A review of high value-added molecules production by microalgae in light of the classification

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This work reviews applications of high added value molecules produced from microalgae. Older forms of valorization - health food and quality feed, polyunsaturated fatty acids, pigments, carbohydrates - are currently penetrating their markets. They are driven by desirable properties : texturer and dye for food industry, antioxidant for cosmetics and the appetite of the general public for biosourced compounds. Most recent developments, such as peptides, vitamins, polyphenols, phytosterols and phytohormones, are struggling to meet their market and reach economical competitiveness. Still they are pushed forward by the very powerful driver that is pharmaceutical industry. In addition this work also proposes to link microalgae phyla and related potential applications. This is done through highlighting of which bioactive compounds can be found in which phyla. While some seem to be restricted to aquaculture, Cyanobacteria, Chlorophyta and Rhodophyta show great promises.

Microalgae | Applications | Classification | Bioactive compounds
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1. Introduction

Algae are a group of organisms that live almost every habitat. While, most part of them are preferentially found in aquatic environments, they can also colonise other spaces including deserts, volcanic waters, highly acidic and frozen soils[1]. They form the basic component of food chains in the world's ecosystems. In addition, they are the main producers of oxygen and contribute to about 40% of global photosynthesis[2–4].

Algae bring together macroalgae, commonly referred to as seaweed which are macroscopic and multicellular organisms, and microalgae, which are microscopic organisms commonly found in marine and freshwater. The later are the focus of this review. Microalgae have been used by man since the dawn of time. It started more than thousand years ago serving as food for indigenous populations. Still, the production of microalgal biomass really began to develop in the middle of the last century, starting first with Germany when post-war societies were apprehensive at a strong demographic growth and its implication to food security[5,6]. However, with the need for sustainable development, microalgae have really sparkled academics and engineers attention over the last half-century for numerous reasons. First of all, as photosynthetic organisms, they can derive their energy from light and carbon from inorganic sources. Compared to higher plants, they show higher annual photon-to-biomass conversion efficiencies of about 3 % (compared to < 1 %) and no intrinsic sensibility to seasonality[7,8]. This feature combined with the great diversity of strains allow valuable molecules such as proteins, lipids, carbohydrates, pigments to be produced with high yields. Second, they can be grown on wastewater or non-agricultural land without pesticides hence not compromising the production of food or others products from crops. Furthermore, they are able to recycle atmospheric carbon dioxide and thus minimising associated environmental impacts. As result, and driven by current energy, environmental and food challenges[4,6,9], microalgal biotechnology steadily rose into power. Nowadays it can be split into four major research fields that are wastewater treatment, CO_2 sequestration, biofuel production and high-added value molecules production.

By having a look at the scientific literature, it is safe to say that the first three fields have already been well explored and reviewed over the former decades. Figure 1 presents the publication trends of those scientific communities. As one can see, very recently, the focus of microalgae applications has changed and is now mainly on the production of high value-added molecules rather than environmental applications. This recent shift in interest is probably related to the high cost of microalgae production even on a large scale. Among the main limitations, the low biomass concentration (about 3 g/L for autotrophic cultures) of microalgae cultures has a significant impact on the downstream proccesing. In particular, additional costs are required at the harvesting stage to successfully concentrate the cultures. These difficulties have led scientists to find new, higher added-value, strategies for valorisation of biomass. From this graph, we can see that the sequestration of CO_2 has a rather linear trend with a low slope suggesting a limited interest (linear fit since 2007, R^2=0.977). As for biofuels, the peak of research intensity seems to be passed (bell curve). Indeed, extensive research has already been led, and the conclusion is that commercial viability will be made possible only if high added value molecules are extracted from biomass beforehand[10]. Finally wastewater treatment and high value-added molecules[1] clearly depict an exponential trend (expo-

[1]It should be noted that for this last stream, broad keywords have been applied. However, unlike other applications, high value-added molecules from microalgae are very diverse and can have different applications. As a result, the volume of publications may have been underestimated with the use of very broad-spectrum keywords. With keywords more focused on the type of molecules such as "carbohydrate", "protein" or else "phytosterol", the trend remains the same but the volume of publication is larger than that presented in the graph.

nential fit since 2007, R^2=0.976 and R^2=0.991 respectively). As a consequence, this review focuses on high-added value molecules production from microalgae and associated applications.

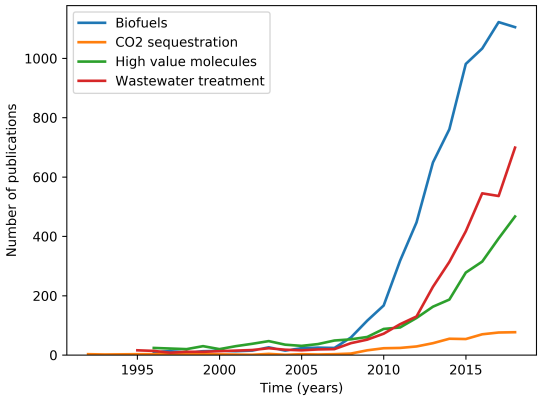

Fig. 1. Number of publications by category of microalgae applications over time. Results obtained on November 8 2019, on the Web of Science search engine over a period until 2018 with the following keywords: TS=(microalgae AND (molecules OR bioactive OR compound)) for high-value molecules, TS=(microalgae AND ((CO2 OR Carbon) AND (sequestration OR mitigation))) for CO_2 sequestration, TS=(microalgae AND (wastewater OR "waste water" OR remediation OR polluted)) for wastewater treatment and TS=(microalgae AND (fuel OR biofuel OR oil OR biooil)) for biofuels.

High added value molecules are a very board category with very different applications. They range from lipids, proteins and carbohydrates with food and nutraceutics applications to pigments and sterols with cosmetics and pharmaceutical aims. The broad range of applications comes from the fact that microalgae are one of the oldest life forms on Earth. They have evolved and adapted over billions of years, yielding a tremendous diversity and complexity. As classification can be of help when assessing the biotechnological potential of a strain, a reminder of a state of the art classification is the first section of this article. Then, for the sake of completeness and the reader interest, environmental applications are briefly mentioned and relevant contributions are pointed out. This is followed by the core of this paper, a review of high-added value molecules production and associated applications. Finally, a link is drawn between classification and applications with the goal to ease strain selection for a specific application.

2. Classification

Microalgae term ties together microscopic algae and oxygenic photosynthetic bacteria. Therefore the first disctinction is between prokaryotes and eukaryotes [11]. The key distinction between both types of cells is the presence of membrane-bound structures in eukaryotic cells which are lacking in prokaryotes. The latter were allegedly acquired by eukaryotes from evolution through endosymbiosis [12,13]. As a result, eukaryotes are larger, more complex, and can be either unicellular or multicellular while prokaryotes are simple and small single-celled organisms.

Traditionally, microalgae have been classified according to their photosynthetic pigments. Yet the current systems of classification take account of others criteria, among them cytological and morphological characters, cell wall constituents and chemical nature of storage products. Based on these features, some methods are commonly employed to identify and classify algal species including morphological observations under a microscope, molecular-based classification using specific short gene sequences [14] or more recently semi-automated or fully automated classification using a flow cytometer combined with computational methods [15–17]. Regardless of the approaches used to identify algal species, the classification system has changed many times over the years. Currently, there is no consensus among the taxonomists around the world to use one classification over another [18,19]. However, one of the lastest classification models includes two main domains, Prokaryota and Eukaryota gathering seven kingdom: Archaebacteria, Eubacteria, Protozoa, Chromista, Fungi, Plantae and Animalia [20].

Keeping in mind that the taxonomic organization may change as information accumulates, the current microalgal classification considers eight major phyla belonging to four of the seven kingdoms depicted in Figure 2. While a large majority of microalgae are nested in the Eukaroyta domain and distributed in seven main phyla, there is only one representative phylum of microalgae in the Prokaryota domain grouped under the name Cyanobacteria. Despite the low representation in this domain, Cyanobacteria are among the most abundant phylum alongside Chlorophyta and Heterokontophyta phyla [21–23].

3. Applications

3 1. Summary of environmental applications

Owing to the increasing deterioration of our environment and the need for energy, research have been focused on recycling and resource recovery. Within this context, microalgae have been studied as an appropriate response to the current environmental issues due to potential benefits they offer [22,24–26], namely:

- Their ability to integrate carbon from combustion gases as a source of carbon [6,24,27–29],
- Their potential of growing on wastewater and incorporating polluants into their metabolism as nutrients [28,30–32],
- The variability of their biochemical composition in micronutrients (mainly nitrogen, potassium and phosphorus) for biofertilizers [4,12,33–35] and in macronutrients (carbohydrates and proteins) for bioplastics production [36–40].

Microalgae have also sparked a major wave of research on the possibility of turning them into biofuels summarized in the Figure 3. Nevertheless, despite the high potential of microalgae, the development of an efficient microalgae-based biofuel production chain remains a major challenge

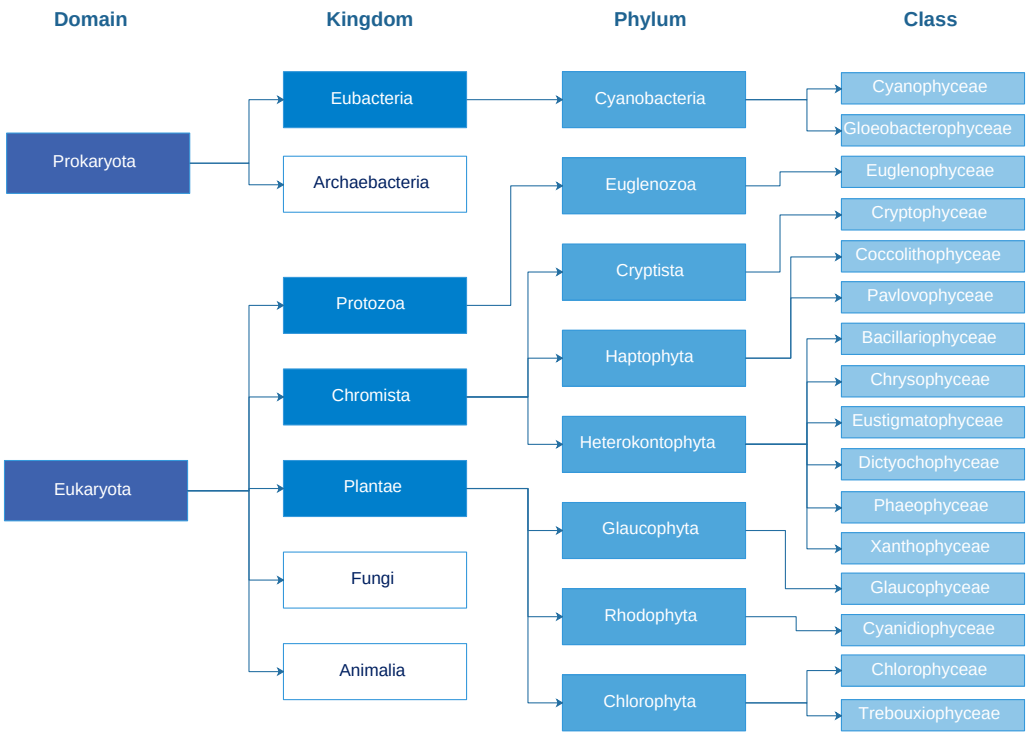

Fig. 2. Major microalgae phyla distribution as per seven-kingdom classification scheme inspired from [20] with classes used for various biotechnological applications

for commercial deployment, both technically and economically [6,41–44].

3 2. Health food and quality feed

Thanks to their composition as well as their simplicity of cultivation, microalgae garnered interest over time as a solution to feed under-nourished populations in the context of malnutrition in developing countries [6]. Furthermore, in recent years, consumer concerns regarding health and safety issues related to the consumption of processed foods have increased [45]. In this respect, microalgae would appear to be potential actors in the trend of using natural additives and are expected to play an important role in the food industry, in particular as nutraceuticals [4–6,23,46]. As a result, many compagnies have started to market functional foods containing microalgal biomass. This latter can either be directly marketed under different forms such as tablets, capsules and liquids or integrated into products and act as a natural nutritional supplement or as a natural rheology improver product [4,12].

Currently, the market is dominated by four genera of microalgae [4,5,45,47] which are *Arthrospira* with more than 12,000 tons of biomass produced every year, followed by *Chlorella* with about 5,000 tons per year. *Dunaliella salina*, mainly marketed for its β-carotene, has an annual production of 3,000 tons and finally *Aphanizomenon* is produced at a level of 1,500 tons per year. Health food production systems also cultivate to a lesser extent the green alga *Scenedesmus* [6,12]. It should be underlined that these species benefit from the GRAS status, *i.e.* Generally Regarded As Safe given by FDA for food purposes and are thus considered as safe and valuable for human consumption [4,5,23,48].

In addition to its use in human food, microalgae have shown a growing interest in animal nutrition as feed additive. Microalgal biomass can be incorporated into the diet of a wide variety of animals ranging from fish to pets and livestock [4,5,12,34,49]. They are mainly used to improve the physiology of animals but also the organoleptic properties of the final consumer product [4]. Currently, about 30% of current global microalgae production is sold to the feed industries [4–6,50].

The perspectives of the use of microalgae as food and feed lies in the diversity of biomass composition. This can be achieved either by strain selection (Table 1) or growth condition manipulation (Table 2). Indeed, they are able to modulate their biochemical composition in response to a change in their environment. As a consequence, researchers have developed strategies based on metabolic imbalances which divert the electron energy towards the selected target [51]. These are usually referred to as *stressing procedures* and feature nutrient depletion, high light irradiance, extreme pH, temperature, high salinity or metal concentration.

Beyond its macronutrient composition, microalgae are able to express and accumulate secondary metabolites under stressful conditions. This paves the way to targetted bioactive compounds production, and eventually penetrate cosmetics and pharmaceutical markets.

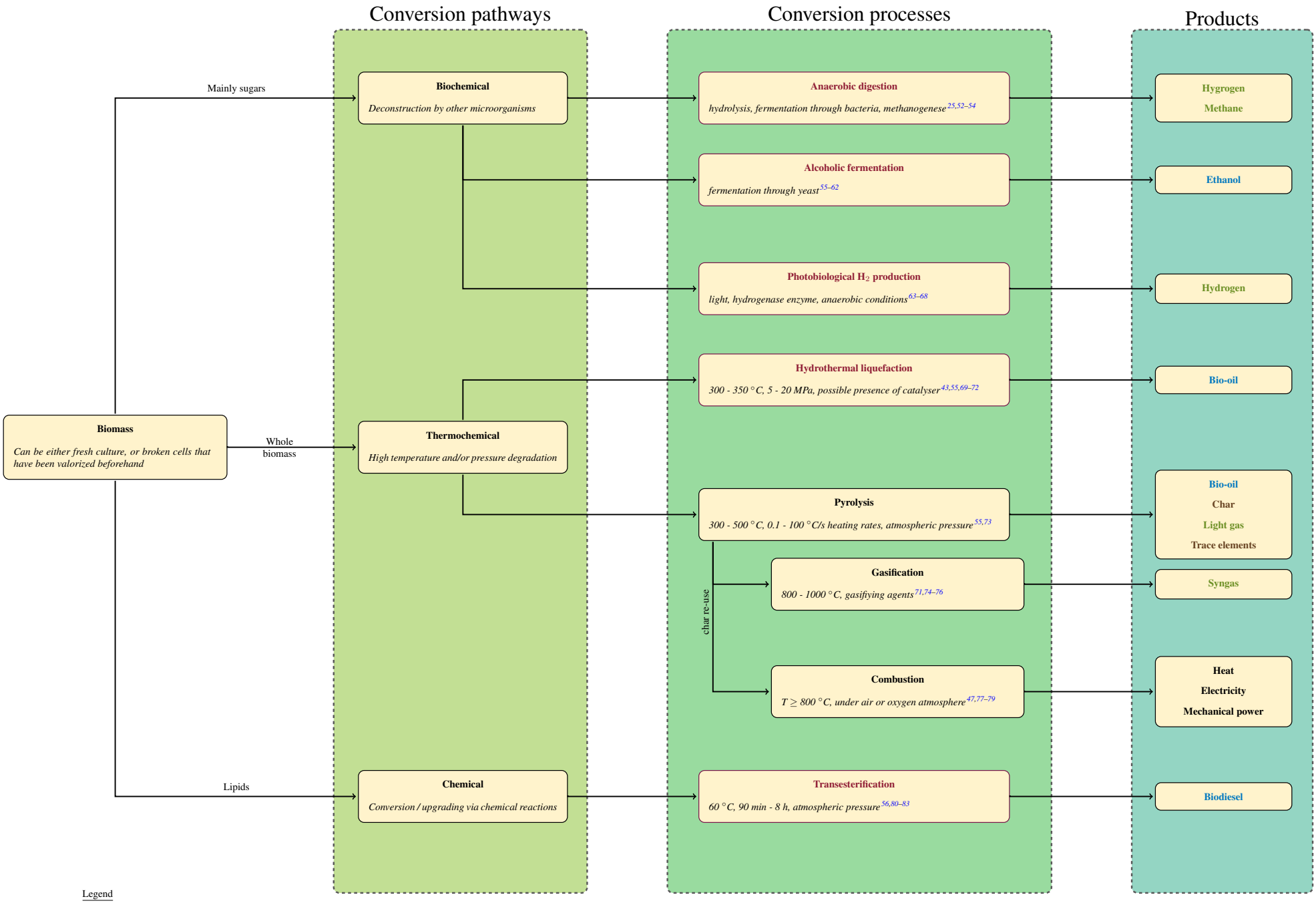

Fig. 3. Scheme of the pathways to produce biofuels from microalgal biomass

3 3. High-value molecules

High-value molecules term can be broken into several subcategories as it covers a very wide range of bioactive compounds. In this review, the are divided into: polyunsaturated fatty acids (PUFAs), pigments, carbohydrates, peptides, vitamins, polyphenols, phytosterols and hormones. For the sake of readability, the applications of those family of molecules extracted from microalgae are synthetically presented in Table 3 with respect to four fields of applications: food, nutraceutics, pharmaceutics and cosmetics. More specific details about their productions and key activities are emphasized in the text hereinafter.

3.3.1. Polyunsaturated fatty acids (PUFAs). There are two main groups of lipids in microalgae: the lipids produced by photosynthesis and stored in the cell known as storage lipids (mainly triglycerides) and lipids being an integral part of the cell structure known as structural lipids (phospholipids and sterols)[4].

Fatty acids belong to the storage lipids. They represent one of the primary metabolites. Within them, polyunsaturated fatty acids (PUFAs) are of note. They are biomolecules made of a long unsaturated hydrocarbon chain containing more than one double bonds with attractive properties for both food and pharmaceutical industries. From a medical point of view, PUFAs have been proven to have health benefits. Several studies highlighted the essential nature for the development of the human nervous system and visual abilities supported by the United States Environmental Protection Agency, the Food and Drug Administration as well as the Food and Agriculture Organisation[121,148,149]. In addition, these fatty acids would also help to reduce the occurrence of various chronic diseases such as diabetes, arthritis, cardiovascular disease, and obesity[4]. Futhermore, a medical review based on both *in vitro* and *in vivo* studies in animals and humans on the ω-3 fatty acids supplementation underlined their anti-inflammatory, anti-proliferative and anticachectic effects[150].

More specifically, ω-3 and ω-6 are essential for human being as they are not able to produce themselves these lipids which are necessary for their basal metabolism[9,119,122,124]. Therefore, they have to obtain them from an exogenous source. It has emerged that one of the promising sources of omega is microalgae, the primary producers of ω-3 eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Accordingly, numerous studies focused on the production of PUFAs from microalgae.

