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Review

Algal Adaptation to Environmental Stresses: Lipidomics Research

Ksenia Chadova

Laboratory of Comparative Biochemistry, A.V. Zhirmunsky National Scientific Center of Marine Biology, Far Eastern Branch, Russian Academy of Sciences, Vladivostok 690041, Russia; chadova_9595@mail.ru; Tel.: +7-9143495830

Abstract: Algal lipidomics is a new field of research that is gaining increasing popularity. The use of high-performance liquid chromatography–mass spectrometry (HPLC-MS) has made it possible to accurately determine the structure of each lipid molecule in a sample. Since algae are considered as a promising source of various compounds with pharmacological and biotechnological potential, including bioactive lipids and polyunsaturated fatty acids, lipidomics research of this group of organisms are of particular interest. The algae lipidome has high plasticity, which is due to the influence of abiotic and biotic environmental factors, and the observed changes in lipid composition are, as a rule, adaptive reactions. This review examines current research in the field of algal lipidomics, discusses the results of studying the influence of various environmental factors, such as temperature, light intensity, nutrient concentration, epi- and endophytic infections on the algae lipidome, and seasonal and geographical plasticity of algae lipidome; questions about the adaptation mechanisms of algae at the level of individual lipid molecular species are considered, and gaps in this area of research are noted.

Keywords: algae; environmental factors; HPLC-MS; lipidome

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1. Introduction

Marine algae play an important role in nature, providing food and habitat for many marine animals. Many biotic and abiotic environmental factors influence the growth and development of algae. In evolution, marine algae have developed numerous adaptation mechanisms to their changing external environments [1]. Cell membranes, based on lipids, are most susceptible to stress. The main lipids of chloroplast membranes of algae are glycoglycerolipid monogalactosyldiacylglycerol (MGDG), digalactosyldiacylglycerol (DGDG), sulfoquinovosyldiacylglycerol (SQDG), phosphoglycerolipid phosphatidylglycerol (PG); in non-chloroplast membranes (cellular, mitochondrial, etc.), the main lipids are phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI), betaine lipids, and other rare specific lipid classes (Figure 1) [2]. The regulation of lipid composition is one of the clue mechanisms of adaptation to changing environmental conditions [3]. In recent years, studies of the lipid composition of algae based on high-performance liquid chromatography–mass spectrometry have become increasingly popular, and the method is constantly improving and expanding worldwide. The use of HPLC-MS has made it possible to determine the structure of all lipid molecules in organisms, including acyl groups and their *sn*-positions. The collection of all lipid molecules in the organism is defined as a lipidome. Currently, many review studies have been published on the methodological aspects of lipidomics [4–10], so in this review we will not touch upon this topic, but will focus on lipidomic studies of marine algae exposed to various environmental factors. Studies of the lipidome dynamics under the influence of abiotic and biotic factors in the natural environment and under controlled conditions have provided new information about adaptive reorganization of lipid matrix of cell membranes. Moreover, since marine algae are a valuable source of bioactive lipids and polyunsaturated fatty acids (PUFAs), the research of lipidome plasticity is of obvious interest for development in

the field of pharmaceutics, nutraceuticals, and biotechnology [11–14]. Recently, microalgae lipids have attracted special attention as a source of last generation biodiesel [15]. Since the properties of biodiesel depend on the unsaturation degree of fatty acids (FAs), studies of the influence of environmental conditions on the FA profile are necessary to develop methods for cultivating algal biomass with the most valuable biochemical composition. In this review, we discuss the studies published to date on the effects of temperature, light intensity, nutrient concentrations, and infestation by epi- and endophytes on lipidome of marine algae, and also the research results of algal lipidome plasticity depending on seasons and geographical location. We also find the main complications and gaps in these studies. In conclusion, we discuss the prospects of the lipidomics of marine algae, and the problems and advantages of using HPLC-MS in this research field.

