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Bioproducts from microalgae biomass: Technology, sustainability, challenges and opportunities

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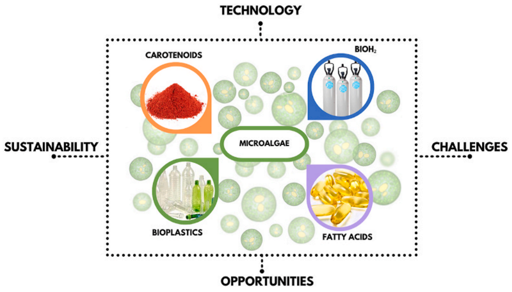
HIGHLIGHTS

- Microalgae biotechnology for sustainable industrial goods.
- Polyunsaturated fatty acids are desirable compounds for human health benefits.
- Microalgae are sustainable sources for the production of carotenoids.
- Microalgae have the potential to be used in the production of bioplastics.
- Microalgae are among the main hydrogen-producing microorganisms.

GRAPHICAL ABSTRACT



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ABSTRACT

Microalgae are a potential feedstock for several bioproducts, mainly from its primary and secondary metabolites. Lipids can be converted in high-value polyunsaturated fatty acids (PUFA) such as omega-3, carbohydrates are potential biohydrogen (bioH$_2$) sources, proteins can be converted into biopolymers (such as bioplastics) and pigments can achieve high concentrations of valuable carotenoids. This work comprehends the current practices for the production of such products from microalgae biomass, with insights on technical performance, environmental and economical sustainability. For each bioproduct, discussion includes insights on bioprocesses, productivity, commercialization, environmental impacts and major challenges. Opportunities for future research, such as wastewater cultivation, arise as environmentally attractive alternatives for sustainable production with high potential for resource recovery and valorization. Still, microalgae biotechnology stands out as an attractive topic for it research and market potential.

1. Introduction

Since the dawn of humankind man has used microalgae, initially as food for wild people (Levasseur et al., 2020). As one of the oldest forms of life on Earth, with evolution and adaptation over billions of years, microalgae cells have diversity and complexity that allow them a range

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of applications (Levasseur et al., 2020). Since 1970s, research on microalgae development and contribution to cost-effective production has been carried out (Siddiki et al., 2022). Moreover, the current feedstock competitiveness and natural resource depletion have increased microalgae relevance, since several bioproducts can be obtained from their biomass.

The attention given to microalgae is mainly related to their bioaccumulation efficiency, nutrient assimilation, and biomass productivity (Rawat et al., 2013). In biomass production for energy and other bioproducts (pigments, bioplastics, fatty acids, among others), microalgae have a range of characteristics that make them advantageous over conventional feedstock, such as non-competition for agricultural land and clean water, favoring food production and other agricultural products (Javed et al., 2019). Moreover, microalgae can fix atmospheric CO_2 and grow in freshwater, wastewater, or seawater. When grown in wastewater, they consume the nutrients there present, favoring bioremediation and, in parallel, reducing the treatment costs (Javed et al., 2019).

Recently, industries have invested in valued bio-based products, such as lipids (feedstock for biofuels), proteins, fatty acids (e.g., omega 3), and carotenoids (e.g., astaxanthin and β-Carotene), making microalgae candidates for transforming “waste into wealth” (Mahapatra et al., 2018), paving the path towards a sustainable future (Siddiki et al., 2022). Due to microalgae’s potential in bioactive compounds production, their biomass use as feedstock can fit the biorefinery concept (Ramesh Kumar et al., 2019), contributing to different nutraceutical, chemical, food, and pharmaceutical production processes (Ramesh Kumar et al., 2019). The microalgae biorefinery concept is based on oil refineries where biomass can be converted into several value-added products (Siddiki et al., 2022). The by-products generated have application in several fields such as food (Torres-Tiji et al., 2020), feed (Kusmayadi et al., 2021), human health and nutraceuticals (polyunsaturated fatty acids (PUFA), carotenoids, vitamins, phytosterols or polyphenols (del Mondo et al., 2021, 2020; Mehariya et al., 2021; Sañé et al., 2021; Zhuang et al., 2022)), materials (biopolymers (Mal et al., 2022), natural dyes, organic fertilizers (Lorentz et al., 2020; Pereira et al., 2021; Silva et al., 2021)) and energy (biofuels such as biogas, biodiesel, bio-oil and biohydrogen (Li et al., 2022a, 2022b; Bianca Barros Marangon et al., 2021)).

Considering biomass composition, cost-effective biorefineries should include valorization of lipid, carbohydrate and protein fractions and other micro-components. Still, optimistic values of productivity and process control are challenges yet to be overcome when considering large scale production and market diffusion of the microalgae bioproducts (Fernández et al., 2021). While products such as biodiesel form transesterification (Karpagam et al., 2021) and biogas from anaerobic digestion (Choudhary et al., 2020) are on later stages of technological development, emerging bioproducts still require insights on their technological status. Moreover, comprehensive reviews focusing on bioprocesses, environmental sustainability and cost-effective cultivation are essential to stablish current status and identify knowledge gaps and opportunities from microalgae biotechnology.

In this context, this study addresses different processing routes for producing bioproducts from microalgae biomass (MB). The routes’ technical, economic, and environmental aspects were integrated under the biorefinery concept, reflecting the study’s main contribution to resource recovery in the industrial sector. Special attention is given to the up-to-date bioproducts from MB such as carotenoids, polyunsaturated fatty acids, bioplastics, and biohydrogen ($bioH_2$). Bioprocesses for extracting and obtaining these products are discussed, along with their technical, financial, and environmental aspects.

2. Value-added products from microalgae

Microalgae cellular composition has become attractive for obtaining products of commercial interest. These microorganisms can synthesize bioactive compounds with high added value and act as feedstock for several industrial routes: pharmaceuticals, cosmetics, animal feed, polymers, chemicals, and energy (Kumar et al., 2021; Premaratne et al., 2021). The bioactive compounds extracted from microalgae are diverse. They are associated with the cellular composition of these microorganisms, which consists mainly of lipids (7–65%), proteins (5–74%), carbohydrates (8–69%), and other metabolites in smaller fractions such as pigments and vitamins (1–14%) (Becker, 2007; Ejike et al., 2017; del Mondo et al., 2020; Siddiki et al., 2022). The metabolites produced by microalgae can be classified as primary (compounds essential for microorganisms survival, such as proteins, carbohydrates, and lipids) and secondary (functional compounds related to physiological systems, such as carotenoids, astaxanthin, and polyhydroxyalkanoates - PHA) (Japar et al., 2021; Liu et al., 2022).

Among the primary metabolites, lipids comprise storage fractions (composed mainly of saturated and monounsaturated fatty acids) and structural (polyunsaturated fatty acids - PUFA) fractions (Steinrücken et al., 2017), with storage lipids indicated for obtaining biodiesel, while PUFA are used as nutraceuticals to supplement human and animal feed (Barta et al., 2021). It is noteworthy that, for obtaining biofuels, the demand for algal biomass volume is greater than for obtaining PUFA, while retail prices are lower (Kumar et al., 2021). MB production and harvesting costs are associated with these retail prices, making it a challenge for large-scale production and hindering the biodiesel viability from microalgae. For this reason, PUFA has attracted commercial attention, especially from the pharmaceutical and cosmetic industries, since the technical and economic viability of this route is more promising than that of biodiesel.

Carbohydrates are also among the primary metabolites of interest in microalgae cellular composition to obtain hydrogen (H_2). This fuel stands out from other hydrocarbon-based energy sources due to its energy potential and conversion efficiency (1 kg of H_2 contains about 120 MJ of energy) (Chen et al., 2021; Li et al., 2022a; Sarkar et al., 2021) Although hydrogen has potential in terms of calorific value, obtaining it in pure form is complex and expensive. The main processes studied for this objective are steam reforming or autothermal reforming (ATR) and partial oxidation. It is noteworthy that such processes are still costly and high-energy (Kalamaras and Efstathiou, 2013), and a potential path to overcome those obstacles is by producing $bioH_2$. Besides being a renewable energy source, it is already known that the biological method for hydrogen production requires less energy and can be carried out under room temperature and pressure (Kraemer et al., 2007; Nishio and Nakashimada, 2004; Wang and Wan, 2009).

