Journal of Environmental Management 401 (2026) 128988

Contents lists available at ScienceDirect

Journal of Environmental Management

journal homepage: www.elsevier.com/locate/jenvman

Review

Integrating microalgae with sludge-based processes for antibiotic removal: Mechanisms, performance, and prospects for sustainable treatment

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ARTICLE INFO

Keywords:
Microalgae
Sludge-based processes
Antibiotic-contaminated wastewater
Antibiotic resistance genes (ARGs)
Sustainable treatment systems

ABSTRACT

The occurrence of antibiotics in wastewater represents a significant environmental and public health challenge due to their persistence and the dissemination of antibiotic resistance genes (ARGs). Conventional sludge-based treatment systems often fail to achieve complete removal of these micropollutants, underscoring the need for innovative strategies. Microalgae–sludge hybrid systems have emerged as a promising, sustainable approach for antibiotic-contaminated wastewater treatment, combining the metabolic versatility of microalgae with the biodegradation potential of bacterial consortia. These integrated systems facilitate antibiotic removal via biosorption, bioaccumulation, biodegradation, and indirect physicochemical mechanisms, while simultaneously enhancing nutrient recovery, oxygen supply, and biomass valorization. This review critically evaluates the performance and underlying mechanisms of microalgae–sludge systems. Additionally, it addresses current challenges and future prospects for Integrating Microalgae with Sludge-Based Processes for optimized performance.

1. Introduction

The occurrence of antibiotics in aquatic environments has become a pressing global concern due to their persistence, ecotoxicity, and capacity to accelerate the spread of antibiotic resistance (Kovalakova et al., 2020; Tan and Xi, 2025). A large amount of antibiotics are used in human medicine, veterinary care, and agriculture, and a considerable fraction is excreted unmetabolized, ultimately entering municipal and agricultural wastewater streams (Meng et al., 2023; Sodhi and Singh, 2021). Conventional wastewater treatment plants (WWTPs), which are primarily designed for the removal of nutrients and organic matter, are often inadequate for eliminating these micropollutants (Matesun et al., 2024; Nishmitha et al., 2025). As a result, residual antibiotics are continuously discharged into natural water bodies, where they can disrupt aquatic ecosystems and promote the proliferation of antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs), both of which pose significant risks to environmental and human health (Heyde et al., 2025; Nishmitha et al., 2025). This growing threat underscores the urgent need for advanced, sustainable treatment strategies capable of reducing antibiotic loads and curbing the spread of antimicrobial resistance.

Microalgae-based technologies have recently gained considerable attention as viable alternatives or complementary approaches to conventional wastewater treatment (Amaro et al., 2023; Law et al., 2022). Microalgae possess unique physiological capabilities: they assimilate nitrogen and phosphorus, fix carbon dioxide (CO_2), and release oxygen through photosynthesis (Abdur Razzak et al., 2024; Onyeaka et al., 2021). These features not only reduce the energy demands of treatment systems but also generate valuable biomass that can be converted into biofuels, biofertilizers, and other bioproducts (Younas et al., 2025). Beyond nutrient recovery, microalgae have demonstrated an ability to remove a wide range of emerging contaminants, including antibiotics, through mechanisms such as biosorption, bioaccumulation, and biodegradation (de Wilt et al., 2016; Lindberg et al., 2021; Mojiri et al., 2021; Mustafa et al., 2021). Their adaptability and multifunctionality make them particularly suitable for integration into existing treatment infrastructures, where they can enhance contaminant removal while contributing to circular bioeconomy objectives (Mustafa et al., 2021;

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https://doi.org/10.1016/j.jenvman.2026.128988
Received 12 November 2025; Received in revised form 30 January 2026; Accepted 10 February 2026
Available online 13 February 2026

Xiong et al., 2018, 2021).

A promising advancement in this field is the coupling of microalgae with sludge-based processes, such as activated sludge and aerobic granular sludge systems (Kosar et al., 2023; X. Wang et al., 2022). These hybrid microalgae–bacteria consortia exploit mutually beneficial interactions: microalgae produce oxygen to support bacterial oxidation of organic matter, while bacteria release carbon dioxide and essential nutrients that promote algal growth. This symbiotic relationship enhances nutrient removal efficiency, reduces aeration energy requirements, and facilitates the degradation of persistent pollutants, including antibiotics (Avila et al., 2022). Moreover, emerging studies suggest that such consortia can mitigate the spread of ARGs, providing an additional layer of protection against antimicrobial resistance. Nonetheless, challenges remain regarding light availability, biomass harvesting, seasonal variability, and the safe handling of antibiotic-laden algal biomass, factors that currently limit large-scale implementation (Borowitzka, 2013; Nwoba et al., 2019; Omokaro et al., 2025; Wendt et al., 2019).

Recent studies have increasingly focused on the integration of microalgae-based technologies into wastewater treatment (WWT) systems as a sustainable approach for resource recovery and pollutant removal (Sun et al., 2022; Tua et al., 2021; Zheng et al., 2022). Pilot-scale demonstrations have shown that coupling microalgae cultivation with sludge co-digestion can enhance nutrient recovery, bioenergy generation, and the overall valorization of waste streams (Avila et al., 2022). Reviews have further highlighted the synergistic utilization of sewage sludge and microalgae, proposing innovative process configurations that improve dewatering efficiency and energy balance while reducing treatment costs (X. Wang et al., 2022). Another review explored process coupling of high-rate activated sludge (HRAS) with aerobic granular sludge (AGS) as energy-efficient upstream options to complement algal systems in sustainable municipal wastewater treatment (Kosar et al., 2023). Also, the coupling of high-rate activated sludge (HRAS) and aerobic granular sludge (AGS) systems has been highlighted as a complementary upstream strategy to increase energy efficiency and support the stable performance of algal-based treatment processes (Kosar et al., 2023). However, existing reviews providing standardized comparative assessments of removal efficiencies for emerging pollutants remain limited. This is particularly true for studies focused on antibiotic removal performance and integration with sludge-based systems, which hinders translation to full-scale applications. This review therefore, critically examines microalgae-based technologies for the treatment of antibiotic-contaminated wastewater, with particular emphasis on their integration with sludge-based processes. The review synthesizes removal mechanisms, system configurations, and performance trends, evaluates microalgae–bacteria consortia, and discusses current limitations and future research directions toward scalable and sustainable treatment solutions. To ensure transparency in literature coverage and trend assessment, the structured review framework used in this study is described in the following section.

1.1. Methodological approach

A structured bibliometric and semi-systematic literature review framework was adopted to evaluate research activity and technological developments related to antibiotic removal in wastewater, with particular emphasis on microalgae-based systems and conventional activated sludge processes. The approach was designed to ensure transparency, reproducibility, and balanced thematic coverage across interdisciplinary sources. The primary bibliographic dataset was obtained from the Web of Science Core Collection database, selected for its high indexing standards, citation tracking capability, and broad coverage of peer-reviewed environmental engineering and water research publications. Searches were conducted in 2025 using Boolean keyword combinations including “removal of antibiotics from wastewater” paired with “conventional activated sludge” and “microalgae-based technology.” Search queries were applied to titles, abstracts, and author keywords to maximize relevance while maintaining topic specificity.

The bibliometric search was limited to journal articles and review papers published between 2016 and 2024. Retrieved records were screened to remove duplicates and clearly unrelated subject areas. Studies were retained when they directly addressed antibiotic or pharmaceutical removal in wastewater treatment contexts and reported process-relevant findings. For the broader thematic review, additional peer-reviewed studies were incorporated to support mechanistic and process-level discussion. Data extracted from the bibliometric dataset included annual publication counts, treatment technology categories, and citation metrics. Records were grouped according to treatment approach (microalgae-based systems versus conventional activated sludge systems). Citation data associated with microalgae-based antibiotic removal studies were obtained using the database analytics tools. The processed data were aggregated and converted into graphical representations to enable trend analysis. Comparative annual publication outputs for each technology category and annual publication–citation relationships for microalgae-based studies were visualized to support quantitative interpretation of research growth and impact patterns.

1.2. Bibliometric trends in antibiotic removal research

Bibliometric analysis of the Web of Science dataset indicates a sustained and accelerating growth in research on wastewater treatment technologies targeting antibiotic removal. Annual publication outputs increased steadily over the 2016–2024 period for both conventional activated sludge systems and microalgae-based technologies (Fig. 1a). While conventional activated sludge research maintained consistent growth, microalgae-based treatment studies exhibited a more pronounced rise in recent years, indicating expanding scientific and technological interest in algal approaches to micropollutant removal. A similar pattern is observed in the citation landscape of microalgae-based antibiotic removal research (Fig. 1b). Both annual publication counts and total citations increased markedly over time, with citation growth accelerating faster than publication output. This pattern suggests not only increasing research activity but also rising scientific influence and recognition of microalgae-based treatment strategies within the wastewater and environmental remediation community. Overall, the observed publication and citation trends reflect a shift toward sustainable and biologically integrated treatment approaches for pharmaceutical and antibiotic contamination. The growing research intensity supports the need for a structured technical synthesis of mechanisms, system designs, and performance outcomes, which is presented in the subsequent sections of this review.