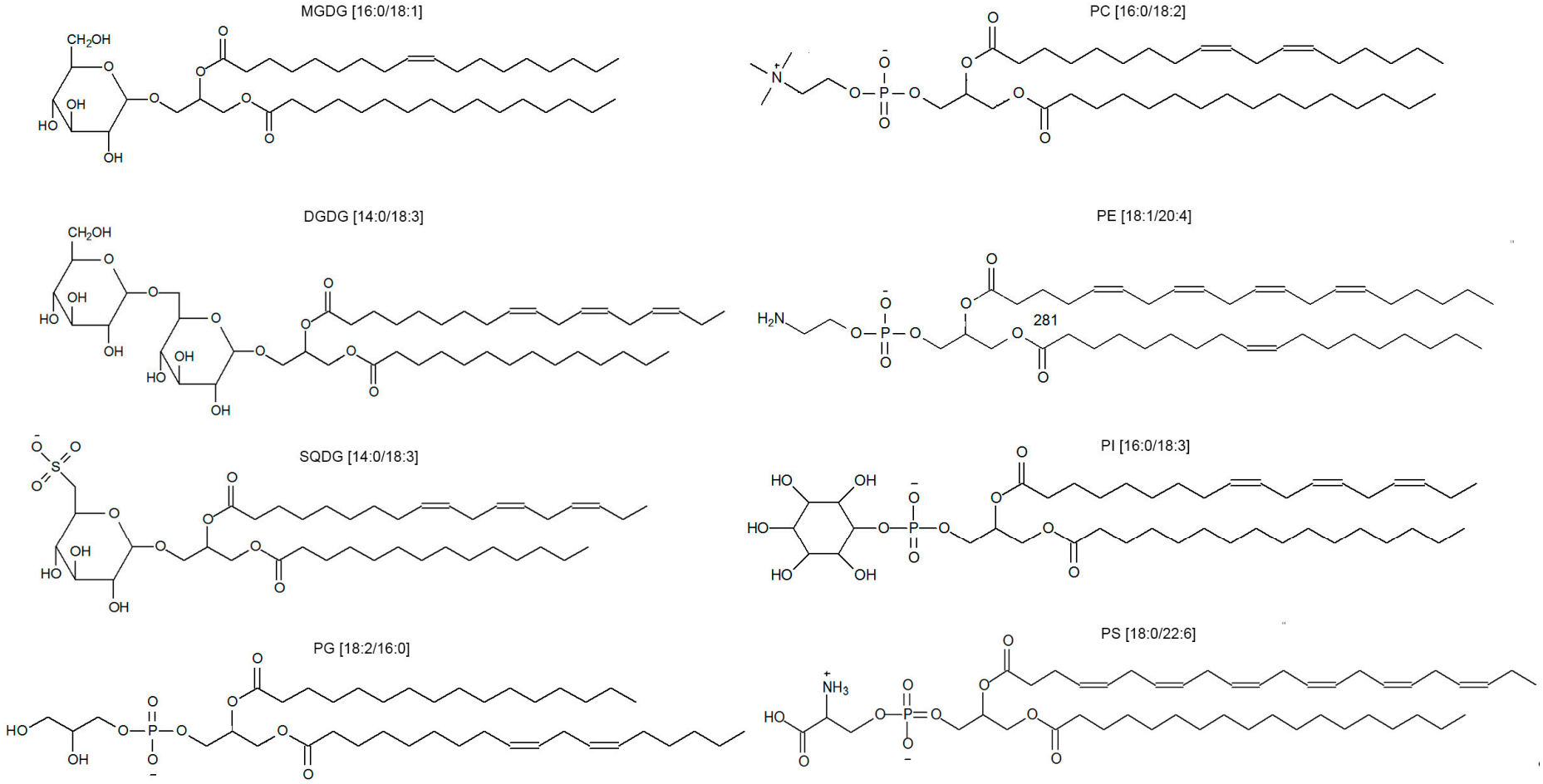

Figure 1. The structure of main algal glyco- and phospholipids. Monogalactosyldiacylglycerol (MGDG), digalactosyldiacylglycerol (DGDG), sulfoquinovosyldiacylglycerol (SQDG), phosphoglycerolipid phosphatidylglycerol (PG); phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylinositol (PI), phosphatidylserine (PS). Lipid molecular species shown as [FA in *sn*-1 position/FA in *sn*-2 position].

