



## Review

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

Huiying Zhang<sup>a,b,c</sup>, Yingzheng Wu<sup>a</sup>, Dong Liu<sup>a</sup>, Siran Feng<sup>d</sup>, Xiaoxin Xuan<sup>a</sup>, Guanghui Dong<sup>c</sup>, Junyi Cheng<sup>c</sup>, Yuan Qin<sup>a,c,\*</sup>, Huu Hao Ngo<sup>d,\*\*</sup>

<sup>a</sup> College of Life Sciences, Fujian Agriculture and Forestry University, Fuzhou, 350002, China

<sup>b</sup> Science Center for Future Foods, Jiangnan University, 1800 Lihu Road, Wuxi, Jiangsu, 214122, China

<sup>c</sup> College of Future Technology, Fujian Agriculture and Forestry University, Fuzhou, 350002, China

<sup>d</sup> Centre for Technology in Water and Wastewater, School of Civil and Environmental Engineering, University of Technology Sydney, Sydney, NSW, 2007, Australia

## ARTICLE INFO

## Keywords:

Carbon sequestration  
Green technology  
Microalgae biotechnology  
Sustainable future development  
Wastewater treatment

## 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

ABA	Absciscic Acid
ABF	Algae–Bacteria Floc
AgNPs	Silver Nanoparticles
AGPase	ADP-glucose Pyrophosphorylase
ARTP	Atmospheric and Room Temperature Plasma
BOD	Biochemical oxygen demand
bZIP	Basic Leucine Zipper
CFD	Computational Fluid Dynamics
COD	Chemical Oxygen Demand
CPR	Closed Photobioreactor
CRISPR/Cas9	Clustered Regularly Interspaced Short Palindromic Repeats/Cas9
DCW	Dry Cell Weight
DGAT	Diacylglycerol Acyltransferase
DHA	Docosahexaenoic acid
EI	Energy Informatics
EPA	Eicosapentaenoic acid

(continued on next column)

## (continued)

EPS	Extracellular Polymeric Substances
EVs	Extracellular Vesicles
FAME	Fatty Acid Methyl Esters
GHG	Greenhouse gas
GMOs	Genetically Modified Organisms
GRAS	Generally Recognized as Safe
HydA	[FeFe]-hydrogenase
ICG	Indocyanine green
LED	Light Emitting Diode
LCA	Life Cycle Assessment
MPBRs	Membrane Photobioreactors
MZF-NPs	Magnesium-Zinc Ferrite Nanoparticles
NO <sub>x</sub>	Nitrogen Oxides
ORP	Open Raceway Pond
PBR	Photobioreactor
PLGA	Poly (lactic-co-glycolic)
PSI	acid photosystem I

(continued on next page)

\* Corresponding author. College of Life Sciences, Fujian Agriculture and Forestry University, Fuzhou, 350002, China.

\*\* Corresponding author.

E-mail addresses: [yuanqin001@foxmail.com](mailto:yuanqin001@foxmail.com) (Y. Qin), [ngohuuhaio121@gmail.com](mailto:ngohuuhaio121@gmail.com) (H.H. Ngo).

<https://doi.org/10.1016/j.jenvman.2025.127263>

Received 8 May 2025; Received in revised form 28 July 2025; Accepted 7 September 2025

Available online 16 September 2025

0301-4797/© 2025 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

(continued)

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-Encinas 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 bio-fuels, 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 bioflocclulants increased the flocculation efficiency of *Tetradlesmus 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.

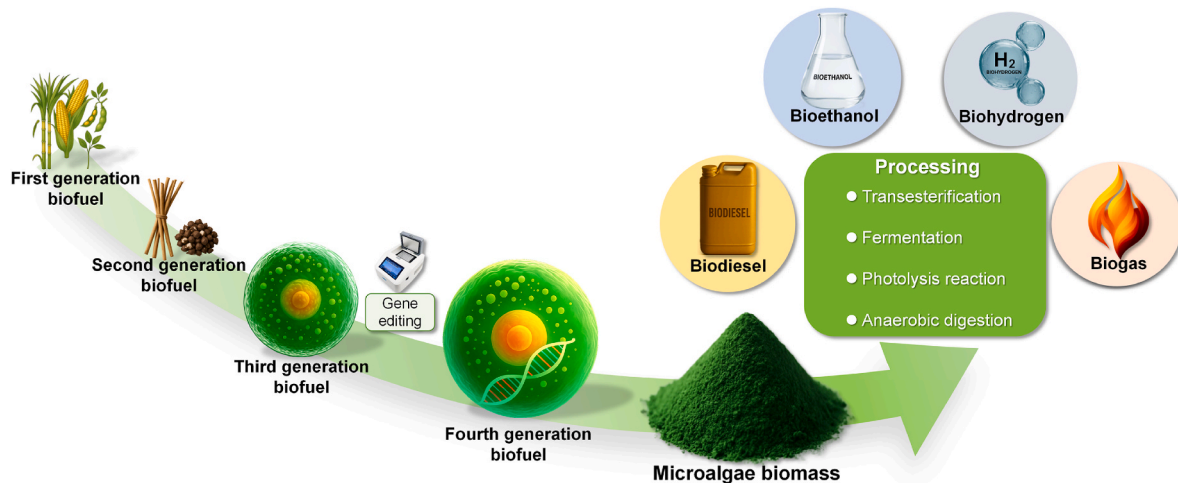


Fig. 2. Biofuel feedstock evolution and microalgae-based fuel production pathways.

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 (Munoz 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*, *Coccoloba*, *Tetraspora*, and *Monoraphidium* (Singh et al., 2023). Among these, *Chlorella* has shown particularly high potential for biohydrogen production (Ošljaj and Mursec, 2010). Notably, a newly discovered strain, *Chlorella* KLS59, 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 microalgal 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</i> <i>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) + Absciscic 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>NT1</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; Velmozhina 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  $\beta$ -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 dendrorhous*, *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 (Jamroz 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).

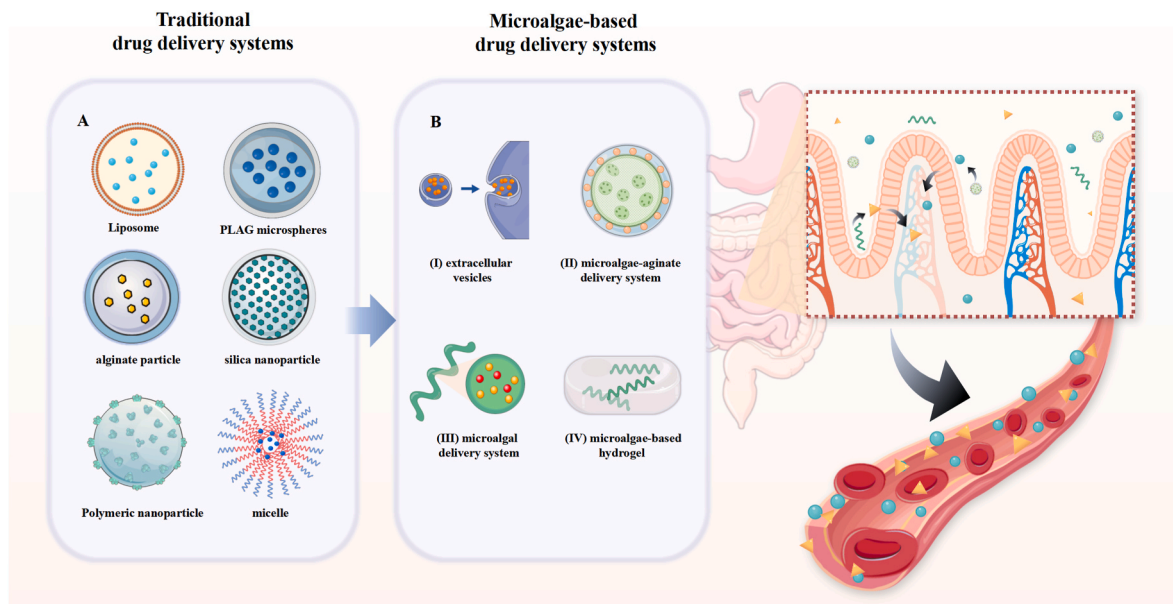
Microalgae also possess reactive cell surfaces that facilitate drug loading. Zhong et al. (2021) constructed an oral delivery system using *Spirulina platensis* to transport the radioprotective agent Amifostine (AMF) selectively to normal tissues (Fig. 3 B-III). Similarly, Zhang et al. (2024c) engineered 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- $\kappa$ B/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).

