

## Review

## Insights into microalgal biotechnology: Current applications, key challenges, and future prospects



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## ABSTRACT

Microalgae have emerged as multifunctional biofactories capable of simultaneously supporting carbon capture, renewable energy production, environmental remediation, and the synthesis of high value bioproducts. Despite this promise, large-scale deployment remains limited by techno-economic barriers, particularly the high costs of biomass harvesting and dewatering. Recent advances including bioflocculation, magnetic separation, and solar-assisted drying are helping to reduce energy inputs and enhance feasibility. In parallel, breakthroughs in synthetic biology, such as CRISPR/Cas genome editing, are enabling the development of engineered strains with enhanced lipid, carbohydrate, and hydrogen productivity. Innovations in photobioreactor design have further improved light-use efficiency, reduced contamination risks, and supported high-density cultivation. Life cycle assessments indicate that integrating microalgal systems with flue gas utilization and wastewater treatment can substantially lower freshwater use and greenhouse gas emissions. To unlock the full potential of this technology, future efforts should prioritize modular biorefinery systems, intelligent process control, and supportive policy frameworks that incentivise negative-emission technologies. These integrated strategies can help position microalgae as a key enabler of a sustainable, circular bioeconomy.

## Abbreviations

(continued)

ABA	Abscisic Acid	EPS	Extracellular Polymeric Substances
ABF	Algae-Bacteria Floc	EVs	Extracellular Vesicles
AgNPs	Silver Nanoparticles	FAME	Fatty Acid Methyl Esters
AGPase	ADP-glucose Pyrophosphorylase	GHG	Greenhouse gas
ARTP	Atmospheric and Room Temperature Plasma	GMOs	Genetically Modified Organisms
BOD	Biochemical oxygen demand	GRAS	Generally Recognized as Safe
bZIP	Basic Leucine Zipper	HydA	[FeFe]-hydrogenase
CFD	Computational Fluid Dynamics	ICG	Indocyanine green
COD	Chemical Oxygen Demand	LED	Light Emitting Diode
CPR	Closed Photobioreactor	LCA	Life Cycle Assessment
CRISPR/Cas9	Clustered Regularly Interspaced Short Palindromic Repeats/Cas9	MPBRs	Membrane Photobioreactors
DCW	Dry Cell Weight	MZF-NPs	Magnesium-Zinc Ferrite Nanoparticles
DGAT	Diacylglycerol Acyltransferase	NO <sub>x</sub>	Nitrogen Oxides
DHA	Docosahexaenoic acid	ORP	Open Raceway Pond
EI	Energy Informatics	PBR	Photobioreactor
EPA	Eicosapentaenoic acid	PLGA	Poly (lactic-co-glycolic) acid photosystem I

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PSII	Photosystem II
PUFAs	Polyunsaturated Fatty Acids
R&D	Research and Development
RNAi	RNA Interference
RNP	Ribonucleoprotein
SO <sub>x</sub>	Sulfur Oxides
SP@Rh-gel	<i>Spirulina</i> -Rhodizonic Acid Hydrogel
TAG	Triacylglycerol
TALENs	Transcription Activator-Like Effector Nucleases
TEA	Techno-Economic Analysis
TF	Transcription Factor
TN	Total Nitrogen
TP	Total Phosphorus
VFA	Volatile Fatty Acid
2,4-D	2,4-Dichlorophenoxyacetic

## 1. Introduction

The escalating threat of climate change, declining fossil fuel reserves, and increasing water pollution have intensified the global demand for renewable energy, clean water, and sustainable technologies. In this context, the bioeconomy has emerged as a promising pathway toward sustainable development, directly supporting the United Nations Sustainable Development Goals (SDGs) (Scapini et al., 2024; Gallego et al., 2025). Among the bio-based platforms under exploration, microalgae have gained significant attention for their versatility and potential in various biotechnological applications (Wang et al., 2024a).

According to the 2024 Global Carbon Budget, fossil fuel combustion generated a record 37.4 gigatonnes of CO<sub>2</sub>, with coal-fired power plants as key contributors (Global Carbon Budget, 2024). Microalgae, through efficient photosynthesis, can capture and convert atmospheric CO<sub>2</sub> into biomass, making them an effective tool for carbon sequestration. Remarkably, 1 kg of microalgae can absorb approximately 1.83 kg of CO<sub>2</sub> daily, and one acre of cultivated microalgae can fix up to 2.7 tonnes of CO<sub>2</sub> per day (Anguselvi et al., 2019). Unlike traditional crops, microalgae do not require arable land and can produce lipid- and protein-rich biomass with greater spatial efficiency (Ullmann and Grimm, 2021). Their rapid growth, high carbon uptake, broad environmental tolerance, and efficient resource utilization make them ideal candidates for integration into circular bioeconomic systems (Olabi et al., 2023).

In recent years, microalgal biotechnology has rapidly advanced across diverse sectors, including environmental remediation (El-Sheekh et al., 2025), renewable energy (Stephy et al., 2025), nutrition (García-Escínas et al., 2025), and pharmaceuticals (He et al., 2025). Technological innovations such as metagenomics, CRISPR-based genome editing, and adaptive evolution have opened new possibilities for enhancing CO<sub>2</sub> fixation and productivity through both natural and synthetic pathways (Naduthodi et al., 2021). These breakthroughs contribute to the economic viability of microalgal applications while delivering combined environmental and economic benefits.

Microalgal biotechnology aligns closely with multiple SDGs, offering synergistic impacts across key development areas. For *Climate Action* (SDG 13), microalgae help mitigate greenhouse gas emissions and support carbon neutrality (Sarker and Karparaju 2024). In the context of *Zero Hunger* (SDG 2), their high protein and micronutrient content makes them a promising food source to combat malnutrition and food insecurity (Sutherland et al., 2021). For *Affordable and Clean Energy* (SDG 7), microalgae provide a high-yield biofuel feedstock that surpasses conventional energy crops (Sundaram et al., 2023). Additionally, for *Industry, Innovation, and Infrastructure* (SDG 9), microalgae offer sustainable industrial applications, such as the purification of wastewater with simultaneous pollutant removal and resource recovery (Sarker and Karparaju 2024). Collectively, these attributes position microalgae as a strategic enabler of integrated, sustainable

development.

Despite notable progress, large-scale commercial deployment of microalgal technologies remains constrained by fragmented research efforts and persistent scale-up challenges. To unlock their full potential, cross-sectoral and interdisciplinary approaches are essential (Vo Hoang Nhat et al., 2018). This review presents a comprehensive synthesis of current advances in microalgal applications, with a focus on biofuel production, pharmaceuticals, and environmental remediation. It highlights the multifaceted role of microalgae in addressing critical global issues such as the energy crisis and environmental degradation.

Future research should prioritize the following key areas: (i) enhancing the efficiency of microalgal carbon capture mechanisms; (ii) applying synthetic biology to develop robust strains capable of thriving in extreme and polluted environments; (iii) scaling up microalgae-based wastewater treatment systems with integrated resource recovery; and (iv) promoting the high-value utilization of microalgal biomass in biofuels, nutrition, and pharmaceuticals. Through these focused efforts, microalgal biotechnology is poised to play an increasingly pivotal role in advancing the global SDGs and fostering a sustainable, low-carbon future.

## 2. Current applications of microalgae biotechnology

Microalgae have attracted considerable attention for renewable energy production, environmental remediation, and the development of nutraceuticals and pharmaceuticals. These biotechnological applications present promising solutions to global challenges such as resource depletion and environmental pollution, while also advancing the development of a sustainable circular economy. As illustrated in Fig. 1, microalgal cultivation can be effectively integrated with carbon capture and wastewater treatment to facilitate nutrient recovery and biomass generation. The harvested biomass can subsequently be converted into high-value products and biochar, while the treated effluent may be reused for aquaculture or irrigation purposes. This integrated approach establishes a resource-efficient, environmentally sustainable closed-loop system.

### 2.1. Microalgae biofuel production

Population growth and industrialization have increased fossil fuel combustion, releasing greenhouse gases like CO, CO<sub>2</sub>, Sulfur Oxides (SO<sub>x</sub>), and Nitrogen Oxides (NO<sub>x</sub>). As a result, global warming and ecological degradation are intensifying. The COVID-19 pandemic further emphasized the urgency of sustainable bioenergy systems (Wicker et al., 2021). As third-generation biofuels, microalgae-based fuels offer significantly higher biomass yields per unit area compared to first-generation biofuels derived from food crops and second-generation fuels produced from non-food lignocellulosic feedstocks. Advances in genetic engineering have paved the way for fourth-generation biofuels by enabling the development of algal strains optimized for high lipid accumulation—an essential trait for biodiesel production (Sobri et al., 2024). In addition to biodiesel, microalgal biomass can be converted into bioethanol, biohydrogen, and biogas (Fig. 2). This section highlights the production of biodiesel, bioethanol, and biohydrogen from microalgae.