In a very general way, microalgal fatty acids profile is relatively preserved within a phylum[151] while their content varies within species according to environmental factors. Though, the ω-3 (EPA and DHA) content in microalgae is naturally relatively low. As an example, 12 strains of microalgae belonging to two distinct phyla were screened in a study[151]. Of all microalgae, only *Chlorella* had quantifiable levels of DHA and EPA (3.24 and 8.9% of total FAME respectively). Thus, EPA and DHA productivity improvement strategies within the cells have been implemented. The first and most well-known approach is to modify environmental parameters to affect internal metabolism. As a result, several studies has been focused on the impact of different environmental factor on the lipids productivity[152,153]. One of the most employed strategy consists in partially or completely depriving microalgae of nitrogen to achieve higher lipid productivity. One of the most striking example is the growth of *Chlamydomonas reinhardtii CC-400 cw15 mt+*. Under normal conditions, the strain is able to express 9% dry matter of lipids while under nitrogen starvation it yields 41% dry matter[89]. Another way to stimulate lipid production is to act directly on the metabolism of the microalgae. It has been shown that under heterotrophic conditions, microalgae obtain higher lipid yields[152,154]. As an example, after 3 days of cultivation, a Thraustochytrid strain 12B is able to express 57.8% lipids in biomass with 43.1% of DHA in it[155]. Besides, increasing experimental evidence seems to highlight that an appropriate level of intracellular Reactive Oxygen Species (ROS) can improve lipid accumulation although the metabolic mechanism is not well known yet[154]. This is made possible by, among other things, the controlled addition of oxygen during cultivation.

However, these conditions, although favourable for lipid accumulation, are not so for microalgae growth leading to reduced growth rates. One way to overcome this problem is to use a two-phase approach. This strategy consists in first the cultivation of microalgae under sufficient nutrients conditions to stimulate higher growth rate and by extension higher biomass. These cells are then exposed to more severe conditions such as nutrient starvation for accumulation of the lipids. As an example, a study following this methodology was conducted on *Nannochloropsis oculata* cells[101]. Under both control conditions, *i.e.* repleted nitrogen, and nitrogen limitation conditions, the final cell yields were similar. However, the cell volume increased under nitrogen limitation from 14.1 to 18.7 μm^3 suggesting a lipid accumulation inside the cells. This was confirmed by analyses. The lipid content increased from 26 to 34% of dry matter. Another way to improve lipid yields without substantial loss of biomass is to combine this approach with strain breeding or genetic engineering approach[152,153].

Currently, the main source of EPA and DHA in food are fatty fish such as salmon. Yet PUFAs derived from this source have low oxidative stability, can contain toxins as well as releasing unpleasant smell and taste, thus limiting their application[49,122,127]. Consequently, microalgae are increasingly emerging as an alternative to the use of fish oil[156]. However, this alternative is limited to the production of DHA[122]. Indeed, until recently, the production of EPA rich algal oil has been restricted to laboratory scale[6]. As a result, DHA is currently the only product on the market[49]. The most common microalgae used for its production are from the genera *Crypthecodinium*, *Schizochytrium* and *Ulkenia* found in the kingdom Chromista[4,157]. These microalgae are capable of accumulating up to more than 40% DHA in fatty acids composition[158]. Other genera such as *Thraustochytrium* and *Labyrinthula* have also been identified as producers of

Table 1. Biochemical composition of different microalgae with controlled growth conditions. Results expressed as % of dry matter

Strains	Original study parameters	Biochemical composition (% dry matter)			References
		Proteins	Carbohydrates	Lipids	
Arthrospira maxima	- Lighting conditions: natural sunlight	56-62	18-23	13	[84]
Arthrospira maxima	- Lighting conditions: 180 µmolphotons/m²/s - Temperature: from 20 to 40 °C	63-70	10-20	6-7	[85]
Arthrospira platensis	- Lighting conditions: 180 µmolphotons/m²/s - Temperature: from 20 to 40 °C	59-72	11-20	6-7	[85]
Arthrospira platensis K-2	- Lighting conditions: 30 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles) - Nitrogen sources: ammonium nitrate or urea	38-53	13-25	6-15	[86]
Arthrospira platensis LEB-52	- Lighting conditions: 31.35 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles) - Temperature: 30 and 35°C - Nitrogen source: sodium nitrate	57-70	-	7-10	[87]
Chlamydomonas reinhardtii	- Lighting conditions: continuous illumination	65	23	-	[88]
Chlamydomonas reinhardtii CC-400 cw15 mt+	- Lighting conditions: continuous illumination of 80 µmolphotons/m²/s - Nitrogen source: ammonium chloride	45	25	9	[89]
Chlorella vulgaris	- Lighting conditions: 150 µmolphotons/m²/s - Photoperiod: 16:8 hours (L/D cycles)	12-45	8-35	3-6	[90]
Chlorella vulgaris	- Lighting conditions: continuous illumination of 60 µmolphotons/m²/s - Nitrogen source: potassium nitrate	7	63	29	[91]
Chlorella vulgaris	- Lighting conditions: daylight illumination	51	18	7	[92]
Chlorella vulgaris ESP-6	- Lighting conditions: 60 µmolphotons/m²/s - Temperature: 28 °C	48	18	13	[93]
Chlorella vulgaris FSP-E	- Lighting conditions: 60 µmolphotons/m²/s - Temperature: 28 °C	60	12	12	[93]
Dunaliella salina	Nothing specific	26	40	18	[94]
Dunaliella tertiolecta	- Lighting conditions: 70-80 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles)	20	12	15	[95]
Isochrysis galbana	- Photoperiod: 12:12 hours (L/D cycles)	16-22	3-6	4-5	[96]
Isochrysis galbana	The strain was received freeze-dried and was analysed without further processing	42	10	25	[97]
Isochrysis galbana	- Lighting conditions: 1000 lux - Temperature 20 °C	29-42	4-10	20-24	[98]
Isochrysis galbana	- Lighting conditions: 70-80 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles)	29	13	23	[95]
Isochrysis galbana TK1	- Temperatures: 15°C and 30°C - Lighting conditions: 200 µmolphotons/m²/s	27-32	25-33	18-25	[99]
Isochrysis sp.	- Lighting conditions: 80 µmolphotons/m²/s - Salinity 25 ‰	30	16	23	[100]
Nannochloropsis oculata	- Lighting conditions: 350 µmol photons/m²/s - Photoperiod: 12:12 hours (L/D cycles) - Salinity: 33 ‰	26	29	26	[101]
Nannochloropsis oculata	- Lighting conditions: 80 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles) - Temperature: 26 °C - [FeCl3]: 0,15 to 63 mg/L	-	-	21-33	[102]
Nannochloropsis oculata	- Lighting conditions: 70-80 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles) - Temperature: 20 °C	35	7,8	18	[95]
Nannochloropsis sp.	- Lighting conditions: different light spectra - Photon flux density <100 µmolphotons/m²/s	20-25	18-30	44-60	[103]
Pavlova salina	- Lighting conditions: 70-80 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles)	26	7	12	[95]
Phaeodactylum tricornutum	- PBR and circular pond comparison - Lighting conditions: daylight	30-59	9-20	24-36	[104]
Phaeodactylum tricornutum	- Lighting conditions: 18-72 µmolphotons/m²/s	38-51	18-28	9-30	[105]
Phaeodactylum tricornutum	- Lighting conditions: 70-80 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles)	30	8	14	[95]
Phaeodactylum tricornutum	- [Nitrogen]: 0.88 mM	32	19	29	[105]
Porphyridium cruentum	- Lighting conditions: 50 and 200 µmolphotons/m²/s - Salinity: 33 ‰ - Nitrogen sources: ammonium and nitrate	5-10	25-37	8-18	[106]
Porphyridium cruentum 161	- Lighting conditions: 60 µmolphotons/m²/s	-	30	10	[107]
Porphyridium cruentum 161	- Mode: continuous mode (dilution rate 10h) - Lighting conditions: daylight	34	32	7	[108]
Scenedesmus obliquus CNW-N	- Lighting conditions: 420 µmolphotons/m²/s - Temperature: 28 °C	15-41	38-52	12-22	[109]
Tetraselmis sp.	- Lighting conditions: 80 µmolphotons/m²/s - Salinity: 25 ‰	13-14	8-9	26-30	[100]
Tetraselmis suecica	- Lighting conditions: 1000 lux	33-34	8-10	6-7	[98]
Tetraselmis suecica	- Lighting conditions: 70-80 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles)	31	12	10	[95]

Table 2. General composition of different microalgae under stressful conditions. Orange: light stress (above 200 µmolphotons/m²/s) ; Red: nitrogen stress (exhausted nitrate source) ; Purple: combined light and nitrogen stress ; and Blue-green: chemical stress.

Strains	Original study parameters	Biochemical composition (% dry matter)			References
		Proteins	Carbohydrates	Lipids	
Chlamydomonas reinhardtii CC-400 cw15 mt+	- Lighting conditions: continuous illumination of 80 µmolphotons/m²/s - Nitrogen starvation	36	17	41	89
Chlamydomonas reinhardtii UTEX 90	- Mode: fed-batch culture for 96 h - Lighting conditions: continuous illumination of 450 µmolphotons/m²/s	9	60	-	110
Chlorella vulgaris	- Lighting conditions: 150 µmolphotons/m²/s - Photoperiod: 16:8 hours (L/D cycle) - Nitrogen limitation - Cadmium stress	10-25	10-59	5-16	58
Chlorella vulgaris ESP-6	- Lighting conditions: 60 µmolphotons/m²/s - Temperature: 28 °C - Nitrogen starvation	23	49	15	109
Chlorella vulgaris FSP-E	- Lighting conditions: 60 µmolphotons/m²/s - Temperature: 28 °C - Nitrogen starvation	21	54	19	109
Isochrysis galbana	- Lighting conditions: continuous illumination of 150 µmolphotons/m²/s - Temperature: 27 °C - Nitrogen starvation	12-30	-	24-47	111
Nannochloropsis oculata	- Lighting conditions: 350 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles) - Salinity: 33 ‰ - Nitrogen starvation	18	29	34	101
Nannochloropsis sp.	- Mode: semicontinuous regime - Lighting conditions: from 0 to 480 µmolphotons/m²/s - Photoperiod: 12:12 hours (L/D cycles)	10-43	20-29	33-61	112
Pavlova sp.	- Lighting conditions: 180-220 µmolphotons/m²/s - Salinity: 34-35 ‰	34-54	30-44	16-29	113
Phaeodactylum tricornutum	- Nitrogen limited and nitrogen free media	16-25	15-17	32-41	105
Porphyridium cruentum 161	- Lighting conditions: 60 µmolphotons/m²/s - Nitrogen limited	-	43	10	107
Porphyridium cruentum VISCHER 1935/107	- Lighting conditions: 8000 lux	27-38	40-57	9-12	114
Scenedesmus obliquus	- Lighting conditions: continuous illumination from 10 to 1,000 µmol/m²/s - Pulsed light at 1,500 µmol/m²/s and 10 Hz	30-40	17-40	35-50	115
Scenedesmus obliquus HM103382	- NaCl stress - Continuous light of 40 µmolphotons/m²/s - Temperature: 27 °C	-	-	18-34	116
Scenedesmus sp. CCNM 1077	- Photoperiod: 12:12 hours (L/D cycles) - Nitrogen limitation and starvation	17-50	16-45	16-29	117
Tetraselmis sp.	- Continuous illumination at 100-120 µmolphotons/m²/s at both sides of PBR - Different sources of nitrogen	22-48	17-42	16-28	118
Tetraselmis sp.	- Continuous illumination at 100-120 µmolphotons/m²/s at both sides of PBR - Nitrogen limitation	17-22	42-55	13-16	118

DHA [155]. More generally, the PUFAs-producing microalgae species are *Phaeodactylum tricornutum*, *Monodus subterraneus*, *Porphyridium cruentum*, *Chaetoceros calcitrans*, *Nannochloropsis sp.*, *Crypthecodinium cohnii*, *Isochrysis galbana*, and *Pavlova salina* [126,127].

3.3.2. Pigments. In addition to PUFAs, microalgae include photosynthetic pigments in their composition. The latter are classified into three groups: chlorophylls, carotenoids and phycobiliproteins responsible for green, yellow/orange and red/blue colours, respectively [4,35]. For several years, these compounds have been shown to have beneficial health properties, such as antioxidant properties, vitamin precursors, immune activators and anti-inflammatory agents [4,33]. Therefore, they are mainly used for food, pharmaceutical or cosmetic applications as natural colours, food supplements or as a source of bioactive molecules [23].

- *Chlorophylls*: Chlorophylls are green pigments, essential for photosynthesis, present in almost all photoautotrophic organisms. Due to their high green pigmentation and growing consumer demand for more natural products, chlorophylls are gaining in importance as a dye agent in the food industries as well as in pharmaceuticals and in cosmetics [49,122]. Naturally present in photosynthetic organisms as chlorophyll *a* and chlorophyll *b*, these molecules can also be found in the form of sodium and cupric derivatives, for example. The latter are mainly used as food additives or in beverages [49].

  Although chlorophylls are mainly extracted from inexpensive sources such as grass or alfalfa, microalgae contain a significant amount of them. The latter are therefore considered as an alternative source to chlorophyll extraction [49,122], which would be potential for covalorization in the scope of biofuel production. Indeed, the chlorophyll content of a cell varies according to environmental conditions as well as the

Table 3. Main molecules of commercial interest extracted from microalgae in relation to their field of application

Molecules	Applications	References
PUFAs *DHA*, *EPA*	***Food***: - ***Nutraceutics***: Enrich formula in omega-3 ***Pharmaceutics***: Positif on blood system (pressure, coagulation), act on the proper function and development of nervous and visual system, reduce occurrence of chronic diseases (diabete, artritis, cardiovascular disease and obesity), reduce the level of chlolestrol triglycerids, prevent arthritis, Alzheimer's disease, psoriasis and certain type of cancer, anti-inflammatory properties ***Cosmetics***: -	9,119–121 4,6,49,122
Chlorophylls *Chlorophyll a and b*	***Food***: Green dyeing agents ***Nutraceutics***: Antioxidant properties ***Pharmaceutics***: Antioxidant properties, vitamin precursors, immune activator, anti-inflammatory properties, cancer prevention (colorectal), cytotoxic towards tumoral cells, stimulate liver function, increase bile secretion, increase hemoglobin, promote rapid cell growth ***Cosmetics***: Dyeing agents, additive agents, antioxidant properties, mask odours	33,49,122
Carotenoids *β-caroten*, *Astaxanthin*, *Lutein*, *Lycopene*, *Violaxanthin*	***Food***: Dyeing agents whose color depends on the molecule (red, orange, yellow) ***Nutraceutics***: Antioxidant properties ***Pharmaceutics***: Antioxidant properties, vitamin precursors,immune activator, anti-inflammatory properties, antihypertensive properties, neuroprotective properties, protective activities against cancer, atherosclerosis, ulcers and carviovascular diseases, prevent macular degeneration, reduce the prevalence of metabolic syndrome, adiposity and serum triglyceride concentrations, strengthen immune resistance to viral, bacterial, fungal and parasitic infections ***Cosmetics***: Antioxidant properties, photoprotective properties, dyeing agents	4,23,33,49,123–125 35,122,123,126,127
Phycobiliproteins *Phycoerythrin*, *Phycocyanin*, *Allophycocyanin*, *Phycoerythrocyanin*	***Food***: Dyeing agents whose color depends on the molecule (red, blue, light blue, magenta) ***Nutraceutics***: - ***Pharmaceutics***: Fluorescent properties, markers of certain immunological methods, antioxidant properties, anti-inflammatory properties, neuroprotective properties, hepatoprotective properties ***Cosmetics***: Dyeing agents	33,122,124,127 4,6,35,49
Exopolysaccharides	***Food***: Water retention capacity, texturing agents, thickening agents, gelling agents, stabilizers, emulsifiers, shelf-life extenders ***Nutraceutics***: - ***Pharmaceutics***: Antioxidant properties, antiviral properties (HIV, Herpes simplex type 1), antitumor properties, anticancer properties, anticoagulant properties, antilipidemic properties, immune activator, anti-inflammatory properties, fight against certain diseases (atherosclerosis, cardiovascular disorders, HIV), thickening and gel-forming properties for drug design ***Cosmetics***: Rheology modifiers, conditioners, anti-inflammatory properties, anti-redness properties, antimicrobial properties, antiviral properties, antioxidant properties, moisturizing agents, healing agents, emulsifiers, substitutes for hyaluronic acid, stimulate collagen synthesis, protective activities against enzymatic proteolysis	48,123,126,128–130
Proteins	***Food***: Emulsifiying agents, foaming agents, thickening agents, gelling agents ***Nutraceutics***: Hypolipidemic, hypoglycemic, anorectic, anorexigenic ***Pharmaceutics***: Anti-inflammatory properties, antihypertensive properties, anticancer properties, antibacterial properties, antioxidant properties, platform for recombinant proteins production ***Cosmetics***: Stimulate collagen synthesis, reduce vascular imperfections, photoprotective properties, antioxidant properties	9,126,131–134 49,123,129,135,136 35,44,137–139
Vitamins	***Food***: - ***Nutraceutics***: Precursor properties of some important enzyme cofactors ***Pharmaceutics***: Antioxidant properties ***Cosmetics***: -	140
Polyphenols	***Food***: - ***Nutraceutics***: - ***Pharmaceutics***: Antioxidant properties, anti-inflammatory properties , anti-cancer properties, anti-allergic properties, anti-diabetes properties, antimicrobial properties, antifungal properties, antimycotoxigenic properties, improve cardiovascular-associated disorders ***Cosmetics***: -	140–143
Phytosterols	***Food***: - ***Nutraceutics***: - ***Pharmaceutics***: Reduce LDL-cholesterol, promote cardiovascular health, anti-inflammatory properties, anti-atherogenicity properties, anti-cancer properties, anti-oxidative properties, protection properties against nervous system disorders ***Cosmetics***: -	144–147

strain from about 0.5 to 4% of dry weight[5,159]. A review highlighted the chlorophyll-inducing conditions in microalgae among which are low light, red light spectrum, a sufficiently high temperature, and a replete nitrogen and phosphorus content[160]. To illustrate this, many studies have been carried out. As an example, a study showed that under high light intensity (400 µmol photon/m^2/s) the chlorophyll *a* content of two microalgae strains underwent a greatly decline compared with low light intensity (40 µmol photon/m^2/s)[161]. *Chlorella sp.* decreased its chlorophyll *a* content from 14 mg/L to 2 mg/L and *Monoraphidium sp.* from 11 mg/L to 3 mg/L. Another study assessed the effect of nitrogen depletion and low light intensity on the chlorophyll content of *Scenedesmus dimorphus*[162]. The authors found a higher chlorophyll content when the cells were cultivated under low light intensity at 16.9 µmol photon/m^2/s (128% higher than the control group grown at 123 µmol photon/m^2/s). Conversely, nitrogen starvation induced an abrupt decrease in chlorophyll content of about 77.53% compared to the initial time. In addition, the proportion of chlorophyll *a* and chlorophyll *b* within the cells was investigated. Microalgae exposed to low light intensities were found to have the same pigment distribution as the control group (81% of chlorophyll *a* and 19% of chlorophyll *b* average percentage relative to the total chlorophyll content). However, nitrogen deprivation induced the production of chlorophyll *b* at the expense of chlorophyll *a* (a decrease in 8.77% in chlorophyll *a* content and an increase by 42.21% in chlorophyll *b* content). In addition to nutrient status and light intensity, the impact of the visible light wavelengths (color spectrum) on the photosynthetic pigment production was also investigated. In this respect, a study emphasizes a difference in pigmentation according to light exposure for the two strains studied[163]. The green microalgae *Chlorella vulgaris* was found to have an increased pigmentation and the highest chlorophyll content (1.29% and 0.38% dry weight for chlorophyll *a* and *b*, respectively) under red light of 650–700 nm compared to the daylight control (0.86% and 0.28% dry weight for chlorophyll *a* and *b*, respectively). Green light yielded the best chlorophyll *a* production in the cyanobacteria *Gloeothece membranacea* with a chlorophyll *a* content of 1.23% dry weight compared with the control at 1.09% dry weight. Light photoperiod is another parameter that can be used to manipulate the cell chlorophyll content[164]. As an example, *Chlorella vulgaris* total chlorophyll content exposed to 60-second periods (215 µmol quanta/m^2/s average light intensity) underwent a 50% increase compared to the continuous light reference[165].

Once the chlorophylls extracted from the cells, the remaining cell fragments can be used to produce biofuels, for example. Among the most exploited strains, the most well known microalgae is from the genus *Chlorella*, whose chlorophyll content represents about 7% of its biomass, five times more than that of *Arthrospira*[44].

