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Microalgae as tools for bio-circular-green economy: Zero-waste approaches for sustainable production and biorefineries of microalgal biomass

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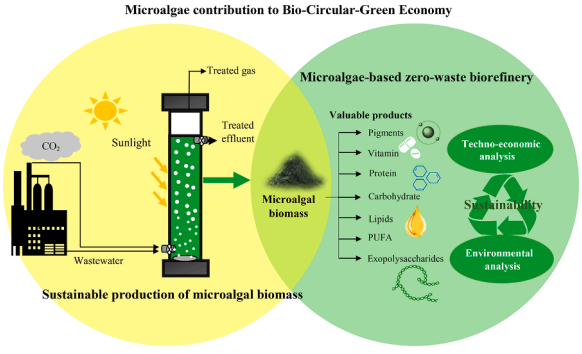
HIGHLIGHTS

- Microalgae are promising tools for zero-waste approaches and biorefinery applications.
- Microalgae are effective in wastewater upcycling and greenhouse gas capture.
- Zero-waste biorefineries would help increase overall profits of microalgae cultivation.
- Cost-effective and innovative integrations with other viable processes are proposed.
- Economic and sustainability of zero-waste microalgal biorefinery are addressed.

GRAPHICAL ABSTRACT



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ABSTRACT

Microalgae are promising organisms that are rapidly gaining much attention due to their numerous advantages and applications, especially in biorefineries for various bioenergy and biochemicals. This review focuses on the microalgae contributions to Bio-Circular-Green (BCG) economy, in which zero-waste approaches for sustainable production and biorefineries of microalgal biomass are introduced and their possible integration is discussed. Firstly, overviews of wastewater upcycling and greenhouse gas capture by microalgae are given. Then, a variety of valuable products from microalgal biomass, e.g., pigments, vitamins, proteins/peptides, carbohydrates, lipids, polyunsaturated fatty acids, and exopolysaccharides, are summarized to emphasize their biorefinery potential. Techno-economic and environmental analyses have been used to evaluate sustainability of microalgal biomass production systems. Finally, key issues, future perspectives, and challenges for zero-waste microalgal

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biorefineries, e.g., cost-effective techniques and innovative integrations with other viable processes, are discussed. These strategies not only make microalgae-based industries commercially feasible and sustainable but also reduce environmental impacts.

1. Introduction

Due to the energy crisis and global environmental protection, replacing fossil fuels, which are not sustainable and also emit greenhouse gases (GHG), with renewable, sustainable and cleaner alternatives should be of immediate concern. Furthermore, using agro-industrial or agricultural wastes as feedstocks for production of renewable bioenergy may ensure sustainability and simultaneously reduce environmental impacts (Machineni et al., 2020). Zero-waste biorefinery refers to the sustainable use of natural resources for a variety of commercial commodities and energy with the least amount of or no emissions and waste. In the circular bioeconomy, wastes constitute a crucial element of biorefineries, where prospects for reuse, recycle, and reproduce, should be practical. Therefore, the key technologies and pathways for conversion of these wastes should be developed. Zero-waste biorefineries have become an attractive alternative for creating renewable biofuels and other biobased products such as biochemicals and biopolymers.

Microalgae have emerged as an environmentally friendly bioremediation for agro-industrial wastewater and CO_2 in industrial flue gas, and as biofuel and biochemical feedstocks. The use of wastewater and CO_2 in flue gas contributes to not only economical production of microalgae-based biofuels and biochemicals but also reduction of environmental impacts as microalgae have an ability to upcycle nutrients from wastewater, mitigate CO_2, and release oxygen (Mustafa et al., 2021; Cheirsilp and Maneechote, 2022). Added to the fact that microalgae have about 20-fold higher photosynthesis efficiency than that of terrestrial plants/crops, they are also great sources of renewable bioenergy, and their biomass may be used to create numerous high-value bioproducts. The crucial stages of a zero-waste microalgal biorefinery include upstream and downstream processing steps. The upstream processing step involves production of microalgal biomass, where nutrients, light, water, and CO_2 are required. The usage of wastewater as nutrient sources, natural sunlight, and industrial flue gas could much lower the cost of upstream processing. In addition to nutrient sources, other significant environmental factors include salinity, light intensity, photoperiod, temperature, mixing and mass-transfer. These factors influence the enzyme activities necessary for microalgal photosynthesis and growth, and the accumulation of biochemicals.

It has been revealed that when microalgae are exposed to various stress conditions, they can adapt themselves by accumulating various macromolecules, namely proteins, lipids and carbohydrates at certain levels (Toledo-Cervantes et al., 2018; Qiu et al., 2020; Li et al., 2021). Several cultural stresses, including extreme temperature, high salinity, and illumination with high light intensity, likely slow down their metabolism and reroute surplus carbons to the synthesis of storage substances, which are mostly starch or lipids depending on the species. Most oleaginous microalgae respond to cultural stress conditions by increasing their lipid content and some valuable biochemicals such as exopolysaccharides and pigments (Maneechote et al., 2021). The downstream processing steps include harvesting, extraction, purification, and applications as valuable products (Koyande et al., 2019a). These procedures are expensive, time-consuming, and complicated. The processes for separation of numerous valuable components in microalgal biomass need to be practical and scalable due to the economic burden incurred by the cost of these downstream processes.

The microalgae contribution to the Bio-Circular-Green (BCG) economy requires sustainable production of microalgal biomass, protection of environment, reducing wasting of resources, and green technologies during processing steps in the upstream and downstream. This review proposes the role of microalgae that contributes to the BCG economy by summarizing the microalgae-based zero-waste approaches and zero-waste biorefineries of microalgal biomass. Firstly, overviews of wastewater upcycling and CO_2 capture by microalgae and a variety of microalgae-based products are introduced in order to pave the way for the integrated processes of using microalgae for waste treatment and production of microalgal biomass as feedstocks for valuable products. The zero-waste microalgal biorefineries are summarized in order to minimize waste generated during microalgae cultivation and processing steps. The techno-economic and environmental analyses for the sustainability of the zero-waste microalgal biorefineries are also reviewed. Finally, key issues, future perspectives, and challenges of the zero-waste microalgae biorefinery are summarized.

2. Microalgae contributions to BCG economy

2.1. Microalgae for upcycling of wastewater

Treatment or upcycling of wastewater using microalgae have demonstrated numerous benefits that can satisfy the growing demand for effective wastewater treatment, waste valorization, and nutrient recovery. Due to the high nutrient uptake capacity and great potential of microalgae for CO_2 fixation through photosynthesis, it is therefore a sustainable and affordable treatment method. The high treatment efficiencies of tertiary wastewater by microalgae have been proven by several researchers (Li et al., 2019; Mohsenpour et al., 2021). Not only are nutrients removed from wastewater, but they can be upcycled into microalgal biomass with high commercial potential because they contain pigments and vitamins, which are of high value, as well as a great amount of lipids, proteins, and carbohydrates. Especially, the microalgal biomass with a high lipid content can be used as biodiesel feedstocks (Table 1).

Several researchers have reported on the cultivation of microalgal biomass integrated with wastewater treatment for low-cost production of high-value products. Microalgae species that have been examined for their wastewater treatment potential include *Botryococcus* spp., *Chlorella* spp., *Chlamydomonas* spp., *Desmodesmus* spp., *Scenedesmus* spp., etc. Yeesang and Cheirsilp (2014) used secondarily pretreated effluent from seafood-processing plant feeding with 2.0 % CO_2 for cultivation of *Botryococcus braunii* and yielded 2.26 g/L microalgal biomass with 30.3 % lipid content. The microalgae also removed nitrate by 91 %. They also evaluated the mixotrophic cultivation using glucose at 0.5 % and molasses at 1.5 % and achieved 3.05 g/L microalgal biomass with 36.9 % lipid content. Patrinou et al. (2020) used *Leptolyngbya*-based microbial consortium to treat poultry litter extract (PLE) and simultaneously produce biodiesel in the attached growth reactors. They achieved high removal efficiency for COD (94.0 %), total phosphorus (TP) (97.4 %), and total nitrogen (TN) (88.2 %), with 335.3 mg/L.d biomass productivity. The amount of lipids in the produced biomass was 19.6 %, and >70 % of the fatty acids were saturated and monounsaturated, indicating their high potential as feedstocks for biodiesel. Sasibunyarat et al. (2014) evaluated the possible use of *Chlorella* sp. cultivation for treatment of digester effluents from seafood-processing plants, palm oil mills, and starch factories. They found that the seafood effluent most promoted the production of microalgal lipids. The highest lipid content obtained was 26.96 ± 1.58 % with the removal of TN and TP by 94.7 % and 77.4 %, respectively. Choi (2016) cultivated *Chlorella vulgaris* for treatment of dairy wastewater and found that the microalgae removed COD, TN, and TP by 80.62 %, 85.47 %, and 65.96 %, respectively, with 1.23 g/L biomass obtained. They also found that the microalgal fatty acids showed high potential as biodiesel feedstocks.

Table 1
Recent reports on microalgae for upcycling of wastewater and CO_2 mitigation.