As for secondary metabolites, carotenoids have aroused interest in the pharmaceutical, cosmetic, animal feed, and health industries since they are natural and healthier pigments than chemically synthesized ones (Liu et al., 2021; Mussagy et al., 2019). Moreover, the present antioxidant and anti-inflammatory properties (Cezare-Gomes et al., 2019). Carotenoids are yellow, orange, or red pigments, subdivided into carotenes, composed only of carbon and hydrogen (α and β-carotene), and xanthophylls, which in addition to carbon and hydrogen, also contain oxygen (astaxanthin and lutein) (Pagels et al., 2020). Carotenoids absorb light mainly at wavelengths between 350 and 600 nm (Begum et al., 2015; Ma et al., 2022).

Protein, starch, and PHA are other metabolites present in the algal cell, which, when synthesized, constitute biopolymers. Meaning, they are bioplastics. There is a growing demand for plastics, also given conventional plastics are made from synthetic polymers from refined petroleum. Beyond that, they cause negative impacts on the environment and health, which raises the interest on researched of bioplastics as an alternative. Moreover, bioplastics from microalgae have also stood out within the scope of the circular economy since they are fully biodegradable, and their production can be integrated with carbon capture and wastewater treatment, minimizing environmental impacts (Karan et al., 2019).

Among the various value-added compounds from microalgae, this study prioritized the technological bioprocesses involved in obtaining PUFA, carotenoids, bioplastics, and biohydrogen (Fig. 1). The investigations of these compounds are at the frontier of knowledge about the MB valorization from pigments, lipid, carbohydrate and protein fractions. Table 1 summarizes the main results addressed and discussed in this article.

2.1. Fatty acids

Lipids are the most studied compound extracted from microalgae, with the highest potential for process scale-up and commercialization (Maltsev and Maltseva, 2021). Algae composition usually ranges from 20 to 50% lipids, reaching 80% depending on strain and cultivation (Sun et al., 2018). Oil yields for similar land occupation are fastest and many folds higher than terrestrial crops (Shahid et al., 2020), which explains attention for the potential use of microalgae as biodiesel feedstock (Sajjadi et al., 2018). Although biofuel valorization routes present a high-volume production, higher market prices are associated with bioactive compounds extracted in small quantities (Kumar et al., 2021).

When targeting high-value-added products from lipids, discussing fatty acid (FA) profiling is necessary. Polyunsaturated fatty acids (PUFA) such as linoleic acid (C18:2 or Omega-6) and linolenic acid (C18:3 or Omega-3) are amongst the most desirable compounds, mainly due to their benefits to human health (Sharma et al., 2020). They can act against numerous conditions, such as coronary heart disease, thrombosis, macular degeneration, dementia, diabetes, allergy, asthma, osteoporosis, some types of cancer, and are currently studied as potential adjuvant therapy for COVID-19 cardiovascular complications (Oliver et al., 2020). Also applied to aquaculture, Omega-3 long-chain PUFA such as Eicosapentaenoic acid (C20:5 or EPA) and Docosahexaenoic acid (C22:6 or DHA) are essential to feed aquatic organisms (Fernández et al., 2021). Microalgae are the predominant source for PUFA, thus representing the major value-added products obtained from them (Kumar et al., 2021). The Omega-3 market is up to USD 2.49 billion (Oliver et al., 2020), and selling prices reached 100 USD/kg for EPA and 120 USD/kg for DHA, with production costs of 39.0 USD/kg (Jacob-Lopes et al., 2019). Comparatively, reported prices for microalgae biodiesel range between 0.49 USD/kg and 21.81 USD/kg (Sun et al., 2019).

When considering environmental issues, life cycle assessment (LCA) studies report that producing omega-3 FA from microalgae is a suitable alternative to reduce biodiversity loss from fish oil production, the traditional source for PUFA in the market (Togarcheti and Padamati, 2021). Feasibility, however, depends on productivity and thus on facts inherent to the production process. Obtaining omega 3 from microalgae requires extraction and purification from microalgae biomass. Cultivation and harvesting can be performed by commonly systems (photobioreactors, open ponds and hybrid systems) and processes (filtration, flocculation and centrifugation). Next, lipid extraction can be done by hexane extraction for large scale facilities or methanol/chloroform for small scale. The following processes depend on the end product desired from microalgae: aquaculture uses fresh or dry pellets to preserve nutritional value, while pharmaceutical industries can need further extraction and purification methods such as supercritical fluid extraction, winterization and fractional distillation (Adarme-Vega et al., 2012).

Strain selection plays a major role in the productivity of high-value compounds, with high lipid content and prominent PUFA producing species such as *Phaeodactylum tricornutum* (up to 41% lipids) and *Nannochloropsis* sp. (up to 61% lipids) with 39% EPA from total FA (Levasseur et al., 2020; Ramesh Kumar et al., 2019). Likewise, *Scenedesmus obliquus* (50% lipids) and *Pavlova salina* (29% lipids) are reportedly high-producing species (Levasseur et al., 2020).

Choosing cultivation systems and controlling operational parameters such as temperature, pH, light, nutrient uptake, salinity, and CO2 availability is strategic to target specific microalgae composition (Ferreira et al., 2019; Levasseur et al., 2020). No statistically significant difference was found for studies comparing different cultivation systems, with open ponds presenting marginally higher lipid content (3.18 ± 0.80%) than closed photobioreactors (2.26 ± 0.51%) for *Chlorella vulgaris* (Jay et al., 2018). Also, when reviewing fatty acid profiling, the systems had similar percentages of the most desirable compounds, such as 6.2% EPA for the closed system compared to 6.0% in the open pond. Hybrid systems are also an effective cultivation strategy for producing PUFA, with closed systems growing a resistant inoculum followed by large-scale open cultivation (Ferreira et al., 2019). Concerning cultivation modes, heterotrophic conditions are reported to result in higher lipid yields (Levasseur et al., 2020). However, the use of heterotrophic cultivation requires major sugar inputs, which in turn is the primary source of impacts in microalgae biomass cultivation chain, reported from LCA studies (Davis et al., 2021).

Regarding operational parameters for cultivation and upon reviewing results for FA profiling, Maltsev & Maltseva (Maltsev and Maltseva, 2021) observed: (i) lipid accumulation can be enhanced by imposing nutrient stress levels from 15 to 54% (Stemmler et al., 2016), but nitrogen and phosphorus deficiencies reportedly also decrease PUFA formation up to 7%; (ii) favoring lower temperatures can increase PUFA from 12 to 21.7% in microalgae FA profiling, but the contrary happens for increasing light intensity, with PUFA decreasing up to 4% under

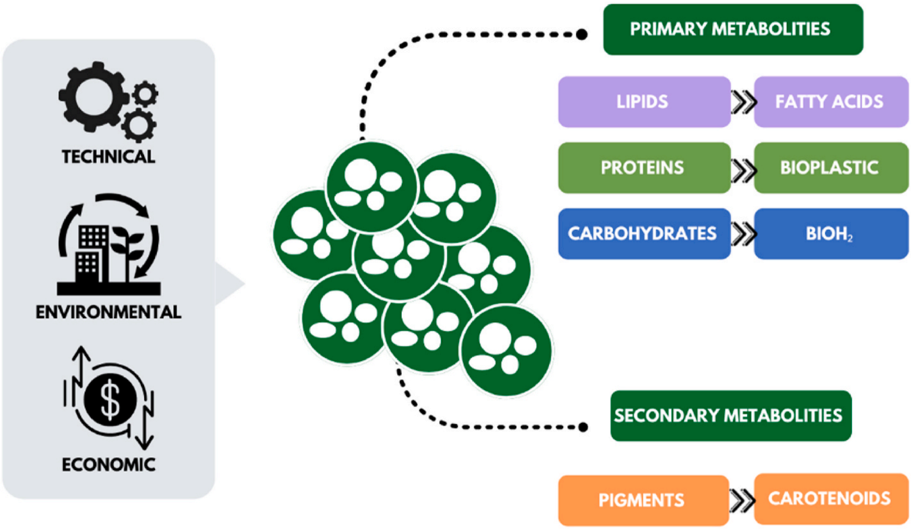

Fig. 1. Bioproducts from microalgae biomass.