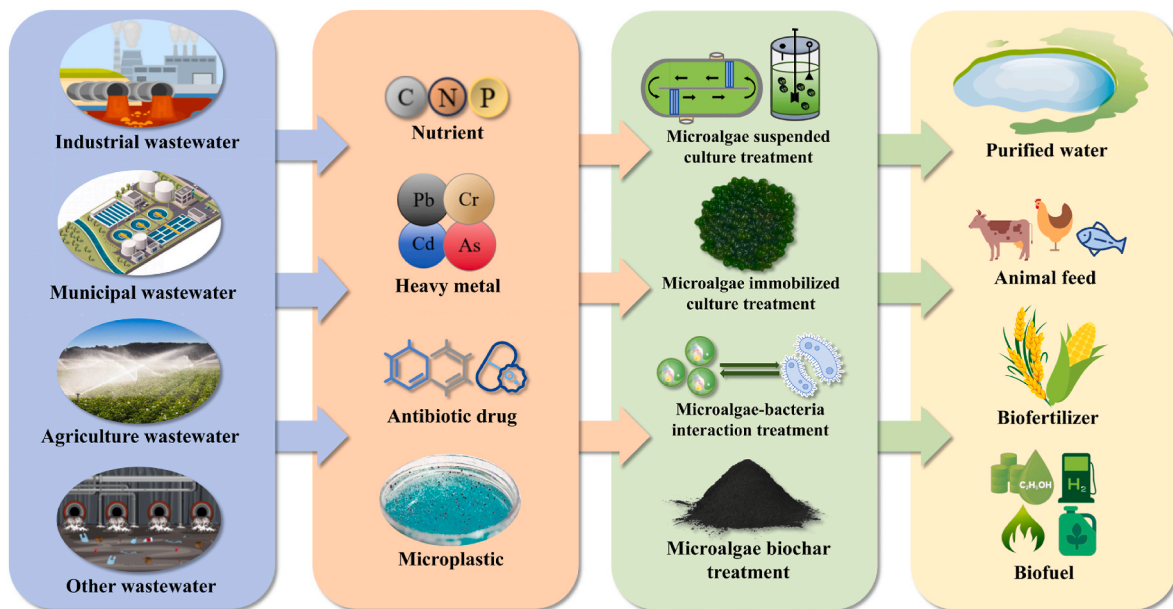
## 2.3. Application of microalgae in wastewater treatment and bioremediation

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-alginate delivery system, (III) Microalgae 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	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	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

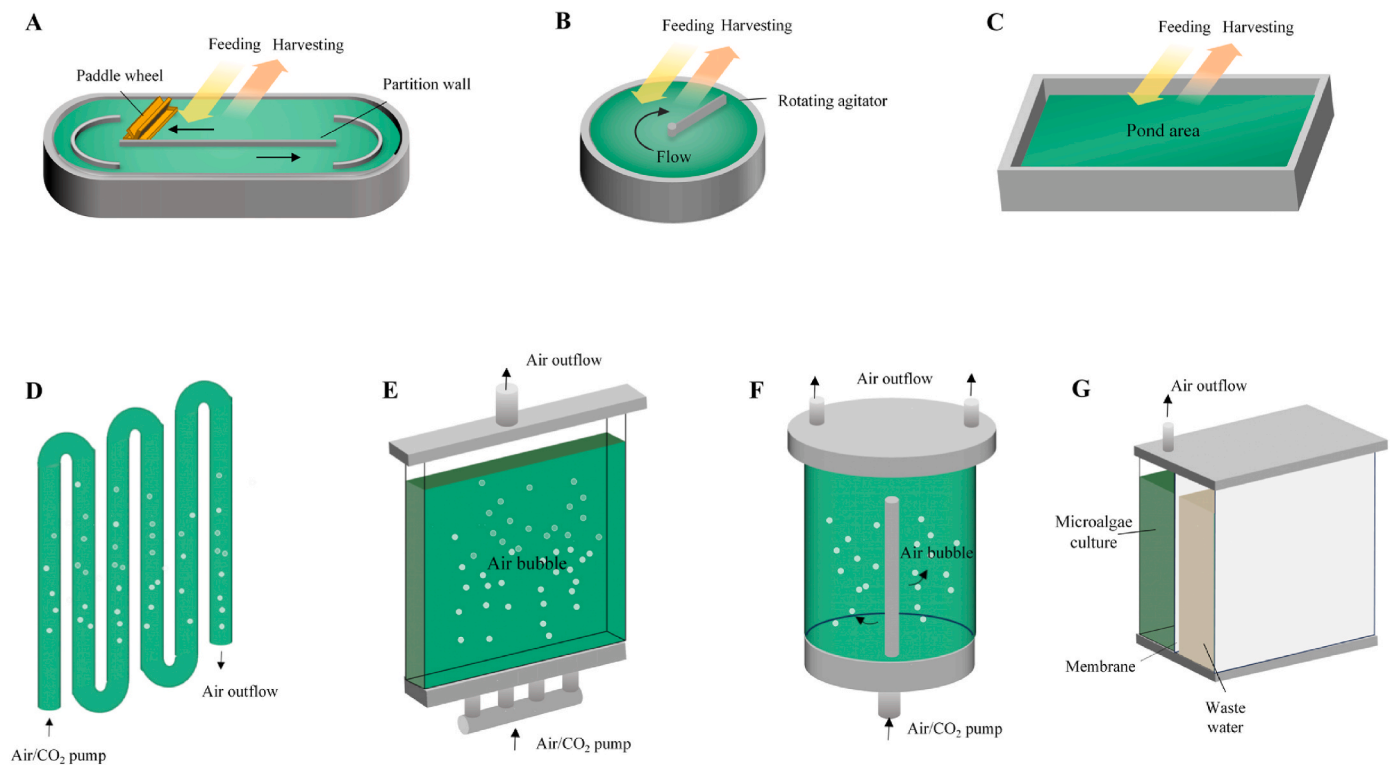
Open raceway ponds (ORPs; Fig. 5A–C) are among the most widely used large-scale systems for microalgae cultivation due to their low capital cost, operational simplicity, and adaptability to diverse environmental conditions (Suparmaniam et al., 2019; Tan et al., 2018). However, ORPs generally yield lower 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 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 zep 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. Brevet (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 Lidian 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	Dai et al. (2024)
	Sedimentation	Low cost, simple operation	Time-consuming, no industrial application	Li et al. (2021)
	Filtration	Low cost, low energy requirements	Membrane contamination	Velten et al. (2024)
	Centrifugation	High efficiency, suitable for almost all microalgae, suitable for research purpose	High equipment and energy cost	Abu-Shamleh and Najjar. (2020)
Extraction method	Physical crushing	High efficiency, no environmental pollution	Non-selective, difficult to separate	Zhang et al. (2024a)
	Organic solvent extraction	High efficiency, pure biomass	Time-consuming,poisonous	Rocha et al. (2023)
	Enzyme extraction	The operating conditions are mild, the selectivity is high, and the extraction product is not damaged	Suitable for high-value products	Sayegh et al. (2025)

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.

Acknowledgement

This research was supported by the Outstanding Research Talents Program of Fujian Agriculture and Forestry University (xjq202008),



Municipal School Science and Technology Achievements Transfer and Transformation Project (2024-G-008), and the University of Technology Sydney, Australia (UTS, RIA NGO). Fig. 3 was partly generated using Servier Medical Art, provided by Servier, licensed under a Creative Commons Attribution 4.0 unported license (<https://creativecommons.org/licenses/by/4.0/>).

## Data availability

Data will be made available on request.

