the best-known explored genera are the unicellular and coenobial coccal algae, such as *Chlorella* and *Scenedesmus*, respectively, or multicellular filamentous algae such as *Arthrospira* (Syn. *Spirulina* p.p.) and *Aphanizomenon* [37,38]. By contrast, flagellate algae are less studied and less utilized, except for a limited number of genera such as *Chlamydomonas*, *Dunaliella*, *Euglena*, *Haematococcus*, and *Tetraselmis* [1,37,39,40]. Due to rich information on their ingredients and utilization, they shall be generally briefly noticed in the current review, which is aimed to show the yet unexplored potential of other, less-elucidated flagellate microscopic algae to provide effective high-value ingredients for modern cosmetics.

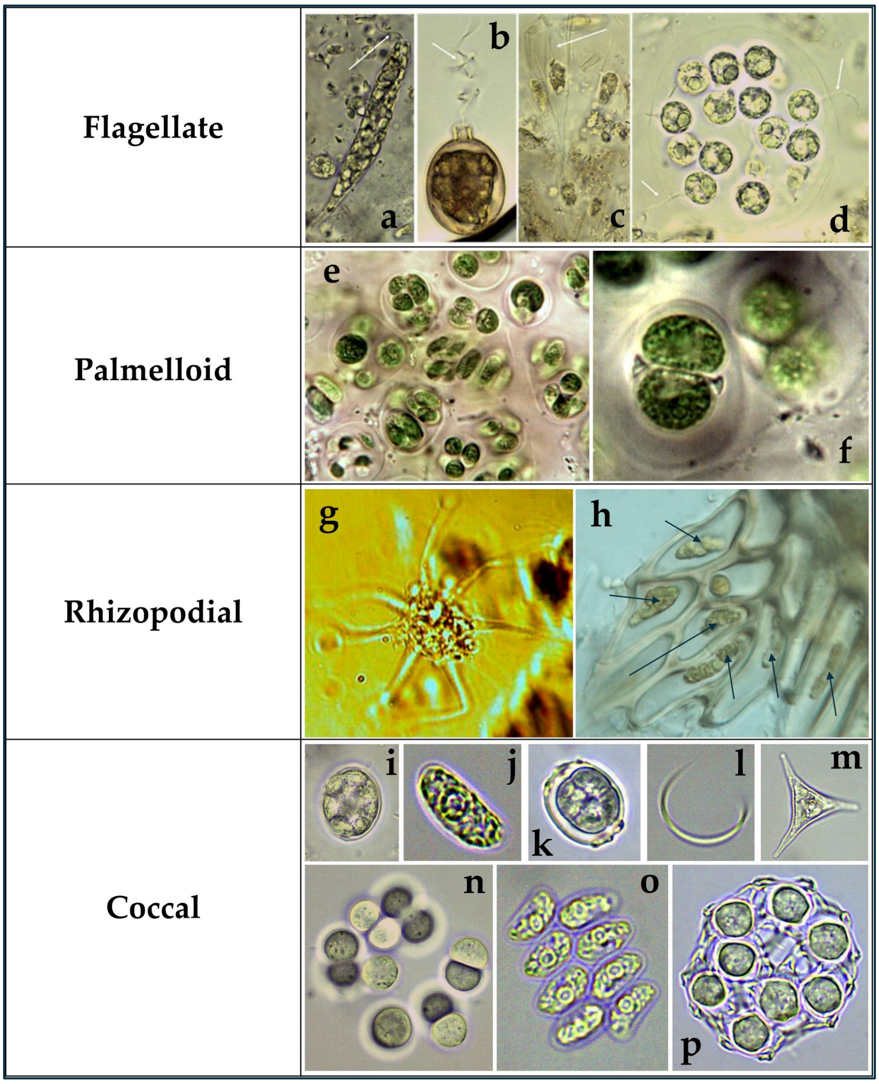

Figure 1. Morphological types of unicellular algae with examples of (1) flagellate type represented by single-celled algae (**a**,**b**), colony (**c**), and coenobium (**d**), with white arrows indicating flagella; (2) palmelloid type—a general view of a colony (**e**) and part of the same colony under high (100×) magnification with immersion (**f**); (3) amoeboid type represented by a single-celled alga (**g**) and plasmodia (**h**), indicated by blue arrows, situated in the hyaline, water-storage cells of a *Sphagnum* moss; (4) coccal type represented by different single cells (**i**–**m**), colony (**n**) and coenobia (**o**,**p**).

2. Materials and Methods

The literature search was performed using the Web of Science, Scopus, Science Direct, PubMed, Google Scholar, and SciFinder databases together with the authors' personal scientific libraries and archives.

In addition to Latin names of species, genera and higher taxonomic categories, keywords included the names of chemical substances, relevant skin and hair disorders, and different biological activities. Research on algae as food or food supplements, important for nutricosmetics [24–26], and on algal extracts or substances relevant only to the medicine or food industries are not included although further research may show possibilities for their application in the cosmetic industry. Due to the limited volume of this paper, when possible, references to more general reviews were preferred.

The term "cosmetics" is used in its broadest sense, embracing also the term "cosmeceutical", in accordance with our previous reviews [12,19].

The classification follows the ten evolutionary lines and relevant eleven phyla (Figure 2) [28,41] with noting of the current taxonomical proposals by Adl et al. [42]. The nomenclature follows Algaebase [43], with the synonyms shown in brackets at the first appearance of the relevant currently accepted Latin name. The taxonomic position in detail and the habitat, or locality, generally are indicated for each species or genus at its first appearance in the text.

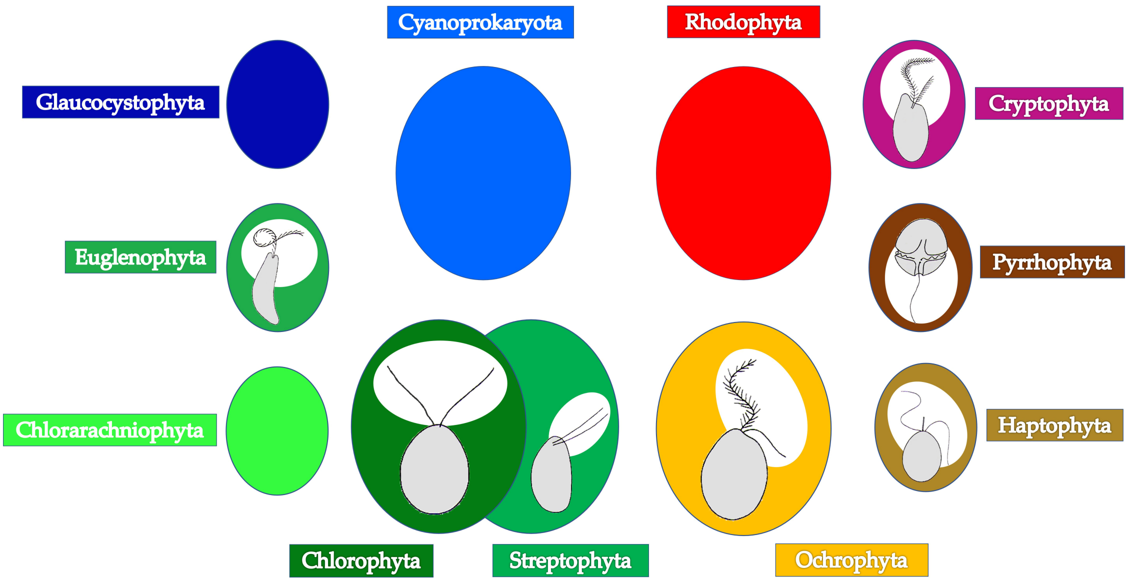

Figure 2. Algal evolutionary lines and relevant taxonomic phyla with indicated distribution of flagellate morphological type. The different size reflects the biodiversity in each phylum.

The flagellate morphological type does not occur only in the blue-green and red algal lineages, as well as in the lines of glaucocystophytes and chlorarachniophytes (Figure 2); in Streptophyta it is known only for the peculiar genus *Mesotigma* and is the only known morphological type in the phyla Cryptohyta, Euglenophyta, and Haptophyta. In the other phyla flagellate, vegetative cells do not appear in all of the species but do appear in some of the classes [28,41].

3. Results

Data on the different natural substances found in more than 411 strains of 161 taxa (159 species, 1 subspecies, and 1 variety) from 110 genera of flagellate algae from 6 evolutionary lines, represented by the phyla Chlorophyta, Ochrophyta, Euglenophyta, Pyrrhophyta, Cryptophyta, and Haptophyta, are presented below in the text. For easier reading, in this review, generally only phyla are mentioned, but for the more specific large phylum Ochrophyta that embraces the whole yellow-brown lineage, here we shall note that data were found on its classes: (1) Synurophyceae (silica-scaled algae), Raphidophyceae (raphidophyceans), and Olisthodiscophyceae (olisthodiscophyceans), in which all cells are monadoid, (2) Chrysophyceae (golden algae), Pelagophyceae (pelagophyceans), and Pinquiophyceae (pinguiophyceans), in which flagellate type occurs together with other morphological types, and (3) Dictyochophyceae (more popular as silicoflagellates), peculiar and disputable regarding its taxonomic position and inclusion in Ochrophyta because in this algae flagellum exists in addition to their general rhizopodial cell organization [41].

3.1. Flagellate Algae as Natural Pigment Sources

The diverse pigments of algae, such as chlorophylls, carotenoids, and phycobilins, are increasingly gaining the attention of the scientific community [44]. Their numerous health-promoting properties are unmatched by synthetic compounds, making algal primary and secondary pigments applicable in many areas, including pharmaceuticals and cosmetics [29,45]. Currently, algae are considered "emerging sources of bioactive natural pigments" [46] since many of their light-harvesting substances used in photosynthesis are only algal specific [47,48] and are produced in cells in high amounts [49].

3.1.1. Chlorophylls

Algae produce different types of chlorophylls (*a*, *b*, *c*, *d*, *f*), which occur in different combinations in each of their evolutionary lines, with only chlorophyll *a* being common in all of them [28,41,44,50,51]. At the end of the sixties of the 20th century, chlorophyll *e* with specific absorption spectra algae was extracted from two yellow-green algae but was not described chemically [51,52]. Chlorophyll content varies significantly depending on the species, cultivation conditions, and age of the culture [53].

Chlorophyll compounds are applicable in skin-care cosmetics because they are able to stimulate tissue growth and have wound-healing, antioxidant, antibacterial, anticancer, antimutagenic, antitumor, and anti-inflammatory properties [29,49,54–56]. The green motile *Chlamydomonas reinhardtii* is a popular model organism, known also for its high chlorophyll content, which can be used in different industries, including cosmetics [14,29,57,58]. Another unicellular flagellate alga considered a chlorophyll source is the marine haptophyte *Diacronema lutheri* (Syn. *Monochrysis lutheri*, *Pavlova lutheri*) [29,57–59] in which a content of 0.47 pg cell^{-1} was achieved [59]. The total content of chlorophyl *a*, c_1, and c_2 in another marine haptophyte, *Isochrysis galbana*, was measured as 2.87 mg g^{-1} dry weight (DW) during its cultivation in 100 L polyethylene bags with seawater [60]. However, up to now, chlorophylls are produced on a commercial scale mainly from spinach, common nettle, lucerne, and corn, although the chlorophyll content (ca. 7%) of microalgae is many-fold greater [38]. Moreover, according to our best knowledge, there is no commercial production of any chlorophyll type from flagellate algae yet.

3.1.2. Carotenoids

Carotenoids are essential live molecules, wellknown as antioxidants that protect cells from photo-oxidation caused in general by overexposure to UV radiation and, therefore, are widely used as anti-aging and sunscreen agents [12,37,61]. Besides photo-aging, the free radicals formed during the process, and their oxygen-containing subset, reactive oxygen species (ROS) in particular, may eventually lead to skin cancer and inflammatory disorder [37,46,61]. Therefore, carotenoids have been studied and applied for health and cancer prevention or treatment, but also for solving almost all problems related to skin beauty.

The most popular and best studied for their antioxidant, anti-inflammatory, immunoprophylactic, and antitumor activities and their UVprotective role carotenoids include astaxanthin, lutein, fucoxanthin, canthaxanthin, zeaxanthin, β-cryptoxanthin, and ß-carotene [37,46]. Some of them, such as lutein, are already used as colorants in cosmetics [37] and have the possibility to improve skin elasticity, in addition to their antioxidant, anti-inflammatory, photoprotection, and anti-carcinogenic activities [62]. The value of lutein derived from algae for industry and for cosmetics in particular is great because in algae it occurs in free, non-esterified forms contrary to the lutein extracted from other sources, where it is ca. 95% esterified [12,23]. Together with lutein, canthaxanthin creates a tan color and has been used in skin tanning and suntan products [12,19,63,64]. Another multifunctional pigment is ß-cryptoxanthin, which has diverse health-promoting functions and may play a role in vitamin A function, but for cosmetics in particular is interesting as a skin-whitening agent [65] and as exhibiting anti-inflammatory properties [66]. Fucoxanthin is the only algal-specific natural pigment [47] among the abovementioned pigments. It has broad therapeutic activities and well-known antioxidant properties [67] that make it important for medicine, pharmacy, and agriculture, but it can also be employed as a functional ingredient in cosmetics [68]. The multifunctional ß-carotene (the precursor of vitamin A) is interesting for cosmetics due to its safety even at high doses and to its dermaprotective abilities against oxidative stress that allow it to not only slow down the skin aging processes and sun damage but also to inhibit proline oxidation in collagen, induced by UV radiation [69]. ß-carotene has strong anti-inflammatory and anti-cancer properties, especially in reducing the risk of developing skin cancer [29,69,70]. It has already been used in hair and personal care products, such as aftershave lotions and makeup [10,69,71,72], and in suntan formulations as well [12,69,71,72]. Application of encapsulated ß-carotene led to improvement of skin appearance by reducing roughness and increasing smoothness and also increased hydration with ca. 25% [69]. The same effect is achieved when it is applied in washing and hand-care creams [69]. In addition to all these multiple benefits, its importance for cosmetics comes from the fact that ca. 16% of ß-carotene permeates the skin, and its application may not only reduce skin pigmentation disorders (such as vitiligo, discolorations, post-acne discolorations, and melasma) but enhance their removal [69]. At the same time, an obstacle to its broader use is the well-established popular belief that this pigment permanently changes skin tone when applied topically since it is concentrated in the uppermost skin layers [69]. This is quite controversial since ß-carotene is able to inhibit melanogenesis and as such is useful in skin-whitening formulations [69]. However, the overall benefits allow this pigment to be pointed out as "one of the most valuable active ingredients used in cosmetics" [69] (p. 212). Microalgal zeaxanthin was suggested as useful in skin-whitening substituents due to its anti-tyrosinase activity [13,73]. Lycopene is another potent natural antioxidant, incorporated in personal care formulations as an antiaging agent, with possible application as a sunscreen and sunburn-preventing agent [12,19,63,64]. Astaxanthin is quite popular as a "superb antioxidant" because its antioxidant activity is stronger in comparison with other carotenoids, such as lutein, beta-carotene, and canthaxanthin [74,75] and it is shown to be 550 times more effective in scavenging ROS than vitamin E [36]. Therefore, astaxanthin is advantageous in many fields, including cosmetics, in which it is applicable as an anti-inflammatory and anticancer agent [1,76–78]. But in the cosmetics industry, it is best known as an attractive constituent in sunscreen and after-sun lotions for endurance and protection of the skin from premature aging and for the alleviation of skin photo-aging, because it reduces age spots and other blemishes or flakes by diminishment of ca. 40% of melanin amount in the trans-epidermal cells [12,13,29,36,78,79].