Microalgae species	Wastewater/CO_2	Operating conditions	Pollutant removal (%)	Microalgal products	References
Microalgae for upcycling of wastewater					
Botryococcus braunii	Secondarily pretreated wastewater from seafood processing plant/CO_2 2.0 %	Light intensity 49.5 μmol photon m^{-2} s^{-1} with a 16:8 light and dark cycle, pH 6.7, 25 °C	Nitrate 91 %	Biomass 2.26 g/L Lipid content 30.3 % Lipid productivity 45.5 mg/L·d	Yeesang and Cheirsilp (2014)
Leptolyngbya sp.	Poultry litter extract (PLE)	Light intensity 200 μmol photon m^{-2} s^{-1} with a 24:0 light and dark cycle, 26 ± 2 °C	COD 94.0 % Nitrogen 88.2 % Phosphorus 97.4 %	Biomass productivity 335.3 mg/L·d Lipid 19.6 %	Patrinou et al. (2020)
Chlorella sp.	Digester effluents from seafood factory/ CO_2 0.03 %	Light intensity 3000 lx with 16:8 light and dark cycle, 25 °C	Nitrogen 94.7 % Phosphorus 77.4 %	Biomass 0.99 ± 0.21 g/L Lipid content 26.96 ± 1.58 % Lipid productivity 263 ± 36 mg/L	Sasibunyarat et al. (2014)
Chlorella vulgaris	Dairy wastewater	Light intensity 200–220 μmol photon m^{-2} s^{-1} with a 16:8h light and dark cycle, 28–32 °C at a shaking rate of 80 rpm	COD 80.62 % TN 85.47 % TP 65.96 %	Biomass 1.23 g/L Unsaturated fatty acids 77.35 % Saturated fatty acids 22.65 %	Choi (2016)
Chlorella sorokiniana	Swine wastewater: 50 % (v/v) diluted/ 2 % CO_2 aeration at 0.1 vvm	Light intensity 150 μmol photon m^{-2} s^{-1} with a 24:0 light and dark cycle, 27 °C	COD 90.1 % TN 97.0 % TP 92.8 %	Biomass 5.45 g/L Protein productivity 0.27 g/L.d	Chen et al., (2020)
Chlorella pyrenoidosa	Poultry excreta leachate 25 % in BG-11 media	Light intensity 700 lx with a 9:15 light and dark cycle, 30 ± 2 ℃	TN 84.2 % NH_3–N 53.1 % TP 96.2 %	Biomass 2.5 g/L Carbohydrates 0.64 g/L Protein 1.02 g/L Lipid 0.49 g/L Chlorophyll 20 μg/mL	Singh *et al.* (2020)
Chlamydomonas sp. QWY37	Swine wastewater/ CO_2 2.5 % in batch-operated vertical alveolar flat panel photobioreactors	Light intensity 500 μmol photon m^{-2} s^{-1} with a 16:8 light and dark cycle, 30 °C	COD 81 % TN 96 % TP 100 %	Biomass 7 g/L Carbohydrate productivity 944 mg/L·d	Qu et al. (2020)
Desmodesmus sp. EJ8-10	Anaerobically-digested (DPE) piggery effluents	Light intensity 120 ± 2 μmol photon m^{-2} s^{-1} with a 14:10 light and dark cycle, 27 ± 1 °C	NH_4^+-N 90 % TN > 80 % PO_4^{3-}-P 100 %	Biomass 0.15–0.35 g/L Lipid content 19.4–28 % Lipid productivity 5.7 mg/L·d	Li et al. (2021)
Haematococcus sp.	Seafood processing plant	Light intensity 40 μmol m^{-2} s^{-1} with a 16:8 light and dark cycle, 30 °C (Two-stage LED: red LED 5 days and blue LED for 5 days)	COD: 50 % TN: 100 % TP: 100 %	Biomass 1.33 g/L Lipid 0.41 g/L (30.81 %) Astaxanthin 3.39 mg/L Chlorophylls 14.3 mg/L Carotenoids 6.22 mg/L	Cheirsilp et al. (2022)
Microalgae for CO_2 mitigation					
Nannochloropsis sp.	Chu 13 medium/CO_2 10 %	Light intensity 60 μmol·photon·m^{-2} s^{-1} with a 24:0 light and dark cycle, 30 °C	CO_2 fixation rate 0.729 ± 0.04 g/L.d	Biomass 0.850 ± 0.16 g/L Lipid content 44.7 ± 1.2 %	Thawechai et al. (2016)
Desmodesmus sp.	BBM/ Undiluted cement flue gas containing CO_2 50 %	LED strips at 10,000 lx light intensity with a 12:12 light and dark cycle, 25 °C	CO_2 fixation rate 0.21 ± 0.02 g/L.d	Biomass 1.11 ± 0.01 g/L Lipid 41.54 ± 1.13 % Carbohydrates 32.44 ± 0.45 %	Premaratne et al. (2021)
Microalgae for wastewater upcycling and CO_2 mitigation					
Scenedesmus obliquus	Cattle wastewater/CO_2 0.35 %	Light intensity 58 μmol photon m^{-2} s^{-1} with a 24:0 light and dark cycle, 21 °C	COD 65–70 % NH_4^+ 98–99 % PO_4^3 69–77.5 % CO_2 fixation 327–547 mg/L·d	Biomass productivity 213–358 mg/L·d	de Mendonça et al. (2018)
Chlorella vulgaris ATCC 13482	Municipal wastewater/ CO_2 5 % at 1.4 L/min flow rate	Light intensity 90 ± 5 μmol photon m^{-2} s^{-1}, with a 14:10 light and dark cycle, 25 °C	COD 76.3 % Ammonia 93.4 % Phosphate 91.5 % CO_2 biofixation rates 140.91 mg/L·d	Biomass 0.94 g/L	Chaudhary et al. (2018)
Scenedesmus obliquus FACHB	Municipal wastewater/ CO_2 5 % at 1.4 L/min flow rate	Light intensity 90 ± 5 μmol photon m^{-2} s^{-1}, with a 14:10 light and dark cycle, 25 °C	COD 75.9 % Ammonia 94.1 % Phosphate 91.3 % CO_2 biofixation rates 129.82 mg/L·d	Biomass 0.86 g/L	Chaudhary et al. (2018)
Chlorella sp. UKM2	Palm oil mill effluent (POME)/ CO_2 10 %	Light intensity 14,000 lx with a 24:0 light and dark cycle, 25 ± 2 °C	COD 48 % TN 86 % Phosphate 85 % CO_2 fixation rate 0.829 g/L.d	Biomass productivity 0.440 ± 0.006 g/L·d	Hariz et al. (2019)

(*continued on next page*)

Table 1 (*continued*)

Microalgae species	Wastewater/CO_2	Operating conditions	Pollutant removal (%)	Microalgal products	References
Scenedesmus sp. SPP immobilized in fungal pellets	Seafood processing effluent	Light intensity 55 μmol photon m^{-2} s^{-1}, with a 16:8 light and dark cycle, 30 °C	COD 98.5 % TN 90.2 % TP 79.5 % CO_2 removal 71.2 %	Biomass 4.46 g/L	Maneechote et al. (2023)

COD: Chemical oxygen demand; TN: total nitrogen; TP: total phosphorus.

Chen et al. (2020a) reported that *Chlorella sorokiniana* cultivated in 50 % (v/v) diluted swine wastewater, could remove pollutants effectively and yielded 5.45 g/L biomass with protein productivity of 0.27 g/L.d. Singh *et al.* (2020) found that *Chlorella pyrenoidosa* efficiently treated 25 % diluted poultry wastewater and gave the biomass, carbohydrates, protein, lipid, and chlorophyll production of 2.5 g/L, 0.64 g/L, 1.02 g/L, 0.49 g/L, and 20 μg/mL, respectively. Interestingly, Qu et al. (2020) reported the bioremediation of non-sterilized and non-diluted swine wastewater by *Chlamydomonas* sp. QWY37. The microalgae reduced COD by 81 %, TN by 96 % and TP by ~100 %, while provided 7 g/L biomass with 944 mg/L.d carbohydrate productivity. Li et al. (2021) treated anaerobically-digested (DPE) piggery effluents by culturing microalga *Desmodesmus* sp. EJ8-10. The ammonia, TN, and phosphate removal efficiencies were 90 %, >80 %, and nearly 100 %, respectively. The microalgae cultivated in DPE reached final biomass of 0.15–0.35 g/L with 19–28 % lipid content. Recently, Cheirsilp et al. (2022) performed the cultivation of *Haematococcus* sp. for valorization of seafood processing wastewater. They found that microalgae could remove COD, TP and TN by 50 %, 100 % and 100 %, respectively, with 1.33 g/L microalgal biomass and 30.81 % lipid content. They also found that the microalgae also accumulated the high-value pigments including astaxanthin of 3.39 mg/L, chlorophylls of 14.3 mg/L and carotenoids of 6.22 mg/L.

2.2. Microalgae for CO_2 mitigation

Among the various techniques for CO_2 capture from flue gas, biological mitigation by microalgal photosynthesis is considered one of the more promising technologies. This is because, compared to terrestrial plants or energy crops, microalgae have a shorter growth cycle and high efficiencies in converting CO_2 into organic compounds using sunlight energy and producing biomass with high potential as feedstocks for food, feed, bioenergy and biochemicals (de Morais et al., 2019; Premaratne et al., 2021). Depending on their ability to tolerate CO_2, microalgae are classified into three groups: i) CO_2-sensitive groups that are repressed by low levels of CO_2 at 2–5 %; ii) CO_2-tolerant groups which tolerate moderate CO_2 levels of 5–20 %; and iii) extreme CO_2-tolerant groups which tolerate very high CO_2 levels of 20–100 %. Table 1 summarizes the recent researches on cultivation of microalgae for CO_2 mitigation. Thawechai et al. (2016) evaluated the ability of the oleaginous microalga Nannochloropsis sp. to mitigate CO_2 in synthetic flue gas and its ability to accumulate pigments and lipids. The combined effects of photoperiod and light intensity were examined for maximizing CO_2 mitigation rate and lipid productivity of microalgae. Under full illumination with light intensity at the saturation level of 60 μmol·photon·m^{-2} s^{-1} and 10 % CO_2 aeration, the microalgal biomass obtained was 850 ± 16 mg/L, with 44.7 ± 1.2 % lipid content, and CO_2 mitigation rate up to 729 ± 40 mg/L·d. Premaratne et al. (2021) used microalga Desmodesmus sp. for CO_2 mitigation from simulated undiluted cement flue gas containing 15.50 % CO_2. The rate of CO_2 mitigation by this microalga over the cultivation period of 8 days was 0.21 ± 0.02 g/L.d. The microalgae also produced 1.11 ± 0.01 g/L biomass with high carbohydrate and lipid contents of 32.44 ± 0.45 % and 41.54 ± 1.13 %, respectively.

2.3. Microalgae for simultaneous wastewater upcycling and CO_2 mitigation

Interestingly, several microalgae have high potential for simultaneous nutrient removal from wastewater and CO_2 capture from flue gas since they can assimilate both organic (sugars and organic acids) and inorganic (CO_2) carbon as well as nitrogen and phosphorus sources. The development of integrated wastewater upcycling with CO_2 mitigation can be a suitable approach for sustainable microalgal biomass production, which also contributes greatly to the BCG economy. Among all widely used bioremediators to achieve simultaneous pollutant removal (80–100 %), it has been shown that wastewater-based microalgae cultivation offers the highest atmospheric CO_2 mitigation rate of 1.83 g CO_2/g of biomass with 40–50 % higher biomass productivity compared to those of the terrestrial crops (Shahid et al., 2020). Recent researches for simultaneous wastewater upcycling and CO_2 mitigation are summarized in Table 1. de Mendonça et al. (2018) studied on bioremediation of cattle wastewater using microalga *Scenedesmus obliquus* cultivated in photobioreactors equipped with vertical alveolar-flat-panels. During cultivation for 12 days in batch mode, the COD, NH_4^+ and PO_4^{3-} removal efficiencies were 65–70 %, 98–99 %, and 69–77.5 %, respectively. The microalga showed CO_2 mitigation rate of 327–547 mg/L.d and biomass productivity of 213–358 mg/L.d. According to Chaudhary et al. (2018), the maximum CO_2 mitigation rate by Chlorella vulgaris ATCC 13482 was 140.91 mg/L.day while that by Scenedesmus obliquus FACHB was slightly lower at 129.82 mg/L.day, when they were grown in municipal wastewater aerated with 5 % CO_2 in air at a flow rate of 1.4 L/min. Hariz et al. (2019) cultivated indigenous microalga *Chlorella* sp. UKM2 using palm oil mill effluent and CO_2. The microalga removed COD, TP, and TN by 48 %, 85 %, and 86 % and fixed CO_2 at a rate of 0.829 g/L.d with the total CO_2 recovery of 12.435 g/L after 15 days of operation. Maneechote et al. (2023) reported the dual bioremediation of non-sterile secondarily treated wastewater using microalgae immobilized in fungal pellets. To increase the reusability, the pellets were coated with chitosan. The removal efficiencies of COD, TP and TN were increased up to 98.5 %, 79.5 %, and 90.2 %, respectively. In this system, the CO_2 from synthetic flue gas was also removed by 71.2 %.