## References

- Abu-Shamleh, A., Najjar, Y.S., 2020. Optimization of mechanical harvesting of microalgae by centrifugation for biofuels production. *Biomass Bioenergy* 143, 105877. <https://doi.org/10.1016/j.biombioe.2020.105877>.
- Adarme-Vega, T.C., Lim, D.K., Timmins, M., Vernen, F., Li, Y., Schenk, P.M., 2012. Microalgal biofactories: a promising approach towards sustainable omega-3 fatty acid production. *Microb. Cell Fact.* 11, 96. <https://doi.org/10.1186/1475-2859-11-96>.
- Ahmed, S.F., Rafa, N., Mofijur, M., Badruddin, I.A., Inayat, A., Ali, M.S., Farrok, O., Yunus Khan, T.M., 2021. Biohydrogen production from biomass sources: Metabolic pathways and economic analysis. *Front. Energy Res.* 9, 753878. <https://doi.org/10.3389/fenrg.2021.753878>.
- Akella, S., Ma, X., Bacova, R., Harmer, Z.P., Kolackova, M., et al., 2021. Co-targeting strategy for precise, scarless gene editing with CRISPR/Cas9 and donor ssODNs in *Chlamydomonas*. *Plant Physiol* 187, 2637–2655. <https://doi.org/10.1093/plphys/kiab418>.
- Alnaief, M., Obaidat, R.M., Alsmadi, M.T.M., 2020. Preparation of hybrid alginate-chitosan aerogel as potential carriers for pulmonary drug delivery. *Polymers* 12, 2223. <https://doi.org/10.3390/polym12102223>.
- Anguselvi, V., Masto, R.E., Mukherjee, A., Singh, P.K., 2019. CO<sub>2</sub> capture for industries by algae. In: *Algae*. IntechOpen.
- Anto, S., Mukherjee, S.S., Muthappa, R., Mathimani, T., Deviram, G., Kumar, S.S., Verma, T.N., Pugazhendhi, A., 2020. Algae as green energy reserve: technological outlook on biofuel production. *Chemosphere* 242, 125079. <https://doi.org/10.1016/j.chemosphere.2019.125079>.
- Assunção, J., Malcata, F.X., 2020. Enclosed “non-conventional” photobioreactors for microalga production: a review. *Algal Res.* 52, 102107. <https://doi.org/10.1016/j.algal.2020.102107>.
- Barboza-Rodríguez, R., Rodríguez-Jasso, R.M., Rosero-Chasoy, G., Rosales Aguado, M.L., Ruiz, H.A., 2024. Photobioreactor configurations in cultivating microalgae biomass for biorefinery. *Bioresour. Technol.* 394, 130208. <https://doi.org/10.1016/j.biortech.2023.130208>.
- Barouk, C., Munoz-Tamayo, R., Steyer, J.P., Bernard, O., 2015. A state of the art of metabolic networks of unicellular microalgae and cyanobacteria for biofuel production. *Metab. Eng.* 30, 49–60. <https://doi.org/10.1016/j.ymben.2015.03.019>.
- Beigbeder, J.-B., Lavoie, J.-M., 2022. Effect of photoperiods and CO<sub>2</sub> concentrations on the cultivation of carbohydrate-rich *P. kessleri* microalgae for the sustainable production of bioethanol. *J. CO<sub>2</sub> Util.* 58, 101934. <https://doi.org/10.1016/j.jcou.2022.101934>.
- Bhatnagar, P., Gururani, P., Bisht, B., Kumar, V., 2021. Algal Biochar: an advance and sustainable method for wastewater treatment. *Octa J. Biosci.* 9.
- Calatrava, V., Ballester, D.G., Dubini, A., 2024. Microalgae for bioremediation: advances, challenges, and public perception on genetic engineering. *BMC Plant Biol.* 24, 1261. <https://doi.org/10.1186/s12870-024-05995-5>.
- Carone, M., Alpe, D., Costantino, V., Derossi, C., Occhipinti, A., Zanetti, M., Riggio, V.A., 2022. Design and characterization of a new pressurized flat panel photobioreactor for microalgae cultivation and CO<sub>2</sub> bio-fixation. *Chemosphere* 307, 135755. <https://doi.org/10.1016/j.chemosphere.2022.135755>.
- Chandra, N., Shukla, P., Mallick, N., 2020. Role of cultural variables in augmenting carbohydrate accumulation in the green microalga *Scenedesmus acuminatus* for bioethanol production. *Biocatal. Agric. Biotechnol.* 26, 101632. <https://doi.org/10.1016/j.bcab.2020.101632>.
- Chandrasekhar, T., Varaprasad, D., Gnaneswari, P., Swapna, B., Riazunnisa, K., Anu Prasanna, V., Korivi, M., Wee, Y.-J., Lebaka, V.R., 2023. Algae: the reservoir of bioethanol. *Fermentation* 9, 712. <https://doi.org/10.3390/fermentation9080712>.
- Cheirsilp, B., Wantip, K., Chai-issarapap, N., Maneechote, W., Pekkoh, J., Duangjan, K., Ruangrit, K., Pumas, C., Pathom-aree, W., Srinuanpan, S., 2022. Enhanced production of astaxanthin and co-bioproducts from microalga *Haematococcus* sp. integrated with valorization of industrial wastewater under two-stage LED light illumination strategy. *Environ. Technol. Innovation* 28, 102620. <https://doi.org/10.1016/j.eti.2022.102620>.
- Chen, B., Li, F., Liu, N., Ge, F., Xiao, H., Yang, Y., 2015. Role of extracellular polymeric substances from *Chlorella vulgaris* in the removal of ammonium and orthophosphate under the stress of cadmium. *Bioresour. Technol.* 190, 299–306. <https://doi.org/10.1016/j.biortech.2015.04.080>.
- Chen, C., Shi, Q., Tong, A., Sun, L., Fan, J., 2023. Screening of microalgae strains for efficient biotransformation of small molecular organic acids from dark fermentation biohydrogen production wastewater. *Bioresour. Technol.* 390, 129872. <https://doi.org/10.1016/j.biortech.2023.129872>.
- China Development, 2023. Green A establishes Li Ye Guang Expert Workstation to promote microalgae R&D integration. <http://www.chinadevelopment.com.cn/zxsds/2023/0510/1837928.shtml>. (Accessed 23 July 2025).
- Dai, D., Qv, M., Wu, Q., Wang, W., Huang, L., Zhu, L., 2024. Investigating flocculation mechanisms and ecological safety of cationic guar gum for rapid harvesting of microalgal cells. *Bioresour. Technol.* 406, 130979. <https://doi.org/10.1016/j.biortech.2024.130979>.
- Deamici, K.M., Figueiredo, D., Guerra, I., Letras, P., Pereira, H., 2025. Global market and future trends of microalgae-based products. In: *Algal Bioreactors*. Elsevier, pp. 11–25.
- Dhokane, D., Shaikh, A., Yadav, A., Giri, N., Bandyopadhyay, A., Dasgupta, S., Bhadra, B., 2023. CRISPR-based bioengineering in microalgae for production of industrially important biomolecules. *Front. Bioeng. Biotechnol.* 11, 1267826. <https://doi.org/10.3389/fbioe.2023.1267826>.
- El-Sheekh, M.M., El-Kassas, H.Y., Ali, S.S., 2025. Microalgae-based bioremediation of refractory pollutants: an approach towards environmental sustainability. *Microb. Cell Fact.* 24, 19. <https://doi.org/10.1186/s12934-024-02638-0>.
- Elsayed, M., Eraky, M., Osman, A.I., Wang, J., Farghali, M., Rashwan, A.K., Yacoub, I.H., Hanelt, D., Abomohra, A., 2023. Sustainable valorization of waste glycerol into bioethanol and biodiesel through biocircular approaches: a review. *Environ. Chem. Lett.* 22, 609–634. <https://doi.org/10.1007/s10311-023-01671-6>.
- Elshobary, M., Abdullah, E., Abdel-Basset, R., Metwally, M., El-Sheekh, M., 2024. Maximizing biofuel production from algal biomass: a study on biohydrogen and bioethanol production using Mg-Zn ferrite nanoparticles. *Algal Res.* 81, 103595. <https://doi.org/10.1016/j.algal.2024.103595>.
- Esmaeili Nasrabadi, A., Eydi, M., Bonyadi, Z., 2023. Utilizing *Chlorella vulgaris* algae as an eco-friendly coagulant for efficient removal of polyethylene microplastics from aquatic environments. *Heliyon* 9, e22338. <https://doi.org/10.1016/j.heliyon.2023.e22338>.
- European Commission, 2024. European green deal and bioeconomy strategy. [https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/european-green-deal\\_en](https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/european-green-deal_en). (Accessed 23 July 2025).
- Fasaei, F., Bitter, J.H., Slegers, P.M., van Bostel, A.J.B., 2018. Techno-economic evaluation of microalgae harvesting and dewatering systems. *Algal Res.* 31, 347–362. <https://doi.org/10.1016/j.algal.2017.11.038>.
- Fayyaz, M., Chew, K.W., Show, P.L., Ling, T.C., Ng, I.S., Chang, J.S., 2020. Genetic engineering of microalgae for enhanced bio refinery capabilities. *Biotechnol. Adv.* 43, 107554. <https://doi.org/10.1016/j.biotechadv.2020.107554>.
- Fenton, O.S., Olafson, K.N., Pillai, P.S., Mitchell, M.J., Langer, R., 2018. Advances in biomaterials for drug delivery. *Adv. Mater.* 30, e1705328. <https://doi.org/10.1002/adma.201705328>.
- Freudenberg, R.A., Witteimer, L., Einhaus, A., Baier, T., Kruse, O., 2022. The spermidine synthase gene *SPD1*: a novel auxotrophic marker for *Chlamydomonas reinhardtii* designed by enhanced CRISPR/Cas9 gene editing. *Cells* 11, 837. <https://doi.org/10.3390/cells11050837>.
- Fulbright, S.P., Robbins-Pianka, A., Berg-Lyons, D., Knight, R., Reardon, K.F., Chisholm, S.T., 2018. Bacterial community changes in an industrial algal production system. *Algal Res.* 31, 147–156. <https://doi.org/10.1016/j.algal.2017.09.010>.
- Gallego, I., Medic, N., Pedersen, J.S., Ramasamy, P.K., Robbins, J., Vereecke, E., Romeis, J., 2025. The microalgal sector in Europe: towards a sustainable bioeconomy. *New Biotechnol* 86, 1–13. <https://doi.org/10.1016/j.nbt.2025.01.002>.
- García-Encinas, J.P., Ruiz-Cruz, S., Juárez, J., Ornelas-Paz, J.D.J., Del Toro-Sánchez, C. L., Márquez-Ríos, E., 2025. Proteins from Microalgae: nutritional, functional and bioactive properties. *Foods* 14, 921. <https://doi.org/10.3390/foods14060921>.
- Gatamaneni Loganathan, B., Orsat, V., Lefsrud, M., Wu, B.S., 2020. A comprehensive study on the effect of light quality imparted by light-emitting diodes (LEDs) on the physiological and biochemical properties of the microalgal consortia of *Chlorella variabilis* and *Scenedesmus obliquus* cultivated in dairy wastewater. *Bioprocess Biosyst. Eng.* 43, 1445–1455. <https://doi.org/10.1007/s00449-020-02338-0>.
- Ghosh, S., Sarkar, B., 2024. Genetically modified algae for biofuel production. In: *Recent Trends and Developments in Algal Biofuels and Biorefinery*. Springer, pp. 441–457.
- Global Carbon Budget, 2024. Fossil fuel CO<sub>2</sub> emissions increase again in 2024. <https://globalcarbonbudget.org/fossil-fuel-co2-emissions-increase-again-in-2024/>. (Accessed 23 July 2025).
- Graesholt, C., Brembu, T., Volpe, C., Bartosova, Z., Serif, M., et al., 2024. Zeaxanthin epoxidase 3 knockout mutants of the model diatom *Phaeodactylum tricornutum* enable commercial production of the bioactive carotenoid diatoxanthin. *Mar. Drugs* 22, 185. <https://doi.org/10.3390/md22040185>.
- Green, A., 2024. Company News-Yunnan Green A Biotechnology Co. Ltd. <http://www.graena.com.cn/list/front.article.articleList/30/44/1476.html>. (Accessed 23 July 2025).
- Gupta, P.L., Lee, S.M., Choi, H.J., 2015. A mini review: photobioreactors for large scale algal cultivation. *World J. Microbiol. Biotechnol.* 31, 1409–1417. <https://doi.org/10.1007/s11274-015-1892-4>.
- Hajjari, M., Tabatabaei, M., Aghbashlo, M., Ghanavati, H., 2017. A review on the prospects of sustainable biodiesel production: a global scenario with an emphasis on waste-oil biodiesel utilization. *Renew. Sustain. Energy Rev.* 72, 445–464. <https://doi.org/10.1016/j.rser.2017.01.034>.
- Hassanien, A., Saadaoui, I., Schipper, K., Al-Marri, S., Dalgamouni, T., Aouida, M., Saeed, S., Al-Jabri, H.M., 2023. Genetic engineering to enhance microalgal-based produced water treatment with emphasis on CRISPR/Cas9: a review. *Front. Bioeng. Biotechnol.* 10, 1104914. <https://doi.org/10.3389/fbioe.2022.1104914>.
- He, T., Liu, Y., Yang, Z., Zhai, S., Wu, Y., Shi, X., Chu, S., 2025. Recent advances in microalgae robots for biomedical applications. *ACS Biomater. Sci. Eng.* 11, 3875–3892. <https://doi.org/10.1021/acsbomaterials.5c00248>.