- Astaxanthin in flagellate algae

Astaxanthin is commonly known as an abundant (45–72–92% of the total pigment pool) secondary pigment in the psychrophilic algae that cause red and orange snow events, namely *Sanguina nivaloides* (currently, according to Leya [80] to this species is transferred *Chlamydomonas nivalis*, with 91% astaxanthin content), *Sanguina aurantia* (72% astaxanthin content), *Chlainomonas rubra*, *Chlainomonas* sp. DR53, *Chlainomonas* sp. AS02, *Chloromonas nivalis*, *Chloromonas hindakii*, *Chloromonas krienitzii*, and *Chloromonas polyptera* [12,40,81–85]. However, in the absence of living cultures of *Chlamydomonas nivalis* [80] and of carotenogenic strains of *Chlainomonas* deposited into public collections [40], they cannot be regarded as promising sources of this important carotenoid [80]. On a commercial scale, currently, astaxanthin is obtained from 11 green microalgae [86] but out of them its main source is the widely spread green freshwater flagellate *Haematococcus lacustris* (Syn. *Haematococcus pluvialis*) [16,29,46,75,77,80,86–90]. In this alga, depending on the cultivation conditions, astaxanthin can reach 3.8–5.0% w/w [86] and even 8% of the cell DW [91]. However, experiments on intraspecific and interspecific variations of astaxanthin production demonstrated that cultivated strains had a lower productivity of this pigment compared to natural isolates of *Haematococcus lacustris*, explainable by possible loss of photoprotective capacity during long-term cultivation [92]. The current study of the astaxanthin derived from *Haematococcus lacustris* clearly demonstrated that it can improve skin conditions in all layers not only in women but also in men after the combination of oral (6 mg per day) and topical (2 mL of

78.9 μM solution per day) applications [93]. Mechanisms for this improvement were clarified after a study of the effects of astaxanthin on the water channel aquaporin-3 (AQP3)—a protein of importance for skin moisture and function [94]. Two more species of the genus *Haematococcus* have been described not long ago from Europe, namely *Haematococcus rubens* and *Haematoccus rubicundus* [95]. Although both of them were proven as astaxanthin producers, *Haematococcus rubicundus* seemed to be more promising as a commercial source due to its higher specific growth rate in comparison with *H. lacustris* [92,95].

Some species of the unicellular flagellate genus *Euglena* from the separate euglenophyte evolutionary line (classified also in the supergroup Discoba in the Tree of Life [42]) can cause red water coloration (red blooms) in freshwater ponds and pools [40]. Such species are *Euglena rubida* and *Euglena sanguinea*, in which astaxanthin is the most abundant (ca. 69 and 75% of the total carotenoid content, respectively) [40,96,97]. In addition to astaxanthin, other valuable carotenoids were recorded in these species, such as mutatoxanthin (another major pigment in *Euglena rubida* [96]) or esters of astaxanthin precursors, adonixanthin, and adonirubin, which occurred in detectable amounts in *Euglena sanguinea* [97]. The high astaxanthin content boosts *Euglena* among the promising carotenogenic algae despite the absence of developed technology for industrial cultivation regarding carotenoid production [98,99]. However, many other experiments have been carried out to achieve its successful cultivation regarding high lipid production for biofuels (e.g., [99,100]). Currently, new genetic engineering methods for its industrial culturing for different biotechnological purposes have been developed [101]. One more freshwater euglenophyte alga, namely *Trachelomonas volvocina*, was proven to accumulate astaxanthin, but there are no available data on its production [40,102] and technologies for industrial cultivation. We note this, since the well-developed lorica around the cell of *Trachelomonas* may require specific techniques and more expenses for pigment extraction.

Red water blooms can also be formed by unicellular flagellate algae from a different evolutionary line—that of pyrrhophytes (known also as dinophytes, classified also in the SAR supergroup in the Tree of Life [42]). The best-known flagellate species (known as dinoflagellates) in this regard are the unicellular freshwater *Tovelia sanguinea*, which accumulates a high amount of astaxanthin esters and contains adonirubin and astacene [103], and *Tovellia rubescens* [104]. Although no industrial cultivation was achieved, both are included in the list of carotenogenic algae of Europe [40].

Astaxanthin was the main secondary carotenoid accumulated at the stationary growth stage of the unicellular marine haptophyte flagellate *Diacronema vlkianum*, in which the maximum carotenoid content was estimated as ca. 0.6–0.8% of cell DW [40,105,106].

- ß-carotene, lycopene, ß-cryptoxanthin, lutein, zeaxanthin, and canthaxanthin in flagellate algae

Currently, ß-carotene is extracted from 14 green microalgal species, 4 of which are flagellates: 2 from the genus *Tetraselmis* (*Tetraselmis wettsteinii*, *Tetraselmis* sp.) and 2 from the genus *Dunaliella* (*Dunaliella salina* (Syn. *Dunaliella bardawii*), and *Dunaliella tertiolecta*) [37,75]. The extracts from *Dunallielia* have been most successfully scaled into industrial production [29,37,76,107–111]. In this case, the ecology of the genus *Dunaliella*, most species of which inhabit waters with high NaCl content, provides additional value due to the possibility for cultivation in salt waters in both low-tech extensive cultivation in lagoons and extensive cultivations in controlled conditions, thus helping to minimize the freshwater water footprint [107]. Moreover, *Dunalilella salina* was enlisted as a commercial source of zeaxanthin together with the snow flagellate *Chlamydomonas nivalis* and the coccal freshwater green *Chlorella ellipsoidea* [37]. Considering the current statement about the absence of living cultures of the extremophilic snow alga *Chlamydomonas nivalis* and its possible transformation to *Sanguinea nivalis* [80], it seems necessary to check taxonomically the strain(s) reported in the earlier literature. This note is valid for all further mentioning of *Chlamydomonas nivalis* in the text. Pigment studies also demonstrated the presence of ß-cryptoxanthin, particularly in *Dunaliella salina* [1,66], and pointed to lutein as another important pigment in different *Dunaliella* species [37,107]. In the extremophilic

Dunaliella acidophila, which lives in freshwaters of low pH (0.2–2.5), lycopene and other major carotenoids (1.4% of the ethyl ether extract), namely, α-carotene, β-carotene, and γ-carotene, were found [112].

On a commercial scale, lutein and zeaxanthin are generally associated with some coccal algae from the green genera *Chlorella* s.l. and *Scenedesmus* s.l. [111]. However, seven green flagellates, namely *Chlamydomonas acidophila*, *Chlamydomonas nivalis*, *Dunaliella tertiolecta*, *Pyramimonas urceolata*, *Pyramimonas* sp., *Tetraselmis wettsteinii*, and *Tetraselmis* sp., were outlined as commercial lutein sources together with 21 green coccal microalgae [37]. In *Chlamydomonas nivalis* in particular, a lutein content of 15.6 mg 100 g^{-1} fresh mass has been reported [113]. Another species from the genus *Chlamydomonas*, the freshwater *Chlamydomonas plantogloea*, was also pointed out as a valuable lutein producer with an estimated content of 7.4 mg g^{-1} [114]. Achievement of high lutein productivity (5.08 mg L^{-1} d^{-1}) under high light irradiation (625 µmol m^{-2} s^{-1}) was also reported for the *Chlamydomonas* strain JSC4, thus demonstrating its great potential for outdoor cultivation [115]. High lutein amounts (4.24 mg g^{-1} and productivity of 3.25 mg L^{-1} per day) were achieved in the freshwater *Chlamydomonas rehinardtii* by controlling the cultivation conditions [39,116]. High lutein content (85.4 mg 100 g^{-1} DW) was detected in the marine green unicellular flagellate *Tetraselmis suecica*, which also contained significant amounts of α-carotene, ß-carotene, and violaxanthin [117]. From a marine strain of the same genus, namely *Tetraselmis* sp. CTP4, which was successfully produced in 100 m^3 photobioreactors, the highest yield of lutein and β-carotene (ca. 622 and 618 µg g^{-1} DW, respectively) was achieved after a mechanical glass bead-assisted cell disruption [118]. Lutein is typical not only for green algae but is a pigment also found in another small evolutionary line—that of unicellular cryptophytes [62]. Considering their broad distribution, it seems promising to find commercially valuable strains among them.

Canthaxanthin was detected in samples that contain red phases of green flagellates inhabiting snow, such as the abovementioned *Chlamydomonas nivalis* [113]. It has been reported to only have been commercially obtained from some strains of *Chlamydomonas nivalis* and *Haematococcus lacustris* [37].

- Fucoxanthin in flagellate algae

Fucoxanthin is an algal-specific pigment, typical for the yellow-brown evolutionary algal line (phylum Ochrophyta) and is commonly extracted on a commercial scale from large brown seaweeds (kelp), such as *Laminaria japonica*, *Undaria pinnatifida*, *Hizikia fusiformis*, *Sargassum* spp., and *Fucus* spp. [68,111]. In the last years, the interest in searching for new sources of this plentiful carotenoid has expanded to microalgae. They seemed to be a more reliable fucoxanthin source compared to macroalgae because of their shorter cultivation period, year-round production, and higher fucoxanthin content in comparison to kelp [67,68,119]. For example, this content has been estimated as 0.28–2.4 mg g^{-1} DW in macroalgae, while in ochrophyte saline microalgae, it is ca. 65 times higher (for details see [120]). Although the production of microalgal fucoxanthin is not yet economically feasible [29,67], the number of studies in this regard is gradually increasing. Most of them concern coccal microscopic algae, such as diatoms [67,121,122], but some also focus on the ochrophyte flagellates. Among them were (1) marine unicellular haptohytes *Isochrysis zhangjiangensis* [123], *Isochrysis galbana* [60,117,119,124–126], *Isochrysis* sp. CCMP1324 [127], *Isochrysis* sp. [128]), *Tisochrysis lutea* [129–133], *Tisochrysis lutea* strain CS-177/7 [120], *Chrysotila carterae strain* CCMP647 [120]), and *Diacronema lutheri* [134]; (2) unicellular golden *Chromulina ochromonoides*, *Poterioochromonas malhamensis, Ochromonas* sp. [135], (3) pelagophycean *Sarcinochrysis marina* [135], (4) olisthodiscophycean *Olisthodiscus luteus* (two strains) [135]; and (5) silica-scaled colonial *Synura petersenii* [135]. Moreover, fucoxanthin obtained from the golden flagellates *Ochromonas danica*, *Ochromonas* sp., from pelagophycean *Sarcinochrysis marina*, and from the haptophytes *Isochrysis galbana*, *Isochrysis* sp. and *Prymensium parvum*, has been used in commercial products [37,75,126]. In the cosmetic industry, for example, the fucoxanthin from *Isochrysis galbana* was exploited as a sunscreen [136].

The comparative experiments with six microalgae considering fucoxanthin production in different concentrations of NaCl showed that the lowest fucoxanthin producer, the unicellular haptophyte *Chrysotila carteriae*, at 35‰ salinity produces about 1.04 mg g^{-1}, which was 60–80% more than that of halotolerant diatoms from the coccal genera *Navicula* and *Amphora* [120]. In *Isochrysis galbana*, the fucoxanthin comprised 1346 mg g^{-1} DW, accounting for ca. 76% of total carotenoids [117]. *Tisochrysis* can produce ca. 10 mg L^{-1} per day [129]. From *Diacronema lutheri* ("*Pavlova lutheri* strain OPMS 30543") with productivity of ca. 5 mg L^{-1} per day, the maximum fucoxanthin titer of 17.8 mg L^{-1} was obtained using sodium nitrate medium [134]. Another microscopic unicellular flagellate from the same yellow-brown evolutionary line, such as the freshwater golden *Poteriochromonas malhamensis*, and especially its strain CMBB-1 [68] and the silica-scaled *Mallomonas* sp. SBV13 [137], has been pointed out to be valuable for commercial fucoxanthin production, showing productivity of 6 and 7 mg L^{-1} per day, respectively. The study of *Poteriochoromnas malhamensis* led to proposing a novel mode for fucoxanthin production by coupling extra illumination with heterotrophic high-cell-density fermentation to obtain a maximum fucoxanthin yield of 50.5 mg L^{-1} [68]. The first study of the golden unicellular flagellate *Hibberdia magna* seems very promising since it demonstrated high fucoxanthin content of ca. 13 mg g^{-1} DW [48].

Fucoxanthin was proved as the major carotenoid in the raphidophycean algae from the same yellow-brown evolutionary algal line. They are mentioned here separately because when species from all known rhaphidophycean genera have been examined; along with some other carotenoids, the unusual joint presence of zeaxanthin and violaxanthin was underlined by the researchers [138]. However, here we have to recall that such a common presence of both pigments (together with 35 other carotenoids) has been pointed out for another ochrophyte class, Eustigmatophyceae, which embraces only coccal algae [139] and is possible in blue-green and red evolutionary lines [28,41]. The current study confirmed the major role of fucoxanthin in strains of the marine *Chattonella subsalsa*, *Chattonella marina*, and *Fibrocapsa japonica* [140] but commercial production from these algae is not known.

- Anthocyanins in flagellate algae

Anthocyanins, commonly known as strong antioxidants, and widely present in fruits and vegetables, are extremely rarely reported in algae [17]. They have been found for the first time in microalgae in small quantities in the peculiar *Chlamydomonas agloeoformis*, currently isolated from a freshwater high alpine lake in Ecuador [17].