Despite their potential, several challenges continue to hinder large-scale adoption. First, cultivation performance remains inconsistent. While nano-additives can enhance growth, reduce conversion temperatures, and be recycled, their release from open-pond systems poses ecological risks and warrants comprehensive environmental assessment (Pohrmen et al., 2025). Second, harvesting and dewatering are cost-intensive, contributing 20–30 % of overall production costs. For instance, the use of waste eggshell-derived bioflocculants increased the flocculation efficiency of *Tetraselmus obliquus* to 98.6 %, yet this approach depends on reliable feedstock supply and process standardization (Roy and Mohanty, 2020). Third, regional feasibility varies



Fig. 1. Microalgae-based biotechnology for building a green, sustainable circular economy.

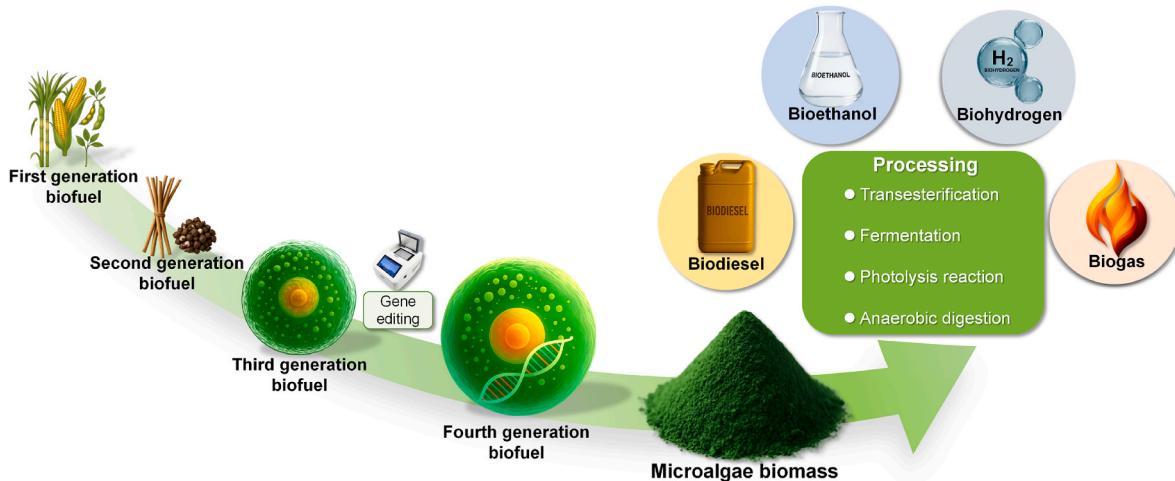


Fig. 2. Biofuel feedstock evolution and microalgae-based fuel production pathways.

considerably, influenced by local energy demands, land availability, and access to freshwater or wastewater resources. Fourth, while single-gene modifications can enhance lipid accumulation without compromising growth, more complex multi-gene engineering strategies, potentially offering greater improvements remain underexplored (Muñoz et al., 2021; Nashath et al., 2025).

Currently, the commercialization of microalgal biofuels is in its infancy. Although small-scale implementations exist and algal fuels are in use in select regional markets, widespread deployment is constrained by low technology readiness and high production costs. Future research

should prioritize enhancing productivity, reducing costs, and improving fuel quality to support the broader adoption of microalgae-derived biofuels.

### 2.1.1. Biodiesel

Biodiesel, composed primarily of fatty acid methyl esters (FAME), offers notable advantages such as high combustion efficiency, excellent lubricity, and ultra-low sulfur content. However, approximately 95% of current biodiesel production relies on edible oils (Hajjari et al., 2017), raising sustainability and food security concerns. Microalgae represent a

promising inedible alternative, with lipid productivities estimated to be 7–31 times higher than those of terrestrial oil crops (Udayan et al., 2023). Moreover, algal lipid profiles can be tailored through controlled cultivation strategies (Table 1).

Cellular lipids are broadly classified as polar or neutral, with triacylglycerols (TAGs)—a neutral lipid being preferred for biodiesel due to their lower degree of unsaturation, which enhances fuel stability. TAG accumulation is typically induced under stress conditions such as nitrogen deprivation, pH fluctuation, or through two-stage cultivation systems. However, excessive or prolonged stress often compromises overall biomass yield. Advances in gene editing now offer more precise metabolic control; for instance, CRISPR/Cas9-mediated overexpression of GAPDH in *Chlamydomonas reinhardtii* has been shown to increase both biomass and fatty acid content (Shin et al., 2024). Furthermore, the combined application of phytohormones and stress treatments has demonstrated synergistic effects on lipid accumulation.

Despite these promising developments, commercial scale microalgal biodiesel production remains constrained by high costs, scalability issues, and regulatory concerns related to chemical catalysts and genetically modified organisms (GMOs). Future research should focus on developing cost-effective cultivation strategies, novel lipid-inducing agents, and standardized, safe gene-editing platforms to facilitate the sustainable, large-scale production of microalgal biodiesel.

### 2.1.2. Bioethanol

Bioethanol derived from biomass is a low-sulfur fuel that generates significantly lower greenhouse gas (GHG) emissions than gasoline. However, its energy content is only about 66 % that of gasoline on a per-volume basis (Anto et al., 2020; Elsayed et al., 2023). Ethanol is typically produced through the fermentation of carbohydrates obtained from crops, lignocellulosic biomass, or microalgae, using yeast or bacterial strains. Among these feedstocks, microalgae are particularly promising due to their high polysaccharide content—including cellulose, agar, starch, and mannitol. Commonly studied and utilized microalgal genera for bioethanol production include *Chlorella*, *Dunaliella salina*, *Chlamydomonas*, *Scenedesmus*, *Spirulina*, *Chlorococcum*, *Tetraselmis*, and *Synechococcus* (Anto et al., 2020; Hebbale et al., 2017).

Microalgae outperform terrestrial biomass for ethanol production due to their lignin-free cell walls, which facilitate polysaccharide decomposition and simplify processing. Their carbohydrates are readily fermented to ethanol with high yields (Siddiki et al., 2022). However, overall efficiency depends on factors such as growth rate, biomass accumulation, sugar composition, and fermentation conditions. These variables are influenced by the species and the cultivation environment.

Several biochemical and environmental factors, such as salinity, light, pH, temperature, nutrients, and vitamins, significantly affect ethanol yields (Chandrasekhar et al., 2023). For instance, Chandra et al. (2020) optimized the initial medium pH increased biomass and carbohydrate content, which boosted ethanol productivity from  $4.1 \pm 0.3$  mg/L/day to  $17.2 \pm 1.2$  mg/L/day. Enhancement strategies for bioethanol production include nutrient supplementation and genetic engineering. Varaprasad et al. (2021) showed that adding vitamins B<sub>1</sub>, B<sub>7</sub>, and B<sub>12</sub> to *Chlorococcum minutum* and *Chlamydomonas reinhardtii* cultures raised reducing sugars and ethanol yields. Maity and Mallick (2024) used a two-stage cultivation, which standard conditions then N starvation to achieve an 86 % ethanol increase in *Leptolyngbya valderiana* BDU 41001. Beigbeder and Lavoie (2022) reported improved ethanol yields from *Parachlorella kessleri* when cultured under 2.5 % (v/v) pig manure, 5 % CO<sub>2</sub>, and a 20 h/4 h light/dark photoperiod. Elshobary et al. (2024) used hydrolysates of magnesium zinc ferrite nanoparticles (MZF-NPs) to pretreat microalgal biomass, resulting in a 4.2-fold increase in ethanol production in *Alkalinema pantanalense* (up to 32.45 g/L) and a 3.48-fold increase in *Chlorella vulgaris* (up to 28.6 g/L). Additionally, Saha et al. (2024) genetically engineered *Chlorella vulgaris* to overexpress the ADP-glucose pyrophosphorylase (AGPase) gene, increasing carbohydrate content to 45.1 % of dry cell weight and ethanol yield to 82.82 mg/L. These advances highlight the potential of targeted strategies to improve bioethanol feedstock quality.