2. Temperature

Temperature is one of the main abiotic factors affecting the physiological state of the organism. It is known that membranes are in a liquid crystal state under normal conditions. Changes in the temperature of the environment causes conformational rearrangements of the acyl groups of membrane lipids. Under cold stress, the degree of membrane order increases due to limited mobility of lipid molecules, and a phase transition of the membrane from a liquid crystal state to a gel occurs. High temperatures lead to a decrease in membrane viscosity and the formation of an isotropic melt. The excessive crystallization and increased fluidity disrupt the activity of all organism systems and are dangerous for it. One of the clue mechanisms for maintaining the cell membranes fluidity under temperature stress is a change in the unsaturation level of membrane lipids [16]. Unsaturated FAs lower packing density of the hydrophobic part of membranes, providing required level of the structural flexibility. Lipids with saturated acyl groups are packed with higher densities and reduce the fluidity of the membrane bilayer. Modern lipidomic studies of marine algae cultured at low or high temperatures have identified the major molecular species of lipids involved in temperature adaptation. Thus, in brown algae from the order Ectocarpales, an increase in the proportion of extremely unsaturated glyco- and phospholipids containing ω3 PUFAs was revealed (18:3 in SQDG, 18:3 and 18:4 in PG, 18:4 and 20:5 in all other lipid classes) at low temperatures [17]. The main molecular species of lipids whose content increased at low temperatures were 18:4/18:4 and 20:5/18:4 MGDG, 18:4/18:4 and 20:5/18:4 DGDG, 14:0/18:3 and 18:3/16:0 SQDG, 18:3/18:3 and 18:3/18:4 PG, 20:4/20:5 and 20:5/20:5 PE, and 20:5/20:5 and SFA/20:5 PC, as well as 20:5/20:4 phosphatidylhydroxyethylglycine (PHEG), which is a brown algae-specific non-chloroplast lipid. Regarding chloroplast lipids, in addition to their structural function, MGDG, DGDG, PG, and SQDG also play a role in the regulation of photosynthetic activity [18–22]. An increased level of PUFAs in the composition of chloroplast lipids is necessary to maintain the efficiency of photosynthesis, as well as to protect photosystems from cold photoinhibition [23,24]. At higher temperatures, there was an increase in the content of SQDG and more saturated molecular species of all classes of lipids containing saturated FAs (SFAs), monounsaturated FAs (MUFAs), and ω6 PUFAs. Since SQDG was the most saturated of all photosynthetic membrane lipids, an increase in its content at high temperature can compensate for the high proportion of highly unsaturated glycolipids and PG. What function ω6 PUFAs play under heat stress is unknown; it is possible that the increase in the content of such PUFAs at high temperatures is associated with a decrease in the activity of temperature-dependent ω3 desaturases in algae [25,26]. Similar results were obtained in a study by Barkina et al. [27,28] who conducted heat acclimation experiments on the brown alga *Saccharina japonica* (J.E. Areschoug) C.E. Lane, C. Mayes, Druehl and G.W. Saunders, 2006 (Laminariales) and the green alga *Ulva lactuca* Linnaeus 1753 (Ulvales). In both algal species, an increase in the ω6/ω3 PUFA ratio was also observed, as well as an increase in the proportion of MGDG and DGDG molecular species with SFAs and MUFAs in *S. japonica* and SQDG with SFAs in *U. lactuca*. On the other hand, the content of some highly unsaturated molecular species of MGDG and DGDG with 18:4 and 20:5 PUFAs increased in both algae with increasing temperature, which contradicted the classical results of similar experiments; the authors attributed this to insufficient thermal acclimation time. Obviously, in both studies, temperature indicators were not critical for the algae life, since typical lipid markers of stress were not observed. For example, in the green microalga *Tetraselmis striata* Butcher 1959 (Chlorodendrales), with an increase in temperature, triacylglycerols (TAGs) accumulated and biomass growth stopped [29]. The accumulation of TAGs, non-membrane storage lipids, typically signals cellular stress [30]. The content of MGDG, DGDG, and SQDG molecular species with PUFAs decreased, and with SFAs it increased (especially 16:0/16:0 DGDG and 18:0/16:0 MGDG). The total amount of glycolipids also decreased, which indicated the destruction of chloroplast membranes. It is worth noting that this study also investigated the effect of salinity level on the content of lipid molecular species, but no significant results were obtained. Another green microalgae, *Chlamydomonas reinhardtii* P. A. Dangeard, nom. cons.

1888 (Chlamodomonadales), also showed an increase in the TAG and diacylglycerol (DAG) content under heat stress, and the observed decrease in the content of 18:3/16:4 MGDG was accompanied by an increase in similar molecular species of DAG and TAG, which indicated the degradation of MGDG and the formation storage lipids from its fragments [31]. The authors suggested that the donor for the third DAG acylation is betaine lipid diacylglyceryltrimethylhomoserine (DGTS) or PE, since the corresponding lysolipid species were increased. Lipidomic analysis of the red alga *Pyropia haitanensis* (T.J. Chang and B.F. Zheng) N. Kikuchi and M. Miyata 2011 (Bangiales) revealed a decrease in the glycolipid level and an increase in the content of glyco- and phospholipid lysoforms under heat stress, which also indicated the destruction of cell membrane lipids [32].

Of particular interest are studies of the influence of environmental temperature on the lipidome of dinoflagellate algae living in symbiosis with corals. Symbiotic dinoflagellates live in the tissue cells of corals and play an important role in providing them with nutrition. Coral bleaching caused by the death of symbiotic dinoflagellate due to the thermal destruction of their membrane lipids is one of the most pressing problems of the world community [33]. Using a lipidomic approach, potential biomarkers of oxidative stress have been identified, including MGDG and DGDG molecular species containing hydroxylated FAs, as well as free oxidized PUFAs, such as 18:2-OH and 22:6-OH [34]. It has been shown that thermotolerance of symbiotic dinoflagellates can be achieved by increasing the content of saturated molecular species of SQDG, increasing the DGDG/MGDG ratio and the proportion of lipid lysoforms [35,36]. These results demonstrate biochemical adaptations associated with thermal tolerance of symbiotic dinoflagellates and suggest that lipidomic analysis is a potential tool for studying the sensitivity of corals to thermal bleaching.