3.1.3. Phycobilins

Phycobilins are accessory pigments, which absorb radiation between 400 nm and 700 nm (but mostly yellow light, 585–575 nm) [141,142]. They occur in three main unique types, such as phycocyanobilins (blue-colored), allophycocyanin, and phycoerythriobilins (red-colored), to each phycourobilin (yellow-colored), and phycoviolobilin (purple-colored, known also as cryptoviolin) were added [141,142]. Phycobilins are algal-specific pigments and even among algae are synthesized only in four evolutionary lines: blue-green, red, glaucocystophyte, and cryptophyte lines [28,41,142,143]. The first three of the types mentioned above appear in certain combinations and are included in specific microbodies, named phycobilisomes [28,41,141,144]. Phycobilisomes are not formed only in cryptophytes [28,41,141], and each organism contains only one type of phycobiliprotein [141]. In two cryptophyte strains, phycocyanins and phycoerythrins were combined with other bilins (bilin 618 and bilin 584), mesobiliverdin, and 15, 16 dihydrobiliversin [145,146].

For years, phycobilins have been applied mainly as fluorescent dyes due to their absorption abilities, but nowadays interest in them as food and nanotechnological, pharmaceutical, medicinal, and cosmetic substances, is increasing [62,141–143,147–151]. It has to be underlined that algal phycobilins are generally found in water-soluble protein-bound forms commonly known as phycobiliproteins (divided into phycoerythrins, allophycocyanin, and phycocyanins), which are commercially used. According to the current summarizing reviews [141,142,148], they are the only natural greenish or bluish colorants and are also pinkish-red colorants that can serve as safe alternatives of the synthetic ones, since no toxicity was recorded in studies using mice, rats, and human cell lines. Phycocyanin and phycoerythrin are constituents of hair and personal care products, in cosmetics and beauty products, and are used in lipsticks, eye-shadows, eyeliners, face make-up, and sun-protecting cream [10,62,143,148,152–156].

In addition, phycobilins have been proven as potent antioxidants able to scavenge ROS, inhibit lipid peroxidation, and chelate iron ions [141,144,157–160]. These properties may explain their multipurpose abilities, including the anti-inflammatory and anticancer effects [141] that serve for their potential application as anti-aging substances [161]. This, together with the discovery of their antiviral, antibacterial, antifungal, dermaprotective, melagonesis-inhibiting, and wound-healing abilities [62,142–144,162–165], is of interest for modern cosmetics.

To date, mainly the phycobilins from the blue-green and red algal evolutionary lines have been explored [142,143,151,164], with less detailed research on the application of the cryptophyte phycobilins [166]. This is valid for the current state-of-the-art related to industrial algal cultivation for phycobilin production, in which, according to our best knowledge, flagellates are not involved despite their extraction and purification from cryptophytes have been successfully achieved [149]. However, currently, the interest in research on the group is rising [62,167].

According to their biliprotein type and its concentration (pg cell^{-1}), cryptophyte genera were ordered as follows: (1) phycoerythrin containing *Cryptomonas* (2.3–40.4), *Rhodomonas* (2.6–13.9), *Rhinomonas* (3.3), *Storeatula* (14.6), *Guillardia* (0.9), *Hanusia* (1.9), *Geminigera* (6.6), *Plagioselmis*, and *Teleaulax* (no data); (2) phycocyanin containing *Proteomonas* (1.2–10.3), *Chroomonas* (6–12.2), *Komma*, and *Flacomonas* (no data); and (3) phycocyanin or phycoertryn containing *Hemiselmis* (PC615 and PC630—0.2–1.6, PC 577 or PE555–0.5) [62,168,169].

A comparative study of eight freshwater *Cryptomonas* strains (namely, *Cryptomonas curvata* CCAP 979/63, *Cryptomonas erosa* CPCC 446, *Cryptomonas lundii* CCAP 979/69, *Cryptomonas marssonii* CCAP 979/70, *Cryptomonas ozolinii* UTEX LB 2782, *Cryptomonas pyrenoidifera* NIVA 2/81, *Cryptomonas pyrenoidifera* CCAP 979/61 (previously *Cryptomonas ovata*), and *Cryptomonas* sp. CPCC 336) with two marine strains (*Rhodomonas salina* CCMP 757, *Proteomonas sulcata* CCMP 704) demonstrated much higher cellular phycoerythrin concentrations in *Cryptomomas*, suggesting that it may be a better source of phycoerythrin than the more extensively studied marine strains [167]. The marine *Rhodomonas* [155] and the freshwater *Cryptomonas* have been considered promising candidates, especially for the production of phycoerythrynes [155,169], whereas the whole genus *Chroomonas* has been reported as a great source of phycocyanin [62,169]. Since from each strain one phycobilin can be obtained, cryptophytes have significant advantages over all other phycobilin producers in which the phycobilisomes contain different pigments and need separation during the production process [62,155,167]. This, together with the lack of a developed cell wall, makes phycobilin processing easy and economically feasible [155]. The other advantages of cryptophytes can be found in the low molecular weight of their pigments compared to those from other algae, which increases their usability in fluorescent labeling [166] and in their ability to produce valuable fatty acids [167].

3.2. Flagellate Algae as Lipid Sources

Lipids are indispensable cell components and precursors to many important molecules. Microalgae accumulate high amounts of lipids (20–50% of the cell DW), mostly fatty acids and wax esters, during their growth [170,171]. Although hundreds of strains capable of such production have been reported, mainly regarding biofuel production [171], most of the studies were oriented towards coccal microalgae and far fewer concerned flagellates.

Comparative lipid analyses of ten oleaginous soil algal isolates, such as three cyanoprokaryotes, five unicellular coccal green algae, and two unidentified green flagellate species from the order Chlamydomonadales TGA3 and TGA5, demonstrated that green algae accumulate more lipids than cyanoprokaryotes [172]. Both flagellates, and the strain TGA3 in particular, were among the best-performing strains for open pond cultivation, exhibiting the highest growth rate 0.28 day^{-1} μexp, lipid accumulation (29.7 %), and biomass yield (134.17 ± 16.87 mg L^{-1} day^{-1}) [172]. A high lipid content was proven also in green unicellular marine algae from the genus *Tetraselmis* [173]. In *Tetraselmis* strain KCTC 12236BP in particular, the highest lipid productivity of 36 mg L^{-1} per day was achieved during cultivation using yeast extract [173].

High lipid content was pointed out also for the freshwater golden unicellular flagellate *Poteriochromonas malhamensis* [68]. Experiments with another golden unicellular non-photosynthetic, but phagotrophic freshwater flagellate *Ochromonas danica*, fermented on ketchup, allowed a high cell yield (40%) to be achieved, with a total lipid content of 9.5 g L^{-1} DW with 38% maximum intracellular content [174].

Findings concerning value-added compounds from the specific lipid categories in flagellates are presented below following the updated LIPID MAPS comprehensive classification [175].

3.2.1. Fatty Acryls: Fatty Acids

Fatty acids comprise the major component of lipids, which can account for 20% to 50% of the dry biomass of microalgae, as was summarized in a review of the application of aeroterrestrial and extremophilic algae in cosmetics [19]. According to this review, in microalgae, 135 fatty acids have been recorded with a variety of applications as emollients, emulsifiers, softeners, and raw materials in soaps. An abundant total content of fatty acids (14% of ethyl ether extract) was discovered in the extremophilic *Dunaliella acidophila* [112]. The study of fatty acids in the marine unicellular raphidophycean flagellate *Heterosigma akashiwo* and two dinoflagellates (*Alexandrium minutum* and *Karlodinium veneficum*) in a bubble column photobioreactors under outdoor culture conditions revealed the highest biomass productivity (0.35 g·L^{-1} day^{-1}), lipid productivity (80.7 mg lipid·L^{-1} day^{-1}), and lipid concentration (252 mg lipid·L^{-1}) for *Alexandrium minutum* [176].

An important type of lipids are polyunsaturated fatty acids (PUFAs), which occur normally in the skin epidermis and play key roles in the regulation of cell membrane fluidity, electron and oxygen transport, and cell and tissue thermal adaptation [16]. PUFAs are also able to prevent intracellular ice crystal formation playing a cryo-protective role [19,177]. In addition, evidence was collected that PUFAs produced by microalgae exhibit antibacterial, antiviral, antioxidant, and detoxifying capacities [75], and can mitigate several inflammatory and allergic reactions [19]. Therefore, PUFAs are significant for proper skin functioning and are used in cosmetics as surfactants in soaps and other skincare products, including those for wound healing and skin whitening [19].

PUFAs are beneficial also for hair care and it has been demonstrated that algal oil rich in omega 3 fatty acids provides deep nourishment to the hair follicles, can decrease dandruff production, reduce scratchy and itchy scalps and hair fall, and make hair stronger and healthier [13]. Of particular use in this regard are Docosahexaenoic Acid (DHA, 22: 6n–3, or also 22:6ω3, 22:6) and Eicosapentaenoic Acid (EPA, 20: 5n–3, or also 20:5ω3, 20:5–3) produced by microalgae, which are desirable constituents regularly used in cosmetic commodities such as hair oils, hair serum, hair gels, and sprays [13].

The high content of unsaturated fatty acids (e.g., Linolenic acid C18:3 from Omega-3 group, and Linoleic Acid C18:2 and Arachidonic Acid C20:4 from Omega-6 group), 69% of total fatty acids, was achieved by changing the culturing conditions mentioned above for its high total lipid content *Poteriochoroomonas malhamensis* [68]. The chemical analysis of another golden unicellular flagellate, the freshwater *Hibberdia magna*, did not reveal high lipid content, but among its lipids, very valuable and diverse PUFAs were found in a non-negligible amount (more than 1 mg g^{-1} DW) [48]. They included three Omega 3 PUFAs (Alpha-linolenic Acid 18:3, Stearidonic Acid 18:4, EPA, and DHA) and four Omega 6 (Linoleic Acid, gamma-Linolenic Acid, Dihomo-γ-Linolenic Acid ethyl ester 20:3, and Docosapentanoic Acid C22:5ω6) [48].

A comparative study of 16 strains of the marine haptophyte genus *Isochrysis* revealed that the strains CL153180 and CCMP1324 are rich in DHA [127,178]. Earlier studies have demonstrated PUFAs in this genus as the predominant fatty acid group (37.93% of the total fatty acids) at 18 °C, and the predominance of saturated fatty acids at 26 °C [60].

Due to the high amount of Omega 3 (ω-3) fatty acids, *Tisochrysis lutea* is used for the production of human food complements and has been used for decades in aquaculture as feedstock for shellfish, oysters, and shrimps [179]. This microalga has a high content of long-chain PUFAs such as DHA [180] and stearidonic acid [179,181].

The percentage contribution of EPA to the total fatty acid content in different marine microalgae allows to point out microflagellates as safe, sustainable, and cheap sources of ω-3 PUFA although their EPA content was lower than those in the coccal green algal species (e.g., 45% in *Mychonastes homosphaera*, former *Chlorella minutissima*) [16]. In more detail, in the unicellular haptophytes *Diacronema lutheri* and *Gephyrocapsa huxleyi* (Syn. *Coccolithus huxleyi*, *Emilianiya huxleyi*), EPA comprises 19% and 17%, respectively, and in the unicellular marine *Pseudopedinella* sp. from the dictyochophycean class of the yellow-brown evolutionary line this percent is even higher—27% [16]. In the green unicellular flagellate *Nephroselmis rotunda* (Syn. Heteromastrix rotunda) EPA constitutes 28%, while in the unicellular cryptophytes Rhodomonas maculata (Syn. Cryptomonas maculata) and Chroomonas sp. it was 17% and 12%, respectively [16]. Examination of fatty acids in all known raphidophycean genera revealed the presence of 15 fatty acids, 5 of which were major, each of them constituting 8–21% of the total fatty acids [138]. Among them were Stearidonic acid and EPA, currently also confirmed as the main acids in the strains of *Chattonella subsalsa*, *Chattonella marina*, and *Fibrocapsa japonica* from the same class [140].

Regarding EPA, we would like to stress the well-known unusually high content of PUFAs in the members of the whole class Pinguiophyceae, and in its marine unicellular flagellate *Phaeomonas parva* and *Phaeomonas* sp. in particular [41,182–184]. This unusually high richness was the basis for choosing the class name using the Latin noun 'pingue' (=fat, grease). Amongst PUFAs, there is a strong predominance of EPA (23.5–56% of total fatty acids), which is typical for the class [41,182–184].

A comprehensive comparative study on the fatty acid composition was performed using 235 microalgal strains from all classes of Ochrophyta, Cryptophyta, and Haptophyta from the Microbial Culture Collection at the National Institute for Environmental Studies [183]. Among these strains, flagellates were spread as follows: (1) 8 golden algae; (2) 7 silica scaled; (3) 16 pelagophyceans; (4) 1 pinguiophycean; (5) 21 raphidophyceans; (6) 3 olisthodiscophyceans; (7) 18 cryptophytes; and (8) 43 haptophytes. EPA was found at >10% of the total fatty acid composition in 119 strains and DHA occurred in more than 10% of the total in 16 strains, most of which were haptophytes, and in two unidentified strains of pelagophycean algae. Strains from all ochrophyte classes, except golden algae and pelagophyceans, as well as the strains from cryptophyte algae, typically contained more EPA than DHA [183].

Other studies also confirm cryptophytes, such as the freshwater species from the genus *Cryptomonas* and marine species from genera *Rhodomonas*, *Teleaulax* and *Proteomonas* as good producers of the ω-3 PUFAs, and especially of EPA and DHA [185–187]. However, only some marine cryptophytes have been suggested for use in biotechnology [167,188], among which *Chroomonas nordstedtii* (Syn. *Chroomonas mesostigmatica*) was pointed for EPA extraction and *Storeatula major*—for both EPA and DHA [186].

The chemical analysis of *Chlamydomonas reinhardtii* demonstrated a content of ca. 20% of lipids [189]. They were composed of saturated fatty acids, monounsaturated fatty acids, or PUFAs with a length between 16 and 20 carbons, especially Alpha-linolenic Acid [39,190]. The current study of *Chlamydomonas agloeformis* revealed a high content of both saturated (particularly palmitic acid C16:0) and unsaturated fatty acids [17]. Considering the last ones, 50% of the total fatty acid content was constituted by two ω-3 fatty acids, namely Alpha-linolenic Acid and Linoleic acid (ca. 32% and 17%, respectively). These levels were much higher in comparison with their amount in another species of the same genus, *Chlamydomonas planctogloea*, characterized in an earlier study [114].