- He, Y., Lian, J., Wang, L., Tan, L., Khan, F., Li, Y., Wang, H., Rebours, C., Han, D., Hu, Q., 2023. Recovery of nutrients from aquaculture wastewater: effects of light quality on the growth, biochemical composition, and nutrient removal of *Chlorella sorokiniana*. *Algal Res.* 69, 102965. <https://doi.org/10.1016/j.algal.2022.102965>.
- Hebbale, D., Chandran, M.D.S., Joshi, N.V., Ramachandra, T.V., 2017. Energy and food security from Macroalgae. *Journal of Biodiversity* 8, 1–11. <https://doi.org/10.1080/09766901.2017.1351511>.
- Hu, H., Zhong, D., Li, W., Lin, X., He, J., Sun, Y., Wu, Y., Shi, M., Chen, X., Xu, F., Zhou, M., 2022. Microalgae-based bioactive hydrogel loaded with quorum sensing inhibitor promotes infected wound healing. *Nano Today* 42, 101368. <https://doi.org/10.1016/j.nantod.2021.101368>.
- Inostroza, C., Solimeno, A., García, J., Fernández-Sevilla, J.M., Acien, F.G., 2021. Improvement of real-scale raceway bioreactors for microalgae production using Computational Fluid Dynamics (CFD). *Algal Res.* 54, 102207. <https://doi.org/10.1016/j.algal.2021.102207>.
- Jamroz, M., Kudlak-Kramarczyk, S., Drabczyk, A., Krzan, M., 2024. Advanced drug carriers: a review of selected protein, polysaccharide, and lipid drug delivery platforms. *Int. J. Mol. Sci.* 25, 786. <https://doi.org/10.3390/ijms25020786>.
- Jiang, W., Brueggeman, A.J., Horken, K.M., Plucinak, T.M., Weeks, D.P., 2014. Successful transient expression of Cas9 and single guide RNA genes in *Chlamydomonas reinhardtii*. *Eukaryot. Cell* 13, 1465–1469. <https://doi.org/10.1128/EC.00213-14>.
- Jing, Y., Wang, Y., Zhou, D., Wang, J., Li, J., Sun, J., Feng, Y., Xin, F., Zhang, W., 2022. Advances in the synthesis of three typical tetraterpenoids including beta-carotene, lycopene and astaxanthin. *Biotechnol. Adv.* 61, 108033. <https://doi.org/10.1016/j.biotechadv.2022.108033>.
- Judd, S.J., Al Momeni, F.A.O., Znad, H., Al Ketife, A.M.D., 2017. The cost benefit of algal technology for combined CO<sub>2</sub> mitigation and nutrient abatement. *Renew. Sustain. Energy Rev.* 71, 379–387. <https://doi.org/10.1016/j.rser.2016.12.068>.
- Khan, M.I., Shin, J.H., Kim, J.D., 2018. The promising future of microalgae: current status, challenges, and optimization of a sustainable and renewable industry for biofuels, feed, and other products. *Microb. Cell Fact.* 17, 36. <https://doi.org/10.1186/s12934-018-0879-x>.
- Kim, J., Chang, K.S., Lee, S., Jin, E., 2021. Establishment of a genome editing tool using CRISPR-Cas9 in *Chlorella vulgaris* UTEX395. *Int. J. Mol. Sci.* 22, 480. <https://doi.org/10.3390/ijms22020480>.
- Kneip, J.S., Kniepkamp, N., Jang, J., Mortaro, M.G., Jin, E., et al., 2024. CRISPR/Cas9-mediated knockout of the lycopene epsilon-cyclase for efficient astaxanthin production in the green microalga *Chlamydomonas reinhardtii*. *Plants* 13, 1393. <https://doi.org/10.3390/plants13101393>.
- Koo, S.Y., Hwang, K.T., Hwang, S., Choi, K.Y., Park, Y.J., Choi, J.H., Truong, T.Q., Kim, S.M., 2023. Nanoencapsulation enhances the bioavailability of fucoxanthin in microalga *Phaeodactylum tricornutum* extract. *Food Chem.* 403, 134348. <https://doi.org/10.1016/j.foodchem.2022.134348>.
- Koul, B., Yadav, D., Singh, S., Kumar, M., Song, M., 2022. Insights into the domestic wastewater treatment (DWWT) regimes: a review. *Water* 14, 3542. <https://doi.org/10.3390/w14213542>.
- Kurita, T., Moroi, K., Iwai, M., Okazaki, K., Shimizu, S., Nomura, S., Saito, F., Maeda, S., Takami, A., Sakamoto, A., Ohta, H., Sakuma, T., Yamamoto, T., 2020. Efficient and multiplexable genome editing using Platinum TALENs in oleaginous microalga, *Nannochloropsis oceanica* NIES-2145. *Genes Cells* 25, 695–702. <https://doi.org/10.1111/gtc.12805>.
- Kusmayadi, A., Ong, H.C., Amir, F., Riayatsyah, T.M.I., Leong, Y.K., Chang, J.-S., 2024. Hydrothermal liquefaction of swine wastewater-cultivated *Chlorella sorokiniana* SU-1 biomass for sustainable biofuel production. *Biochem. Eng. J.* 209, 109383. <https://doi.org/10.1016/j.bej.2024.109383>.
- Kusmayadi, A., Suyono, E.A., Nagarajan, D., Chang, J.S., Yen, H.W., 2020. Application of computational fluid dynamics (CFD) on the raceway design for the cultivation of microalgae: a review. *J. Microbiol. Biotechnol.* 47, 373–382. <https://doi.org/10.1007/s10295-020-02273-9>.
- Lam, T.P., Lee, T.M., Chen, C.Y., Chang, J.S., 2018. Strategies to control biological contaminants during microalgal cultivation in open ponds. *Bioresour. Technol.* 252, 180–187. <https://doi.org/10.1016/j.biortech.2017.12.088>.
- Leong, W.H., Saman, N.A.M., Kiatkittipong, W., Assabumrungrat, S., Najdanovic-Visak, V., Wang, J., Khoo, K.S., Lam, M.K., Mohamad, M., Lim, J.W., 2022. Photoperiod-induced mixotrophic metabolism in *Chlorella vulgaris* for high biomass and lipid to biodiesel productions using municipal wastewater medium. *Fuel* 313, 123052. <https://doi.org/10.1016/j.fuel.2021.123052>.
- Li, D.W., Balamurugan, S., Yang, Y.F., Zheng, J.W., Huang, D., Zou, L.G., Yang, W.D., Liu, J.S., Guan, Y., Li, H.Y., 2019. Transcriptional regulation of microalgae for concurrent lipid overproduction and secretion. *Sci. Adv.* 5, eaau3795. <https://doi.org/10.1126/sciadv.aau3795>.
- Li, L., Chai, W., Sun, C., Huang, L., Sheng, T., Song, Z., Ma, F., 2024a. Role of microalgae-bacterial consortium in wastewater treatment: a review. *J. Environ. Manag.* 360, 121226. <https://doi.org/10.1016/j.jenvman.2024.121226>.
- Li, L., Xue, S., Zhang, Y., Gao, Y., Yang, J., Zhang, X., Zhang, W., 2024b. A chemical-free magnetophoretic approach for recovering magnetic particles in microalgae removal through magnetic separation. *J. Clean. Prod.* 467, 143025. <https://doi.org/10.1016/j.jclepro.2024.143025>.
- Li, T., Hu, J., Zhu, L., 2021. Self-Flocculation as an efficient method to harvest microalgae: a mini-review. *Water* 13, 2585. <https://doi.org/10.3390/w13182585>.
- Li, Y., Huang, F., Dong, S., Liu, L., Lin, L., Li, Z., Zheng, Y., Hu, Z., 2024c. Microbiota succession, species interactions, and metabolic functions during autotrophic biofloc formation in zero-water-exchange shrimp farming without organic carbon supplements. *Bioresour. Technol.* 414, 131584. <https://doi.org/10.1016/j.biortech.2024.131584>.