2. Microalgae-based WWT technology

2.1. Overview of microalgae and their general role in wastewater treatment

Protecting the aquatic environment has encouraged astonishing research for sustainable treatment technologies (Hussain et al., 2017, 2021), taking into account that conventional treatment methods often present drawbacks, such as requiring large amounts of energy and high operation and maintenance costs. In this frame, microalgae offer an alternative biological treatment approach, as they can remove nutrients from wastewater and convert them into valuable biomass (Mohd Udaiyappan et al., 2017). Microalgae are microscopic photosynthetic organism (ranging from a few to several micro-meters, that, unlike higher plants, lack complex organs such as roots, stems, and leaves. They are generally unicellular, although some species can form simple multicellular structures (Mustafa et al., 2021). Microalgal growth depends on multiple factors, including light availability, temperature, and nutrient concentrations in the growth medium (Aslam et al., 2018; Hussain et al., 2021). Key nutrients such as nitrogen and phosphorus are essential for growth and the production of value-added compounds (Ota

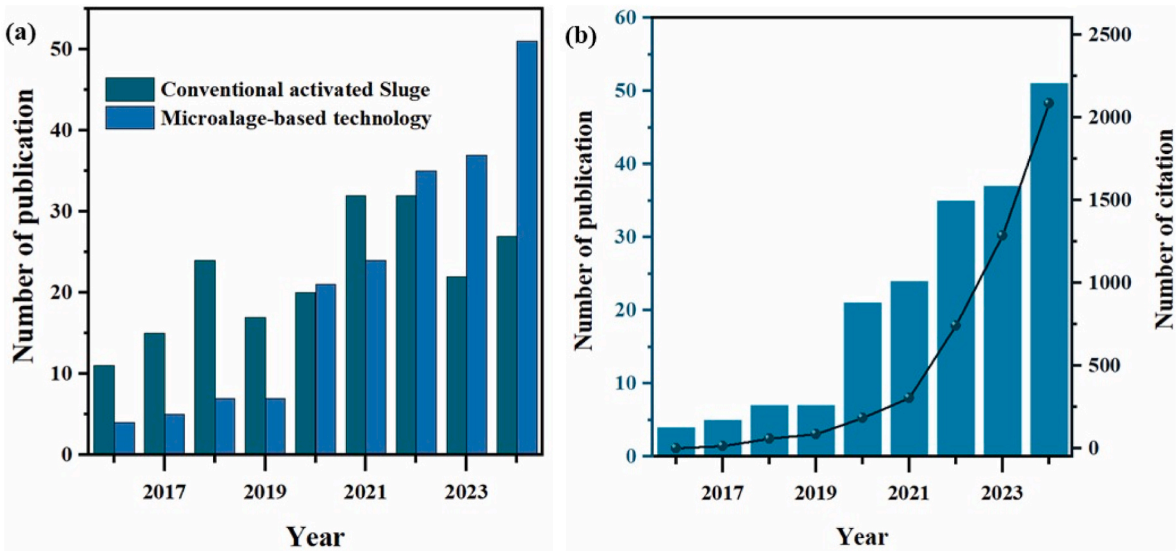

Fig. 1. Summary of published articles on the removal of antibiotics using (a) conventional activated sludge and microalgae-based technologies, and (b) the annual number of publications and citations related to antibiotic removal by microalgae-based technology from 2016 to 2024. Data were obtained from the Web of Science database (2025) using the search terms “removal of antibiotics from wastewater” in combination with “conventional activated sludge” and “microalgae-based technology.

et al., 2016; Yang et al., 2018; Yodsuwan et al., 2017), although concentrations above the optimal range may be toxic (Metin and Altınbaş, 2024).

The microalgae-based remediation technologies presents several advantages, such as efficient CO_2 fixation, environmentally friendliness, solar energy-driven activity, and the potential for biorefinery applications, such as the production of fertilizers, biofuels or other high-value biochemicals. Some microalgae species can tolerate a range of environmental stresses, although growth and activity usually occur within specific pH, temperature, and salinity ranges (Berge et al., 2012; Yu et al., 2022). For example, *Chlorella sorokiniana* exhibits species-specific tolerance to environmental conditions, growing optimally at pH 9 and 30 °C, while maintaining growth between pH 6–11 and temperatures up to 42 °C (Li et al., 2013; Wan et al., 2012). Integrating microalgal cultivation with existing wastewater treatment technologies is an efficient strategy to reduce production costs. Due to their high nutrient uptake capacity and biomass productivity, research into the commercial application of microalgae for wastewater treatment has been steadily increasing.

Compared to vascular plants, microalgae present significantly higher growth rates and a minimal environmental footprint since their use does not cause harmful impacts on the environment. Their large surface area facilitates the uptake of water, nutrients and carbon dioxide (CO_2) (Mohd Udaiyappan et al., 2017; Prajapati et al., 2013). Remarkably, under optimal cultivation conditions such as nutrient-rich media, adequate light, and favorable temperature, some microalgal species can double its original biomass less than 24 h during the exponential growth phase (Abdelfattah et al., 2023). For example, a mass doubling time of approximately 19 h has been reported for *Chlorella vulgaris* under highly controlled laboratory conditions (Daliry et al., 2017; Trisakti et al., 2025).

Furthermore, microalgae can survive under various environmental stresses, although tolerance is species- and habitat-dependent (Arora et al., 2023; Frascaroli et al., 2024; Paliwal et al., 2017; Rastogi et al., 2020). Marine microalgae can thrive in high-salinity conditions, whereas freshwater species are generally limited to low-salinity environments (Dao et al., 2024; Pan et al., 2024). Both freshwater and marine microalgae can tolerate certain ranges of heavy metals and pH variations, although extreme pH or toxic metal concentrations may inhibit growth (Berge et al., 2012; Yu et al., 2022; Zhang et al., 2014). In addition, microalgae require relatively little land area for cultivation, minimizing competition with agriculture, animal farming, industry, and residential zones (Abdelfattah et al., 2023). These characteristics position microalgae as a sustainable and multifunctional solution for modern wastewater management.

Typically, microalgae cultivation is conducted in photobioreactors (PBRs) and high-rate algal ponds (HRAP) (Abinandan and Shanthakumar, 2015). During growth, microalgae efficiently fix CO_2, thereby reducing greenhouse gas emissions and contributing to climate change mitigation (Mustafa et al., 2021; Sutherland and Ralph, 2019). The key advantages and current challenges of microalgae-based technology are summarized in Fig. 2.

While these system configurations and sustainability advantages underpin the growing adoption of microalgae-based wastewater treatment, their effectiveness in antibiotic removal ultimately depends on underlying physicochemical and biological mechanisms. These mechanisms are discussed in Section 2.2.

2.2. Microalgal removal mechanisms

The microalgae-based technologies have been widely employed for the treatment of wastewater containing antibiotics such as amoxicillin, erythromycin, levofloxacin, sulfamethoxazole, tetracycline, cephalexin and oxytetracycline, as summarized in Table 1. Microalgae that are highly resistant to these emerging contaminants include species of the genus: *Microcystis, Spirulina, Euglena, Nitzschia, Chlamydomonas, Chlorella, Scenedesmus* and *Neochloris* (Xiong et al., 2018). Upon exposure to antibiotics, microalgae activate stress-response mechanisms that facilitate the degradation of these contaminants (Aderemi et al., 2018; L. Chen et al., 2025).

Studies indicate that microalgae remove antibiotic by various mechanisms, namely biosorption, bioaccumulation, intracellular/extracellular biodegradation, photodegradation, and hydrolysis (Nguyen et al., 2021; Oberoi et al., 2019; Xiong et al., 2018). The initial step typically involves the quick and passive adsorption of pollutants through physicochemical interactions between the cell surface and the pollutants. This interaction allows the pollutants to adhere to the surface of the microalgae cells (Chia et al., 2020). Following the biosorption, there is a comparatively slower process of molecule transfer through the cell membrane. This step involves the movement of the adsorbed

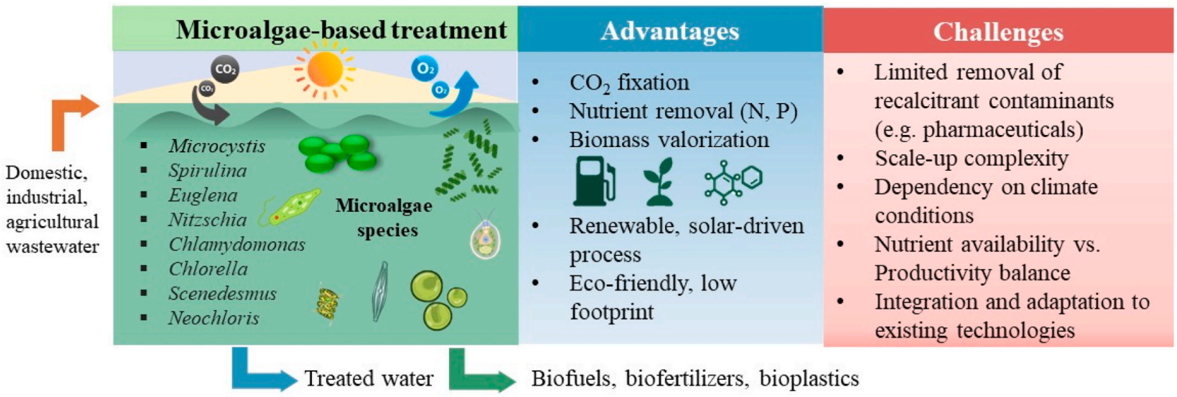

Fig. 2. Overview of wastewater treatment using microalgae, including key advantages and current challenges.

pollutants from the cell surface into the interior of the microalgae cells. The transferred pollutants can either undergo bioaccumulation, where they accumulate within the microalgae cells, or undergo biodegradation, where they are broken down by the microalgae cells. In some cases, both bioaccumulation and biodegradation may occur simultaneously (Yu et al., 2017). However, the occurrence of photodegradation and hydrolysis during micro-algae-mediated removal of antibiotics is limited and, in most cases, these pathways only contribute marginally to the overall removal of pollutants (Nguyen et al., 2021).

Photodegradation and hydrolysis generally play minor roles in antibiotic removal mediated by microalgae, as these pathways depend strongly on environmental conditions. Photodegradation requires adequate sunlight, specific photochemical properties of the contaminants, and favorable physicochemical conditions, whereas hydrolysis effectiveness is influenced by factors like high vapor pressure or specific pH levels (Nguyen et al., 2021; Xiong et al., 2021).