Table 1
Value-added products from microalgae.

Products		Microalgae cultivation medium	Results	Units	References
Polyunsaturated Fatty Acids (PUFA)	EPA	Wastewater	3.7–7.6	mg.g^{-1} algal biomass	Tossavainen et al. (2019)
	DHA		2.3–4.5		
	DHA	Freshwater	48.3–58.2	% of total fatty acids	Lee Chang et al. (2014)
			41–75	% of total fatty acids	Chalima et al. (2017)
	DHA	Marine	1.1–5.6	g.L^{-1}.d^{-1}	Hong et al. (2013)
	EPA + DHA		2.0–7.5	ton ha^{-1} year^{-1}	Chauton et al. (2015)
Carotenoids	Lutein	Freshwater	6.2	mg.g^{-1}	Chen et al. (2021)
	Lutein	Corn starch wastewater	8.5	mg. g^{-1}	Zheng et al. (2022)
	Astaxanthin	Saline Synthetic Medium	6.0	mg. g^{-1}	Kou et al. (2020)
	Astaxanthin	Wastewater	28.7	μg mg^{-1} dry biomass	Singh et al. (2019)
	β-Carotene	Optimized artificial sea water	7.9	% β-Carotene	Xi et al. (2020)
	β-Carotene	Wastewater	47.0	μg mg^{-1} dry biomass	Singh et al. (2020)
Bioplastics	PHA	Freshwater	71–78	% dcw	Bhati and Mallick (2015)
	PHA	Freshwater	12–16	% dcw	Costa et al. (2018)
	PHA	Wastewater	30	% PHA VSS^{-1}	Fradinho et al. (2013)
	Starch	Freshwater	40	% dw	Gifuni et al. (2017)
	Starch	Freshwater	58	ton.ha^{-1}.year^{-1}	
	Starch	Freshwater	19.5–38.2	% dw	Gifuni et al. (2018)
	Amido	Freshwater	49	% wt	Mathiot et al. (2019)
	Proteins	Freshwater	26–29	% wt	González-Balderas et al. (2021)
	Proteins	Freshwater	15.1–45.5	% dw	Gifuni et al. (2018)
	Proteins	Wastewater	48	% wt	González-Balderas et al. (2021)
Biohydrogen (bioH$_2$)	H$_2$	Freshwater	48.0	% total biomass	Liu et al. (2020)
	H$_2$	Freshwater	47.2	ml.g VS^{-1}	Phanduang et al. (2019)
	H$_2$	Freshwater	16.2	ml.g VS^{-1}	Lunprom et al. (2019)
	H$_2$	Freshwater	116.0	ml.g TS^{-1}	Kumar et al. (2018)
	H$_2$	Freshwater	2.87	mmol.g TS^{-1}	Chen et al. (2016)
	H$_2$	Freshwater	0.96	dm^3. g VS^{-1}	
	H$_2$	Freshwater	1.47	mol H$_2$	Si et al. (2015)

Note: EPA = Eicosapentaenoic acid; DHA = Docosahexaenoic acid; dcw = dry cell weight; dw = dry weight; wt = weight; TS = Total solids; VS = Volatile solids; VSS = Volatile suspended solids.

bright light; (iii) promoting alkaline pH levels can also enhance PUFA production up to 16%; and (iv) salt stress can enhance lipid production, but the effect on FA profiling is highly variable. Bioprocesses for obtaining PUFA from microalgae as shown in Fig. 2.

Moreover, studies report that a major drawback from replacing the traditional fish oil feedstock with algae is associated with production expenses (Ferreira et al., 2019), with high capital costs, energy consumption, and consumables such as water, fertilizers, and CO$_2$ (Barsanti and Gualtieri, 2018). Using wastewater as a culture media, water, nitrogen, phosphorus, organic carbon, and other nutrients can be consumed for microalgae growth (Xin et al., 2016). Studies suggest that although wastewater cultivation may reduce lipid accumulation, the microalgae fatty acid profile may not be negatively affected (Ferreira et al., 2019). When assessing the potential applications for wastewater-grown microalgae, Do et al. (Do et al., 2019) reached satisfactory FA profiling for both biofuel and bio-lubricant.

LCA studies also support using waste streams for PUFA production from microalgae, arguing that even with higher production costs, the lower environmental burdens and resource recovery justifies their use in a bioeconomy perspective, when compared to fish oil omega 3 (Bartek et al., 2021). Still, most environmental assessments are reported for lab, pilot scale and literature data studies, or use synthetic cultivation with

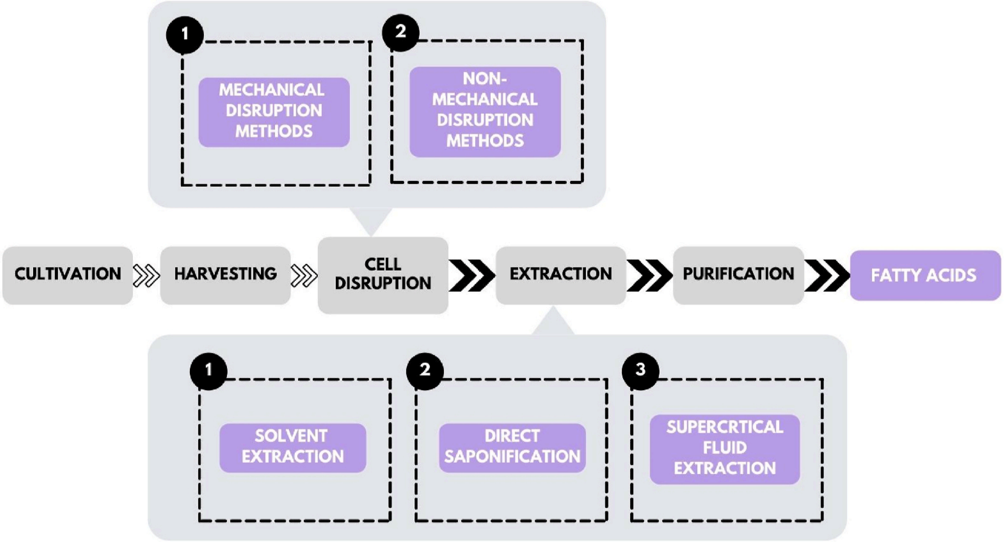

Fig. 2. Bioprocesses for obtaining PUFA from microalgae. Based on Li et al. (2019).

fresh or marine water as culture media (Davis et al., 2021). Also, contamination issues from wastewater-grown biomass are still pending research for more noble uses such as food and cosmetics (Ferreira et al., 2019). In addition, the extent to which microalgae absolve pathogens from waste streams and the guidelines for acceptable pollutant concentrations in the biomass still need a risk assessment, which will guarantee safe utilization for feed supplements (Li et al., 2021).

2.2. *Carotenoids*

Carotenoids are fat-soluble yellow, orange, or red pigments, subdivided into carotenes, composed only of carbon and hydrogen (α and β-carotene), and xanthophylls that, in addition to carbon and hydrogen, also contain oxygen. (Astaxanthin and lutein) (Pagels et al., 2020). Microalgae are increasingly recognized as a sustainable source for carotenoid production due to their growth rate, adaptability, and photosynthetic efficiency (Zheng et al., 2022b).

Among the carotenoids produced from microalgae, β-carotene, lutein, and astaxanthin are the ones of greatest commercial interest (Hu et al., 2018; Rammuni et al., 2019). This growing interest is due to the antioxidant, anti-inflammatory, vitamin A precursor, and neuroprotective properties of these carotenoids extracted from microalgae (Cezare-Gomes et al., 2019; D'Alessandro and Antoniosi Filho, 2016; Hu et al., 2018). According to Ambati et al. (2019) algae's carotenoids such as astaxanthin, β-carotene, fucoxanthin, and lutein are receiving much more attention in recent research. The reason is that they are obtained from natural sources and have great potential for value-added compounds production. In addition, carotenoids such as diatoxanthin, diadinoxanthin, alloxanthin, or peridinin from microalgae, are also relevant given their bioactive levels, benefits to human health and potential application to biotechnology (Pistelli et al., 2021). However, according to Saini and Keum (2019), 80–90% of the demand for carotenoids is met through chemical synthesis derived from petrochemicals.

