

Review

Aeroterrestrial and Extremophilic Microalgae as Promising Sources for Lipids and Lipid Nanoparticles in Dermal Cosmetics

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Abstract: Microscopic prokaryotic and eukaryotic algae (microalgae), which can be effectively grown in mass cultures, are gaining increasing interest in cosmetics. Up to now, the main attention was on aquatic algae, while species from aeroterrestrial and extreme environments remained underestimated. In these habitats, algae accumulate high amounts of some chemical substances or develop specific compounds, which cause them to thrive in inimical conditions. Among such biologically active molecules is a large family of lipids, which are significant constituents in living organisms and valuable ingredients in cosmetic formulations. Therefore, natural sources of lipids are increasingly in demand in the modern cosmetic industry and its innovative technologies. Among novelties in skin care products is the use of lipid nanoparticles as carriers of dermatologically active ingredients, which enhance their penetration and release in the skin strata. This review is an attempt to comprehensively cover the available literature on the high-value lipids from microalgae, which inhabit aeroterrestrial and extreme habitats (AEM). Data on different compounds of 87 species, subspecies and varieties from 53 genera (represented by more than 141 strains) from five phyla are provided and, despite some gaps in the current knowledge, demonstrate the promising potential of AEM as sources of valuable lipids for novel skin care products.

Keywords: carotenoids; Cyanoprokaryota; fatty acids; morphological type; PUFA; Ochrophyta; Rhodophyta; Chlorophyta; Streptophyta; sterols



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1. Introduction

The increasing use of microalgae in the cosmetic industry as extraordinary rich source of novel high-value functional products, obtained in eco-friendly and cost-effective processes, is widely recognized [1,2]. To date, more than 15,000 novel compounds of algal origin have been identified [3]. Many bio-based microalgal products are often “multipurposed” and are applied in dermal cosmetics as sunscreens, skin sensitizers and colorants, as well as agents for moisturizing, water-binding, texturizing, thickening, tanning, whitening, etc. [2,4–8]. In such skin-related applications, the chemically and functionally diverse group of lipids and their derivatives comprise a significant gradient [9,10]. Apart from the fact that deficiencies in cutaneous lipids cause discomfort, which may lead to serious skin diseases (e.g., atopic dermatitis, psoriasis, acne, rosacea, hereditary ichthyoses, allergic and irritant contact dermatitis and hidradenitis suppurativa), the broad usage of lipids is based also on their ability to form a protective multifunction skin barrier and on their role as emollients or emulsifiers in the bulk of care and make-up products as well [9,11]. Today, with the flourishing development of nanotechnology, which leads to a fast product innovation [12,13], the potential of lipid nanoparticles (LNP), which seem to be both effective and economic, has been recognized as promising [14]. For example, in dermal cosmetics, about a decade ago,

it was already demonstrated that nano-sized sunscreen products have better performance than micron-sized materials [15].

Therefore, currently, nano-sized systems are being increasingly studied and applied to encapsulate active ingredients in order to enhance the efficacy of their percutaneous delivery to targeted cells and are also used to improve the physiochemical stability of skin-based cosmetic products [16]. Such loaded LNP have the advantage of a cumulative effect achieved by a combination of their easier penetration with the enhanced and prolonged release of the carried ingredient to the targeted cellular and subcellular regions [17–19]. In this way, the overall functionality of the final product is improved, allowing LNP-based cosmetic formulations to be highly effective in skin protection, in treating dermatological disorders and in antiaging therapy [17–19]. In addition, many loaded LNP may provide glowing skin [19]. All these positive effects can be achieved not only by topical skin administrations but also by oral applications [19], and it is easily explainable that the modern dermal cosmetic industry is searching for new high-value functional lipid products of natural origins.

Moreover, in the recent conditions of our society, with growing consumer demands for vegetal oils, there is a rapidly increasing general interest in lipid-rich microalgae (>20% of lipids on a cell dry weight basis), named oleaginous [10,20]. Evidence has been accumulated that the average lipid content in microalgae varies between 1 and 70%, but in certain conditions, it can reach 90% of dry weight (for details, see Reference [21]). This commercial interest is strongly supported by the fact that many oleaginous microalgae can be cultivated at a production scale both autotrophically and heterotrophically, mostly with inexpensive nutrient regimes, and have faster growth rates with high biomass productivity as compared to terrestrial crops [2,22–24]. Further comparisons show that microalgae have even more advantages, since they can be grown all-year-round without the use of arable land, have low water consumption and have low environmental impact [25]. Another important fact that has to be taken into account is the great general biodiversity of microalgae, which is far away from being thoroughly studied and is gaining increasing attention due to recent surge in searching for indigenous commercially important strains or phycoprospecting [2,26,27].

Lipids produced by microalgae belong to two major groups of polar lipids and non-polar, or neutral lipids [25,28,29]. Polar lipids have an important role in cell structure and cell signaling processes and are commonly known also as structural or membrane lipids [28,29]. They comprise a small part of the total lipid fraction in cells (ca. 20%) and usually have long chains of extractable fatty acids (FtAs) [25,28–30]. Nonpolar lipids have diverse biological functions, but most of them, triglycerides in particular, are often pointed out as responsible for energy storage [28]. Most oleaginous microalgae have the capacity to produce significant amounts of nonpolar lipids (up to 80% of the total cell lipid content), the accumulation of which can be influenced, especially in conditions of a lack of nutrients or in stress environments [25,28].

The capacity of microalgae to produce lipids in such appreciable amounts, combined with the advantages of their growing, has stimulated considerable interest in their screening for useful and unusual lipid compositions and their mass cultivation as a feedstock for various biotechnological products [29]. Until now, most research has been oriented towards freshwater, marine and hyperhaline aquatic species from the genera *Aphanizomenon*, *Arthrospira*, *Chlorella*, *Desmodesmus*, *Dunaliella*, *Haematococcus*, *Nannochloropsis*, *Scenedesmus* and *Spirulina* [2]. However, the commercial potential of microalgae inhabiting many other aeroterrestrial or extreme habitats remains untapped [2]. The species from these inimical environments had to develop ultrastructural, physiological and biochemical adaptive features, which include a series of protective natural compounds of special interest for future applications in human life and cosmetics in particular [2]. Moreover, such microalgae can be successfully cultivated in outdoor conditions detrimental for standard crops and other algae [31].

The aim of the present review is to summarize the current knowledge on the aeroterrestrial and extremophilic microalgae (AEM) with a promising potential for obtaining

lipids and LNP with dermal cosmetic applications. In addition, considering that: (1) experiments have demonstrated the successful increase of the oral bioavailability of lipophilic carotenoids obtained through their combination with other lipid-based formulations (e.g., palm oil and polysorbate) [32] and (2) the nanoparticle-based cosmetic products recently available on the market (for details, see Reference [19]) do not contain microalgal lipids, this review summarizes the data on diverse bioactive lipid compounds recorded in AEM. We believe that this review will encourage the further investigation of microalgae from these underestimated ecological groups and their commercial use in modern cosmetics.

2. Materials and Methods

The present review is based on the relevant sources from known databases, including Google Scholar, Science Direct, MEDLINE (PubMed), Web of Science, Scopus and SciFinder and our private scientific libraries and archives as well. In this way, the found publications on the topic covered a period of the last 56 years starting from 1965. The keywords used for search included all lipid classes and subclasses, skin diseases, cosmetic products and ways of application, and names of taxonomic and ecological groups of algae, as well as the names of certain species and genera. Due to the limited volume of the paper, when possible, references to more general reviews were preferred.

In lack of an internationally agreed-upon definition, lipids are loosely considered as biological substances that are generally hydrophobic in nature and, in many cases, soluble in organic solvents [10,33]. Different approaches have been applied to classify lipids, but in the present review, we follow the eight categories in the extended LIPID MAPS comprehensive classification with their relevant abbreviations: fatty acyls (FA), glycerolipids (GL), glycerophospholipids (GP), sphingolipids (SP), sterol lipids (ST), prenol lipids (PR), saccharolipids (SL) and polyketides (PK) [34].

Beyond the scope of this review are the methods for the preparation and characterization of LNP for skin care applications and the mechanisms of their penetration, which have been described in detail [14,19]. Although we use the general term “lipid nanoparticles” with the abbreviation LNP, whenever possible, according to the data availability, we indicate the exact class of lipid-based nanoparticulate systems utilized in cosmetic products recognized by Reference [19]: solid LNP, nanostructured lipid carriers, liposomes and nanoemulsions.

In the review, the terms “cosmetics/cosmetic industry” are used in their broadest sense, embracing the recently proposed but still debatable terms “cosmeceutics/cosmeceutical”, which consolidate between cosmetics and pharmaceuticals, based on the medicinal utility of biologically active compounds (for details, see References [2,5]), and “cosmotherapy”, which considers therapeutically efficacious cosmetics (for details, see Reference [19]).

Since the term “algae” has no taxonomic standing, its scope and understanding of AEM in particular, as well as of their ecological groups, are in accordance with the definitions provided in References [2,35]. In this approach, algae from soils, rock, bark and leaf surfaces and building facades are named aeroterrestrial, while algae from caves, ice, snow, permafrost, cryoconites and thermal springs, as well as from unusual acidic habitats, are considered extremophilic. The algal nomenclature follows Algaebase [36], with the synonyms shown at the first appearance of the relevant Latin name.

3. Results

Data on the lipids, detected in more than 141 strains of 87 species, subspecies and varieties from 53 genera of AEM, are presented below in the text, following the order of the major lipid categories in the extended LIPID MAPS comprehensive classification [34].

3.1. Fatty Acyls (FA) from AEM

FA are a diverse group of molecules, included in one of the most fundamental categories of biological lipids, because the fatty acyl structure represents the major lipid building block of complex lipids (i.e., lipids that yield three or more products on hydrol-

ysis) [33]. It is characterized by a repeating series of methylene groups, responsible for the hydrophobic characteristic of this category [33]. FA are subdivided into classes, which include FtAs, fatty acid esters (FAEs), fatty alcohols, fatty amides, monoradylglycerols, diradylglycerols, triaradylglycerols, etc. [33].

3.1.1. Fatty Acids (FtAs) from AEM

In microalgae, a variety of 135 FtAs has been recorded [37]. FtAs comprise the major component of lipids, which can account from 20% to 50% of the dry biomass, but also, other values (1–70%) have been reported [22,38]. This peculiarity makes microalgae essentially beneficial for industrial cosmetics, in which FtAs have broad applications as raw materials in soaps, as emollients, emulsifiers, softeners, etc. [39].

There are different ways to classify FtAs, but quite commonly in microalgal studies, they are discussed in three categories based on their saturation, such as polyunsaturated fatty acids (PUFA), saturated acids (SAFA) and monounsaturated fatty acids (MUFA). PUFA are largely spread in structural polar lipids, but SAFA and MUFA comprise the storage lipid fraction [25,28–30]. Another often-used term is “essential fatty acids” (EFA), which refers to necessary for health PUFA that cannot be synthesized in the body and must be obtained from foods [40]. EFAs embrace mostly PUFA from the families of the so-called Omega 3 (ω 3) and Omega 6 (ω 6) FtAs, such as eicosapentaenoic acid (EPA, 20:5 ω 3) and docosahexaenoic acid (DHA, 22:6 ω 3), with their intermediate, docosapentaenoic acid (DPA, 22:5 ω 3) [28].