3. Valuable products from microalgal biomass

Various cultivation modes and physicochemical factors can influence the biochemical compositions of the microalgal biomass. Typically, there are basic three modes, namely photoautotrophic, heterotrophic, and mixotrophic modes, for microalgae cultivation. In the phototrophic mode, the microalgae assimilate inorganic carbon, CO_2, and absorb light energy to create chemical energy through their photosynthesis system. This mode is a common mode for microalgae cultivation. While in the heterotrophic mode, the microalgae assimilate organic carbon, sugars or organic acids, as their energy source without light. The problem of limited light can be avoided using this mode. Mixotrophic cultivation mode is the combined mode of photoautotrophic and heterotrophic modes. Under this mode, the microalgae can grow through either photoautotrophic or heterotrophic metabolisms, or both (Kuravi and Mohan, 2021). A variety of valuable products, e.g., pigments, vitamins, proteins/peptides, carbohydrates, lipids, polyunsaturated fatty acids, and exopolysaccharides, can be produced by microalgae under specific

Table 2
Valuable products from microalgae under different cultivation conditions.

Products	Modes	Microalgae species	Cultivation/Production conditions	Product yield	References
Pigments	Photoautotrophic	*Nannochloropsis* sp.	Modified Chu 13 medium, white light at 80 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 30 °C	Chlorophylls 230 mg/g Carotenoids 140 mg/g	Thawechai et al. (2016)
		Asterarcys quadricellulare PUMCC 5.1.1	Bold basal medium, nitrate 10 mM, phosphate 3.5 mM, salinity 0.17 mM, blue light at 60 μmol photon m^{-2} s^{-1} with 14:10 h light:dark cycle, 28 ± 2 °C	Carotenoids 118 μg/mg	Singh et al. (2019)
		Chlamydomonas reinhardtii	Tris-acetate-phosphate (TAP) medium, white light at 50 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 15 °C	Chlorophylls 55.18 mg/L.d Carotenoids 13.48 mg/L.d	Potijun et al. (2021)
		Mixed *Scenedesmus dimorphus* (50 %) and *Chlorella* sp. (50 %)	Aquaculture wastewater (AW), light at 36 μmol photon m^{-2} s^{-1} with a 24:0 light:dark cycle, 25 ± 2 °C	Chlorophylls 1253.17 μg/L	Pekkoh et al. (2022)
		Dunaliella salina	f/2 medium with 1 N:1P ($NaNO_3$ 75 mg/L, $NaH_2PO_4{\cdot}2H_2O$ 5.65 mg/L), light at 50 μmol photon m^{-2} s^{-1} with a 12:12 light:dark cycle, 24 ± 1 °C	β-carotene 57.5 mg/g	Cezare-Gomes et al. (2023)
		Haematococcus sp.	Non-sterile secondary effluent from an aerobic pond of seafood processing industry, two-stage LED: red LED 5 days and blue LED for 5 days light at 40 μmol m^{-2} s^{-1} with a 16:8 light and dark cycle, 30 °C	Astaxanthin 3.39 mg/L Chlorophylls 14.3 mg/L Carotenoids 6.22 mg/L	Cheirsilp et al. (2022)
		Scenedesmus obliquus FSP-3	Detmer's Medium (DM), white light at 150 μmol m^{-2} s^{-1}s, CO_2 concentration, 2.5 %; CO_2 flow rate, 0.4 vvm; with a 24:0 light:dark cycle, 30 °C	Lutein 4.84 mg/g	Ho et al. (2014)
		Phaeodactylum tricornutum	Swine wastewater (SW):water 1:1, white light at 100 μmol photon m^{-2} s^{-1}, 3 % CO_2 at a flow rate of 0.7 L min^{-1}, 25 ± 2 °C	Fucoxanthin 28.41 mg/L	Jiang et al. (2022)
Vitamins	Photoautotrophic	*Anabaena cylindrica*	Modified ASM-1 medium (MLA), nitrate1700 mg/L, white light at 320 μmol photon m^{-2} s^{-1} with 12:12 h light:dark cycle, 23 °C	Vitamin K1 content of 200 μg/g (22 μg//L.d)	Tarento et al. (2018)
		Nannochloropsis oceanica	Zarrouk medium, UVB at 36 kJ·m^{-2} with 24:0h light:dark cycle, 23 ± 1 °C	Vitamin D3 1 μg/g	Ljubic et al. (2020)
Proteins/ Peptides	Photoautotrophic	*Scenedesmus obiquus*	Modified BG11 medium, white light at 150 μmol photon m^{-2} s^{-1} with 12:12 h light:dark cycle, 25 ℃	Proteins 56 %	Zhang et al. (2019)
		Pseudopediastrum boryanum	ASM1 medium, white light at 40 μmol photon m^{-2} s^{-1} with 12:12 h light:dark cycle, 30 °C	Proteins 67.3 %	Militao et al. (2019)
		Porphyridium purpureum	Modified F/2 medium, white light at 100 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 15 °C	Peptides with ORAC 13.98 μmol TE/g and FRAP 478.94 μmol TE/g	Stack et al. (2018)
		Arthrospira maxima OF15	30 % diluted sugarcane vinasse, white light at 2,500 Lux with 12:12 h light:dark cycle, 30 °C	Protein 57.04 ± 0.031 % Peptides 2395–2831 μg/mL	Montalvo et al. (2019)
	Mixotrophic	*Chlorella protothecoides*	Bold's Basal medium modified, added with 0.30 g of glucose, white light at 118.74 μmol photon m^{-2} s^{-1} with 12:12 h light:dark cycle, 25 °C	Peptides with scavenging DPPH 33.47 ± 0.68 % and hydroxyl radicals 46.81 ± 2.38 %	Olena et al. (2022)
		Dunaliella salina	Glucose 15 g/L and NaCl 2.5 M, white light at 40 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 25 °C	Proteins 1.6 g/100 g	Kadkhodaei et al. (2015)
Carbohydrates	Photoautotrophic	*Chlorella vulgaris* FSP-E	Basal medium with 4-day nitrogen starvation aerated with 2.0 % CO_2, white light at 60 μmol photon m^{-2} s^{-1} with 16:18 h light:dark cycle, 28 °C	Carbohydrates 51.3 %	Ho et al. (2013)
		Tribonema sp.	BG-11 medium, white light at 2500 Lux with 24:0h light:dark cycle, 25 ± 1 °C	Carbohydrates 43 %	Huo et al. (2020)
		Scenedesmus sp.	BG11 medium, white light at 50 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 27 ± 1 °C	Polysaccharides 122 mg/L	Sivaramakrishnan et al. (2020)
		Tribonema sp.	Simulated acrylonitrile butadiene styrene (ABS) based wastewater aerated with 2 % CO_2, white light at 300 μmol photon m^{-2} s^{-1} with 12:12 h light:dark cycle, 25 °C	Carbohydrates 0.201 g/L.d	Zheng et al. (2022)
	Mixotrophic	*Chlorella minutissima*	BMM medium, arabinose 20 mg/L, white light at 33.75 μmol photon m^{-2} s^{-1} with 12:12 h light:dark cycle, 30 °C	Carbohydrates 53.8 %	Freitas et al. (2017)
		Scenedesmus obliquus UTEX 393	Bold 3 N medium, glucose 3.33 g/L, urea 126.77 mg/L, white light at 100 μmol photon m^{-2} s^{-1} with 16:8h light:dark cycle, 27.65 °C	Carbohydrates 270 mg/L.d	Singh et al. (2019)

(*continued on next page*)

Table 2 (*continued*)