The demand for carotenoids obtained from microorganisms' sources is increasing due to the improvement of biotechnology, high efficiency, and the possibility of cost reduction compared to natural carotenoids derived from plants (Liu et al., 2021). Additionally, synthetic carotenoids such as synthetic astaxanthin cannot be used directly for human consumption in foods or supplements. This is because its synthetic production involves petrochemical compounds, originating a final product with potential toxicity, besides environmentally unsustainable (Cezare-Gomes et al., 2019; Panis and Carreon, 2016).

Bioprocesses for obtaining carotenoids from microalgae involve the stages of biomass production and harvesting, cell disruption and extraction, and, finally, purification when necessary (Ambati et al., 2019; García-Vaquero et al., 2021; Pagels et al., 2020), as shown in Fig. 3. The operational variables and ideal production conditions vary according to the desired carotenoid type at the end of the production line.

Light intensity, salinity, temperature, nutrients, and pH are the main factors influencing carotenoid production in the cultivation stage. Several studies investigate the influence of these parameters on biomass productivity and carotenoid production (Pourkarimi et al., 2020; Rammuni et al., 2019; Singh et al., 2020). According to Bueno et al. (2020), the temperature is a determining factor for microorganisms' development and growth, affecting enzyme concentrations and, consequently, controlling the produced carotenoid level.

The experiment conducted by Wu et al. (2020) investigated the stress caused by high light (HL) (200 μmol m^{-2}. s^{-1}), nitrogen depletion (ND) (NH_4NO_3 0.016 g. L^{-1}), and high salt (HS) (NaCl 175.5 g. L^{-1}) on β-carotene and lutein carotenoids productivity. The results showed that the β-carotene content was 31.5% (HL) and 50.6% (ND) higher than control, although saline stress did not increase this carotenoid. As for the lutein content, the authors observed results of 95.9% (HL), 50.6% (ND), and 34.5% (HS) compared to the control treatment. The ideal conditions for higher β-carotene yields, lutein, and astaxanthin were high light exposure, low nitrogen demand, and high salinity. Furthermore, each microalgae species used to obtain the specific carotenoid will have optimal production intervals (Liu et al., 2021; Lu et al., 2021; Pourkarimi et al., 2020; Zheng et al., 2022b).

The pH control may also influence carotenoid yields during production, and ideal values can vary by species. For example, the ideal pH for β-carotene from *Dunaliella salina* is 7.5 (Pagels et al., 2020); the higher astaxanthin yield from *Haematococcus pluvialis* is in the range from 7.5 to 8.0 (Panis and Carreon, 2016); for lutein the optimal range is from 7.0 to 8.0 for *Chlorella minutissima* (Zheng et al., 2022a). Furthermore, metabolic pathways also play a significant role in higher yields (Kalra et al., 2021). In this context, heterotrophic cultivation is the best alternative for increasing biomass and carotenoid production and is more cost-effective (Hu et al., 2018).

Few microalgae strains are highlighted for a specific carotenoid at the commercial production level, despite Chlorophyceae family strains being highlighted for storing carotenoids (Kalra et al., 2021). Currently, research has focused its efforts on *Dunaliella salina* for β-carotene production (Pourkarimi et al., 2020; Wu et al., 2020; Xi et al., 2020), *Haematococcus pluvialis* to obtain astaxanthin (Li et al., 2011; Panis and

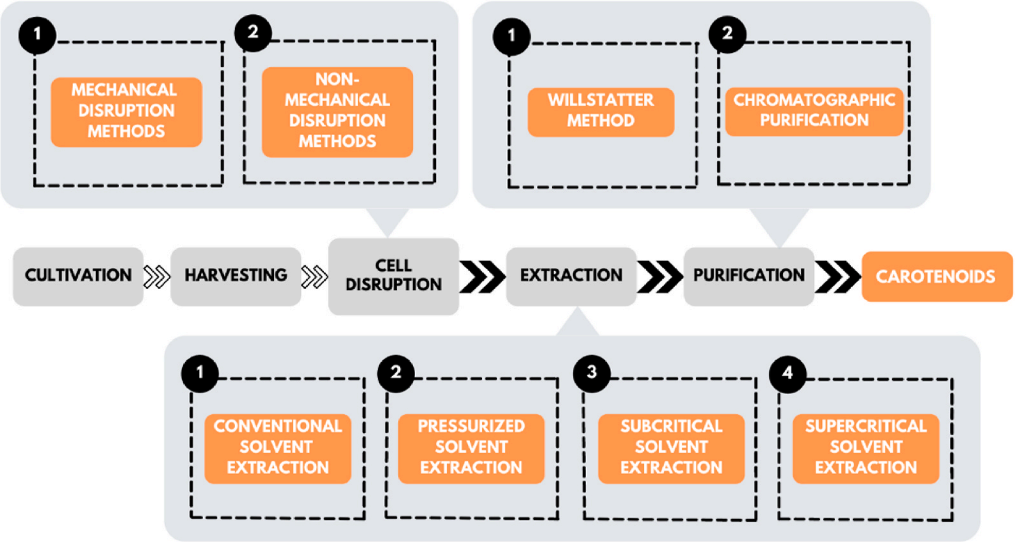

Fig. 3. Bioprocesses for obtaining carotenoids from microalgae. Based on García-Vaquero et al. (2021).

Carreon, 2016; Rammuni et al., 2019), and *Murielopsis* sp. and *S. almeriensis* for lutein (Pagels et al., 2020). Even so, Silva et al. (2020) gathered trends on the brightest pigments and microalgae sources in the last ten years and indicated the strains *Chlorella vulgaris*, *Spirulina platensis*, *Haematococcus pluvialis* and *Dunaliella salina* as the most studied.

Regarding the cultivation method for carotenoids production, open and closed systems can be used, but closed photobioreactors are preferred (Carvalho et al., 2014; Zheng et al., 2022b). In these reactors, it is possible to provide greater control over the cultivation parameters such as temperature, light, and carbon dioxide diffusion (Hu et al., 2018). However, according to Cezare-Gomes et al., 2019a), astaxanthin's large scale production from *Haematococcus pluvialis* can occur through hybrid cultivation systems. According to the authors, this production takes place through two stages: (i) incubation and vegetative growth phase (green phase), in a closed photobioreactor; followed by (ii) the red phase, in which there is carotenoid accumulation, through ponds (open reactors).

Most research related to wastewater use is conducted on a laboratory scale. This culture medium is a sustainable option for environmental management and carotenoid production from microalgae (Kalra et al., 2021; Zheng et al., 2022b). Heavy metals, pathogenic organisms, suspended solids, variation in the content and molecular form of nutrients, and environmental factors influence microalgae growth in wastewater treatment and limit carotenoid production. This fact may also restrict carotenoid pigments used to produce food coloring and nutraceuticals (Guldhe et al., 2017; Oyebamiji et al., 2019). In addition, variation in nutrients' content and molecular form, and metal ions can affect carotenoid production (Kalra et al., 2021).

For the harvesting stage, priority should be given to processes that avoid cell degradation and toxic processes, such as flocculation and electro flocculation. These processes can cause Al^{3+} bioaccumulation in carotenoid products (Lu et al., 2021; Zheng et al., 2022b). Methods such as centrifugation are usually applied on a laboratory and small industrial scale to harvest biomass. However, they are related to high energy consumption and high costs (Panis and Carreon, 2016; Zheng et al., 2022b).

Generally, carotenoids are stored inside microalgae cells, protected by a rigid cell wall, hindering or limiting their extraction and, consequently, their bioaccessibility (Bernaerts et al., 2020). In this way, some mechanical or non-mechanical cell rupture techniques are applied before extraction (Kalra et al., 2021). The first uses physical force to break cells and can be applied to all microalgae species, but involves higher costs due to high energy consumption. The most used techniques are manual grinding, ball mill, and high-pressure homogenization (Kalra et al., 2021; McMillan et al., 2013). Meanwhile, non-mechanical techniques are related to chemical substances use (alcohols, acids, or surfactants), microwaves, sonication, electroporation, or enzymes application to promote microalgae cells breakdown (Kalra et al., 2021; Zheng et al., 2022b). It is noteworthy that the harvesting technology choice must be made considering the next carotenoid biosynthesis stages (rupture and extraction) to consider the chemical inputs and the transformation processes involved in the stages.