- Li, Y., Wu, X., Liu, Y., Taidi, B., 2024d. Immobilized microalgae: principles, processes and its applications in wastewater treatment. *World J. Microbiol. Biotechnol.* 40, 150. <https://doi.org/10.1007/s11274-024-03930-2>.
- Li, Z., Peng, S., Li, Q., Wei, S., Zhang, Q., An, X., Li, H., 2023. Exploration of two-stage cultivation strategy using nitrogen limited and phosphorus sufficient to simultaneously improve the biomass and lipid productivity in *Desmodesmus intermedius* 28. *Fuel* 338, 127306. <https://doi.org/10.1016/j.fuel.2022.127306>.
- Liang, W., Wei, L., Wang, Q., You, W., Poetsch, A., et al., 2024. Knocking out chloroplast aldolases/Rubisco lysine methyltransferase enhances biomass accumulation in *Nannochloropsis oceanica* under high-light stress. *Int. J. Mol. Sci.* 25, 3756. <https://doi.org/10.3390/ijms25073756>.
- Lin, J.Y., Lin, W.R., Ng, I.S., 2022. CRISPRa/i with adaptive single guide assisted regulation DNA (ASGARD) mediated control of *Chlorella sorokiniana* to enhance lipid and protein production. *Biotechnol. J.* 17, e2100514. <https://doi.org/10.1002/biot.202100514>.
- López Pastor, R., Pinna-Hernández, M.G., Acien Fernández, F.G., 2023. Technical and economic viability of using solar thermal energy for microalgae drying. *Energy Rep.* 10, 989–1003. <https://doi.org/10.1016/j.egyr.2023.07.040>.
- Luo, Q., Zou, X., Wang, C., Li, Y., Hu, Z., 2021. The roles of cullins E3 ubiquitin ligases in the lipid biosynthesis of the Green Microalgae *Chlamydomonas reinhardtii*. *Int. J. Mol. Sci.* 22, 4695. <https://doi.org/10.3390/ijms22094695>.
- Mahata, C., Mishra, S., Dhar, S., Ray, S., Mohanty, K., Das, D., 2023. Utilization of dark fermentation effluent for algal cultivation in a modified airlift photobioreactor for biomass and biocrude production. *J. Environ. Manag.* 330, 117121. <https://doi.org/10.1016/j.jenvman.2022.117121>.
- Mahjoub, M.A., Dadashzadeh, S., Haeri, A., Shahhosseini, S., Abbasian, Z., Nowroozi, F., 2023. Doxorubicin-Loaded multivesicular liposomes (DepoFoam) as a sustained release carrier intended for locoregional delivery in cancer treatment: development, characterization, and cytotoxicity evaluation. *Iran. J. Pharm. Res. (IJPR)* 21, e134190. <https://doi.org/10.5812/ijpr-134190>.
- Maity, S., Mallick, N., 2024. Role of cultivation parameters in carbohydrate accretion for production of bioethanol and C-phycoerythrin from a marine cyanobacterium *Leptolyngbya valderiana* BDU 41001: a sustainable approach. *Bioresour. Technol.* 411, 131209. <https://doi.org/10.1016/j.biortech.2024.131209>.
- Melero-Cobo, X., Gallemí, M., Carnicer, M., Monte, E., Planas, A., Leivar, P., 2025. MoCloro: an extension of the *Chlamydomonas reinhardtii* modular cloning toolkit for microalgal chloroplast engineering. *Physiol. Plantarum* 177, e70088. <https://doi.org/10.1111/ppl.70088>.
- Michalak, I., Baślańska, S., Mokrzycki, J., Rutkowski, P., 2019. Biochar from A freshwater macroalga as a potential biosorbent for wastewater treatment. *Water* 11, 1390. <https://doi.org/10.3390/w11071390>.
- Mishra, N., Gupta, E., Singh, P., Prasad, R., 2021. Application of microalgae metabolites in food and pharmaceutical industry. In: *Preparation of Phytopharmaceuticals for the Management of Disorders*. Elsevier, pp. 391–408.
- Morya, R., Raj, T., Lee, Y., Kumar Pandey, A., Kumar, D., Rani Singhania, R., Singh, S., Prakash Verma, J., Kim, S.H., 2022. Recent updates in biohydrogen production strategies and life-cycle assessment for sustainable future. *Bioresour. Technol.* 366, 128159. <https://doi.org/10.1016/j.biortech.2022.128159>.
- Munoz, C.F., Sudfield, C., Naduthodi, M.I.S., Weusthuis, R.A., Barbosa, M.J., Wijffels, R.H., D'Adamo, S., 2021. Genetic engineering of microalgae for enhanced lipid production. *Biotechnol. Adv.* 52, 107836. <https://doi.org/10.1016/j.biotechadv.2021.107836>.
- Mustafa, G., Zahid, M.T., Kurade, M.B., Alvi, A., Ullah, F., Yadav, N., Park, H.K., Khan, M.A., Jeon, B.H., 2024. Microalgal and activated sludge processing for biodegradation of textile dyes. *Environ. Pollut.* 349, 123902. <https://doi.org/10.1016/j.envpol.2024.123902>.
- Naduthodi, M.I.S., Claessens, N.J., D'Adamo, S., van der Oost, J., Barbosa, M.J., 2021. Synthetic biology approaches to enhance microalgal productivity. *Trends Biotechnol.* 39, 1019–1036. <https://doi.org/10.1016/j.tibtech.2020.12.010>.
- Nagy, V., Dabosi, Z., Kuntam, S., Csankó, K., Kovács, L., Tóth, S.Z., 2024. Photoautotrophic and sustained H<sub>2</sub> production by the *pgr5* mutant of *Chlamydomonas reinhardtii* in simulated daily light conditions. *Int. J. Hydrogen Energy* 53, 760–769. <https://doi.org/10.1016/j.ijhydene.2023.12.126>.
- Nair, V.R., Das, D., Maiti, S.K., 2020. A novel bubble-driven internal mixer for improving productivities of algal biomass and biodiesel in a bubble-column photobioreactor under natural sunlight. *Renew. Energy* 157, 605–615. <https://doi.org/10.1016/j.renene.2020.05.079>.
- Nashath, F.Z., Ng, Y.J., Khoo, K.S., Show, P.L., 2025. Current contributions of microalgae in global biofuel production: cultivation techniques, biofuel varieties and promising industrial ventures. *Biomass Bioenergy* 201, 108092. <https://doi.org/10.1016/j.biombioe.2025.108092>.
- Nguyen, T.T., Nguyen, T.T., An Binh, Q., Bui, X.T., Ngo, H.H., Vo, H.N.P., Andrew Lin, K.Y., Vo, T.D., Guo, W., Lin, C., Breider, F., 2020. Co-culture of microalgae-activated sludge for wastewater treatment and biomass production: exploring their role under different inoculation ratios. *Bioresour. Technol.* 314, 123754. <https://doi.org/10.1016/j.biortech.2020.123754>.
- Nie, X., Yu, Z., Li, Y., Ouyang, S., Wang, Z., Wang, G., 2024. Simultaneous removal of Cyanobacteria and algal organic matter (AOM) by CaCO<sub>3</sub> precipitation combined with Polyaluminum chloride (PACl) flocculation. *J. Water Process Eng.* 66, 105994. <https://doi.org/10.1016/j.jwpe.2024.105994>.
- Nomura, T., Kim, J.S., Ishikawa, M., Suzuki, K., Mochida, K., 2024. High-efficiency genome editing by Cas12a ribonucleoprotein complex in *Euglena gracilis*. *Microb. Biotechnol.* 17, e14393. <https://doi.org/10.1111/1751-7915.14393>.
- Nzayisenga, J.C., Farge, X., Groll, S.L., Sellstedt, A., 2020. Effects of light intensity on growth and lipid production in microalgae grown in wastewater. *Biotechnol. Biofuels* 13, 4. <https://doi.org/10.1186/s13068-019-1646-x>.