### 2.1.3. Biohydrogen

Biohydrogen, a completely carbon-free fuel with a high calorific value of 120–140 MJ/kg, is anticipated to contribute up to 10 % of the global energy demand by 2025 (Rady et al., 2024). Despite its environmental benefits and energy potential, widespread adoption remains constrained by high production costs, logistical complexities, and technical limitations. Microalgae have emerged as promising platforms for sustainable biohydrogen production due to their rapid growth rates and efficient CO<sub>2</sub> fixation capabilities. To date, over 70 species across more than 30 genera have been investigated, including *Chlorella*, *Chlamydomonas*, *Scenedesmus*, *Anabaena*, *Spirulina*, *Nostoc*, *Platymonas*, *Coccolastrella*, *Tetraspora*, and *Monoraphidium* (Singh et al., 2023). Among these, *Chlorella* has shown particularly high potential for biohydrogen production (Ošlaj and Muršec, 2010). Notably, a newly discovered strain, *Chlorella KLSc59*, has demonstrated biohydrogen yields of up to 281 mmol H<sub>2</sub>/mg Chl (Sirawattanamongkol et al., 2020).

In microalgae, light-driven water splitting generates electrons and protons, which are subsequently recombined into hydrogen (H<sub>2</sub>) by hydrogenase or nitrogenase enzymes (Show et al., 2019). Targeted

**Table 1**  
Assessment of various strategies for enhancing microalgae biodiesel production.

Strategy	Specific approach	Key Regulation Parameters	Species	Performance	References
Environmental stress regulation	Constant pH treatment	pH = 9.5 (CHES buffer)	<i>Phaeodactylum tricornutum</i>	Redirects carbon flux to lipid synthesis	Zhang et al. (2024b)
	Nitrogen starvation	Total nitrogen deprivation (0 N BG11 medium)	<i>Chlorophycean Desmodesmus</i> sp.	Lipid content: 23 % (dry basis) but growth inhibition	Rios et al. (2015)
Two-stage cultivation strategy	Nutrient phased supplementation	N (750 mg/L) and P (40 mg/L) added on Day 2	<i>Desmodesmus intermedius</i> Z8	Lipid productivity: 244.69 mg/L/d; fatty acids meet biodiesel standards	Li et al. (2023)
	2,4-Dichlorophenoxyacetic (2,4-D) + Abscisic Acid (ABA) sequential treatment	2.5 mg/L 2,4-D (Days 0–5) + 2 mg/L ABA (Days 5–8)	<i>Phaeodactylum tricornutum</i>	Synergistic increase in biomass and lipid content	Zhang et al. (2021)
Genetic engineering	Key genes overexpression	<i>DGTT2/3/4</i> , <i>DYRK</i> , <i>DGAT2</i> , etc.	Multiple microalgae	Targeted lipid pathway engineering	Ghosh and Sarkar. (2024)
	Malic enzyme overexpression	Malic enzyme cloning and overexpression	<i>Chlorella protothecoides</i>	2.8 folds increase in total lipid accumulation	Yan et al. (2019)
	GAPDH overexpression	Chloroplast GAPDH under <i>NIT1</i> promoter	<i>Chlamydomonas reinhardtii</i> mutant PNG#7	Biomass increased 44 % (Day 4) and 76 % (Day 16); 2.4 folds increase in FAME content	Shin et al. (2024)
Transcription factor engineering	<i>bZIP1</i> overexpression	<i>bZIP1</i> TF	<i>Nannochloropsis oceanica</i>	Enhanced lipid accumulation/secretion without physiological trade-offs	Li et al. (2019)

genetic engineering can significantly enhance this process. For example, single and double mutations in the *HydA* gene of *Chlorella* sp. DT led to up to a 30-fold increase in H<sub>2</sub> evolution under variable oxygen conditions (Yang et al., 2019). Similarly, a *pgr5* mutant of *Chlamydomonas reinhardtii* produced 2.5 times more H<sub>2</sub> than the wild type under simulated sunlight. This enhancement is attributed to the loss of cyclic electron flow around photosystem I (PSI), which reduces the proton motive force and relaxes photosynthetic control thereby facilitating electron transfer to hydrogenase and sustaining hydrogen production under anaerobic, carbon-limited conditions (Nagy et al., 2024).

Hydrogen production by microalgae can proceed through either direct or indirect biological photolysis. In direct photolysis, water molecules are split by photosystem II (PSII) to generate oxygen, protons, and electrons, with hydrogenase facilitating hydrogen production (Morya et al., 2022). In contrast, indirect photolysis involves the initial production of carbohydrates via photosynthesis, followed by hydrogen generation through anaerobic metabolism of accumulated glycogen and starch (Ahmed et al., 2021). Dark fermentation of microalgal biomass presents a cost-effective, light-independent pathway for biohydrogen production. However, its efficiency is often hindered by oxygen intrusion and the accumulation of acidic byproducts. Integrating this process with algal cultivation and recycling volatile fatty acid (VFA)-rich effluents can help mitigate these limitations, establishing a circular, carbon-neutral bioenergy system (Chen et al., 2023; Velozhina et al., 2023).

Recent advances in nanotechnology offer promising strategies to boost hydrogenase activity. For instance, Subramani et al. (2024) demonstrated that supplementing *Chlorella* cultures with 0.24 mg/L of biosynthesized silver nanoparticles (AgNPs) from *Azadirachta indica* increased hydrogenase activity fivefold and elevated peak H<sub>2</sub> production to 10.8 mmol/L compared to untreated controls. These results highlight the potential of nanotechnology-enhanced microalgal systems to improve hydrogen yields and contribute to CO<sub>2</sub> mitigation, reinforcing biohydrogen's role as a sustainable energy source.

## 2.2. Microalgae for pharmaceutical and nutraceutical products

### 2.2.1. Biologically active metabolites of microalgae

Microalgae are prolific sources of bioactive carbohydrates, vitamins, flavonoids, carotenoids, pigments, phenolics, and mycosporine-like amino acids with potent antioxidant, anti-inflammatory, antiviral, and anticancer activities (Subramani et al., 2024). A diverse array of microalgal taxa illustrates the broad spectrum of bioactive functions they offer. *Phaeodactylum tricornutum*, *Haematococcus pluvialis*, and *Skeletonema costatum* exhibit notable antimicrobial properties; *Navicula directa* demonstrates antiviral activity; while *Chlorella vulgaris*, *Fucus vesiculosus*, *Undaria pinnatifida*, and *Spirulina platensis* show promising anticancer potential. Additionally, *Tetraselmis* spp. and *Porphyridium* spp. provide anti-inflammatory and neuroactive effects (Mishra et al., 2021).

Among their bioactive compounds, polyunsaturated fatty acids (PUFAs) derived from microalgae are especially valued for their anti-inflammatory, cardioprotective, and neurocognitive benefits (Adarme-Vega et al., 2012). Notably, key omega-3 PUFAs such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are now being produced at industrial scale by various biotechnology companies (Khan et al., 2018). Microalgae-derived pigments such as β-carotene, astaxanthin, and fucoxanthin have received Generally Recognized as Safe (GRAS) status from the U.S. FDA (Jing et al., 2022). Astaxanthin stands out as a particularly prominent compound, with *Haematococcus pluvialis* capable of accumulating it up to 3–5 % of its dry weight. Other notable producers include *Chlorella* spp., *Xanthophyllomyces dendrophous*, *Brevundimonas* spp., *Paracoccus* spp., and *Rhodotorula* spp. (Jing et al., 2022). Fucoxanthin, another high-value carotenoid, is abundant in diatoms and golden-brown algae, with some strains producing over 25 mg/g (Wang et al., 2021). Additionally, microalgal polysaccharides

are attracting growing interest as natural polymers due to their low toxicity, biodegradability, and excellent biocompatibility (Sami et al., 2021).

### 2.2.2. Microalgae as a new drug carrier

In addition to being rich in bioactive compounds, microalgae can serve as biodegradable drug carriers capable of encapsulating both hydrophilic and hydrophobic molecules for targeted delivery (Vieira et al., 2020). Unlike conventional non-biodegradable carriers, which may persist in the body and necessitate the use of chelating or reducing agents for elimination (Fenton et al., 2018), microalgal carriers are inherently biocompatible, biodegradable, and non-toxic. This minimizes the risk of residual toxicity and provides a more sustainable, environmentally friendly alternative (Fig. 3).

Traditional delivery methods, including oral, intravenous, dermal, and intramuscular routes often face issues such as poor solubility, short half-life, toxicity, and rapid drug degradation (Vargason et al., 2021). Sustained-release carriers such as liposomes (Mahjoub et al., 2023), PLGA microspheres (Su et al., 2021), and alginate-based particles (Alnaief et al., 2020) (Fig. 3A) provide controlled delivery (Jamrozy et al., 2024).