Products	Modes	Microalgae species	Cultivation/Production conditions	Product yield	References
		Chlamydomonas sp. QWY37	Swine wastewater, white light at 500 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 30 °C	Carbohydrates 944 mg/L.d	Qu et al. (2020)
Lipids	Photoautotrophic	*Botryococcus* spp.	Modified Chu 13 medium, iron 0.74 mM, without nitrogen, white light at 82.5 μmol photon m^{-2} s^{-1} with 16:8h light:dark cycle, 25 ± 1 °C	Lipids 35.9 %	Yeesang and Cheirsilp (2011)
		Nannochloropsis sp.	Modified Chu 13 medium aerated with CO_2 10 %, white light at 47 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 30 ± 2 °C	Lipids 0.36 g/L	Cheirsilp et al. (2017)
		Micractinium reisseri SIT04 and *Scenedesmus obliquus* SIT06	Modified Chu13 medium without addition of KNO_3 (N starvation), white light at 90 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 28 °C	Lipids 36.6 % and 56.8 %	Srinuanpan et al. (2018)
		Scenedesmus sp. SPP	Modified Chu13 medium (nitrogen rich and 0.5 % salt), white light at 55 μmol photon m^{-2} s^{-1}h light:dark cycle, 30 °C	Lipids 26.8 %	Maneechote et al. (2021)
		Scenedesmus sp. SPP	Modified Chu13 medium (nitrogen rich and 0.5 % salt) aeration at 0.05 vvm, white light at 4.0 klux with 16:8h light:dark cycle, 30 °C	Lipids 44.1 ± 1.5 %	Maneechote et al. (2021)
	Mixotrophic	Marine *Chlorella* sp. and *Nannochloropsis* sp.	BG-11 medium with fed-batch of glucose, white light at 3000 lx with 16:8h light:dark cycle, 30 °C	Lipids 22–26 %	Cheirsilp and Torpee (2012)
		Chlorella sp.	Seafood effluent with total phosphorus of 45.24 ± 3.80 mg/L, white light at 3000 lx with 16:8h light:dark cycle, 30 °C	Lipids 26.96 ± 1.58 %	Sasibunyarat et al. (2014)
		Botryococcus braunii	Modified Chu 13 medium with glucose 5 g/L and molasses15 g/L, white light at 49.5 μmol photon m^{-2} s^{-1} with 16:8h light:dark cycle, 25 °C	Lipids 36.9 %	Yeesang and Cheirsilp (2014)
		Co-culture of *Chlorella vulgaris* -*Rhodotorula glutinis*	Molasses 1 %, yeast:microalga (1:1), white light at 5.0 klux with 16:8h light:dark cycle, 30 °C	Lipids 2.88 ± 0.16 g/L	Cheirsilp et al. (2011)
		Co-culture of *Chlorella vulgaris* -*Trichosporonoides spathulata*	Crude glycerol-based medium, white light at 2,000 lx with 16:8h light:dark cycle, 28 °C	Lipids 47 %	Kitcha and Cheirsilp (2014)
		Chlorella pyrenoidosa	Furfural wastewater added with $NaNO_3$ 0.75 g/L, with light intensity at 120 μmol photon m^{-2} s^{-1}, 25 ± 2 °C	Lipids 16.84 %	Cheng et al. (2022)
	Heterotrophic	*Chlorella pyrenoidosa*	Furfural wastewater added with $NaNO_3$ 0.75 g/L, without light, 25 ± 2 °C	Lipids 18.53 %	Cheng et al. (2022)
	Two-stage mixotrophic	*Scenedesmus* sp. SPP	First stage: modified Chu 13 medium with nitrogen rich, glucose 1 %, CO_2 13 %, white light at 4.8 klux, with 16:8h light:dark cycle, 30 °C	Lipids 39 %	Maneechote et al. (2023)
Polyunsaturated fatty acids (PUFAs)	Photoautotrophic	*Phaeodactylum tricornutum*	BG11 medium with nitrogen replete and enriched air with 2 % CO_2, white light at 60 μmol photon m^{-2} s^{-1} with 16:8h light:dark cycle, 25 °C	PUFAs 6 ± 12 mg/L.d	Remmers et al. (2017)
		Nannochloropsis oceanica	Modified f/2 medium, white light at 250 μmol photon m^{-2} s^{-1} with 24:0h light:dark cycle, 5 °C	ALA 52 % EPA 96 % DHA 77 %	Sirisuk et al. (2018)
		Nannochloropsis sp. BR2	f/2 medium, light at 150 μmol photon m^{-2} s^{-1} with royal blue LEDs in a 16:8h light:dark cycle, 25 °C	EPA 30 mg/L	Ma et al. (2018)
		Phaeodactylum tricornutum CCMP-2561	Artificial seawater added with f/2 medium with fulvic acid 15 mg/L under 70 % salinity, white light at 50 μmol photon m^{-2} s^{-1} with 12:12 h light:dark cycle, 10 °C	EPA 13.9 %	Wang et al. (2019)
		Scenedesmus sp. SPP	Modified Chu 13 medium with 0.5 % salt, white light at 55 μmol photon m^{-2} s^{-1} with 16:8h light:dark cycle, 30 °C	PUFA 27–28 % of total lipids	Maneechote et al. (2021)
Exopolysaccharides (EPS)	Photoautotrophic	*Chlorella vulgaris* FACHB-6	OECD medium, Cd^{2+} 1.0 mg/L, white light at 30 μmol photon m^{-2} s^{-1} with 12:12 h light:dark cycle, 25 °C	Soluble EPS 0.22 mg/L, Bound EPS 0.603 mg/L	Chen et al. (2015)
		Scenedesmus sp. SB1	BG-11 medium, NaCl 1 %, white light at 1500 lx with 12:12 h light:dark cycle, 25 °C	EPS 0.086 ± 0.04 mg/mL	Angelaalincy et al. (2017)
		Scenedesmus abundans	Modified Chu-13 media with replacing KNO_3 by urea, white light at 2162 μmol photon m^{-2} s^{-1} with 14:10 h light:dark cycle, 24 °C	EPS 37 mg/g biomass	Mahesh et al. (2019)
	Mixotrophic	Marine *Chlorella* sp.	BG11 medium with CO_2 10 % and glucose 1 %, white light at 65 μmol photon m^{-2} s^{-1} with 16:8h light:dark cycle, 30 °C	EPS 1.46 g/L	Cheirsilp et al. (2016)

ORAC: oxygen radical absorbance capacity; FRAP: ferric reducing power; TE: Trolox Equivalent; DPPH: 2,2-diphenyl-1-picryl-hydrazyl-hydrate.
ALA: Alpha-Linolenic acid; EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid.

cultivation modes as shown in Table 2. In addition, there are several types of wastewater which are relatively safe and suitable for microalgae cultivation due to their high organic content and low toxicity. Therefore, Table 2 also summarizes the microalgae cultivated on wastewater those can be used for production of high valuable products.

3.1. Pigments

Microalgal pigments greatly contribute to the profitability of microalgal biorefineries. Microalgal pigments are verified to have numerous functional properties that are beneficial to health of both human and animal i.e., antioxidant, anti-obesity, anticarcinogenic, anti-angiogenic, anti-inflammatory, and neuroprotective-properties (Lee et al., 2021). Furthermore, the microalgal pigments are widely applied as additives in food and feed industries and also in pharmaceutical and cosmetic industries because of their functional properties and intensified colors (Patel et al., 2022). Due to the great biological activities of the microalgal pigments, researches on their productions and applications have significantly grown in recent years. The main pigments present in various microalgal species include chlorophylls and carotenoids. In some specific microalgae, carotenes and xanthophylls are also found. Carotenes (such as lycopene and β-carotene) consist of hydrocarbons ($C_{40}H_{56}$), whereas xanthophylls (such as astaxanthin, zeaxanthin, and lutein) consist of carbon, hydrogen, and oxygen ($C_{40}H_{56}O_2$). Chlorophyceae, a prominent carotenoid-producing group among microalgal species, can also produce carotenes and xanthophylls but at low levels. Compared to lycopene, β-carotene, zeaxanthin, and lutein, astaxanthin has much higher antioxidant capacity, even ten times higher than that of vitamin C and 100 times higher than that of vitamin E (Patel et al., 2022). This efficacy comes from the thirteen conjugated double-bond in its structure. Several researchers have determined the optimal conditions for pigment production by microalgae, as shown in Table 2.

Among various microalgal pigments, chlorophylls and carotenoids have been reported as the main pigments in various microalgae under photoautotrophic cultivation mode. Thawechai et al. (2016) have reported the effects of light intensity and photoperiod on the pigment accumulation in oleaginous microalga *Nannochloropsis* sp. They found that the content of pigments was improved with increased loads of light energy. When the photoperiod was prolonged to be full illumination for 24 h with the high light intensity of 80 μmol photon m^{-2} s^{-1}, both chlorophylls and carotenoids contents increased up to 230 mg/g and 140 mg/g, respectively. Singh et al. (2019) revealed that the use of blue-light at moderate intensity of 60 μmol photon m^{-2} s^{-1} for cultivation of *Asterarcys quadricellulare* PUMCC 5.1.1, did increase the carotenoids content up to 118 μg/mg dry biomass. In addition, cold temperatures also stimulated hyper-accumulation of chlorophylls and carotenoids. A cold temperature of 15 °C coupled with full illumination at 50 μmol·photon·m^{-2} s^{-1} light intensity, was the best condition for the hyper-accumulation of pigments by *Chlamydomonas reinhardtii*. The maximum productivity of chlorophylls was 55.18 mg/L.d and that of carotenoids was 13.48 mg/L.d. It has been suggested that to sustain the cellular activities under the cold temperature stress, the microalgal cells need a number of protective morphological and physiological mechanisms. One of them is the hyper-synthesis of the pigments (Potijun et al., 2021). Recently, the mixed *Scenedesmus dimorphus* (50 %) and *Chlorella* sp. (50 %) has been used to bioremediate aquaculture wastewater added with agricultural wastes. With this system, the chlorophylls production of 1253.17 μg/L was recorded (Pekkoh et al., 2022). Among the microalgal species studies, β-carotene is predominantly found in *Dunaliella salina*. Since several studies have shown that the human body can convert β-carotene into vitamin A, the uptake of microalgal biomass has been suggested to help meet the physiological need for vitamin A (Khanra et al., 2018; Cezare-Gomes et al., 2023).

The secondly most used microalgae pigment, besides β-carotene, is the red-colored xanthophylls known as astaxanthin (Koyande et al., 2019b). *Haematococcus pluvialis*, a type of microalgae, produces the most astaxanthin, at a rate of about 81 % of total carotenoid yield (Levasseur et al., 2020; Cheirsilp et al., 2022). In addition to *Haematococcus pluvialis*, other species such as *Chlorella zofingiensis*, *Scenedesmus* sp., and *Chlorococcum* sp. are also able to accumulate astaxanthin, but at a limited level. Zeaxanthin is mainly accumulated by *Nannochloropsis oculate* and *Scenedesmus almeriensis* (Pereira et al., 2021). Zeaxanthin has strong capacity to absorb blue light and also has protective function against retinal damages (Koyande et al., 2019b). *Chlorella* genus has been suggested as the best natural source for lutein pigment. Among them, *Chlorella protothecoides* was found to be the dominant strain to accumulate high lutein (Ho et al., 2014). Other microalgal species including *Scenedesmus almeriensis*, *Muriellopsis* sp., *Galdieria sulphuraria,* and *D. salina* are also exploited for lutein accumulation (Sun et al., 2021). The contents of lutein found in *Muriellopsis* sp. and *Chlorella protothecoides* were 18 and 150 folds greater than that in marigold (Lin et al., 2015). Fucoxanthin is a lipophilic pigment containing carotene structure with oxygenated backbone. It also contains functional groups like carboxyl, hydroxyl, epoxy, and carbonyl moieties (Pereira et al., 2021; Jiang et al., 2022). It transforms visible spectrum light from the blue-green to yellow-green regions by absorbing light with wavelengths of 450–540 nm. Fucoxanthin-rich foods have been shown in prior research to have beneficial bioactive effects, including antihypertensive, antioxidant, anticancer, antimicrobial, and many others (Bae et al., 2020).