3. Light

Light is another important environmental factor affecting the growth, development and photosynthetic activity of plants and algae. Changes in the light intensity is reflected in the lipid composition of algae. It is known that the mechanisms of light adaptation vary, which may be due both to the peculiarities of the FA composition in different species of algae and to different photosensitivity. For example, in some algae the PUFA concentration increased in low light conditions [37], while in others it increased under high light conditions [38,39]. This species-specific regulation of FA content may be a result of various strategies for adapting to changes in light levels. It was found that light intensity mainly affects the molecular species composition of chloroplast lipids. In brown algae *Streblonema corymbiferum* Setchell and N.L. Gardner 1922 and *Streblonema* sp. (Ectocarpales), accumulation of MGDG with ω3 PUFAs (18:4/18:4, 20:5/18:3, 20:5/18:4) and the 18:3/16:1Δ3t PG molecular species was detected at low and high light, as well as the accumulation of DGDG with ω3 PUFAs (20:5/18:3, 20:5/18:4) at high light [17]. The fatty acid composition of photosynthetic membrane lipids is important for the photosynthesis. For example, at low light levels, the accumulation of 20:5ω3 PUFA in MGDG leads to increased photosynthetic activity [40], and at high light levels, the accumulation of PUFAs in MGDG may be associated with the function of this lipid in the violaxanthin cycle, which protects the algae from excess irradiation [41]. The accumulation of 16:1Δ3t PG-specific FA at low and high light intensities, as noted by Gray et al. [42], is required for the assembly of light-gathering complex II, the main function of which is to absorb the light and transfer of the excitation energy to the reaction center of photosystem II. It is worth noting that changes in light intensity did not affect the composition of the SQDG molecular species of brown algae, and in the composition of the non-chloroplast lipid PE, an accumulation of extremely unsaturated PUFA was observed at high light intensity, which was most likely associated with increased photosynthesis [17]. Lipidomic analysis of the green algae *Codium tomentosum* Stackhouse 1797 and *Bryopsis plumosa* (Hudson) C. Agardh 1823 (Briopsidales) also showed accumulation of highly unsaturated molecular species of phospholipids and betaine lipids at high light intensity [43]. For example, in *C. tomentosum*, the content of PG and PC molecular species with 18:3 and 18:4 PUFAs increased; the same was observed

in *B. plumosa*, where another class of phospholipids, PE, containing C18- and C20-PUFAs, makes an additional contribution to light adaptation. Regarding glycolipids, an increase in the proportion of the more saturated molecular species of MGDG, DGDG, and SQDG (e.g., 18:1/16:0, 18:2/16:0) in both species at high light intensity was found, as well as an increase in the content of MGDG lysoforms and DGTS. On the contrary, the content of highly unsaturated molecular species of glycolipids, including C16 acyl chains with different levels of unsaturation, decreased. This may indicate degradation of photosynthetic membranes, inhibition of photosynthesis, and, consequently, high photosensitivity of these algae. A decrease in glycolipid content and accumulation of TAG, as markers of photo-oxidative stress, were found in the green freshwater microalga *Haematococcus pluvialis* Flotow 1844 (Chlamydomonadales) cultivated under high light [44]. However, analysis of the transcriptome did not reveal changes in the expression level of genes responsible for the glycerolipid synthesis. This indicated an increase in *de novo* lipid synthesis under high irradiation, which, according to the authors, should have replaced damaged lipids in cell membranes. TAG accumulation may also be a defense mechanism to safely dissipate excess carbon, energy, and electrons under unfavorable conditions [45].