Carotenoid extraction is a resource-demanding process, and the most appropriate method must be chosen considering the target carotenoid chemical structure and microalgae species cultivated (Kalra et al., 2021; Rammuni et al., 2019). This step can be performed using conventional extraction methods that use non-polar solvents such as chloroform, dichloromethane, chloroform/methanol and hexane/isopropanol (Kalra et al., 2021). This is a more common, simple and easily applied method for bench scale extraction (Liu et al., 2021). However, to obtain lutein and β-carotene, higher yields were observed using a biphasic system, through solvent combination (Soares et al., 2016). Additionally, there are also advanced extraction techniques such as ultrasonication assisted extraction, press2urized liquid extraction, subcritical and supercritical solvent extraction. These techniques are a more sustainable alternative to organic solvents (Kwan et al., 2018). Furthermore, extraction with supercritical carbon dioxide is fast, non-flammable, non-toxic, inexpensive, and efficient method for extracting carotenoids (Ambati et al., 2019).

The carotenoid fraction from natural sources, such as microalgae, is reduced due to the high costs involved in the production process. Still, it is gaining market space due to its various nutritional properties. While the synthetic carotenoids market value is relatively low (250–2,000 $USD.kg^{-1}$), natural carotenoids from plant sources are between 350 and 7,500 $USD.kg^{-1}$ (Ram et al., 2020).

Regarding the production costs of carotenoid pigments from microalgae, there is still a gap in scale-up technologies to enable greater production and cost-reduction (Pagels et al., 2020). According to Pérez-López et al. (2014), there are large-scale facilities dedicated to the natural production of astaxanthin from *H. pluvialis*. Jacob-Lopes et al. (2019) estimated the costs involved in β-Carotene and astaxanthin production from microalgae and obtained 105 and 552 $USD.kg^{-1}$. Furthermore, the selling price was 790 and 2,500 $USD.kg^{-1}$, respectively.

The high production costs for obtaining carotenoid pigments from microalgae imply the need to develop sustainable and profitable production processes to compete and replace synthetic carotenoids. Li et al. (2011) obtained a lower astaxanthin cost (882 $USD.kg^{-1}$) concerning synthetic astaxanthin production (1,000 $USD.kg^{-1}$). It was possible because the authors optimized the production process through a two-step approach to cultivate *Haematococcus* in tubular photobioreactors. In addition, under environmental conditions of high temperatures and high solar intensities, they present greater economic viability (Li et al., 2011). It is because during the "red phase", these conditions inhibit cell proliferation and induce the astaxanthin accumulation. Therefore, astaxanthin production is greater and more advantageous in countries with a hot climate (Panis and Carreon, 2016). According to Guldhe et al. (2017), wastewater use can significantly reduce pigment production costs. Still, due to the low cell density and reduced cell size, high costs are involved in the microalgae harvesting process (Cezare-Gomes et al., 2019), representing 20–30% of the total biomass production costs (Panis and Carreon, 2016; Zheng et al., 2022b).

Synthetic astaxanthin is known to be produced from a petrochemical source, raising questions about food and nutritional safety (potential toxicity in the final product), environmental sustainability, in addition to making human consumption impossible (Li et al., 2011). Thus, efforts have been concentrated to boost alternative biotechnologies use and the development of environmentally-friendly production systems (Onorato and Rösch, 2020; Pérez-López et al., 2014).

The life cycle assessment of astaxanthin production from microalgae on a laboratory and pilot scale conducted by Pérez-López et al. (2014) showed that electricity has a great environmental impact in both cases with the cultivation stage being the determining factor due to artificial lighting usage. In addition, the authors performed a sensitivity analysis in which artificial lighting replacement by sunlight favored impact reduction, followed by a decrease in biomass productivity.

Kyriakopoulou et al. (2015) performed a comparative analysis between different matrices to obtain β-carotene from microalgae (*Dunaliella salina*) and carrot (conventional extraction). The comparative analysis performed by the authors for both matrices revealed that the cultivation and harvesting of *D. salina* in open ponds exhibit a greater environmental impact than the cultivation of carrots. However, the high β-carotene content in *D. salina* leads to higher extraction yields and, therefore, it leads to extraction processes with lower environmental impacts.

2.3. *Bioplastics*

Plastics are synthetic polymers obtained from refined petroleum products. Considering they are derived from oil, they are associated with fossil resources depletion, climate change, and greenhouse gas emissions. On the other hand, bioplastics are biopolymers obtained from biological resources, including components from animals, plants, algae, and microorganisms. It can be produced totally or partially from biomass or other renewable sources and have the same function as petroleum-based plastics. Agricultural crops such as corn, wheat, soy proteins, milk, collagen, and gelatin are common raw materials for industrial-scale bioplastics. Bioplastics belong to the biodegradable plastics class, which break down when they interact with water, enzymes, ultraviolet rays, and gradual changes in pH. However, there is a concern about bioplastic feedstock sustainability given they compete for land and water resources (Karan et al., 2019; Onen Cinar et al., 2020).

Therefore, microalgae have the potential to be used in bioplastics production (Vieira de Mendonça et al., 2021), in addition to the advantages compared to other green plastics sources (Karan et al., 2019), highlighting their production during wastewater treatment. In this way, microalgae act to prevent water body eutrophication, promoting sanitation resources use (Castro et al., 2020; B.B. B.B. Marangon et al., 2021), in addition to not competing for arable areas and clean water, a situation that occurs with the mentioned feedstocks (Karan et al., 2019). Polyhydroxyalkanoates (PHA), starch, and protein are biopolymers synthesized by the algal cell.

However, to increase microalgae bioplastics viability, techniques for accumulating biopolymers during microalgae growth, such as nutrients excess/deprivation and light/dark cycles, have been researched (Lutzu et al., 2021; Roja et al., 2019). Nitrogen and phosphorus-deficient growing media favor PHA accumulation since carbon-rich compounds (such as PHAs) are produced for energy storage (Costa et al., 2019, 2018). Protein accumulation occurs due to the culture medium increased temperature and nitrogen supply in abundance (López Rocha et al., 2020; Wu et al., 2021). Starch accumulates in response to a lack of certain nutrients and day/night cycles since this polysaccharide is produced by cells to be used as an energy reservoir (Gifuni et al., 2017; Mathiot et al., 2019). Gifuni et al. (2018) obtained a 96% increase in the starch composition of *Chlorella sorokiniana* when the authors using a nitrogen deprivation technique during the microalgae growth phase. Mathiot et al. (2019) achieved a 14-fold increase in starch in the cellular composition of *Chlamydomonas reinhardtii* grown in a sulfur-deprived environment. These results corroborate the use of microalgae as a feedstock for bioplastic production. However, it is essential to evaluate the target biopolymer and more likely to be accumulated by the cultivated algal species and which technique should be applied in the growth of microalgae to achieve this goal. This is due to the enormous diversity of these microorganisms. The most used microalgae species for PHA production are *Botryococcus braunii, Synechocystis salina, Synechococcus elongatus,* and *Spirulina* sp. (Costa et al., 2019). The species *Spirulina* sp., *Scenedesmus* sp, and *Desmodesmus* sp were studied, seeking the production of protein-based bioplastic (López Rocha et al., 2020; Wu et al., 2021). Aiming at starch production, the following species were studied: *Ankistrodesmus falcatus, Chlamydomonas reinhardtii, Chlorella sorokiniana, Chlorella variabilis, Chlorella vulgaris, Parachlorella kessleri, Scenedesmus acutus, Scenedesmus obliquus* and *Scenedesmus* sp (Mathiot et al., 2019).

MB can be used wet or dry, as shown in Fig. 4, depending on the bioplastic conversion route. The three main approaches for obtaining bioplastics from microalgae are the use of the whole cell (route 1), biopolymers extraction and utilization (route 2), and volatile organic acids and polymerization production (route 3).