Among these materials, microalgal polysaccharides, such as carrageenan and alginate are particularly attractive due to their biodegradability, non-toxicity, and effectiveness in drug delivery applications (Yang et al., 2013). Koo et al. (2023) developed alginate-casein nanoparticles encapsulating fucoidan, enabling controlled release and improved absorption in simulated gastrointestinal conditions. Extracellular vesicles (EVs)-membrane bound nanoparticles naturally secreted by cells, have emerged as one of the most promising bio-nanocarriers for sustainable drug delivery (Fig. 3B-I). For instance, Ren et al. (2023) cross-linked *Chlorella vulgaris* with sodium alginate to create an oral insulin system (Fig. 3B-II).

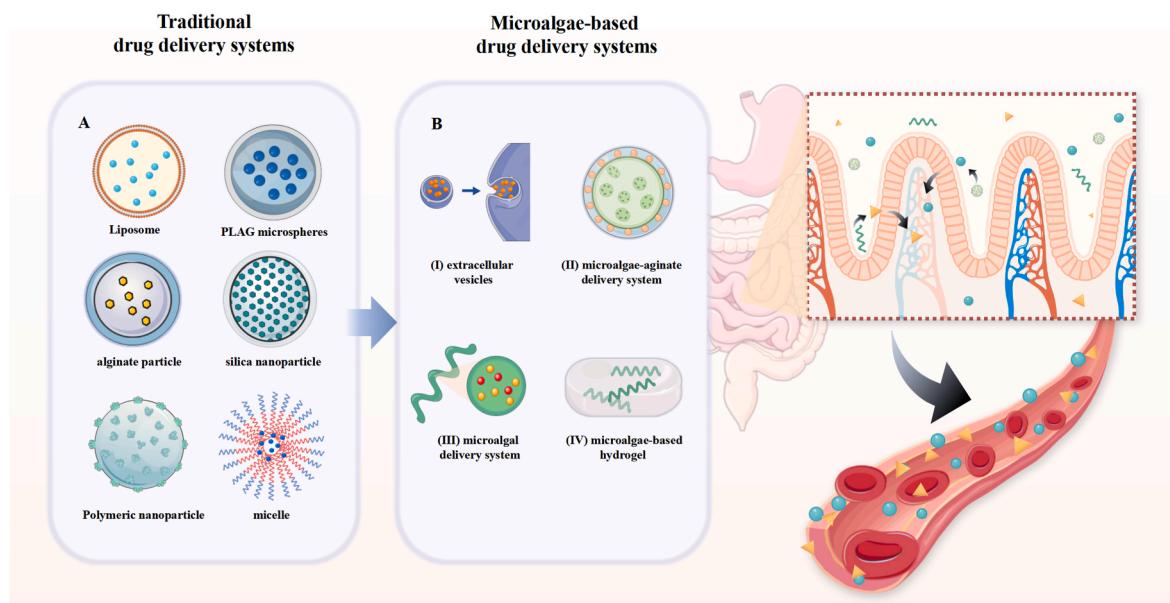
Microalgae also possess reactive cell surfaces that facilitate drug loading. Zhong et al. (2021) constructed an oral delivery system using *Spirulina platensis* to transport the radioprotective agent Amifostine (AMF) selectively to normal tissues (Fig. 3 B-III). Similarly, Zhang et al. (2024c) engineered a bioactive drug carrier derived from *Chlorella pyrenoidosa*, loading it with the photosensitizer Indocyanine Green (ICG). When administered to tumor-bearing mice, the carrier not only targeted tumors effectively but also generated oxygen through photosynthesis by decomposing excess water in the tumor microenvironment (Hu et al., 2022).

Another innovative strategy involves the use of a spirulina-rhodizonic acid hydrogel (SP@Rh-gel), which enhances drug solubility, enables controlled release, and extends gastrointestinal retention time. In a murine model of chronic colitis, SP@Rh-gel effectively attenuated NF-κB/caspase-1 signaling, reduced colonic inflammation, suppressed microglial activation and neuroinflammation, and promoted neurogenesis. These effects collectively alleviated colitis-associated anxiety and depression (Zhong et al., 2024) (Fig. 3B-IV).

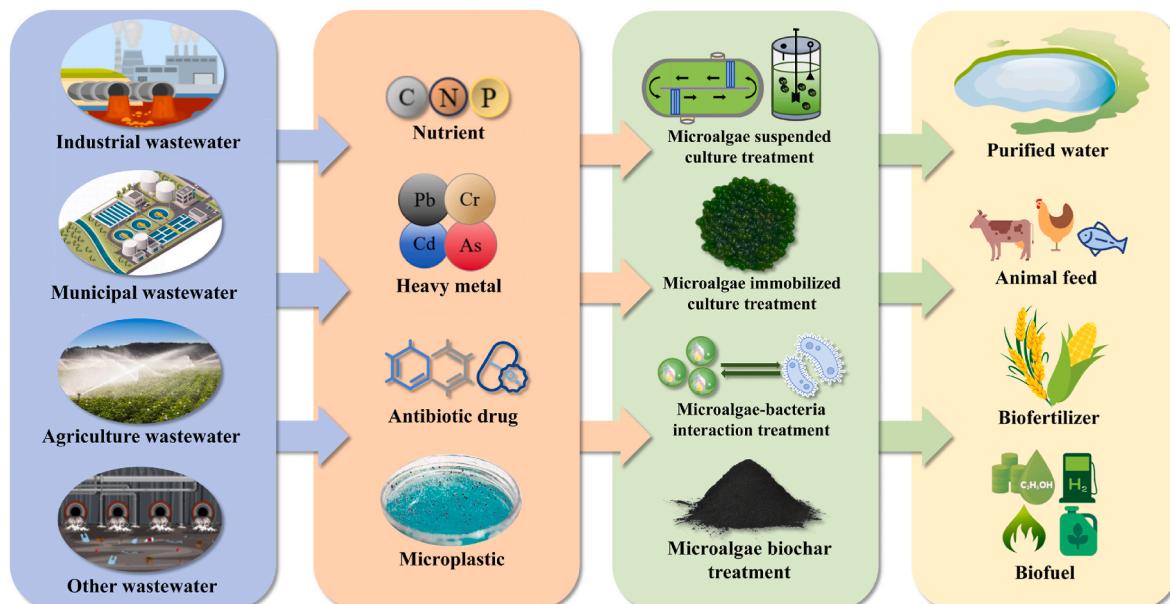
## 2.3. Application of microalgae in wastewater treatment and bioremediation

Rapid industrialization and economic expansion have intensified water pollution, positioning wastewater remediation as a pressing global challenge. Wastewater from industrial, agricultural and municipal sources carry diverse contaminants chemicals, microplastics, heavy metals and high loads of C, N, and P (Fig. 4). Integrating microalgae cultivation with wastewater treatment presents a cost-effective and sustainable approach, simultaneously lowering culture medium costs, enhancing pollutant removal efficiency, and contributing to CO<sub>2</sub> sequestration.

Microalgae can effectively remove pollutants from wastewater through mechanisms such as adsorption, bioaccumulation, and biotransformation (Touliabah et al., 2022), thereby contributing to



**Fig. 3.** Microalgae as a new drug carrier. A. Traditional drug delivery systems. B. Microalgae-based drug delivery systems. (I) Extracellular vesicles, (II) Microalgae-agarate delivery system, (III) Microalgal drug carrier, (IV) Microalgae-based hydrogel.



**Fig. 4.** Microalgae-based wastewater remediation pathways (i) suspended culture treatment, (ii) immobilized culture treatment, (iii) microalgae-bacteria consortia, and (iv) microalgal biochar conversion transforming nutrient, heavy-metal, antibiotic and microplastic pollutants into purified water, animal feed, biofertilizer and biofuel.

substantial water purification. When cultivated in wastewater, the resulting microalgal biomass can be harvested and processed through biorefining to enable resource recovery and the production of value-added products, including protein-rich animal feed, biofertilizers, biofuels, and biopolymers. A wide range of microalgal species has been successfully applied to treat various types of wastewater (Table 2). Assessing the feasibility of such systems requires consideration of pollutant removal efficiency, biomass harvesting capabilities, and the economic potential of the resulting by-products.