Fig. 3 displays the schematic diagram of the main mechanisms involved in microalgae mediated removal for degradation of antibiotics. The following subsections provide a detailed discussion of the major microalgae-mediated antibiotic removal pathways, beginning with biosorption, then bioaccumulation, and finally biodegradation, highlighting their roles, limitations, and interactions in the context of wastewater treatment.

2.2.1. *Biosorption*

Biosorption is the process by which a dissolved or suspended contaminant (sorbate) is captured by a solid-phase bio sorbent. The important factor that draws sorbate species is the biosorbent's exceptional affinity for the target sorbate. Additionally, the total capacity of the biosorbent determines the number of sorbate molecules that can be effectively adsorbed (Mustafa et al., 2021). The biosorption process continues until the adsorbed substance reaches equilibrium with the residual concentration in the liquid. The distribution of a specific sorbate between the liquid and solid phases is determined by the biosorbent's affinity for sorbate molecules (Mantzorou et al., 2018).

During the microalgae-mediated antibiotic removal, biosorption is observed when antibiotics attach to the cell wall of microalgae or onto organic compounds like extracellular polymeric substances (EPS) (Fomina and Gadd, 2014). EPS consist of polysaccharides, proteins, lipids, nucleic acids, and humic compounds, thereby offering functional groups such as hydroxyl, carboxyl, amine, and hydrophobic regions that act as binding sites for a variety of substances (d'Abzac et al., 2010; D'Abzac et al., 2010). Upon exposure to antibiotics, microorganisms tend to release more EPS-protecting cells as a response to the harsh environment (More et al., 2014; Wang et al., 2018). The interaction between antibiotics and microalgal cell surfaces is a passive process without any metabolic involvement (Sheng et al., 2010), occurring through processes like ion exchange, electrostatic interaction, surface complexation, absorption, chelation, adsorption, and micro-precipitation (Chia et al., 2020; Guo et al., 2016). Furthermore, non-living microalgae biomass has demonstrated significant potential as a biosorbent for removing antibiotics (Angulo et al., 2018; Daneshvar et al., 2018). The biomaterial used can include dead or living microbes and their components.

The effectiveness of microalgae-based biosorption is highly dependent on the characteristics of the target antibiotic (such as its hydrophobicity and functional groups available for chemisorption), the microalgal species acting as sorbent, and environmental conditions. Previous studies have shown that the adsorption performance varies, based on hydrophilicity, structure, and functional groups of different antibiotics (Xiong et al., 2018). Generally, lipophilic compounds have high bioadsorption affinity values to microalgae due to electrostatic interactions, while hydrophilic compounds exhibit low bioadsorption affinities and are more persistent in the growth medium (Xiong et al., 2018). The lipophilicity or hydrophobicity of a substance can be evaluated in terms of log K_{ow} (octanol–water partition coefficient), with a higher log K_{ow} value implying elevated adsorption of compounds onto the surface of microorganisms or the solid phase. Antibiotics with high log K_{ow} values ≥ 5 are easily absorbed than those with low log K_{ow} values ≤ 2.5) (Sutherland and Ralph, 2019; Tiwari et al., 2017).

Environmental conditions influencing biosorption are mainly the pH and temperature: pH impacts the ionization/dissociation of antibiotics in water and the surface charge of the biosorbent, while temperature influences the rate of antibiotics adsorption on the microalgal cell surface (Daneshvar et al., 2018). However, by optimizing these variables as well as the biosorbent dosage, initial adsorbate concentration, and contact time can improve the overall biosorption efficiency (Hena et al., 2020; Sutherland and Ralph, 2019).

2.2.2. *Bioaccumulation*

Bioaccumulation is reasonably slower than biosorption and an active metabolic process that requires energy to store antibiotics within the cell (Rempel et al., 2021). To quantify the extent of bioaccumulation, a parameter called the bioconcentration factor (BCF) is used, defined as the ratio of the contaminant concentration within the microalga to that in the surrounding medium. It provides a measure of the accumulation of antibiotics within the microalgae cells (Abdelfattah et al., 2023; Mustafa et al., 2021). Antibiotics can traverse the microalgal cell membrane through three primary pathways: passive diffusion, passive-facilitated diffusion, and energy-dependent/active uptake (Sutherland and Ralph, 2019; Wu et al., 2012).

a) Passive diffusion is an energy-independent process where antibiotics can pass through the microalgal cell membrane from an area of high concentration to low concentration. Antibiotics, particularly those with low molecular weight and hydrophobic properties, can diffuse

Table 1
Removal efficiencies of antibiotics by microalgae.

Microalgae species	Reaction medium	Operating conditions	Antibiotics	Initial concentration	Treatment duration (day)	Removal efficiency (%)	Removal mechanism	Ref.
Chlorella vulgaris	Bold's Basal Medium (BBM)	0.14 g/L microalgal suspension; 27 °C	LVX	200 mg/L	11	80	Biodegradation	Xiong et al. (2017a)
Chlorella vulgaris	Synthetic wastewater	1 × 10^6 cells/mL microalgal concentration; 25 ± 2 °C	LOM	100 μg/L	40	78	Biodegradation	Kiki et al. (2020)
Chlorella pyrenoidosa	BG-11 medium	OD_{680} = 1 × 10^6 cells/mL microalgal concentration; 25 ± 1 °C; 8 mM sodium acetate	SMX	0.4 μM	11	99.3	Biodegradation	Xiong et al. (2020)
Selenastrum capricornutum	Synthetic wastewater	1 × 10^6 cells/mL microalgal concentration; 25 ± 2 °C	LOM	20 μg/L	40	98	Biodegradation	Kiki et al. (2020)
Scenedesmus quadricauda	Synthetic wastewater	1 × 10^6 cells/mL microalgal concentration; 25 ± 2 °C	LOM	20 μg/L	40	94	Biodegradation	Kiki et al. (2020)
Chlorella vulgaris	Synthetic wastewater	1 × 10^6 cells/mL microalgal concentration; 25 ± 2 °C	LOM	20 μg/L	40	92	Biodegradation	Kiki et al. (2020)
Haematococcus pluvialis	Synthetic wastewater	1 × 10^6 cells/mL microalgal concentration; 25 ± 2 °C	LOM	20 μg/L	40	99	Biodegradation	Kiki et al. (2020)
Chlorella pyrenoidosa	BG-11 medium	7.50 × 10^5 cell/mL microalgal concentration; 28 ± 1 °C	TC	100 mg/L	13	93.9	Hydrolysis and biodegradation	Pan et al. (2021)
Microcystis aeruginosa	BG-11 medium	7.12 × 10^6 cell/mL microalgal concentration; 28 ± 1 °C	TC	100 mg/L		98.0	Biodegradation	Pan et al. (2021)
Chromochloris zofingiensis	Synthetic wastewater	0.14 g/L of concentration; 30 g/L glucose, 25 °C	LVX	100 mg/L	30	76	Bioaccumulation and biodegradation	Peng et al. (2022)
Chlamydomonas reinhardtii	Simulated wastewater	12.5 mg/L microalgal concentration; 25 ± 1 °C	MOX	1 mg/L	12	77.67	Biodegradation	Wan et al. (2022)
Scenedesmus quadricauda	Dairy wastewater	0.052 g/L microalgal concentration; pH = 6.5–7.0; 25 °C	TC	80 mg/L	12	67.87	Biosorption	Daneshvar et al. (2018)
Tetraselmis suecica	Dairy wastewater	0.073 g/L microalgal concentration; pH = 6.5–7.0; 25 °C	TC	80 mg/L	12	57.61	Biosorption	
Chlorella sp	Swine wastewater	5 × 10^6 cell/mL microalgal concentration; 25 ± 1 °C	AMX	150 mg/L	10	85.6	Biodegradation	Shi et al. (2018)
Scenedesmus obliquus	Synthetic wastewater	1.0% (v/v); OD680 = 1.0; 27 °C	SMT	0.1 mg/L	11	17.3	Biodegradation	Xiong et al. (2019b)
	Synthetic wastewater	1.0% (v/v); OD680 = 1.0; 27 °C	SMX	0.2 mg/L	11	29.3	Biodegradation	
Haematococcus pluvialis	Synthetic wastewater	1 × 10^6 cells/mL microalgal concentration; 25 ± 2 °C	AZM	20 μg/L	40	78	Biodegradation	Kiki et al. (2020)
Selenastrum capricornutum	Synthetic wastewater	1 × 10^6 cells/mL microalgal concentration; 25 ± 2 °C	AZM	20 μg/L	40	87	Biodegradation	Kiki et al. (2020)
Chlorella vulgaris	Synthetic wastewater	1 × 10^6 cells/mL microalgal concentration; 25 ± 2 °C	AZM	20 μg/L	40	93	Biodegradation	Kiki et al. (2020)
Chlorella vulgaris	Aquaculture wastewater	0.075 g/L microalgal concentration	SMT	0.046 mg/L	70	31.17	Adsorption bioaccumulation and degradation	Peng et al. (2020)

(*continued on next page*)

Table 1 (*continued*)