- *Carotenoids:* Carotenoids are another class of pigments that are abundantly found in microalgae. These richly coloured molecules ranging from yellow to red are mainly known for their antioxidant property as well as dyeing power[49,122,123]. Thanks to their properties, carotenoids are frequently encountered in food and feed industries as well as cosmetics and pharmaceutical area[35]. With more than 600 representatives, carotenoids form the most diverse and widespread class of pigments[122,166]. Most of them share a common chemical structure composed of a 18-carbon conjugated double bond chain with two hexacarbon rings at each end[122]. Within this large class, carotenoids are divided into two groups: carotenes and xanthophylls. The former are oxygen-free hydrocarbons such as α-carotene and β-carotene, while the latter are oxygenated derivatives of carotenes (lutein, violaxanthin, zeaxanthin, fucoxanthin, astaxanthin, among others)[167]. The main sources of carotenoids are microalgae belonging to the Chlorophyceae class. These microalgae are capable of producing a wide range of pigments: carotenes (β-carotene, lycopene) as well as xanthophylls (astaxanthin, violaxanthin, anteraxanthin, zeaxanthin, neoxanthin and lutein, among others). Other pigments, such as fucoxanthin, diatoxanthin and diadinoxanthin are produced by other microalgae phyla[123]. On average, carotenoids represent 0.1 to 0.2% of the dry matter[5]. However, under unfavourable conditions, these pigments can be expressed up to 12% in the phylum Chlorophyta[167]. Currently, the two pigments having the highest demand in global carotenoid market are β-carotene and astaxanthin from the genera *Dunaliella* and *Haematococcus*, respectively[6,123,168].

  β-carotene is the first ever high-value product to be commercially produced from microalgae[168]. It is commonly produced by *Scenedesmus almeriensis*, *Dunaliella bardawil* and *Dunaliella tertiolecta*[4,33,44,49,123,126,127]. However, the richest source for commercial production of natural β-carotene is the microalgae *Dunaliella salina* which is capable of expressing up to 98.5% β-carotene in relation to its total carotenoids and about 13% of its dry biomass[168,169]. Although the latter is in competition with its synthetic equivalent, natural β-carotene would have the advantage to be the unique source of 9-cis β-carotene. This isomers plays a major role in quenching oxygen free radicals and preventing oxidative damage to the cell[168].

  Astaxanthin, a red xanthophyll pigment, is the second most industrially exploited carotenoid. It is naturally produced by the microalgae *Chlorella zofingiensis*, *Chlorococcum sp.* and *Scenedesmus sp.* as well as the yeast *Xanthophyllomyces dendrorhous*[49,122,127].

However, the microalga *Haematococcus pluvalis*[4,35] is able to accumulate up to 81% of astaxanthin of its total carotenoids and about 7% of dry weight[169]. Therefore, this microorganism is seen as the most favourable specie for industrial scale production of natural astaxanthin[168,170]. Due to its high red dyeing power, this carotenoid pigment is mainly used in aquaculture feed as a dye agent for fish and shellfish flesh[4,35,49]. However, the use of astaxanthin is not limited to its pigmentation. It is particularly known to have antioxidant properties ten times greater than other carotenoids, making it the most potent natural antioxidant[4,33,123,126]. In this respect, astaxanthin is linked to biological activities with positive effects on human health. However, despite its attractive biological properties, the cost of production of natural astaxanthin is higher than that of synthetic astaxanthin (2,500 to 7,000$/kg and 1,000$/kg, respectively)[171], which is a barrier to the industrial exploitation of this microalgae[127].

Lutein is another yellow carotenoid found in microalgae. It is mainly involved in the formulation of drugs and cosmetics. Particularly, they are mainly know to have protective activity against photoinduced damage to the lens and retina of eyes[172]. Currently, most of the lutein production comes from marigold flowers (lutein content in marigold granules: 20 g/kg)[49,127,173]. However, lutein production from microalgae is gaining more and more ground due to higher productivity[127]. Indeed, although they have a lower lutein content than flowers (on average 5 g/kg), the annual production of microalgae is estimated to be 70-150 tons/hectare, 11.5-25 times higher than that of marigold flowers (6 tons)[173]. Lutein-producing strains include *Muriellopsis sp.*, *Chlorella protothecoides*, *Chlorella zofingiensis*, *Chlorococcum citriforme*, *Neospongiococcus gelatinosum* and *Scenedesmus almeriensis* as the largest producers with the ability to produce up to 0.5% lutein on a dry basis[49,127,171].

Other carotenoid pigments with industrial applications include lycopene, violaxanthin and zeaxanthin. Lycopene is a natural red antioxidant found in the cosmetics industry as a sunscreen and in anti-aging care formulations[33,127]. It is also used for pharmacological purposes because of its anti-carcinogenic and antiatherogenic properties[127]. Violaxanthin, an orange carotenoid pigment, is particularly known for its anti-inflammatory and anti-cancer properties. It is naturally produced by the strains *Chlorella ellipsoidea* and *Dunaliella tertiolecta*[123,126]. Zeaxanthin is a yellow carotenoid. It is mainly used in the pharmaceutical, cosmetic and food industries. For its production, the strains *Scenedesmus almeriensis* and *Nannochloropsis oculata* are used[4,127]. Finally, other carotenoids such as canthaxanthin, β-cryptoxanthin or fucoxanthin are used for pharmaceutical or cosmetic purposes because of their tanning, anti-inflammatory and anti-cancer properties, respectively[33].

- *Phycobiliproteins:* Phycobiliproteins are the last class of pigments found in photosynthetic organisms. They are hydrophilic protein-pigments complexes present only in cyanobacteria, and microalgae of the Rhodophyta phylum as well as in some Cryptophytes and Glaucophytes[124,167,174]. Like chlorophylls *b/c/d/f* and carotenoids, phycobiliproteins are accessory photosynthetic pigments used to extend the range of light absorption needed for photosynthesis (from 450 to 650 nm)[167,175,176]. They are classified into four major subgroups according to their absorption spectra[122,127]: the red phycoerythrin (PE, λ_{max} = 540 - 570 nm), the magenta phycoerythrocyanin (PEC, λ_{max} = 560 - 600 nm), the blue phycocyanin (PC, λ_{max} = 610 - 620 nm), and the light blue allophycocyanin (APC, λ_{max} = 650 - 6500 nm). Their composition varies with the species and environmental conditions. Under certain conditions, they can represent up to 13% of the dry biomass of some microalgae[174]. As a matter of fact, researchers have investigated the effects of different culture conditions (light source and growth media) on the expression of phycobiliproteins of *Pseudanabaena mucicola* freshwater cyanobacteria[177]. The highest total phycobiliprotein content (237 mg/g) was reached when the cyanobacteria was cultured on wastewater under white light. When zooming in on the different pigments individually, it appeared that phycocyanin was produced in larger quantities in blue light on BBM medium (0.419 mg/L), while allophycocyanin had better performance under white light on wastewater (0.523 mg/L). The phycoerythrin content was mainly influenced by changes in pH rather than light. As a result, its content in the study was found to be very low (> 0.05 mg/L). However, another study aiming at maximizing its content in *Porphyridium marinum* found the greatest amount to be 40 mg/g dry weight under 70 µmol photons/m^2/s, $NaNO_3$ = 3.4 g/L and metal solution = 1.5 mL/L[178]. Hence, strategies need to be investigated to optimize phycocyanin production. In this regard, a study aimed at identifying the optimal growth conditions to obtain the highest phycocyanin content from *Spirulina platensis*[179]. To do so, they set the following parameters: light intensity = 400 µmol photons/m^2/s, CO_2 aeration = 2.5% and flow rate = 0.2 vvm. Then, they varied different parameters such as the source of the illumination, the photoperiod, the nature of the culture medium. They finally found the highest phycocyanin content and productivity (14.9% and 101.1 mg/L/d, respectively) under white LED light source, 30:30 min light/dark cycles, recycled medium (50% replacement), and nitrate addition (45 mM).

  Due to their powerful and highly sensitive fluorescent properties, phycobiliproteins are used as markers for certain immunological methods, in flow cytometry, microscopy and DNA tests[4,6,35,49,122]. On an industrial

scale, these pigments are produced from the species *Porphyridium sp.*, *Arthrospira sp.* and *Aphanizomenon flos-aquae* [4,33,49,122,126,127].

3.3.3. Carbohydrates. Carbohydrates are synthesized intracellularly and represent the major part of the compounds derived from photosynthesis. Their content can reach up to 50% of dry weight of certain microalgae [180]. Among the genera and species most commonly used for the production of polysaccharides extracted from microalgae are *Tetraselmis sp.*, *Isochrysis sp.*, *Porphyridium cruentum*, *Porphyridium purpureum*, *Chlorella sp.* and *Rhodella reticulata* [126].

Once synthesized, these carbohydrates can serve a variety of biological functions. Depending on their physiological role, polysaccharides are usually grouped into three classes: energy reserve polysaccharides, structural polysaccharides that participate in cell wall formation and polysaccharides involved in cell communication [137,181]. From a biotechnological point of view, only the first two categories of polysaccharides have industrial potential and are therefore developed in the following paragraphs. Furthermore, energy reserve polysaccharides have been studied in great depth mainly in the context of biofuel production. While structural polysaccharides show great promises for pharmaceutical, cosmetic and food applications thanks to the diversity of molecules, the studies dealing with them are very recent and remain few.

- *Energy reserve polysaccharides*: Carbohydrates, as storage compounds, provide energy for the metabolic processes of organisms and allow, if necessary, temporary survival in the dark [182]. The synthesis of these reserve polysaccharides is a species-dependent process. Generally, polymers used as a storage product differ from those used as components of cell walls. In most microalgae species, the energy reserves are in the form of starch. The latter is a complex carbohydrate composed of amylose and amylopectin, two glucose polymers. Its degree of polymerization as well as its location within the cell differ according to the species of microalgae. In red microalgae, the Rhodophytes, starch is called floridian, *i.e.* it is stored as a vesicle in the cytoplasm outside the chloroplast. In green microalgae, the Chlorophyceae, starch is stored intraplastidially. In addition to starch and floridean starch, other types of storage polysaccharides including chrysolaminarin, paramylon and glycogen can be found [137,183]. Although most microalgae store their reserves as starch, cyanobacteria tend to accumulate glycogen, sucrose or glucosylglycerol [182,184].

  The constitution of energy reserves is not equivalent in all microalgae. For example, the strain *Porphyridium cruentum* is able to accumulate carbohydrates up to 57% of its dry matter content while *Chlamydomonas sp.* does not exceed 17% [182,184]. As pointed out earlier, carbohydrates content can be manipulate through growth conditions. As a consequence, highly fluctuating carbohydrate levels have been reported in the literature. For instance, *Chlorella vulgaris* may be able to accumulate carbohydrates between 9 and 41% of its dry matter content depending on growth conditions [184,185]. The same is true for *Scenedesmus obliquus*, which could accumulate between 10 and 47% of carbohydrates in its dry matter content [184]. However, in the literature, an antagonistic mechanism to the accumulation of carbohydrates has also been observed. Indeed, microalgae are able to modify the composition of their biomass and redirect their metabolic pathway under stress conditions to maintain cellular activities [182]. As a result, several studies have documented a conversion of carbohydrates to lipids when cells were exposed to different stress conditions. In this respect, a study showed that a salinity of 1 g NaCl/l induced a 58.68% conversion of carbohydrates to lipids in a microalgal consortium [186]. Temperature is another abiotic factor that can induce metabolic changes. Studies have shown that a temperature of 30°C and 40°C caused the conversion of 57.8% and 42% of carbohydrates to lipids, respectively [187,188].

  The main application of reserve polysaccharides is biofuels [180]. Indeed, their ability to be easily digested without requiring pre-treatment makes them a good choice for biomass conversion technologies, in particular for anaerobic digestion. However, in order to maximize biofuel production from microalgae, it is necessary to combine the high innate carbohydrate content of a species with its ability to produce biomass in a significant way [182].

- *Structural polysaccharides*: Structural polysaccharides are gaining increasing importance in the literature. These cell wall related polysaccharides were firstly exploited for their rheological properties as thickening or gelling agents. Yet they have recently received much attention because of the detection of different biological activities well reviewed [189] in addition to being relatively easy to extract [137,181]. Consequently, these macromolecules can find applications in the food [23,35,48,130], cosmetics [126,129,180] and pharmaceuticals [23,35,123,126,128,130,180] industries. Some polysaccharides are also thought to have biosurfactant activities used in bioremediation of water and soil [35].

  Except for a few species, the microalgal cell is surrounded by a cell wall whose composition differs whithin a phylum, class or even species [137]. It is generally rigid, homogeneous and multi-layered. In eukaryotic microalgae, the cell wall consists of microfibrils embedded in a mucilage composed in part of polysaccharides, called fibrillar polysaccharides, such as cellulose and hemicellulose. A mixture of others polysaccharides such as xylose, mannose or sulfated polysaccharides are also found in different proportions. All these polysaccharides are related to the rigidity of the cell wall as well as the resistance to mechanical disruption techniques [137]. Unlike eukaryotic microalgae, cyanobacteria have a peptidoglycan-based

cell wall made up of N-acetylglucosamine and N-acetylmuramic acid residues connected by β-1,4 linkages that are easily breakable [137,190].

Furthermore, several eukaryotic and prokaryotic microalgae can produce and excrete extracellular polymeric substances either non-covalently bonded to the surface of cells or in their surrounding environment. Most of the time, these polymers are referred to as exopolysaccharides although the terminology remains unclear [35,180,191]. Contrarily to both intracellular and cell wall polysaccharides, these exopolysaccharides have a very complex structure. As a result, there is still limited information available on the structural characterization of carbohydrates from microalgae [192]. This phenomenon is all the more amplified by the fact that the interest in exopolysaccharides is rather recent [137,181,192,193]. However, several potential functions have been identified. Exopolysaccharides are known to promote the formation of cell adhesion or aggregates playing a role in the formation of biofilms [137,181]. In addition, their expression would be an adaptive response of microalgae to both mechanical and environmental stresses providing a protection to the cell. It is therefore not surprising that microalgae have been recognized as a good source for exopolysaccharides production ranging from about 0.5 g/L to up to 20 g/L [192]. However, to date, only few studies have been done on the subject. It also appears that, most of the time, the name used in the literature does not allow to distinguish between exopolysaccharides and cell wall related polysaccharides making comparison difficult [192].

Carbohydrates from microalgae are generally made up of a mixture of neutral sugars, amino sugars and uronic acids in their structure. Their nature is species-dependent and therefore vary from one species to another [130,184,193–195]. However, the 12 most common monosaccharides constituting the carbohydrates in microalgae are glucose, rhamnose, xylose, mannose, galactose, fucose, arabinose, ribose, glucosamine, galactosamine, glucuronic acid and galacturonic acid [35,137,193]. Their detection is not always easy as their synthesis depends on the culture conditions, as well as the growth phases. One of the most commonly used strategies for the accumulation of exopolysaccharides is nutrient limitation. A study investigated the influence of different nitrogen sources on exopolysaccharide synthesis by *Botryococcus braunii* UC 58 [196]. The results highlight the strain ability to produce exopolysaccharides regardless of the nitrogen source but at different concentrations (2.4 g/L with nitrate, 1.8 g/L with urea and 2.1 g/L with ammonium after 14 days of culture). However, the nitrogen limitation had no effect on the composition of *Tetraselmis suecica* cell wall [197]. Regardless of the initial nitrate concentration (62 and 90 ppm), the cell walls were found to have a similar monosaccharide composition consisting of 54% 3-deoxy-D-manno-oct-2-ulosonic acid (Kdo), 17% 3-deoxy-lyxo-2-heptulosaric acid (Dha), 21% galacturonic acid and 6% galactose. However, nitrate depletion at a concentration of 3 ppm induced an accumulation of intracellular starch up to 45% of dry biomass.

Apart from culture media, physico-chemical culture paramaters such as light, temperature, aeration can affect the exopolysaccahrides composition and production. In this context, a study demonstrated that the production of exopolysaccharides from *Arthrospira platensis* was a light-dependent process and was also influenced by the temperature [198]. The authors found an optimum for exopolysaccahrides production at light intensity higher than 180 µmol photons/m^2/s and temperature at 35°C. In addition to light intensity, wavelengths and therefore light spectrum also influence the production and monosaccharide composition of exopolysaccharides without changing their structure. A study conduced on *Nostoc flagelliforme* revealed that blue light was more suitable than white light for exopolysaccharides production [199]. The effect of CO_2 concentration was also investigated on exopolysaccharides production [200]. The same aeration (2% of CO_2) was applied to four different strains of *Chlorella*. Within the same species, different polysaccharides profiles were found. *Chlorella vulgaris* and *Chlorella variabilis* showed a different content of total carbohydrates in their cell wall (48% and 33% of total carbohydrates in cell wall, respectively) but their neutral cell wall monosaccharides profiles were quite similar (about 14% of arabinose, 36% of rhamnose, 43% of xylose+galactose+mannose and 7% of glucose). Conversely, *Chlorella sorokiniana* and *Chlorella minutissima* had the same total cell wall carbohydrates content (about 30%) but presented different cell wall composition: 0% arabinose, 38% rhamnose, 58% xylose+galactose+mannose and 4% glucose ; and 0% arabinose, 3% rhamnose, 74% xylose+galactose+mannose and 23% glucose, respectively.

To date, there is poor knowledge of the structure of exopolysaccharides. In order to maximize their biotechnological exploitation, it is necessary to have access to their structural information to establish relationships between structure and biological activity. For this, further studies are necessary and expected in the coming years.

3.3.4. Proteins, peptides and amino acids. Depending on the species and environmental factors, the protein content varies from 6 to 70% of their dry weight, although the majority of them have protein levels around 50% [131]. Microalgae also have a rich and varied composition of amino acids, among which the most abundantly found are aspartate (Asp) and glutamate (Glu) [201]. These molecules have different biological functions that can be used in the nutritional, cosmetics and pharmaceutical fields.

Proteins from microalgae are mainly used as nutraceuticals or included in the formulation of functional foods[35,44]. Due to the high protein content of microalgae, mainly in *Arthrospira*, *Chlorella* and *Dunaliella salina*, they are considered to be an unconventional source of protein for human consumption, particularly for developing countries[9,131,135]. It would be estimated that by 2054, about 50% of the replacement protein market would be covered by proteins derived from algae or insects[44]. Furthermore, microalgae contain well-balanced essential amino acids profiles, however, they may have lower digestibility than standard protein sources[131,137]. In this respect, *in vitro* microalgae digestibility tests have been performed on different microalgae species. The results showed a large variability in protein digestibility values depending on the species analyzed ranging from 50 to 82%[202,203]. In the high range, *N. sphaeroides*, *A. platensis* and *C. vulgaris* were found with crude protein digestibility values of 82%, 81% and 76%, respectively. These microalgae have a higher digestibility than some standard protein sources such as beans, oats and wheat (78%, 72% and 77%, respectively)[202]. Conversely, other microalgae such as *N. oceanica* and *C. sorokiniana* exhibited relatively low protein digestibility values (50 and 55%, respectively). The reduced digestibility of some microalgae is explained by the composition of the cell wall. The thick, rigid and cellulosic cell wall in some microalgae is considered to be a barrier to digestibility[204]. Conversely, cyanobacteria have a thinner cell wall that is more easily hydrolysable. Nevertheless, the digestibility of microalgae can be improved by exposing the cells to different processes[204]. In this sense, a study has shown digestibility values of sixteen microalgae increased when the cells were subjected to a cell disruption process[203]. In untreated cells, the highest average digestibility was found in *Chlorella sp.*. (79%) and the lowest in *Nannochloropsis sp.*. (54%). The process of cell disruption increased the average digestibility of all types of microalgae (78-84% on average), but with different gains. The largest increase was obtained in *Nannochloropsis sp.*. (49% increase), while for the other genera the increase was less significant: *Arthrospira sp.* (5%), *Chlorella sp.* (6%) and *Phaeodactylum sp.*. (8%). In addition to nutraceuticals, proteins of microalgal origin would present promising technological functionalities for the agri-food industry. For example, *Chlorella vulgaris* and *Tetraselmis sp.* would have emulsifying and foaming properties[137]. Thickening or gelling properties have also been reported for *Arthrospira platensis* and *Tetraselmis suecica* proteins[137].