3.2. Vitamins

Several kinds of vitamins are found in microalgal biomass such as provitamin-A, vitamin B, vitamin C and vitamin K (Galasso et al., 2019; Ljubic et al., 2020; Mehariya et al., 2021) as shown in Table 2. The microalgae species, physiological/nutritional factors, especially in photoautotrophic mode, and climatic conditions all affect the synthesis of vitamins in microalgae (Levasseur et al., 2020). Although microalgae do not naturally make vitamin A, they can accumulate precursors to vitamin A like retinol, α- and β-carotenes (Koyande et al., 2019b). Edelmann et al. (2019) reported that when *Nannochloropsis* sp. and *Chlorella* sp. biomass were formulated as powders, they contain 20.8 and 25.9 μg/g of vitamin B9, respectively. Vitamin B12 is an essential vitamin, but its availability in plant foods is restricted, making it particularly important for good health. In addition, the availability of nitrogen (N) also affects the ability of microalgae to produce vitamins. It was shown that cyanobacteria generated less vitamin B12 content under nitrogen-deficient conditions when compared to that under nitrogen-replete conditions (Bonnet et al., 2010). Riboflavin, an essential vitamin for mariculture animals, is another vitamin that may be found in microalgal biomass (Chew et al., 2017). *Anabaena cylindrica* is recognized as the most abundant source of vitamin K1, also known as phylloquinone, which is essential for various physiological activities, including bone and vascular health and blood coagulation. The optimal nitrate concentration of 1700 mg/L combined with extremely high light intensity at 320 μmol photons m^{-2} s^{-1} increased the productivity of phylloquinone by 4 folds, to 22 μg L^{-1} day^{-1} and also the vitamin K1 content to 200 μg/g (Tarento et al., 2018). Ljubic et al. (2020) found that *Nannochloropsis oceanica* accumulated vitamin D3 at 1 μg/g, and its content was increased by increasing the UVB radiation up to 6 kJ/m^2.

3.3. Proteins/peptides

Proteins are amino acids linked by peptide bonds. By 2054, proteins from insects and microalgae may replace those from plants, which currently account for 50 % of the world's market for proteins and peptides (Khanra et al., 2018). The availability of nitrogen in the medium affects the protein content of microalgal biomass. Most of studies reported the protein production under photoautotrophic mode but the mixotrophic mode was also used for microalgal protein production (Table 2). Increasing nitrogen concentration appears to be the main

factor for enhancing protein biosynthesis and also indirectly influences other components such as pigments (Kadkhodaei et al., 2015). Usually, rapidly growing microalgal biomass has high protein content but low lipid or carbohydrate content. Zhang et al. (2019) found that the protein content of Scenedesmus obiquus could be maximal at 56 % when cultivated at pH 10.0, 25 °C and 150 μmol photon m^{-2} s^{-1} light intensity. With increasing temperature and light intensity beyond the optimum, the efficiency of protein synthesis was reduced resulting in a low content of protein. Kadkhodaei et al. (2015) found that the protein content of *Dunaliella salina* cultivated under mixotrophic modes increased when glucose and salt was added. However, with glucose and salt concentrations higher than 1.5 % and 2.5 M, respectively, the protein content dropped dramatically. With using light intensity of 40 μmol m^{-2} s^{-1} coupled with photoperiod of 12:12 h, the protein content of *Pseudopediastrum boryanum* significantly increased to 672.6 mg/g-dried weight (67.3 %) at 30 °C (Militao et al., 2019). It has been reported that the defatted *Nannochloropsis* sp. biomass contained protein content of about 45.2 %, which could be extracted through the hydrothermal liquefaction process. This protein fraction can be used as a human protein supplement or an ingredient in animal feed. These microalgal proteins may replace as an alternative to soybean protein and be preferable to consumers with soy allergies (Valente et al., 2019).

Microalgal protein can be hydrolyzed into peptides those contain short-chain amino acids (20–50 units). Peptides have been experimentally confirmed their biological functions (Levasseur et al., 2020). Stack et al. (2018) cultivated red microalga *Porphyridium purpureum* for their high protein contents and the production of bioactive peptides. The peptides showed oxygen-radical-absorbance-capacity (ORAC) of 13.98 ± 0.97 μmol Trolox Equivalent (TE) per gram-dry matter and ferric reducing power (FRAP) of 478.94 ± 34.43 μmol TE/g. Montalvo et al. (2019) performed the enzymatic production of biopeptides from microalga *Arthrospira maxima* OF15, which was cultivated on diluted sugarcane vinasse. The protein content of *A. maxima* OF15 was as high as 57.04 ± 0.031 %. The peptides concentration obtained were 2395–2831 μg/mL. Recently, Olena et al. (2022) revealed that the enzymatic hydrolysis of microalgal protein followed by centrifugation could generate large amount of bioactive peptides. In their study, *Chlorella protothecoides* (FACHB-2) cultivated under mixotrophic condition was used for enzymatic hydrolysis. The protein hydrolysates contained peptides with scavenging activities of 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) radicals (33.47 ± 0.68 %) and hydroxyl radicals (46.81 ± 2.38 %).

3.4. Carbohydrates

Typically, microalgal biomass has high carbohydrate content, which is around 50 % of their dry weight. This is because their relatively high photoconversion efficiency to produce glucose and accumulate in the form of carbohydrates. Carbohydrates in microalgal biomass are mainly in the forms of cellulose, starch, and many polysaccharides. Among these forms, microalgal starch is usually applied as feedstock for bioenergy production such as bioethanol, biogas and biohydrogen, while polysaccharides from microalgal biomass have various functions and activities such as storage, structural molecules, and protective substances. They can be applied as functional ingredients, additives for cosmetics, and natural pharmaceutical agents. They also have ability to improve immune system and inflammatory responses (Chew et al., 2017). Factors affecting microalgal carbohydrate production include microalgal species, nutrients, medium composition, CO_2 concentration, light intensity, pH, temperature and agitation. Many studies have reported the production of microalgal carbohydrate under both photoautotrophic and mixotrophic modes (Table 2).

Generally, nutrient starvation and other stress factors can be used to induce microalgal phenotypes that can accumulate high content of carbohydrates (Singh et al., 2019). The nitrogen starvation is often used as effective stressor for stimulating carbohydrate accumulation in microalgae. Under photoautotrophic mode, *Chlorella vulgaris* FSP-E accumulated carbohydrates up to 51.3 % when it was cultivated using 2.0 % CO_2 at light intensity of 60 μmol photon m^{-2} s^{-1} and temperature of 28 °C under nitrogen depletion for 4 days (Ho et al., 2013). Huo et al. (2020) cultivated *Tribonema* sp., a filamentous microalga, in BG-11 medium at various temperatures of 25–35 °C. The optimal temperature was 25 °C giving the highest carbohydrate accumulation of 43 % in 9 days. Sivaramakrishnan et al. (2020) found that the polysaccharides extracted from *Scenedesmus* sp. biomass after microwave treatment could be applied in food industry as thickening agents, emulsifiers and stabilizers and in other industries as bioflocculants, water-soluble lubricants, cosmetics, antioxidants, antitumor agents. Recently, carbohydrate-rich microalga *Tribonema* sp. has been used to remove acetophenone and acrylonitrile from simulated wastewater containing acrylonitrile, butadiene and styrene. The feeding of 2 % CO_2 with the presence of acetophenone at 100 mg/L increased biomass, biomass productivity, and carbohydrates productivity up to 3.97 g/L, 0.419 g/L.d, and 0.201 g/L.d, respectively. This microalga also completely degraded acetophenone within 9 days (Zheng et al., 2022).

Freitas et al. (2017) studied the effects of pentose addition and light fluctuation on carbohydrate accumulation by *Chlorella minutissima*. The cultures were performend under mixotrophic mode in a raceway photobioreactor. The carbohydrate content in the microalga was increased up to 53.8 %. They also suggested that the microalgal carbohydrates could be used as ethanol feedstock with a theoretical yield of 39.1 mL per 100 g. Another study maximized the biomass and carbohydrate productivities of S. obliquus UTEX 393 by using multiple-factor optimizing strategies. After optimization, the maximum productivities of biomass and carbohydrate obtained were 491 and 270 mg/L.d, respectively. The optimized conditions were: initial pH of 6.69, temperature of 27.65 °C, glucose and urea concentrations of 3.33 g/L and 126.77 mg/L, respectively (Singh et al., 2019). The optimal conditions for carbohydrate productivity of *Chlamydomonas* sp. QWY37 cultivated in swine wastewater were: very high light intensity at 500 μmol photon m^{-2} s^{-1} and temperature of 30 °C. The maximum carbohydrate productivity obtained was 944 mg/L.d (Qu et al., 2020).

3.5. Lipids

Oleaginous microalgal species can accumulate lipids > 20 % of their biomass, and the lipid content might be as high as 30 % to 70 % of their biomass when cultivated under specific conditions. The most effective strategies to increase lipid accumulation are cultural stresses such as nutrient limitation/starvation (e.g., nitrogen, phosphorus and ferrous ion), high light intensity/long photoperiod, and high or low temperature profiles. Most of these cultural stresses repress cell growth but stimulate lipid accumulation. There are two types of lipids that are accumulated in microalgae. The first type has fatty acid chains with 14 to 19 carbon atoms, whereas the second type has fatty acid chains with > 19 carbon atoms. The former type can be commonly converted to biodiesel and the latter type is rather used as polyunsaturated fatty acids in food industry. Recently, microalgae have gained attention for biodiesel production since they have much higher lipid productivity than conventional oil crops (Koyande et al., 2019a). There are several researches attempted to increase the lipid production of microalgae by manipulating cultivation modes as shown in Table 2.

Green microalga *Botryococcus* sp. TRG photoautotrophically cultivated in nitrogen-rich medium grew better but accumulated lower lipid content than that in nitrogen-deficient medium by two to three folds (Yeesang and Cheirsilp, 2011). Furthermore, by combining a nitrogen-deficient medium with a high Fe concentration of 0.74 mM and a high light intensity of 82.5 μmol photon m^{-2} s^{-1}, the lipid content of the TRG strain was increased from 25.8 % to 35.9 %. According to Srinuanpan *et al.* (2018), limiting phosphorus or ferrous iron had less effect on cell growth but increased lipid accumulation by 1.2 folds for *Scenedesmus obliquus* SIT06 and *Micractinium reisseri* SIT04. However, at conditions of

light intensity of 90 μmol photon m^{-2} s^{-1} and 24:0h light:dark cycles, nitrogen starvation resulted in improved lipid content by 1.5–1.6 times while severely inhibiting microalgal growth. Moreover, nitrogen starvation also increased the content of saturated fatty acids, which then gave higher cetane number and better oxidative stability than other fuels. In addition, Figueroa-Torres et al. (2021) suggested a co-limiting nitrogen and phosphorus strategy to increase starch and lipid contents while supplying acetate as organic carbon source to enhance biomass production. Under optimization, the starch and lipid contents of the microalgal biomass was increased by 27 % and 74 %, respectively.