PUFA, and the essential ω 6 linoleic acid (18:2 ω 6), in particular, as a natural part of the skin epidermis, are important for proper skin functioning, and their application shows beneficial effects on the skin [39–43]. For example, a deficiency of linoleic acid results in a scaly skin disorder and excessive epidermal water loss [39,42,44,45], but its application is useful in the treatment of hyperplasia of the skin [2,7]. The use of PUFA (ω 3, ω 6 and ω 9 PUFA in particular) for skin protection is gaining increased attention, because they have been proven helpful for maintaining membrane fluidity, improving skin barrier function and skin homeostasis, reducing of trans-epidermal skin loss, the acceleration of skin wound healing, ensuring photoprotection, the prevention of skin cancer development and the alleviation of skin impairments (e.g., acne), photoaging, allergy, dermatitis, cutaneous wounds and melanogenesis (thus treating hyperpigmentation) [2,10,41,43,46–60]. The application of PUFA as surfactants in soaps and other skin care products is well-known. To exemplify once more the great potential of PUFA in dermal human cosmetics, we note here the prepared solid emulsion gel for cell-targeted PUFA delivery to skin wounds [61] and the linoleic acid-loaded liposomes as NP carriers for skin whitening [62]. The effect was greater for liposomal (0.1%) than for free linoleic acid, and liposomal encapsulation protected the unstable linoleic from oxidation [62]. Higher effects of a final cosmetic product, obtained by application of the nanoemulsion matrix enriched on long-chain PUFA, were also reported [12].

In addition to all the beneficial effects enlisted above, PUFA are supposed to have a cryo-protective role, which helps to prevent intracellular ice crystal formation [63]. Considering this, here, we outline the high PUFA levels (58.1–65.8% of the total lipids, mainly the ω 3 essential α -linolenic acid, 18:3 ω 3) in the extremophilic unicellular green *Chloromonas hindakii*, which causes “orange snow” [64]. This species, like other cryophilic algae from Chlamydomonadaceae, produces two types of cells during its life cycle: green-colored flagellated (monadal) cells, which dwell in melting snow, and nonmotile resting thick-walled cells of orange-reddish color, which thrive on the snow surface. The SAFA (mainly palmitic acid, 16:0) and MUFAs (mainly oleic acid, 18:1 ω 9) comprised 23% and 9.4%, respectively, of the total lipid content [64]. These relatively high levels of palmitic and oleic acid in *C. hindakii* correspond to their similar amounts in other strains of *Chloromonas* [64,65]. In *C. hindakii*, also, ω 3 polyunsaturated stearidonic acid (18:4 ω 3, 4.7–5.9% of the total FtAs) and hexadecatetraenoic acid (16:4 ω 3, 25.6–31.6% of the total FtAs) were recorded [64]. The same production of hexadecatetraenoic acid was detected earlier in another snow alga,

Chloromonas remiasii CCCryo 005–99, kept under nitrogen-deficient conditions [63]. This acid is of interest for modern dermal cosmetics, because it can mitigate several inflammatory and allergic reactions [49].

A high content (45–50% of all FtAs) of PUFA with lower amounts of SAFA (30–40%) and MUFA (10–15%) was detected also in the “red snow” samples containing mainly the cryophilic green unicellular algae *Chloromonas alpina*, *Chloromonas nivalis* (incl. subsp. *tatrae*), *Chloromonas polyptera* and *Chloromonas* spp.; some uncultured species of the family Chlamydomonadaceae and in the filamentous *Raphidonema sempervirens* [66,67]. High levels of PUFA are also common for two cryophilic strains of green algae isolated from lake ice, the filamentous *Ulothrix zonata* [68] and unicellular *Monoraphidium* sp. [31]. The last strain was recognized as a prospective candidate for low-temperature biotechnology because of its successful outdoor cultivation under early winter conditions with average temperatures of 10.0 °C [31]. In these conditions, it had a lipid productivity of 162 mg L⁻¹ day⁻¹, with a production of 16:4 and 18:4 FtAs reaching 27.5 and 43.7 mg L⁻¹ day⁻¹, respectively, which is one order of magnitude higher than the previously reported values. The proportion of these acids of total FtAs was up to 19.1% and/or 34.7%, respectively [31].

A high FtAs content was detected in the aeroterrestrial unicellular green *Coelastrrella striolata* var. *multistriata* isolated from the rock surface [69]. During cultivation, this alga changed the cell color from green to reddish, depending on the nitrogen concentration in the culture media [69]. Both green and red cells contained SAFA (mostly palmitic acid) and PUFA, but differences in the amount of specific PUFA were registered. For example, in the green cells, linoleic acid predominated, reaching 22.7 mg per g dry weight cells (mg g⁻¹ dwt) from the total lipid content of 90 mg g⁻¹ dwt. In the orange-reddish cells, oleic acid was the most abundant, reaching 113.4 mg g⁻¹ dwt from the total lipid content of 319 mg g⁻¹ dwt [69].

In the aeroterrestrial coenobial green *Tetradismus obliquus* (Syn. *Scenedesmus obliquus*), the total lipids comprised 10.3% g 100 g⁻¹, PUFA were 47.31% from all unsaturated FtAs, representing predominantly ω3 linolenic acid (16.74%), and by ca. 9.70% of ω6 FtAs, such as linoleic and linoleic acids (18:2 ω6) [70]. These results correspond to earlier data on FtAs profiles of this alga [71–73] with high amounts of linolenic acid (>15%), oleic acid (>14%) and linoleic acid (>10%) [72] and suggest its use as their potential source [70].

The analysis of three aeroterrestrial filamentous cyanoprokaryotes, namely *Anabaena cylindrica*, “*Nostoc canina*” (we suppose that this is an isolated photobiont of the lichen *Peltigera canina*) and *Desmonostoc muscorum* (Syn. *Nostoc muscorum*), revealed that their total lipid content varied between 10.7 and 12.3% of the dry weight with a high content (>50%) of PUFA [74]. Some species-specific differences in FtAs compositions were detected: palmitic acid, linoleic acid and linolenic acid were predominant in *Anabaena cylindrica*; palmitic, palmitoleic, oleic and linoleic acids were the most abundant in *Nostoc canina* and palmitic, palmitoleic, hexadecadienoic, oleic and linoleic acids dominated in *D. muscorum* [74]. The authors outlined the differences with another species of *Nostoc*, namely *N. calcicola* (strain 1453-1), in which linolenic acid was dominant [75].

The lipid analyses of ten oleaginous soil algal isolates, comprised by three filamentous cyanoprokaryotes (*Tolypothrix* sp. PBGA1, *Tolypothrix* sp. PBGA2 and *Oscillatoria* sp. PBGA3) and seven unicellular green algae (*Acutodesmus dissociatus* TGA1, *Chlorella* sp. TGA2, *Chlorella* sp. TGA4, *Chlorella* sp. PGA2, *Hindakia tetrachotoma* PGA1 and two unidentified species from the order Chlamydomonadales (“Chlamydomonadales species” TGA3 and “Chlamydomonadales species” TGA5), indicated that green algae accumulate more lipids than cyanoprokaryotes [76]. The study proved the high lipid productivity of *Acutodesmus dissociatus* TGA1 (22 mg L⁻¹ d⁻¹) caused by its greater biomass productivity (119 mg L⁻¹ d⁻¹) and fast specific growth rate (μ_{exp} −0.23 day⁻¹). Similarly, high lipid content, high lipid productivity and beneficial biomass yield were shown by *Chlorella* sp. TGA2 (28%, 27 mg L⁻¹ d⁻¹ and 115 mg L⁻¹ d⁻¹, respectively) and by *Hindakia tetrachotoma* PGA1 (25.70%, 20 mg L⁻¹ d⁻¹ and 89 mg L⁻¹ d⁻¹, respectively) [76]. In *Acutodesmus dissociatus* TGA1, *Chlorella* sp. TGA2 and *Hindakia tetrachotoma*, the most abundant was palmitic acid, followed by oleic acid [76]. These data were in agreement with the formerly published

predominance of palmitic acid in most algae with common values between 20 and 27% but with a possibility to reach 49–50% [77]. In addition, the strain “Chlamydomonadales species” TGA3 was outlined as a promising feedstock for biotechnology as “considerably thermotolerant” [76].

An interesting strain (K-1) of the unicellular green species *Parietochloris alveolaris* (Syn. *Lobosphaera incisa*), described from alpine soils and reported as occurring as a photobiont in lichens, was recently isolated from a tidal flat [78]. K-1 has higher proportions of ω 3 FtAs (including α -linolenic acid and EPA) than other strains of the same species investigated earlier [79] and was outlined as a strongly promising source of ω PUFA [78]. Before this study, *P. alveolaris* was already declared to be the richest natural source of the peculiar, high-value polyunsaturated ω 6 arachidonic acid (AA, 20:4 ω 6) [80], with high contents in its all studied strains [81]. Its specific delta5 desaturase mutant was proven as a novel source for the large-scale production of the valuable long-chain polyunsaturated dihomogamma-linolenic acid (20:3n6), a precursor of the AA [82]. Dihomogamma-linolenic acid is of particular interest for dermal applications due to its successful implementation in the treatment of inflammatory disorders, such as atopic eczema and psoriasis [82,83].

Another alga, rich in the relatively rare AA, is the unicellular red *Porphyridium purpureum* (Syn. *P. cruentum*) [84], which develops in various habitats, including soil surfaces [36]. Besides AA, this aeroterrestrial alga also contains beneficial amounts of EPA [84]. A high content of both valuable long-chain PUFAs was detected on the background of a total lipid content ranging between 9 and 19% dry weight biomass and a lipid productivity up to 34 mg L⁻¹ day⁻¹ [21,25,85–89]. Since the total AA and EPA recoveries reached 39.5% and 50.8%, respectively, for a purity ~97% for both FtAs, *P. purpureum* was considered promising for lipid-based industrial applications [21,25,84,89]. High proportions of EPA were also detected in another soil inhabitant, the unicellular eustigmatophycean alga *Monodopsis subterraneus* (Syn. *Monodus subterranea*) from division Ochrophyta [90]. Since EPA accounted up to 36.7% of all FtAs and up to 4.4% of dry weight, *M. subterraneus* was declared as one of the most promising candidates for its phototrophic production [91,92]. Later, through the manipulation of culture conditions and strain selection, EPA productivity reached 56 mg L⁻¹ 24 h⁻¹ [93], and a yield of 96.3 mg L⁻¹ was obtained from its strain UTEX 151 [94].