Microalgal proteins, maily from *Arthrospira* and *Chlorella* genera, have also penetrated the cosmetics field, and more particularly the skin market[136,205]. In general, protein extracts are found in the formulation of beauty products because of their attractive biological activities. These activites have already been well reviewed[205]. At present, some beauty products containing protein extracts from microalgae can be found in the market. For example, Dermochlorella DG ® is a product developed from *Chlorella vulgaris* extracts containing oligopeptides. This microalgae-based ingredient, by stimulating collagen production, acts as a restructuring agent that gives firmness to the skin, reduces the morphology of stretch marks and reduces vascular imperfections[49,129,136]. *Arthrospira* proteins are also used in cosmetics to repair the signs of early skin aging[136]. Micosporin-like amino acids have also attracted a lot of interest as potential cosmetic agents[123,126]. The latter specifically have photoprotective and antioxidant actions to fight against photoinduced skin aging[35,126].

From a pharmacological point of view, peptides from microalgae have gained more attention as alternative bioactive compounds due to their safety status. They are mainly known to have anti-inflammatory[132], antihypertensive, anticancer[133], antibacterial and antioxidant[134] properties that can be applied in human health promotion[140]. These peptides are generally obtained following enzymatic hydrolysis of various proteins[135,206]. Proteins usually contain 3–20 amino acid residues, and their activity depends on their amino acid composition and sequence[135]. One of the main producers of peptides is *Chlorella sp.*[206]. As such, many studies have been conducted on this genus. One of them was performed *in vitro* on hydrolyzed proteins from *Chlorella ellipsiodea*[207]. This study identified a specific pentapeptide (Leu-Asn-Gly-Asp-Val-Trp) showing to have peroxyl radical, 1,1-Diphenyl-2-picrylhydrazyl (DPPH) and hydroxyl radicals scavenging antioxidant activities at the half maximal inhibitory concentrations (IC_{50}) values of 0.02, 0.92 and 1.42 mM, respectively. Once purified, the peptide was cultured with monkey kidney cells. The latter has improved both cellular viability against hydrochloride-induced cytotoxicity on normal cells (56.3%, 72.3%, and 79.4% at the concentrations of 25, 50, and 100 μM, respectively) and reduced the proportion of necrotic apoptotic cells hydrochloride-induced by 32.95%. The same author conduced another study on *Chlorella ellipsiodea* hydrolysates in order to identify anti-hypertensive properties[208]. In this respect, another peptide (Val-Glu-Gly-Tyr) was reported to have both *in vitro* angiotensensin I-converting enzyme (ACE) inhibitory activity (IC_{50} value = 128.4 μM) and *in vivo* systolic blood pressure lowering effects when orally administrered in rats. A similar study has been conduced on both *Chlorella vulgaris* and *Spirulina platensis* peptides showing different peptides with different inhibition activity[209]. In *Chlorella vulgaris*, 4 peptides of the 5 peptides studied inhibited the ACE acitivy with lower IC_{50} than in the previous study: Ala-Phe-Leu (63.8 μM), Phe-Ala-Leu (26.3 μM), Ala-Glu-Leu (57.1 μM), and Val-Val-Pro-Pro-Ala (79.5 μM). Five peptides have been identified from *Spirulina platensis*: Ile-Ala-Glu (34.7 μM), Phe-Ala-Leu, Ala-Glu-Leu, Ile-Ala-Pro-Gly (11.4 μM), and Val-Ala-Phe (35.8 μM). *In vitro* cytotoxic effects of *Dunaliella salina* peptides have also been reported in the literature[210]. The antimicrobial activity was performed against *Escherichia coli*, *Staphylococcus aureus* and *Helicobacter pylori*. The highest inhibitory effect was obtained from peptids with > 10 kDa molecular weights for *E. coli* and peptids with 3-10 kDa molecular weights after 16 h of culture (16.8% and 17.2% inhibitory effect, respectively). The bioactive pep-

tides with highest bacterial inhibition effect were observed on *H. pylori* culture with a minimum inhibitory concentration of 0.175 mg compared to *E. coli* and *S. aureus* (0.58 and 0.81 mg, respectively). Antiproliferative properties of *Dunaliella salina* peptides was analysed on human colon cancer cell lines (SW480). Among the three peptide fractions and concentrations studied, the most effective concentration appeared to be the peptides < 3 kDa in 0.1 µg/mL concentration after 72 h with about 30% viability. Although a large number of studies have been conducted using *in vitro* and cell-based assays for identifying properties, there are an increasing number of *in vivo* studies, mainly in rats. To our knowledge, the latest one to date was on the oral toxicity of microalgal protein hydrolysates on Wistar rats. This study has revealed the safety of these hydrolysates and thus supports their use in functional foods or nutraceuticals[211].

These proteins, once synthesized, require extraction and purification steps. These must be monitored and tested to ensure that no changes in protein integrity occur as a result of these treatments[139].

3.3.5. Vitamins. Microalgae are an essential primary food source in the rearing of all stages of marine bivalve molluscs, larvae of several marine fish species and shrimps, and zooplankton providing them with nutritional intakes. In addition to their balanced macronutrient composition, microalgae provide them with vitamins essential to their development as they are not able to synthesize them. These bioactive compounds are important metabolites because of their precursor properties of some important enzyme cofactors. Besides, they play an essential antioxidant role in the scavenger of ROS. Thus, the majority of studies on vitamin production by microalgae have been conducted on strains used in aquaculture.

In the context of aquaculture, marine microalgae are able of synthesizing and accumulating a wide range of vitamins including pro-vitamin A, some vitamins of the B group (B1, B2, B3, B5, B6, B8, B9 and B12), vitamin C, and vitamin E, among others[140]. The vitamin content from microalgae is both species-dependent[212–215] and correlated with the growth phase and growth conditions[215]. For instance, a study demonstrated that riboflavin (vitamin B2) content of six microalgae species used in mariculture all increased during the onset of stationary growth phase[216]. Later, the same author studied the effect of photoperiod and harvest stages on *Nannochloropsis* sp. CS-246 vitamins content[215]. Under different light conditions, the content of most of the vitamins changed. Both vitamin B2 and B6 were found in larger quantities under constant light (62 and 9.5 µg/g, respectively compared with 25 and 3.6 obtained under light/dark cycles of 12:12h) while pro-vitamin A content was found to be lower (0.29 compared with 0.50 mg/g). Harvest stage also affected the vitamin content. Some vitamins such as vitamin C and vitamin E are expressed in greater quantities when the culture is harvested during the exponential phase. In constrast, the pro-vitamin A and vitamin B2 contents decreased as the culture grown and was harvested during the stationary phase. Another study also investigated the relationship between light availability and vitamin yield in *Dunaliella tertiolecta*[217]. The vitamin C content of the cells increased from 1.72 to 3.48 mg/g with increasing average light intensity (from 84 to 430 µmol/m^2/s). Unlike vitamin C, the authors found a negative correlation between the amount of vitamin E produced per mole of photons absorbed and the average light intensity inside the reactor. Two years earlier, a study had shown the same trend[218]. However, the authors highlighted that vitamin E production was not only a function of light, but also of the strain and growth phase. Under the same conditions, *Tetraselmis suecica* expressed the highest vitamin E content during the exponential phase (1.08 mg/gDW). However, this content gradually declined over the rest of the growth to reach a final value of 0.4 mg/gDW. In contrast, in *Dunaliella tertiolecta*, the vitamin E content increased with increasing cell density to reach up to 0.5 mg/gDW. Finally, the availability of nutrients in the culture medium is also likely to affect vitamin synthesis in microalgae. As an example, a study investigated the effects of the nitrogen source (sodium nitrate and ammonium chloride) and their concentration (882 and 441 µmol/L) on the accumulation of vitamin E in *Nannochloropsis oculata*[219]. The authors identified the highest vitamin E content (2325.8 µg/g dry weight) at 441 µmol/L sodium nitrate in the late stationary phase, *i.e.* 34 days of culture suggesting that decreasing nitrogen concentrations led to an increase in vitamin E accumulation. All these results support that vitamin expression is a species-dependent process and is adjusted according to the environmental conditions to which they are exposed (light, nutrients) as well as the harvesting stage.

In addition to aquaculture, studies have been carried out on the contribution of vitamins from microalgae in human nutrition. In this respect, a study has shown that commercial microalgae powders intended for consumption are a source of vitamins B2, B3, B9 and B12[220]. The vitamin B2 content of *Spirulina* powders showed a low variability between the samples tested with a maximum content of 40.9 µg/g. Vitamin B3 is expressed more strongly in *Chlorella* (0.24 mg/g) than *Spirulina* (0.16 mg/g) powders, although the difference observed was not significant. However, overall, these powders represent only a small portion of the recommended daily allowances of riboflavin (B2) and niacin (B3) for adults, which are 1.3 and 16 mg, respectively. In contrast, *Chlorella* and *N. gaditana* powders have been shown to be a good source of vitamin B9. Their content (maximum content of 25.9 µg/g and 20.8 µg/g, respectively) is 6 times higher than that of *Spirulina* (maximum content of 4.7 µg/g), representing a quarter of the daily intake (400 µg) for a consumption of 5 g of microalgal powder. Moreover, another recent study has identified microalgae, in particular the cyanobacterium *Anabaena cylindrica*, as a non-toxic source of vitamin K1[221]. This vitamin, which plays a role in the prevention of chronic diseases, is mainly produced chemically. Cyanobacterial production of vitamin K1 offers an interesting biological alternative since it allows only active isomers to be produced (as opposed to 10 to 20% inactive by chemical means). Additionally, its very high concentration of around 200 µg/g dry weight (six times higher than the 37 µg/g found in parsley, a rich vitamin

K1 food source) provides three times the daily needs of an adult for a 1 g intake of powder. Futhermore, others studies point out that the microalgal vitamin content is superior to certain vegetable commodities. Notably, some microalgae would have higher vitamin pro-vitamin A, vitamins E, B1 and B9 contents than conventional foods such as orange, carrot, wheat flour, corn flour, rye flour or soy flour[212]. Besides, fruits and vegetables do not represent a good source of vitamin B12 because the latter is neither synthesized nor required by the plants[222]. Consequently, a vegetarian or vegan diet can lead to a deficiency of this vitamin. To make up for this deficiency, microalgae are considered as an essential source of vitamin B12 for people following these diets[222]. Studies have shown that microalgae powders would be a good alternative. For example, *Chlorella*-based powder can contain up to 2.4 µg/g of vitamin B12, thus covering 5 times the recommended daily intake of 2.4 µg for an intake of 5 g of powder[220]. In addition, one gram of *Anabaena cylindrica* powder provides 64% of the adult vitamin B12 intake[221]. Still, the bioavailability of these vitamins is species-dependent[140].

Thus, depending on the desired product, different strategies are to be implemented. Moreover, a special attention must be paid to post-harvesting treatments as drying processes. These latter could have a considerable effect on the vitamin content, especially on the heat unstable vitamins such as B1, B2, B3 and C.

3.3.6. Polyphenols. Polyphenols are a wide group of secondary metabolites comprising phenolic acids, flavonoids, isoflavonoids, stilbenes, lignans and phenolic polymers[140]. Their basic structure consists of one or more hydroxyl groups bound to an aromatic ring, making them polar compounds. These molecules display a wide range of biological activities including antioxidant activites as well as anti-inflammatory, anti-cancer, anti-allergic, anti-diabetes, anti-aging and antimicrobial properties[140,141]. A recent review focusing on both preclinical and clinical studies of polyphenols from seaweeds suggests that these latter would improve cardiovascular-associated disorders, but the authors point out that further data are needed to make this clear[142]. Recently,a study was carried out on polyphenols extracted from two different microalgae species: *Nannochloropsis sp.* and *Spirulina sp.*[143]. These extracts were used to study antifungal and antimycotoxigenic properties on trichothecenes mycotoxins from *in vitro* cultures of *Fusarium graminearum*. This study revealed that after 168 h of culture, 40 µg/mL of phenolic extracts from *Nannochloropsis sp.* completely inhibited nivalenol and deoxynivalenol and dramatically hindered acetylates production by 98%. Polyphenol extracts from *Spirulina sp.* totally inhibited nivalenol and significantly decreased deoxynivalenol production by 62% and reduced acetylates contents by 78%.

Extensive information on polyphenols exist on macroalgae[223], however, production of polyphenols from microalgae was also studied. Like all other active biological compounds, both the composition and content of polyphenol from microalgae are species-dependent. A screening of 32 different species was performed to determine among other the polyphenol contents[224]. From this study, it has been shown that polyphenols range between 54 mg Gallic Acid Equivalent (GAE)/100g DW (*Haematococcus pluvialis*) to 375 mg GAE/100g DW (*Phaeodactylum tricornutum*). *Tetraselmis sp.* and *Neochloris oleoabundans* are also great producers with 374 and 373 mg GAE/100g DW, respectively. Other studies on microalgal polyphenols have found results within this range. For instance, a study found that *Arthrospira platensis* exhibits 334 mg GAE/100g DW while *Chlorella vulgaris* expresses 217 mg GAE/100g DW[225]. Moreover, when compared to other sources of polyphenols, it has been observed that microalgae have total polyphenolic content similar to or higher than several vegetables and fruits[226]. However, the greatest polyphenolic producers remain red berries.

Despite this step forward, further studies are needed to explore the production mechanism of polyphenols in more detail to determine the advantageous conditions to their expression.

3.3.7. Phytosterols. Sterols are components of the cellular membrane acting on its stability, permeability and fluidity by controlling movement of fatty acid chains within it[140,147,227]. They are nitrogen-free complex polycyclic alcohols that originate from isoprenoid biosynthesis. Among the 200 reported phytosterols, β-sitosterol is the most abundant in higher plants, but in a number of microalgae it appeared that 24-ethylcholesterol was dominant[140,147,227]. In addition, the sterols present in microalgae display both a great diversity of structures and occurrence variety. These compounds are species-dependent and their composition can also be influenced by environmental factors such as light intensity, temperature, salinity and growth stage[227,228].

Phytosterols have already been the subject of numerous reviews because of their beneficial effects on human health[145,147]. Particularly, they are well-know for their ability to reduce low density lipoprotein (LDL)-cholesterol and promote cardiovascular health with an intake of 2-3 g/days minimum. Besides, they present anti-inflammatory, anti-atherogenicity, anti-cancer and anti-oxidative activities[144]. An *in vivo* study conducted on mice also highlighted some protection properties of β-sitosterol against nervous system disorders[146]. In addition to their properties, the biodisponibility of phytosterols has been studied by exploring their absorption on different animal species. It has been reported that rabbits do not absorb phytosterols while rats and humans absorb a small fraction (4% and 1.5% to 5%, respectively)[145].

In microalgae, a screnning of 10 species commonly used in aquaculture and the nutraceuticals industry was conducted to determine the best candidates for phytosterols production[147]. From this study, it emerged that *Pavlova lutheri*, *Tetraselmis sp. M8* and *Nannochloropsis sp. BR2* were the greatest producers of total phytosterols (from 0.4 to 2.6% dry weight). In addition, when stressed, *Pavlova lutheri* was able of expressing sterols up to 5% DW (day 14 at 35 ‰salinity)[147].

Currently, the main industrial sources of phytosterols are tallow and vegetable oils. For instance, corn and rapeseed are capable to synthesize 850 mg/100g and 820 mg/100g of

phytosterols, respectively [147]. Microalgae are also good producers of phytosterols, especially *Pavlova lutheri* with 5186 mg/100g of phytosterols. However, further efforts are needed to induce overexpression of phytosterols from microalgae through metabolic or genetic engineering, as well as on recovery and purification methods.

3.3.8. Hormones. Phytohormones are a class of molecules produced in very low concentrations serving as chemical messengers to coordinate cellular processes in higher plants [229]. Most of the microalgal lineages are able to produce phytohormones. Among the classical phytohormones, there are auxin, abscisic acid, cytokinin, ethylene, gibberellins, polyamines, jasmonides, salicylates, signal peptides, and brassinosteroids [126,229,230]. Although their functional roles are not well known to date, they have recently been studied [126,229]. Depending on strains, phytohormones can act on development, growth, light response, stress tolerance, secondary metabolite synthesis and senescence of microalgae and thus regulating homoeostasis to cope with variable environmental factors [229,230]. As a result, understanding phytohormone pathways can be considered as a strategy for the selection of microalgae species for specific industrial purposes in particular for enhanced biofuel production [229]. Indeed, the manipulation of phytohormone metabolism could improve important industrial and economic characteristics of microalgae such as increased biomass productivity, or secondary metabolites, and better tolerance to adverse environmental conditions, among others. In addition, microalgae-based hormones could play a role in counteracting the signs of skin ageing in the field of cosmetics [126].

4. Current and projected market share

In 2017, the global market for microalgae-based products was estimated at 32.60 billion USD and is projected to reach approximately 53.43 billion USD by 2026 [231]. This general enthusiasm for microalgae is partly due to the various beneficial properties that their diversity offers, affecting various sectors. The first market niche to have developed is that of colouring agents with 300 million USD in 2009, followed by nutraceuticals (30 million USD in 2009) [231]. Since then, other potential markets have emerged. As such, it is estimated that in 2020, colouring agents will still be the leading microalgae product on the market with 800 million USD, closely followed by pharmaceuticals/chemicals (500 million USD), nutraceuticals (300 million USD) and finally cosmetics (30 million USD) [231]. Currently, the market for mcroalgae-based products is dominated by the United States, Asia and Oceania. However, in the coming years, it is likely that Europe will become one of the leaders in the field of microalgae-based bioproducts [231].

Considering the total market volume of microalgae-based products, more than 75% of the production of microalgae-derived products is dedicated to food, feed or nutraceutical applications [231]. Two species, *Arthrospira* (trade name *Spirulina*) and *Chlorella*, are at the head of the world market with a production of 12,000 tons per year and 5,000 tons per year, respectively [232,233] . These production figures are expected to increase further due to the evolution and growing consumer demand for a healthier diet. As an example, it is estimated that by 2050 more than 18% of protein sources will be derived from microalgae [234]. As a result, the increase in the market value of *Spirulina* powder is estimated at over 380 million USD by 2027 compared to 220.5 million USD in 2017 [232].

If we take a closer look at the market shares of current microalgae products (Table 4), one can see that only certain high value-added molecules from microalgae have really made inroads into the world market. Among these molecules are PUFAs, in particular omega-3 with a current market share of 2.5 billion USD in 2014, and carotenoids with 1.5 billion USD in 2017. Currently, the largest share of the PUFAs market is held by the United States. However, this market is expected to grow at an average annual growth rate of 13.5% [233]. The market for carotenoids is also growing steadily due to the health benefits of these molecules. Of the 600 existing carotenoids, only a few have commercial potential: astaxanthin and β-carotene. The global market for astaxanthin was estimated at 1.2 billion USD in 2010 with only 1% of this value corresponding to the production of naturally occurring astaxanthin. However, with the emergence of natural and organic products, the market value for natural astaxanthin can be expected to increase. To this end, it has been estimated that the market share of astaxanthin derived from microalgae would be 770 million USD by 2024. The same phenomenon can be observed for β-carotene.

5. Discussion

From the proposed review, one can see that microalgae have a great potential for high added-value molecules production. Still, the levels of maturity of the aforementioned categories variate, while pigments and PUFAs have started to penetrate their markets, other molecules are still under active research. In particular, exopolysaccharides, polyphenols, phytosterols and hormones are classes of molecules whose research wave is relatively recent. Further research efforts to better understand the structures and/or mechanisms of production are needed to hopefully make them emerging technologies in the coming years.

With this focus, microalgae cultures will be product driven. Still subsequent capital will be needed for both culture protocol and product development, making the early choice of the relevant strain all the more relevant. In the light of microalgae diversity, this choice may not be an easy task. With this aim, Figure 4 ties together classification, phyla specific bioactive compounds and their properties to biotechnological applications.