The amount of PUFAs and their detailed composition in extremophilic and aeroterrestrial algae regarding their utilization in cosmetics was currently reviewed [19]. Here, considering the potential of flagellates as PUFA sources for cosmetics, we shall recall that studies concerned cryophilic unicellular green *Chloromonas alpina*, *Chloromonas hindakii*, *Chloromonas nivalis* (incl. subsp. *tatrae*), *Chloromonas polyptera*, *Chloromonas remiasii* CCCryo 005–99, *Chloromonas* spp. and some uncultured species of the family Chlamydomonadaceae. In all of them, PUFAs (mostly ω3) were the major component of their total lipid content (45–50% of all fatty acids), predominating over saturated fatty acids (30–40%) and monounsaturated fatty acids (10–15%) [83,177,191–193].

3.2.2. Fatty Acryls: Fatty Acid Esters

Fatty acid esters comprise wax monoesters, wax diesters, lactones, etc. [175]. The sources and application of microalgal waxes in cosmetics were summarized [19], showing them as important and dermatologically well tolerated ingredients that may serve as texturizer agents for regulation of the viscosity of formulations and increasing their protective and lubricant properties for improving the rigidity, hardness, texture, and stability of lipsticks [194]. Waxes of flagellates are very poorly known, but one of the commercial sources of PUFAs and wax esters is *Euglena gracilis* [195]. Although its general content of lipids is not so high as in other microalgae, it has been stated by different authors that this euglenophyte flagellate has a competitive advantage due to the better wax esters/total lipid ratio (up to 0.8 g g^{-1}), as lipids produced by most microalgae are typically fatty acids [196,197].

Lactones represent the second group of fatty acid esters and, by contrast with other organisms, including seaweeds, have been poorly studied in microscopic flagellates [19]. As in other algae, most research addressed the oxylipins (oxygenated derivatives of PUFA) due to their antibacterial, anti-inflammatory, and antiallergic activity and ability to alleviate damages caused by diverse kinds of stress, desiccation, wounds, and pathogen infections [19,198–200]. The endogenous lipoxygenase-derived oxylipins were determined in the green unicellular freshwater/soil *Edaphochlamys debaryana* (Syn. *Chlamydomonas debaryana*) [199]. In *Dunaliella acidophila*, three methyl esters were identified as new for algae: methyl (9Z,13E,15Z)-18-hydroxyoctadeca-9,13,15-trienoic acid, methyl (9S)-hydroxyoctadeca-10E, 12Z,15Z-trienoic acid and methyl (9Z,12R)-12-Hydroxyoctadec-9-enoate [112].

3.2.3. Fatty Acryls: Hydrocarbons and Triadylglycerols

Hydrocarbons are a separate class in the category of fatty acids that embraces isoprenoids (terpenoids) and alkanes/alkenes (commonly written as alka(e)nes) and have an essential role in preventing water loss of tissues [201,202]. Therefore, they are applied in different ingredients, including those used in cosmetics [203]. Hydrocarbons are better explored in higher plants and cyanoprokaryotes but less studied in eukaryotic microalgae. Among them, research was focused mainly on green algae and on the well-known model alga *Chlamydomonas reinhardtii* [19,201,202,204]. In this species, a C17 alkene, n-heptadecene, was detected and a new, light-dependent pathway to convert C16 and C18 fatty acids into alka(e)nes was pointed out in microalgae [201]. Currently, hydrocarbons and their possible biosynthetic pathways are gaining more attention combined with bioengineering attempts to increase their production mainly in relation to their importance in biofuels [201,202]. Additionally, regarding the role of hydrocarbons in carotenoid synthesis, the number of examined species is enlarging, including for example the green flagellate *Haematococcus lacustris* [205].

Triacylglycerols are a separate class of fatty acids [175]. Their content in *Dunaliella acidophila* reached 5.2% of the ethyl ether extract, including trilinolenin, triolein, trielaidin, and tristearin [112].

3.2.4. Glycerolipids

Glycerolipids include (1) mono-, di- and tri-substituted glycerols, from which the best-known are acylglycerols [175], and (2) betaine lipids [206]. Glycerolipids have anti-cancer, antiviral, and anti-inflammatory activities, which make them attractive in dermal cosmetics [19]. However, data on their content in flagellates are scarce, despite the presence of betaine lipids has been proved in the plastids of green microalgae [19]. In particular, in *Chlamydomonas reinhardtii*, betaine lipids replace phospholipids, which is typical for most eukaryotes [207].

3.2.5. Glycerophospolipids

Glycerophospholipids commonly occur in microalgae as key components of cell membranes, which may participate in responses to stress and are used in cosmetic ingredients as excellent emulsifying agents that can stabilize oil–water emulsions [19,194,208,209]. Yet, few investigations are available on their content in flagellates, among which is that of *Chloromonas hindakii* [83]. Its detailed study demonstrated that the content of Alpha-linolenic acid was up to twice higher in phospholipids than in neutral lipids and glycolipids [83].

3.2.6. Sphingolipids

This lipid class embraces ceramides, phosphosphingolipids, glycosphingolipids, and some others, including protein adducts [175]. Sphingolipids have great industrial potential due to their significant role in maintaining cell membrane integrity and antibiotic (antimicrobial and antiviral) activity [19]. This is especially valid for ceramides, which are spread in the stratum corneum of the skin and are significant for protective skin functions, serving as barriers for undesirable water loss or ingress of potentially harmful substances [210]. Their role in the alleviation of atopic dermatitis [210,211], enhancement of psoriasis treatment [212], prevention of tumor formation [213], and reduction in UV-induced wrinkle formation in skin photoaging [214], as well as the increasing of gene expression related to ceramide delivery in normal human epidermal keratinocytes [215], makes them important and desirable ingredients in cosmetic formulations for topical application [19].

Although most investigations have been oriented towards marine green and red macroalgae [19,216], results obtained on the structure and functions of sphingolipids in microalgae, and in flagellates in particular, look very promising for their cosmetic utilization. Identification and quantitative profiling of ceramides and glycosphingolipids in total lipid extracts from three strains of dinoflagellates *Alexandrium minutum*, *Prorocentrum donghaiense*, and Karlodinium veneficum, and from three strains of haptophytes, *Isochtysis galbana*, *Isochrysis zhanjiangensis* and *Pleurochrysis carterae*, revealed miscellaneous composition of ceramides with structural diversity in different species [217]. Moreover, in both microalgal groups, sphingolid long-chain bases different from those in high plants were discovered. The total amount of sphingolipids ranged significantly from 0.45 to 53 nmol mg^{-1} DW, with similarly notable ranges in different classes: ceramides (0.03–7.37 nmol mg^{-1} DW), monosaccharide ceramides (0.08–14.85 nmol mg^{-1} DW), disaccharide ceramides (0.12–12.45 nmol mg^{-1} DW), and trisaccharide ceramides (0.06–7.41 nmol mg^{-1} DW), respectively [217]. A novel ceramide bearing a 2-hydroxy-15-methyl-3-octadecenoyl moiety was isolated as a cellular constituent in the marine epiphytic dinoflagellate *Coolia monotis* [218]. Glycosylceramides have been detected in the marine *Tetraselmis* sp. [219]. In freshwater unicellular flagellates, sphingolipids were studied in *Ochromonas danica* [220] and in *Euglena gracilis*, in which monohexosylceramides have been identified and recommended for use as moisturizers in cosmetics [221].

3.2.7. Sterol Lipids

Sterol lipids, commonly known as sterols, are a specific lipid group, produced by all types of organisms with essential roles in their cell membrane structures and functioning [19]. Of special interest for cosmetics are the antioxidant, anti-cancer, anti-inflammatory, and antibacterial properties of the sterols [19,62]. Although plant sterols (phytosterols) in general are commercially obtained from higher plants, currently, algae and microalgae, in particular, are regarded as their promising source due to their great variety and health benefits [10,19,222].

Sterol diversity in microalgae was documented by different authors. Data were summarized on detailed sterol composition of marine microalgae from the following taxonomic groups that contain flagellates: Ochrophyta (Chrysophyceae, Synurophyceae, Dictyophyceae, Raphidophyceae), Pyrrhophyta, Cryptophyta, Haptophyta (Coccolithophyceae, Pavlovaphyceae), Euglenophyta, Chlorophyta (Chlorophyceae) [223,224]. The most studied were *Diacronema lutheri*, *Isochrysis galbana*, and *Dunaliella salina*, out of which *Diacronema lutheri* achieved a total sterol accumulation of 5.1%. DW was suggested as a source for commercial phytosterol production [225]. In the same study, another flagellate, *Tetraselmis* sp. M8, was pointed as a top phytosterol producer (0.4–2.6% DW).

In *Dunaliella acidophila*, the sterol content was 6.4% of the ethyl ether extract, comprising β-sitosterol, isofucosterol, 24-methylenlophenol, and (24S)-methyllophenol (isolated for the first time in green algae) together with new, unidentified sterols [112]. Some novel compounds with important bioactivities have also been discovered in euglenophytes. Astasin, extracted from the colorless euglenophyte *Astasia longa*, which contains ergosterol, xylopyranose, and oxalic acid, significantly inhibits the growth of human lymphoma HL-60 cells [226].

The examination of 19 cryptophytes revealed that the major sterol in these flagellates is brassicasterol ($C_{28}H_{46}O$), but four others different phytosterols, including crinosterol (also named epibrassicasterol, $C_{28}H_{46}O$), β-sitosterol ($C_{29}H_{50}O$) campesterol ($C_{28}H_{48}O$), and stigmasterol ($C_{29}H_{48}O$), were also identified [62]. Brasisicasterol can act in blood vessel formation and is considered to have wound-healing potential [227]. This compound has been reported as having skin conditioning properties used in anti-aging cosmetic products, moisturizers, sunscreen, and body wash [228,229]. Crinosterol can be also used as an anti-aging factor [229] but stigmasterol is still considered to be the most valuable due to its anti-inflammatory effects and health-promoting benefits [62,230,231]. Stigmasterol was identified as the major sterol of *Isochrysis galbana* [60].

Although the diversity was revealed, commercial sterol extraction from microalgae is in its infancy due to low sterol content [224].

3.3. Flagellate Algae as Polysaccharide Producers

Polysaccharides are important macromolecules, consisting of connected monosaccharide units, which have specific gelling, texturizing, thickening, and stabilizing properties valuable for different industries, and for cosmetics in particular [39,232]. Moreover, they are known to act as immunomodulators, antioxidants, antitumor drugs, anticoagulants, antibacterial, and antiviral agents [233,234]. Algae produce polysaccharides in significant amounts and are recognized as their abundant resource, especially concerning the families of exopolysaccharides and sulfated polysaccharides [39,235].

Regarding flagellates, the production of polysaccharides is extensively studied in *Chlamydomonas* [39]. The exopolysaccharides of two *Chlamydomonas* species, namely *Chlamydomonas oblonga* (Syn. *C. mexicana*), *Chlamydomonas reinhardtii*, and *Lobochlamys segnis* (Syn. *Chlamydomonas sajao*), contained 6 to 9 monomers, in which dominant sugars were glucose, galactose, fucose, rhamnose, and arabinose [39]. According to the same study, the sulfated polysaccharides of *Chlamydomonas* demonstrated notable activity against different pathogenic bacteria, including *Streptococcus* spp. Earlier, other noteworthy activities, such as antioxidant and efficient anticancer properties against HepG2, HeLa, melanoma B16, and MCF-7 have been demonstrated for the sulfate polysaccharides of *Chlamydomonas reinhardtii* [236].

Cryptophytes are another group of flagellates, known for the ability to synthesize exopolysaccharides [167]. Although they produce large amounts of these compounds, they have received little attention in this regard [237–239]. The first isolation of exopolysaccharides from a temperate soil strain of the genus *Cryptomonas* revealed its structure with two fractions, the first with 12 and the second with 16 different linkages, with a predominance of 1,4-linked galacturonic acid and 1,3-linked galactose in both fractions [237]. By contrast, the isolation of a complex heteropolysaccharide with 23 different linkages in the weak acid fraction and 14 in the strong acid fraction from a tropical reservoir strain of *Cryptomonas tetrapyrenoidosa* revealed that major components of the first fraction were fucose, N-acetyl glucosamine, galactose, and mannose [238]. From a strain of *Cryptomonas obovata*, isolated from a tropical shallow oxbow lake, extracellular sulfated fucose-rich polysaccharide was obtained [239]. In addition to fucose (42%), it contained also N-acetyl-galactosamine (26%), rhamnose (15%), and glucuronic acid, mannose, galactose, xylose, and glucose in small amounts [239]. Here, the rich fucose content is noticed, especially considering the studies that demonstrated the potential of fucose-containing sulfated polysaccharides from algae as skin-cancer preventive factors [233] and as strong anticoagulants [62,234].

Paramylon (β-1,3-glucan), a glucose polymer that is similar to cellulose, is a specific intracellular storage product of euglenophyte algae that can constitute over 80% of the DW [195,197,240] with 16 g L^{-1} culture reported as one of the highest paramylon titers (e.g., [197,241]). Paramylon and other β-1,3-glucans have multiple bioactivities, among which their antimicrobial properties are of interest for cosmetics [197]. Moreover, it can be applied in cosmeceuticals since it has been demonstrated that topical treatment by paramylon can promote wound healing [242]. An increase in this effect was observed when both paramylon and hyaluronic acid at a concentration of 200 mg L^{-1} on rats were applied and was explained by the increased corneal epithelial cell migration and suppression of the acute inflammatory reaction by corneal alkali burns [242]. The commercial microalgal source of paramylon is *Euglena gracilis* [195], considered unique in this respect among other microalgae [101]. Numerous studies regarding possibilities to enhance paramylon production by using different cultivation techniques and cost-effective media have been published (for details, see [243]).

Another flagellate, capable of storing β-1,3-glucan in a soluble form, is *Poterioochromonas malhamensis* [244]. The accumulation of this valuable product in high enough amounts feasible for commercial production (up to 55% of the cell DW) was achieved during high-cell density cultivation under heterotrophic conditions [244].

3.4. Flagellate Algae as Alcohol Sources

Glycerol, known also as glycerine, is an organic osmolyte applied in different fields and widely used in cosmetic products, especially in hand creams for increasing skin moisture in long-lasting skin hydration [13,37]. It is concentrated in significant amounts in *Dunaliella salina* (e.g., 94.26 pg $cell^{-1}$ [245]), but also in *Chlamydomonas reinhardtii* [37].