PUFA profiles of the polyextremophilic unicellular red alga, isolated from acidic thermal spring and identified as *Galdieria* sp. USBA-GBX-832, provided the first evidence for the synthesis of AA and EPA in this genus [95]. However, both FtAs were detected only in trace concentrations (<0.25%) [95]. The amount of total lipids ranged between 4.0 and 5.0 mg and was higher under autotrophic culture conditions (15.3% of dry biomass) than under heterotrophic and mixotrophic conditions (ca. 3.7% of dry biomass) [95]. In the same study, SAFA (mostly palmitic acid, 27.9%) and stearic acid (C18:0), 24.3%) comprised 25% of all FtAs produced under autotrophic conditions. By contrast, SAFA, obtained under hetero- and mixotrophic conditions and, especially, palmitic acid (~27%), accounted for 40–47% of FtAs. In autotrophic conditions, no MUFA were detected, while, under hetero- and mixotrophic conditions, the most abundant MUFA was oleic acid (28.2% and 34.1%, respectively). PUFA (predominantly linoleic acid) comprised 17% under autotrophic conditions and accounted for ca. 21% in both other cases [95]. These results on PUFA correspond to earlier reports on 45 other strains of *G. sulphuraria* [65,96]. These two studies revealed low amounts of lipids (in comparison with 26–32% proteins and 63–69% polysaccharides) but demonstrated the presence of valuable palmitic, oleic, linoleic and linolenic acids, with small amounts (traces) of myristic, palmitoleic and stearic acids [65,96]. The comparison of these polyextremophilic strains of *G. sulphuraria*, isolated from acid thermal springs (pH = 0–4, water temperature up to 56 °C) with its acidic but non-thermophilic strain (growth optimum of 30–35 °C), showed no obvious differences in FtAs [97].

In another acidophilic alga, the unicellular green *Dunaliella acidophila*, which grows at pH 0.2–2.5, the nonpolar lipids consisted predominantly of FtAs (14% of ethyl ether extract), namely linolenic, γ -linolenic, linoleic, oleic and elaidic acids [98]. In the same

study, three hydroxy fatty acids, which have never been detected in other algae, were identified as methyl esters: methyl (12R)-hydroxyoctadeca-9Z,13E,15Z-trienoate, methyl (9S)-hydroxyoctadeca-10E and 12Z,15Z-trienoate and methyl ricinoleate.

3.1.2. Fatty Acid Esters (FAEs) from AEM

FAEs are represented by wax monoesters, wax diesters, lactones, etc. [33]. In cosmetics, waxes are used as texturizer agents to regulate the viscosity of formulations and increase their protective and lubricant properties [9,10,17,99,100]. Therefore, waxes are important and dermatologically well-tolerated ingredients that improve the rigidity, hardness, texture and stability of lipsticks [10]. However, today, waxes from AEM are very poorly known. They have been found among the main constituents of lipids in the unicellular green *Chlorella vulgaris*, together with glycolipids, hydrocarbons, phospholipids and small amounts of free FtAs [24,101,102]. This aeroterrestrial alga can produce 11–40 mg L⁻¹ day⁻¹ lipids, which account from 5 to 58% of the dry biomass [21].

Lactones are natural secondary metabolites, constituted from cyclic carboxylic esters, which have received considerable attention from the scientific community due to the broad range of their biological activities [103–105]. Regarding dermal cosmetics, their general antimicrobial, antibacterial, antifungal, insect-repellent, anti-inflammatory and antitumor properties are important [103,104]. For example, the furanocoumarins, a subclass of lactones, are extremely important in the treating of skin disorders, such as vitiligo, psoriasis, dermatitis, eczema, leukoderma and different mycoses, because they can promote the pigmentation of affected areas [103].

Lactones have been isolated from a wide range of living organisms, mostly plants, fungi and marine sponges [103,105]. Concerning algae, the studies have been based mainly on marine and few freshwater species [105–114]. In marine algae, apart from common oxygenated FtAs derivatives, a number of complex and unique compounds were found (e.g., cyclopropyl hydroxyeicosanoids, egregiachlorides, ecklonialactones, hybridalactones, bicyclic cymathere ethers, cymatherelactones and cymatherols—for details, see Reference [108]). New lactones were also discovered in freshwater species (e.g., sesquiterpenes 3 α ,4 α ,8 α -trihydroxy-10 α -methoxy-1 α ,5 α ,7 α ,11 β H-guaia,6 α ,12-olide and 4 α ,8 α -dihydroxy-10 α -methoxy-1 α ,5 α ,7 α ,11- β H-guaia,6 α ,12-olide [106]), and for the first time, coriolic acid, a precursor of δ -decalactone, was reported in cyanoprokaryotes [114].

In contrast with aquatic algae, lactones from AEM are yet poorly known. Studies have mainly addressed the oxygenated derivatives of PUFA, collectively termed oxylipins, which showed antibacterial, anti-inflammatory and antiallergic activity and alleviated the effects from diverse kinds of stress, desiccation, wounds and pathogen infections [108,112,114]. The endogenous lipoxygenase (LOX)-derived oxylipins were determined in aeroterrestrial filamentous *Nostoc punctiforme* PCC73102 and *Nostoc* sp. PCC7120 [115,116] and in the green unicellular *Edaphochlamys debaryana* (Syn. *Chlamydomonas debaryana*) [112]. In another green, but extremophilic, alga, *Dunaliella acidophila*, three new methyl esters were identified as new for algae: methyl (12R)-hydroxyoctadeca-9Z,13E,15Z-trienoate, methyl (9S)-hydroxyoctadeca-10E, 12Z,15Z-trienoate and methyl ricinoleate [98]. The findings of these compounds and earlier data, obtained on the antibacterial properties of *Chlorella vulgaris* [117], allow to suppose the great untapped potential of AEM as lactone sources and to encourage their future research.

3.1.3. Fatty Alcohols, Hydrocarbons and Triacylglycerols from AEM

Fatty alcohols and hydrocarbons represent separate classes without subclasses in the FA category, whereas the class of triacylglycerols contains several subclasses, including triacylglycerols [33]. Data collected from the few reports of long-chain alcohols in microalgae allowed to suppose that microalgae are not a major source of these lipids [118].

Hydrocarbons derived from FtAs, such as alkanes and alkenes, commonly occur in plants and insects and play an essential role in preventing water loss from their tissues [119]. The synthesis of hydrocarbons is widespread in cyanoprokaryotes [120], but in general, in

eukaryotic microalgae (except the aquatic *Botryococcus braunii* [121]) and, particularly, in AEM, it has received little attention [119]. In the aeroterrestrial unicellular green *Chlamydomonas reinhardtii*, a C17 alkene, n-heptadecene, was detected, and in *Chlorella variabilis* NC64A eptadecane, pentadecane, as well as 7- and 8-heptadecene, were found [119]. The same study showed that microalgae have the ability to convert C16 and C18 FtAs into alka(e)nes by a new, light-dependent pathway [119].

Triacylglycerols in *Dunaliella acidophila* comprised 5.2% of the ethyl ether extract and were represented by trilinolenin, triolein, trielaidin and tristearin [98]. In another green unicellular extremophilic alga, *Pseudochorocystis ellipsoidea* MBIC11204, isolated from a hot spring, a high amount of triacylglycerols (82% of the total lipid content and about 21% of the dry weight) was detected in conditions of nitrogen starvation [122]. In the same study, the major FtAs were C18:1 and C16:0, and the maximum growth rate was $3.46 \text{ g L}^{-1} \text{ day}^{-1}$ or $0.144 \text{ g L}^{-1} \text{ h}^{-1}$. Therefore, *P. ellipsoidea* MBIC11204 was considered as a promising fast-growing oleaginous algal strain from which hydrocarbons and triglycerides can be produced photoautotrophically, reaching up to 30% of the dried biomass [122].

3.2. Glycerolipids (GL) from AEM

Glycerolipids (GL) encompass all glycerol-containing lipids of an amphiphilic nature (assembly of FtAs, glycerol and polar heads) [33,123]. GL include: (1) mono-, di- and tri-substituted glycerols, from which the best-known are acylglycerols (FAEs of glycerol) [33], and (2) betaine lipids, which are characterized by a non-phosphorous polar head group connected by an ether bond with a diacylglycerol (DAG) backbone [124]. Three types of betaine lipids have been identified: diacylglyceryl-*N,N,N*-trimethylhomo-Ser (DGTS), diacylglyceryl-hydroxymethyl-*N,N,N*-trimethyl- β -Ala (DGTA) and diacylglyceryl-carboxyhydroxymethylcholine (DGCC) [124–126]. All GL are currently very attractive in dermal cosmetics due to exerting therapeutic anticancer, antiviral and anti-inflammatory activities through interactions with other biological molecules (for details, see Reference [123]).

Monogalactosylglycerol (MGD), digalactosylglycerol (DGD), triagalactosylglycerol (TGD), sulphoquinovosyl diacylglycerol (SQD) and phosphatidylglycerol (PSD) in *Anabaena cylindrica* 1403-2, *Nostoc calcicola* 1453-1, *Oscillatoria chalybea* 1459-2 and *Tolypothrix tenuis* B 1482-3 were analyzed [75]. In the lipid extracts from these aeroterrestrial filamentous cyanoprokaryotes, MGD had the highest proportion (19.2–28.6 weight %) and was followed by DGD (6.9–9.3%), SQD (5.6–7.1%) and PSD (3.3–8.5%). Only TGD was not detected in *Anabaena* and *Nostoc* but comprised 2 and 5% in *Oscillatoria* and *Tolypothrix*, respectively [75]. A later study of *Anabaena cylindrica*, "*Nostoc canina*" and *Desmonostoc muscorum* demonstrated a similar dominance of MGD, DGD, SQD and PSD and reported the occurrence of a highly polar unknown glycolipid in all of them [74]. Experiments with the soil ochrophyte *Monodopsis subterraneus* showed a decrease of saturated 16:0–16:0 DGD with a parallel increase of unsaturated 20:5–16:1 DGD under phosphate starvation [127].

The study of GL in the red polyextremophilic *Galdieria sulphuraria* also demonstrated the presence of MGD, DGD and SQD [128]. The same investigation revealed the presence of betaine lipids DGTA and DGTS, the contents of which decreased with the increase of the pH, while the contents of the other glycolipids (i.e., MGD, DGD and SQD) and of the phospholipids (phosphatidylglycerol—PG, phosphatidylcholine/lecithin—PC, phosphatidyletanolamine/cephalin—PE, phosphatidylinositol—PI, phosphatidylserine—PS and phosphatidate) increased. This phenomenon was related to the lack of available phosphorus in the culture media, but in general, the replacement of phospholipids by betaine lipids in *G. sulphuraria* was recognized as a major change in the adaptation to low pH and high temperatures [128]. However, in six other red algae, including unicellular polyextremophilic *Cyanidium caldarium*, which develops in low pH hot springs, and aeroterrestrial *Porphyridium purpureum*, betaine lipids were not found [128,129]. Considering the complicated taxonomy of *Cyanidium*, from which *Galdieria* was derived [36], we suppose that the lack of betaine lipids in *Cyanidium* needs further proof.

Betaine lipids are relatively better investigated in marine and freshwater microalgae [126,129,130], with DGTS and DGTA found in the plastid and thylakoid membranes of green algae [125]. It has been demonstrated that, in organisms like *Chlamydomonas reinhardtii*, betaine lipids (DGTS) seem to replace phospholipids (and particularly PC), a major phospholipid class in most eukaryotes, and instead produces a substantial amount of DGTS regardless of the P concentration [131]. However, betaine lipids remained poorly known in AEM, although there was empirical evidence that glycine betaine is among the essential compounds that allow halophytes to grow in high saline conditions [132].