Cheirsilp and Torpee (2012) evaluated the fed-batch mixotrophic cultivation for enhancing lipid production by two microalgae, marine *Chlorella* sp. and *Nannochloropsis* sp. In the fed-batch mixotrophic cultivation, glucose was intermittently added and light intensity was gradually increased to supply sufficient carbon and energy sources during microalgae growth. This strategy produced two-fold higher lipids than the batch cultivation. In addition, Cheirsilp et al. (2017) also evaluated the use of *Nannochloropsis* sp. entrapped in alginate gel beads under repeated-batch cultivation for production of microalgal lipids. The optimal conditions were: aeration with 10 % CO_2 and illumination for 24 h at 47 μmol photon m^{-2} s^{-1} light intensity for 7 days. The repeated-batch cultivation increased microalgal biomass by 2.66 folds and lipid production by 1.41 folds. The fatty acid compositions were found suitable as feedstocks for biodiesel. However, Cheng et al. (2022) claimed that the lipid content of *Chlorella pyrenoidosa* obtained with heterotrophic growth (18.53 %) was higher than that with mixotrophic growth (16.84 %).

In addition to the pure culture, Cheirsilp et al. (2011) suggested co-cultivating microalga *Chlorella vulgaris* with oleaginous yeast *Rhodotorula glutinis* using molasses as a cheap carbon source. The optimal microalga to yeast ratio was 1 per 1. The optimal molasses concentration and initial pH were 1 % and 5.0, respectively. The optimal light intensity was at 5,000 Lux with 16:8h photoperiod. These optimized conditions achieved the maximum level of lipid production of 2.88 ± 0.16 g/L. These findings agreed with those reported by Kitcha and Cheirsilp (2014), who also used oleaginous yeast *Trichosporonoides spathulate* JU4-57 for co-cultivating with *Chlorella vulgaris* TISTR 8261. The co-culture was entrapped in alginate gel beads. Under light intensity of 2 klux with 16:8h photoperiod, the microalgae-yeast biomass obtained was as high as 12.2 g/L and the lipid content was 47 %. Additionally, due to their similar fatty acid compositions to those of plant oils, microalgae-yeast lipids are considered as potential feedstocks for the production of biodiesel.

3.6. Polyunsaturated fatty acids

Microalgae can accumulate polyunsaturated fatty acids (PUFA), which are necessary for human health and nutrition. Due to their year-round viability and high biomass and lipid productivity, they are considered sustainable sources for PUFA production (Chew et al., 2017). Consumption of omega-3 PUFA has shown efficacy in the prevention of diseases including inflammatory bowel disorders, type-II diabetes, cancer, depression, arthritis, schizophrenia, asthma, and cardiovascular disorders. The stress conditions, i.e. nitrogen starvation not only increased the yield of docosahexaenoic acid (DHA) but also upregulated gene expression, indicating high PUFA synthase activity (Chen et al., 2020). Remmers et al. (2017) found that *Phaeodactylum tricornutum* accumulated PUFAs at the highest level when using 60 μmol photon m^{-2} s^{-1} light intensity and nitrogen-replete condition. Interestingly, the use of green LED-wavelengths was also a practical technique to enhance PUFA content in *Nannochloropsis oceanica* under stress conditions (Ra et al., 2016). In addition to green-wavelength stress, low culture temperatures also could be used to increase the PUFAs content (Sirisuk et al., 2018). Ma et al. (2018) found that microalga *Nannochloropsis* sp. produced high-value omega-3-rich PUFAs, specifically eicosapentaenoic acid (EPA), at a higher level when using 50 μmol photon m^{-2} s^{-1} light intensity. Wang et al. (2019) reported a strategy to improve PUFA production by microalga *Phaeodactylum tricornutum* CCMP-2561 through fulvic acid-empowered adaptive evolution. They found that the use of fulvic acid at 15 mg/L could promote microalgal growth and increase EPA production up to the highest content of 13.9 %. This was because fortification with fulvic acid could increase antioxidant capacity and re-allocated carbon metabolic precursors to lipogenesis. These then improved both microalgal growth and lipid content. Maneechote et al. (2021) shown that two newly isolated microalgae, *Chlorella* sp. PPS and *Scenedesmus* sp. SPP, were promising PUFA sources as they contained PUFA as high as 18–27 % of total lipids under nitrogen-rich conditions.

3.7. Exopolysaccharides

Exopolysaccharides produced by microalgae could be used as biodegradable polymers, bioflocculents, and bioactive compounds with many health benefits for human, for example anticancer, antithrombotic, immunomodulatory agents, and anticoagulants. During their life cycle, microalgae can produce a lot of polysaccharides that they can secrete into the extracellular medium, where they combine with other biomolecules like lipids, nucleic acids, and proteins providing backbone structure for defensive bio-films. The microalgal exopolysaccharides could be harvested as byproducts from the culture medium after biomass separation with no waste generated (Manirafasha et al., 2018). Most microalgae species produce polysaccharides that are heteropolymers consisted of several sugars including glucose, galactose, and xylose relating to cultivation conditions. While *Gyrodinium impudicum* and *Chlorella vulgaris* produced homopolysaccharides containing glucose as parts of their cell walls.

The production of microalgal EPS is greatly affected by the medium components such as nitrogen or carbon sources (Angelaalincy et al., 2017). Chen et al. (2015) examined the effect of heavy metal stress at 1.0 mg-Cd^{2+}/L on production of two forms of EPSs, namely cell bound (B-EPS) and soluble (S-EPS) forms by *Chlorella vulgaris* FACHB-6. With this heavy metal stress, the culture conditions under 12 h daily light illumination at 30 μmol photons m^{-2} s^{-1} and temperature of 25 °C improved B-EPS and S-EPS production by 50.6 % and 19.7 %, respectively. Similarly, Angelaalincy et al. (2017) also found that *Scenedesmus* sp. SB1 produced EPS 1.67 folds higher than the control when 1 % salt was added to the medium to induce salinity stress condition. Mahesh et al. (2019) studied the EPS production by cultivation of *Scenedesmus abundans* in a flat-panel photobioreactor. They found that the nitrogen starvation combined with high extremely light intensity (2162 μmol photons m^{-2} s^{-1}), did increase the EPS production to 236 mg/L yielding 37 mg EPS/g-biomass. Cheirsilp et al. (2016) revealed that oleaginous marine *Chlorella* sp. was promising microalga as it could accumulate high content of lipids > 30 % of its biomass and also released EPS as by-product into the culture medium. The optimized conditions for maximizing microalgal biomass and product formation were: mixotrophic mode added with 1 % w/v glucose and aerated with CO_2 of 10 % in air and 65 μmol photon m^{-2} s^{-1} light intensity. It was also reported that both microalgal EPS and lipids showed high potential as bioflocculant and biodiesel feedstocks, respectively.

4. Sustainability of zero-waste microalgal biorefinery

4.1. Valorization of wastes from microalgae cultivation

The wastes derived from microalgae cultivation can be categorized as liquid and solid wastes. Sustainable biorefinery of microalgal biomass requires processes those are energy-efficient and can upcycle or recycle both liquid and solid wastes. Recently, many researches have proposed the valorization of wastes from microalgae cultivation for the production of valuable products based on the zero-waste biorefinery concept (Laurens et al., 2017; Chandra et al., 2019).

a) Liquid waste, during microalgae cultivation and processing of

microalgal biomass, a substantial volume of spent medium is generated as liquid waste. The discharge of this liquid waste might lead to the environmental problem. Upcycling or recycling the spent medium is a great idea to reduce liquid waste streams and decrease environmental effects as well as the need for nutrients because the amount of unused nutrients may remain in the spent medium (Mishra et al., 2019). However, the effluent property and subsequent valorization of the spent medium depend on biomass separation methods, i.e. centrifugation, filtration, and flocculation. Thus, the use of microalgae strains with auto-flocculation characteristics can greatly reduce high energy input and reduce or eliminate the usage of chemical flocculants and consequently allow spent culture media to be reused (Zhang et al., 2021).

b) Solid waste, different types of solid wastes are generated after processing of microalgal biomass depending on their main products. For example, the lipid-free biomass come from the production of microalgae-based biodiesel and anaerobic digestate comes from the production of biohydrogen and biomethane. Based on the concept of zero-waste biorefinery, these solid wastes should be used to create other valuable co-products (Mishra et al., 2019; Maneechote et al., 2021). However, to avoid using energy-intensive downstream processes, i.e. neutralizing, drying, grinding, and other processes, it is imperative to choose the suitable solid-waste valorization pathway. It has been reported that several valuable components, i.e., proteins, lipids, carbohydrates, polysaccharides, and other minor components, remained in the solid wastes after the processing of microalgal biomass (Song et al., 2019). Pretreatment of the solid wastes by individual or combined techniques (chemical, physical, thermo-chemical, and enzymatic) have been used to degrade the complex molecules into simpler substances prior to further conversion to other high-value products. The solid wastes may be recycled through anaerobic digestion to produce biofuel production, namely methane and hydrogen, since they are rich in organic carbon and nutrients. It has been reported that the anaerobic digestion of microalgal biomass for production of hydrogen could improve methane content in subsequent anaerobic digestion (Mussgnug et al., 2010). Gu et al. (2015) also revealed that the microalgal solid residues could be upcycled as nutrient sources for subsequent microalgae cultivation. With this strategy, both heterotrophic microalgal growth and lipid production were improved. Another recent research proposed the combination of fermentation and ethanol-assisted liquefaction of *Nannochloropsis* sp. biomass for improved biofuel production (Rahman et al., 2019).

4.2. Techno-economic and environmental sustainability

Sustainability refers to the ability to maintain something indefinitely while still being capable of meeting future demands. The development of integrated techniques that can extract all components from microalgal biomass and use them for production of valuable biofuel and bioproducts, would make microalgae-based industries not only economically feasible but also sustainable. However, it is also crucial to involve the valorization of wastes from microalgae cultivation, and balance between the techno-economic sustainability and the environmental sustainability to develop the zero-waste microalgal biorefinery (Fig. 1). These two aspects are likely interconnected in a way that one's performance might hinder another's.

a) Techno-economic sustainability: The aspect of techno-economic sustainability is frequently considered by evaluation of profitability and techno-economic analysis (TEA), where technical dimensions are examined in terms of process economics. To sustainably produce a specific product, several biorefinery scenarios should be compared, and their economic performance has to be evaluated by cost indicators (Yadav and Sen, 2018). The TEA of microalgae production is rather inconstant. There are many factors affecting the TEA of the process, i.e., design of the cultivation system, the nutrient and CO_2 sources for cultivation, facility scale, biomass productivity, and downstream processing techniques (Subhash et al., 2022). The impacts of these factors on the costs and performance of each scenario is evaluated using a techno-economic model in order to maximize overall profits. This model also provides the input and output inventory necessary for subsequent life cycle analysis. One report on the TEA of jet-biofuels made from microalgae indicated the minimum sale price at 5.89 $/L. This price was 14 times more expensive than that of fossil-based jet fuel, which was only 0.43 $/L (Ewurum, 2019). Therefore, the combined strategies have been reported for cost reduction in microalgae-based biofuel production. Some strategies focused on cost reduction in detailed unit operations such as cultivation, harvesting, or downstream processes; others focused on cost reduction across the board, including cultivation inputs, i.e., the utilization of wastewater and CO_2 in flue gas (Subhash et al., 2022).