In route 1, proteins, carbohydrates, and starch, especially, are targets for plasticization and transformation into fibers and thin films through the mechanical extrusion process. In this route, the total biomass can be used directly after harvesting and drying. However, cellular microalgae components, such as lipids, will also be plasticized when using the whole biomass. Therefore, the produced bioplastic may have inferior mechanical properties (Beckstrom et al., 2020). Hence, when whole microalgae cells are used as feedstock for bioplastic production, mixtures between algal biomass, synthetic polymers, and plasticizing agents, such as glycerol, are performed to obtain a product with better mechanical properties (Zeller et al., 2013; Mathiot et al., 2019).

In route 2, the wet biomass undergoes biopolymer extraction processes, involving steps such as cell destabilization and/or rupture, recovery, and purification. In this route, the PHA content, starch, and proteins in microalgae cells can make this biomass as feedstock for bioplastics unfeasible. This unfeasibility is due to the abovementioned steps that demand intensive energy and solvents (Lutzu et al., 2021). PHA, although it is already a bioplastic (polyester), is produced in small amounts by microalgae (Costa et al., 2019), compared to cyanobacteria specialized in the production of this biopolymer (Bhati and Mallick, 2015). With this, microalgae can be used together with other sanitation resources as a substrate for PHA-producing bacteria, as suggested in route 3. In this sense, microalgae could undergo biological processes (digestion or fermentation) and sludge from other wastewater treatment steps to produce substrate for biopolymer synthesis (Lutzu et al., 2021).

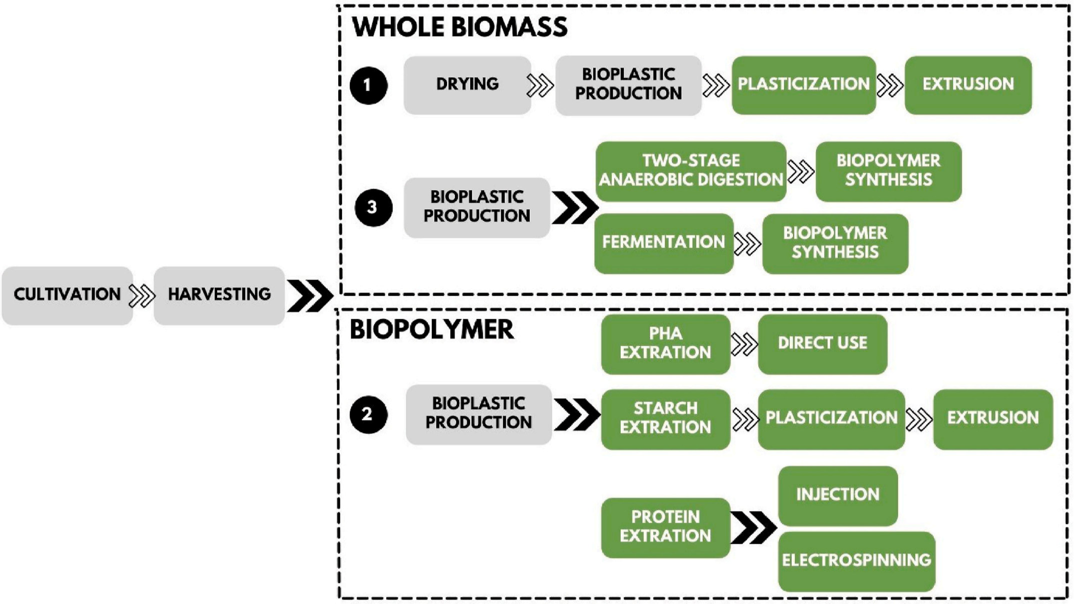

Fig. 4. Bioprocesses for obtaining bioplastics from microalgae.

On the other hand, microalgae can reach starch productivity of about 57 tons. $ha^{-1}.yr^{-1}$ (Gifuni et al., 2017), which may be higher than that of cereals such as corn (6 tons. $ha^{-1}.yr^{-1}$) and rice (8 tons. $ha^{-1}.yr^{-1}$) (FAO, 2019). However, extracting starch from microalgae is complex (Lutzu et al., 2021).

González-Balderas et al. (2021) improved protein functionality for biopolymer production purposes through ultrasound pretreatment and protein extraction applied to biomass obtained from wastewater. However, complete biomass is also used to reduce steps and costs when producing protein-based bioplastics (Lutzu et al., 2021). López Rocha et al.,2020 found a mixing ratio with glycerol that caused domestic wastewater biomass bioplastic (45% protein) to achieve better mechanical properties than bioplastic from commercial microalgae (66% protein).

Beckstrom et al. (2020) carried out a technical-economic and environmental analysis of microalgae production (with 40% of proteins) as a feedstock for protein-based bioplastic production and biofuel generation by different technologies. The authors reported that techno-economically, the most viable biorefinery configuration did not involve the production of biofuels. This is because operating costs were increased, and the sale price of the biofuel did not comprise financial gains. However, bioplastic had a sales price of 970 $USD.ton^{-1}$, within the range of 800–1200 $USD.ton^{-1}$, a value considered profitable for the plastics industry. Environmentally, this biorefinery configuration had emissions of −0.315 kg of CO_2 equivalent per kg of feedstock for bioplastic, benefiting the environment by capturing CO_2 (Beckstrom et al., 2020). Moreover, these emissions were lower than those of synthetic nylon and polypropylene plastic resins (Beckstrom et al., 2020; Wernet et al., 2016).

Technically-economically, biopolymers extraction routes need to be optimized, although there is the option of using total biomass, mixing with plasticizing agents, and synthetic polymers. Increasing target biopolymer accumulation, be it PHA, starch, or protein, is necessary to make the process more profitable. Environmentally, CO_2 capture in microalgae growth makes them attractive (Beckstrom et al., 2020). In addition, during bioplastic production containing biopolymer and synthetic polymer, non-biodegradable polymer encapsulation occurs, capturing and storing CO_2 in the form of biomass permanently, preventing these emissions (Lutzu et al., 2021). This MB utilization route can promote wastewater treatment without impeding bioplastic production (González-Balderas et al., 2021; López Rocha et al., 2020). Additionally, the use of microalgae to produce bioplastics reduces competition for arable land and drinking water (Karan et al., 2019).

2.4. *Biohydrogen*

Hydrogen is the most abundant element in the universe and Earth's crust (Zohuri, 2019). Besides, this element has the highest calorific value among fuels (on average 142 MJ kg^{-1}), being 68% higher than petroleum (45 MJ kg^{-1}), the most used fuel in the world (Kayfeci et al., 2019). Although hydrogen has potential in energy generation terms, it is complex and expensive to obtain it in pure form. The main processes studied for this purpose are steam or autothermal reforming and partial oxidation (Cappelletti and Martelli, 2017). It is also noteworthy that such processes involve costs and energy, being obstacles that still need to be overcome (Kalamaras and Efstathiou, 2013).

One way to overcome these challenges is by producing biohydrogen ($bioH_2$), defined as biologically produced hydrogen. Microalgae, bacteria, and archaea are the main producers of $bioH_2$ (Wang and Wan, 2009). The main $bioH_2$ production process is fermentation, in which organisms break down organic matter into carbon dioxide (CO_2) and hydrogen (H_2) (Wang and Yin, 2018). Furthermore, $bioH_2$ can be obtained by thermochemical transformations when biomass is used as a substrate in this reaction type (Mohan and Pandey, 2013).

Although microalgae are among the main $bioH_2$ producers, several factors can affect this production. Among them are the microalgae species, light intensity, cell density, substrate type, pH of the medium, and temperature. Each of the above factors is explored in more detail below.

Genetic engineering techniques have been used to optimize the species applied to target this product. For example, *S. elongates PCC7942* is a microalga developed to generate compounds that increase $bioH_2$ production (El-Dalatony et al., 2020). Considering the light intensity, Oncel et al. (2014) detected an optimal light intensity range between 100 and 200 μmol $photons.m^{-2}.s^{-1}$ for the microalgae *Chlamydomonas reinhardtii*, and 137 $ml.L^{-1}.d^{-1}$ $bioH_2$ production, approximately.