Microalgae species	Reaction medium	Operating conditions	Antibiotics	Initial concentration	Treatment duration (day)	Removal efficiency (%)	Removal mechanism	Ref.
Chlorella vulgaris	Aquaculture wastewater	0.075 g/L microalgal concentration	SDZ	0.12 mg/L	70	32.06	Adsorption bioaccumulation and degradation	Peng et al. (2020)
Chlorella vulgaris	Aquaculture wastewater	0.075 g/L microalgal concentration	SMX	0.14 mg/L	70	34.07	Adsorption bioaccumulation and degradation	Peng et al. (2020)
Chlamydomonas mexicana	Bold's Basal Medium (BBM)	1.5% (v/v) culture added; OD_{680} = 1.0; 4 g/L sodium acetate	CIP	2 mg/L	11	56	Biodegradation, bioaccumulation and bioadsorption.	Xiong et al. (2017c)
Microcystis aeruginosa	BG11 medium	4 × 10^5 cells/mL microalgal concentration; 25 ± 1 °C	SPM	50 ng/L	7	32.9	Biodegradation	Liu et al. (2012)
		4 × 10^5 cells/mL microalgal concentration; 25 ± 1 °C	AMX	50 ng/L		33.6		
Microcystis aeruginosa	BG11 medium	4 × 10^5 cells/mL microalgal concentration; 25 ± 1 °C; Nitrogen = 5 mg/L	AMX	200 ng/L	7	18.2%	Biodegradation	Liu et al. (2015)
	BG11 medium	4 × 10^5 cells/mL microalgal concentration; 25 ± 1 °C; Nitrogen = 5 mg/L		500 ng/L	7	30.5	Biodegradation	Liu et al. (2015)
Chlorella sp. L38 *Chlorella sp. UTEX1602*	BG11 medium BG11 medium	/	TAP	46.2 mg/L	14	95 97	Biodegradation, bioaccumulation and biosorption	Song et al. (2020)
Chlorella sp. Cha-01	BG11 medium, 26 ± 1 °C, 2.5% CO_2	26 ± 1 °C, 2.5% CO_2	7-ACA	100 mg/L	13	75	Biosorption	Guo et al. (2016)
Chlorella pyrenoidosa	BG11 medium 25 ± 1 °C	20 × 10^7 cells/mL microalgae concentration; 25 ± 1 °C	CFD	60 mg/L,	4	76	Bioaccumulation	Chen et al. (2015)
Chlamydomonas sp. Tai-03	Synthetic wastewater,	30 °C, 2% CO_2 30 °C, 2% CO_2	CIP SDZ	10 mg/L	9	65.05 17.05	Biodegradation	Xie et al. (2020)
Chlorella vulgaris	BG11 medium	0.1 g/L microalgae concentration; 25 ± 4 °C	MTZ	5 μM	20	100	Biosorption	Hena et al. (2020)
Chlorella sorokiniana	Bold's Basal Medium (BBM)	25 °C, pH = 7.2	OFX	1 μg/L	12	65	Bioaccumulation	Gojkovic et al. (2019)
Chlorella vulgaris	Bold's Basal Medium (BBM)	25 °C, pH = 7.2	OFX	1 μg/L	12	69	Bioaccumulation	Gojkovic et al. (2019)
Desmodesmus sp. RUC2	Bold's Basal Medium (BBM)	25 °C, pH = 7.2	OFX	1 μg/L	12	77	Bioaccumulation	Gojkovic et al. (2019)
Scenedesmu obliquus RISE (UTEX 417)	Bold's Basal Medium (BBM)	25 °C, pH = 7.2	OFX	1 μg/L	12	89	Bioaccumulation	Gojkovic et al. (2019)
Coelastrum astroideum RW10	Bold's Basal Medium (BBM)	25 °C, pH = 7.2	OFX	1 μg/L	12	61	Bioaccumulation	Gojkovic et al. (2019)
Coelastrella sp. 3–4	Bold's Basal Medium (BBM)	25 °C, pH = 7.2	OFX	1 μg/L	12	90	Bioaccumulation	Gojkovic et al. (2019)
Phaeodactylum tricornutum	Natural seawater and ALGAL medium	18 ± 2 °C	OTC	2.5 mg/L	0.5	97	Biosorption	Santaeufemia et al. (2016)
Chlorella sorokiniana	M−8a medium	1.66 × 10^5 cell/ml microalgae concentration; 25 °C, 3% CO_2	TMP	200 μg/L	23	60	Biodegradation and photolysis	de Wilt et al. (2016)

Abbreviation list: LEV: Levofloxacin; LOM: Lomefloxacin; SMX: Sulfamethoxazole; TC: Tetracycline; MOX: Moxifloxacin; AMX: Amoxicillin; SMT: Sulfamethazine; AZM: Azithromycin; SDZ: Sulfadiazine; CIP: Ciprofloxacin; SPM: Spiramycin; TAP: Thiamphenicol; 7-ACA: 7-Aminocephalosporanic acid; CFD: Cefradine; ENR: Enrofloxacin; MTZ: Metronidazole; OFX: Ofloxacin; OTC: Oxytetracycline; TMP: Trimethoprim; BG-11: Blue-Green medium; OD: optical density.

through the cell membrane due to their lipid solubility. The permeability of the cell membrane can also be influenced by factors such as antibiotic exposure or environmental stress, leading to changes in membrane permeability and facilitating passive diffusion. This phenomenon is often associated with membrane depolarization or hyperpolarization (Sutherland and Ralph, 2019). The passive diffusion of antibiotics can occur when the integrity of the cell membrane is compromised. For example, the addition of 1% (w/v) NaCl increased the removal efficiency of levofloxacin from 16% to over 80%, while the intracellular concentration increased from 34.0 μg/g to 101.0 μg/g in *Chlorella vulgaris* (Xiong et al., 2017a). Similar passive diffusion has been observed during the removal of florfenicol and carbamazepine by microalgae (Song et al., 2019; Xiong et al., 2016).

b) Passive-facilitated diffusion involves the movement of antibiotics across the cell membrane with the assistance of transporter proteins.

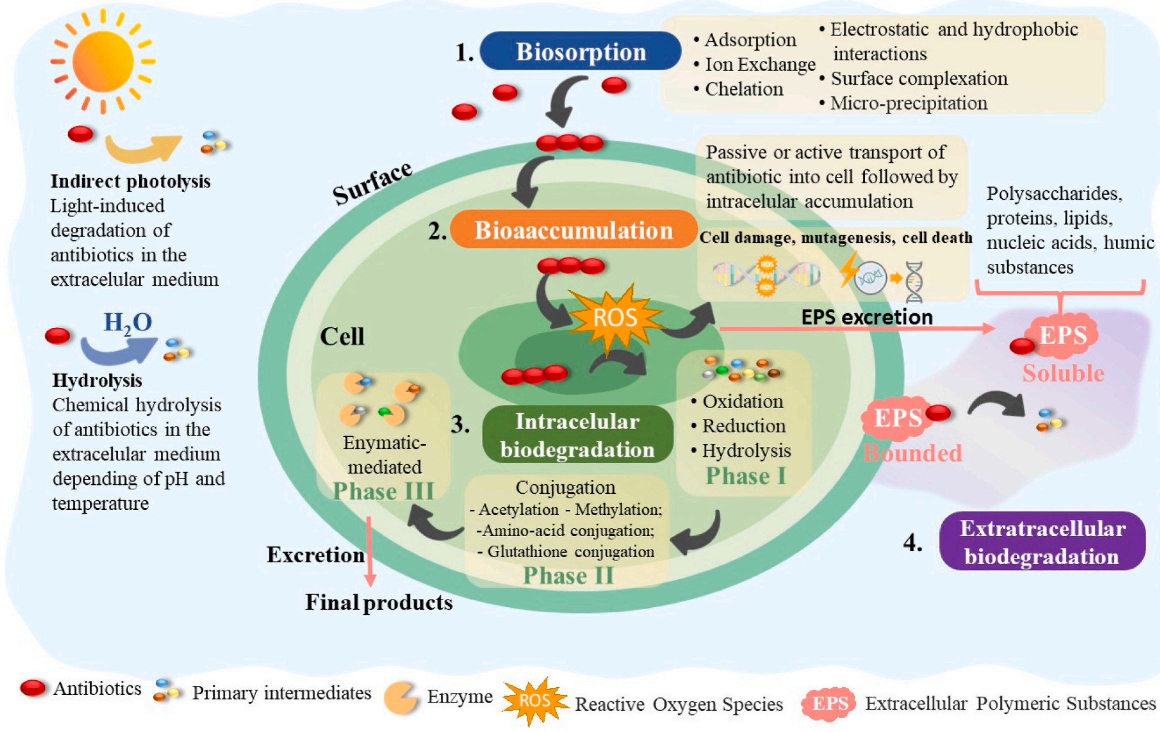

Fig. 3. Schematic diagram of the main mechanisms involved in microalgae mediated removal for degradation of antibiotics. The process includes: (1) biosorption; (2) bioaccumulation; (3) intracellular biodegradation (Phase I, II and III); and (4) extracellular biodegradation mediated by extracellular polymeric substances (EPS). Abiotic processes, such as are indirect photolysis and chemical hydrolysis, play a minor role.

These proteins play a crucial role in facilitating the influx of polar molecules into the cell.

c) Active transport is a process that requires metabolic energy to transport antibiotics against a concentration gradient, allowing them to move into the cell (Sutherland and Ralph, 2019).

Furthermore, bioaccumulation efficiency is influenced by several parameters, mainly contact time (Salah et al., 2024), antibiotic concentration (Chu et al., 2023), pH, and temperature (Gojkovic et al., 2019; Song et al., 2019; Tang et al., 2020; Xiong et al., 2016). Thus, optimizing these parameters can improve both the rate and extent of antibiotic accumulation in microalgae, while also protecting cells from potential toxicity (Chu et al., 2023; Frascaroli et al., 2024; Tang et al., 2020). This optimization is crucial for promoting antibiotic removal (Li et al., 2022). Consequently, recent studies have focused on screen microalgal species that combine high tolerance to expected antibiotic concentration and high rates of bioaccumulation (J. Chen et al., 2025; Tan et al., 2025; Wang et al., 2024).

After bioaccumulation, antibiotics can trigger the production of reactive oxygen species (ROS), including superoxide radical, perhydroxyl radical, hydroxyl radical, and singlet oxygen, which can promote the metabolism-driven depletion of the accumulated antibiotics by intracellular biodegradation (Kurade et al., 2016). Studies have demonstrated that combined accumulation and intracellular biodegradation play significant roles in the metabolism of certain antibiotics like levofloxacin and florfenicol by microalgae (Song et al., 2019; Xiong et al., 2017a). Specifically, these mechanisms have been identified as the primary pathways for levofloxacin removal by *Chlorella vulgaris* (Nagarajan et al., 2019; Xiong et al., 2017a).