Light wavelength also influences the algae lipidome, with the correlation between light wavelength and lipid composition of algae is species-specific. For example, in the green microalga *Chlorella vulgaris* Beijerinck 1890 (Chlorellales), irradiation with red and white LED lamps resulted in faster growth rates and higher lipid content, while the content of proteins and other substances remained relatively constant [46]. However, another study showed that the highest lipid content in samples of *Chlorella* sp. and *Nannochloropsis oculate* (Droop) D.J.Hibberd 1981 (Eustigmatales) was observed when cultivated under blue light [47]. In *U. lactuca* and *Sargassum salicifolium* Naccari 1828 (Fucales), the maximum amount of lipids was observed under white light, in *Ulva intestinalis* Linnaeus 1753 (Ulvales) and *Gelidium latifolium* (Greville) Bornet 1883 (Gelidiales) under blue light, and in *Codium tomentosum* Stackhouse 1797 (Bryopsidales) under red and blue light [48]. A lipidomic study of the arctic diatom *Porosira glacialis* (Grunow) Jørgensen 1905 (Thalassiosirales) showed that blue light induces the PUFA accumulation in the structural phospho- and galactolipids, while in *Coscinodiscus radiatus* Ehrenberg 1840 (Coscinodiscales) PUFAs accumulated as a part of TAG. At the same time, *C. radiatus* demonstrated more effective adaptation to changes in light conditions, and also a higher growth rate, reaching a maximum under red light [49]. In the green microalga *H. pluvialis* [50], blue light promoted rapid cell division compared to red or white light, while lipid content was higher under red or white light compared to blue light. Lipidome analysis showed a clear correlation between the content of lipid molecular species in algae cultured under different light conditions, which seems to be related to different rates of cell division.

4. Nutrition

Changes in the concentration of nutrients in the environment, namely nitrogen and phosphorus, significantly affect the processes of growth and development of algae. Many studies have shown a tendency to decrease the growth rate of algae with nitrogen deficiency; however, lipid synthesis did not stop, but on the contrary, significantly increased, with concomitant accumulation in the form of TAGs [51–53]. This feature has attracted attention in the fields of wastewater treatment and biofuel production [54]. Wang et al. [55] conducted a lipidomic study of the freshwater green microalgae *Scenedesmus* sp. (Sphaeropleales) and the diatom *Cylindrotheca closterium* (Ehrenberg) Reimann and J.C. Lewin 1964 (Bacillariales), cultivated under conditions of nitrogen deficiency. Total glycolipids and highly unsaturated molecular species of MGDG (16:4/18:3 in *Scenedesmus* sp., 16:3/20:5 in *C. closterium*) decreased in both algae, which was probably due to chloroplast degradation. However, in *Scenedesmus* sp. total level of DGDG, and in particular the proportion of the 16:0/18:3 DGDG molecular species, increased, which may be a species-specific adaptive response to maintain the integrity of photosynthetic membranes. During the entire cultivation time, TAG molecular species containing both 16:0 and C18 FAs with varying

degrees of saturation accumulated in *Scenedesmus* sp., while TAGs containing more than three double bonds (in total) were absent under normal conditions. The response of *C. closterium* to nitrogen starvation was different: the proportion of TAGs decreased after 12 h, then increased after 96 h, and the molecular species contained predominantly 14:0, 16:0, 18:1 FAs, and C20-PUFAs. In 2022, Wang and Miao [56] investigated the effects of nitrogen starvation on the lipidome of the freshwater green microalga *Chlorella pyrenoidosa* (H. Chick) Molinari and Calvo-Pérez 2015 (Chlorellales). As in *Scenedesmus* sp., nitrogen deprivation caused the accumulation of TAG molecular species containing predominantly 16:0 and C18 FAs with varying degrees of saturation, while the proportion of glycolipids with C16- and C18-PUFAs decreased. The authors also demonstrated that in the early stages of nitrogen starvation, the exchange of acyl groups between lipids makes a large contribution to the reorganization of the lipid composition of cell membranes, and in later stages, the Kennedy pathway (the classical pathway of *de novo* lipid synthesis). Similar results were observed in a study conducted on the green microalga *Chromochloris zofingiensis* (Dönz) Fucíková and L.A. Lewis 2012 (Sphaeropleales): nitrogen deficiency increased the proportion of TAG molecular species with 16:0, 18:1, 18:2, and 18:3 FAs, and decreased the content of MGDG and DGDG molecular species with 18:2 and 18:3 FAs [57], indicating that these lipids may be donors of PUFAs for TAG synthesis, while SFAs and MUFAs for TAGs may be synthesized *de novo*. In the green microalga *Lobosphaera incisa* (Reisigl) Karsten et al. 2005 (Trebouxiales), under conditions of nitrogen deficiency, 20:4ω6 PUFA accumulated in TAG, and destruction of chloroplasts was also observed [58]. In the diatom *Phaeodactylum tricornutum* Bohlin 1898 (Bacillariophyceae ordo incertae sedis), nitrogen starvation caused the accumulation of 16:0 and 16:1ω7 FAs in TAG, which, from the data of lipidomic analysis, was mediated by remodeling of the betaine lipid DGTS, although the authors did not exclude the possible remodeling of MGDG [59]. A decrease in the PG, DGTS, and PC content was observed in *N. oceanica* under nitrogen starvation, and the expression of genes for the synthesis of these lipids did not change, indicating their participation in adaptive membrane remodeling [60]. Redirection of synthesized fatty acids from structural lipids to TAGs has also been found in *Chlorella* sp. and *Nannochloropsis* sp. [61], *Pseudochoricystis ellipsoidea* MBIC 11204 (Trebouxiales) [62], *Ettlia oleoabundans* (S. Chantanachat and Bold) J.Komárek 1989 (Chlamydomonadales) [63], and *C. reinhardtii* [64], and appears to be a general metabolic feature of microalgae. Interesting results were obtained in the study of Lowenstein et al. [65]; the authors conducted a lipidomic comparative analysis of four species of haptophyte algae: *Emiliania huxleyi* (Lohmann) W.W. Hay and H. Mohler 1967 (Isochrysidales), *Isochrysis galbana* Parke 1949 (Isochrysidales), *Pavlova gyrans* Butcher 1952 (Pavlovales), and *Prymnesium parvum* N. Carter 1937 (Prymnesiales), cultivated in an environment with low concentrations of nitrogen and phosphorus. In response to nitrogen deficiency in all algae species with exception *P. gyrans*, accumulation of various forms of TAG was observed with a concomitant decrease in the proportion of structural lipids. However, species-specific responses were noted, such as a decrease in the proportion of the betaine lipid diacylglycerylcarboxyhydroxymethylcholine (DGCC) and the glycolipids DGDG and SQDG in *P. parvum*, as well as a significant increase in the proportion of the sulphophospholipid phosphatidyl-*S*,*S*,-dimethylpropanethiol in *E. huxleyi*. Interestingly, in *P. gyrans*, the changes in the lipidome in response to low concentrations of either nitrogen or phosphorus in the medium were not observed, which may indicate the absence of a mechanism for adaptive reorganization of the lipid composition in this algae species with limited nutrients.