Another relevant factor is that, when carrying out photosynthesis, microalgae accumulate starch and lipids. In the dark phase, an anaerobic condition occurs proportional to the light amount previously exposed, helping the hydrogenase enzyme maximize $bioH_2$ production, increasing the consumption rate of sulfur (S) and oxygen (O). S and O inhibit the production of $bioH_2$, so when consumed, there is greater $bioH_2$ production (Bala Amutha and Murugesan, 2011). Cell density, in turn, is also an important factor because, when microalgae have high density, there is a risk of anaerobic transition due to self-shading, increasing the starch amount in the medium, decreasing $bioH_2$ productivity (Hemschemeier et al., 2009). Studies carried out with the species *Chlamydomonas reinhardtii* showed that the optimal cell density range is equal to 20–25 μg chlorophyll-*a*.ml^{-1} (Hemschemeier et al., 2009). Regarding the substrate, although more studies are needed to define the ideal relationship, previous work shows that there must be a balance between carbohydrate, organic nitrogen, and phosphate (Razu et al., 2019). Finally, studies show that, during $bioH_2$ production by microalgae, the ideal pH range is between 5.2 and 6.0 reported in a study on the use of *Chlorella vulgaris* MSU 01 strain (Bala Amutha and Murugesan, 2011), and the temperature is between 28 °C and 32 °C considering a mixed culture (Ahmed et al., 2021).

Along with the factors that affect the production of $bioH_2$ from microalgae, recent works (Ahmed et al., 2021; Razu et al., 2019) have evaluated the challenges related to this production. One of these challenges is the sensitivity to oxygen since these molecules inhibit hydrogenase and, consequently, $bioH_2$ production. Another challenge is thylakoid alteration. The altered thylakoid constitution is often responsible for disrupting proton transfer during microalgae-based $bioH_2$ production. There is also light capture interruption. Light-harvesting complex proteins of photosynthetic microorganisms receive photons and scatter them as light energy. The activities of this complex are often disrupted. Changing the genetic makeup of the light-gathering complex protein is expected to solve this problem (Razu et al., 2019). Other challenges to be explored are contaminants production and high construction and operating costs (Ahmed et al., 2021).

Considering these challenges, it is necessary to improve the $bioH_2$ production paths from MB (Ahmed et al., 2021; Show et al., 2019). Recent studies have addressed the direct (Ban et al., 2019, 2018; Ziara et al., 2019) and indirect $bioH_2$ production (Adnan et al., 2019; Adnan and Hossain, 2018; Florio et al., 2019; Kim and Logan, 2019; Krishnan et al., 2019). The main bioprocesses for direct $bioH_2$ production are photofermentation, and direct and indirect photolysis. Regarding indirect production, dark fermentation, gasification and pyrolysis have been used as chemical conversion bioprocesses, and microbial cells have been used for electrochemical processes for $bioH_2$ production. Fig. 5 shows a flowchart of the main bioprocesses for producing $bioH_2$ from microalgae.

Direct $bioH_2$ production must take place in a closed reactor to guarantee the storage of the produced gas. Furthermore, it is light-dependent during microalgae cultivation, in which the hydrogenase enzyme can break down the water molecule, producing $bioH_2$ (Khetkorn et al., 2017). $BioH_2$ production occurs in photobioreactors, the most used currently: tubular fence, tubular helical, horizontal tubular, vertical panel, airlift, accordion, stirring tank, and bubble column (Khetkorn et al., 2017). These reactors are mostly on a lab-scale, requiring further studies to scale up (Skjånes et al., 2013). Furthermore, studies show that

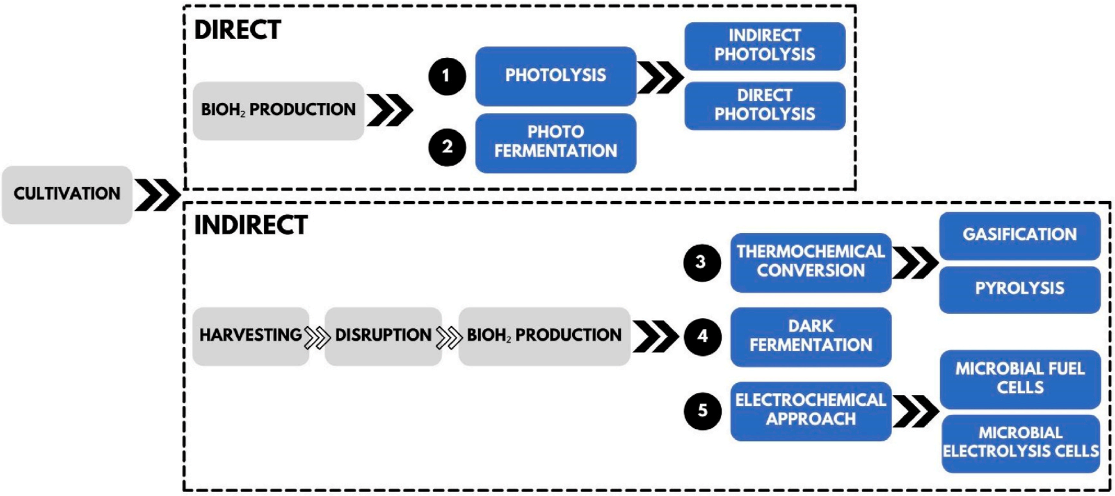

Fig. 5. Bioprocesses for obtaining bioH_2 from microalgae cultivation.

a photobioreactor suitable for bioH_2 production should have a low hydraulic retention time without removing the biomass from the reactor (Arimi et al., 2015).

Therefore, the reactors mentioned earlier aim to increase bioH_2 production through proper microalgae species selection, collection techniques, and constructive aspects. It is relevant to know the microalgae species used to know if its genetic code allows it to produce this biofuel (Ahmed et al., 2021). Among the species currently used are *Chlorella* sp.*, Spirulina obliquus, Spirulina platensis, Pseudomonas* sp.*, Synechocystis* sp.*, Rhodobacter sphaeroides, Chlamydomonas reinhardtii, Lysinibacillus sphaericus,* and *Pseudomoas aeroginosa* (Duangjan et al., 2017).

Unlike direct production, there is no dependence on light for indirect bioH_2 production (Singh and Das, 2020). Additionally, biomass is inserted into thermochemical processes to produce the fuel. After the combustion process, there is a gas generation that may contain carbon monoxide (CO), carbon dioxide (CO_2), methane gas (CH_4), H_2, and water vapor (Kumar et al., 2009). The reactor must be closed to collect and store the generated gas as in direct production.

To optimize bioH_2 production, pretreatments are necessary to ensure adequate bioH_2 production in indirect processes. In this context, such treatments aim to rupture cells to increase carbohydrate availability (Ahmed et al., 2021). Among the main pretreatments currently used are ultrasonic (Choi et al., 2011), enzymatic (Nguyen et al., 2010), chemical (Phanduang et al., 2019), and thermal (Xia et al., 2013). It is noteworthy that acid is more appropriate for some microalgae species, while for other species, the alkaline treatment is appropriate. This is because acids hydrolyze cell wall polymers, resulting in their rupture, while bases hydrolyze cell wall lipids, disintegrating their structure (Nagarajan et al., 2020).

After pretreatment, the biomass can be inserted into various thermochemical, photobiological, fermentation, or electrochemical conversion processes. Ahmed et al. (2021) point out several advantages and disadvantages of such processes. Among the thermochemical processes, gasification and pyrolysis are the most used. Gasification has the advantage of being a consolidated process. On the other hand, it produces ash and tar. Pyrolysis is more energy-efficient than gasification, but it is complex and expensive and produces ash and tar. Indirect biophotolysis has the advantage of not involving oxygen, which inhibits the production of H_2. However, the separation of H_2 is expensive, and the reactor still cannot be used on a large scale. Dark fermentation has the advantage of not needing light or oxygen and low energy demand. However, the production of bioH_2 is low, and the separation of the produced gas is still a bottleneck. Microbial cells allow low detention time and rapid acquisition of H_2. On the other hand, they require continuous electrical energy, and more studies are needed for scaling up.