However, antibiotics stored in microalgal biomass can also be transferred and amplified through the food chain, posing potential risks to human health by contributing to the development and spread of antibiotic resistance (Xie et al., 2017). Therefore, controlling antibiotic concentrations in aquatic systems is therefore essential to prevent excessive accumulation in microalgal cells and the related ecological hazards.

2.2.3. Biodegradation

Biodegradation involves the breakdown of target pollutants through two primary mechanisms: (i) complete mineralization, which converts parent molecules into CO_2, H_2O, and inorganic ions, and (ii) biotransformation, a process that utilizes a series of enzymatic reactions to generate various metabolic intermediates (Sutherland and Ralph, 2019; Xiong et al., 2017a). Microalgae-mediated biodegradation of antibiotics involves both extracellular and intracellular degradation processes. Initially, extracellular degradation occurs through the excretion of EPS, which act on dissolved antibiotics near the cell surface, serving as an external digestive system (Tiwari et al., 2017; Xiong et al., 2018). Furthermore, EPS also functions as a biosurfactant, enhancing the bioavailability of antibiotics and promoting their subsequent bioaccumulation by microalgae (Leng et al., 2020; Sheng et al., 2010). In contrast, intracellular degradation relies on the antibiotics accumulated within microalgal cells, where they are metabolized by enzymatic systems (Abdelfattah et al., 2023).

Microalgae-mediated biodegradation of antibiotics is dependent on the intricate cellular metabolism of microalgae, which encompasses a series of complex enzymatic reactions. This biodegradation process can be categorized as a three-phase enzymatic catalysis process, characterized by the functionality of the enzymes involved (Leng et al., 2020; Wang et al., 2017).

Phase I involve the introduction of reactive functional groups through oxidation, reduction, or hydrolysis reactions. These reactions are catalyzed by NADPH cytochrome P450 enzymes, including hydroxylase, carboxylase, decarboxylase, and monooxygenase. As a result, various enzymatic reactions such as carboxylation, decarboxylation, oxidation, hydroxylation, dehydroxylation, hydrogenation, methylation, demethylation, and ring cleavage have been observed (Leng et al., 2020; Xiong et al., 2019b, 2021, 2020). Additionally, the metabolites produced in Phase I reactions enhance the polarity and hydrophilicity of xenobiotics, facilitating their transformation or subsequent excretion (Xiong et al., 2021). Phase II involves conjugation reactions, where enzymes such as glutathione-S-transferases and glucosyltransferases catalyze the attachment of glutathione or other functional groups to compounds containing electrophilic centers (e.g., $CONH_2$, epoxide rings, and COOH), enhancing detoxification and protecting cells against oxidative damage (Xiong et al., 2019b, 2021). Phase III encompasses further biotransformation mediated by a variety of enzymes, including dehydrogenase, glutamyl-tRNA reductase, carboxylase, oxygenase, dehydratase transferase, and hydrolases, that biotransform these molecules into less or non-toxic intermediates (Ding et al., 2017). For example, *Chlorella pyrenoidosa* was found to biodegrade sulfamethoxazole through Phase I reactions involving oxidation and hydroxylation of the amine group, followed by Phase II reactions involving formylation and pterin-related conjugation (Xiong et al., 2020). It should be noted that eukaryotic algae are not susceptible to antibiotics that hinder cell wall synthesis, such as the β-lactam group (Välitalo et al., 2017). In a laboratory treatability test, acclimated *Chlorella sp*. demonstrated over 99% amoxicillin removal, while a continuous operation using a membrane photobioreactor achieved an 85% removal efficiency (Nagarajan et al., 2019; Shi et al., 2018). Additionally, acclimated *C. vulgaris* exhibited a 16% levofloxacin removal at a concentration of 1 mg/L (Nagarajan et al., 2019; Xiong et al., 2017a).

Overall, biodegradation of antibiotics mediated by microalgae is a highly intricate process that requires the involvement of enzymes across multiple phases. However, the specific enzymes that govern this process and their respective functions have not been comprehensively studied thus far. In practical wastewater environments, these transformation processes rarely occur in isolated algal cultures but instead take place within mixed microbial communities. This underscores the importance of examining microalgae interactions and consortium-based antibiotic removal performance, as discussed in the following section.

3. Microalga consortia for antibiotic removal

Microalga consortium are a promising method for antibiotic removal due to their greater resistance to environmental fluctuations and higher removal efficiency compared to monocultures of microalgae. Xiao et al. (2021) demonstrated that an equal mixture of *C. proteinosa* and *M. aeruginosa* achieved 44% and 59% higher cefradine (50 mg/L) removal, respectively, compared to monocultures after 24 h. According to Xiao et al. (2021), this enhanced performance can be attributed to synergistic interactions within the consortium, including the production of metabolites that improve cell permeability and enzyme activity, thereby facilitating antibiotic adsorption and degradation. The same study further showed that removal efficiency can depend on the direction of metabolite exchange:, with *C. proteinosa* removed 75% of cefradine when grown in the filtered medium of *M. aeruginosa*, whereas *M. aeruginosa* removed only 13% when exposed to metabolites from *C. proteinosa* (Xiao et al., 2021). These findings suggest that metabolite exchange during co-cultivation can enhance biomass accumulation and nutrient or micropollutant removal (Xiong et al., 2021). Similarly, Ndlela et al. (2023) demonstrated that a consortium of *Chlorella protothecoides* and *Chlorella vulgaris* remained viable and effectively removed sulfamethoxazole (77.3% at 10 ppb and 46.5% at 100 ppb) and ofloxacin (43.5% and 55.1%, respectively) from South African wastewater ponds, highlighting the potential of consortia in real-world, resource-limited settings.

While these findings highlight the potential benefits of cooperation within consortia, they also underscore that interactions among species can be complex, sometimes limiting overall performance. For instance, the ecotoxicity and removal of enrofloxacin by five individual microalgae species *Chlorella vulgaris*, *Micractinium resseri*, *Scenedesmus obliquus*, *Ourococcus multisporus*, and *Chlamydomonas mexicana*, alongside their consortium showed that the consortium was more sensitive to enrofloxacin (lower EC50) than the individual species, even though it achieved removal comparable to the most effective monoculture (*C. vulgaris*) (Xiong et al., 2017b, 2017d). Although it exhibited a relatively high kinetic removal rate ($k = 0.0256\ d^{-1}$; $T_{1/2} = 55.2$ days), it did not surpass *C. vulgaris* ($k = 0.027\ d^{-1}$; $T_{1/2} = 52.4$ days), likely due to antagonistic interactions such as competition for nutrients, light, or allelopathic effects (Xiong et al., 2017b). These observations indicate that cooperation and competition coexist in algal cultures, and co-cultures do not always maximize antibiotic removal. Supporting this, Huang et al. (2023) reported that as the sulfamethoxazole (SMX) concentration increased, the removal capacity of all treatment algae consortia declined. As shown in Fig. 4a and b, *Chlorella pyrenoidosa* and consortia containing *Chlorella pyrenoidosa*, and *Scenedesmus quadricauda* exhibited the highest removal efficiencies, reaching 11.1% and 10.9%, respectively, at 10 mg/L SMX. In addition, the consortia containing *Chlorella pyrenoidosa*, and *Dictyosphaerium sp.*, and the other group of consortia containing *C. pyrenoidosa*, *S. quadricauda*, and *Dictyosphaerium sp*., displayed lower removal efficiency of SMX across the tested concentration. Furthermore, the enzyme activity analysis revealed dynamic changes under SMX stress as displayed in Fig. 4c and d. Seven extracellular enzymes were detected, with esterase (C4 and C8) activity emerging on day 7 and decreasing at higher SMX concentrations. Aminopeptidase activities were highest on day 3, particularly in consortia with *C. pyrenoidosa* and *Dictyosphaerium sp.*, but lowest in the *C. pyrenoidosa* and S. *quadricauda* group. Phosphatase activity declined with increasing SMX, although it was higher on day 7 than on day 3. Additionally, increased intracellular antioxidant activity and sustained high levels in the *C. pyrenoidosa*, *S. quadricauda*, and *Dictyosphaerium sp*. consortium indicated that SMX stress disrupted the balance between reactive oxygen species generation and elimination, resulting in increased physiological stress (Huang et al., 2023).

Overall, most microalgal consortia do not consistently outperform the best individual monocultures in terms of antibiotic removal efficiency. Antibiotic exposure can adversely affect key biochemical parameters, including photosynthetic pigment content, chlorophyll fluorescence, extracellular enzyme activity, and reactive oxygen species generation, highlighting the susceptibility of multi-species algal consortia to antibiotic-induced stress. These limitations indicate that algal-only consortia may not be sufficient for optimal remediation performance. Consequently, increasing attention has shifted toward engineered microalgae–bacteria consortia, which are discussed in the following section.