Rapid industrialization has significantly exacerbated water pollution, introducing high concentrations of organic matter, heavy metals, antibiotics, and pathogenic microorganisms into aquatic systems (Koul et al., 2022). These complex pollutants pose considerable challenges for

microalgal-based wastewater treatment. Nevertheless, various microalgal species have demonstrated strong pollutant-removal capabilities. *Chlamydomonas mexicana* can decolorize textile dyes (Mustafa et al., 2024), while *Synechocystis* sp. PCC6803 effectively removes cadmium (Cd) from contaminated water (Wang et al., 2024b). Additionally, *Chlorella pyrenoidosa* and *Microcystis aeruginosa* are capable of degrading antibiotics. *Scenedesmus obliquus* efficiently assimilates carbon (C), nitrogen (N), and phosphorus (P) from piggery effluent, and *Chlorella vulgaris* achieves substantial reductions in brewery wastewater pollutants—lowering biochemical oxygen demand (BOD) by 88 %, total nitrogen (TN) by 82 %, and total phosphorus (TP) by 54 % (Pan et al., 2021).

Microalgae remove heavy metals from wastewater via biosorption,

**Table 2**

Assessment of various microalgae in wastewater treatment and resource utilization.

Species	Cultivation medium	Phycoremediation efficiency	Productivity	Biochemical composition	References
<i>Chlorella vulgaris</i>	Domestic wastewater	COD, TN>94 %	0.89 g/L	0.16 g/L Lipid	Leong et al. (2022)
<i>Chlorella variabilis</i> and <i>Scenedesmus obliquus</i>	Dairy wastewater	—	673 mg/L	7.22 mg/L lutein, 56 % protein, 24 % carbohydrate	Gatamaneni (2020)
<i>Desmodesmus</i> sp and <i>Scenedesmus obliquus</i>	Domestic wastewater	TN, TP>75 %	1.1 g/L	6.2 % fatty acid	Nzayisenga et al. (2020)
<i>Chlorella sorokiniana</i>	Domestic wastewater	TN: 60 %, TP: 85 %	548 mg/L/d	12 mg/L carotenoid, 15 % protein, 5 % carbohydrate	Rani and Ojha. (2021)
<i>Chlorella sorokiniana</i>	Aquaculture wastewater	TOC: 82.27 %, TN: 86.42 %, NH <sub>4</sub> <sup>+</sup> -N: 93.25 %	1.93 g/L	55.52 % carbohydrate, 28.55 % lipid, 17.25 % protein, 3.39 mg/L Astaxanthin	He et al. (2023)
<i>Haematococcus</i> sp.	Wastewater from the seafood processing industry	TN: 93 %, TP: 97 %	1.33 g/L	3.39 mg/L of astaxanthin, 14.3 mg/L of chlorophylls, 6.22 mg/L of carotenoids, and 0.41 g/L of lipids	Cheirsilp et al. (2022)
<i>Parachlorella kessleri</i> QWY28	Pig farming wastewater	COD: 88 %, TN: 95 %, TP: 100 %	9.2 g/L	carbohydrate production at 646 mg/L/d	Qu et al. (2019)
<i>Scenedesmus</i> sp. HXY5	potato wastewater	TN: 59 %, TP: 32 %, COD: 93 %	2.64 g/L	total pigment yield (18.45 mg/L), with a lutein yield of 11.46 mg/L	Yuan et al. (2021)
<i>Scenedesmus</i> sp. LX1	domestic wastewater	NH <sub>4</sub> <sup>+</sup> -N: 93.81 % TP: 87.72 %	0.55 g/L	protein, with a highest content of 54.64 %	Wang et al. (2022)
<i>Chlorella sorokiniana</i> SU-1	50 % swine wastewater	COD: 92.29 % TP: 93.7 % NH <sub>4</sub> <sup>+</sup> -N: 95.64 %	6.53 g/L	56.65 % carbohydrate content, 33.5 % protein content, and 4.35 % lipid content	Kusmayadi et al. (2024)

bioaccumulation, and biotransformation, aided by extracellular polymeric substances (EPS) that bind pollutants (Sarma et al., 2024; Chen et al., 2015). Under Cd stress, EPS and protein production increases, illustrating the synergy of adsorption, chelation, and precipitation in metal removal mechanisms (Wang et al., 2024b).

Microplastics pose a rising threat (Priya et al., 2022). Recent studies highlight microalgae's capability to intercept, entrap, and aggregate microplastics, aided by EPS secretion. Esmaeili Nasrabadi et al. (2023) demonstrated that *Chlorella vulgaris* can intercept, entrap, and aggregate particles with EPS enhanced binding, achieved up to 84 % removal of polyethylene microplastics at pH 10.

Certain microalgae have adapted to thrive in extreme wastewater conditions, offering unique advantages for treatment processes. *Galdieria sulphuraria*, for example, grows optimally at pH 1.8 and 56 °C, reducing the need for external pH regulation through active proton extrusion. This makes it particularly well-suited for treating acidic waste streams with high chemical oxygen demand (COD). Likewise, the thermophilic microalga *Chlorella sorokiniana* effectively removes nitrogen and phosphorus under heterotrophic conditions at 43 °C, broadening its applicability in diverse wastewater treatment scenarios (Wollmann et al., 2019).

While suspended microalgae cultivation systems are effective, they often involve high harvesting costs. Consequently, immobilized microalgae systems are gaining attention for their higher pollutant removal efficiency and easier biomass recovery. Immobilized microalgae have demonstrated strong potential for removing nutrients, heavy metals, pesticides, and antibiotics (Li et al., 2024d). For example, *Lobosphaera* sp. IPPAS 2047 immobilized in cross-linked chitosan polymers maintained high photosynthetic activity and demonstrated significantly greater nutrient removal efficiency compared to suspended cultures. Moreover, the harvested biomass was effectively repurposed as a slow-release biofertilizer (Vasilieva et al., 2021).

Microalgae-bacteria co-culture systems further enhance wastewater treatment performance. Microalgae supply oxygen through photosynthesis, supporting bacterial degradation of organic matter, while bacteria provide CO<sub>2</sub> to sustain microalgal growth (Li et al., 2024a). Nguyen et al. (2020) identified an optimal 3:1 *Chlorella* sp. to activated sludge

ratio that achieved 86 %, 79 %, and 99 % removal of TN, TP, and COD, respectively, with a biomass concentration of 1.12 g/L. More recently, Li et al. (2024c) developed a bio-microalgae-bacteria floc (ABF) system for commercial shrimp aquaculture, which maintained non-toxic ammonia and nitrite levels even under low carbon-to-nitrogen ratios. Integrating co-culture and immobilization technologies significantly enhances wastewater remediation efficiency, advancing sustainable development goals.

Finally, biochar derived from microalgae through pyrolysis, microwave-assisted pyrolysis, or hydrothermal carbonization has emerged as a sustainable adsorbent material. Its abundance of polar functional groups, such as carboxyl, hydroxyl, ketone, and aldehyde significantly enhances its adsorption capacity (Bhatnagar et al., 2021). For example, *Cladophora glomerata*-based biochar achieved removal rates of 89.9 %, 97.1 %, and 93.7 % for Cr<sup>3+</sup>, Cu<sup>2+</sup>, and Zn<sup>2+</sup>, respectively (Michalak et al., 2019). These findings confirm microalgal biochar as a renewable, cost-effective material for advanced wastewater remediation.

### 3. The cutting-edge in microalgae biotechnology

#### 3.1. Synthetic biology and CRISPR/Cas9 system

Synthetic biology has transformed microalgal biotechnology by leveraging genomic data and precise editing tools to boost sustainable bioproduction. Over 25 species including *Chlamydomonas reinhardtii* and *Nannochloropsis* spp. now utilize established genetic toolkits (Baroukh et al., 2015; Sun et al., 2021). Modern methods like RNA interference (RNAi) and transcription activator-like effector nucleases (TALENs) have enabled targeted lipid enhancement and dual gene knockouts, respectively (Fayyaz et al., 2020; Schaeffer and Nakata, 2015). For instance, RNAi has been used to silence CrCULs genes in *C. reinhardtii*, increasing lipid accumulation for biofuel applications (Luo et al., 2021). Similarly, TALENs have enabled dual gene knockouts in *Nannochloropsis oceanica* through the use of Platinum TALENs (Kurita et al., 2020).