As one can see, Chlorophyta phylum is the one with the most diverse applications. It is followed by Cyanobacteria and Heterokontophyta phyla. Other phyla, usually cultivated for aquaculture (Cryptista, Haptophyta) seem to have potential for higher value application, such as PUFA. At the other end of the list, Euglenozoa phylum has no identified high added-value application and seems to be restricted to wastew-

Table 4. Current and projected market share for microalgae-based products (N.A.: Not Available)

Products	Current demand	Projected demand	Main producing strains
Omega-3 PUFAs	2.5 billion USD in 2014 [233]	5 billion USD by 2020 [233]	
EPA	300 million USD in 2010 [231]	4 billion USD for EPA/DHA by 2022 [232]	*Isochrysis galbana, Nannochloropsis oculata, Phaeodactylum tricornutum*
DHA	1.5 billion USD in 2010 [231]		*Crypthecodinium cohnii, Schizochytrium limacinum, Ulkenia sp.*
Carotenoids	1.5 billion in 2017 [235–237]	2.0 billion beetween 2019-2022 [235,236]	
Astaxanthin	both synthetic and natural forms: 555.4 million USD in 2016 [231]	1.5 billion USD by 2020 [236] to 2.57 billion by 2025 [232]. Microalgae-based form: 770 million USD by 2024 [232]	*Haematococcus pluvialis*
β-carotene	224 - 285 million in 2019 [231,232]	N.A.	*Dunaliella salina*
Phycobiliproteins	Greater than 60 million USD in 2010 [233]	N.A.	
Phycoerythrin	10 – 50 million USD in 2019 [235]	N.A.	*Porphyridium sp. and Rhodella sp.*
Phycocyanin	112.3 million USD in 2018 [232]	232.9 million USD by 2025 [232]	*Arthrospira sp., Porphyridium aerugineum*

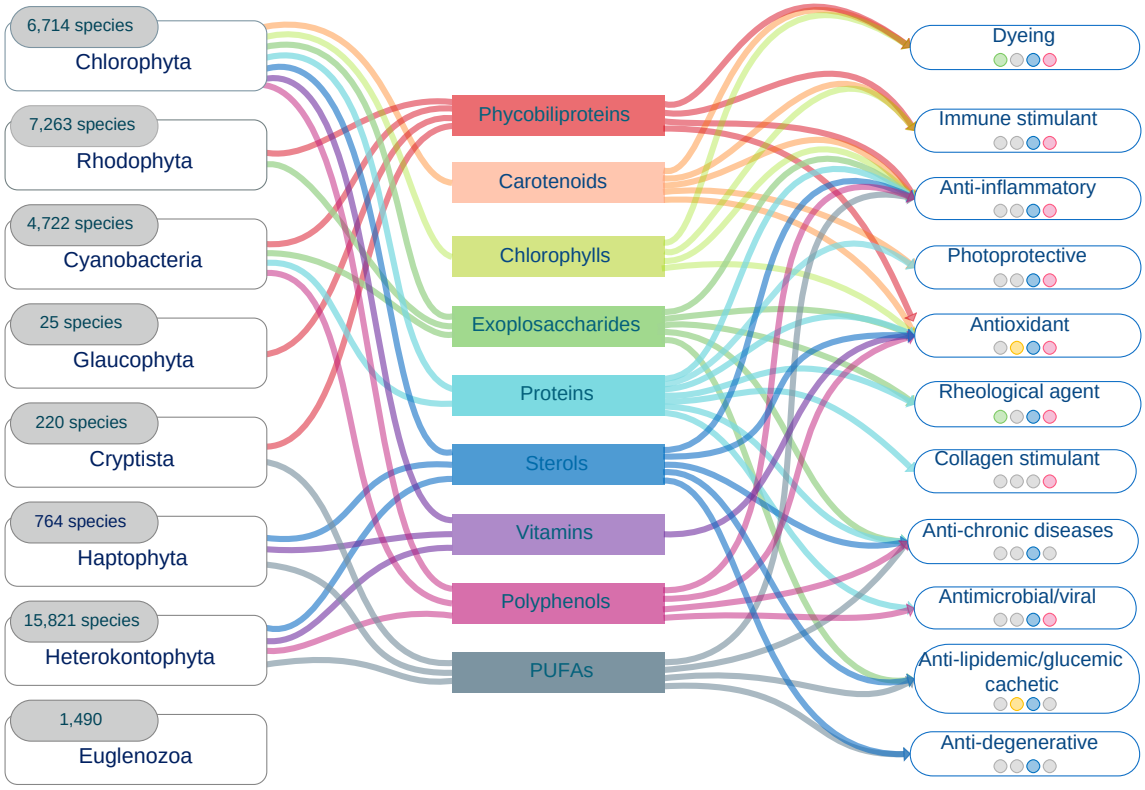

Fig. 4. Main bioactive compounds expressed in microalgae in relation to their classification and possible applications as high value added products. Numbers of species obtained from [238,239]. Blue circle: pharmaceutics ; pink circle: cosmetics ; yellow circle: nutraceutics and green circle: food.

ater treatment. In addition, to identify potential valorisation for a given strain, Figure 4 highlights that some compounds can only be produced by a very restricted set of phyla. It is specifically the case for chlorophylls and carotenoids which are produced at relevant levels by Chlorophyta, or for technical proteins produced by Chlorophyta and Cyanobacteria. Still, no matter which molecule would be extracted, it could be valorised in different configurations thanks to several positive effects (except for vitamins whose have only one). Regarding applications, despite their diversity, the potential sectors of applications for microalgae extracted bioactive compounds mostly belong to cosmetics and pharmaceutical industries. Finally, food industry may consider microalgae for technical purposes restricted to dyeing and rheological agents.

Despite the benefits of microalgae, there are many bottlenecks throughout the process of their exploitation [51]. During the culture stage, strain selection, which this article aims at helping, strain engineering and nutrient supply strategies need to be optimized for the hyperaccumulation of a single product. In addition, the growth of microalgae in culture is strongly limited by the degree of light penetration, resulting in dilute cultures with low biomass concentrations (about 3 g/L for autotrophic cultures compared to 30-100 g/L for heterotrophic fermentations). The diluted nature of the culture has major repercussions on processes downstream of the

value chain, which represent 40% of the total costs of the entire process, and in particular on the harvesting stage[240]. Finally, the extraction of metabolites of interest is also limiting due to the capacity of microalgae to effectively resist cell disruption processes due to the nature of the biochemical composition of their cell wall[25,52]. At present, these bottlenecks have not been resolved. The most optimitic projections envision a whole biomass cost of 0.62 €/kg dry weight (accounting for 0.20 €/kg dry weight cost reduction associated to wastewater treatment valorisation)[241]. Still, the diversity of applications widen the valorisation horizon as it is an edge that may alleviate the cost burden associated with biomass low cost (biofuel, feed) valorisation. Depending on the market value associated to the targeted bioactive compounds, two strategies can be envisioned. For high price molecule such as astaxanthin, its sole hyperaccumulation may bring economic viability to the production process. In addition, after extraction of this flagship molecule, spend biomass can be turn to biofuel. An alternative strategy would be the production of two or more medium added value compounds without paying the additional production costs associated to hyperaccumulation promoting growth conditions[51].

Still, one can note that, in recent years, genetic and metabolic engineering has emerged as a potential tool for promoting economical viablity of microalgal biotechnology. Indeed, it allows to modify existing strains to improve their performances hence reducing associated production costs. Several examples can be given in this regard. First, in order to make the production of biofuels from microalgae profitable, strains can be modified to overexpress lipid production[4,47]. Another relevant example is the production of recombinant proteins. A recombinant protein is a protein produced by a cell whose genetic material that has been modified by genetic recombination. Recombinant proteins obtained from microalgae include antibodies, vaccines and enzymes such as[138,139]. Microalgae have been considered and studied as a platform for the production of these proteins. Being eukaryotic cells, their main advantage is to contain the cellular machinery allowing them to synthesize complex human proteins in a cost effective manner[242]. Thanks to the complete sequencing of the genome of *Chlamydomonas reinhardtii*, the latter has great potential for the production of recombinant proteins[138,139,242]. Other strains such as *Chlorella ellipsoidea*, *Dunaliella tertiolecta* or *Dunaliella salina* have also been studied[139]. Some of the notable successes, although many, are the expressions of an anti-glycoprotein D antibody of herpes simplex virus, a monoclonal antibody IgG1 directed against anthrax protective antigen or the human protein TRAIL known to induce apoptosis in tumor cells infected with a virus[138,139,242]. However, routine genetic manipulation has been limited to a few species until recently[42]. To date, few - about thirty - species have undergone transformations[4,12,243]. As for other genetically modified organisms, modified microalgae would have to face two challenges regulations and consumer acceptance.

6. Conclusion and perspectives

This work reviewed applications of high added value molecules produced from microalgae. From this, it can be stated that, older forms of valorization - health food and quality feed, polyunsaturated fatty acids, pigments, carbohydrates - are currently penetrating their markets. For some they can even be found on supermarkets shelves. They are driven by two factors. For general public goods, the consumer appetite for healthy food and biosourced molecules in cosmetics. For industrial applications, desirable technical properties : e.g. texturer and dye for food industry, antioxidant for cosmetics. Most recent developments, such as peptides, vitamins, polyphenols, phytosterols and phytohormones, are struggling to meet their market and reach economical competitiveness. Still they are pushed forward by the very powerful driver that is pharmaceutical industry and the hope to gain new drugs and therapy. Regarding those, only time, research and development will tell us if they fulfill their expectations.

This work not only reviewed the aforementioned applications, it also tried to link microalgae classification and related potential applications. This is done through highlighting of which bioactive compounds can be found in which phyla. While some seem to be restricted to aquaculture, Cyanobacteria, Chlorophyta and Rhodophyta show great promises. This diversity of potential can be explained by two factors: the low number of strains in some phyla (25 and 220 species currently described for Glaucophyta and Cryptista, respectively), meaning low intrinsic potential, and the past direction of global research effort which may have biased our perception toward some phyla.

Finally, in addition to unravelling microalgae capabilities, academics and engineers still have to focus on alleviating large scale production bottlenecks, namely, high density cultures, harvest and molecules extraction. This could be done by strain genetic engineering, rising concerns about regulation and consumer acceptance, or conventional process optimization.

ACKNOWLEDGEMENTS

The authors would like to thank Département de la Marne, Région Grand Est and Grand Reims for their financial support.

AUTHOR CONTRIBUTIONS

WL and VP initiated and planned the project. WL drafted the manuscript. PP and VP performed critical revision of the manuscript. All the authors read and approved the final manuscript and take responsibility for the integrity of the work as a whole, from inception to finished article.

COMPETING FINANCIAL INTERESTS

Authors have no conflict of interest to disclose.

Bibliography

1. David KY Lim and Peer M. Schenk. Microalgae selection and improvement as oil crops: GM vs non-GM strain engineering. *AIMS Bioeng*, 4(1):151–161, 2017.
2. R. A. Andersen. Diversity of eukaryotic algae. *Biodiversity & Conservation*, 1(4):267–292, December 1992. ISSN 1572-9710. .
3. Naveen Sharma and Ak Rai. Biodiversity and biogeography of microalgae: Progress and pitfalls. *Environmental Reviews*, 19, December 2011. .
4. Imen Hamed. The Evolution and Versatility of Microalgal Biotechnology: A Review. *Comprehensive Reviews in Food Science and Food Safety*, 15(6):1104–1123, November 2016. ISSN 1541-4337. .
5. Pauline Spolaore, Claire Joannis-Cassan, Elie Duran, and Arsène Isambert. Commercial applications of microalgae. *Journal of Bioscience and Bioengineering*, 101(2):87–96, February 2006. ISSN 1389-1723. .

6. John J. Milledge. Commercial application of microalgae other than as biofuels: a brief review. *Reviews in Environmental Science and Bio/Technology*, 10(1):31–41, March 2011. ISSN 1572-9826. .
7. Robert E. Blankenship, David M. Tiede, James Barber, Gary W. Brudvig, Graham Fleming, Maria Ghirardi, M. R. Gunner, Wolfgang Junge, David M. Kramer, Anastasios Melis, Thomas A. Moore, Christopher C. Moser, Daniel G. Nocera, Arthur J. Nozik, Donald R. Ort, William W. Parson, Roger C. Prince, and Richard T. Sayre. Comparing photosynthetic and photovoltaic efficiencies and recognizing the potential for improvement. *Science (New York, N.Y.)*, 332(6031):805–809, May 2011. ISSN 1095-9203. .
8. Giorgio Perin, Alessandra Bellan, Andrea Bernardi, Fabrizio Bezzo, and Tomas Morosinotto. The potential of quantitative models to improve microalgae photosynthetic efficiency. *Physiologia Plantarum*, 166(1):380–391, 2019. ISSN 1399-3054. .
9. Efterpi Christaki, Panagiota Florou-Paneri, and Eleftherios Bonos. Microalgae: a novel ingredient in nutrition. *International Journal of Food Sciences and Nutrition*, 62(8):794–799, December 2011. ISSN 0963-7486. .
10. Muhammad Rizwan, Ghulam Mujtaba, Sheraz Ahmed Memon, Kisay Lee, and Naim Rashid. Exploring the potential of microalgae for new biotechnology applications and beyond: A review. *Renewable and Sustainable Energy Reviews*, 92:394–404, September 2018. ISSN 1364-0321. .
11. Melissa Stark and Ian O'Gara. An Introduction to Photosynthetic Microalgae. *Disruptive Science and Technology*, 1(2):65–67, June 2012. ISSN 2163-310X. .
12. Otto Pulz and Wolfgang Gross. Valuable products from biotechnology of microalgae. *Applied Microbiology and Biotechnology*, 65(6):635–648, November 2004. ISSN 1432-0614. .
13. Nathan C. Rockwell, J. Clark Lagarias, and Debashish Bhattacharya. Primary endosymbiosis and the evolution of light and oxygen sensing in photosynthetic eukaryotes. *Frontiers in ecology and evolution*, 2:66, 2014.
14. Sophie Groendahl, Maria Kahlert, and Patrick Fink. The best of both worlds: A combined approach for analyzing microalgal diversity via metabarcoding and morphology-based methods. *PLOS ONE*, 12(2):e0172808, February 2017. ISSN 1932-6203. .
15. Heidi M. Sosik and Robert J. Olson. Automated taxonomic classification of phytoplankton sampled with imaging-in-flow cytometry. *Limnology and Oceanography: Methods*, 5(6): 204–216, 2007. ISSN 1541-5856. .
16. Paulo Drews, Rafael G. Colares, Pablo Machado, Matheus de Faria, Amália Detoni, and Virgínia Tavano. Microalgae classification using semi-supervised and active learning based on Gaussian mixture models. *Journal of the Brazilian Computer Society*, 19(4): 411, November 2013. ISSN 1678-4804. .
17. I. Correa, P. Drews, S. Botelho, M. S. de Souza, and V. M. Tavano. Deep Learning for Microalgae Classification. In *2017 16th IEEE International Conference on Machine Learning and Applications (ICMLA)*, pages 20–25, December 2017. .
18. Kirsten Heimann and Roger Huerlimann. Chapter 3 - Microalgal Classification: Major Classes and Genera of Commercial Microalgal Species. In Se-Kwon Kim, editor, *Handbook of Marine Microalgae*, pages 25–41. Academic Press, Boston, January 2015. ISBN 978-0-12-800776-1. .
19. F. Xavier Malcata, Isabel Sousa Pinto, A. Catarina Guedes, Isabel Sousa Pinto, and A. Catarina Guedes. *Marine Macro- and Microalgae : An Overview*. CRC Press, December 2018. ISBN 978-1-4987-0534-9. .
20. Michael A. Ruggiero, Dennis P. Gordon, Thomas M. Orrell, Nicolas Bailly, Thierry Bourgoin, Richard C. Brusca, Thomas Cavalier-Smith, Michael D. Guiry, and Paul M. Kirk. A Higher Level Classification of All Living Organisms. *PLoS ONE*, 10(4), April 2015. ISSN 1932-6203. .
21. Jasvinder Singh and Rakesh Chandra Saxena. Chapter 2 - An Introduction to Microalgae: Diversity and Significance. In Se-Kwon Kim, editor, *Handbook of Marine Microalgae*, pages 11–24. Academic Press, Boston, January 2015. ISBN 978-0-12-800776-1. .
22. Jayachandran Venkatesan, Panchanathan Manivasagan, and Se-Kwon Kim. Chapter 1 - Marine Microalgae Biotechnology: Present Trends and Future Advances. In Se-Kwon Kim, editor, *Handbook of Marine Microalgae*, pages 1–9. Academic Press, Boston, January 2015. ISBN 978-0-12-800776-1. .
23. José L. García, Marta de Vicente, and Beatriz Galán. Microalgae, old sustainable food and fashion nutraceuticals. *Microbial Biotechnology*, 10(5):1017–1024, August 2017. ISSN 1751-7915. .
24. Andy Shilton and Benoit Guieysse. Sustainable sunlight to biogas is via marginal organics. *Current Opinion in Biotechnology*, 21(3):287–291, June 2010. ISSN 0958-1669. .
25. A. J. Ward, D. M. Lewis, and F. B. Green. Anaerobic digestion of algae biomass: A review. *Algal Research*, 5:204–214, July 2014. ISSN 2211-9264. .
26. Jason C. Quinn and Ryan Davis. The potentials and challenges of algae based biofuels: a review of the techno-economic, life cycle, and resource assessment modeling. *Bioresource Technology*, 184:444–452, May 2015. ISSN 1873-2976. .
27. Shaikh A. Razzak, Mohammad M. Hossain, Rahima A. Lucky, Amarjeet S. Bassi, and Hugo de Lasa. Integrated CO2 capture, wastewater treatment and biofuel production by microalgae culturing—a review. *Renewable and sustainable energy reviews*, 27:622–653, 2013.
28. Laura Soto Sierra, Chelsea K. Dixon, and Lisa R. Wilken. Enzymatic cell disruption of the microalgae Chlamydomonas reinhardtii for lipid and protein extraction. *Algal Research*, 25:149–159, July 2017. ISSN 2211-9264. .
29. Shih-Hsin Ho, Chun-Yen Chen, Duu-Jong Lee, and Jo-Shu Chang. Perspectives on microalgal CO2-emission mitigation systems—a review. *Biotechnology advances*, 29(2): 189–198, 2011.
30. S. Abinandan and S. Shanthakumar. Challenges and opportunities in application of microalgae (Chlorophyta) for wastewater treatment: a review. *Renewable and Sustainable Energy Reviews*, 52:123–132, 2015.
31. Raul Muñoz and Benoit Guieysse. Algal–bacterial processes for the treatment of hazardous contaminants: A review. *Water Research*, 40(15):2799–2815, August 2006. ISSN 0043-1354. .
32. Ana L. Goncalves, José CM Pires, and Manuel Simoes. A review on the use of microalgal consortia for wastewater treatment. *Algal Research*, 24:403–415, 2017.
33. Michael A. Borowitzka. Microalgae as sources of pharmaceuticals and other biologically active compounds. *Journal of Applied Phycology*, 7(1):3–15, February 1995. ISSN 1573-5176. .
34. Indira Priyadarshani and Biswajit Rath. Commercial and industrial applications of micro algae – A review. page 12, 2012.
35. Stefania Fortes Siqueira, Maria Isabel Queiroz, and Leila Queiroz Zepka and Eduardo Jacob-Lopes. Introductory Chapter: Microalgae Biotechnology - A Brief Introduction. *Microalgal Biotechnology*, June 2018. .
36. Farao Zhang, Hiroshi Kabeya, Ryouichi Kitagawa, Takahiro Hirotsu, Masatada Yamashita, and Toshi Otsuki. Preparation and Characterization of a Novel Polyethylene-Chlorella Composite. *Chemistry of Materials*, 11(8):1952–1956, August 1999. ISSN 0897-4756. .
37. Farao Zhang, Takashi Endo, Ryouichi Kitagawa, Hiroshi Kabeya, and Takahiro Hirotsu. Synthesis and characterization of a novel blendof polypropylene with Chlorella. *Journal of Materials Chemistry*, 10(12):2666–2672, January 2000. ISSN 1364-5501. .
38. Franziska Hempel, Andrew S. Bozarth, Nicole Lindenkamp, Andreas Klingl, Stefan Zauner, Uwe Linne, Alexander Steinbüchel, and Uwe G. Maier. Microalgae as bioreactors for bioplastic production. *Microbial Cell Factories*, 10:81, October 2011. ISSN 1475-2859. .
39. Mark Ashton Zeller, Ryan Hunt, Alexander Jones, and Suraj Sharma. Bioplastics and their thermoplastic blends from Spirulina and Chlorella microalgae. *Journal of Applied Polymer Science*, 130(5):3263–3275, December 2013. ISSN 0021-8995. .
40. A. Rahman and C. D. Miller. Chapter 6 - Microalgae as a Source of Bioplastics. In Rajesh Prasad Rastogi, Datta Madamwar, and Ashok Pandey, editors, *Algal Green Chemistry*, pages 121–138. Elsevier, Amsterdam, January 2017. ISBN 978-0-444-63784-0. .
41. René H. Wijffels. Potential of sponges and microalgae for marine biotechnology. *Trends in Biotechnology*, 26(1):26–31, January 2008. ISSN 0167-7799. .
42. Federico Valverde, Francisco J. Romero-Campero, Rosa León, Miguel G. Guerrero, and Aurelio Serrano. New challenges in microalgae biotechnology. *European journal of protistology*, 55:95–101, 2016.
43. David Chiaramonti, Matteo Prussi, Marco Buffi, Andrea Maria Rizzo, and Luigi Pari. Review and experimental study on pyrolysis and hydrothermal liquefaction of microalgae for biofuel production. *Applied Energy*, 185:963–972, January 2017. ISSN 0306-2619. .
44. Saumyakanti Khanra, Madhumanti Mondal, Gopinath Halder, O. N. Tiwari, Kalyan Gayen, and Tridib Kumar Bhowmick. Downstream processing of microalgae for pigments, protein and carbohydrate in industrial application: A review. *Food and Bioproducts Processing*, 110:60–84, July 2018. ISSN 0960-3085. .
45. Bruna da Silva Vaz, Juliana Botelho Moreira, Michele Greque de Morais, and Jorge Alberto Vieira Costa. Microalgae as a new source of bioactive compounds in food supplements. *Current Opinion in Food Science*, 7:73–77, February 2016. ISSN 2214-7993. .
46. W. M. Bishop and H. M. Zubeck. Evaluation of microalgae for use as nutraceuticals and nutritional supplements. *J Nutr Food Sci*, 2(5):1–6, 2012.
47. Liam Brennan and Philip Owende. Biofuels from microalgae—A review of technologies for production, processing, and extractions of biofuels and co-products. *Renewable and Sustainable Energy Reviews*, 14(2):557–577, February 2010. ISSN 1364-0321. .
48. Joel de la Noue and Niels de Pauw. The potential of microalgal biotechnology: A review of production and uses of microalgae. *Biotechnology Advances*, 6(4):725–770, January 1988. ISSN 0734-9750. .
49. Zahira Yaakob, Ehsan Ali, Afifi Zainal, Masita Mohamad, and Mohd Sobri Takriff. An overview: biomolecules from microalgae for animal feed and aquaculture. *Journal of Biological Research-Thessaloniki*, 21(1):6, May 2014. ISSN 2241-5793. .
50. R. Raja, S. Hemaiswarya, N. Ashok Kumar, S. Sridhar, and R. Rengasamy. A perspective on the biotechnological potential of microalgae. *Critical Reviews in Microbiology*, 34(2): 77–88, 2008. ISSN 1549-7828. .
51. Imma Gifuni, Antonino Pollio, Carl Safi, Antonio Marzocchella, and Giuseppe Olivieri. Current Bottlenecks and Challenges of the Microalgal Biorefinery. *Trends in Biotechnology*, 37(3):242–252, March 2019. ISSN 0167-7799. .
52. Bruno Sialve, Nicolas Bernet, and Olivier Bernard. Anaerobic digestion of microalgae as a necessary step to make microalgal biodiesel sustainable. July 2009.
53. Rijuta Ganesh Saratale, Gopalakrishnan Kumar, Rajesh Banu, Ao Xia, Sivagurunathan Periyasamy, and Ganesh Dattatraya Saratale. A critical review on anaerobic digestion of microalgae and macroalgae and co-digestion of biomass for enhanced methane generation. *Bioresource Technology*, 262:319–332, August 2018. ISSN 0960-8524. .
54. Glenda Cea-Barcia, Jaime Pérez, and Germán Buitrón. Co-digestion of microalga-bacteria biomass with papaya waste for methane production. *Water Science and Technology*, 78 (1):125–131, August 2018. ISSN 0273-1223. .
55. Pratima Bajpai. Production of Biofuel from Microalgae. In Pratima Bajpai, editor, *Third Generation Biofuels*, SpringerBriefs in Energy, pages 45–66. Springer Singapore, Singapore, 2019. ISBN 9789811323782. .
56. Jorge Alberto Vieira Costa and Michele Greque de Morais. The role of biochemical engineering in the production of biofuels from microalgae. *Bioresource Technology*, 102(1): 2–9, January 2011. ISSN 0960-8524. .
57. Inamuddin, Mohammad Faraz Ahmer, and Abdullah M. Asiri. *Microbial Fuel Cells: Materials and Applications*. Materials Research Forum LLC, March 2019. ISBN 978-1-64490-011-6.
58. Mathias Ahii Chia, Ana Teresa Lombardi, Maria da Graça Gama Melão, and Christopher C. Parrish. Combined nitrogen limitation and cadmium stress stimulate total carbohydrates, lipids, protein and amino acid accumulation in Chlorella vulgaris (Trebouxiophyceae). *Aquatic Toxicology*, 160:87–95, March 2015. ISSN 0166-445X. .
59. Marwa M. El-Dalatony, Mayur B. Kurade, Reda A. I. Abou-Shanab, Hoo Kim, El-Sayed Salama, and Byong-Hun Jeon. Long-term production of bioethanol in repeated-batch fermentation of microalgal biomass using immobilized Saccharomyces cerevisiae. *Bioresource Technology*, 219:98–105, November 2016. ISSN 0960-8524. .
60. Yoshiyuki Ueno, Norihide Kurano, and Shigetoh Miyachi. Ethanol production by dark fermentation in the marine green alga, Chlorococcum littorale. *Journal of Fermentation and Bioengineering*, 86(1):38–43, January 1998. ISSN 0922-338X. .
61. Cinzia Formighieri. Bioethanol from Algae Polysaccharides. In Cinzia Formighieri, edi-