3.1. Microalgae -bacteria consortia in wastewater treatment

Bacteria are effective microorganisms for improving wastewater treatment processes. Some genera of bacteria have been reported to oxidize a wide range of antibiotics and other micropollutants, such as *Acinetobacter*, *Streptomyces*, *Pseudomonas*, and *Sphingomonas.* Most studies focus on aerobic degradation (Deng et al., 2018; Eheneden et al., 2023; Van Epps and Blaney, 2016); however, the supply of oxygen to the consortium incurs additional operational costs, which have been reported as a disadvantage. Antibiotic inhibitory effects constitute another limitation of bacterial consortiums for antibiotic removal (Eheneden et al., 2023). The microalgae-bacteria consortium, combining photosynthetic microalgae and heterotrophic bacteria, offers a variety of benefits, including antibiotic removal in actual, complex wastewater matrices and great tolerance to high-concentration loads of antibiotics (Eheneden et al., 2023; Zambrano et al., 2021). The interactions between microalgae and bacteria in the microalgae-bacteria consortium cover a wide range of relationships from cooperation to competition. Generally, oxygen produced from photosynthesis by microalgae is available to heterotrophic bacteria for the oxidation of organic carbons, while CO_2 released during bacterial mineralization in return can be fed to microalgae for photosynthesis (Quijano et al., 2017). Additionally, bacteria can supply fixed nitrogen, vitamin B_{12}, and siderophores for

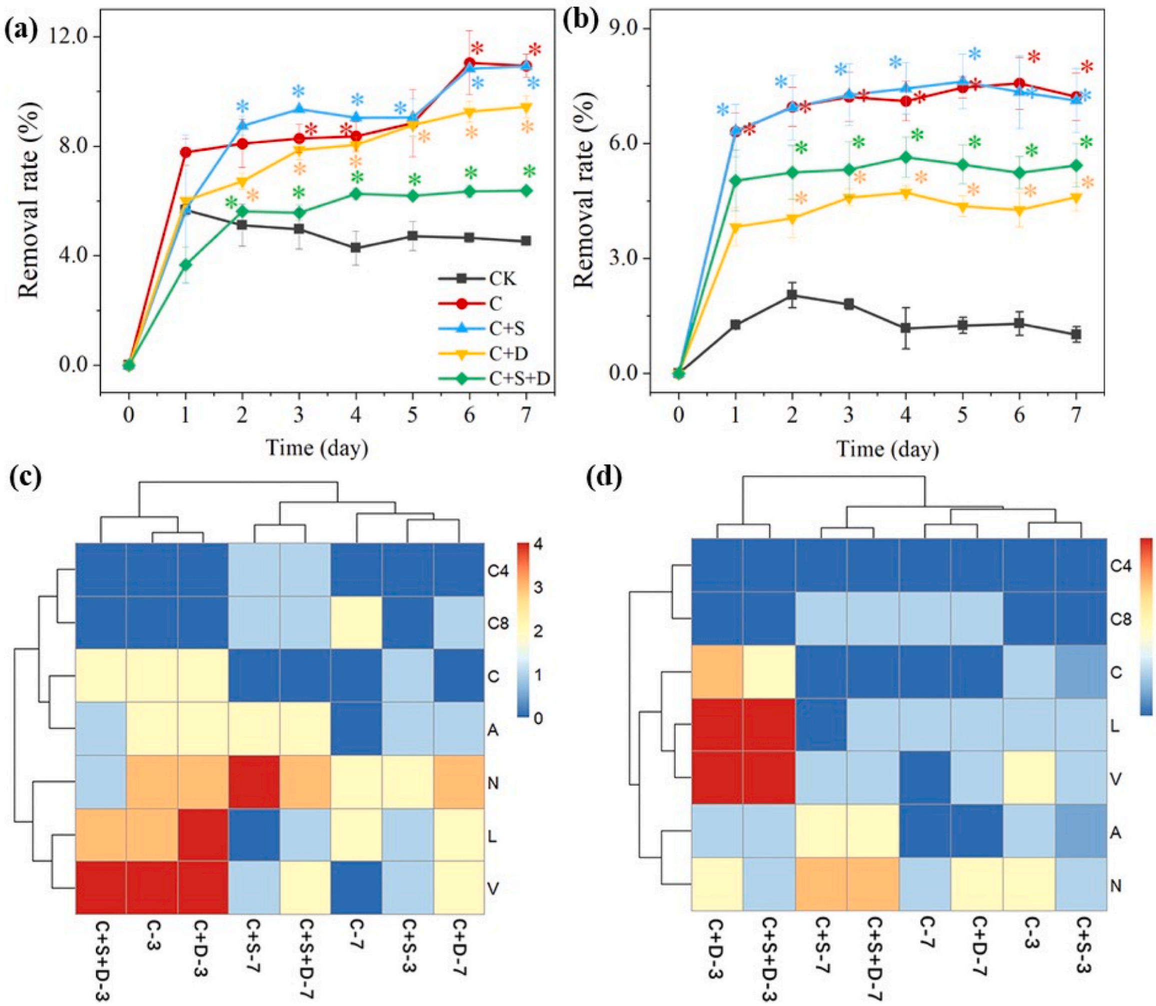

Fig. 4. Removal efficiency of sulfamethoxazole at different concentrations in three microalgae consortia treatment groups: (A) 10 mg/L and (B) 50 mg/L. Heatmap analysis of extracellular enzyme activities in the consortia on days 3 and 7 of SMX exposure at the two concentrations. Abbreviations for consortia: CK = Abiotic control group; C = *Chlorella pyrenoidosa*; C + S = *Chlorella pyrenoidosa* + *Scenedesmus quadricauda*; C + D = *Chlorella pyrenoidosa* + *Dictyosphaerium* sp.; C + S + D = *Chlorella pyrenoidosa* + *Scenedesmus quadricauda* + *Dictyosphaerium* sp. Adapted from Huang et al. (2023).

microalgal growth, and microalgae provide dissolved organic carbon to bacteria (Buchan et al., 2014). The direct or indirect cooperative interactions facilitate the microalgae-bacteria consortium with a better and broader removal efficiency of contaminants than the single- and poly-microalgae consortium (Gonçalves et al., 2017; Subashchandrabose et al., 2013; B. Zhang et al., 2020, 2020).

Alongside the cooperative interactions between microalgae and bacteria, it is crucial to acknowledge the potential antagonistic effects they can have on each other's physiology and metabolism. One such example is the ability of bacteria to generate toxic metabolites that hinder excessive microalgal growth. Conversely, microalgae can release exotoxins that function as allelochemicals or growth inhibitors for bacteria. These interactions play a significant role in shaping the dynamics between microalgae and bacteria. Fig. 5 provides an overview of

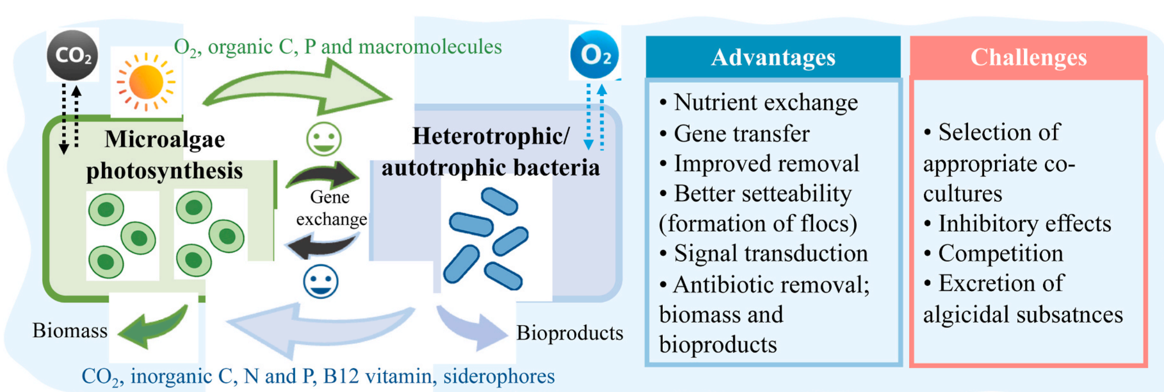

Fig. 5. Overview of wastewater treatment using microalgae-bacterial consortium, including key advantages and current challenges.

wastewater treatment using microalgae-bacteria consortia, highlighting key advantages and current challenges.

Microalgae-bacteria consortia have emerged as highly effective systems for the removal of antibiotics and other emerging contaminants from wastewater. Both microalgae and bacteria act as biosorbents, with extracellular polymeric substances (EPS) providing essential binding sites that enhance adsorption, enzyme retention, and structural stability (Wang et al., 2017). Beyond biosorption, synergistic interactions within these consortia further improve biodegradation and tolerance to contaminants. For example, Ismail et al. (2016) demonstrated that co-cultivation of *Chlorella* sp. with specific bacterial strains achieved highly efficient ketoprofen biodegradation and enhanced tolerance. Similarly, Guo and Chen (2015) developed a novel microalgae-activated sludge mixed system for the degradation of cephalosporins. The integration of microalgae with activated sludge systems has proven effective for cephalosporin removal, achieving total removal efficiencies exceeding 97% (Guo and Chen, 2015).

Predominant microalgal genera in these consortia, including *Chlorella* (da Silva Rodrigues et al., 2021, 2020; Shi et al., 2018), *Dictyosphaerium* (Zhang et al., 2022), *Scenedesmus* (Y. Wang et al., 2022c; Zambrano et al., 2023) and *Haematococcus* (Aydin et al., 2022), are favored due to their robust growth, high biosorption capacity, and adaptability, with co-cultivation also supporting bioenergy production. The mechanisms underlying contaminant removal are multifaceted, encompassing biosorption (Shashirekha et al., 2011; Yang et al., 2021), bioaccumulation (Beigbeder et al., 2019; Zhou et al., 2021), biodegradation, photolysis (Gatamaneni Loganathan et al., 2021; López-Pacheco et al., 2019), and hydrolysis (Gupta and Marchetti, 2026; Zhou et al., 2022). Although emerging contaminants can inhibit microalgal growth and reduce treatment efficiency, strategies such as acclimation, co-metabolism, and consortium formation can mitigate these effects (Abdelfattah et al., 2023; Zhou et al., 2022). Furthermore, microalgae play a critical role in shaping bacterial community composition, enhancing antibiotic removal and limiting the spread of ARGs in wastewater (Lin et al., 2026; Liu et al., 2022; Wang et al., 2024). For instance, Kiki et al. (2020) evaluated the antibiotic removal potential of four microalgae species, *Haematococcus pluvialis*, *Selenastrum capricornutum*, *Scenedesmus quadricauda*, and *Chlorella vulgaris*, in batch cultures exposed to ten antibiotics, including sulfonamides, trimethoprim, macrolides, and fluoroquinolones. All four species demonstrated significant antibiotic removal, but with differing specificities: *H. pluvialis* and *S. quadricauda* showed higher affinity for sulfonamides, while *S. capricornutum* and *C. vulgaris* were more effective at removing macrolides and fluoroquinolones. These findings underscore the importance of selecting and optimizing microalgal species, and their consortia for targeted and efficient antibiotic removal in sustainable wastewater treatment (Kiki et al., 2020). Together, these interactions highlight the importance of optimizing microalgae-bacteria consortia to achieve efficient, sustainable wastewater treatment. Table 2 summarizes recent studies on microalgae and bacteria consortium antibiotic removal efficiency, mode of removal, and treatment duration.