Phosphorus deficiency, as a rule, leads to a decrease in the content of phosphorus-containing lipids and an increase in the proportion of glycolipids and betaine lipids [66]. The change in the ratio between these lipid classes is considered to be one of the adaptation mechanisms of algae to phosphorus deprivation. For example, it is known that with the lack of sulfur or phosphorus, the anionic lipids of chloroplast membranes SQDG and PG can replace each other [67]. It has also been shown that another anionic glycolipid glucuronosyldiacylglycerol (GlcADG), identified in some algal species [17,68,69], can also

replace PG, since it was found in plant cells its content increases with a lack of phosphorus in the medium [70]. However, judging from the above studies, the composition of the molecular species of SQDG (or GlcADG) and PG are radically different from each other, so the question arises which molecular species of these lipids may be interchangeable and how this may affect the work of the photosynthetic apparatus. On the other hand, a recent study by Hunter et al. [71], conducted on the diatom algae *Thalassiosira pseudonana* Hasle and Heimdal 1970 (Thalassiosirales), showed that the content of 16:1/16:0, 20:5/16:0, 20:5/16:1, 16:1/14:0, and 32:2 PG molecular species decreases under phosphorus starvation conditions. However, the content of SQDG and its molecular species remained stable, which the authors interpreted as the algae adapting to the reduced PG content without the need to replace it. There was also a decrease in content of PC, which, judging by the FA distribution analysis, was replaced by PE and the betaine lipid DGCC. Moreover, the molecular species content with highly unsaturated FAs, such as 20:5/20:5 and 22:6/20:5, increased sharply in the first 12–24 h followed by a decrease, which the authors regarded as a mechanism for maintaining the physicochemical properties of cell membranes with adaptive replacement of lipid classes in response to insufficient phosphorus concentration in the medium. In a study by Lowenstein et al. [65], the authors also found an increase in DGCC content under phosphorus starvation in three species of haptophyte algae. Curiously, *E. huxleyi* also showed an increase in the proportion of SQDG, while the content of PG and PC remained stable; in *I. galbana* the proportion of DGDG and TAG increased, and in *P. parvum* the level of GlcADG increased. Thus, the question arises as to what causes differences in the lipidomic reactions of closely related algal species to nutrient deficiencies. In *N. oceanica* and *L. incisa*, phosphorus starvation induced a decrease in the content of phospholipids and was also accompanied by an increase in the content of SQDG and the betaine lipid DGTS [58,72]. It was previously shown that DGTS may also play an important role under phosphorus starvation, as well as at low temperatures in algae [73]. In general, it is believed that when there is a lack of phosphorus in the environment, betaine lipids can perform the functions of phospholipids, the synthesis of which is limited under these conditions. This is confirmed by the fact that in some green algae PC is completely replaced by DGTS, and in some brown algae, PC is completely replaced by DGTA [2,74]. This is true when these structural lipids have the same FA composition as betaine lipids. For example, it was shown by Murakami et al. [73] that DGTS is highly enriched in 20:5 PUFA in the green microalga *N. oceanica*, and the content of this lipid is correlated with MGDG, which also contains this FA. In the green macroalga *U. fenestrata*, DGTS was enriched in 16:0, 18:1, and 18:4 FAs, like PC and PE, and played an important role in winter acclimation along with these lipids [75]. The FA composition of betaine lipids is species-specific; in addition, in some algae, the FA composition of DGTS and DGTA differs from the FA composition of any of the structural lipids [17,76], which complicates the interpretation of the results and suggests the presence of a different role for betaine lipids, which remains unclear.