tor, *Solar-to-fuel conversion in algae and cyanobacteria*, SpringerBriefs in Environmental Science, pages 13–17. Springer International Publishing, Cham, 2015. ISBN 978-3-319-16730-5. .

62. Jae-Hoon Hwang, Akhil N. Kabra, Min-Kyu Ji, Jaeyoung Choi, Marwa M. El-Dalatony, and Byong-Hun Jeon. Enhancement of continuous fermentative bioethanol production using combined treatment of mixed microalgal biomass. *Algal Research*, 17:14–20, July 2016. ISSN 2211-9264. .
63. Patrick C. Hallenbeck and John R. Benemann. Biological hydrogen production; fundamentals and limiting processes. *International Journal of Hydrogen Energy*, 27(11):1185–1193, November 2002. ISSN 0360-3199. .
64. Wanthanee Khetkorn, Rajesh P. Rastogi, Aran Incharoensakdi, Peter Lindblad, Datta Madamwar, Ashok Pandey, and Christian Larroche. Microalgal hydrogen production – A review. *Bioresource Technology*, 243:1194–1206, November 2017. ISSN 0960-8524. .
65. James B McKinlay and Caroline S Harwood. Photobiological production of hydrogen gas as a biofuel. *Current Opinion in Biotechnology*, 21(3):244–251, June 2010. ISSN 0958-1669. .
66. John R. Benemann. Hydrogen production by microalgae. *Journal of Applied Phycology*, 12(3):291–300, October 2000. ISSN 1573-5176. .
67. Melanie Oey, Anne Linda Sawyer, Ian Lawrence Ross, and Ben Hankamer. Challenges and opportunities for hydrogen production from microalgae. *Plant Biotechnology Journal*, 14(7):1487–1499, 2016. ISSN 1467-7652. .
68. Olaf Kruse and Ben Hankamer. Microalgal hydrogen production. *Current Opinion in Biotechnology*, 21(3):238–243, June 2010. ISSN 0958-1669. .
69. S Sawayama, T Minowa, and S-Y Yokoyama. Possibility of renewable energy production and CO2 mitigation by thermochemical liquefaction of microalgae. *Biomass and Bioenergy*, 17(1):33–39, July 1999. ISSN 0961-9534. .
70. John Benemann. Microalgae for Biofuels and Animal Feeds. *Energies*, 6(11):5869–5886, November 2013. .
71. Sherif Elsayed, Nikolaos Boukis, Dominik Patzelt, Stefan Hindersin, Martin Kerner, and Jörg Sauer. Gasification of Microalgae Using Supercritical Water and the Potential of Effluent Recycling. *Chemical Engineering & Technology*, 39(2):335–342, February 2016. ISSN 1521-4125. .
72. Diego López Barreiro, Wolter Prins, Frederik Ronsse, and Wim Brilman. Hydrothermal liquefaction (HTL) of microalgae for biofuel production: state of the art review and future prospects. *Biomass and Bioenergy*, 53:113–127, 2013.
73. J. Fermoso, J. M. Coronado, D. P. Serrano, and P. Pizarro. 11 - Pyrolysis of microalgae for fuel production. In Cristina Gonzalez-Fernandez and Raúl Muñoz, editors, *Microalgae-Based Biofuels and Bioproducts*, Woodhead Publishing Series in Energy, pages 259–281. Woodhead Publishing, January 2017. ISBN 978-0-08-101023-5. .
74. Muflih A. Adnan and Mohammad M. Hossain. Gasification of various biomasses including microalgae using CO2 – A thermodynamic study. *Renewable Energy*, 119:598–607, April 2018. ISSN 0960-1481. .
75. Guicai Liu, Yanfen Liao, Yuting Wu, Xiaoqian Ma, and Limei Chen. Characteristics of microalgae gasification through chemical looping in the presence of steam. *International Journal of Hydrogen Energy*, 42(36):22730–22742, September 2017. ISSN 0360-3199. .
76. Muflih A. Adnan, Herri Susanto, Housam Binous, Oki Muraza, and Mohammad M. Hossain. Feed compositions and gasification potential of several biomasses including a microalgae: A thermodynamic modeling approach. *International Journal of Hydrogen Energy*, 42(27):17009–17019, July 2017. ISSN 0360-3199. .
77. Chunxiang Chen, Xiaoqian Ma, and Kai Liu. Thermogravimetric analysis of microalgae combustion under different oxygen supply concentrations. *Applied Energy*, 88(9):3189–3196, September 2011. ISSN 0306-2619. .
78. L. Sanchez-Silva, D. López-González, A. M. Garcia-Minguillan, and J. L. Valverde. Pyrolysis, combustion and gasification characteristics of Nannochloropsis gaditana microalgae. *Bioresource Technology*, 130:321–331, February 2013. ISSN 0960-8524. .
79. Hong Il Choi, Jeong Seop Lee, Jin Won Choi, Ye Sol Shin, Young Joon Sung, Min Eui Hong, Ho Seok Kwak, Chan Young Kim, and Sang Jun Sim. Performance and potential appraisal of various microalgae as direct combustion fuel. *Bioresource Technology*, 273: 341–349, February 2019. ISSN 0960-8524. .
80. I. Rawat, R. Ranjith Kumar, T. Mutanda, and F. Bux. Biodiesel from microalgae: A critical evaluation from laboratory to large scale production. *Applied Energy*, 103:444–467, March 2013. ISSN 0306-2619. .
81. René H. Wijffels and Maria J. Barbosa. An Outlook on Microalgal Biofuels. *Science*, 329 (5993):796–799, August 2010. ISSN 0036-8075, 1095-9203. .
82. Yusuf Chisti. Biodiesel from microalgae. *Biotechnology Advances*, 25(3):294–306, May 2007. ISSN 0734-9750. .
83. Chung Hong Tan, Dillirani Nagarajan, Pau Loke Show, and Jo-Shu Chang. Chapter 25 - Biodiesel From Microalgae. In Ashok Pandey, Christian Larroche, Claude-Gilles Dussap, Edgard Gnansounou, Samir Kumar Khanal, and Steven Ricke, editors, *Biofuels: Alternative Feedstocks and Conversion Processes for the Production of Liquid and Gaseous Biofuels (Second Edition)*, Biomass, Biofuels, Biochemicals, pages 601–628. Academic Press, January 2019. ISBN 978-0-12-816856-1. .
84. G. Torzillo, B. Pushparaj, F. Bocci, W. Balloni, R. Materassi, and G. Florenzano. Production of Spirulina biomass in closed photobioreactors. *Biomass*, 11(1):61–74, January 1986. ISSN 0144-4565. .
85. M.A.C.L. de Oliveira, M.P.C. Monteiro, P.G. Robbs, and S.G.F. Leite. Growth and Chemical Composition of Spirulina Maxima and Spirulina Platensis Biomass at Different Temperatures. *Aquaculture International*, 7(4):261–275, July 1999. ISSN 1573-143X. .
86. Fedekar Fadel Madkour, Abd El-Wahab Kamil, and Hoda Shafik Nasr. Production and nutritive value of Spirulina platensis in reduced cost media. *The Egyptian Journal of Aquatic Research*, 38(1):51–57, January 2012. ISSN 1687-4285. .
87. Christa L. Colyer, Christopher S. Kinkade, Pertti J. Viskari, and James P. Landers. Analysis of cyanobacterial pigments and proteins by electrophoretic and chromatographic methods. *Analytical and Bioanalytical Chemistry*, 382(3):559–569, June 2005. ISSN 1618-2642. .
88. Ahmed Mahdy, Lara Mendez, Mercedes Ballesteros, and Cristina González-Fernández. Enhanced methane production of Chlorella vulgaris and Chlamydomonas reinhardtii by hydrolytic enzymes addition. *Energy conversion and management*, 85:551–557, 2014.
89. Jeong-Jin Park, Hongxia Wang, Mahmoud Gargouri, Rahul R. Deshpande, Jeremy N. Skepper, F. Omar Holguin, Matthew T. Juergens, Yair Shachar-Hill, Leslie M. Hicks, and David R. Gang. The response of Chlamydomonas reinhardtii to nitrogen deprivation: a systems biology analysis. *The Plant Journal*, 81(4):611–624, February 2015. ISSN 0960-7412. .
90. Mathias A. Chia, Ana T. Lombardi, and Maria Da Graca G. Melao. Growth and biochemical composition of Chlorella vulgaris in different growth media. *Anais da Academia Brasileira de Ciências*, 85(4):1427–1438, 2013.
91. Jian-Ming Lv, Li-Hua Cheng, Xin-Hua Xu, Lin Zhang, and Huan-Lin Chen. Enhanced lipid production of Chlorella vulgaris by adjustment of cultivation conditions. *Bioresource Technology*, 101(17):6797–6804, September 2010. ISSN 0960-8524. .
92. Humberto J. Morris, Angel Almarales, Olimpia Carrillo, and Rosa C. Bermúdez. Utilisation of Chlorellavulgaris cell biomass for the production of enzymatic protein hydrolysates. *Bioresource Technology*, 99(16):7723–7729, November 2008. ISSN 0960-8524. .
93. Shih-Hsin Ho, Shu-Wen Huang, Chun-Yen Chen, Tomohisa Hasunuma, Akihiko Kondo, and Jo-Shu Chang. Characterization and optimization of carbohydrate production from an indigenous microalga Chlorella vulgaris FSP-E. *Bioresource Technology*, 135:157–165, May 2013. ISSN 0960-8524. .
94. Moh Muhaemin Moh Muhaemin and Richardus F. Kaswadji. Biomass Nutrient Profiles of Marine Microalgae Dunaliella salina. *Jurnal Penelitian Sains*, 13(3), September 2010. ISSN 2597-7059.
95. Malcolm R. Brown. The amino-acid and sugar composition of 16 species of microalgae used in mariculture. *Journal of Experimental Marine Biology and Ecology*, 145(1):79–99, March 1991. ISSN 0022-0981. .
96. Asma Gnouma, Irina Sadovskaya, Anissa Souissi, Khaled Sebai, Amel Medhioub, Thierry Grard, and Sami Souissi. Changes in fatty acids profile, monosaccharide profile and protein content during batch growth of Isochrysis galbana (T.iso). *Aquaculture Research*, 48 (9):4982–4990, 2017. ISSN 1365-2109. .
97. C. Bonfanti, C. Cardoso, C. Afonso, J. Matos, T. Garcia, S. Tanni, and N. M. Bandarra. Potential of microalga Isochrysis galbana: Bioactivity and bioaccessibility. *Algal Research*, 29:242–248, January 2018. ISSN 2211-9264. .
98. John N. C. Whyte. Biochemical composition and energy content of six species of phytoplankton used in mariculture of bivalves. *Aquaculture*, 60(3):231–241, February 1987. ISSN 0044-8486. .
99. C. J. Zhu, Y. K. Lee, and T. M. Chao. Effects of temperature and growth phase on lipid and biochemical composition of Isochrysis galbana TK1. *Journal of Applied Phycology*, 9(5): 451–457, October 1997. ISSN 1573-5176. .
100. Susan M Renaud, Luong-Van Thinh, and David L Parry. The gross chemical composition and fatty acid composition of 18 species of tropical Australian microalgae for possible use in mariculture. *Aquaculture*, 170(2):147–159, January 1999. ISSN 0044-8486. .
101. Caroline R. P. S. Paes, Gabrielle R. Faria, Natália A. B. Tinoco, Dominique J. F. A. Castro, Elisabete Barbarino, and Sergio O. Lourenço. Growth, nutrient uptake and chemical composition of Chlorella sp. and Nannochloropsis oculata under nitrogen starvation. *Latin American Journal of Aquatic Research*, 44(2):275–292, 2016. ISSN 0718-560X. .
102. Soheila Sabzi, Mehdi Shamsaie Mehrgan, Houman Rajabi Islami, and Seyed Pezhman Hosseini Shekarabi. Changes in biochemical composition and fatty acid accumulation of Nannochloropsis oculata in response to different iron concentrations. *Biofuels*, 0(0):1–7, October 2018. ISSN 1759-7269. .
103. Ashiwin Vadiveloo, Navid R. Moheimani, Jeffrey J. Cosgrove, Parisa A. Bahri, and David Parlevliet. Effect of different light spectra on the growth and productivity of acclimated Nannochloropsis sp. (Eustigmatophyceae). *Algal Research*, 8:121–127, March 2015. ISSN 2211-9264. .
104. Ana M. Silva Benavides, Giuseppe Torzillo, Jiřka Kopecký, and Jiří Masojídek. Productivity and biochemical composition of Phaeodactylum tricornutum (Bacillariophyceae) cultures grown outdoors in tubular photobioreactors and open ponds. *Biomass and Bioenergy*, 54: 115–122, July 2013. ISSN 0961-9534. .
105. Qian KaiXian and Michael A. Borowitzka. Light and nitrogen deficiency effects on the growth and composition ofPhaeodactylum tricornutum. *Applied Biochemistry and Biotechnology*, 38(1):93–103, January 1993. ISSN 1559-0291. .
106. M. del Pilar Sánchez-Saavedra, Fátima Y. Castro-Ochoa, Viridiana Margarita Nava-Ruiz, Duahmet A. Ruiz-Güereca, Ana Laura Villagómez-Aranda, Fabián Siqueiros-Vargas, and Ceres A. Molina-Cárdenas. Effects of nitrogen source and irradiance on Porphyridium cruentum. *Journal of Applied Phycology*, 30(2):783–792, April 2018. ISSN 1573-5176. .
107. Seong-Joo Hong, Yong Sung Park, Mi-Ae Han, Z.-Hun Kim, Byung-Kwan Cho, Hookeun Lee, Hyung-Kyoon Choi, and Choul-Gyun Lee. Enhanced production of fatty acids in three strains of microalgae using a combination of nitrogen starvation and chemical inhibitors of carbohydrate synthesis. *Biotechnology and Bioprocess Engineering*, 22(1):60–67, February 2017. ISSN 1976-3816. .
108. M. M Rebolloso Fuentes, G. G Acién Fernández, J. A Sánchez Pérez, and J. L Guil Guerrero. Biomass nutrient profiles of the microalga Porphyridium cruentum. *Food Chemistry*, 70(3):345–353, August 2000. ISSN 0308-8146. .
109. Shih-Hsin Ho, Chun-Yen Chen, and Jo-Shu Chang. Effect of light intensity and nitrogen starvation on CO2 fixation and lipid/carbohydrate production of an indigenous microalga Scenedesmus obliquus CNW-N. *Bioresource Technology*, 113:244–252, June 2012. ISSN 0960-8524. .
110. Seung Phill Choi, Minh Thu Nguyen, and Sang Jun Sim. Enzymatic pretreatment of Chlamydomonas reinhardtii biomass for ethanol production. *Bioresource Technology*, 101 (14):5330–5336, July 2010. ISSN 0960-8524. .
111. Drora Kaplan, Zvi Cohen, and Aharon Abeliovich. Optimal growth conditions for Isochrysis galbana. *Biomass*, 9(1):37–48, January 1986. ISSN 0144-4565. .
112. Jaime Fábregas, Ana Maseda, Adolfo Domínguez, and Ana Otero. The cell composition of Nannochloropsis sp. changes under different irradiances in semicontinuous culture. *World Journal of Microbiology and Biotechnology*, 20(1):31–35, February 2004. ISSN 1573-0972. .
113. E. Ponis, I. Probert, B. Véron, J. R. Le Coz, M. Mathieu, and R. Robert. Nutritional value of

six Pavlovophyceae for Crassostrea gigas and Pecten maximus larvae. *Aquaculture*, 254 (1):544–553, April 2006. ISSN 0044-8486. .