3.3. Glycerophospholipids (GP) from AEM

Glycerophospholipids (GP) are natural lipids, widely spread in living organisms as key components in cell membranes with distinct differences in the structures between domains Eubacteria and Eukarya and domain Archaea (for details, see References [33,133]). In addition to their structural functions, GP can serve as precursors, or as membrane-derived messengers, but can participate in responses to stress [10,33]. GP contain a phosphate (or phosphonate) group esterified to one of the glycerol hydroxyl groups, but it has to be noted that a large number of trivial names are associated with this category [33].

GP commonly occur in microalgae and are used in cosmetic ingredients as excellent emulsifying agents that can stabilize oil–water emulsions as delivery systems [10,134,135]. The distribution of major GP in comparison with betaine lipids was discussed in the text above according to their distribution in unicellular red and green AEM. Data on PUFA domination (65.1%) over SAFA (18.4%) and MUFA (16.6%) and the detailed participation of FtAs in phospholipids of cryophilic *Chloromonas hindakii* have been published, with a note that the content of alpha-linolenic acid was up to twice higher in phospholipids than in neutral lipids and glycolipids [64].

3.4. Sphingolipids (SP) from AEM

Sphingolipids (SP) are a group of diverse molecules, which have a sphingoid base backbone (synthesized de novo from serine) and a long-chain fatty acyl-CoA [33]. The common name of this base, “sphingosine”, means similar to the Sphinx and is connected with the enigmatic (Sphinx-like) properties of these peculiar lipids (for details, see Reference [136]). SP comprise ceramides (which are also precursors of more complex SP), phosphosphingolipids, glycosphingolipids and some others, including protein adducts [33]. SP have a high potential for industry due to their important structural functions in maintaining the integrity of cell membranes and participation in extracellular signaling [137–139]. In addition, SP have demonstrated antimicrobial and antiviral activity [138,140–148].

Ceramides occur in high concentrations in the stratum corneum of the skin and are essential in maintaining the skin barrier properties, such as inhibiting water loss and protecting the ingress of potentially harmful substances [143]. Decreased levels of ceramides lead to the disruption of these barrier functions, which have been impaired in skin diseases such as psoriasis and atopic dermatitis [11,143,149,150]. The topical administration of ceramides was shown to be effective in preventing trans-epidermal water loss [151]. Glycosylceramide can alleviate atopic dermatitis by oral application via dietary intake [151–154], whereas its topical administration improves UV A-induced wrinkle formation and helps in preventing tumor metastasis in mice [155–157]. In addition, glycosylceramides increase the expression of genes involved in tight junctions and ceramide delivery in normal human epidermal keratinocytes [158].

SP have been known more than 100 years [136] but only currently has the accumulated evidence on beneficial skin applications led to their expanded utilization [151]. Despite this gradually increasing focus with a demand for natural sources of SP, up to now, their structural diversity in algae was poorly studied in comparison with mammals, higher plants and fungi [137]. Data on SP are available for aquatic macro- and microalgae from different taxonomic groups [142,144,145,148,151–171]. However, according to our best knowledge, there are no investigations regarding AEM. Considering that new structures

and new microalgal sources of SP are regularly discovered [159,167,169,170], and that the importance of SP for dermal cosmetics is increasing, future stronger interest in this class of valuable lipids from AEM can be expected.

3.5. Sterol Lipids (ST) from AEM

Sterol lipids (ST) are secondary triterpenoid metabolites, which are essential components of cell membranes [172]. They play a role in controlling the membrane stability, fluidity and permeability and influence the functionality of enzymes, receptors and channels [172–175]. ST have anti-inflammatory, anticarcinogenic, antibacterial and antiviral properties and demonstrate strong antioxidant abilities, which support the hypothesis for their origin as protective molecules in the response to reactive oxygen species [172,173,175–178]. ST are divided mainly according to their biological functions and, as a major lipid category, contain the following classes: cholesterol and derivatives, steroids (mainly with hormonal functions and a role in signaling molecules), secosteroids, bile acids and derivatives; steroid conjugates (including taurine conjugates, glycine conjugates, glucuronides and sulfates) and hopanoids [33].

ST show fascinating diversity, but their types and combinations differ between organismic groups [172,175]. ST of microalgae, despite not being comprehensively studied, also show great structural diversity and include some rare and unusual compounds but commonly occur in low amounts [137,179,180]. Studies of cyanoprokaryotes have provided debatable results on the presence/absence of ST, depending on the species and analytical tests, but when detected, ST were in low amounts (<0.03% of the dwc) [172]. However, genetic sequencing revealed several genes with a close sequence match to the genes related to sterol biosynthesis [172].

By contrast, it was stated that all eukaryotic microalgae contain ST [172,175,177]. C27 D5-unsaturated sterol cholesterol, usually considered animal sterol, is surprisingly common in microalgae [172]. However, in comparison with animals, ST profiles of algae show high compositional diversity and are of great interest for natural product research [180,181]. Algae produce cycloartenol and utilize the phytosterol biosynthetic pathway in a similar way to the higher plants [175]. Moreover, according to their ST contents, unicellular algae exhibit greater diversity than multicellular algae and plants, being an evolutionary precursor for the cycloartenol-based pathways in higher plants, and are supposed to be an evolutionary transition point for sterols [175]. The free-occurring microalgal ST are frequently, if not always, accompanied by conjugated forms (e.g., steryl glycosides, acyl steryl glycosides, esters (bearing fatty acid residues) and sulfates) of great diversity [137]. Usually, the compositional changes in ST profiles dependent on external factors are small, but some exceptions have been reported, indicating that, besides the taxonomic characteristics, the culturing conditions also need to be considered when comparing data on different species (for details, see Reference [172]).

An analysis of the available publications showed that, regarding ST, the most extensively examined were marine algae (for details, see References [137,178,180]). After the first studies in the 1960s indicating chondrillasterol in *Scenedesmus* [182], there was an increase in interest in freshwater green microalgae [183,184]. Their highly diverse sterolomic profiles were demonstrated, proving that even species from one genus can perform substantial differences (for details, see Reference [180]). Likewise, an investigation of marine microalgae (based on 106 cultures of diatoms) revealed their great ST diversity, represented by 44 types, all common with other algae [175,185]. Despite the obtained results on ST diversity in microalgae, there are very few investigations concerning AEM.

Historically, the first study of the aeroterrestrial filamentous cyanoporkaryote *Drouetiella lurida* (Syn. *Phormidium luridum*) was conducted in 1968 and led to the discovery of seven unsaturated ST [186]. It was followed by analyses on the other seven filamentous aeroterrestrial cyanoprokaryotes, namely *Anabaena cylindrica*, *Calothrix* sp., *Desmonostoc muscorum*, *Microcoleus autumnalis* (Syn. *Phormidium autumnale*), “*Nostoc canina*”, *Nostoc carneum* and *Nostoc commune* [74,173,187–189]. In *Microcoleus autumnalis*, the main ST were cholesterol, β -sitosterol and stigmasterol, with squalene as a precursor, and high amounts of

ergosterol were produced in a glucose culture [189]. For *N. canina*, “considerable amounts” of cholesterol and lanosterol were reported [74], while campesterol, sitosterol and clionasterol were detected in *Nostoc commune* var. *sphaeroides* [177,188,190]. Two unidentified ST were found, and thirteen unsaturated ST were determined in another filamentous aeroterrestrial cyanoprokaryote *Scytonema* sp. [191]. Among them, cholest-5-en-3 β -ol (18.9%), 3 β -methoxycholest-5-ene (16.2%) and 3 β -acetoxycholest-5-ene (11.2%) dominated [191]. In the same alga, only one tetraenoic sterol, namely ergosta-5,7,22,24(28)-tetraen-3 β -ol, was determined [191].

The first detection of this rare ST was in the polyextremophilic red *Cyanidium caldarium* and *Galdieria sulphuraria* [192]. These species grew on the soil and rocks of the acid hot springs, but a large part of their populations was cryptoendolithic and showed additional possibilities to adapt to low-light regimes inside the rocks [193]. Studies on *Galdieria sulphuraria* conducted in different light regimes and culture conditions have identified higher levels of ergosterol, the precursor of vitamin D₂, under high-light exposure and when glucose was added to the culture [194].

In *Chlorella vulgaris*, ergosterol, 7-dehydroporiferasterol, ergosterol peroxide, 7-dehydroporiferasterol peroxide and 7-oxocholesterol with anti-inflammatory and anticancer activities were detected [195]. Later, the examination of the ST composition of four other aeroterrestrial unicellular green algae, namely *Chlorella variabilis* NC64A (symbiotic), *Chlorella sorokiniana*, *Coccomyxa subellipsoidea* and *Chlamydomonas reinhardtii*, also revealed that, in *Chlorella*, and *Chlamydomonas* as well, the major sterol was ergosterol, whereas, in *Coccomyxa subellipsoidea*, which is able to grow at much lower, near-polar temperatures, three phytosterols occurred instead of ergosterol [175].

In *Dunaliella acidophila*, the ST were 6.4% of the ethyl ether extract, comprising β -sitosterol, isofucosterol, 24-methylenlophenol and (24S)-methyllophenol (isolated for the first time in green algae), and, in addition, two unidentified sterols were detected [98]. Other lipids, identified in this green extremophilic alga, were acylsterols (5.4%) and phytol (6.4%) [98].

Since microalgae have been declared as “the most prominent strains” for ST production [173], it has to be noted that almost all the studies cited above have demonstrated that the external conditions and type of cultivation (auto-, hetero- or mixotrophic) influence the amounts of ST. In spite of the great structural diversity and revealed promising sources, one of the limitations in the development of microalgae-derived phytosterols is their low sterol content [172,177], and the commercial exploitation of sterols from microalgae is yet in its infancy [172].

3.6. Prenol Lipids (PR) from AEM

Prenol lipids (PR) are synthesized from five-carbon isoprene units and comprise extremely important natural compounds, such as carotenoids, vitamins E and K, diverse terpenes, etc. [33].

Carotenoids are natural pigments from which currently more than 850 types have been identified [10,196,197]. Carotenoids are “multipurpose” strong antioxidants and scavenging agents, applied in dermal cosmetic formulations such as antiaging, anti-inflammatory, tanning and sunscreen compounds [2,5,197–202]. In addition, they have nutritional value to the skin and hair [201]. Therefore, carotenoids are used in both topical treatments, as active ingredients in creams and lotions, and in oral applications via dietary means [201,203]. Although these pigments are spread in all algal phyla, their types are peculiar for each taxonomic group, and they occur in different amounts with variations even among the strains of the same species (for details, see References [2,199]). Carotenoids have different disposition and function in cells, where they can be found in photosynthetic plastids (primary carotenoids) or in the cytoplasm (secondary carotenoids), and they have protective and nutritional functions [10]. Here, it is necessary to also recall that different harvesting techniques and extraction approaches lead to different carotenoids yields, and until now, no single uniform method has been accepted [197,201,204].

The best-known UV protectors with dermal topical application and rejuvenating function among the algal carotenoids are astaxanthin (ASX), β -carotene and lutein [2,3,6,7,17,197,205–217]. More than a single contribution could be attributed to these important pigments, all of which are able to decrease hyperpigmentation, while β -carotene has also a strong provitamin A activity and is applied in the formulation of suntan products, and ASX is valuable for its ability to inhibit skin cancer and to be effective in ulcer prevention [2,4–7,9,10,212].