Among gene-editing technologies, CRISPR/Cas9 has emerged as the most widely adopted tool in microalgal research due to its high

efficiency, low off-target activity, and consistent performance across diverse species (Hassanien et al., 2023). Initially applied in *Chlamydomonas reinhardtii*, the system has since been successfully implemented in *Phaeodactylum tricornutum*, *Porphyridium purpureum*, and several other taxa. Early studies revealed that constitutive expression of Cas9 could compromise cell viability (Jiang et al., 2014), leading to the development of transient delivery methods using Cas9-sgRNA ribonucleoprotein (RNP) complexes. This approach not only minimizes off-target effects but also enhances editing efficiency (Onn et al., 2024). Interestingly, *P. tricornutum* is tolerant of stable Cas9 expression and achieves higher disruption efficiencies for the *CpSRP54* gene compared to *C. reinhardtii*, underscoring species-specific differences in Cas9 response.

The RNA-DNA complementarity of CRISPR/Cas9 enables precise and multiplexed genome editing to enhance microalgal traits such as biomass productivity, stress tolerance, lipid accumulation, and the synthesis of high-value metabolites (Onn et al., 2024). More recently, Cas12a RNPs have achieved mutagenesis efficiencies of 77.2–94.5 % in various microalgal species (Nomura et al., 2024). Representative CRISPR/Cas applications are summarised in Table 3.

Recent developments in modular genetic toolkits have overcome long-standing challenges in microalgal engineering. For instance, the MoClo system for *C. reinhardtii* provides standardized genetic parts and chloroplast transformation vectors, facilitating precise multi-cassette assembly and stable plastome integration (Melero-Cobo et al., 2025). These advances streamline the construction of microalgal cell factories for the sustainable production of biofuels, nutraceuticals, and specialty chemicals, with reduced environmental footprints (Dhokane et al., 2023).

Collectively, these technological innovations position microalgae as promising methods for circular bioeconomy applications, supporting renewable biomass conversion and carbon neutral biomanufacturing in line with cleaner production principles.

### 3.2. Progress in microalgae culture system

Microalgae cultivation systems are broadly categorized into two main configurations: open ponds and enclosed photobioreactors (PBRs), each with distinct sustainability trade offs (Fig. 5). Open raceway ponds (ORPs) are still the main commercial option and can offer high lipid yields (Sharma et al., 2021). However, ORPs face several inherent challenges, including susceptibility to contamination (Lam et al., 2018), relying on solar irradiation with only moderate productivity (0.2–0.5 g/L/day), and instability caused by evaporation-driven salinity changes (Tan et al., 2018).

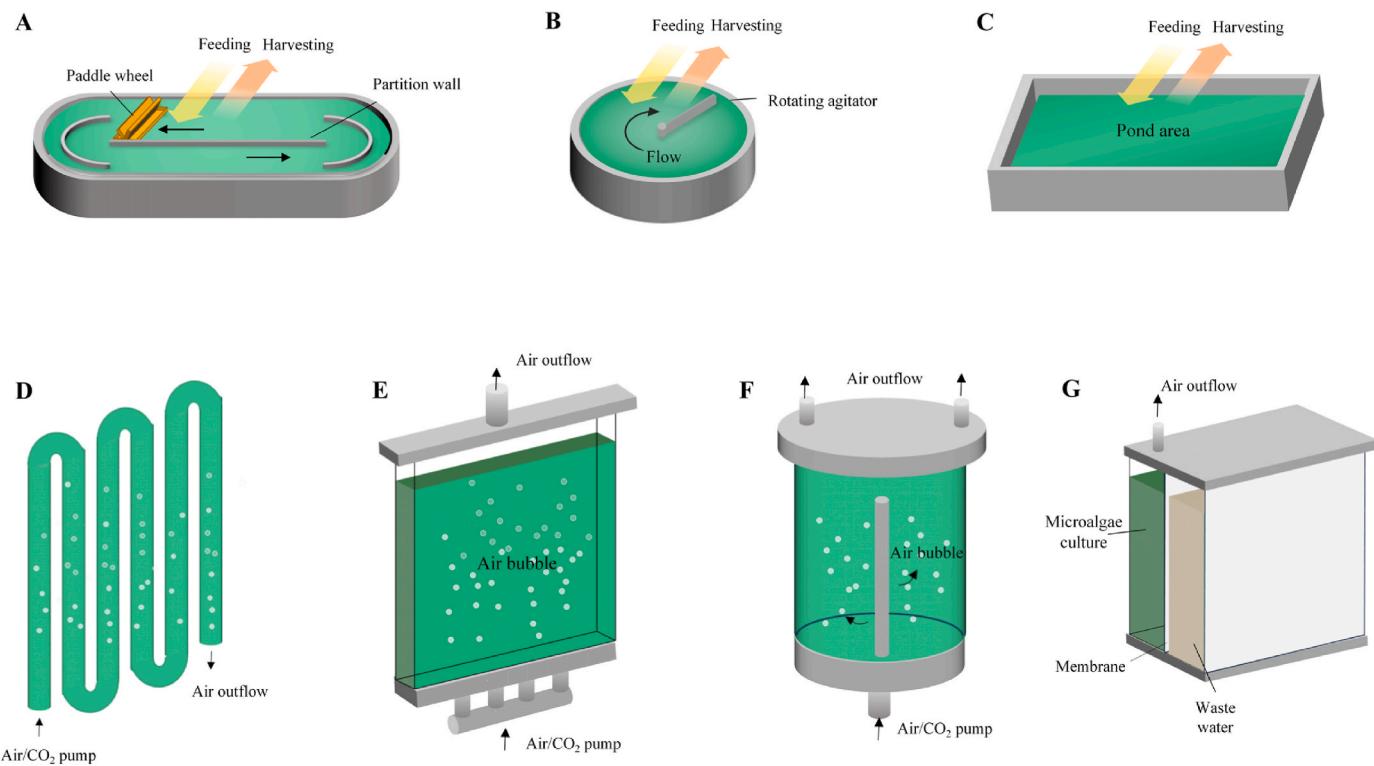
#### 3.2.1. Open pond systems

Open raceway ponds (ORPs; Fig. 5A–C) are among the most widely used large-scale systems for microalgae cultivation due to their low capital cost, operational simplicity, and adaptability to diverse environmental conditions (Suparmaniam et al., 2019; Tan et al., 2018). However, ORPs generally yield lower cell densities compared to closed photobioreactors and require efficient harvesting strategies to remain economically viable (Barboza-Rodriguez et al., 2024). Their open design increases susceptibility to contamination, and environmental factors such as rainfall and evaporation can alter salinity and pH, thereby affecting culture productivity (Lam et al., 2018). Moreover, reliance on natural sunlight and inadequate mixing often limit photosynthetic efficiency and biomass output. As a result, robust, fast-growing strains like *Chlorella vulgaris* are commonly employed (Barboza-Rodriguez et al., 2024; Tan et al., 2018). For instance, Sharma et al. (2021) reported a lipid yield of 19.98 wt% from *Chlorella minutissima* cultivated semi-continuously in a 1500 L ORP.

Recent advances have focused on optimizing hydrodynamics to enhance performance. CFD simulations have been used to improve flow uniformity and minimize dead zones (Inostroza et al., 2021). Raceway ponds with length-to-width ratios greater than 10 provide superior

**Table 3**  
Recent CRISPR/Cas system in microalgae.

Microalgae strain	CRISPR/Cas system	Targeted gene (s)	Products	References
<i>Chlamydomonas reinhardtii</i>	Cas9	<i>PPX1,FTSY, WDTC1</i>	Generation of individual strains with precise mutations in multiple target gene	Akella et al. (2021)
<i>Chlamydomonas reinhardtii</i>	Cas9	<i>SPD1</i>	Targeted knockout of CrSPD1 induces spermidine auxotroph, which could be used as a selectable marker in biotechnology	Freudenberg et al. (2022)
<i>Chlamydomonas reinhardtii</i>	Cas9	<i>LCYE</i>	A 2.3-fold increase in astaxanthin accumulation	Kneip et al. (2024)
<i>Nannochloropsis</i> spp.	dCas9	<i>g1248</i>	Growth and photosynthetic parameters of the mutants increased by 23 % and 12 %, respectively, compared to the wild type under ambient CO <sub>2</sub> levels	Wei et al. (2022)
<i>Nannochloropsis</i> spp.	Cas9	<i>LSMT</i>	Mutation induced 18–20 % reduction in fructose1, 6-bisphosphate aldolases, along with 9.7–13.8 % increase in dry weight and enhanced growth	Liang et al. (2024)
<i>Phaeodactylum tricornutum</i>	Cas9	<i>CryP</i>	Increased light-harvesting protein levels in <i>CryP</i> knockout mutants	Yang et al. (2022)
<i>Phaeodactylum tricornutum</i>	Cas9	<i>ZEP2, ZEP3</i>	Generation of <i>zep</i> mutants as a platform for diatoxanthin production	Graesholt et al. (2024)
<i>Chlorella</i> sp.	Cas9	<i>NR, APT</i>	Generation of auxotrophic strains	Kim et al. (2021)
<i>Chlorella</i> sp.	CRISPRi and CRISPRa	Randomly mediate gene regulation	Mutants with protein content of 60 %–65 % (w/w) of dry cell weight	Lin et al. (2022)
<i>Euglena gracilis</i>	LbCas12a	<i>EgGSL2, EgcrTB</i>	High-efficiency genome editing system using direct delivery of LbCas12a RNP complexes	Nomura et al. (2024)
<i>Euglena gracilis</i>	Cas9	Knockout of 16 Carotenoid biosynthetic genes present in <i>E. gracilis</i>	Mutants with different carotenoid compositions	Tamaki et al. (2023)