Recent metagenomic and physiological studies reveal that

Table 2
Removal efficiencies of antibiotics by microalgae-bacteria consortium.

Microalgae-bacteria consortium	Antibiotic	Wastewater category	Concentration	Treatment duration (day)	Mode of removal	Removal efficiency (%)	Ref.
Scenedesmus almeriensis-bacteria consortium	TC	Piggery wastewater	20−1000 μg/L	4	Biosorption	75–82	Zambrano et al. (2021)
Scenedesmus almeriensis-bacteria consortium	CIP	Piggery wastewater	20−1000 μg/L	4	Biosorption	43–100	Zambrano et al. (2021)
microalgae-bacteria consortium	SMX	WWTP effluent	52 μg/L	7	Biodegradation	54.34	da Silva Rodrigues et al. (2020)
Scenedesmus obliquus bacteria consortium	SMX SDZ	Stimulated wastewater	10 mg/L 1 mg/L	9 9	Biodegradation	5.85 40.84	Y. Wang et al. (2022c)
Scenedesmus obliquus bacteria consortium enrich with 10 mM glucose	SDZ SMX	Biological wastewater treatment	40 mg/L	6 6	Biodegradation	289 ± 8 181 ± 8	Y. Wang et al. (2022b) Y. Wang et al. (2022b)
Scenedesmus almeriensis -bacteria consortium	TC CIP SDZ SMX	Synthetic wastewater	1000,500, 100 and 20 μg/L	4	Biosorption and biodegradation	99.9 78.0 52.6 5.0	Zambrano et al. (2023)
Chlorella vulgaris and *Bacillus subtilis* consortium	TC	Simulated wastewater	500 μg/L	15	Biodegradation	74.20	Zhou et al. (2023)
Desmodesmus sp and *Klebsiella pneumoniae* (1:2) *consortium*	TC	Synthetic wastewater	50 mg/L 100 mg/L	14	Biodegradation	95% 82.11	Jingrui et al. (2022)
Haematococcus pluvialis-Proteobacteria consortium	SMX TC ENR	Synthetic wastewater	100 mg/L 37.3 mg/L 100 mg/L	0.5	Biodegradation	97.08 89.73 98.15	Aydin et al. (2022)
Natural microalgae-bacteria *(Dictyosphaerium and Pseudomonas consortium)*	OTC OFX	Swine wastewater	1 mg/L	10	Biodegradation	100.0 60.1	Zhang et al. (2022)
Natural microalgae-bacteria consortium *(mainly C. sorokiniana)*	SMX	WWTP secondary effluents	52 μg/L	7	Biodegradation	54.3	da Silva Rodrigues et al. (2020)
Natural microalgae-bacteria consortium *(Chlorella sorokiniana and Brevundimonas basaltis)*	CFD ENR	WWTP secondary effluents	50 μg/	4 7	Biodegradation	96.5 92.4	da Silva Rodrigues et al. (2021)
Scenedesmus obliquus FACHB-12 - *bacteria consortium*	CTC	BG-11 medium	60 mg/L	0.5	Biosorption and enzymatic degradation	76.2	Y. Wang et al. (2022a)
Microalgae-bacteria consortia	AMX CIP SMX	Synthetic wastewater	1 mg/L	5	Biodegradation and biosorption	93 72 20.59	Gupta and Philip (2025)

Abbreviation list: TC: Tetracycline; CIP: Ciprofloxacin; SMX: Sulfamethoxazole; SDZ: Sulfadiazine; ENR: Enrofloxacin.
OTC: Oxytetracycline; OFX: Ofloxacin; CFD: Cefradine; CTC: Chlortetracycline; AMX: Amoxicillin; WWTP: Wastewater treatment plant.

microalgae-bacteria consortia exposed to fluoroquinolones or sulfamethoxazole undergo shifts in microbial community composition, including enrichment of resistant bacterial taxa and changes in key microalgal species (Qv et al., 2025; Zhang et al., 2025). These shifts are coupled with altered metabolic gene expression in pathways related to antibiotic degradation, nutrient cycling, and stress response, indicating active metabolic adjustment by both partners. Concurrently, EPS composition changes, such as increased protein content and modified polysaccharide ratios, enhance structural stability and provide additional antibiotic-binding sites, supporting continued biosorption and partial removal (Qv et al., 2025). Collectively, these findings highlight the dynamic, context-dependent interactions that underpin consortia resilience. Strategic selection of complementary species and monitoring of EPS, gene expression, and stress-related pathways can optimize consortia for sustained antibiotic removal, improved nutrient recovery, and reduced spread of antibiotic resistance genes. However, for practical implementation, consortia performance must be evaluated within established biological treatment infrastructures rather than as standalone systems. One of the most promising implementation pathways is the integration of microalgal consortia with sludge-based processes, where complementary metabolic functions and operational synergies can be leveraged at the system scale. These integrated sludge–microalgae treatment strategies are discussed in the following section.

3.2. Coupling microalgae with sludge-based processes

The conventional activated sludge (CAS) process is one of the most widely used biological treatments for municipal and industrial wastewater (Hamid and Eskicioglu, 2012). CAS operates through the biological oxidation of organic matter, converting it into CO_2, new biomass, and water (X. Zhang et al., 2020). In these systems, adsorption is often the dominant mechanism for antibiotic removal, surpassing biodegradation. Antibiotics are adsorbed onto sludge flocs, leading to the generation of significant amounts of activated sludge as a by-product. The adsorption efficiency depends on factors such as the antibiotic's chemical structure and hydrophobicity, as well as the physicochemical characteristics of the sludge (Suto et al., 2017). The CAS process offers several advantages, including minimal secondary pollution and relatively low operating costs (X. Zhang et al., 2020). For example, bench-scale aerobic degradation experiments using activated sludge demonstrated the mineralization of sulfonamides (SAs) into nitrogen and carbon sources. The co-metabolic breakdown of SMX yielded stable metabolites such as 3-amino-5-methyl-isoxazole and hydroxyl-N-(5-methyl-1,2-oxazole-3-yl)-benzene-1-sulfonamide (Müller et al., 2013). Despite extensive research, however, the exact mechanisms underlying antibiotic removal in CAS remain incompletely understood and may vary depending on the antibiotic type (Li and Zhang, 2010).

A major concern associated with CAS is the proliferation of antibiotic resistance genes (ARGs) and antibiotic-resistant bacteria (ARB). The system's high nutrient load, dense biomass, and prolonged exposure to sub-inhibitory antibiotic concentrations create conditions favorable for ARG propagation (Guo et al., 2017; Hou et al., 2019). Additionally, recycling activated sludge can further enhance ARG and ARB dissemination (Manaia et al., 2018). The composition and abundance of ARGs in CAS systems vary widely across treatment plants (Liu et al., 2019; Manaia et al., 2018; Yang et al., 2013). For instance, Liu et al. (2019) reported diverse ARG profiles across three wastewater treatment plants, reflecting differences in wastewater sources. Sabri et al. (2020) found that most targeted ARGs decreased in abundance within a full-scale CAS system, achieving up to 2.45 log removal for macrolides resistance gene *ermB*, while sulfonamide resistance gene *sul1* and integrase gene class 1 *intI1* increased. The *intI1* gene, which is associated with horizontal gene transfer and multidrug resistance, is frequently detected in CAS and other biological wastewater treatment plants (Zheng et al., 2020). Similarly, Pazda et al. (2020) observed significant enrichment (up to 10-fold) of tetracycline resistance genes tetB, *tetK*, *tetL*, *tetO*, and sulfonamide resistance gene *sulIII*, indicating that CAS operations can inadvertently promote ARG persistence. The proliferation of ARGs and ARB within CAS systems poses a significant public health and environmental risk, as these genes can be disseminated into receiving water bodies, facilitating the spread of antimicrobial resistance in natural ecosystems. This highlights a critical limitation of conventional wastewater treatment, emphasizing the need for advanced or alternative treatment strategies capable of effectively mitigating ARG propagation.

Currently, there is no consensus on the overall efficiency of CAS in removing antibiotics and ARGs, as treatment performance is influenced by operational parameters, environmental conditions, and microbial community composition (Hazra et al., 2024; Li et al., 2016; Muoghalu et al., 2025; Zhang et al., 2015). Numerous studies have reported highly variable removal efficiencies across treatment plants and target compounds, highlighting the context-dependent nature of CAS performance (Le et al., 2018; Li et al., 2016; Muoghalu et al., 2025; Sabri et al., 2020; Xing et al., 2022; Zhang et al., 2015). For instance, Zhang et al. (2015) showed that antibiotics were not completely removed by wastewater treatment plants, with significantly lower removal efficiencies observed during winter due to seasonal effects. Similarly, Luo et al. (2025) reported that metagenomic analysis of effluent samples from WWTPs with different process configurations revealed the persistence of high-risk ARGs co-occurring with pathogenic bacteria such as *Pseudomonas aeruginosa* and *Salmonella enterica*. (Luo et al., 2025). These findings highlight that CAS systems do not consistently achieve complete removal of antibiotics and ARGs. Even with further optimization, CAS is unlikely to meet future treatment requirements (Zhang et al., 2019). For example, substantial energy input is required to drive the biological oxidation of organic matter and ammonia, which also generates greenhouse gas (GHG) emissions. In 2017, municipal wastewater treatment accounted for approximately 0.3–0.5% of global electricity consumption, reaching 3–5% in some developed countries, and contributed to about 1.6% of global GHG emissions in 2010 (Zhang et al., 2021). Upgrading CAS systems typically involves adding advanced post-treatment units, which increases complexity and cost while offering only short-term improvements (Zhang et al., 2019).