ASX has gained increasing acceptance due to its beneficial external and internal applications in dermal cosmetics [217]. ASX is available on the market in the forms of cream, powder, soft gel, capsule, tablet, biomass, energy drink, oil and extract, and its products are often made in combination with other carotenoids, multivitamins, herbal extracts and omega-3, 6 fatty acids [218]. There is accumulated evidence, and different patent applications are available on ASX for preventing bacterial infection, inflammation and cancer and improving skin thickness [218]. During clinical studies, ASX suppressed hyperpigmentation with the inhibition of melanin synthesis and photoaging through topical application as a cream (containing also other ingredients) or consuming it as a dietary supplement (single or including tocotrienol from palm oil) [219–223]. Later, clinical studies on female and male subjects demonstrated the improvement of skin conditions in all layers (i.e., corneocyte layer, epidermis, basal layer and dermis) with increased elasticity, decreased age spots and skin wrinkles and diminished trans-epidermal water loss and sebum oil level after combined oral (6 mg day^{-1}) and topical application (2 mL day^{-1} of a $78.9\text{-}\mu\text{M}$ solution) of microalgal ASX (derived from its well-known producer *Haematococcus pluvialis*) [217]. The authors underlined the positive effects obtained not only in women but also in men and stressed that a combination technique may be very beneficial for the skin. The successful prevention of UV-induced skin damages, such as skin thickening, collagen reduction and increased melanin production, was also achieved using the topical administration of a liposomal formulation containing ASX [224]. An experiment with 40 healthy males demonstrated that the oral bioavailability of ASX increased 1.7–3.7 times when lipid-based formulations were incorporated [32].

ASX, β -carotene and lutein in different amounts were represented together with 34 other carotenoids in the peculiar class Eustigmatophyceae from the phylum Ochrophyta, for which lutein was reported for first time [199]. Particularly in the strains of its unicellular aeroterrestrial genera *Eustigmatos*, *Monodus* and *Vischeria*, they reached 60–85% of the total carotenoid content and over 5% of the dry weight [199]. High β -carotene and lutein contents were proven in another unicellular alga—the acidophilic ($\text{pH} < 2.5$) green *Coccomyxa acidophila*, which accumulated up to 3.55 mg g^{-1} when grown in mixotrophic conditions in the urea [225]. This extremophilic species, which could be efficiently cultivated outdoors, has to be noted especially as a potential commercial lutein source, because it contrasts with the most acidophilic algae, which are slow-growing [225].

The lutein derived from microalgae is in a non-esterified form and, therefore, is an advantageous alternative to conventional plant sources [3]. Regarding the promising microalgal species for lutein production in bioreactors, the analysis of Fernández-Sevilla et al. [226] revealed two unicellular oleaginous AEM: (1): the green aeroterrestrial *Muriellopsis* sp., which can produce $4.3\text{--}5.5 \text{ mg g}^{-1}$ in a laboratory batch and outdoor tubular systems [227–230], and (2) the acidophilic and aeroterrestrial *Auxenochlorella protothecoides* (Syn. *Chlorella protothecoides*) [3,231–237], which is capable of growing both autotrophically and heterotrophically, accumulating large amounts of lipids and lutein especially (4.6 mg g^{-1}) under heterotrophic laboratory growth conditions [225,233]. The aeroterrestrial green unicellular *Chromochloris zofingiensis* (Syn. *Chlorella zofingiensis*) is able to accumulate high amounts of carotenoids that contain a ketone group, named keto-carotenoids (including ASX, canthaxanthin and lutein), when growing heterotrophically or mixotrophically, or under stress conditions [3,197,200,218,238–246]. Therefore, this species and its Cz-bkt1–5 mutants in particular were suggested as a natural source for the production of zeaxanthin, lutein and β -carotene [244]. Besides *C. zofingiensis*, the aeroterrestrial green *Neochloris wimmeri*, *Scenedesmus vacuolatus*, *Coelastrella oocystiformis* (Syn. *Scotiellop-*

sis oocystiformis) and *Protosiphon botryoides* accumulate significant quantities of secondary carotenoids, mainly as ASX esters and canthaxanthin, when grown in conditions of nitrogen deficiency and high light intensity [239]. The proportions of these secondary carotenoids to the rest of the pigments in the green and red cells of these species comprised between 50% in *C. oocystiformis* and *C. zofingiensis* and more than 80% in *Neochloris wimmeri* and *Protosiphon botryoides*, with canthaxanthin predominating in *S. vacuolatus* [239]. Although being lower than ASX in *Haematococcus* (22.7 mg g⁻¹ biomass), the accumulation of this carotenoid reached relatively high values in *Neochloris wimmeri*, *Protosiphon botryoides*, *Coelastrella oocystiformis*, *Chromochloris zofingiensis* and *Scenedesmus vacuolatus* of 19.2, 14.3, 10.9, 6.8 and 2.7 mg g⁻¹ biomass, respectively [247]. Evidence has accumulated that *Tetradesmus obliquus* can synthesize ASX from β -carotene through three possible pathways, but the accumulation and metabolism of ASX can be controlled by cultivated conditions [248].

Zeaxanthin was found to be abundant (4.26 mg g⁻¹) in the aeroterrestrial green *Chlorodinium ellipsoideum* (Syn. *Chlorella ellipsoidea*), “with a total level more than nine times that of red pepper, a plant source of zeaxanthin” [249]. The additional value of this microalgal zeaxanthin is its occurrence in the free form, while those in other plants exist as mono- and diesters [249]. Another aeroterrestrial green alga, *Coelastrella striolata* var. *multistriata*, is also promising for large-scale cultivation, because it synthesizes very high amounts of major secondary carotenoids (56.0 mg g⁻¹ biomass) in its reddish-orange cells, with the contents of canthaxanthin, ASX and β -carotene reaching 47.5, 1.5, and 7.0 mg g⁻¹ cell dry weight, respectively [69].

ASX, zeaxanthin, canthaxanthin and lutein comprise significantly the carotenoid content of aeroterrestrial *Chlorella vulgaris* and *Auxenochlorella pyrenoidosa* (Syn. *Chlorella pyrenoidosa*) [197,205,250–254]. For example, by improving the extraction process, the yield of lutein 3.16–3.36 mg g⁻¹ (wet weight) from *C. vulgaris* was achieved [255], or, when saponification was applied, the yield was 85–91%, with the final purity of lutein obtained at 90–98% [256]. Here, we would like to note that, despite finding strain-specific differences, according to its high total lipid content (58% dry weight), *C. vulgaris* was declared as one of the “winners” among the candidates for industrial lipid producers [25,257]. Regarding the possible beneficial effects in dermal cosmetics after oral application, we have to recall that *C. vulgaris* is one of the few microalgae that can be found on the market as a food supplement or additive, food emulsion or colorant (after carotenogenesis) in different forms (capsules, tablets, extracts and powder) (for details, see Reference [24]).

A high lutein content (0.25%) with achieved stability of about 90% was obtained in a developed method for efficient commercial lutein extraction at a lower cost, based on experiments with *Tetradesmus obliquus* and its strain “*Scenedesmus obliquus* CNW-N” in particular [258]. Light-related strategies applied to enhance the lutein production of the same species (strain “*Scenedesmus obliquus* FSP-3”) allowed to obtain the optimal productivity of 4.08 mg L⁻¹ d⁻¹ [259]. *Tetradesmus obliquus*, with up to a 50% dry weight lipid content, was also included in the list of “winners” among the microalgal candidates for commercial lipid producers [21,25]. In different cultures of species from the genus *Scenedesmus* s.l. (from which *Tetradesmus* was derived), lutein was accumulated as the major carotenoid in the cells, with an achieved increase of lutein and ASX under stress conditions [70,258,260].

Similar results on extremely high ketocarotenoid contents (up to 103 mg total ketocarotenoids L⁻¹) with 32 mg ASX L⁻¹ were obtained from the specific MA-1 strain of the unicellular green *Chlorococcum* sp. [261]. It accumulates twice as much as the wild thermotolerant type, which was already proposed for the commercial production of these pigments [261–263]. In the strains of the same species, ASX (in a free form and as esters) was reported together with adonixanthin (in a free form and as esters), lutein, canthaxanthin and β -carotene [200,218,264,265]. Although the total carotenoid content (2 mg g⁻¹ dw) was lower in comparison to the large-scale producer *Haematococcus*, *Chlorococcum*, with its higher growth rate, was suggested as a potentially interesting source for secondary carotenoid production [265].

A high β -carotene and lutein content was also reported for the green extremophilic algae developing on snow, such as the cryophilic unicellular *Chlorococcum* sp. (4.9 mg per 100-g⁻¹ fresh mass and 30.1 mg per 100-g⁻¹ fresh mass, respectively) and filamentous *Raphidonema nivale* (5.5 mg per 100-g⁻¹ fresh mass and 37.4 mg per 100-g⁻¹ fresh mass, respectively) [266]. In samples from reddish and greenish snow, lutein accomplished 77.6 (15.6% of the total pigment content) and 194.8 mg g⁻¹ (19.2%), and β -carotene reached 11.9 (2%) and 28.8 mg g⁻¹ (3%), respectively [267].

Generally, in red snow with 10³ to 10⁴ red pigmented algal cells mL⁻¹ (mainly *Chloromonas alpina*, *Chloromonas nivalis*, *Chloromonas polyptera*, *Raphidonema sempervirens* and some uncultured species of Chlamydomonadaceae), the UV-protective secondary carotenoids comprise between 70 and 90% [66]. Among them, ASX (trans-ASX) dominates [66], as was shown earlier for *Chlamydomonas nivalis* [268,269]. Similar results on a high ASX content were obtained for the eurythermic and desiccation-resistant red or orange cysts of other green unicellular snow algae, *Sanguina nivalis* and *Sanguina aurantia* [270]. ASX was the only pigment detected in the class of secondary carotenoids in *Chloromonas polyptera* that caused orange snow in the vicinity of penguin rockeries [271]. In the orange cysts of *Chloromonas hindakii*, ASX comprised 19.8–22.1% of all the pigments, with amounts comparable to that in *Chlamydomonas nivalis* [64,268,269]. The chemotaxonomical comparison revealed that the high abundance of nonpolar ASX diesters differentiated the green unicellular *Chlamydomonas*, which caused orange snow, from the other two main groups of Chlamydomonadalean snow algae, the “*Chloromonas*-snow” clade and the “*Chlamydomonas*-red snow” clade [272]. All the evidence accumulated from different studies suggests that the secondary carotenoids like ASX dominate over chlorophylls in green algae snow, which causes red, orange and pink snow during their mass development [64,268,269,271,273] and that these snow algae should be considered valuable sources of these pigments for cosmetic and other industries.