- Olabi, A.G., Shehata, N., Sayed, E.T., Rodriguez, C., Anyanwu, R.C., Russell, C., Abdelkareem, M.A., 2023. Role of microalgae in achieving sustainable development goals and circular economy. *Sci. Total Environ.* 854, 158689. <https://doi.org/10.1016/j.scitotenv.2022.158689>.
- Onn, S.M., Koh, G.J., Yap, W.H., Teoh, M.-L., Low, C.-F., Goh, B.-H., 2024. Recent advances in genetic engineering of microalgae: bioengineering strategies, regulatory challenges and future perspectives. *J. Appl. Phycol.* 37, 247–264. <https://doi.org/10.1007/s10811-024-03367-y>.
- Ošljaj, M., Muršec, B., 2010. BIOGAS AS A RENEWABLE ENERGY SOURCE, vol. 17. TEH. VJESN.
- Pan, M., Lyu, T., Zhan, L., Matamoros, V., Angelidaki, I., Cooper, M., Pan, G., 2021. Mitigating antibiotic pollution using cyanobacteria: removal efficiency, pathways and metabolism. *Water Res.* 190, 116735. <https://doi.org/10.1016/j.watres.2020.116735>.
- Pawar, S.B., 2016. Process engineering aspects of vertical column photobioreactors for mass production of microalgae. *ChemBioEng Rev.* 3, 101–115. <https://doi.org/10.1002/cben.201600003>.
- Pohrmen, C.B., Jaiswal, K.K., Jaiswal, A.K., 2025. Application of biosynthesized nanocatalysts in microalgae biofuel conversion processes: challenges, technological advances, and environmental impacts. *Microalgal Biofuels* 485–504. <https://doi.org/10.1016/B978-0-443-24110-9.00022-0>.
- Porto, B.F.C.V., Silva, T., Gonçalves, A.L., Esteves, A.F., de Souza, S.M.A.G.U., de Souza, A.A.U., Pires, J.C.M., Vilar, V.J.P., 2022. Tubular photobioreactors illuminated with LEDs to boost microalgal biomass production. *Chem. Eng. J.* 435, 134747. <https://doi.org/10.1016/j.cej.2022.134747>.
- PRC State Council, 2021. Outline of the 14th five-year plan for marine economic development. [https://www.gov.cn/zhengce/zhengceku/2021-12/27/content\\_5664783.htm](https://www.gov.cn/zhengce/zhengceku/2021-12/27/content_5664783.htm). (Accessed 23 July 2025).
- Priya, A.K., Jalil, A.A., Dutta, K., Rajendran, S., Vasseghian, Y., Karimi-Maleh, H., Soto-Moscato, M., 2022. Algal degradation of microplastic from the environment: mechanism, challenges, and future prospects. *Algal Res.* 67, 102848. <https://doi.org/10.1016/j.algal.2022.102848>.
- Qu, W., Zhang, C., Zhang, Y., Ho, S.H., 2019. Optimizing real swine wastewater treatment with maximum carbohydrate production by a newly isolated indigenous microalga *Parachlorella kessleri* QWY28. *Bioresour. Technol.* 289, 121702. <https://doi.org/10.1016/j.biortech.2019.121702>.
- Rady, H.A., Ali, S.S., El-Sheekh, M.M., 2024. Strategies to enhance biohydrogen production from microalgae: a comprehensive review. *J. Environ. Manag.* 356, 120611. <https://doi.org/10.1016/j.jenvman.2024.120611>.
- Rani, S., Ojha, C.S.P., 2021. *Chlorella sorokiniana* for integrated wastewater treatment, biomass accumulation and value-added product estimation under varying photoperiod regimes: a comparative study. *J. Water Process Eng.* 39, 101889. <https://doi.org/10.1016/j.jwpe.2020.101889>.
- Ren, C., Zhong, D., Qi, Y., Liu, C., Liu, X., Chen, S., Yan, S., Zhou, M., 2023. Bioinspired pH-Responsive microalgal hydrogels for oral insulin delivery with both hypoglycemic and insulin sensitizing effects. *ACS Nano* 17, 14161–14175. <https://doi.org/10.1021/acs.nano.3c04897>.
- Rios, L.F., Klein, B.C., Luz Jr., L.F., Maciel Filho, R., Wolf Maciel, M.R., 2015. Nitrogen starvation for lipid accumulation in the microalga species *Desmodesmus* sp. *Appl. Biochem. Biotechnol.* 175, 469–476. <https://doi.org/10.1007/s12010-014-1283-6>.
- Rocha, D.N., Rosa, A.P., Borges, A.C., Falconi, J.H.H., Covell, L., Martins, M.A., 2023. Impacts of organic solvent toxicity on resource recovery from *Senedesmus obliquus* biomass after lipid extraction. *Biomass Bioenergy* 177, 106948. <https://doi.org/10.1016/j.biombioe.2023.106948>.
- Roy, M., Mohanty, K., 2020. Valorization of waste eggshell-derived bioflocculant for harvesting *T. obliquus*: process optimization, kinetic studies and recyclability of the spent medium for circular bioeconomy. *Bioresour. Technol.* 307, 123205. <https://doi.org/10.1016/j.biortech.2020.123205>.
- Saha, S., Maji, S., Ghosh, S.K., Maiti, M.K., 2024. Engineered *Chlorella vulgaris* improves bioethanol production and promotes prebiotic application. *World J. Microbiol. Biotechnol.* 40, 271. <https://doi.org/10.1007/s11274-024-04074-z>.
- Sarker, N.K., Kaparaju, P., 2024. Microalgal bioeconomy: a green economy approach towards achieving sustainable development goals. *Sustainability* 16, 11218. <https://doi.org/10.3390/su162411218>.
- Sami, N., Ahmad, R., Fatma, T., 2021. Exploring algae and Cyanobacteria as a promising natural source of antiviral drug against SARS-CoV-2. *Biomed. J.* 44, 54–62. <https://doi.org/10.1016/j.bj.2020.11.014>.
- Sarma, U., Hoque, M.E., Thekkangil, A., Venkatarayappa, N., Rajagopal, S., 2024. Microalgae in removing heavy metals from wastewater-An advanced green technology for urban wastewater treatment. *J. Hazard. Mater. Adv.* 15, 100444. <https://doi.org/10.1016/j.hazadv.2024.100444>.
- Sawant, S.S., Gosavi, S.N., Khadamkar, H.P., Mathpati, C.S., Pandit, R., Lali, A.M., 2019. Energy efficient design of high depth raceway pond using computational fluid dynamics. *Renew. Energy* 133, 528–537. <https://doi.org/10.1016/j.renene.2018.10.016>.
- Sayegh, F., Al-naghriani, M.J., Amran, R.H., Jamal, M.T., Nass, N.M., Felemban, W.F., Satheesh, S., 2025. Extraction of beta-carotene from the microalga *Dunaliella salina* using bacterial lipase enzyme and organic solvent under varying stress conditions. *Front. Mar. Sci.* 12, 1543147. <https://doi.org/10.3389/fmars.2025.1543147>.
- Scapini, T., Woiciechowski, A.L., Manzoki, M.C., Molina-Aulestia, D.T., Martinez-Burgos, W.J., Fanka, L.S., et al., 2024. Microalgae-mediated biofixation as an innovative technology for flue gases towards carbon neutrality: a comprehensive review. *J. Environ. Manag.* 363, 121329. <https://doi.org/10.1016/j.jenvman.2024.121329>.