3.5. Flagellate Algae as Phenolic Sources

Phenols (also known as phenolics), the largest group of plants' secondary metabolites, are commonly divided into simple phenols and polyphenols, the last group in the classes of phenolic acids, flavonoids, isoflavonoids, stilbenes, lignans, and phenolic polymers [246]. Their quantity and composition vary in a broad range (e.g., 0 to 2820 mg GAE/100 [247]) depending on the species and growth conditions [17,53,247]. Polyphenols are important as cosmetic ingredients because they show chemical protecting mechanisms against damages caused by UV radiation and act against melanin formation [12,35,62,248,249]. One of the most frequently reported phenols derived by algae is verbascoside [250]. It is multifunctional, but its anti-inflammatory and antioxidant activities [251,252] are of special interest for inclusion in cosmetic products.

Although phenols of microalgae have been less explored in comparison with marine macroalgae [12], some authors suggest that the phenols are involved in the remarkable antioxidant activities of microalgae [250,253–256], generally associated with carotenoids (e.g., [257]). For example, there was evidence for a significant increase in the total phenolic content in the snow alga *Chlamydomonas nivalis*, after five to seven days of exposure to UV radiation [258]. An increase in polyphenols under light exposure has been demonstrated in experiments with *Chlamydomonas reinhardtii* [259]. Similar results after experiments with light exposure were obtained in a study of *Chlamydomoans agloeaformis*, in which the main phenolic component was verbascoside (158.17 $\pm$ 16.67 out of a total of 169.14 μg g^{-1} DW) with well-known antimicrobial properties, detected together with a good amount of flavonols (quercetin in particular), and flavan-3-ols (mainly epicatechin) and traces of phenolic acids and flavones [17]. The detected amounts of polyphenols were similar to the average total polyphenol content of 211 mg GAE/100 g DW reported after examination of 32 microalgal species, among which were the flagellates *Tetraselmis suecica* and *Isochrysis* sp. [256].

A specific flavonoid class, 2-styrylchromones (2-SC, $C_{17}H_{12}O_2$), was discovered in extracts from the marine pelagophycean *Chrysophaeum taylori* [62].

3.6. Flagellate Algae as Sources of Enzymes and Peptides

Microalgae have great capacity to synthesize enzymes, and 16 microalgal species, mainly cyanoprokaryotes, have been enlisted as their industrial sources [260]. Only one of them was a flagellate, namely *Poterioochromonas malhamensis*, which is included in this list as a source for the α-galactosidase production. There is a bulk of studies related to the discovery of genes that code enzyme production in microalgae and reveal the activity of different enzymes at the laboratory scale, analyzed in detail in [260]. For example, α-amylase activity in *Chlamydomonas reinhardtii* was registered in culture conditions and genes for lipases were identified in the *Chlamydomonas* genome. α-amylase, oligo-1,6-glucosidase, and starch phosphorylase were identified in *Dunaliella tertilecta*, and α-amylase, β-amylase, and glycogen phosphorylase were found in *Dunaliella parva*. *Dunaliella* can also produce gluthathione, a low-molecular-weight thiol-tripeptide constituted by amino acids glycine, cysteine, and glutamic acid [37,261]. Gluthathione, with its high antioxidant capacity and antimelanogenic properties, gained popularity as a powerful sunscreen, skin protector from photo-aging, and skin-lightening agent, applied in many cosmetic products, mainly creams and lotions [37,261]. Since gluthathione is available on the market in oral, parenteral, and topical forms, it has to be noted that, up to now, safety has been proven only for its oral and topical application [261].

Tetraselmis suecica produces antimicrobial peptides with bactericidal effects against gram-negative and Gram-positive bacteria [262], some of which can affect skin wounds.

3.7. Flagellate Algae as Sources of Mycosporine-like Aminoacids (MAAS)

Mycosporine-like aminoacids (MAAs) are natural compounds biosynthesized by algae considered responsible for protection from UV radiation [263–265]. They have been identified in different groups of algae. It has to be underlined that algal MAAs have already resulted in commercially stable and effective skin-care UV-protective products [16,37,266]. Besides the sunscreen function and anti-aging abilities [62], MAAS can be strong antioxidants [16,265] and anti-cancer agents [62], and it has been suggested that some of them have anti-inflammatory effects [267]. Additionally, they can improve skin smoothness [62,268] and inhibit elastane decomposition and wrinkle formation [269]. All these effects significantly increase their potential for application in modern cosmeceuticals.

Comparative study on MAAs in 206 strains of 152 cultured marine microalgal species included the following number of flagellates from different taxonomic groups: (1) 4 raphidophyceans; (2) 35 haptophytes; (3) 1 euglenophyte; (4) 47 dinoflagellates; (5) 10 cryptophytes; and (6) 22 green algal strains. The highest amounts of these compounds in dinoflagellates, cryptophytes, haptophytes, and raphidophyceans were discovered [270]. The richest in UV absorptive compounds were the raphidophycean *Fibrocapsa* sp., the haptophyte *Phaeocystis pochetii*, and the dinoflagellates *Alexandrium margalefi* and *Gymnodinium catenatum*, whereas the green *Tetraselmis chui* had the lowest content comparable with this in the coccal colonial diatom *Asterionella glacialis* [270]. Moreover, the results obtained showed that concentrations of UV absorptive compounds differed strongly among species and strains, with the highest variation of diversity in the group of dinoflagellates. When field phytoplankton samples were also examined, it was concluded that the highest UV-screening capacity in both types of samples processed was demonstrated by dinoflagellates that are bloom-forming in nature (e.g., *Gymnodinium catenatum*, *Alexandrium*, *Scrippsiella*, *Heterocapsa*, and *Woloszynskaya*) followed by haptophytes (*Chrysochromulina*, *Gephyrocapsa*, *Haptolina*, *Dicrateria*, and *Phaeocystis*), cryptophytes (*Chroomonas* and *Rhodomonas*), and by raphidophyceans (*Chattonella* and *Fibrocapsa*). The same authors also found three yet-unknown MAAs in *Gymnodinium catenatum* in addition to the well-known mycosporine-glycine, porphyra 344, and shinorine. The main conclusions from this comprehensive study led to the understanding of the prevalence of MAAs in bloom-forming marine flagellates as the best "sun-adapted" phytoplankters [270], indicating their great potential for future research for effective sunscreen products.

Further study of 33 algal strains (31 marine, 1 freshwater, 1 soil species), 23 of which were flagellates, provided new data on the diversity and abundance of MAAs, pointing also to their application as potential source of natural alternatives to synthetic sunscreens [271]. In this study, shinorin was outlined as the most spread compound. MAAS were detected in 20 (60%) of all examined species and their frequent occurrence in high amounts as well as their diversity in dinoflagellates were proved. The highest MAAs concentrations (>6000 fg cell^{-1}) were measured in the dinoflagellates of *Kryptoperidinium foliaceum* (Syn. *Glenodinuim foliaceum*) and *Scripsiella acuminata* (Syn. *Scrippsiella trochoidea*), followed by *Karlodinium veneficum* (Syn. *Gymnodinium galatheanum*, *Gymnodinium venificum*; >1500 fg cell^{-1}) [271]. In addition, in the same study, the ability to synthesize MAAS was supposed for the first time for the heterotophic dinoflagellate *Oxyrrhis marina*. A novel UV-absorbing compound λmax 342 nm (peak 12) in the cultures of *Gyrodinium* sp. and *Gymnodiniun* spp. was found, and a relatively high amount of MAAs was measured in the cryptophyte *Rhodomonas baltica* (140 fg cell^{-1}).

In 2007, a database on UV-absorbing mycosporines and MAAs reported in different organisms from aquatic and terrestrial habitats, including 44 strains of flagellate algae, was published [272]. Considering extremophilic algae, MAAs were found as produced in significant amounts by snow inhabitants [12]. They have been identified in the green flagellates inhabiting the snow surface, such as *Chlamydomonas nivalis* [37,273] or *Chlamydomonas hedleyi* from a non-indicated habitat [263]. In the samples from "reddish" and "greenish" snow collected near the penguin rockeries on King George Island, different amounts of MAAs were measured, coinciding with a different spectral profiling [274]. For example, the average MAA concentration in the reddish snow was lower (278.2 µg g^{-1}) in comparison with that of the greenish snow (316.0 µg g^{-1}), which showed a specific high absorbance between 450 and 600 nm. Interestingly, there was no difference in the composition of pigments and fatty acids between both samples [274].

3.8. Flagellate Algae as Vitamin Sources

Vitamin C (ascorbate) is a strong antioxidant [197] essential for collagen biosynthesis and currently becomes popular in anti-pigmentation skin treatment. It is accumulated in high amounts in *Dunaliella* [37]. Although the titer of ascorbate produced by *Euglena gracilis* strongly varies depending on the culture conditions (from 8 to 85 mg L^{-1}), it is considered a valuable commercial source [197,275]. A significant amount (6.45 pg cell^{-1}) of vitamin C in *Cryptomonas maculata* was reported [276].

Microalgae that produce vitamin E (tocopherol) are known to be included in photoprotective skin creams [37]. Earlier studies on the biochemical composition of microalgae demonstrated differences in their tocopherol content dependent on their taxonomic position and culture conditions (e.g., [277]). The best producers on a commercial scale are *Dunaliella tertiolecta*, *Tetraselmis suecica*, and *Euglena gracilis* [37]. The last species is valuable in exclusive production only of the α-tocoferol, the yield of which can be increased by long incubation times and the addition of a carbon source (ethanol) to the culture medium, with the highest achieved titer of 44.2 mg L^{-1} culture, or 1.1 mg g^{-1} DW [197]. However, there is no reported commercial production of tocopherol from *Euglena gracilis* [197]. HPLC investigations proved three flagellates as promising sources of this vitamin depending on the cultivation and method of extraction: *Dunaliella* (228 $\mu g\ g^{-1}$ DW of α-tocopherol, 35 $\mu g\ g^{-1}$ DW of γ-tocopherol, and 1 $\mu g\ g^{-1}$ DW of δ-tocopherol), *Tetraselmis* (49–289 $\mu g\ g^{-1}$ DW of α-tocopherol), and *Isochrysis* (101–302 $\mu g\ g^{-1}$ DW of α-tocopherol, 5 $\mu g\ g^{-1}$ DW of γ-tocopherol, and 2 $\mu g\ g^{-1}$ DW of δ-tocopherol) [277]. More currently, a high yield of α-tocopherol (concentration of 5.22 mg/100 g DW) was obtained from the marine *Isochrysis galbana* cultivated in 100 L polyethylene bags with seawater [60]. In another haptophyte, *Diacronema vlkianum*, the maximum obtained level of α-tocopherol in laboratory conditions was $257.7 \pm 21.6\ \mu g\ g^{-1}$ DW at 18 °C [106].

Vitamin A is produced only by animals and its increased demand boosted a high search for the plant-derived provitamin A, which is the photosynthetic pigment ß-carotene [197]. Currently, one of the most important commercial sources of (pro)vitamins is *Euglena gracilis* [195,197]. However, large-scale cultivation of this flagellate requires supplying the media with the essential vitamins B1 and B12, which are expensive. It was suggested this limitation could be overcome by using co-cultures with microorganisms able to synthesize sufficient amounts of these vitamins [195,278]. Successful co-culturing for long time periods with a dramatical decrease in costs was achieved by adding the fungus *Cladosporium* westerdijkiae, and bacteria *Lysinibacillus* boronitolerans and *Pseudobacillus badius* [278]. Moreover, it was demonstrated that these cultures may enhance the harvesting of *Euglena biomass* through bio-flocculation [195,278].

Although some unresolved problems regarding the stability and sensitivity to environmental factors (heat, oxygen, and light), vitamins of the B group are common ingredients in different cosmetic products due to their versatile favorable effects on the skin [279,280]. Vitamin B_1 (thiamine) has an antipruritic effect and is used in the treatment of rosacea and seborrhea together with riboflabin (vitamin B_2), which has an anti-inflammatory effect [279,280]. Thiamine in a concentration of ca. 358.8 nmol g $cell^{-1}$ was measured in the cryptophyte *Rhodomonas salina* [281]. Riboflavin is applied in cosmetic products as an excipient (natural colorant) [280]. Niacin (vitamin B3) is essential for skin health due to its multifunctional activities, such as being sebostatic, antipruritic, vasoactive, barrier- and photo-protective, lightening, anti-microbial, and anti-inflammatory [280,282]. It is useful in dermatological formulations for the treatment of skin aging, hyperpigmentation, light damage of the skin, acne, atopic dermatitis, melasma, psoriasis, pellagra, nonmelanoma, and skin cancer [280,282,283]. Pantothenic acid (vitamin B5) in the form of its alcohol analog, dexpanthenol, is a moisturizer, has anti-inflammatory properties, and influences fibroblast proliferation. Therefore, it is applied topically for care of damaged skin, wound healing, atopic dermatitis, and scar management [280,284]. Vitamin B6 in its methanol form, pyridoxine, and Vitamin B12 (cobalamin) are promising candidates for the treatment of atopical dermatitis due to the ability of B6 to stimulate filaggrin production in human epidermal keratinocytes [285], and to the suppression of cytokine production, cell proliferation enhancement, and modulation of lymphocyte activity by B12 [280,286]. Due to the reduction in nitric oxide production, B12 may be applied topically in the treatment of childhood eczema [287].

Some flagellates are important as common potential sources of different vitamins. Examples are *Dunaliella tertiolecta*, which contains vitamins B_{12}, B_2, E, and provitamin A, and *Tetraselmis suecica*, which is rich in vitamins B_1, B_3, B_5, B_6, and C [62].

3.9. Extracts of Flagellate Algae as Cosmetic Ingredients

During the literature search, we found information on different algal extracts that exhibited strong effects in skin and hair protection, improvement of appearance, or other treatment regarding beauty products or in treatment of skin and hair disorders, but their exact composition and active compound were not always indicated.

The exception is the freeze-dried methanolic extract of *Chlamydomonas agloeformis* with the following content of bioactive compounds: total phenols, 177.55 ± 25.94 mg GAE/100 g DW; flavonoids, 440.15 ± 152.38 mg CE/100 g DW; and flavonols, 203.80 ± 97.02 mg

QE/100 g DW, examined for its antioxidant properties [17]. According to the results obtained, the extract was non-toxic and had a role in preventing oxidative damage to molecules [17], which suggested its potential as a safe ingredient in anti-aging cosmetic products. A peptide extract of *Chlamydomonas acidophila* for the prevention of skin disorders in cosmetics has already been patented under the international number WO2020/136283 A1 [288].