In the red-phase samples of unicellular green snow algae *Chlamydomonas nivalis*, *Chlamydocapsa* sp. and *Chlorococcum* sp., another secondary carotenoid, canthaxanthin, was found to be responsible for their yellow-to-orange pigmentation [266]. The values varied between (12–28)–388 and 921 μ g g⁻¹ freeze-dried dry mass, being the highest in *Chlamydocapsa* sp. and *Chlorococcum* sp. [266]. The relative high content (65.1%) of canthaxanthin was detected in the soil cold-tolerant green alga *Tetracystis* sp., resulting in its dark orange coloration [274]. More recently, this ketocarotenoid was found in four aeroterrestrial oleaginous *Visheria*/*Eustigmatos* strains, accounting for 3–7% of their total carotenoid content [2,199]. Two ketolase genes, *crtW38* and *crtW148*, for the heterologous production of canthaxanthin and astaxanthin were cloned from the aeroterrestrial cyanoprokaryote *Nostoc punctiforme* (strain PCC 73102 [275]). Although its ecophysiological role has to be further clarified, canthaxanthin has been used in tanning products [2,207,276].

β -carotene was detected as the main carotenoid in a study of 43 strains of the thermophilic red *Galdieria sulphuraria*, and lutein comprised 0.4 mg g⁻¹, but its total lipid content was low [96]. Similar results on the low lipid content (3–4.6% weight) contrasting to a high percentage of proteins (22–37%) and carbohydrates (20–58.4%) were obtained in a more recent study on biomass composition of this alga grown under heterotrophic conditions [277,278].

Another carotenoid, lycopene, a potent natural antioxidant, is used in personal care formulations as an antiaging agent, and its application as a sunscreen and sunburn-preventing agent has been suggested [2,207,279]. Two strains of the aeroterrestrial cyanoprokaryote *Anabaena vaginicola* contain substantially higher contents of lycopene (24.6 and 19.3 mg g⁻¹ dw) in comparison with all the previously reported natural sources [2,280]. The same *Anabaena* strains and the soil *Nostoc calcarea* also contained high amounts of β -carotene (1.2–8.1 mg g⁻¹ dry weight) “comparable with the best natural β -carotene sources” [280]. In all isolated *Anabaena* and *Nostoc* strains, lycopene and β -carotene were combined with lutein and zeaxanthin, which allowed the authors to outline these strains as “rich sources of major carotenoids” [280]. Lycopene in combination with other major carotenoids (1.4%

of the ethyl ether extract), namely, α -carotene, β -carotene and γ -carotene, was isolated in the extremophilic green *Dunaliella acidophila* [98].

Tocopherols (vitamin E) with their strong antioxidant activity are of special interest for the cosmetics industry [4,281]. However, they are relatively rarely studied in microalgae, and only a small amount of data are available on AEM, among which are some aeroterrestrial species belonging to Chlorophyta (*Bracteacoccus* sp., *Coccomyxa* sp., *Muriella terrestris* and *Stichococcus bacillaris*); Ochrophyta (yellow-green *Botrydiopsis intercedens*, *Heterococcus* sp., *Xanthonema* sp. and eustigmatophycean *Monodus guttula*) and both green cryophilic species *Chlamydocapsa* sp. and *Raphidonema sempervirens* (for details on the amounts, see Reference [2]).

3.7. Saccharolipids (SL) from AEM

Saccharolipids (SL) describe compounds in which fatty acids are linked directly to a sugar backbone, forming structures that are compatible with membrane bilayers [33]. However, only a small amount of studies have provided data on SL from microalgae, all of which are from aquatic habitats (for details, see References [10,282]).

3.8. Polyketides (PK) from AEM

There are three types of polyketide synthases (PKS; I, II and III) that catalyze the biosynthesis of the structurally and functionally diverse natural products, polyketides (PK) [283]. In general, it is believed that PKS type I is typical for fungi, and type II has been found in bacteria, mitochondria and plastids, while type III occurs mostly in land plants [283]. In algae, type I PKS genes were discovered by genome sequencing but have patchy occurrence, being distributed mostly in green algae [283,284]. Among them, *Chlamydomonas reinhardtii*, *Chlorella variabilis* and *Coccomyxa subellipsoidea* (strain C-169, formerly designated “*Coccomyxa* sp. C-169”) belong to AEM [283–285]. PKS II was discovered in the aeroterrestrial filamentous *Klebsormidium flaccidum* from Streptophyta and, in unicellular red polyextremophiles inhabitants of acid thermal springs, *Cyanidioschyzon merolae* and *Galdieria sulphuraria* [283]. The results from a study of 32 species from different phyla allowed us to demonstrate that PKS I is phylogenetically scattered in algae, suggesting a large potential for the production of PK and non-ribosomal peptides in some phyla, whereas others completely lack this ability [283]. Regarding the safety of cosmetic products, it is necessary to note that PK synthesis plays a role in the biosynthesis of non-ribosomal cyanoprokaryote toxins, namely microcystins, and in some dinoflagellate toxins (for details, see Reference [283]). PKS related to PUFA synthase are involved in the biosynthesis of long-chain polyhydroxy alcohols and contribute to the formation of the glycolipid envelope in specific nitrogen-fixing cells of Cyanoprokaryota known as heterocysts [75,283,286,287].

3.9. Safety Aspects

Most compounds included in this review are commonly considered safe and nontoxic, but we have to note that some microalgae can produce toxic metabolites (algal toxins), which are of a great safety concern due to their serious impact on human health (for details, see References [2,35]). From the lipids discussed in the review, PK play a role in the biosynthesis of some algal toxins [283]. Therefore, these lipids and their sources have to be carefully investigated before being utilized in cosmetic products. However, studies oriented towards the checking of algal toxicity are mostly exceptional, and only a few targeted experiments proving the safety of the biomass of oleaginous algae have been conducted [288,289].

Although it has been widely accepted that, among AEM, the number of potential toxin producers is much lower in comparison with their counterparts from aquatic habitats, according to our recent analysis, algal toxins and their producers occur in all general types of detrimental habitats [35]. All nine genera from Cyanoprokaryota, which have been examined for lipids, have already been enlisted among the potential toxin-producers and algae with allergenic potential [35,290]. However, due to the lack of precise taxonomic

information in most publications that address lipid studies, more detailed comparisons are not well-grounded, but we would like to stress the need for specific studies targeted on the toxicity for all novel sources and their products proposed for cosmetical formulations.

4. Discussion

The conducted analysis of publications on lipids from AEM issued in the last 56 years showed that most studies addressed PR and FA, specifically carotenoids and FtAs (mainly PUFA), but even these two lipid categories and their accumulation in AEM deserve more attention. In fact, from the eight major groups accepted in LIPID MAPS classification [33,34], only five (i.e., FA, GL, GP, ST, PR and PK) have been examined in different phyla of AEM, as follows: Cyanoprokaryota (FA, GL, ST and PR); Rhodophyta (FA, GL, ST, PR and PK); Ochrophyta (FA, GL and PR); Chlorophyta (FA, GL, GP, ST, PR and PK) and Streptophyta (PK)—Table 1. However, according to the data obtained, it is possible to state that stronger efforts are necessary to improve our knowledge regarding GL, GP and SL and their spread in AEM. Special attention has to be paid to SP, which, according to our best knowledge, remain unknown in AEM.

Table 1. Main lipid classes investigated in aeroterrestrial (AET) and extremophilic (EXT) microalgae of different taxonomic phyla and classes. Abbreviations: AA—arachidonic acid, ASX—astaxanthin, DGD—digalactosylglycerol, DGTA—diacylglycerol-hydroxymethyl-*N,N,N*-trimethyl- β -Ala, DGTS—diacylglycerol-*N,N,N*-trimethylhomo-Ser, EPA—eicosapentaenoic acid, FA—fatty acyls, FtAs—fatty acids, FAEs—fatty acid esters, GL—glycerolipids, GP—glycerophospholipids, MGD—monogalactosylglycerol, PC—phosphatidylcholine/lecithin, PE- phosphatidyletanolamine/cephalin, PG—phosphatidylglycerol, PI—phosphatidylinositol, PK—polyketides, PR—prenol lipids, PS—phosphatidylserine, PSD—phosphatidylglycerol, SQD—sulphoquinovosyl diacylglycerol, ST—sterol lipids, TGD—triagalactosylglycerol. In Bold are outlined AEM, noted in the cited literature as promising for commercial production and relevant lipids.

Taxonomic Group/Alga	Ecological Group	Investigated Lipid Classes with Examples of Detected Lipids	References
CYANOPROKARYOTA			
<i>Anabaena cylindrica</i>	AET	FA (PUFA—linoleic and linolenic acids, SAFA—palmitic acid and MUFA); GL; ST	[74]
<i>Anabaena cylindrica</i> 1403-2	AET	GL (MGD, DGD, SQD and PSD)	[75]
<i>Anabaena vaginicola</i>	AET	PR (lycopene, lutein, beta-carotene, zeaxanthin)	[280]
<i>Calothrix</i> sp.	AET	ST	[74,173,187–189]
<i>Desmonostoc muscorum</i>	AET	FA (PUFA—hexadecadienoic and linoleic acids, SAFA—palmitic acid, MUFA—oleic and palmitoleic acids); GL; ST	[74,173,187–189]
<i>Drouetiella lurida</i>	AET—soil, subaerial	ST (seven unsaturated ST)	[186]
<i>Microcoleus autumnalis</i>	AET—soil, subaerial	ST (cholesterol, β -sitosterol and stigmaterol with squalene as a precursor; ergosterol)	[189]
<i>Nostoc calcarea</i>	AET—soil, subaerial	PR (lycopene, lutein, beta-carotene, zeaxanthin)	[280]
<i>Nostoc calcicola</i> B 1459-2	AET—soil, subaerial	FA (PUFA—linolenic acid, SAFA, MUFA), GL—MGD, DGD, SQD and PSD	[75]

Table 1. Cont.