5. Infection

In the natural environment, populations of macrophytic algae are often infected by epi- and endophytic algae. The frequency of this phenomenon can vary depending on the life stage of the host algae [77], species specificity [78], season [79,80], environmental conditions, and region [79,81,82]. It is known that some endophyte species can infect up to 100% of the host algal population [83]. The relationship between epi- and endophytic algae and host macrophytes is not always neutral. As a result of infection, the growth and reproduction of macrophytes was suppressed, which reduces their commercial value [84,85]. Epi- and endophytic infections are often accompanied by the formation of spots on the surface of the host leaf blade, the formation of galls, morphological deformations of thalli, in particular compaction and twisting of the blade and stalk, as well as damage to the tissue cells of the host macrophyte [86–90]. In such cases, epi- and endophytism are quite legitimately considered as a type of infection. However, not all infected macrophyte hosts exhibit

morphological changes. The underlying molecular mechanisms of this interaction and the advantages or disadvantages for either organism are still unclear.

To date, defensive reactions in marine algae to pathogen infection have been well studied [91,92]. The accumulation of reactive oxygen species is considered to be the primary defense response; other mechanisms include the accumulation of oxylipins and the production of halogenated secondary metabolites [93]. In the red alga *Chondrus crispus* Stackhouse 1797 (Gigartinales) infected with the green endophytic alga *Acrochaete operculata* J.A. Correa and R. Nielsen 1988 (Ulvales), an increase in the activity of a number of oxidative enzymes, in particular lipoxygenase, and an increase in the concentration of some oxylipins, such as hydroxy-, hydroperoxy-, oxo- and epoxy-C18-, and C20-PUFAs were found [94]. The study of the epiphyte-infected red alga *Gracilaria chilensis* C.J. Bird, McLachlan and E.C. Oliveira 1986 (Gracilariales) also revealed the accumulation of free FAs, and the formation of hydroxy- and dihydroxy-C20 PUFAs were detected [95]. Recently, it has been shown that co-cultivation of the brown endophytic alga *Laminarionema elsbetiae* H. Kawai and Tokuyama 1995 (Ectocarpales) and brown algae-host is accompanied by the activation of several protective genes, including those encoding a protein homolog of oxidase that mediates the oxidative burst, and proteins with lipase and lipoxygenase activities, as well as suppression of gene expression, related to photosynthesis and FA synthesis [96]. Chadova and Velansky [69] studied the effect of infection with the brown filamentous endophytic alga *Laminariocolax aecidioides* A.F. Peters 1998 (Ectocarpales) on the lipidome of the brown alga *Undaria pinnatifida* (Harvey) Suringar 1873 (Laminariales) *in vivo*. The study revealed an increase in the content of saturated FAs, such as 16:0 and 18:0, in TAGs, both in infected and adjacent intact areas of the leaf blade of the host macrophyte, which, according to the authors, was a sign of the presence of secondary viral or bacterial infection. In endophyte-infected tissues, an increase in the relative abundance of phospholipid molecular species containing PUFAs at both *sn*-positions were found (e.g., 18:3/18:4 and 18:4/18:4 PG, 20:4/20:5 and 20:5/20:5 PE, 20:5/18:3 and 20:5/20:5 PC, 20:5/20:4 and 20:5/20:5 PHEG), which the authors associated with the mechanical effect of the endophyte on *U. pinnatifida* cells.