As previously presented, obtaining bioH_2 from microalgae is still a challenge. Furthermore, there are still few environmental and economic studies to determine the feasibility of this biofuel. Among the existing works, Gholkar et al. (2021) carried out such evaluations considering the production of the microalgae *Scenedesmus* sp., processing 12,790 kg of microalga.h^{-1}. The authors performed computational modeling to evaluate the production of bioH_2 from MB, using a gasifier as a reactor for biofuel production. Considering ideal experimental conditions, the system's H_2 production was 12 kt yr^{-1}. Comparatively, the conventional H_2 production by electrolysis is about 30 kt yr^{-1} (IEA, 2021). Therefore, although the production is about 60% of that of the conventional system, microalgae is an alternative way of producing this fuel that is constantly being improved. As for the environmental analysis, the authors observed that the major impacts were associated with climate change due to the source of electrical energy used in the gasifier (75% fossil fuels, 20% hydroelectricity, and 5% other renewable energies). Although environmental impacts have been registered, the authors report that bioH_2 production is environmentally viable. Comparatively, biomethane production in the system presented impacts on climate change 36.74% greater than that of bioH_2, demonstrating the potential of bioH_2 as biofuel. The authors suggest replacing the energy matrix with sources such as hydroelectricity to reduce environmental impacts when using non-renewable energy sources. Furthermore, the authors point out that this reduction can be even greater if the microalgae are cultivated in wastewater.

As indicated by Gholkar et al. (2021), using wastewater is an alternative to mitigate environmental impacts for bioH_2 production from microalgae. However, Ahmed et al. (2021) point out that the indirect bioH_2 production from microalgae grown in wastewater can generate contaminants such as contaminated coal, tar, carbon dioxide, carbon monoxide, methane, and other pollutants. It is noteworthy that, although the generation of these contaminants is common in reactors for indirect production of bioH_2, the characteristics of MB from wastewater can increase unwanted products production (Ahmed et al., 2021). Such results demonstrate that contaminants production mitigation is important to increase the viability of bioH_2 production from microalgae cultivated in pure culture medium or wastewater.

Allied to environmental analysis, it is necessary to address the economic feasibility of producing bioH_2 from microalgae. In this context, the economic analysis carried out by Gholkar et al. (2021) showed that the microalgae production cost is equal to 0.5 USD.kg^{-1} microalgae, the payback period equal to 3.78 years, with a total investment of USD 144.6 million. When using a gasifier, this reactor represents 11% of material costs. Furthermore, electricity for microalgae cultivation represents 76% of operating expenses. In direct production, on the other hand, photobioreactors are considered very expensive in terms of implementation and operational costs. This is a major challenge for large-scale $bioH_2$ generation from microalgae grown in wastewater (Ahmed et al., 2021). These costs must be reduced to promote acceptance of these technologies by stakeholders at different levels. It is important to note that no studies were found that performed economic and environmental analysis of other bioprocesses to produce $bioH_2$ from microalgae.

Furthermore, although more studies are still needed to enable the production of $bioH_2$ on a commercial scale, the International Energy Agency (IEA, 2006) sets as a target the retail cost for hydrogen production in the competitive market in 0.30 $USD.kg^{-1}$ H_2. Comparatively, the gasoline price reference equals 0.33 $USD.kg^{-1}$ (Show et al., 2019). In this context, future studies should focus on the routes and bioprocesses, the factors affecting $bioH_2$ production, and the current technical, economic and environmental feasibility scenario to guarantee the insertion of this biofuel in the competitive market.

3. Prospects and challenges

Although obtaining valued products from MB has numerous benefits, ranging from nutrient recovery (when grown in wastewater) to feedstock formation for various industrial products, some limitations still make its commercialization difficult. For example, concerning obtaining fatty acids, the biggest challenges are associated with biomass cultivation. Strategies to improve the production of high value-added FA from microalgae include two-stage cultivation (Liyanaarachchi et al., 2021), with the first phase on sufficient nutrients to stimulate biomass yields, and a second step with severe conditions to achieve higher lipid content (Levasseur et al., 2020). The most prominent step towards sustainability, however, lies in genetic engineering (Barsanti and Gualtieri, 2018). Selecting PUFA producing strains with high lipid yields is the key factor to make large-scale production feasible. Most studies in this area focus on modifying a single metabolic pathway to channel carbon towards lipid synthesis (Muñoz et al., 2021). From all the above mentioned, it is still possible to affirm that microalgae are an attractive source of high-value fatty acids, with many research fields open for improvement in technical, environmental, and economic feasibility.

Concerning obtaining carotenoids, some strategies consist of culture medium pretreatment (in the case of wastewater) to remove or reduce the presence of undesirable organisms and suspended solids; nutrient supplementation to increase productivity; selection of more stress-tolerant or genetically modified species; and diluting concentrated wastewater with pure water or using wastewater from low nutrients sources and contaminants (Guldhe et al., 2017; Kalra et al., 2021). In addition, recent research has been carried out on pigment production from microalgae grown in wastewater, and the strategy used that allowed pigment yield was the use of pre-treated wastewater (Arashiro et al., 2020) or with lower concentrations of organic matter and supplemented by nutrients (Cardoso et al., 2020).

Regarding microalgae bioplastics, many advances are still needed for their industrial production. The research found in the literature uses technologies for growing, separating, and harvesting biomass both on a laboratory and pilot scale, but microalgae bioplastic production is still at the laboratory level (Onen Cinar et al., 2020). One reason is that there are other renewable sources for obtaining each of these biopolymers synthesized by microalgae, even though this may lead to competition for arable land and drinking water. However, bioplastics or biodegradable plastics are gaining more space in the global market (Lutzu et al., 2021; Onen Cinar et al., 2020). For this microalgae product, the high production costs must be considered. Despite that, according to Acién Fernández et al. (2021), when it comes to the wastewater treatment service, microalgae production costs can be reduced to 1.1 to 1.2 $euro.m^{-3}$. However, they are still higher than conventional systems (0.2 $euro.m^{-3}$).

The prospects for $bioH_2$ production from microalgae are motivating to enable this form of renewable fuel generation. Among them, the aforementioned genetic engineering techniques, which contribute to microalgae species improvement, have been widely explored (Ahmed et al., 2021). Biological pretreatments have also been explored. Operating costs, energy consumption, and resource requirements can be reduced by using hybrid pretreatment methods, reusing biological components of the process (such as by-products, enzymes, and microalgae), and promoting enzyme production (Show et al., 2019). Bacterial-algae co-culture studies are promising, as the oxygen consumption by the bacteria creates a favorable anaerobic environment for $bioH_2$ formation (Ahmed et al., 2021).

Finally, it is noteworthy that, regardless of the route used to obtain value-added products from microalgae, it is interesting to study the use of the remaining biomass and, when applicable, its integration with other resources and routes. This approach is a suitable match for wastewater treatment through microalgae biomass cultivation, strengthening the circular economy concept. The recovery of resources such as nutrients, organic matter, and water as feedstock for the production of added-value products makes this path closer to feasibility from a technical-economic point of view while contributing to reducing environmental impacts.

4. Final considerations

Microalgae are potential sources of several value-added products, capable of ecologically contributing to numerous industrial sectors. These contributions include supplying the growing demand for plastics, products aimed at promoting human and animal health (such as nutraceuticals and pharmaceuticals), and renewable fuels with high energy potential. In this work, the main biotechnological processes for obtaining PUFA, carotenoids, bioplastics, and $bioH_2$ were explored, from the cultivation and separation of the product to its economic and environmental viability. The expectation is that these products have the potential to become sustainable industrial goods. However, some limitations still need to be overcome, mainly concerning cultivation stages optimization (including nutritional balance, strain selection, and scaling up) and biomass pretreatments to improve bioproducts extraction.

Still, microalgae biotechnology and the valorization of its primary and secondary metabolites firm themselves as a path towards sustainable product development. Several emerging biomass application routes are increasingly becoming attractive both research and marketwise. Thus, future trends on microalgae biotechnology are expected soon to overcome its major challenges, given its high technological, environmental and economic potential as a feedstock for sustainable biorefineries.

Credit

Maria Lúcia Calijuri: Investigation, Visualization, Supervision. **Thiago Abrantes Silva:** Conceptualization, Writing - original draft. **Iara Barbosa Magalhães:** Conceptualization, Writing - original draft. **Alexia Saleme Aona de Paula Pereira:** Conceptualization, Writing - original draft. **Bianca Barros Marangon:** Conceptualization, Writing - original draft. **Letícia Rodrigues de Assis:** Investigation, Visualization, Methodology, Writing - review & editing. **Juliana Ferreira Lorentz:** Investigation, Visualization, Methodology, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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