Taxonomic Group/Alga	Ecological Group	Investigated Lipid Classes with Examples of Detected Lipids	References
<i>Nostoc carneum</i>	AET—soil, subaerial	ST	[74,173,187–189]
“ <i>Nostoc canina</i> ”	AET (symbiont?)	FA (PUFA—linoleic acid, SAFA -palmitic acid, MUFA—palmitoleic and oleic acids); GL; ST (cholesterol and lanosterol)	[74]
<i>Nostoc commune</i>	AET	ST	[74,173,187–189]
<i>Nostoc commune</i> var. <i>sphaeroides</i>	AET	ST (campesterol, sitosterol and clionasterol)	[177,188,190]
<i>Nostoc punctiforme</i> PCC73102	AET	FA (FAEs—oxylipins), PR (genes for ASX and canthaxanthin)	[115,275]
<i>Nostoc</i> sp. PCC7120	AET	FA (FAEs—oxylipins)	[116]
<i>Oscillatoria chalybea</i> B1459-2	AET	GL (MGD, DGD, TGD, SQD and PSD)	
<i>Oscillatoria</i> sp. PBGA3	AET—soil	FA (FtAs)	[76]
<i>Scytonema</i> sp.	AET	ST (cholest-5-en-3 β -ol (18.9 %), 3 β -methoxycholest-5-ene (16.2 %) and 3 β -acetoxcholest-5-ene (11.2 %), ergosta-5,7,22,24(28)-tetraen-3 β -ol)	[191]
<i>Tolypothrix tenuis</i> B1482-3	AET	GL (MGD, DGD, TGD, SQD and PSD)	[75]
<i>Tolypothrix</i> sp. PBGA1	AET	FA (FtAs)	[76]
<i>Tolypothrix</i> sp. PBGA2	AET	FA (FtAs)	[76]
RHODOPHYTA			
<i>Cyanidium caldarium</i>	EXT—thermal springs	GL; ST (ergosta-5,7,22,24(28)-tetraen-3 β -ol)	[192]
<i>Cyanidioschyzon merolae</i>	EXT—thermal springs	PK	[283]
<i>Galdieria sulfuraria</i> (>47 strains)	EXT—thermal springs/AET—cryptoendolith	FA (PUFA—linoleic and linolenic acid, SAFA—palmitic acid, MUFA—oleic and palmitoleic acids); GL (MGD, DGD and SQD); PG, PC, PE, PI, PS and phosphatidate); GP; ST (ergosta-5,7,22,24(28)-tetraen-3 β -ol and ergosterol); PR (β -carotene, lutein); PK	[64,96,128,192,283]
<i>Galdieria sulfuraria</i> / <i>Galdieria</i> sp.?	EXT—acidic but non-thermophilic	FA (PUFA—linoleic and linolenic acids, SAFA—palmitic, myristic and stearic acids, MUFA—oleic and palmitoleic acids)	[64,96]
<i>Galdieria</i> sp. USB-GBX-832	EXT—thermal springs	FA (PUFA—linoleic acid, AA and EPA; SAFA—palmitic and stearic acid, MUFA—oleic acid)	[95]
<i>Pophyridium purpureum</i>	AET-soil	FA (PUFA—AA and EPA); GL	[84]
OCHROPHYTA Eustigmatophyceae			
<i>Monodopsis subterraneus</i>	AET—soil	FA (PUFA—EPA), GL (DGD)	[90–94,127]
<i>Monodus guttula</i>	AET	PR (tocopherols)	[2]
<i>Monodus</i> sp.	AET	PR (carotenoids—ASX, beta-carotene and lutein)	[199]
<i>Vischeria/Eustigmatos</i>	AET—soil, subaerial	PR (total carotenoids; ASX, beta-carotene, lutein and canthaxanthin)	[199]
Tribophyceae (=Xanthophyceae)			
<i>Botrydiopsis interdecens</i>	AET	PR (tocopherols)	[2]
<i>Heterococcus</i> sp.	AET	PR (tocopherols)	[2]
<i>Xanthonema</i> sp.	AET	PR (tocopherols)	[2]
CHLOROPHYTA			
<i>Acutodesmus dissociatus</i> TGA1	AET—soil	FA (SAFA—palmitic acid and MUFA—oleic acid)	[76]

Table 1. Cont.

Taxonomic Group/Alga	Ecological Group	Investigated Lipid Classes with Examples of Detected Lipids	References
<i>Auxenochlorella protothecoides</i>	AET/EXT—acidic	PR (carotenoids— lutein)	[231–237]
<i>Auxenochlorella pyrenoidosa</i>	AET	PR (carotenoids—ASX, zeaxanthin, canthaxanthin, lutein)	[197,205,250,254]
<i>Bracteacoccus</i> sp.	AET	PR (tocopherols)	[2]
<i>Chlamydocapsa</i> sp.	EXT—snow	PR (canthaxanthin, tocopherols)	[2,266]
<i>Chlamydomonas nivalis</i>	EXT—snow	PR (ASX, canthaxanthin)	[266,268,269]
<i>Chlamydomonas reinhardtii</i>	AET	FA (hydrocarbons—C17 alkene n-heptadecene), GL (betaine lipids—DGTS); GP; ST (ergosterol); PK	[119,131,175,283–285]
<i>Chlainomonas</i> sp.	EXT—snow	PR (ASX)	[272]
<i>Chlorella sorokiniana</i>	AET	ST (ergosterol)	[175]
<i>Chlorella variabilis</i>	AET	PK	[283–285]
<i>Chlorella variabilis</i> NC64A	AET (symbiotic)	ST (ergosterol)	[175]
<i>Chlorella vulgaris</i>	AET	FA (free FtAs, FAEs—lactones; hydrocarbons—NC64A eptadecane pentadecane, as well as 7- and 8-heptadecene); GL; ST (ergosterol, 7-dehydroporiferasterol, ergosterol peroxide, 7-dehydroporiferasterol per-oxide and 7-oxocholesterol); PR (carotenoids—ASX, zeaxanthin, canthaxanthin and lutein), PK	[21,24,101,102,119,195,197,205,250,254]
<i>Chlorella</i> sp. PGA2	AET—soil	FA (SAFA, MUFA)	[76]
<i>Chlorella</i> sp. TGA2	AET—soil	FA (SAFA- palmitic acid, MUFA—oleic acid)	[76]
<i>Chlorella</i> sp. TGA4	AET—soil	FA (SAFA, MUFA)	[76]
<i>Chlorococcum</i> sp. (1)	AET	PR (carotenoids—ASX (in a free form and as esters), adonixanthin (in a free form and as esters), lutein, canthaxanthin and β -carotene)	[200,218,261–265]
<i>Chlorococcum</i> sp. MA-1	AET	PR (total carotenoids; ASX, lutein, canthaxanthin and β -carotene)	[261]
<i>Chlorococcum</i> spp.	EXT—snow	PR (β -carotene, lutein and canthaxanthin)	[64,65,266,268,269,271,273]
<i>Chloroidium ellipsoideum</i>	AET	PR (carotenoids— zeaxanthin)	[249]
<i>Chloromonas alpina</i>	EXT—snow	FA (PUFA, SAFA, MUFA), PR (ASX)	[64–67,268,269,271,273]
<i>Chloromonas hindakii</i>	EXT—snow	FA (PUFA— α -linolenic, steredonic and hexadecatetraenoic acids, SAFA—palmitic acid and MUFA—oleic acid); GP; PR (ASX)	[64–67,268,269,271,273]
<i>Chloromonas nivalis</i>	EXT—snow	FA (PUFA—hexadecatetraenoic, SAFA and MUFA); PR (ASX, canthaxanthin)	[64–67,266,268,269,271,273]
<i>Chloromonas nivalis</i> subsp. <i>tatrae</i>	EXT—snow	FA (PUFA, SAFA and MUFA); PR (ASX)	[67]
<i>Chloromonas polyptera</i>	EXT—snow	FA (PUFA, SAFA and MUFA), PR (ASX)	[64–67,268,269,271,273]
<i>Chloromonas remiasii</i> CCCryo 005–99	EXT—snow	FA (PUFA-hexadecatetraenoic acid, SAFA and MUFA), PR	[63–67,268,269,271,273]
<i>Chloromonas</i> spp.	EXT—snow	FA (PUFA, SAFA—palmitic acid and MUFA—oleic acid), PR	[65–67,268,269,271,273]
<i>Chromochloris zofingiensis</i>	AET	PR (carotenoids—ASX, canthaxanthin, zeaxanthin , lutein and β - carotene)	[197,200,218,238–247]
<i>Coccomyxa acidophila</i>	EXT—acidic	PR (carotenoids— β -carotene and lutein)	[255]
<i>Coccomyxa subellipsoidea</i>	AET	ST (phytosterols)	[175]
<i>Coccomyxa subellipsoidea</i> C-169	AET	PK	[283–285]

Table 1. Cont.

Taxonomic Group/Alga	Ecological Group	Investigated Lipid Classes with Examples of Detected Lipids	References
<i>Coccomyxa</i> sp.	AET	PR (tocopherols)	[2]
<i>Coelastrella oocystiformis</i>	AET	PR (carotenoids—ASX esters and canthaxanthin)	[239,247]
<i>Coelastrella striolata</i> var. <i>multistriolata</i>	AET—subaerial, soils	FA (PUFA—linoleic acid, SAFA—palmitic acid and MUFA—oleic acid); PR (carotenoids— canthaxanthin , ASX and β-carotene)	[68,69]
<i>Dunaliella acidophila</i>	EXT-acidic	FA (PUFA—linolenic, γ-linolenic and linoleic acids; SAFA; MUFA—oleic and elaidic acids; FAEs—lactones, methyl (12R)-hydroxyoctadeca-9Z,13E,15Z-trienoate, methyl (9S)-hydroxyoctadeca-10E, 12Z,15Z-trienoate and methyl ricinoleate; triacylglycerols—trilinolenin, triolein, trielaidin and tristearin); ST (β-sitosterol, isofucosterol, 24-methylenlophenol, (24S)-methyllophenol and two unidentified sterols, acylsterols and phytol); PR (lycopene, alpha-, beta and gamma-carotene)	[98,119]
<i>Edaphochlamys debaryana</i>	AET—soil	FA (FAEs—oxylipins)	[112]
<i>Hindakia tetrachotoma</i> PGA1	AET—soil	FA (SAFA—palmitic acid and MUFA—oleic acid)	[76]
<i>Monoraphidium</i> sp.	EXT—ice	FA (PUFA)	[31]
<i>Muriella terrestris</i>	AET	PR (tocopherols)	[2]
<i>Muriellopsis</i> sp.	AET	PR (carotenoids— lutein)	[226–230]
<i>Neochloris wimmeri</i>	AET	PR (carotenoids—ASX esters and canthaxanthin)	[239,247]
<i>Parietochloris alveolaris</i>	AET—oil, symbiont	FA (PUFA—EPA, AA and its precursor dihomo-γ-linolenic acid)	[80,82]
<i>Parietochloris alveolaris</i> K-1	AET	FA (PUFA—α-linolenic acid and EPA)	[78,79]
<i>Protosiphon botryoides</i>	AET—soil	PR (carotenoids—ASX esters and canthaxanthin)	[239,247]
<i>Pseudochoricystis ellipsoidea</i> MBIC11204	EXT—thermal springs	FA (FtAs and FAEs— hydrocarbons and triacylglycerols)	[122]
<i>Raphidonema sempervirens</i>	EXT—snow	FA (PUFA, SAFA and MUFA); PR (β-carotene, ASX, lutein and tocopherols)	[2,65–67,266]
<i>Sanguina aurantia</i>	EXT—snow	PR (ASX)	[270]
<i>Sanguina nivalis</i>	EXT—snow	PR (ASX)	[270]
<i>Scenedesmus vacuolatus</i>	AET	PR (carotenoids—ASX esters and canthaxanthin)	[239,247]
<i>Scenedesmus</i> spp.	AET	PR (total carotenoids, ASX and lutein)	[69,258,260]
<i>Stichococcus bacillaris</i>	AET	PR (tocopherols)	[2]
<i>Tetracystis</i> sp.	AET/EXT—cryotolerant	PR (canthaxanthin)	[274]
<i>Tetradesmus obliquus</i>	AET	FA (PUFA—linolenic, linoleic and linoleic acids and SAFA—oleic acid); PR (carotenoids—ASX and lutein)	[21,25,69–73,248,258,260]
<i>Tetradesmus obliquus</i> (strain <i>Scenedesmus obliquus</i> SNW-N)	AET	PR (lutein)	[258]
<i>Tetradesmus obliquus</i> (strain <i>Scenedesmus obliquus</i> FSP-3)	AET	PR (lutein)	[259]
<i>Ulothrix zonata</i>	EXT—ice	FA (PUFA)	[68]
“Unidentified Chlamydomonadaceae”	EXT—snow	FA (PUFA, SAFA and MUFA); PR (ASX)	[76]

Table 1. Cont.