Acne is a multifactorial skin disease, visually expressed by eruptions on the skin surface that seriously affects the emotions, self-image, and self-esteem of the patients [289]. Therefore, the improvement of the skin appearance can seriously positively influence the lifestyle, and dermatological treatment of various acne lesions is important. The effectiveness of a hydrating product in topical treatment of acne-prone skin of adult women, which contained an extract of *Chlamydomonas reinhardtii*, was proved [289]. In this case, the green algal extract was included to act as a cellular stimulant.

A novel, n-Hexane extract with a high content of palmitic acid was obtained from a specific strain of *Haematococcus lacustris*, isolated from the river Nile (deposited in the GenBank as *Haematococcus lacustris* isolate REH10 with accession number OK336515) [290]. This extract inhibited multi-antibiotic resistant pathogens with its strong activity being proved after examination of seven fractions of *H. lacustris* hexanolic extracts [290].

An extract from the robust marine *Tetraselmis* sp. CTP4, rich in carotenoids together with other bioactive substances, has been shown to diminish hyperpigmentation by reducing the size of melanocytes and reducing skin tension through stimulation of the growth of the epidermal tissue [10,118].

An extract of the bioluminescent marine dinoflagellate *Noctiluca* offered the skin a new source of radiance [13].

The methanol extract (BIO1631) of marine *Isochrysis* sp. Tahitian strain (T-Iso) was highly effective in increasing the number of hair follicles and in hair shaft elongation even at low concentrations and was suggested as a highly promising candidate for inclusion in a cosmetic active for the prevention of hair loss [291]. However, an opinion was published that such a product is unreliable for consumption in the human body considering the toxicity of methanol extract [13]. However, other *Isochrysis* sp. extracts have been applied in sunscreen formulation that contain organic and inorganic filters with SPF 15 to prevent UV transmission [13].

3.10. Flagellate Algae as Nanoparticle Sources

A current review of aeroterrestrial and extremophilic algae showed their potential for the production of lipid nanoparticles for use in cosmetic formulations [19]. However, to our best knowledge there is no commercial exploration of flagellates in this respect. According to our recent search, the only data on the potential application of flagellates in nanoproducts are provided on the ability of the green unicellular marine algae from the genus *Platymonas* to synthesize silver nanoparticles with antibacterial activity against pathogens, which are able to infect different wounds such as *Vibrio alginolyticus*, *Bacillus flexus*, and *Streptococcus* sp. [292].

3.11. Safety Aspects

The compounds included in this review are commonly considered safe and nontoxic, especially when applied topically. However, it is noteworthy to recall that some microalgae can produce toxic metabolites (algal toxins), which are a great safety concern due to their serious impact on human health (for details, see [31,293,294]). Since their detailed discussion is out of the scope of the present study, we shall enlist them briefly for completeness of data on the species producers of valuable cosmetic products. Up to now, toxins have been identified in flagellates from four of the taxonomic groups discussed in this paper, namely Euglenophyta, Pyrrhophyta, Haptophyta, and Ochrophyta (Class Raphidophyceae) (e.g., [293–298]. They have been reported for the following genera, mentioned in this paper: (1) Euglenophyte genera *Euglena* (some strains of *Euglena sanguinea* in particular, as well as strains of two more species of *Euglena* not mentioned in the text, such as *Euglena socialbilis* and *Euglena stellata*) and *Trachelomonas* (but only in the species *Trachelomonas ellipsoideus* and not in *Trachelomonas volvocina* noted here) are producers of euglenophycin, less than 20% of which may be released extracellularly mainly in old cultures of *E. sanguinea* [295,296]; (2) Haptophyte genus *Prymnesium* (*Prymnesium parvum* in particular) release prymnesins, which are categorized into at least three types—A, B, and C [298,299]; (3) Pyrrhophyte genera *Alexandrium*, *Amphidinium*, *Gymnodinium*, *Gyrodinium*, *Prorocentrum* and *Pyrodinium*—saxitoxins, gonyatoxins, pectenotoxins, yessotoxins, and okadaic acid [293,294,297]; (4) Raphidophyceans *Chatonella* (*Chattonela marina* and its variety *antiqua*), *Fibrocapsa* (*Fibrocapsa japonica*) and *Heterosigma* (*Heterocapsa akashiwo*) release brevetoxins [297]. However, euglenophycins and prymnesins were proved as producers of ichtyotoxins that cause fish mortalities without direct effect on humans, while for saxitoxins, gonyatoxins, yessotoxins, pectenotoxins, okadaic acid, and brevetoxins, the main exposure routes are through contaminated water, consumption of poisoned food, or respiration of infested aerosols. According to our best knowledge, negative effects of these toxins via topical application have never been reported, which in the state-of-the-art makes them harmless for cosmetical formulations. However, we would like to stress again the necessity of specific studies targeted on the toxicity of all novel sources and their products proposed for cosmetical formulations [19].

4. Discussion

The growing global cosmetic market is inevitably demanding innovative, more and more specific natural cosmetic ingredients that are not only beneficial in many aspects but are safe for human health and are obtained via eco-friendly processes from less conventional sources [6]. In this regard, microalgae become more and more attractive due to many reasons besides their abilities to function as living factories that provide year-round production and are fast-growing in various types of cultivation systems, including out-door cultivation and culturing in extremophilic conditions inimical for many other organisms (e.g., [13,67,68,119]). Their almost unknown world, especially of algae from some peculiar ecological and morphological groups, offers a rich palette of unexplored natural substances with unique, sometimes intricate structures and functions, and there is growing evidence of findings of novel algal metabolites that exhibit strong and often multipurpose biological activities [12,13,19]. Although there is progressively increasing interest in diving in this fascinating and promising realm, a very small part of algal metabolites from a limited number of algal species have been utilized at a commercial scale. This is especially valid for the microscopical algae from different evolutionary lines that are capable of active motion using specific organelles named flagella, and that inhabit various environments from conventional aquatic systems to hypersaline or acidophilic waterbodies, soils, or snow surfaces. Continued exploration of their structures, functions, and applications not only deepens our understanding of their diversity and improves the taxonomy, but also allows the discovery of new, valuable sources for modern biotechnologically based industries, including cosmetics. A great challenge for future exploitation of these flagellates lies not only in identifying their chemical composition but also in discovering the best-performing strains of these organisms in terms of growth and yields of the products of interest and finding proper ways for their cost-effective specific cultivation and harvesting, including sophisticated genome editing techniques. Based on our long-lasting phycological expertise, the present review summarized research broadly spread in different sources, which was sometimes poorly documented and even included controversial data on natural substances of microscopic flagellates and their potential applications in the field of modern cosmetics.

According to the data obtained, more than 411 strains of flagellates have been investigated. Their distribution according to the evolutionary lines and relevant phyla with clearly visible prevalence of studies of cryptophytes (27%) and haptophytes (23%) is shown in Figure 3.

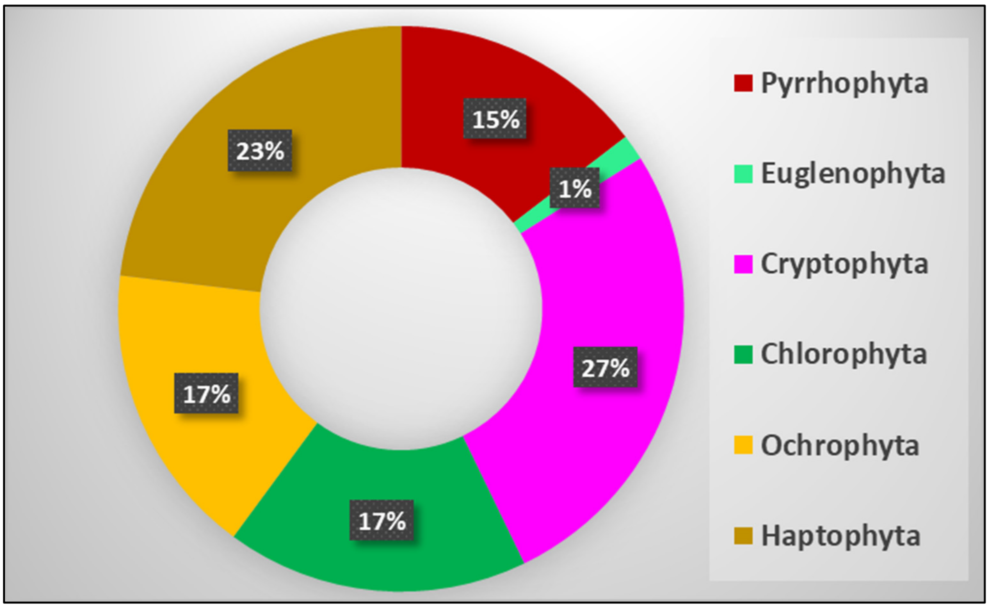

Figure 3. Distribution of number of investigated strains of flagellate algae according to the main taxonomic groups (algal phyla). Colors reflect the natural dyes of algae in the relevant groups.

The biodiversity of the examined flagellates, expressed by the number of species (incl. varieties and forms, and all unidentified species counted separately), is as follows: Chlorophyta—55, Cryptophyta—56, Pyrrhophyta—33, Haptophyta—65, Ochrophyta—37, and. Euglenophyta—5 (Figure 4). Regarding the taxonomic richness, it becomes evident that Haptophytes are the best-investigated groups, followed by almost equally investigated species of green algae and cryptophytes. However, considering the enormous diversity of green flagellates in nature incompatible with this of cryptophytes, this result can be interpreted differently—it shows that much more research on green flagellates is needed in the future. Lack of relevant information on the flagellate species from the phylum Streptophyta from the green evolutionary line (e.g., *Mesostigma*), as well as from some ochrophyte classes with a small number of flagellates (e.g., Bolidophyceae, Tribophyceae), also broadens the field for future research.

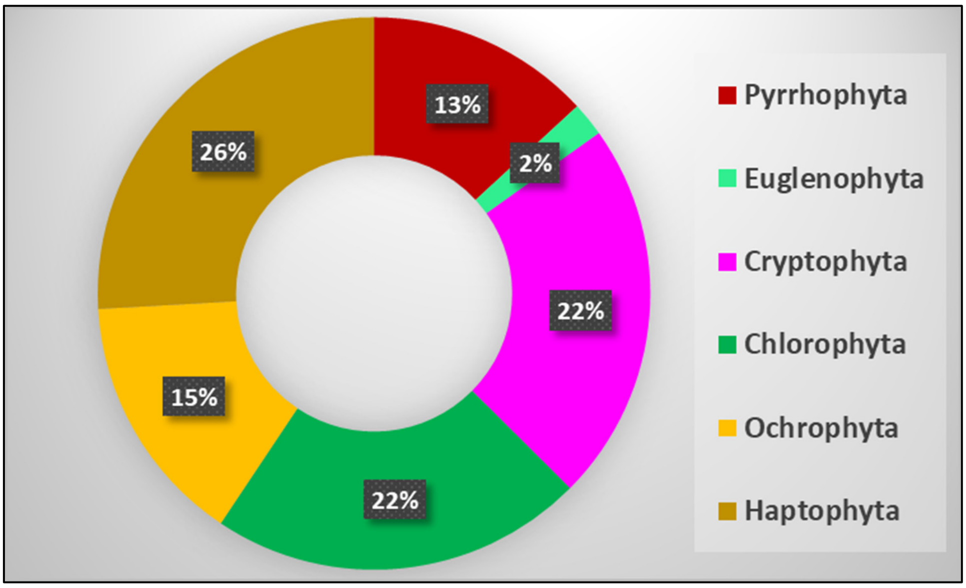

Figure 4. The biodiversity of investigated flagellate species according to the main taxonomic groups (algal phyla). Colors reflect the natural dyes of algae in the relevant groups.

According to the results from the analysis of the distribution of examined algal genera by taxonomical phyla, the best studied were haptophytes and ochrophytes (Figure 5).

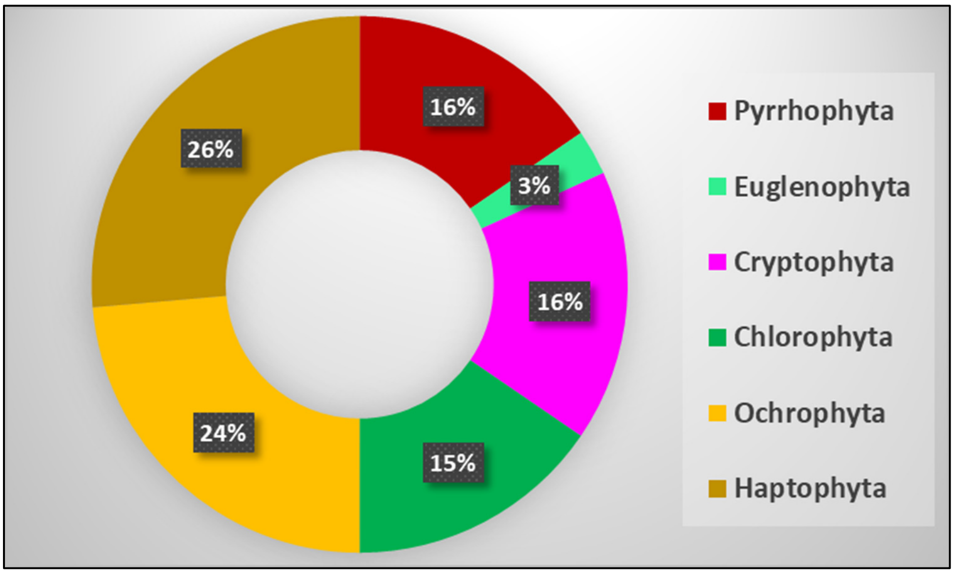

Figure 5. Distribution of the flagellate algal genera in the main taxonomic groups (algal phyla). Colors reflect the natural dyes of algae in the relevant groups.

All the abovementioned differences in the biodiversity of investigated strains, species, and genera did not allow for only one phylum to be pointed to as the best clarified regarding bioactive compounds valuable for the cosmetic industry (Figure 6).