**Fig. 5.** Configuration of different open systems and photobioreactor (PBR). A. Open raceway pond B. Circular pond C. Natural pond D. tubular PBS E. flat PBS F. Column PBS G. Membrane PBS.

velocity distributions, while innovations such as advanced slurry wheels and hydrofoil impellers have further improved mixing efficiency and scalability. These enhancements enable deeper (up to 1 m) systems with 15–30 % higher productivity (Sawant et al., 2019; Kusmayadi et al., 2020).

### 3.2.2. Closed photobioreactors

Photobioreactors (PBRs) utilize transparent vessels to isolate cultures while enabling precise control over environmental parameters such as light intensity, nutrient availability, temperature, pH, and CO<sub>2</sub> concentration. This controlled environment minimizes risks of contamination and evaporation (Assunção and Malcata, 2020; Sirohi et al., 2022). These advantages make PBRs particularly well-suited for the production of high-value compounds, including pharmaceuticals and nutraceuticals (Yen et al., 2019).

Significant technological innovations have improved various PBR configurations.

- Tubular PBRs (Fig. 5D) consist of interconnected tubes in horizontal, vertical, or spiral layouts to maximize light capture and space efficiency (Fulbright et al., 2018; Tan et al., 2018). Porto et al. (2022) developed LED-illuminated tubular PBRs with reflective surfaces, which enhance light use and reduce energy costs and thermal stress, enabling scalable and energy-efficient operation.
- Flat-plate PBRs (Fig. 5E) use narrow panels with a high surface-area-to-volume ratio, supporting high-density cultures. Transparent materials like glass or polycarbonate ensure effective light penetration. Carone et al. (2022) designed an alveolar cultivating *Acutodesmus obliquus*, achieved 1.9 g/L biomass and 64 % CO<sub>2</sub> fixation at 27–46 Wh/m<sup>3</sup>.
- Column PBRs (Fig. 5F), including bubble and airlift designs, use gas injection and internal baffles or mixers to enhance mass transfer. Naira et al. (2020) introduced a self rotating mixer within a bubble column PBR, resulting in 13 % and 62 % improvements in biomass and biodiesel productivity, respectively. Modified airlift reactors

achieved 30 % higher biomass productivity compared to conventional columns (Mahata et al., 2023). However, limited light penetration and surface area constraints still challenge scale up (Gupta et al., 2015; Pawar, 2016).

Membrane Photobioreactors (MPBRs) (Fig. 5 G) combine cultivation with membrane filtration for concurrent biomass growth, wastewater treatment, and nutrient recovery. Segredo-Morales et al. (2024) introduced a vertical upflow multi-column MPBR, achieving 15.0–15.4 g/L biomass productivity, 48–75 % COD removal, and 97–98 % NH<sub>4</sub><sup>+</sup> removal efficiencies.

Future research should prioritize the development of intelligent control systems and comprehensive life cycle assessments to optimize the balance between environmental impact and economic viability. Innovations in light management, shear stress mitigation, and overall process optimization will be key to enabling the scalability, energy efficiency, and sustainability of next-generation photobioreactors (PBRs) for biomass production and resource recovery.

## 4. Commercialization applications and policy environment of microalgae biotechnology

### 4.1. Commercialization applications of microalgae biotechnology

The growing global demand for sustainable food and energy is driving the rapid expansion of microalgae production. Backed by targeted policies and significant biotechnological advancements, China has emerged as a global leader in the sector, sustaining a comprehensive value chain from research and development to large-scale manufacturing (Deamici et al., 2025). Flagship operations include Yunnan Green A's RMB 480 - million facility at Chenghai Lake, supplying 3000 tonnes of *Spirulina* annually nearly 40 % of the global supply (Green A, 2024), and Fuqing King Dnarmsa, which supplies 2000 tonnes per year of *Spirulina*, *Chlorella*, *phycocyanin*, and *Dunaliella* products to international markets (Xindaze, 2025). Internationally, innovators are

transforming algal biomass into high-value products. Brevel (Israel) has reduced algal protein production costs by over 90%; Arborea (UK) deploys “Bio-Solar Leaf” panels that operate without the need for arable land; and MiAlgae (Scotland) upcycles whisky distillery by-products into  $\omega$ -3-rich oils. Meanwhile, AGS Therapeutics (France) leverages algal extracellular vesicles for targeted drug delivery applications (VentureRadar, 2025).

Algal-based wastewater treatment is also advancing at scale. Jiangsu Algae Chain’s RMB 2.25 billion Lindian complex (2024) integrates aquaculture, algal raceways, and photovoltaics to simultaneously achieve carbon capture, nutrient removal, and biomass valorization (Weizaowang, 2024). In the USA, Algae Systems deploys floating photobioreactors on municipal effluents, while OneWater’s AlgaeWheel combines algal–bacterial consortia with membrane technologies to produce bio-compost and renewable fuels (Calatrava et al., 2024).

Although high capital and operational costs, regulatory complexity, and limited market familiarity present challenges, the commercial outlook remains promising. Circular economy strategies such as repurposing industrial byproducts as feedstocks enhance both economic performance and life-cycle sustainability. Integrated biorefineries further maximize value by co-extracting high-value compounds including proteins, pigments, and lipids. Meanwhile, CRISPR-enabled strain engineering accelerates the tailored production of pharmaceuticals, cosmetics, and specialty chemicals. Together, these innovations position microalgae as a promising and sustainable cornerstone of the emerging global bioeconomy.

#### 4.2. Policy environment of microalgae biotechnology

China, the EU, and the U.S. are advancing national strategies that position microalgae as a key component of sustainable development. China’s 14th Five-Year Plan for Marine Economic Development lists microalgae as a strategic resource; provincial “blue-bio” parks and national R&D hubs (PRC State Council, 2021). For example, the Yunnan Green A Biotechnology Park enhanced product quality and yield through collaboration with the Li Ye Guang Expert Workstation at the Wuhan Botanical Garden, Chinese Academy of Sciences (China Development, 2023).

The European Green Deal and the Bioeconomy Strategy both highlight the strategic importance of algae for sustainable food, feed, fuel, and biomaterial production. In parallel, the Renewable Energy Directive mandates that 14 % of transport fuels must come from renewable sources, thereby stimulating demand for algal biodiesel. Additionally, Horizon Europe (2021–2027), with a budget of €95.5 billion, supports research and development across the entire algae value chain, including impact assessments and commercialization pathways (European Commission, 2024).

In the United States, the Department of Energy’s Algae Program targets reducing algal biofuel costs to \$2.50 per gallon by 2030. State-level incentives in California and Arizona promote the use of algae for carbon capture and wastewater treatment. The Algae Biomass Organization advocates for sustained federal support, while collaborative initiatives with the U.S. EPA help align deployment strategies with regulatory objectives (Wiatrowski and Davis, 2021).

### 5. Challenges and future limitations

In advancing microalgae biotechnology for sustainable resource development, each stage—from selecting cultivation techniques to biomass harvesting and product extraction—requires a careful balance between technical feasibility and economic viability. At the same time, environmental impact and long-term sustainability must be thoroughly evaluated to ensure responsible resource utilization. Achieving ecological sustainability alongside efficient resource use and economic profitability remains a central challenge in current research.

#### 5.1. Economic analysis of microalgae technology

Microalgae biotechnology holds significant promise for advancing sustainable development, but its widespread adoption requires robust evidence of technical feasibility, economic viability, and environmental sustainability. Integrating algal cultivation with wastewater treatment is particularly compelling, as it enables simultaneous water recovery, nutrient sequestration, and biomass generation, thereby reducing operational costs and promoting closed-loop resource cycles.