In response to these limitations, the microalgal-bacterial granular sludge (MBGS) process has emerged as a promising alternative for wastewater treatment. This symbiotic system combines the metabolic capabilities of microalgae and bacteria, offering advantages such as high biomass retention, excellent settling properties, efficient pollutant removal, and reduced operational costs (Liu et al., 2022). The superior settleability of granular sludge allows for compact reactor design and simpler biomass–effluent separation using smaller clarifiers (Abouhend et al., 2020; Quijano et al., 2017). Moreover, mutualistic interactions between microalgae and bacteria are stronger in granular sludge systems compared to suspended sludge, enhancing overall treatment performance (Zambrano et al., 2016; B. Zhang et al., 2020). Notably, algae-based systems can degrade antibiotics without promoting ARG formation (Guo et al., 2016). For instance, it was observed that the *Scenedesmus obliquus* was reported to remove 31.4-62.3% of sulfamethazine and 27.7-46.8% of sulfamethoxazole after 12 days of cultivation (Xiong et al., 2019a). Similarly, Wang et al. (2020) investigated the response of MBGS to transient high concentrations of tetracycline (1–10 mg/L) over ten operational cycles and found that the system produced more low-molecular-weight polysaccharides as a protective response. These findings highlight the resilience and potential of microalgal–bacterial systems as sustainable alternatives to conventional sludge-based wastewater treatment processes. (Wang et al., 2020).

Although long-term studies on algal–bacterial granular sludge (ABGS) systems for antibiotic removal and the attenuation of antibiotic resistance genes (ARGs) and their hosts remain limited, emerging evidence highlights their significant potential for advanced wastewater treatment. Most existing research has focused on nutrient removal, as demonstrated by Tang et al. (2018), who reported efficient total nitrogen (69.9%) and total phosphorus (94.8%) removal in a novel algal–bacterial symbiosis system based on a sequencing batch suspended biofilm reactor. Subsequent work by Tang et al. (2021) revealed that extracellular polymeric substances (EPS) play a vital role in nutrient storage, transfer, and microbial aggregation in algal–bacterial symbiotic systems. Further studies have expanded these findings, showing that algal–bacterial consortia such as *Chlorella-Bacillus* can achieve simultaneous nutrient removal and effective ARG mitigation, with up to 97% removal of the *sul1* gene, a widely used marker for sulfonamide resistance in bacteria, and 98.5% total nitrogen removal (Tang et al., 2022). Furthermore, EPS dynamics have been recognized as key drivers of microbial interaction, pollutant adsorption, and system stability, particularly under stress conditions such as antibiotic exposure and salinity fluctuations (Bute et al., 2024; Liu et al., 2024). These developments suggest that integrating algal–bacterial symbiosis with granular sludge technology offers a promising and sustainable strategy for simultaneous nutrient removal, antibiotic degradation, and ARG mitigation. Nevertheless, further long-term and mechanistic investigations are essential to elucidate the underlying pathways, resilience mechanisms, and scalability of ABGS systems for comprehensive antibiotic and ARG control in complex wastewater environments. Fig. 6 illustrates the wastewater treatment process in microalgae-sludge systems, emphasizing key benefits and existing limitations.

Taken together, these findings show that microalgae–sludge integrated systems are promising platforms for antibiotic and antibiotic resistance gene control in wastewater treatment. However, operational, economic, and environmental uncertainties still limit confidence in long-term and full-scale performance. The key prospects and implementation challenges are discussed in the following section.

4. Prospects and challenges

Coupling microalgae with sludge-based processes presents exciting opportunities for advancing antibiotic wastewater treatment. These integrated systems offer multiple benefits beyond contaminant removal, including nutrient recovery, oxygen production that reduces the need for energy-intensive aeration, and the generation of biomass that can be valorized for biofuels, biofertilizers, or other bioproducts. The multi-functionality of microalgal–bacterial systems aligns well with circular economy principles, positioning them as sustainable alternatives to conventional treatment methods. Importantly, these systems not only target antibiotics directly but also show potential to curb the spread of antibiotic resistance genes by reducing selective pressure and altering microbial community dynamics. Their adaptability across different wastewater sources, from municipal effluents to industrial and agricultural discharges, further highlights their promise.

Despite these prospects, several challenges must be addressed before a large-scale implementation can be realized:

- Light availability remains a central limitation, as efficient photosynthesis is often hindered in dense cultures and under seasonal or geographic constraints. The design of photobioreactors or open ponds must therefore ensure sufficient illumination while maintaining cost-effectiveness.
- Selection of proper microalgae-sludge/acclimation/genetic engineering
- Biomass harvesting and downstream management also pose practical obstacles, particularly when the biomass contains residual antibiotics or resistance genes that could re-enter the environment if not handled appropriately.
- Antibiotic removal efficiency varies widely depending on the compound, algal strain, and operational conditions, making system performance difficult to predict and standardize.
- The economic and regulatory barriers add further complexity. The capital and maintenance costs associated with cultivating and harvesting microalgae remain significant, although reduced aeration can lower operational energy demands. At present, regulatory frameworks do not fully accommodate mictroalgae–sludge technologies, and limited pilot-scale demonstrations contribute to uncertainties about their reliability and scalability.
- Most studies have been conducted at the laboratory scale, while pilot-scale investigations remain scarce but are critically important for understanding technical and operational conditions and for conducting more accurate economic evaluations. Therefore, greater efforts directed to advance the technology readiness level are needed to enable full-scale implementation in the near future.
- Knowledge gaps persist regarding the fate of transformation products, the long-term effectiveness of resistance gene reduction, and the ecological safety of discharging or reusing algal biomass.

Future progress will depend on innovations in reactor design, strain selection, and the integration of algal systems with complementary technologies such as advanced oxidation processes or membrane filtration. Addressing these scientific, technical, and regulatory challenges will be essential to unlocking the full potential of microalgae–sludge systems and enabling their transition from promising laboratory concepts to practical, sustainable solutions for antibiotic-contaminated wastewater.

5. Conclusion

The persistence of antibiotics and antibiotic resistance genes in wastewater represents a growing threat to environmental and human health, highlighting the urgent need for treatment solutions that go beyond the capabilities of conventional sludge-based processes. Microalgae offer unique advantages in this context, combining nutrient recovery, carbon dioxide fixation, and oxygen generation with the ability

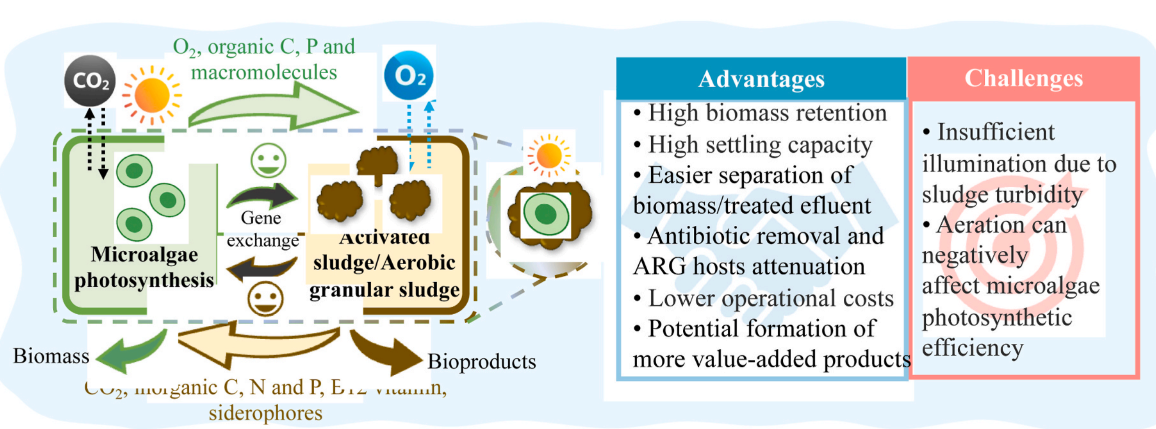

Fig. 6. Overview of wastewater treatment using microalgae-sludge, including key advantages and current challenges.

to remove antibiotics through biosorption, bioaccumulation, biodegradation, and indirect physicochemical pathways. When coupled with sludge-based processes, microalgae create synergistic consortia that not only enhance contaminant removal but also improve microbial stability, reduce aeration energy demand, and open new opportunities for biomass valorization.

The evidence reviewed here demonstrates the considerable potential of algal–bacterial systems to mitigate antibiotic contamination and attenuate the spread of resistance determinants. At the same time, these technologies face persistent challenges related to light requirements, biomass harvesting, seasonal variability, and the safe handling of antibiotic-laden biomass. Economic costs, regulatory uncertainties, and limited large-scale demonstrations further restrict their near-term deployment. Addressing these barriers will require interdisciplinary efforts in reactor engineering, strain development, process optimization, and environmental risk assessment, as well as stronger integration with complementary technologies such as advanced oxidation or membrane processes.

This review highlights that coupling microalgae with sludge-based treatment represents a promising pathway toward sustainable management of antibiotic-contaminated wastewater. With continued innovation, genetic engineering, pilot-scale validation, and supportive regulatory frameworks, these systems could evolve from experimental concepts into practical technologies that contribute both to water quality protection and to the global fight against antimicrobial resistance.

CRediT authorship contribution statement

Ehiaghe Agbovhimen Elimian: Writing – original draft, Visualization, Data curation, Conceptualization. **Géssica de Oliveira Santiago:** Writing – review & editing, Visualization, Supervision.

Declaration of competing interest

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

Data availability

Data will be made available on request.

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