114. Iv Vasileva and J. Ivanova. BIOCHEMICAL PROFILE OF GREEN AND RED ALGAE–A KEY FOR UNDERSTANDING THEIR POTENTIAL APPLICATION AS FOOD ADDITIVES. *Trakia Journal of Sciences*, 17(1):1, 2019.
115. Barbara Gris, Tomas Morosinotto, Giorgio M. Giacometti, Alberto Bertucco, and Eleonora Sforza. Cultivation of Scenedesmus obliquus in Photobioreactors: Effects of Light Intensities and Light–Dark Cycles on Growth, Productivity, and Biochemical Composition. *Applied Biochemistry and Biotechnology*, 172(5):2377–2389, March 2014. ISSN 1559-0291. .
116. El-Sayed Salama, Hyun-Chul Kim, Reda A. I. Abou-Shanab, Min-Kyu Ji, You-Kwan Oh, Seong-Heon Kim, and Byong-Hun Jeon. Biomass, lipid content, and fatty acid composition of freshwater Chlamydomonas mexicana and Scenedesmus obliquus grown under salt stress. *Bioprocess and Biosystems Engineering*, 36(6):827–833, June 2013. ISSN 1615-7605. .
117. Imran Pancha, Kaumeel Chokshi, Basil George, Tonmoy Ghosh, Chetan Paliwal, Rahulkumar Maurya, and Sandhya Mishra. Nitrogen stress triggered biochemical and morphological changes in the microalgae Scenedesmus sp. CCNM 1077. *Bioresource Technology*, 156:146–154, March 2014. ISSN 0960-8524. .
118. Garam Kim, Ghulam Mujtaba, Kisay Lee, Garam Kim, Ghulam Mujtaba, and Kisay Lee. Effects of nitrogen sources on cell growth and biochemical composition of marine chlorophyte \textlessitalic\textgreaterTetraselmis\textless/italic\textgreater sp. for lipid production. *ALGAE*, 31(3):257–266, September 2016. ISSN 1226-2617, 2093-0860. .
119. Scott D. Doughman, Srirama Krupanidhi, and Carani B. Sanjeevi. Omega-3 fatty acids for nutrition and medicine: considering microalgae oil as a vegetarian source of EPA and DHA. *Current Diabetes Reviews*, 3(3):198–203, August 2007. ISSN 1573-3998.
120. T Catalina Adarme-Vega, David K Y Lim, Matthew Timmins, Felicitas Vernen, Yan Li, and Peer M Schenk. Microalgal biofactories: a promising approach towards sustainable omega-3 fatty acid production. *Microbial Cell Factories*, 11:96, July 2012. ISSN 1475-2859. .
121. OW US EPA. *2017 EPA-FDA Advice about Eating Fish and Shellfish*. July 2015.
122. Ejovwokoghene C. Odjadjare, Taurai Mutanda, and Ademola O. Olaniran. Potential biotechnological application of microalgae: a critical review. *Critical Reviews in Biotechnology*, 37(1):37–52, January 2017. ISSN 0738-8551. .
123. Jean-Yves Berthon, Rachida Nachat-Kappes, Mathieu Bey, Jean-Paul Cadoret, Isabelle Renimel, and Edith Filaire. Marine algae as attractive source to skin care. *Free Radical Research*, 51(6):555–567, June 2017. ISSN 1029-2470. .
124. Luísa Gouveia, Ana Evangelista Marques, João M. Sousa, Patrícia Moura, and Narcisa Bandarra. Microalgae – source of natural bioactive molecules as functional ingredients. *Food Science & Technology Bulletin: Functional Foods*, 7:21–37, June 2010. .
125. Isabel Sousa, L. Gouveia, Ana Paula Batista, Anabela Raymundo, and N. M. Bandarra. Microalgae in novel food products. *Food Chemistry Research Developments*, pages 75–112, 2008.
126. María Lourdes Mourelle, Carmen Gómez, and José L. Legido. The Potential Use of Marine Microalgae and Cyanobacteria in Cosmetics and Thalassotherapy. *Cosmetics*, 4:46, November 2017. .
127. Gatamaneni Loganathan Bhalamur, Orsat Valerie, and Lefsrud Mark. Valuable bioproducts obtained from microalgal biomass and their commercial applications: A review. *Environmental Engineering Research*, 23(3):229–241, September 2018. ISSN 1226-1025.
128. Abdul Bakrudeen Ali Ahmed, Mohaddeseh Adel, Pegah Karimi, and Mahvash Peidayesh. Chapter Ten - Pharmaceutical, Cosmeceutical, and Traditional Applications of Marine Carbohydrates. In Se-Kwon Kim, editor, *Advances in Food and Nutrition Research*, volume 73 of *Marine Carbohydrates: Fundamentals and Applications, Part B*, pages 197–220. Academic Press, January 2014. .
129. Ana Martins, Helena Vieira, Helena Gaspar, Susana Santos, Ana Martins, Helena Vieira, Helena Gaspar, and Susana Santos. Marketed Marine Natural Products in the Pharmaceutical and Cosmeceutical Industries: Tips for Success. *Marine Drugs*, 12(2):1066–1101, February 2014. .
130. Vazhiyil Venugopal. *Marine polysaccharides: Food applications*. CRC Press, 2016. ISBN 1-4398-1527-5.
131. E. W. Becker. Micro-algae as a source of protein. *Biotechnology Advances*, 25(2):207–210, March 2007. ISSN 0734-9750. .
132. Thanh-Sang Vo, BoMi Ryu, and Se-Kwon Kim. Purification of novel anti-inflammatory peptides from enzymatic hydrolysate of the edible microalgal Spirulina maxima. *Journal of Functional Foods*, 5(3):1336–1346, July 2013. ISSN 1756-4646. .
133. S. Sadeghi, H. Jalili, S. O. Ranaei Siadat, and M. Sedighi. Anticancer and Antibacterial Properties in Peptide Fractions from Hydrolyzed Spirulina Protein. *Journal of Agricultural Science and Technology*, 20(4):673–683, October 2018.
134. I.-Chuan Sheih, Tung-Kung Wu, and Tony J. Fang. Antioxidant properties of a new antioxidative peptide from algae protein waste hydrolysate in different oxidation systems. *Bioresource Technology*, 100(13):3419–3425, July 2009. ISSN 1873-2976. .
135. Se-Kwon Kim and Kyong-Hwa Kang. Chapter 25 - Medicinal Effects of Peptides from Marine Microalgae. In Se-Kwon Kim, editor, *Advances in Food and Nutrition Research*, volume 64 of *Marine Medicinal Foods*, pages 313–323. Academic Press, January 2011. .
136. Patrick Stolz. Manufacturing microalgae for skin care. *Cosmetics Toiletries*, 120:99–106, March 2005.
137. Tom M. M. Bernaerts, Lore Gheysen, Imogen Foubert, Marc E. Hendrickx, and Ann M. Van Loey. The potential of microalgae and their biopolymers as structuring ingredients in food: A review. *Biotechnology Advances*, page 107419, July 2019. ISSN 0734-9750. .
138. Yangmin Gong, Hanhua Hu, Yuan Gao, Xudong Xu, and Hong Gao. Microalgae as platforms for production of recombinant proteins and valuable compounds: progress and prospects. *Journal of Industrial Microbiology & Biotechnology*, 38(12):1879–1890, December 2011. ISSN 1476-5535. .
139. Chelsea Dixon and Lisa R. Wilken. Green microalgae biomolecule separations and recovery. *Bioresources and Bioprocessing*, 5:14, March 2018. ISSN 2197-4365. .
140. Christian Galasso, Antonio Gentile, Ida Orefice, Adrianna Ianora, Antonino Bruno, Douglas M. Noonan, Clementina Sansone, Adriana Albini, and Christophe Brunet. Microalgal Derivatives as Potential Nutraceutical and Food Supplements for Human Health: A Focus on Cancer Prevention and Interception. *Nutrients*, 11(6):1226, June 2019. .
141. Hua-Bin Li, Ka-Wing Cheng, Chi-Chun Wong, King-Wai Fan, Feng Chen, and Yue Jiang. Evaluation of antioxidant capacity and total phenolic content of different fractions of selected microalgae. *Food Chemistry*, 102(3):771–776, January 2007. ISSN 0308-8146. .
142. Manuel Gómez-Guzmán, Alba Rodríguez-Nogales, Francesca Algieri, and Julio Gálvez. Potential Role of Seaweed Polyphenols in Cardiovascular-Associated Disorders. *Marine Drugs*, 16(8):250, August 2018. .
143. Priscila Tessmer Scaglioni, Sabrina de Oliveira Garcia, and Eliana Badiale-Furlong. Inhibition of in vitro trichothecenes production by microalgae phenolic extracts. *Food Research International*, 124:175–180, October 2019. ISSN 0963-9969. .
144. T. A. Woyengo, V. R. Ramprasath, and P. J. H. Jones. Anticancer effects of phytosterols. *European Journal of Clinical Nutrition*, 63(7):813–820, July 2009. ISSN 1476-5640. .
145. David Kritchevsky and Shirley C. Chen. Phytosterols—health benefits and potential concerns: a review. *Nutrition Research*, 25(5):413–428, May 2005. ISSN 0271-5317. .
146. Hyun-Jin Kim, Xiaotang Fan, Chiara Gabbi, Konstantin Yakimchuk, Paolo Parini, Margaret Warner, and Jan-Åke Gustafsson. Liver X receptor β (LXRβ): A link between β-sitosterol and amyotrophic lateral sclerosis–Parkinson's dementia. *Proceedings of the National Academy of Sciences*, 105(6):2094–2099, February 2008. ISSN 0027-8424, 1091-6490. .
147. Faruq Ahmed, Wenxu Zhou, and Peer M. Schenk. Pavlova lutheri is a high-level producer of phytosterols. *Algal research*, 10:210–217, 2015.
148. Food and Agriculture Organization of the United Nations. Fats and fatty acids in human nutrition: report of an expert consultation. *FAO Food Nutr Pap*, 91:1–166, 2010.
149. Meharban Singh. Essential fatty acids, DHA and human brain. *The Indian Journal of Pediatrics*, 72(3):239–242, March 2005. ISSN 0973-7693. .
150. David H. Jho, Shawn M. Cole, Ellyn M. Lee, and N. Joseph Espat. Role of Omega-3 Fatty Acid Supplementation in Inflammation and Malignancy. *Integrative Cancer Therapies*, 3 (2):98–111, June 2004. ISSN 1534-7354. .
151. Abhishek Sahu, Imran Pancha, Deepti Jain, Chetan Paliwal, Tonmoy Ghosh, Shailesh Patidar, Sourish Bhattacharya, and Sandhya Mishra. Fatty acids as biomarkers of microalgae. *Phytochemistry*, 89:53–58, May 2013. ISSN 0031-9422. .
152. B. Ramesh Kumar, Garlapati Deviram, Thangavel Mathimani, Pham Anh Duc, and Arivalagan Pugazhendhi. Microalgae as rich source of polyunsaturated fatty acids. *Biocatalysis and Agricultural Biotechnology*, 17:583–588, January 2019. ISSN 1878-8181. .
153. Xinxin Wang, Hilde Karoline Fosse, Keshuai Li, Matilde Skogen Chauton, Olav Vadstein, and Kjell Inge Reitan. Influence of nitrogen limitation on lipid accumulation and EPA and DHA content in four marine microalgae for possible use in aquafeed. *Frontiers in Marine Science*, March 2019. ISSN 2296-7745. .
154. Xiao-Man Sun, Ling-Jun Geng, Lu-Jing Ren, Xiao-Jun Ji, Ning Hao, Ke-Quan Chen, and He Huang. Influence of oxygen on the biosynthesis of polyunsaturated fatty acids in microalgae. *Bioresource Technology*, 250:868–876, February 2018. ISSN 0960-8524. .
155. Seshagiri Raghukumar. Thraustochytrid Marine Protists: Production of PUFAs and Other Emerging Technologies. *Marine Biotechnology*, 10(6):631–640, December 2008. ISSN 1436-2236. .
156. Owen P. Ward and Ajay Singh. Omega-3/6 fatty acids: Alternative sources of production. *Process Biochemistry*, 40(12):3627–3652, December 2005. ISSN 1359-5113. .
157. Robert J. Winwood. Recent developments in the commercial production of DHA and EPA rich oils from micro-algae. *OCL*, 20(6):D604, November 2013. ISSN 2257-6614. .
158. Deniz Sahin, Ezgi Tas, and Ulkü Hüma Altindag. Enhancement of docosahexaenoic acid (DHA) production from Schizochytrium sp. S31 using different growth medium conditions. *AMB Express*, 8, January 2018. ISSN 2191-0855. .
159. Razif Harun, Manjinder Singh, Gareth M. Forde, and Michael K. Danquah. Bioprocess engineering of microalgae to produce a variety of consumer products. *Renewable and Sustainable Energy Reviews*, 14(3):1037–1047, April 2010. ISSN 1364-0321. .
160. Veronica da Silva Ferreira and Celso Sant'Anna. Impact of culture conditions on the chlorophyll content of microalgae for biotechnological applications. *World Journal of Microbiology and Biotechnology*, 33(1):20, December 2016. ISSN 1573-0972. .
161. Qiaoning He, Haijian Yang, Lei Wu, and Chunxiang Hu. Effect of light intensity on physiological changes, carbon allocation and neutral lipid accumulation in oleaginous microalgae. *Bioresource Technology*, 191:219–228, September 2015. ISSN 1873-2976. .
162. V.s. Ferreira, R.f. Pinto, and C. Sant'Anna. Low light intensity and nitrogen starvation modulate the chlorophyll content of Scenedesmus dimorphus. *Journal of Applied Microbiology*, 120(3):661–670, March 2016. ISSN 1364-5072. .
163. Seyedeh Fatemeh Mohsenpour, Bryce Richards, and Nik Willoughby. Spectral conversion of light for enhanced microalgae growth rates and photosynthetic pigment production. *Bioresource Technology*, 125(Supplement C):75–81, December 2012. ISSN 0960-8524. .
164. Vanessa Daneluz Gonçalves, Marcia Regina Fagundes-Klen, Daniela Estelita Goes Trigueros, Alexander Dimitrov Kroumov, and Aparecido Nivaldo Módenes. Statistical and optimization strategies to carotenoids production by Tetradesmus acuminatus (LC192133.1) cultivated in photobioreactors. *Biochemical Engineering Journal*, 152: 107351, December 2019. ISSN 1369-703X. .
165. Wendie Levasseur, Behnam Taidi, Robin Lacombe, Patrick Perré, and Victor Pozzobon. Impact of seconds to minutes photoperiods on Chlorella vulgaris growth rate and chlorophyll a and b content. *Algal Research*, 36:10–16, December 2018. ISSN 2211-9264. .
166. Mengyue Gong and Amarjeet Bassi. Carotenoids from microalgae: A review of recent developments. *Biotechnology Advances*, 34(8):1396–1412, December 2016. ISSN 0734-9750. .
167. Robert Edward Lee. *Phycology*. Cambridge University Press, March 2018. ISBN 978-1-107-55565-5.
168. M. N. Rammuni, Thilini U. Ariyadasa, P. H. V. Nimarshana, and R. A. Attalage. Comparative assessment on the extraction of carotenoids from microalgal sources: Astaxanthin from H. pluvialis and β-carotene from D. salina. *Food Chemistry*, 277:128–134, March 2019. ISSN 0308-8146. .
169. Antonio Molino, Angela Iovine, Patrizia Casella, Sanjeet Mehariya, Simeone Chianese,

Antonietta Cerbone, Juri Rimauro, and Dino Musmarra. Microalgae Characterization for Consolidated and New Application in Human Food, Animal Feed and Nutraceuticals. *International Journal of Environmental Research and Public Health*, 15(11):2436, November 2018. .