To lower the costs for microalgal biomass production, the integrations of waste valorization with microalgae cultivation have been explored. However, the costs of using microalgae to treat the wastes must be at the same level as conventional methods. In the case of wastewater treatment by microalgae, the cultivation costs should not be

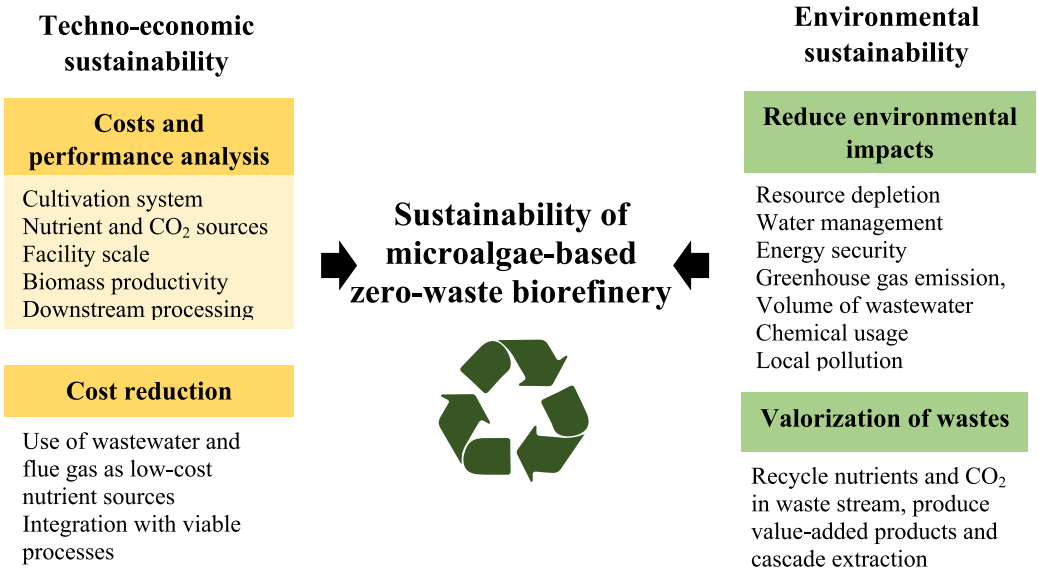

Fig. 1. Some sustainable practices for microalgae-based zero-waste biorefinery.

higher than that of conventional wastewater treatment (0.2€/m^3) (Gouveia et al., 2016). In one study, volatile fatty acids obtained during the fermentation of food wastes were utilized as cheap nutrient sources for the heterotrophic growth of microalgae, which not only improved microalgal lipid yield but also decreased the production costs of biodiesel to $2.3/gallon (Fei et al., 2015). The TEA has revealed that the bio-oil production from microalgal biomass when integrated with the protein extraction process could generate extra revenues from the extracted proteins. This combined process may significantly contribute to the development of zero-waste microalgal biorefineries (Phusunti and Cheirsilp, 2020). In the biorefinery concept, the pigments of the oleaginous microalga *Chlorella* sp. were extracted before biodiesel production via direct transesterification reaction, and the carbohydrate fraction of the defatted microalgal biomass was subsequently acid-hydrolyzed to produce sugars, and finally, the protein hydrolysate was recovered (Mandik et al., 2020). In addition, the TEA for co-productions of biofuels, namely biodiesel, and ethanol, from microalgal biomass have shown prerequisite investment settings with low environmental impact. The integration of microalgae cultivation with other viable processes could also reduce life-cycle GHG emissions, heat recovery, and CO_2 recycling (Wu et al., 2018). Microalgae cultivation using wastewater, allowing nutrient recovery in microalgal biomass and subsequent biofuel production, is considered a promising path to promote the sustainability of microalgae-based zero-waste industries (Li et al., 2022).

b) Environmental sustainability: this aspect involves the methods that demonstrate the environmental burden of the products or processes and the social impacts by analyzing the damage to ecosystem resources, human health, climate, etc. The procedure starts with the selection of the cultivation region and sustainable nutrient sources for microalgal growth and product formation, the biomass harvesting methods, and the methods, and solvents for lipid extraction and conversion into biodiesel or other valuable products. All steps should contribute to environmental sustainability. The index for long-term sustainability can be confirmed by the use of certain indicators, including soil and resource depletion, water management, energy security, local pollution, GHG emissions, the volume of wastewater, chemical usage, and local pollution, etc. (Subramanian et al., 2016; Patnaik and Mallick, 2021). Valorizing wastewater is a common scheme to reutilize nutrients and water, reduce the volume of wastewater being transported and treated, and consequently lessen environmental impacts. Microalgae are considered an excellent candidate to be explored in these scenarios. Emerging microalgae cultivation systems that can help reduce GHG through CO_2 capture while producing an alternative biofuel for fossil fuels are the keys to being valuable and sustainable (Kamyaba et al., 2019). Environmentally friendly cascade extraction/separation of the valuable components in the microalgal biomass as well as their suitable conversions to economically viable products should be developed to increase the technical-economics feasibility of zero-waste biorefinery of microalgal biomass and maintain environmental sustainability (Yadav and Sen, 2018).

The mixotrophy, the strategy to utilize the mechanism of microalgae to simultaneously assimilate both inorganic carbon and organic carbon, is one of the crucial approaches for microalgal biorefineries because it can boost microalgal biomass productivities, CO_2 fixation rates, and lipid accumulation; together with wastewater bioremediation (Subramanian et al., 2016). It should be also emphasized that the applications of microalgal biomass as sources of bioenergy have been restricted by the high energy requirements and high costs of downstream processing steps. One study has reported the use of switchable-ionic liquids (S-ILs) induced by CO_2 coupled with hydrophobic-hydrophilic reversible conversion for lipid extraction and separation. S-IL based lipid extraction is advantageous because it combines extraction, separation, and recovery processes with no additional chemicals. It was therefore considered a promising downstream process for sustainable microalgae-based bioenergy production (Tang and Ho Row, 2020).

5. Key issues and future perspectives

5.1. Key issues

Microalgae are considered promising sources to substitute fossil fuels as they are more environmental friendly and can solve environmental problems. Though a scenario with processes that use environmentally friendly fuels with a positive energy balance needs to be designed, one problem needs to be solved is the economic hurdles. The main hurdles are their productivity and industrial scalability. In the case of using photobioreactors with artificial light, the cultivation cost of microalgae would be much higher than that of bacterial fermentation. The low cell concentration and high cost of downstream process (about 40 % based on total cost) also makes microalgal biorefinery difficult (Koyande et al., 2019a). Although the zero-waste biorefinery concept involves the full valorization of wastes from microalgae cultivation, the full utilization of microalgal biomass for valuable products, this concept also faces the problem of low final yields for each product because of many processing steps are needed to get a particular purity. There are also numerous other concerns that need to be taken into account. These include the rather small market for each product, the product loss and degradation during processing steps, and the stability of the extracted compounds. The studies on those concerns are important (Chew et al., 2017).

Moreover, a technically and economically viable biorefinery should have a positive energy balance because many processes involving mixing and mass transfer, and downstream processing including harvesting and drying of biomass and lipid extraction, require high energy input. Although microalgae-based biofuel production has been considered one of the cleanest and most sustainable processes, its commercialization still has numerous key issues to overcome. These include the screening of promising microalgal strains, the requirements of nutrients and water, the large-scale cultivation, the climate impact, the harvesting and drying process of biomass, and the suitable conversion process. Among them, the critical issue that should be concerned is the harvesting of microalgal biomass (Chew et al., 2017). It should be mentioned that due to the low concentration of microalgal biomass, the operations of collecting and drying require a significant amount of energy. As far as energy inputs are concerned, it is crucial to select a set of processes that can produce more energy than those consumed. An energy analysis is an approach that can be applied for this purpose. It estimates the irreversibilities of the processes and compares the energy used in the processes (Peralta et al., 2010).

The greatest limitations of microalgae-based zero-waste biorefineries would be the cost limitations and restrictions on large-scale microalgae cultivation. The policy considerations for the successful implementation of microalgae-based zero-waste biorefineries would be: microalgae cultivation systems with high efficiency; tolerance of microalgae to fluctuations of environmental conditions, such as temperature and light intensity; prevention of contamination from microorganisms; efficient energy consumption of the biorefinery procession of microalgal biomass; biosafety risk and governmental policy issues for microalgal biomass produced from wastewater and flue gas aeration; and a strong and reliable policy and regulatory framework supporting microalgae commercialization (Kuo et al., 2021).