However, several critical challenges persist. Chief among them are enhancing areal productivity and extracting high-value products without increasing energy consumption or greenhouse gas emissions.

Commercial-scale systems are generally classified into two types. Closed photobioreactors (CPRs) offer superior process control and higher lipid quality but come at a higher cost—approximately \$32.57 per gallon at a 10-million-gallon production scale. In contrast, ORPs can produce the same volume at a substantially lower cost of \$12.74 per gallon but are hindered by lower light utilization efficiency and greater susceptibility to contamination (Sharmila et al., 2022). Therefore, system design must carefully balance capital and operating expenditures with productivity and product quality: CPRs provide premium outputs, whereas ORPs offer economic scalability.

Downstream processing remains the primary bottleneck in the algal biorefinery value chain. Harvesting alone accounts for 20–30 % of total production costs (Fasaei et al., 2018), and the rigid cell walls of many microalgal species complicate product extraction, often necessitating energy-intensive, solvent-based techniques. Table 4 summarizes current methods and their associated trade-offs.

Emerging research is increasingly focused on developing milder, low-carbon alternatives. Promising innovations include solar-thermal drying systems (López Pastor et al., 2023), pH-responsive, charge-switchable membranes for biofilm support and dewatering (Zhao et al., 2021), and magnetic separation technologies employing functionalized particles for selective biomass recovery (Li et al., 2024b). These approaches aim to reduce energy demand, minimize chemical usage, and support the scalable deployment of microalgae-based biorefineries in alignment with circular economy principles.

Optimizing existing unit operations and rigorously evaluating new methods through techno-economic analysis are critical to reducing the cost and energy demands of microalgal biomass conversion. Early collaboration with industry partners further facilitates scale-up and commercialization. Although microalgae can produce significant quantities of bulk products such as lipids and biodiesel, current production costs vary widely—from \$150 to \$6000 per tonne, depending on cultivation systems and processing technologies. CPRs provide superior environmental control but incur higher operational costs compared to open raceway ORPs. For instance, producing 10,000 tonnes of biomass with 30 % lipid content is estimated to cost approximately \$2.80 per liter of biodiesel, rendering it economically uncompetitive with fossil fuels. Nevertheless, strategies such as co-cultivation of synergistic strains have shown promise in enhancing lipid yields and reducing production costs (Judd et al., 2017).

Ongoing innovation in cultivation, harvesting, extraction, and process integration is essential to bridging the cost gap and improving sustainability metrics, ultimately positioning microalgae as a robust, low-carbon cornerstone of the emerging circular bioeconomy.

#### 5.2. Environmental impacts and sustainability concerns

Microalgae present significant opportunities for sustainable development but face challenges related to water, energy, and waste management. Cultivation is water-intensive; however, the use of wastewater can reduce freshwater consumption by up to 90 % while simultaneously supplying nutrients and enabling bioremediation (Yang et al., 2011). Integrating renewable energy, such as solar-powered photobioreactors and wind-driven systems, can enhance sustainability by optimizing

**Table 4**

Merits and demerits of microalgae harvesting and biomass extraction methods.

Method	Advantages		Disadvantages	References
Harvesting method	Flocculation	High efficiency	Flocculant pollution, unsuitable for food industry	<a href="#">Dai et al. (2024)</a>
	Sedimentation	Low cost, simple operation	Time-consuming, no industrial application	<a href="#">Li et al. (2021)</a>
	Filtration	Low cost, low energy requirements	Membrane contamination	<a href="#">Velten et al. (2024)</a>
Extraction method	Centrifugation	High efficiency, suitable for almost all microalgae, suitable for research purpose	High equipment and energy cost	<a href="#">Abu-Shamleh and Najjar. (2020)</a>
	Physical crushing	High efficiency, no environmental pollution	Non-selective, difficult to separate	<a href="#">Zhang et al. (2024a)</a>
	Organic solvent extraction	High efficiency, pure biomass	Time-consuming, poisonous	<a href="#">Rocha et al. (2023)</a>
	Enzyme extraction	The operating conditions are mild, the selectivity is high, and the extraction product is not damaged	Suitable for high-value products	<a href="#">Sayegh et al. (2025)</a>

water circulation, temperature regulation, and light delivery. Developing energy-efficient cultivation technologies is essential to minimize environmental impact and support large-scale implementation.

Effective waste management is critical: post harvest media contain residual nutrients and cells that may cause contamination or harmful algal blooms, such as those caused by *Karenia mikimotoi*, have been linked to mass die-offs in marine aquaculture ([Nie et al., 2024](#)). Residual organic matter can hinder downstream water treatment processes by interfering with coagulation and filtration. However, spent biomass and growth media represent valuable resources. Through processes such as fermentation, anaerobic digestion, or hydrothermal liquefaction, these residues can be converted into bioethanol, biogas, or biodiesel, contributing to material loop closure and resource recovery.

Digital tools, including Energy Informatics (EI) integrated with Life Cycle Assessment (LCA), facilitate real-time resource optimization and comprehensive environmental impact evaluation. By integrating wastewater reuse, renewable energy utilization, residue valorization, and digital monitoring, microalgal systems offer a promising pathway toward low-carbon, circular production models.

To fully realize this potential, continued technological innovation and supportive policy frameworks are essential. These frameworks should aim to internalize environmental benefits and provide incentives for the cost-effective deployment of sustainable microalgal technologies.

## 6. Future sustainable development directions and opportunities

Future research on microalgae resource utilization should prioritize targeted strain selection, genetic enhancement, intelligent and energy-efficient cultivation strategies, and low-energy harvesting techniques. Equally important are streamlined biomass conversion processes, the development of diverse high-value applications, and rigorous sustainability assessments. Breakthroughs in this field will increasingly depend on system-level optimization enabled by advances in synthetic biology and precision gene editing. Achieving these goals will require robust interdisciplinary collaboration to accelerate the integration of microalgae into global sustainability efforts and industrial innovation.

Based on the review of existing research findings, current challenges, and emerging trends, the following areas deserve focused attention and thorough exploration.

- **Efficient Biomass Conversion and Product Diversification:** Environmentally sustainable pretreatment strategies are essential for effectively disrupting the rigid cell walls of microalgae to enhance downstream extraction and conversion processes. In parallel, innovative bioconversion pathways should be developed to enable the production of a diverse array of value-added products, including biofuels, specialty chemicals, and functional food ingredients.
- **Integrated System Optimization and Sustainability Assessment:** Employ LCA and Techno-Economic Analysis (TEA) to systematically evaluate environmental impacts and economic viability. These tools will inform the optimization of resource-efficient, circular bio-

production systems and support the development of sustainable microalgae-based value chains.

## 7. Conclusion

Microalgal biotechnology represents a promising and multifaceted platform for advancing global sustainability. It offers efficient pathways for carbon sequestration, renewable biofuel production, high-value bioproduct synthesis, and environmental remediation, particularly through wastewater treatment and CO<sub>2</sub> capture. This review has highlighted recent advances in strain engineering and cultivation process optimization, underscoring the considerable potential of this field. Nevertheless, the large-scale deployment of microalgae remains constrained by several techno-economic challenges, including high production costs especially harvesting and dewatering, which account for 20–30 % of total costs limited biomass productivity in open cultivation systems, and difficulties in achieving cost-competitive biofuel production. To overcome these barriers, future research should prioritize: (i) Engineering robust and high-yielding strains using synthetic biology tools to enhance productivity and stress tolerance; (ii) Integrating cultivation with resource recovery systems, such as using wastewater and flue gas, to reduce energy and nutrient input; and (iii) Establishing algal biorefineries that enable the co-production of biofuels, animal feed, and high-value bioproducts to improve economic viability. Progress in these areas driven by interdisciplinary collaboration will be critical to positioning microalgae as a central component of the circular bioeconomy, contributing to decarbonization, sustainable resource utilization, and environmental restoration.

## CRediT authorship contribution statement

**Huiying Zhang:** Writing – original draft, Project administration, Formal analysis, Data curation, Conceptualization. **Yingzheng Wu:** Writing – original draft, Resources. **Dong Liu:** Writing – review & editing, Data curation. **Siran Feng:** Writing – original draft, Visualization. **Xiaoxin Xuan:** Resources, Formal analysis. **Guanghui Dong:** Visualization, Data curation. **Junyi Cheng:** Visualization, Validation. **Yuan Qin:** Writing – review & editing, Supervision. **Huu Hao Ngo:** Writing – review & editing, Supervision, Project administration, Conceptualization.

## 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.

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## Data availability

Data will be made available on request.

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