170. Maria Filomena de Jesus Raposo, Alcina Maria Miranda Bernardo de Morais, and Rui Manuel Santos Costa de Morais. Carotenoids from Marine Microalgae: A Valuable Natural Source for the Prevention of Chronic Diseases. *Marine Drugs*, 13(8):5128–5155, August 2015. ISSN 1660-3397. .
171. Antonio Molino, Juri Rimauro, Patrizia Casella, Antonietta Cerbone, Vincenzo Larocca, Simeone Chianese, Despina Karatza, Sanjeet Mehariya, Angelo Ferraro, Evangelos Hristoforou, and Dino Musmarra. Extraction of astaxanthin from microalga Haematococcus pluvialis in red phase by using generally recognized as safe solvents and accelerated extraction. *Journal of Biotechnology*, 283:51–61, October 2018. ISSN 0168-1656. .
172. Joan E. Roberts and Jessica Dennison. The photobiology of lutein and zeaxanthin in the eye. *Journal of ophthalmology*, 2015, 2015.
173. Jian-Hao Lin, Duu-Jong Lee, and Jo-Shu Chang. Lutein production from biomass: Marigold flowers versus microalgae. *Bioresource Technology*, 184:421–428, May 2015. ISSN 0960-8524. .
174. S. (Malis) Arad and A. Yaron. Natural pigments from red microalgae for use in foods and cosmetics. *Trends in Food Science & Technology*, 3:92–97, January 1992. ISSN 0924-2244. .
175. J Masojidek, Michal Koblizek, and Giuseppe Torzillo. Photosynthesis in Microalgae. *Handbook of Microalgal Culture: Biotechnology and Applied Phycology*, pages 20–39, April 2013. .
176. Emmanuel Manirafasha, Theoneste Ndikubwimana, Xianhai Zeng, Yinghua Lu, and Keju Jing. Phycobiliprotein: Potential microalgae derived pharmaceutical and biological reagent. *Biochemical Engineering Journal*, 109:282–296, May 2016. ISSN 1369-703X. .
177. Helena Khatoon, Lai Kok Leong, Norazira Abdu Rahman, Sohel Mian, Hasina Begum, Sanjoy Banerjee, and Azizah Endut. Effects of different light source and media on growth and production of phycobiliprotein from freshwater cyanobacteria. *Bioresource Technology*, 249:652–658, February 2018. ISSN 0960-8524. .
178. Nesrine Gargouch, Ines Karkouch, Jihen Elleuch, Salem Elkahoui, Phillipe Michaud, Slim Abdelkafi, Céline Laroche, and Imen Fendri. Enhanced B-phycoerythrin production by the red microalga Porphyridium marinum: A powerful agent in industrial applications. *International Journal of Biological Macromolecules*, 120:2106–2114, December 2018. ISSN 0141-8130. .
179. Shih-Hsin Ho, Jing-Fu Liao, Chun-Yen Chen, and Jo-Shu Chang. Combining light strategies with recycled medium to enhance the economic feasibility of phycocyanin production with Spirulina platensis. *Bioresource Technology*, 247:669–675, January 2018. ISSN 0960-8524. .
180. Hong-Wei Yen, I. Chen Hu, Chun-Yen Chen, Shih-Hsin Ho, Duu-Jong Lee, and Jo-Shu Chang. Microalgae-based biorefinery – From biofuels to natural products. *Bioresource Technology*, 135:166–174, May 2013. ISSN 0960-8524. .
181. Olivier Pignolet, Sébastien Jubeau, Carlos Vaca-Garcia, and Philippe Michaud. Highly valuable microalgae: biochemical and topological aspects. *Journal of Industrial Microbiology & Biotechnology*, 40(8):781–796, August 2013. ISSN 1476-5535. .
182. Giorgos Markou, Irini Angelidaki, and Dimitris Georgakakis. Microalgal carbohydrates: an overview of the factors influencing carbohydrates production, and of main bioconversion technologies for production of biofuels. *Applied Microbiology and Biotechnology*, 96(3): 631–645, November 2012. ISSN 1432-0614. .
183. Tom M. M. Bernaerts, Lore Gheysen, Clare Kyomugasho, Zahra Jamsazzadeh Kermani, Stéphanie Vandionant, Imogen Foubert, Marc E. Hendrickx, and Ann M. Van Loey. Comparison of microalgal biomasses as functional food ingredients: Focus on the composition of cell wall related polysaccharides. *Algal Research*, 32:150–161, June 2018. ISSN 2211-9264. .
184. Cristina González-Fernández and Mercedes Ballesteros. Linking microalgae and cyanobacteria culture conditions and key-enzymes for carbohydrate accumulation. *Biotechnology Advances*, 30(6):1655–1661, November 2012. ISSN 0734-9750. .
185. Giuliano Dragone, Bruno D. Fernandes, Ana P. Abreu, António A. Vicente, and José A. Teixeira. Nutrient limitation as a strategy for increasing starch accumulation in microalgae. *Applied Energy*, 88(10):3331–3335, October 2011. ISSN 0306-2619. .
186. S. Venkata Mohan and M. Prathima Devi. Salinity stress induced lipid synthesis to harness biodiesel during dual mode cultivation of mixotrophic microalgae. *Bioresource Technology*, 165:288–294, August 2014. ISSN 0960-8524. .
187. G. Venkata Subhash, M. V. Rohit, M. Prathima Devi, Y. V. Swamy, and S. Venkata Mohan. Temperature induced stress influence on biodiesel productivity during mixotrophic microalgae cultivation with wastewater. *Bioresource Technology*, 169:789–793, October 2014. ISSN 0960-8524. .
188. Fei Han, Haiyan Pei, Wenrong Hu, Lin Han, Shuo Zhang, and Guixia Ma. Effect of high-temperature stress on microalgae at the end of the logarithmic phase for the efficient production of lipid. *Environmental Technology*, 37(20):2649–2657, October 2016. ISSN 0959-3330. .
189. Maria Filomena de Jesus Raposo, Rui Manuel Santos Costa De Morais, and Alcina Maria Miranda Bernardo de Morais. Bioactivity and Applications of Sulphated Polysaccharides from Marine Microalgae. *Marine Drugs*, 11(1):233–252, January 2013. .
190. E. D'Hondt, J. Martín-Juárez, S. Bolado, J. Kasperoviciene, J. Koreiviene, S. Sulcius, K. Elst, and L. Bastiaens. 6 - Cell disruption technologies. In Cristina Gonzalez-Fernandez and Raúl Muñoz, editors, *Microalgae-Based Biofuels and Bioproducts*, Woodhead Publishing Series in Energy, pages 133–154. Woodhead Publishing, January 2017. ISBN 978-0-08-101023-5. .
191. Chun-Yen Chen, Xin-Qing Zhao, Hong-Wei Yen, Shih-Hsin Ho, Chieh-Lun Cheng, Duu-Jong Lee, Feng-Wu Bai, and Jo-Shu Chang. Microalgae-based carbohydrates for biofuel production. *Biochemical Engineering Journal*, 78:1–10, September 2013. ISSN 1369-703X. .
192. Cédric Delattre, Guillaume Pierre, Céline Laroche, and Philippe Michaud. Production, extraction and characterization of microalgal and cyanobacterial exopolysaccharides. *Biotechnology Advances*, 34(7):1159–1179, November 2016. ISSN 0734-9750. .
193. David W. Templeton, Matthew Quinn, Stefanie Van Wychen, Deborah Hyman, and Lieve M. L. Laurens. Separation and quantification of microalgal carbohydrates. *Journal of Chromatography A*, 1270:225–234, December 2012. ISSN 0021-9673. .
194. S. Geresh and S. Arad. The extracellular polysaccharides of the red microalgae: Chemistry and rheology. *Bioresource Technology*, 38(2):195–201, January 1991. ISSN 0960-8524. .
195. Rui Xiao and Yi Zheng. Overview of microalgal extracellular polymeric substances (EPS) and their applications. *Biotechnology Advances*, 34(7):1225–1244, November 2016. ISSN 0734-9750. .
196. F. M. Lupi, H. M. L. Fernandes, M. M. Tomé, I. Sá-Correia, and J. M. Novais. Influence of nitrogen source and photoperiod on exopolysaccharide synthesis by the microalga Botryococcus braunii UC 58. *Enzyme and Microbial Technology*, 16(7):546–550, July 1994. ISSN 0141-0229. .
197. Azadeh Kermanshahi-pour, Toby J. Sommer, Paul T. Anastas, and Julie B. Zimmerman. Enzymatic and acid hydrolysis of Tetraselmis suecica for polysaccharide characterization. *Bioresource Technology*, 173:415–421, December 2014. ISSN 0960-8524. .
198. Lamia Trabelsi, Hatem Ben Ouada, Hassen Bacha, and Mohamed Ghoul. Combined effect of temperature and light intensity on growth and extracellular polymeric substance production by the cyanobacterium Arthrospira platensis. *Journal of Applied Phycology*, 21 (4):405–412, August 2009. ISSN 1573-5176. .
199. Pei-pei Han, Ying Sun, Shi-ru Jia, Cheng Zhong, and Zhi-lei Tan. Effects of light wavelengths on extracellular and capsular polysaccharide production by Nostoc flagelliforme. *Carbohydrate Polymers*, 105:145–151, May 2014. ISSN 0144-8617. .
200. Y.-S. Cheng, J. M. Labavitch, and J. S. VanderGheynst. Elevated CO2 concentration impacts cell wall polysaccharide composition of green microalgae of the genus Chlorella. *Letters in Applied Microbiology*, 60(1):1–7, 2015. ISSN 1472-765X. .
201. E. Conde, E. M. Balboa, M. Parada, and E. Falqué. 4 - Algal proteins, peptides and amino acids. In Herminia Domínguez, editor, *Functional Ingredients from Algae for Foods and Nutraceuticals*, Woodhead Publishing Series in Food Science, Technology and Nutrition, pages 135–180. Woodhead Publishing, January 2013. ISBN 978-0-85709-512-1. .
202. Alberto Niccolai, Graziella Chini Zittelli, Liliana Rodolfi, Natascia Biondi, and Mario R. Tredici. Microalgae of interest as food source: Biochemical composition and digestibility. *Algal Research*, 42:101617, September 2019. ISSN 2211-9264. .
203. Katharina Judith Wild, Herbert Steingaß, and Markus Rodehutscord. Variability in nutrient composition and in vitro crude protein digestibility of 16 microalgae products. *Journal of Animal Physiology and Animal Nutrition*, 102(5):1306–1319, 2018. ISSN 1439-0396. .
204. Ayse Kose, Mehmet O. Ozen, Murat Elibol, and Suphi S. Oncel. Investigation of in vitro digestibility of dietary microalga Chlorella vulgaris and cyanobacterium Spirulina platensis as a nutritional supplement. *3 Biotech*, 7(3):170, June 2017. ISSN 2190-5738. .
205. Fabio Apone, Ani Barbulova, and Maria Gabriella Colucci. Plant and Microalgae Derived Peptides Are Advantageously Employed as Bioactive Compounds in Cosmetics. *Frontiers in Plant Science*, 10, 2019. ISSN 1664-462X. .
206. Chukwunonso E. C. C. Ejike, Stephanie A. Collins, Nileeka Balasuriya, Andrew K. Swanson, Beth Mason, and Chibuike C. Udenigwe. Prospects of microalgae proteins in producing peptide-based functional foods for promoting cardiovascular health. *Trends in Food Science & Technology*, 59:30–36, January 2017. ISSN 0924-2244. .
207. Seok-Chun Ko, Daekyung Kim, and You-Jin Jeon. Protective effect of a novel antioxidative peptide purified from a marine Chlorella ellipsoidea protein against free radical-induced oxidative stress. *Food and Chemical Toxicology*, 50(7):2294–2302, July 2012. ISSN 0278-6915. .
208. Seok-Chun Ko, Nalae Kang, Eun-A. Kim, Min Cheol Kang, Seung-Hong Lee, Sung-Myung Kang, Joon-Baek Lee, Byong-Tae Jeon, Se-Kwon Kim, Sun-Joo Park, Pyo-Jam Park, Won-Kyo Jung, Daekyung Kim, and You-Jin Jeon. A novel angiotensin I-converting enzyme (ACE) inhibitory peptide from a marine Chlorella ellipsoidea and its antihypertensive effect in spontaneously hypertensive rats. *Process Biochemistry*, 47(12):2005–2011, December 2012. ISSN 1359-5113. .
209. Kunio Suetsuna and Jiun-Rong Chen. Identification of Antihypertensive Peptides from Peptic Digest of Two Microalgae, Chlorella vulgaris and Spirulina platensis. *Marine Biotechnology*, 3(4):305–309, July 2001. ISSN 1436-2228. .
210. Maliheh Darvish, Hasan Jalili, Seyed-Omid Ranaei-Siadat, and Mahsa Sedighi. Potential cytotoxic effects of peptide fractions from Dunaliella salina protein hydrolyzed by gastric proteases. *Journal of aquatic food product technology*, 27(2):165–175, 2018.
211. Ines Barkia, Hanen Ketata Bouaziz, Tahiya Sellami Boudawara, Lotfi Aleya, Ali Faouzi Gargouri, and Nazamid Saari. Acute oral toxicity study on Wistar rats fed microalgal protein hydrolysates from Bellerochea malleus. *Environmental Science and Pollution Research*, January 2019. ISSN 1614-7499. .
212. Jaime Fabregas and Concepcion Herrero. Vitamin content of four marine microalgae. Potential use as source of vitamins in nutrition. *Journal of Industrial Microbiology*, 5(4): 259–263, June 1990. ISSN 0169-4146, 1476-5535. .
213. Yannick De Roeck-Holtzhauer, Isabelle Quere, and Corinne Claire. Vitamin analysis of five planktonic microalgae and one macroalga. *Journal of Applied Phycology*, 3(3):259–264, September 1991. ISSN 1573-5176. .
214. Peter Coutteau and Patrick Sorgeloos. Manipulation of dietary lipids, fatty acids and vitamins in zooplankton cultures. *Freshwater Biology*, 38(3):501–512, December 1997. ISSN 1365-2427. .
215. M.R. Brown, M. Mular, I. Miller, C. Farmer, and C. Trenerry. The vitamin content of microalgae used in aquaculture. *Journal of Applied Phycology*, 11(3):247–255, June 1999. ISSN 1573-5176. .
216. Malcolm R. Brown and Christine L. Farmer. Riboflavin content of six species of microalgae used in mariculture. *Journal of Applied Phycology*, 6(1):61–65, February 1994. ISSN 1573-5176. .
217. Maria J. Barbosa, Jan Willem Zijffers, Adrian Nisworo, Woulter Vaes, Jan van Schoonhoven, and René H. Wijffels. Optimization of biomass, vitamins, and carotenoid yield on light energy in a flat-panel reactor using the A-stat technique. *Biotechnology and Bioengineering*, 89(2):233–242, January 2005. ISSN 0006-3592. .
218. Eira C. Carballo-Cárdenas, Pham Minh Tuan, Marcel Janssen, and René H. Wijffels. Vi-

tamin E (α-tocopherol) production by the marine microalgae Dunaliella tertiolecta and Tetraselmis suecica in batch cultivation. *Biomolecular Engineering*, 20(4):139–147, July 2003. ISSN 1389-0344. .

219. Yaşar Durmaz. Vitamin E (α-tocopherol) production by the marine microalgae Nannochloropsis oculata (Eustigmatophyceae) in nitrogen limitation. *Aquaculture*, 272(1):717–722, November 2007. ISSN 0044-8486. .
220. Minnamari Edelmann, Sanni Aalto, Bhawani Chamlagain, Susanna Kariluoto, and Vieno Piironen. Riboflavin, niacin, folate and vitamin B12 in commercial microalgae powders. *Journal of Food Composition and Analysis*, 82:103226, September 2019. ISSN 0889-1575. .
221. Thomas D. C. Tarento, Dale D. McClure, Emily Vasiljevski, Aaron Schindeler, Fariba Dehghani, and John M. Kavanagh. Microalgae as a source of vitamin K1. *Algal Research*, 36:77–87, December 2018. ISSN 2211-9264. .
222. Apurav Krishna Koyande, Kit Wayne Chew, Krishnamoorthy Rambabu, Yang Tao, Dinh-Toi Chu, and Pau-Loke Show. Microalgae: A potential alternative to health supplementation for humans. *Food Science and Human Wellness*, 8(1):16–24, March 2019. ISSN 2213-4530. .
223. Lidia Montero, Andrea del Pilar Sánchez-Camargo, Elena Ibáñez, and Bienvenida Gilbert-López. Phenolic compounds from edible algae: Bioactivity and health benefits. *Current medicinal chemistry*, 25(37):4808–4826, 2018.
224. Koen Goiris, Koenraad Muylaert, Ilse Fraeye, Imogen Foubert, Jos De Brabanter, and Luc De Cooman. Antioxidant potential of microalgae in relation to their phenolic and carotenoid content. *Journal of Applied Phycology*, 24(6):1477–1486, December 2012. ISSN 1573-5176. .
225. Joana Matos, Carlos L. Cardoso, Pedro Falé, Cláudia M. Afonso, and Narcisa M. Bandarra. Investigation of nutraceutical potential of the microalgae Chlorella vulgaris and Arthrospira platensis. *International Journal of Food Science & Technology*, 2019.
226. Claudine Manach, Augustin Scalbert, Christine Morand, Christian Rémésy, and Liliana Jiménez. Polyphenols: food sources and bioavailability. *The American Journal of Clinical Nutrition*, 79(5):727–747, May 2004. ISSN 0002-9165. .
227. J. Volkman. Sterols in microorganisms. *Applied Microbiology and Biotechnology*, 60(5): 495–506, January 2003. ISSN 1432-0614. .
228. Manon Le Goff, Eric Le Ferrec, Claire Mayer, Virginie Mimouni, Dominique Lagadic-Gossmann, Benoît Schoefs, and Lionel Ulmann. Microalgal carotenoids and phytosterols regulate biochemical mechanisms involved in human health and disease prevention. *Biochimie*, 167:106–118, December 2019. ISSN 0300-9084. .
229. Yandu Lu and Jian Xu. Phytohormones in microalgae: a new opportunity for microalgal biotechnology? *Trends in Plant Science*, 20(5):273–282, May 2015. ISSN 1360-1385. .
230. Andrzej Bajguz. Brassinosteroids in Microalgae: Application for Growth Improvement and Protection Against Abiotic Stresses. In Shamsul Hayat, Mohammad Yusuf, Renu Bhardwaj, and Andrzej Bajguz, editors, *Brassinosteroids: Plant Growth and Development*, pages 45–58. Springer Singapore, Singapore, 2019. ISBN 9789811360589. .
231. Khondokar M. Rahman. Food and High Value Products from Microalgae: Market Opportunities and Challenges. In Md. Asraful Alam, Jing-Liang Xu, and Zhongming Wang, editors, *Microalgae Biotechnology for Food, Health and High Value Products*, pages 3–27. Springer, Singapore, 2020. ISBN 9789811501692. .
232. Nethravathy M. U, Jitendra G. Mehar, Sandeep N. Mudliar, and Ajam Y. Shekh. Recent Advances in Microalgal Bioactives for Food, Feed, and Healthcare Products: Commercial Potential, Market Space, and Sustainability. *Comprehensive Reviews in Food Science and Food Safety*, 18(6):1882–1897, 2019. ISSN 1541-4337. .
233. Alex Wang, Kosmo Yan, Derek Chu, Mohamed Nazer, Nga Ting Lin, Eshan Samaranayake, and James Chang. Microalgae as a Mainstream Food Ingredient: Demand and Supply Perspective. In Md. Asraful Alam, Jing-Liang Xu, and Zhongming Wang, editors, *Microalgae Biotechnology for Food, Health and High Value Products*, pages 29–79. Springer, Singapore, 2020. ISBN 9789811501692. .
234. Martín P. Caporgno and Alexander Mathys. Trends in Microalgae Incorporation Into Innovative Food Products With Potential Health Benefits. *Frontiers in Nutrition*, 5, 2018. ISSN 2296-861X. .
235. Emeka G. Nwoba, Christiana N. Ogbonna, Tasneema Ishika, and Ashiwin Vadiveloo. Microalgal Pigments: A Source of Natural Food Colors. In Md. Asraful Alam, Jing-Liang Xu, and Zhongming Wang, editors, *Microalgae Biotechnology for Food, Health and High Value Products*, pages 81–123. Springer, Singapore, 2020. ISBN 9789811501692. .
236. Thomas Butler and Yonatan Golan. Astaxanthin Production from Microalgae. In Md. Asraful Alam, Jing-Liang Xu, and Zhongming Wang, editors, *Microalgae Biotechnology for Food, Health and High Value Products*, pages 175–242. Springer, Singapore, 2020. ISBN 9789811501692. .
237. Jesús Ruiz, Giuseppe Olivieri, Jeroen de Vree, Rouke Bosma, Philippe Willems, J. Hans Reith, Michel H. M. Eppink, Dorinde M. M. Kleinegris, René H. Wijffels, and Maria J. Barbosa. Towards industrial products from microalgae. *Energy & Environmental Science*, 9(10):3036–3043, 2016. .
238. Michael D. Guiry. How many species of algae are there? *Journal of Phycology*, 48(5): 1057–1063, October 2012. ISSN 0022-3646. .
239. M.D. Guiry and G.M. Guiry. AlgaeBase, 2020.
240. F. Fasaei, J. H. Bitter, P. M. Slegers, and A. J. B. van Boxtel. Techno-economic evaluation of microalgae harvesting and dewatering systems. *Algal Research*, 31:347–362, April 2018. ISSN 2211-9264. .
241. F. G. Acién Fernández, José María Fernández Sevilla, and Emilio Molina Grima. Chapter 21 - Costs analysis of microalgae production. In Ashok Pandey, Jo-Shu Chang, Carlos Ricardo Soccol, Duu-Jong Lee, and Yusuf Chisti, editors, *Biofuels from Algae (Second Edition)*, Biomass, Biofuels, Biochemicals, pages 551–566. Elsevier, January 2019. ISBN 978-0-444-64192-2. .
242. Elizabeth Specht, Shigeki Miyake-Stoner, and Stephen Mayfield. Micro-algae come of age as a platform for recombinant protein production. *Biotechnology Letters*, 32(10):1373–1383, October 2010. ISSN 1573-6776. .
243. René H Wijffels, Olaf Kruse, and Klaas J Hellingwerf. Potential of industrial biotechnology with cyanobacteria and eukaryotic microalgae. *Current Opinion in Biotechnology*, 24(3): 405–413, June 2013. ISSN 0958-1669. .