Taxonomic Group/Alga	Ecological Group	Investigated Lipid Classes with Examples of Detected Lipids	References
Unidentified "Chlamydomonadales species" TGA3	AET—soil, thermotolerant	FA (SAFA and MUFA)	[76]
Unidentified "Chlamydomonadales species" TGA5	AET—soil	FA (SAFA and MUFA)	[76]
STREPTOPHYTA			
<i>Klebsormidium flaccidum</i>	AET	PK	[283]

The taxonomic diversity of the examined AEM, expressed by the number of species, is as follows: Cyanoprokaryota—20, Rhodophyta—6, Ochrophyta—7, Chlorophyta—53 and Streptophyta—1 (Figure 1A and Table 1). Thus, AEM from green evolutionary lineages (Chlorophyta and Streptophyta) are the most investigated, but a strong discrepancy between the studies inside the green lineages is obvious, with only one species from Streptophyta (i.e., *Klebsormidium flaccidum*) investigated in comparison with 53 species of 34 genera from Chlorophyta. The next most-studied group is represented by prokaryotic blue-green algae, Cyanoprokaryota, from which 20 species of nine genera have been analyzed. The number of species investigated in Rhodophyta and Ochrophyta is significantly lower and almost similar (six and seven, respectively), but more genera have been covered by studies on Ochrophyta (seven) than from Rhodophyta (four). However, much more strains from Rhodophyta have been examined, with more than 47 strains investigated from a single species (i.e., the extremophilic *Galdieria sulfuraria*). Most of the studied AEM are unicellular (59), followed by filamentous (26) and coenobial algae (2). The highest morphological diversity has been found in the studied chlorophyte algae, while, from Cyanoprokaryota, only filamentous species and, from Rhodophyta, only unicellular species were examined for different lipids.

Regarding the ecological affiliation of the examined microalgae (Figure 1B,C), it could be stated that the highest number (66) of studied species are aeroterrestrial, and they are the most taxonomically diverse, including representatives from all five major algal phyla (Figure 1C). By contrast, the number of examined extremophilic species is lower (21), with only two phyla studied (i.e., Rhodophyta and Chlorophyta) (Figure 1B). Despite this generally low number, ten extremophilic algae (ca. 50%) have been considered as promising lipid sources (Table 1). However, it has to be boldly underlined that this analysis is based only on Latin species names provided in the available publications, since, for most of the strains, there are neither data from genetic studies nor detailed morphological and ecological descriptions. In the recent times of rapid taxonomical changes, providing such data in future publications is strongly recommended in order to obtain more precise information on the biochemical compositions of the studied microalgae.

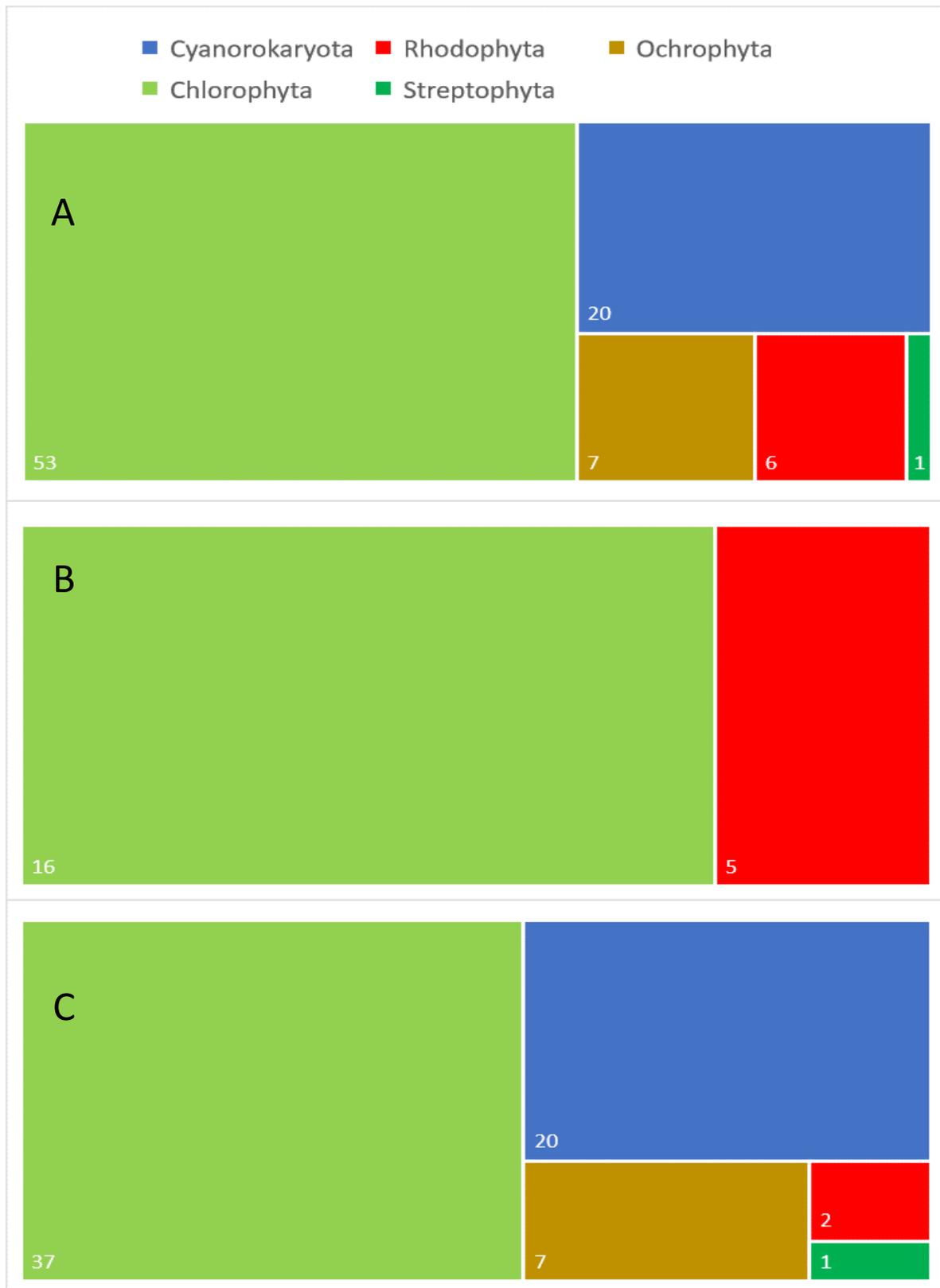


Figure 1. Taxonomic diversity of aeroterrestrial and extremophilic microalgae analyzed for different lipids: (A) general taxonomic diversity of the analyzed algal species, (B) taxonomic diversity of the examined extremophilic species and (C) taxonomic diversity of the investigated aeroterrestrial species. Numbers in white indicate the exact number in each category.

The results obtained clearly showed that very few known AEM have been investigated for their lipid content, with most of the studies being quite scarce and oriented towards certain compounds. Less studies were comparative, but the differences in lipid contents were demonstrated with field materials and cultivated in different conditions algae, or ecologically different strains (e.g., thermophilic and non-thermophilic) were investigated. These results may stimulate further research for the best physiological and cultural conditions, which would lead to the optimal yield of algal biomass and certain lipids. As we have shown in the text above, data on all lipid classes in AEM are far away from being complete, and more investigations on certain compounds and in more AEM are needed in the future. Nevertheless, all collected evidence until now suggests the great potential of AEM as novel commercial lipid sources for versatile cosmetic substances and products for skin care. In this regard AEM are comparable with their aquatic (marine and freshwater) counterparts and land plants, which have been much more intensively studied [1,2,291]. Twenty-three AEM have been already pointed out as promising for obtaining certain compounds, most of them from Chlorophyta (Table 1). The potential of AEM as beneficial lipid sources can be recognized in two aspects, separately or in combination: (1) quantitative, since, in some AEM, the contents of valuable lipids are higher in comparison with other algae or plants (e.g., *Parietochloris alveolaris* is considered to be the richest natural source of the high value polyunsaturated ω 6 AA, or *Chlorodinium ellipsoideum*, in which zeaxanthin exceeded more than nine times that of red pepper, a plant source of zeaxanthin) and (2) qualitative, since, in some AEM, rare and unusual lipids were discovered (e.g., the three hydroxy FtAs in *Dunaliella acidophila*, such as methyl (12R)-hydroxyoctadeca-9Z,13E,15Z-trienoate, methyl (9S)-hydroxyoctadeca-10E, 12Z,15Z-trienoate and methyl ricinoleate, or the unidentified ST of *Scytonema* sp. and *Dunaliella acidophila*). These compositional peculiarities in AEM, as it has been shown earlier, are due to their specific ecology and adaptations to survive inimically in other organism environments, and this potential is still untapped [2]. However, among the AEM examined for lipids occur species from genera that have already been recognized as potential toxin producers or allergic-causative agents [34,290]. On that account, in order to answer safety concerns, we strongly underline that all algae, chosen as lipid sources for direct use or for transformation to LNP, must be subjected to chemical analyses before introducing them into mass cultures and cosmetics formulations.

5. Conclusions

The cosmetics industry is increasingly exploring new compounds derived from natural products, preferably from plant origins, due to strong consumer demands [2,291]. In addition, nanotechnologies are delving deeper into people's lives, including the field of skin cosmetics [16]. It is well-known that skin lipid compositions and structures are significant for proper skin functioning, and their deficit leads to skin diseases and disorders [9–11]. Therefore, in addition to traditional topical and oral lipid applications, there is a rising interest in enhancing the targeted lipid transport to different skin layers using nanosized systems, including LNP [12–19]. Currently, different methods for obtaining nanoparticles from lipids have been developed and standardized [14,19]. Since algae from different ecological and taxonomic groups are rich in biologically active compounds, including lipids, they are increasingly becoming the focus of biotechnology [1–8]. However, to date, mostly aquatic micro- and macroalgae have been investigated, whereas the algae from aeroterrestrial and versatile extremophilic habitats have been more neglected. At the same time, due to their peculiar ecology, AEM produce many specific compounds that are not available from other algae or accumulate higher amounts of other chemicals than other algae and plants [2]. To the best of our knowledge, there are no commercially produced skin care preparations, or LNP, yet based on lipids from AEM, despite some AEM being outlined as promising commercial lipid sources (Table 1). Therefore, we summarized the available, but quite scattered, data on the lipid contents of different species of AEM issued during the last 56 years.

According to the analysis of this knowledge, considering: (1) the successes in the clinical experiments for the treatment, alleviation or prevention of different skin disorders, as well as all other beneficial effects of versatile lipids, which occur in AEM; (2) the fact that both standard and unusual lipids have been detected, and most of them can be obtained in profitable amounts from AEM; (3) the possibilities to benefit from the direct application of lipids or from their enhanced penetration using LNP; (4) the developed methods for obtaining LNP [13]; (5) the advantages of the effective mass cultivation of AEM species even outdoor, unfavorable for algae from “standard” aquatic habitats, conditions, which can make more cost-effective and beneficial yields of both unusual and standard lipids; (6) the gradually increasing phycoprospection in the background of the enormous biodiversity of microalgae, which has been recognized but is far away from being utilized, we believe that all the provided data will serve as the groundwork to enhance and further encourage studies for broader applications of AEM-derived lipids in novel products of the future dermal cosmetics bioindustry.

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