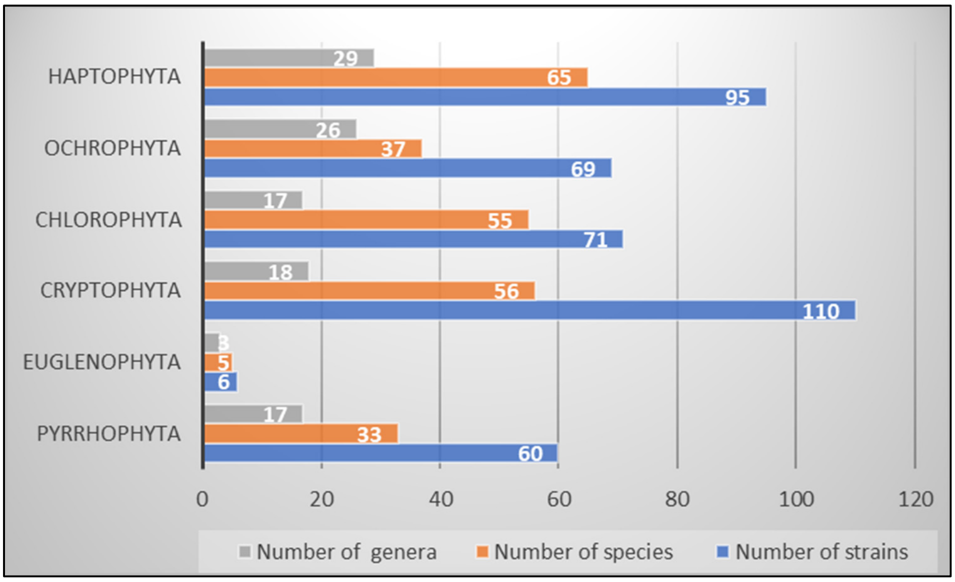

Figure 6. Number of investigated flagellate strains, species, and genera in the main taxonomic groups. Digits in white show the number in each of the categories.

With respect to morphological features, it has to be stressed that all investigated algae were unicellular, except the colonial *Dinobryon divergens Synura petersenii*, *Synura sphagnicola*, *Synura spinosa*, and *Uroglena americana*, included in the investigations of algal fatty acids [183] and fucoxanthin (only *Synura petersenii* [135]).

The ecological affiliation of the examined microalgae is difficult to evaluate correctly since for some of the strains data on habitats are not available. However, according to the strains with provided data, it is possible to summarize that the best studied were flagellates from the phytoplankton of conventional aquatic environments (with the predominance of marine and brackish flagellates). One was marine epiphyte, much less were the extremophilic strains investigated (inhabitants of hypersaline waters, acidic freshwaters, or snow surface) and only four were strains obtained from the soil. All investigated extremophiles and three soil inhabitants belong to the green algae, to phylum Chlorophyta in particular, with only one soil strain of cryptophytes.

However, it has to be boldly underlined that these results are based only on Latin species or strain names enlisted in the available publications. Many of these strains are labeled as "unidentified", pointing to a supposed group, or, in the best case, are given a generic name. In the absence of more taxonomic data, it is practically impossible to estimate the real biodiversity of examined microalgae. In many cases, the same is valid for the strains labelled with species names. However, we found data on labeled strains pointed to a given taxonomic group which contradicts the provided name. Whenever possible, we actualized the synonymy based on the names provided, but here we would like to confirm our previous statement that in the recent times of rapid classification and relevant nomenclatural changes, supplying biochemical data with those from genetic studies and with detailed morphological and ecological descriptions in future publications is strongly recommended [12,19]. Moreover, we would suggest proceeding taxonomically with each strain before publishing data on its biochemistry, cultivation, etc. The reliable identification will allow not only a feasible cultivation process to be realized [300,301] but also more precise and correct information on the sources of biologically active metabolites to be obtained.

Although the number of examined taxa at first glimpse seems to be high and satisfying, we would like to stress that it is quite low on the background of general microalgal diversity, and on the natural wealth of flagellate species and genera, in particular. The same is valid for the investigated strains and in this respect, the increasing importance of living culture collections with taxonomically correctly identified strains has to be underlined. The role of these living archives in screening and identifying valuable Indigenous strains, phycoprospecting [302], and thus in enhancing upstreaming bioprocessing, is practically irreplaceable.

The analysis of the results obtained shows not only the low number of investigated taxa but also the low number of certain investigated substances, grouped according to their presentation in the text (Table 1).

Table 1. Main bioactive substances investigated in flagellate algae with indication of their properties, real or potential application in cosmetics, studied strains (organized alphabetically in the taxonomic groups), and relevant references. For details of application and commercially utilized sources, please, follow the text.

Substance	Activity Important for Cosmetics	Use/Potential Use in Cosmetics	Species/Strains	References
1. Pigments				
1.1. Chloropohylls	Stimulate tissue growth; wound-healing, antioxidant, antibacterial, anticancer, antimutagenic, antitumor, anti-inflammatory properties	Skin-care products	*Chlamydomonas reinhardtii*, *Diacronema lutheri*, *Isochrysis galbana*	[14,29,49,54–60]
1.2. Carotenoids	Antioxidant, anti-inflammatory, immunoprophylactic, and antitumor activities and UV-protective role	Skin-beauty products, products that slow down skin aging and sun damage, and formulations against skin cancer and inflammatory disorders		[37,46,61]

Table 1. *Cont.*

Substance	Activity Important for Cosmetics	Use/Potential Use in Cosmetics	Species/Strains	References
• Lutein	Improves skin elasticity	Colorant; skin tanning and sun-tan products	*Chlamydomonas acidophila*, *Chlamydomonas nivalis*, *Chlamydomonas plantogloea*, *Chlamydomonas rehinardtii*, *Chlamydomonas* strain JSC4, *Dunaliella tertiolecta*, *Dunaliella* spp., *Pyramimonas urceolata*, *Pyramimonas* sp., *Tetraselmis suecica*, *Tetraselmis wettsteinii*, *Tetraselmis* sp., cryptophytes	[12,19,23,37,39,62–64,107,113–117]
• Canthaxanthin	Tan color	Skin tanning and suntan products	*Chlamydomonas nivalis*, *Haematococcus lacustris*	[12,19,37,63,64]
• ß-cryptoxanthin	Skin whitening		*Dunaliella salina*	[1,65,66]
• Fucoxanthin		Functional antioxidant ingredient	*Hibberdia magna*, *Isochrysis galbana*, *Isochrysis zhangjiangensis*, *Isochrysis* sp. CCMP1324, *Isochrysis* sp., *Tisochrysis lutea*, *Tisochrysis lutea* CS-177/7, *Chrysotila carteriae*, *Chrysotila carterae* CCMP647, *Diacronema lutheri*, *Chromulina ochromonoides*, *Poterioochromonas malhamensis*, *Poteriochromonas malhamensis* CMBB-1, *Ochromonas danica*, *Ochromonas* spp., *Mallomonas* sp. SBV13, *Sarcinochrysis marina*, *Olisthodiscus luteus*, *Synura petersenii*, *Chattonella subsalsa*, *Chattonella marina*, *Fibrocapsa japonica*	[37,47,48,60,67,68,76,117–120,123–138,140]
• ß-carotene	Inhibits proline oxidation in collagen, induced by UV radiation; improvement of a skin appearance by reducing the roughness and increasing the smoothness and hydration; reduction in skin pigmentation disorders and enhance their removal; inhibits melanogenesis	Hair and personal care products (aftershave lotions and makeup) and suntan formulations; washing and hand creams; skin-whitening formulations	*Chlamydomonas nivalis*, *Dunaliella salina*, *Dunaliella tertiolectra*, *Tetraselmis wettsteinii*, *Tetraselmis suecica*, *Tetraselmis* sp.	[10,29,37,66,69–72,75,76,107–111,117]
• Zeaxanthin	Anti-tyrosinase activity	Skin-whitening substituents	*Chlamydomonas nivalis*, *Dunaliella salina*	[13,73]
• Lycopene		Personal care formulations as an antiaging agent, with possible application as a sunscreen and sunburn-preventing agent	*Dunaliella acidophila*	[12,19,63,64,112]

Table 1. *Cont.*

Substance	Activity Important for Cosmetics	Use/Potential Use in Cosmetics	Species/Strains	References
• Astaxanthin	Diminishment of melanin	Sunscreen and after sun lotions	*Sanguina nivaloides*, *Sanguina aurantia*, *Chlainomonas rubra*, *Chlainomonas* sp. DR53, *Chlainomonas* sp. AS02, *Chloromonas nivalis*, *Chloromonas hindakii*, *Chloromonas krienitzii* and *Chloromonas polyptera*, *Haematococcus lacustris*, *Haematococcus rubens*, *Haematoccus rubicundus*, *Euglena rubida*, *Euglena sanguinea*, *Trachelomonas volvocina*, *Tovellia rubescens*, *Tovelia sanguinea*, *Diacronema vlkianum*	[1,12,13,16,29,36,40,46, 75–106]
• Anthocyanins			*Chlamydomonas agloeoformis*	[17]
1.1.3. Phycobilins	The only natural greenish or bluish colorants; pinkish colorants; antioxidant, anti-inflammatory and anticancer activities; antiviral, antibacterial, antifungal, dermaprotective, melagonesis inhibiting and wound-healing abilities	Hair and personal care products; lipsticks, eye-shadows, eyeliners, face make-up and sun-protecting cream; anti-ageing formulations	*Cryptomonas curvata* CCAP 979/63, *Cryptomonas erosa* CPCC 446, *Cryptomonas lundii* CCAP 979/69, *Cryptomonas marssonii* CCAP 979/70, *Cryptomonas ozolinii* UTEX LB 2782, *Cryptomonas pyrenoidifera* NIVA 2/81, *Cryptomonas pyrenoidifera* CCAP 979/61, *Cryptomonas* sp. CPCC 336, *Rhodomonas salina* CCMP 757, *Proteomonas sulcata* CCMP 704), *Rhinomonas*, *Storeatula*, *Guillardia*, *Hanusia*, *Geminigera*, *Plagioselmis* and *Teleaulax*; *Proteomonas*, *Chroomonas*, *Komma*, *Flacomonas*; *Hemiselmis*	[10,62,141–144,148,152–156,162–165,168,169]
2. Lipids	Indispensable cell components and precursors to many important molecules.	Nanoparticles	*Chlamydomonas reinhardtii*, Chlamydomonadales strains TGA3 and TGA5; *Tetrasemis suecica*, *Poteriochromonas malhamensi*, *Ochromonas danicas*	[68,172–174,189]
2.1. Fatty acryls				
2.1.1. Fatty acids	The major component of lipids in microalgae	Emollients, emulsifiers, softeners, and as raw material in soaps as well	*Chlamydomonas agloeformis*, *Dunaliella acidophila*; *Heterosigma akashiwo*, *Alexandrium minutum*, *Karlodinium veneficum*	[17,19,112,176]

Table 1. *Cont.*

Substance	Activity Important for Cosmetics	Use/Potential Use in Cosmetics	Species/Strains	References
• PUFAs	Regulation of cell membrane fluidity, electron and oxygen transport; role in cell and tissue thermal adaptation as well; cryo-protective role; antibacterial, antiviral, antioxidant and detoxifying capacities with ability to mitigate several inflammatory and allergic reactions; hair nourishment and protection	Surfactants in soaps and other skin care products, including those for wound-healing and skin whitening; hair oils, hair serum, hair gels and sprays	*Chlamydomonas agloeformis*, *Chlamydomonas planctogloea*, *Chloromonas alpina*, *Chloromonas hindakii*, *Chloromonas nivalis* (incl. subsp. *tatrae*), *Chloromonas polyptera*, *Chloromonas remiasii* CCCryo 005–99, *Chloromonas* spp.; *Hibberdia magna*, *Poteriochoroomonas malhamensis*; *Isochrysis* spp., *Diacronema lutheri*, *Gephyrocapsa huxleyi*; *Tisochrysis lutea*; *Pseudopedinella* sp.; *Nephroselmis rotunda*; *Chroomonas nordstedtii*, *Chroomonas* sp., *Cryptomonas* spp., *Rhodomonas maculata*, *Rhodomonas* spp., *Storeatula major*, *Teleaulax* spp., *Proteomonas* spp.; *Chattonella subsalsa*, *Chattonella marina*, *Fibrocapsa japonica*, other raphidophyceans; *Phaeomonas parva*, *Phaeomonas* sp., all other Pinguiphyceae; 235 strains	[13,16,17,19,41,48,60,68, 75,83,114,127,138,140, 167,177–190,192]
2.1.2. Fatty acid esters	Texturizing properties to regulate viscosity of formulations and to increase their protective and lubricant properties for improvement the rigidity, hardness, texture and stability	Texturizer agents in cosmetic formulations; Lipsticks	*Euglena gracilis*; *Dunaliella acidophila*, *Edaphochlamys debaryana*	[19,112,134,195–197,199]
2.1.3. Hydrocarbons and triadylglycerols	Essential role in preventing water loss of tissues	Skin-care formulations (potential)	*Chlamydomonas reinhardtii*. *Haematococcus lacustris*	[19,201–205]
2.2. Glycerolipids	Anticancer, antiviral and anti-inflammatory activities	Dermal cosmetics (potential)	*Chlamydomonas reinhardtii*	[19]
2.3. Glycerophospolipids	Key components of cell membrane which may participate in responses to the stress	Excellent emulsifying agents to stabilize oil–water emulsions	*Chloromonas hindakii*	[19,83,194,208,209]
2.4. Sphingolipids	Significant role in maintaining cell membrane integrity; antimicrobial and antiviral activity; alleviation of atopic dermatitis; enhancement of psoriasis treatment; preventing of tumor formation; reduction in UV-induced wrinkle formation in a skin photoaging	Ingredients in cosmetic formulations for topical application	*Alexandrium minutum*, *Coolia monotis*; *Karlodinium veneficum*; *Prorocentrum donghaiense*; *Isochtysis galbana*, *Isochrysis zhanjiangensis*, *Pleurochrysis carterae*; *Ochromonas danica*; *Tetraselmis* sp.; *Euglena gracilis*	[19,210–214,217,219–221]