- Schaeffer, S.M., Nakata, P.A., 2015. CRISPR/Cas9-mediated genome editing and gene replacement in plants: transitioning from lab to field. *Plant Sci.* 240, 130–142. <https://doi.org/10.1016/j.plantsci.2015.09.011>.
- Segredo-Morales, E., González, E., González-Martín, C., Vera, L., 2024. Novel vertical upflow multi-column configured membrane photobioreactor with a filtration control system for outdoor microalgae-bacteria cultivation, harvesting and wastewater reclamation. *Chem. Eng. J.* 482, 148799. <https://doi.org/10.1016/j.cej.2024.148799>.
- Sharma, A.K., Sharma, A., Singh, Y., Chen, W.-H., 2021. Production of a sustainable fuel from microalgae *Chlorella minutissima* grown in a 1500 L open raceway ponds. *Biomass Bioenergy* 149, 106073. <https://doi.org/10.1016/j.biombioe.2021.106073>.
- Sharmila, V.G., Rajesh Banu, J., Dinesh Kumar, M., Adish Kumar, S., Kumar, G., 2022. Algal biorefinery towards decarbonization: economic and environmental consideration. *Bioresour. Technol.* 364, 128103. <https://doi.org/10.1016/j.biortech.2022.128103>.
- Shin, S.E., Koh, H.G., Park, K., Park, S.H., Chang, Y.K., Kang, N.K., 2024. Increasing lipid production in *Chlamydomonas reinhardtii* through genetic introduction for the overexpression of glyceraldehyde-3-phosphate dehydrogenase. *Front. Bioeng. Biotechnol.* 12, 1396127. <https://doi.org/10.3389/fbioe.2024.1396127>.
- Show, K.Y., Yan, Y., Zong, C., Guo, N., Chang, J.S., Lee, D.J., 2019. State of the art and challenges of biohydrogen from microalgae. *Bioresour. Technol.* 289, 121747. <https://doi.org/10.1016/j.biortech.2019.121747>.
- Siddiki, S.Y.A., Mofijur, M., Kumar, P.S., Ahmed, S.F., Inayat, A., Kusumo, F., Badruddin, I.A., Khan, T.M.Y., Nghiem, L.D., Ong, H.C., Mahlia, T.M.I., 2022. Microalgae biomass as a sustainable source for biofuel, biochemical and biobased value-added products: an integrated biorefinery concept. *Fuel* 307, 121782. <https://doi.org/10.1016/j.fuel.2021.121782>.
- Singh, T., Sehgal, A., Singh, R., Sharma, S., Pal, D.B., Tashkandi, H.M., Raddadi, R., Harakeh, S., Haque, S., Srivastava, M., Aly Hassan, A., Srivastava, N., Gupta, V.K., 2023. Algal biohydrogen production: impact of biodiversity and nanomaterials induction. *Renew. Sustain. Energy Rev.* 183, 113389. <https://doi.org/10.1016/j.rser.2023.113389>.
- Sirawattanamongkol, T., Maswana, T., Maneeruttanarungroj, C., 2020. A newly isolated green alga *Chlorella* sp. KLSc59: potential for biohydrogen production. *J. Appl. Phycol.* 32, 2927–2936. <https://doi.org/10.1007/s10811-020-02140-1>.
- Sirohi, R., Kumar Pandey, A., Ranganathan, P., Singh, S., Udayan, A., Kumar Awasthi, M., Hoang, A.T., Chilakamarry, C.R., Kim, S.H., Sim, S.J., 2022. Design and applications of photobioreactors-a review. *Bioresour. Technol.* 349, 126858. <https://doi.org/10.1016/j.biortech.2022.126858>.
- Sobri, M.Z.A., Khoo, K.S., Liew, C.S., Lim, J.W., Tong, W.Y., Zhou, Y., et al., 2024. Abreast insights of harnessing microalgal lipids for producing biodiesel: a review of improving and advancing the technical aspects of cultivation. *J. Environ. Manag.* 360, 121138. <https://doi.org/10.1016/j.jenvman.2024.121138>.
- Stephy, G.M., Surendarnath, S., Flora, G., Amesko, K.T., 2025. Microalgae for sustainable biofuel generation: innovations, bottlenecks, and future directions. *Environ. Qual. Manag.* 34, e70019. <https://doi.org/10.1002/eqem.70019>.
- Su, Y., Zhang, B., Sun, R., Liu, W., Zhu, Q., Zhang, X., Wang, R., Chen, C., 2021. PLGA-based biodegradable microspheres in drug delivery: recent advances in research and application. *Drug Deliv.* 28, 1397–1418. <https://doi.org/10.1080/10717544.2021.1938756>.
- Subramani, K., Wuthithien, P., Saha, R., Lindblad, P., Incharoensakdi, A., 2024. Characterization and potentiality of plant-derived silver nanoparticles for enhancement of biomass and hydrogen production in *Chlorella* sp. under nitrogen deprived condition. *Chemosphere* 361, 142514. <https://doi.org/10.1016/j.chemosphere.2024.142514>.
- Sundaram, T., Rajendran, S., Gnanasekaran, L., Rachmadona, N., Jiang, J.J., Khoo, K.S., Show, P.L., 2023. Bioengineering strategies of microalgae biomass for biofuel production: recent advancement and insight. *Bioengineered* 14, 2252228. <https://doi.org/10.1080/21655979.2023.2252228>.
- Sun, H., Wu, T., Chen, S.H.Y., Ren, Y., Yang, S., Huang, J., Mou, H., Chen, F., 2021. Powerful tools for productivity improvements in microalgal production. *Renew. Sustain. Energy Rev.* 152, 111609. <https://doi.org/10.1016/j.rser.2021.111609>.
- Suparmaniam, U., Lam, M.K., Uemura, Y., Lim, J.W., Lee, K.T., Shuit, S.H., 2019. Insights into the microalgae cultivation technology and harvesting process for biofuel production: a review. *Renew. Sustain. Energy Rev.* 115, 109361. <https://doi.org/10.1016/j.rser.2019.109361>.
- Sutherland, D.L., McCauley, J., Labeeuw, L., Ray, P., Kuzhiumparambil, U., Hall, C., et al., 2021. How microalgal biotechnology can assist with the UN Sustainable Development Goals for natural resource management. *Curr Res Environ Sus* 3, 100050. <https://doi.org/10.1016/j.crsust.2021.100050>.
- Tamaki, S., Ozasa, K., Nomura, T., Ishikawa, M., Yamada, K., Suzuki, K., et al., 2023. Zeaxanthin is required for eyespot formation and phototaxis in *Euglena gracilis*. *Plant Physiol* 191, 2414–2426. <https://doi.org/10.1093/plphys/kiad001>.
- Tan, X.B., Lam, M.K., Uemura, Y., Lim, J.W., Wong, C.Y., Lee, K.T., 2018. Cultivation of microalgae for biodiesel production: a review on upstream and downstream processing. *Chin. J. Chem. Eng.* 26, 17–30. <https://doi.org/10.1016/j.cjche.2017.08.010>.
- Touliabab, H.E., El-Sheekh, M.M., Ismail, M.M., El-Kassas, H., 2022. A review of Microalgae- and Cyanobacteria-Based biodegradation of organic pollutants. *Molecules* 27, 1141. <https://doi.org/10.3390/molecules27031141>.
- Udayan, A., Pandey, A.K., Sirohi, R., Sreekumar, N., Sang, B.I., Sim, S.J., Kim, S.H., Pandey, A., 2023. Production of microalgae with high lipid content and their potential as sources of nutraceuticals. *Phytochem. Rev.* 22, 1–28. <https://doi.org/10.1007/s11101-021-09784-y>.