5.2. Perspectives and challenges

The perspectives for achieving the sustainable zero-waste microalgal biorefinery are the development of cost-effective technologies and their integration with other viable processes. Some guidelines for the development of sustainable zero-waste microalgal biorefinery can be elaborated as follows (Fig. 2):

1) Lowering harvesting costs by using self-sedimenting strains or fungal pellets: The use of microalgal strains with self-sedimenting properties would help avoid the use of flocculating agents and other energy-intensive methods to harvest the microalgal biomass. This then,

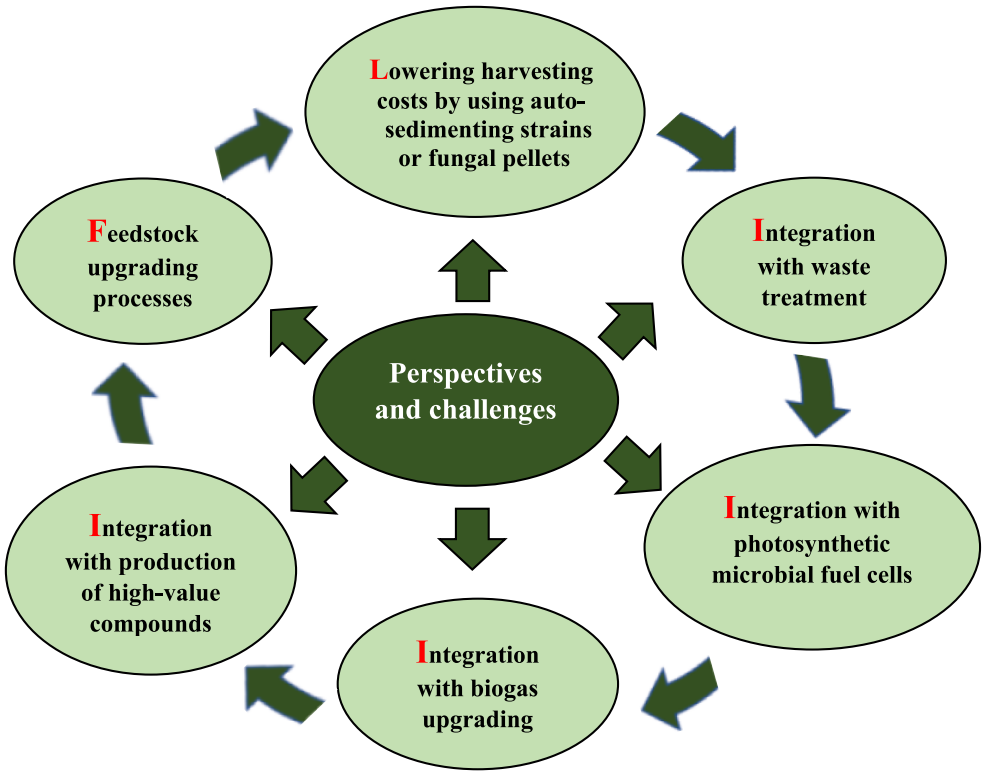

Fig. 2. Perspectives and challenges to achieve sustainable microalgae-based zero-waste biorefinery.

in turn, enables the reusability and recycling of the effluents for subsequent cultivation and/or other bioproductions. Furthermore, the microalgal biomass without the contamination of flocculants also improves their potential as biofuel feedstocks (Mishra et al., 2019). Nie et al. (2018) reported that *Golenkinia* sp. SDEC-16 had cell diameters ranging from 7 to 18 mm and self-sedimenting properties. Srinuanpan *et al.* (2018) reported a promising approach to rapidly harvest *Scenedesmus* sp. cells using the fungal pellets of *Trichoderma reesei* QM 9414. The optimal fungal pellets volume ratio to the microalgae culture broth was 1:2. With this method, the microalgal cells>94 % were rapidly harvested within 10 min.

2) Integration of microalgae cultivation with waste treatment: the processes to reduce, reuse, recycle, and treat effluents, solid wastes, and emitted CO_2 should be developed under BCG economy model. The viable production of microalgal biomass can be accomplished by integrating the microalgae cultivation with treatment of waste streams. The use of anaerobic digestate and wastewater can supply macro- and micronutrients for microalgal metabolism and growth (Ghimire et al., 2017). Recent literatures have revealed various microalgae biorefinery approaches those integrated microalgae cultivation with biovalorization of wastes and biofuel production (Chandra et al., 2019; De Bhowmick et al., 2019). The studies showed that innovative biorefinery approaches such as combined wastewater treatment with industrial CO_2 mitigation would enable effective bioremediation and reduction of GHG emissions. While the combined use of biomass feedstocks i.e., food wastes, sewage, lignocellulosic wastes, and agricultural wastes, would facilitate infinite factory operation (Wang et al., 2019). Microalgae can adapt to new environments and therefore grow in various types of wastewater. They can uptake a wide variety of carbon, nitrogen, and phosphorous and can adsorb or uptake pollutants like heavy metals. However, when integrating microalgae cultivation with wastewater treatment, the levels of carbon, nitrogen, and phosphorous, as well as pollutants, that can be toxic to microalgae, should be considered (Plöhn et al., 2021).

3) Integration of microalgae cultivation with bioelectricity generation: This approach is well known as photosynthetic microbial fuel cells (MFC). It comprises of two chambers, cathodic and anodic chambers, with a proton-exchange-membrane set between the chambers. The anaerobic bacteria in the anodic chamber produce electrons while oxidizing organic substances. When these electrons are transported to a cathode in the cathodic chamber through an external wire circuit, electricity will be generated. The advantage of MFC is that the system can generate electricity while degrading organic wastes. In photosynthetic MFC, microalgae that are cultivated in the cathodic chamber fix CO_2 and produce oxygen as an electron acceptor through their photosynthetic activity, and this could enhance the production of bioelectricity (Uggetti and Puigagut, 2016). Nookwam et al. (2022), who cultivated the oleaginous microalga *Scenedesmus* sp. in the cathodic chamber of MFC, found that the microalgae could increase oxygen availability and enhance the production of bioelectricity while simultaneously secondarily treating effluent from the anodic chamber and producing lipids that can be used as biodiesel feedstocks.

4) Integration of microalgae cultivation with biogas upgrading: Biogas is a biofuel that is anaerobically produced from the anaerobic digestion of organic wastes. It is mainly composed of methane and CO_2, with small amounts of hydrogen, nitrogen, and water. It may also contain a trace amount of hydrogen sulfide depending on the wastes used. Biogas has been produced from various organic wastes, such as food wastes, crop wastes, municipal wastes, agricultural wastes, agro-industrial wastes, lignocellulosic wastes, aquatic wastes, and microalgae and macroalgae (Saratale et al., 2018). For effective energy conversion, the biogas should be purified to increase the methane content to >90 % before combustion. The biological CO_2 removal from biogas using microalgae was established by Mann et al. (2009). The microalgae can purify biogas by removal of CO_2. As the CO_2 content decreases, the methane content increases. Srinuanpan et al. (2017) could effectively remove CO_2 in biogas by cultivating oleaginous *Scenedesmus* sp. The methane content was improved up to be >90 %. This strategy not only purified biogas but also economically produced microalgal biomass with high lipids content. Moreover, Srinuanpan et al. (2019) also developed a two-phase purifying unit for simultaneous phycoremediation of

effluents from anaerobic digestor and upgrading biogas by using oleaginous *Scenedesmus* sp. entrapped in alginate-gel beads. After optimization, the CO_2 in biogas was efficiently removed by the microalgae, and resulted in the increased methane content to > 95 %. Cao et al. (2017) also reported the CO_2 removal in biogas by microalgae. In their study, the microalgae not only removed CO_2 by 75.61 % but also removed COD by 78.09 %, nitrogen by 86.24 % and phosphorus by 86.74 %. Recently, Scarcelli et al. (2021) proposed the domestic sewage treatment system in an anoxic-aerobic photobioreactor and integrated it with the anaerobic digestion system of bacterial-microalgal biomass harvested from the photobioreactor. This system also included photosynthetic biogas upgrading unit. This integrated system removed total organic carbon (TOC) by 98.9 ± 1.1 % and TN by 90.8 ± 8.0 %. The photosynthetic biogas upgrading also removed CO_2 by 74.7 ± 3.0 % and hydrogen sulfide by 99.0 ± 2.8 %. This integrated system would provide an ideal setting for the establishment of a large-scale anoxic-aerobic photobioreactor combined with anaerobic digestion and photosynthetic biogas upgrading using microalgae.

5) Coupling microalgae cultivation with co-production of high-value components: Certain microalgal strains can accumulate large amounts of high-value compounds, including pigments, vitamins, and PUFAs, in addition to the main compounds of lipids, proteins, and carbohydrates. Therefore, co-production and challenges for the recovery of those components have been reported. Nevertheless, the viability and scalability of cultivation and extraction methods, as well as their energy consumption, should be of concern (Chew et al., 2017). Gifuni et al. (2019), who evaluated various research studies on microalgal biorefinery, have concluded that cascade extraction is one of the most suitable approaches to fully utilizing microalgal components. Several studies have performed cascade extraction to fully recover high-value pigments from microalgal biomass, namely carotene, astaxanthin, and lutein before the extraction of other by-products including proteins, lipids, and carbohydrates (Gilbert-López et al., 2017; Lupatini et al., 2017). The possibility of recovering as much as possible from microalgal components depends on the severity of the extraction method. The use of a mild liquid for extraction was suggested, as it caused less damage to other components. Moreover, the extraction method that allows the direct use of wet microalgal biomass also helps decrease the drying process costs (Koyande et al., 2019a). In the biorefinery concept, if a number of chemicals can be simultaneously recovered from the microalgal biomass, it is therefore possible to achieve a higher market value than the production costs. Pigments are one of the main targets for microalgal biorefinery when it comes to fine chemical compounds. Although cascade extraction of high-value components can boost the overall value of microalgal biomass, it is also crucial to implement green techniques for pretreating, extracting, and processing all valuable components for further applications in various sectors. Therefore, a key challenge is to integrate platforms not only for efficiently extracting or fractionating the target components but also for meeting the principles of green chemistry and attaining sustainability (Gilbert-López et al., 2017).

6) Feedstock upgrading processes: microalgal biorefineries should also involve feedstock upgrading processes, the processes that continuously upgrade and refine raw materials. In other words, a feedstock should not be directly burned without any upgrading processes. Therefore, microalgal biorefineries should recover and upgrade the components of the feedstock through a series of processes to attain pure chemical species at high concentrations. In addition, a biorefinery plant should also operate through sustainable processes. The energy input for feedstock conversion processes should be internally obtained from the heat and electricity produced by the combustion of residues. Through the biorefinery concept, production and conversion costs should be significantly reduced. It has been reported that although 13.8 MJ is spent to recover 1 kg of microalgal biomass using the centrifugation method (Wan et al., 2015), the total energy return can offset these energy expenses comparing with other sources of bioenergy. The production costs of microalgal biomass should not go beyond an ideal theoretical cost (0.55 cents) for manufacturing bulk microalgae-based products, namely biofuels and biochemicals, which would help microalgae viable in the view point of commercialization (dos Santos et al., 2017).

6. Concluding remarks

Zero-waste microalgal biorefineries with commercial feasibility, sustainability, and environmental benefits require: i) screening of promising microalgae with superior biomass productivity and unique compositions; ii) cultivation techniques that maximize both photosynthetic efficiency, growth, and high-value components; iii) co-location strategies to valorize industrial wastes and CO_2 flue gas; iv) cascade extraction/separation of high-value components that help increase the overall value of microalgal biomass; and v) utilizing environmentally friendly methods to harvest, pretreat, extract, and process useful components for use in a variety of sectors. The key issues and perspectives include sustainable microalgal biomass production, cost-effective technologies, and innovative integration with viable processes

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

Data will be made available on request.

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