Table 1. *Cont.*

Substance	Activity Important for Cosmetics	Use/Potential Use in Cosmetics	Species/Strains	References
2.5. Sterol lipids	Essential role in cell membrane structures and functioning; antioxidant, anti-cancer, anti-inflammatory, and antibacterial properties; health-promoting benefits	Anti-aging cosmetic products, moisturizers, sunscreens and body washes	*Diacronema lutheri*, *Isochrysis galbana*; *Dunaliella acidophila*, *Dunaliella salina*, *Tetrselmis* sp. and other strains from Ochrophyta (Chrysophyceae, Synurophyceae, Dictyophyceae, Raphidophyceae), Pyrrhophyta, Cryptophyta, Haptophyta (Coccolithophyceae, Pavlovaphyceae), Euglenophyta, Chlorophyta (Chlorophyceae); *Astasia longa*; 19 cryptophytes	[10,19,60,62,112,222–227,230,231]
3. Polysaccharides	S gelling, texturizing, thickening, and stabilizing properties		*Chlamydomonas oblonga*, *Chlamydomonas reinhardtii*, *Lobochlamys segnis*; *Cryptomonas obovata*, *Cryptomonas tetrapyrenoidosa*, *Cryptomonas* soil strain; *Euglena gracilis* and all euglenophytes; *Poterioochromonas malhamensis*	[39,167,195,197,232,234, 236–240,243,244]
4. Alcohols	Organic osmolytes	In hand creams for increasing the skin moisture in long-lasting skin hydration	*Chlamydomonas reinhardtii*, *Dunaliella salina*	[13,37,245]
5. Phenolics	Antioxidants; chemical protectors against UV radiation and anti-melanogenic properties	Cosmetic ingredients	*Chlamydomoans agloeaformis*, *Chlamydomonas nivalis*, *Chlamydomonas reinhardtii*, *Tetraselmis suecica*; *Isochrysis* sp.; *Chrysophaeum taylori*	[17,62,250,253–259]
6. Enzymes and peptides	Antioxidant capacity; anti-melanogenic properties; antibacterial activities	Sunscreens, skin protectors from photo-ageing and skin-lightening agents in many cosmetic products, mainly creams and lotions	*Chlamydomonas reinhardtii*, *Dunaliella parva*, *Dunaliella tertilecta*, *Tetraselmis suecica*; *Poterioochromonas malhamensis*	[37,260–262]

Table 1. *Cont.*

Substance	Activity Important for Cosmetics	Use/Potential Use in Cosmetics	Species/Strains	References
7. Mycosporine-like aminoacids (MAAs)	Protection from UV radiation (sun-screen function and anti-aging abilities); strong antioxidants; anti-cancer agents; anti-inflammatory effects; inhibition of elastane decomposition	Stable and effective skin-care UV protective products; formulations to improve skin smoothness and inhibit wrinkle formation	239 strains of 152 cultured marine microalgal species from raphidophyceans (incl. *Chattonella*, *Fibrocapsa*), haptophytes (incl. *Chrysochromulina*, *Gephyrocapsa*, *Haptolina*, *Dicrateria* and *Phaeocystis pochetii*, *Phaeocystis* sp.), euglenophyte, dinoflagellates (incl. *Alexandrium margalefi*, *Gymnodinium catenatum*, *Gymnodiniun* spp., *Gyrodinium* sp., *Karlodinium veneficum*, *Kryptoperidinium foliaceum*, *Oxyrrhis marina*, *Scripsiella acuminata*, *Scrippsiella* sp., *Heterocapsa* and *Woloszynskaya*), cryptophytes (*Chroomonas*, *Rhodomonas baltica*, *Rhodomonas* sp.) and green algae (incl. *Tetraselmis chui*); *Chlamydomonas nivalis*, *Chlamydomonas hedleyi*; strains from "reddish" and "greenish" snow	[12,16,37,62,263–265,267,269–274]
8. Vitamins				
8.1. Vitamin C	Strong antioxidant essential for collagen synthesis	Anti-pigmentation skin treatment	*Dunaliella* spp., *Tetraselmis suecica*; *Euglena gracilis*; *Cryptomonas maculata*	[37,62,195,197,275,276]
8.2. Vitamin E		Photoprotective skin creams	*Dunaliella tertiolecta*, *Tetraselmis suecica*; *Euglena gracilis*; *Diacronema vlkianum*, *Isochrysis galbana*	[37,106,197,277]
8.3. Vitamin A (see also ß-carotene)			*Euglena gracilis*, *Dunaliella tertiolecta*	[62,195,197,278]
8.4. Vitamin B (B_1, B_2, B_3, B_5, B_6, B_{12})	Multiple favorable effects on the skin: antipruritic effect (B_1, B_3); anti-inflammatory effect (B_2, B_3, B_5); sebostatic, antipruritic, vasoactive, barrier- and photo-protective, lightening, anti-microbial (B_3); moisturizer; effect on the fibroblast proliferation (B_5); stimulation of filaggrin production in human epidermal keratinocytes (B_6); suppression of cytokine production, reduction of nitric oxide production, cell proliferation enhancement, modulation of lymphocyte activity (B_{12})	Ingredients in versatile skin-care formulations for topical application (against acne, atopic dermatitis, childhood eczema, skin aging, photo damages on the skin, etc.)	*Rhodomonas salina*; *Dunaliella tertiolecta*, *Tetraselmis suecica*	[62,279–288]

Table 1. *Cont.*

Substance		Activity Important for Cosmetics	Use/Potential Use in Cosmetics	Species/Strains	References
9.	Extracts	Strong effects in skin and hair protection, improvement of appearance, or other treatment regarding beauty-products or in treatment of skin and hair disorders	Anti-aging cosmetic products; anti-acne formulation; diminishment of hyperpigmentation	*Chlamydomonas agloeformis*, *Chlamydomonas reinhardtii*, *Haematococcus lacustris* REH10, *Tetraselmis* sp. CTP4; *Isochrysis* sp. Tahitian strain (T-Iso), *Isochrysis* sp.	[10,13,17,118,289–292]
10.	Nanoparticle sources	Ability to synthesize silver nanoparticles with antibacterial activity against pathogens, able to infect different wounds	Topical application in wound-healing formulations	*Platymonas* sp.	[293]

It has to be noted that for the analysis provided below, we counted total lipids, extracts, and data on nanoparticles as three separate types, and in the same way, as separate types, data were counted on pigments (chlorophylls, carotenoids, and phycobilins) due to their specificity. The low number of examined compounds concerns both their total number and the numbers investigated in each strain, or species. In most strains, 371, or 90%, only one compound type was investigated. Regarding species, logically, considering the popularity of *Chlamydomonas reinhardtii* as a model organism, it is a leader according to the number of investigated main groups of substances (11) and is followed by *Isochrysis galbana* (9) and *Euglena gracilis* (7). Five compound groups have been investigated in *Diacronema lutheri*, *Dunaliella salina*, *Poterioochromonas malhamensis*, and *Tetraselmis suecica*, and four groups were investigated in *Chlamydomonas agloeoformis*, *Dunaliella acidophila*, *Dunaliella tertiolecta*, and *Ochromonas danica*. Since for many strains species names were not available, a more detailed analysis will be made on the basis of the genera below.

The summarized data on the number of compound types investigated in flagellate genera show results almost similar to those obtained from species analysis. The most examined different substance types of genera were *Chlamydomonas* (12), *Isochrysis* (11), and *Tetraselmis* (10), followed by *Dunaliella* (9), *Euglena* (7), *Diacronema* (6), and *Poterioochromonas* (5). Four types of compounds were investigated in *Ochromonas* and *Rhodomonas*, three groups have been studied in nine genera: *Alexandrium*, *Chattonella*, *Chloromonas*, *Chroomonas*, *Chrysotilla*, *Cryptomonas*, *Fibrocapsa*, *Haematococcus*, and *Prymnesium*, whereas two compounds were studied in 21 genera, In the remaining 86 genera (or 79%), only one compound type was investigated. According to the spread of these genera by taxonomic groups (Figure 7), it can be stated that the highest diversity of substances in flagellate algae was investigated in the green algae and haptophytes, followed by ochrophytes. By contrast, far fewer bioactive substances were examined in euglenophytes, dinoflagellates, and cryptophytes.

The analysis of data obtained on different substances shows that the best-studied compounds were the fatty acids (181 records, and among them PUFAs (with 161 records, mainly on EPA and DHA), and MAAs (with 131 records), followed by carotenoids (54 records, mainly fucoxanthin—21 records, astaxanthin—18 records, and lutein—13 records), phycobilins (25 records) and sphingolipids (10 records)). All other compound types have been poorly documented in flagellates, leaving a wide field for future research. Despite these generally scarce studies, it has to be noted that some novel compounds have been identified in the following types: phycobilins (3), fatty acid esters (3), polysaccharides (1), MAAs (3), sterols (3), and sphingolipids (1). Several more need feed chemical identification [112,145,146,218,226,239,270]. Additionally, noteworthy is the finding of anthocyanins, considered as spreading generally in higher plants, in one species of *Chlamydomonas* [17], and the abundance of easier and more cost-effectively obtained phycobilins in cryptophytes [62,155,167]. Since the chlorophyll content of microalgae is higher than in vascular plants [38], its commercial extraction in the future can be strongly recommended, Of special importance is the fact that many, if not all flagellates, produce more than one high-value substance, the combined effect of which may contribute to the higher efficacy of cosmetic formulations. For example, the combination of vitamin C and glutathione in *Dunaliella* [37,261] could enhance skin depigmentation in the fight against dark spots caused by aging or UV radiation. In this aspect, it is valuable to note the obtaining of interesting algal extracts with successful application in cosmetics [10,13,18,288–290]. Resulting from the laboratory studies, several strains have been outlined in addition to the already recognized species as promising sources for biotechnological utilization, including the field of cosmetics (Chlamydomonadales TGA3 and TGA5, *Diacronema lutheri*, *Haematoccus rubicundus*, *Hibberdia magna*, freshwater *Chlamydomonas plantogloea*, *Chroomonas*, *Cryptomonas*, *Isochrysis galbana*, *Mallomonas* sp. SBV13, *Ochromonas danica*, *Poteriochromonas malhamensis* CMBB-1, *Rhodomonas*, *Tetraselmis*, *Tisochrysis*, etc. [48,57,58,60,62,68,92,95,114,117,137,155,169,172–174]). It could be predicted that this number will increase with the development of proper cultivation technologies, conditions, and media to achieve faster growth and higher yields. Last but not least, our search proved that one and the same species can be used as a producer of different high-value compounds, which is important for cost-effective processing. According to the current knowledge, most of the examined flagellates and their isolated and cultivated strains can be considered as safe sources since they do not produce toxic compounds. Exceptions of some potentially toxin-producing strains and genera have been discussed in the text regarding the safety concern, but it has been underlined that the toxins produced still have not been reported as harmful for cosmetic formulations. However, considering the ability of algae to produce toxins, we underlined the need for tests on the toxicity of both producers and harvested compounds [19].

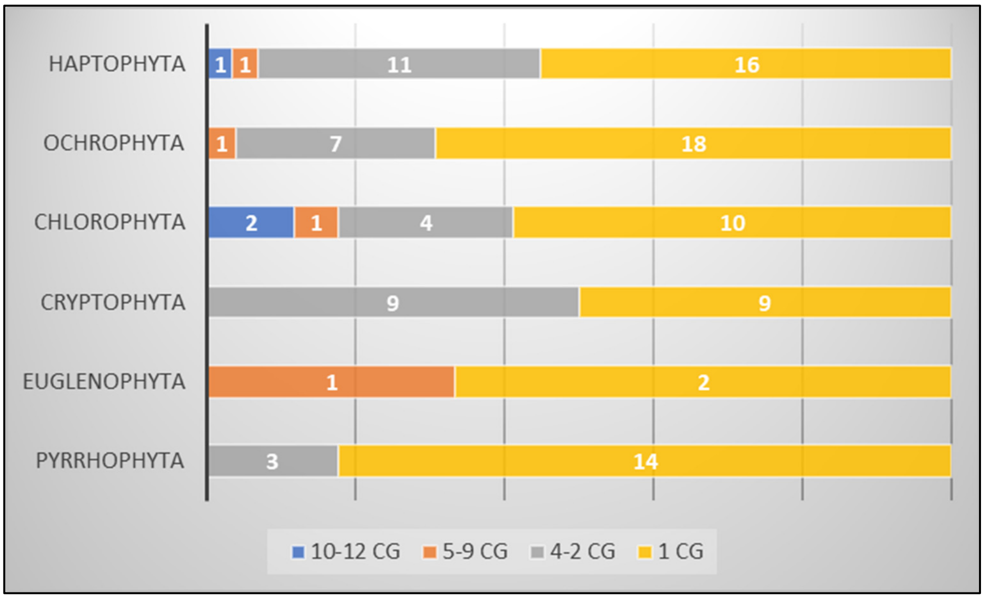

Figure 7. Percentage distribution of genera in main taxonomic groups with one, two-four, five-nine, and ten-twelve compound groups (CGs) investigated. White digits show the real numbers of investigated compounds.

Different methods for obtaining algal metabolites during downstream bioprocessing have been developed (e.g., [39,49,60,86,87,91,92,101,106,107,115,116,134,173,195,243,244]), but only a few species have been commercially utilized contrasting to the great number of strains existing in the nature. More investigations are needed in the future with comparisons of the extraction yields from wet and dry biomasses using different combinations of cultivation, harvesting, and cell disruption methods. The literature analysis shows that most research in such technical aspect deals with already well-known genera and species, such as the widely recognized not only by the scientific community but also by the broad audience of consumer algae like *Dunalliella salina*, *Haematococcus lacustris*, and *Euglena gracilis*. Fewer studies concern other green and euglenophyte algae, as well as smaller algal groups, such as raphidophyceans, chrysophyceans, cryptophytes, haptophytes, and even dinoflagellates in regard to their commercial utilities. At the same time, considering the gaps in the knowledge, even expanding investigations of the abovementioned popular algae can be stimulated. But also, more efforts are necessary in the field of upstreaming processing, especially focused on phycoprospective discovery of new promising species and strains from yet unexplored genera.

All collected data show inevitably that microscopic flagellate algae offer significant potential for modern cosmetics, although more investigations regarding their availability, cosmetic efficacy, and safety may be encouraged as well as the development of stronger links between laboratory researchers and industrial technologists. However, it can be optimistically expected that the successful application in different cosmetic preparations of high-valued natural substances from the novel sources, highlighted in this review, could be achieved in the nearest decades.

5. Conclusions

The current review shows once more that algae are generating considerable interest in terms of value-added metabolites. Although there is a great deal of potential to be further investigated in the near future, a thorough exploration of the existing literature makes evident the promising abilities of yet poorly explored microscopic flagellate algae as beneficial commodities for modern cosmetics. The rising environmental stress from increased air pollution and stronger UV radiation causes skin and hair damage, and at the same time augments consumer demand for stronger preventive, protective, and repairing cosmetic products. All collected data highlight the microscopic flagellates as novel sources of such innovative biologically derived substances that serve as the best replacement to chemical entities available on the market with great possibilities for commercial utilization especially in less processed products. Their utility for developing modern cosmetic formulations that are tailor-made to actual consumer needs and desires is suggested.

Author Contributions: Conceptualization, M.S.-G.; methodology, M.S.-G. and G.G.; writing—original draft preparation, M.S.-G.; writing—review and editing, B.U. and G.G.; visualization, M.S.-G., B.U. and G.G.; supervision, G.G.; project administration, B.U.; funding acquisition, B.U. All authors have read and agreed to the published version of the manuscript.

Funding: This study is financed by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project No. BG-RRP-2.004-0008.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

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