- Ullmann, J., Grimm, D., 2021. Algae and their potential for a future bioeconomy, landless food production, and the socio-economic impact of an algae industry. *Org. Agric. For.* 11, 261–267. <https://doi.org/10.1007/s13165-020-00337-9>.
- Varaprasad, D., Narasimham, D., Paramesh, K., Sudha, N.R., Himabindu, Y., Kumari, Keerthi, et al., 2021. Improvement of ethanol production using green alga *Chlorococcum minutum*. *Environ. Technol.* 42, 1383–1391. <https://doi.org/10.1080/09593330.2019.1669719>.
- Vargason, A.M., Anselmo, A.C., Mitragotri, S., 2021. The evolution of commercial drug delivery technologies. *Nat. Biomed. Eng.* 5, 951–967. <https://doi.org/10.1038/s41551-021-00698-w>.
- Vasilieva, S., Lobakova, E., Grigorov, T., Selyakh, I., Semenova, L., Chivkunova, O., Gotovtsev, P., Antipova, C., Zagoskin, Y., Scherbakov, P., Lukyanov, A., Lukanina, K., Solovchenko, A., 2021. Bio-inspired materials for nutrient biocapture from wastewater: microalgal cells immobilized on chitosan-based carriers. *J. Water Process Eng.* 40, 101774. <https://doi.org/10.1016/j.jwpe.2020.101774>.
- Velmozhdina, K., Shinkovich, P., Zhazhkov, V., Politaeva, N., Korabiev, V., Vladimirov, I., Morales, T.C., 2023. Production of biohydrogen from Microalgae biomass after wastewater treatment and air purification from CO<sub>2</sub>. *Processes* 11, 2978. <https://doi.org/10.3390/pr11102978>.
- Velten, H., Krahe, D., Hasport, N., Thomas, F., Ulrich, G., Linda, K., Ulf, T., 2024. Pile cloth media filtration for harvesting microalgae used for wastewater treatment. *Fermentation* 10. <https://doi.org/10.3390/fermentation10060325>, 325–325.
- VentureRadar, 2025. Top micro-algae companies. <https://www.ventureradar.com/keyword/Micro-Algae>. (Accessed 23 July 2025).
- Vieira, M.V., Pastrana, L.M., Fucinos, P., 2020. Microalgae encapsulation systems for food, pharmaceutical and cosmetics applications. *Mar. Drugs* 18, 644. <https://doi.org/10.3390/md18120644>.
- Vo Hoang Nhat, P., Ngo, H.H., Guo, W.S., Chang, S.W., Nguyen, D.D., Nguyen, P.D., Bui, X.T., Zhang, X.B., Guo, J.B., 2018. Can algae-based technologies be an affordable green process for biofuel production and wastewater remediation? *Bioresour. Technol.* 256, 491–501. <https://doi.org/10.1016/j.biortech.2018.02.031>.
- Wang, X., Ma, S., Kong, F., 2024a. Microalgae biotechnology: methods and applications. *Bioengineering* 11, 965. <https://doi.org/10.3390/bioengineering11100965>.
- Wang, J., Tian, Q., Zhou, H., Kang, J., Yu, X., Qiu, G., Shen, L., 2024b. Physiological regulation of microalgae under cadmium stress and response mechanisms of time-series analysis using metabolomics. *Sci. Total Environ.* 916, 170278. <https://doi.org/10.1016/j.scitotenv.2024.170278>.
- Wang, Q., Wang, X., Hong, Y., Liu, X., Zhao, G., Zhang, H., Zhai, Q., 2022. Microalgae cultivation in domestic wastewater for wastewater treatment and high value-added production: species selection and comparison. *Biochem. Eng. J.* 185, 108493. <https://doi.org/10.1016/j.bej.2022.108493>.
- Wang, S., Wu, S., Yang, G., Pan, K., Wang, L., Hu, Z., 2021. A review on the progress, challenges and prospects in commercializing microalgal fucoxanthin. *Biotechnol. Adv.* 53, 107865. <https://doi.org/10.1016/j.biotechadv.2021.107865>.
- Wei, L., Jiang, Z., Liu, B., 2022. A CRISPR/dCas9-based transcription activated system developed in marine microalga *Nannochloropsis oceanica*. *Aquaculture* 546, 737064. <https://doi.org/10.1016/j.aquaculture.2021.737064>.
- Weizaowang, 2024. Jiangsu Algae chain's lindsay integrated complex Project introduction. <http://weizaowang.com/view/wzwPc/1/13/view/1012.html>. (Accessed 23 July 2025).
- Wiatrowski, M., Davis, R., 2021. Algal Biomass Conversion to Fuels via Combined Algae Processing (CAP): 2020 State of Technology and Future Research. National Renewable Energy Lab.(NREL), Golden, CO (United States). No. NREL/TP-5100-79935). <https://www.nrel.gov/docs/fy22osti/82502.pdf>.
- Wicker, R.J., Kumar, G., Khan, E., Bhatnagar, A., 2021. Emergent green technologies for cost-effective valorization of microalgal biomass to renewable fuel products under a biorefinery scheme. *Chem. Eng. J.* 415, 128932. <https://doi.org/10.1016/j.cej.2021.128932>.
- Wollmann, F., Dietze, S., Ackermann, J.U., Bley, T., Walther, T., Steingroewer, J., Krutz, F., 2019. Microalgae wastewater treatment: biological and technological approaches. *Eng. Life Sci.* 19, 860–871. <https://doi.org/10.1002/elsc.201900071>.
- Xindaze, 2025. Company profile. [http://xindaze.com/html/cn/pc/cn\\_about.html](http://xindaze.com/html/cn/pc/cn_about.html). (Accessed 23 July 2025).
- Yan, J., Kuang, Y., Gui, X., Han, X., Yan, Y., 2019. Engineering a malic enzyme to enhance lipid accumulation in *Chlorella protothecoides* and direct production of biodiesel from the microalgal biomass. *Biomass Bioenergy* 122, 298–304. <https://doi.org/10.1016/j.biombioe.2019.01.046>.
- Yang, W., Zhou, L., Wang, J., Wang, L., Gao, S., et al., 2022. Knockout of a diatom cryptochrome by CRISPR/Cas9 causes an increase in light-harvesting protein levels and accumulation of fucoxanthin. *Algal Res.* 66, 102822. <https://doi.org/10.1016/j.algal.2022.102822>.
- Yang, D.-W., Syn, J.-W., Hsieh, C.-H., Huang, C.-C., Chien, L.-F., 2019. Genetically engineered hydrogenases promote biophotocatalysis-mediated H<sub>2</sub> production in the green alga *Chlorella* sp. DT. *Int. J. Hydrogen Energy* 44, 2533–2545. <https://doi.org/10.1016/j.ijhydene.2018.11.088>.
- Yang, J., Chen, J., Pan, D., Wan, Y., Wang, Z., 2013. pH-sensitive interpenetrating network hydrogels based on chitosan derivatives and alginate for oral drug delivery. *Carbohydr. Polym.* 92, 719–725. <https://doi.org/10.1016/j.carbpol.2012.09.036>.
- Yang, J., Xu, M., Zhang, X., Hu, Q., Sommerfeld, M., Chen, Y., 2011. Life-cycle analysis on biodiesel production from microalgae: water footprint and nutrients balance. *Bioresour. Technol.* 102, 159–165. <https://doi.org/10.1016/j.biortech.2010.07.017>.
- Yen, H.-W., Hu, I.C., Chen, C.-Y., Nagarajan, D., Chang, J.-S., 2019. Design of photobioreactors for algal cultivation. In: *Biofuels Algae*. Elsevier, pp. 225–256.
- Yuan, S., Ye, S., Yang, S., Luo, G., 2021. Purification of potato wastewater and production of byproducts using microalgae *Scenedesmus* and *Desmodesmus*. *J. Water Process Eng.* 43, 102237. <https://doi.org/10.1016/j.jwpe.2021.102237>.
- Zhang, H., Wen, H., Qin, W., Yin, H., Wang, Y., Liu, X., Kong, X., Zhang, S., 2024a. Multi-objective optimization of a novel microalgae harvesting method based on buoy-bead flotation and feasibility analysis by life cycle assessment. *Sep. Purif. Technol.* 329, 125143. <https://doi.org/10.1016/j.seppur.2023.125143>.
- Zhang, H., Yin, W., Liao, G., Liu, J., Dong, G., Wang, J., Guo, W., Ngo, H.H., 2024b. The identification of a correlation between lipid content in the model diatom *Phaeodactylum tricornutum* and pH treatment strategies. *Sci. Total Environ.* 915, 169897. <https://doi.org/10.1016/j.scitotenv.2024.169897>.
- Zhang, H., Yin, W., Ma, D., Liu, X., Xu, K., Liu, J., 2021. Phytohormone supplementation significantly increases fatty acid content of *Phaeodactylum tricornutum* in two-phase culture. *J. Appl. Phycol.* 33, 13–23. <https://doi.org/10.1007/s10811-020-02074-8>.
- Zhang, X., Zhang, X., Liu, S., Zhang, W., Dai, L., Lan, X., Wang, D., Tu, W., He, Y., Gao, D., 2024c. Achieving deep intratumoral penetration and multimodal combined therapy for tumor through algal photosynthesis. *J. Nanobiotechnol.* 22, 227. <https://doi.org/10.1186/s12951-024-02476-7>.
- Zhao, Z., Muylaert, K., Szymczyk, A., Vankelecom, I.F.J., 2021. Enhanced microalgal biofilm formation and facilitated microalgae harvesting using a novel pH-responsive, crosslinked patterned and vibrating membrane. *Chem. Eng. J.* 410, 127390. <https://doi.org/10.1016/j.cej.2020.127390>.
- Zhong, D., Jin, K., Wang, R., Chen, B., Zhang, J., Ren, C., Chen, X., Lu, J., Zhou, M., 2024. Microalgae-Based hydrogel for inflammatory bowel disease and its associated anxiety and depression. *Adv. Mater.* 36, e2312275. <https://doi.org/10.1002/adma.202312275>.
- Zhong, D., Zhang, D., Chen, W., He, J., Ren, C., Zhang, X., Kong, N., Tao, W., Zhou, M., 2021. Orally deliverable strategy based on microalgal biomass for intestinal disease treatment. *Sci. Adv.* 7, eabi9265. <https://doi.org/10.1126/sciadv.abi9265>.