6. Season and Geographic Location

In the environment, the composition and content of lipids in algae varies significantly, which is associated with both the stage of ontogenesis and the influence of a combination of various environmental factors, which complicates the interpretation of research results. The study of the lipidome seasonal dynamics of the annual brown alga *U. pinnatifida* revealed an increased content of 18:4/18:4 and 20:5/18:4 MGDG molecular species, 20:5/18:4, 18:4/18:4, and 16:0/18:4 DGDG, and PG with 18:3 FA in winter and spring (since December to April), when the water temperature was about 0–1 °C [69]. The proportion of less unsaturated species of these lipids was increased in autumn and summer (November, June), when water temperatures were 5 and 18 °C, respectively. The minimum content of the 18:3/16:1Δ3t PG molecular species was in June, which the authors associated with optimal light conditions for photosynthesis during this period. Accumulation of highly unsaturated non-chloroplast lipids, namely PE (16:0/20:5, 18:1/20:5, 20:5/18:3, 20:5/20:5, 20:4/18:3), PC (20:4/18:3, 16:0/20:5, and 20:5/20:5), and PHEG (20:5/20:4 and 20:5/20:5), was also observed during the winter-spring period. The authors concluded that temperature changes are decisive in the restructuring of the composition of hydrophobic parts of non-chloroplast lipids during seasonal adaptation, whereas changes in the composition of glycolipids and PG were influenced by both water temperature and light conditions. In a study conducted on the perennial brown alga *Fucus vesiculosus* Linnaeus 1753 (Fucales), changes were observed mainly in the chloroplast lipid composition [97]. It was found that in winter (February, water temperature approximately 13 °C) there was an increased content of the 36:8 MGDG molecular species, 38:6 DGDG, 34:3 and 34:4 PG, 16:1 lyso-PG, and 32:2 and 32:3 SQDG, while in spring (May, water temperature approximately 17 °C) 32:1, 38:5, and 40:8 MGDG, 38:6 DGDG, 32:1, 34:1, 36:2, and 36:4 PG, and 16:0 lyso-SQDG increased.

Although molecular species were defined as the sum of FAs in this study, which complicates the interpretation of the data, analysis of the total FA composition confirmed that the lipid composition was dominated by ω3 PUFAs, such as 18:3, 18:4, and 20:5 in winter, and 16:0, 18:0, and 18:1 and ω-6 PUFAs, such as 18:2 and 20:4, in spring, which is consistent with previous study. Lipidomic analysis of the green alga *Ulva rigida* C. Agardh 1823 (Ulvales), collected in different seasons, revealed a decrease in the content of the most unsaturated molecular species of lipids (34:8 MGDG, 38:5 SQDG, 36:3 PG, 38:6 PC, and 40:6 DGTS) from winter (March, water temperature approximately 13 °C) to summer (August, water temperature approximately 22 °C) [98]. The content of 32:1 DGDG molecular species, as well as 30:1 and 32:1 DGTS, on the contrary, was maximum in summer and spring (May, water temperature about 18 °C). Monteiro et al. [99] performed a comparative lipidomic analysis of the brown alga *Saccharina latissima* (Linnaeus) C.E. Lane, C. Mayes, Druehl and G.W. Saunders 2006 (Laminariales), collected from three different locations (France, Norway, and the United Kingdom) and showing both quantitative and qualitative differences. For example, samples from France were characterized by a high content of various lysoforms of MGDG, SQDG, and DGDG, which may indicate the presence of stressful conditions in this location. Unlike samples from France and the United Kingdom, algae collected from Norway, where water temperatures are lower, had low levels of structural lipid molecular species with SFAs, such as 36:1 and 38:0 SQDG and 36:1 DGTS, as well as lipid lysoforms. These data confirm that a detailed study of the algae lipidome in the process of seasonal adaptation provides a deeper understanding of adaptive changes determined by a combination of various environmental factors affecting the organism, which vary geographically, creating different conditions for life. It is worth considering that in addition to environmental factors, the lipid composition of algae is also influenced by the development stage of the samples.

7. Future Direction

Studies using a lipidomic approach are necessary to expand our knowledge of the structure, diversity, and biosynthesis of algal lipids, as well as the chemotaxonomy and physiology of this group of organisms. The information obtained from research of lipidome dynamics under the influence of various environmental factors can be used by a wide range of specialists to select optimal conditions for cultivating algae with nutritional, pharmacological, and biotechnological value, as well as to develop new options for industrial applications and methods for monitoring the aquaculture state. It is worth noting that there are currently few comprehensive studies of the algal lipidome, and only a few studies have established the structure of lipids down to the determination of the *sn*-positions of fatty acids in each molecule. The complexity of such studies is due to the great diversity of lipid molecules, as well as the presence of a large number of their structural isomers, for the identification of which requires modification of chromatographic separation techniques. In general, the use of HPLC-MS has a wide range of advantages, such as a large range of molecular weights of substances that can be worked with, high speed and accuracy of analysis, high sensitivity allowing the determination of microquantities of substances, and flexibility in changing the composition of mixtures used as the mobile phase, ensuring the separation of compounds of different nature and improving their fragmentation; in addition, the selectivity of this method is usually higher than that of other chromatography options. In the field of marine organism lipidomics, this method has only begun to be used relatively recently, but it has already demonstrated advantages for understanding complex metabolic processes.

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