Microalgae-based biotechnology as a promising strategy for removing antibiotics from wastewater: opportunities, challenges and future directions

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1 Introduction

As potentially important pharmaceuticals, antibiotics have extensively been used to improve public health, prevent infectious diseases, and promote productivity of domestic and some economical animals (Zhang et al., 2017). Every year, more than 100,000 tons of antibiotics would be consumed worldwide (Danner et al., 2019). Based on the published literatures, it can be concluded that 1) 30%–90% of antibiotics would be excreted into various environments via feces or urine because they are partially absorbed or metabolized by humans and animals (Wang et al., 2023); 2) wastewater, such as industrial (pharmaceutical industries), hospital, household, and livestock wastewater, is a sink of antibiotic residues, and a source of environmental antibiotics (Rizzo et al., 2013); 3) different concentrations of antibiotics have been detected in various wastewaters, such as industrial wastewater (26 ng L^{-1}–31 mg L^{-1}) (Larsson et al., 2007; Okeke et al., 2022), hospital wastewater (0.1–157 µg L^{-1}) (Parida et al., 2022), and domestic wastewater (0.001–32 µg L^{-1}) (Verlicchi et al., 2012); and 4) antibiotics pose a serious threat to ecological environment and human health (Wang et al., 2021). Thus, how to remove antibiotics from wastewater has attracted increasing global concern and public attention in recent years.

In conventional wastewater treatment systems, only 20%–90% of antibiotics could be removed through the process of sludge adsorption (Perini et al., 2018), and natural degradation of some antibiotics (Becker et al., 2016). In order to enhance the removal efficiency of antibiotics from wastewater, various physicochemical techniques (e.g., adsorption, flocculation, coagulation, ozonation, ion exchange, membrane filtration, electrochemical degradation, chemical oxidation, and advanced oxidation) have been developed until now (Nabilah Mohd Noor et al., 2023). Additionally, some biological methods, such as microalgae, biochars, and ligninolytic fungi, have been invented to remove antibiotics from wastewater due to their unique benefits, such as being environmentally-friendly and having low economic costs (Rambabu et al., 2020; Russell and Yost, 2021; Li et al., 2022c). Among these biological methods, microalgae-based biotechnology has attracted extensive attention recently because it possesses some merits (e.g., low cost, wastewater purification, CO_2 sequestration, and microalgae biomass production) (Guo et al., 2016; Bhatt et al., 2022). Thus, this biotechnology is considered as an environmentally friendly strategy for removing antibiotics from wastewater and improving the quality of wastewater. However, some key challenges (e.g., low removal efficiency of antibiotics, toxicity of antibiotics and their intermediate transformation products, undefined

antibiotic removal mechanisms, and effects of wastewater-born bacteria) hindering the large-scale application of this biotechnology are often not noticed in previous literatures. In this paper, opportunities, challenges and future directions about this biotechnology were described, which would help to provide new opinions into microalgae-based removal of antibiotics from wastewater, and spur researchers to carry out more investigations for obtaining practically-feasible solutions.

2 Opportunities, challenges and future directions

2.1 Opportunities of microalgae-based biotechnology used for removing antibiotics

In order to remove antibiotics from wastewater, some physicochemical methods (e.g., adsorbent adsorption, advanced oxidation, and photocatalysis) have been performed in previous studies (Mulla et al., 2023). However, the above methods have some disadvantages, which have been reviewed and listed by Leng et al. (2020) and Wang et al. (2022). Thus, novel antibiotics removal techniques need to be developed urgently according to physicochemical characteristics of wastewater.

Recently, microalgae-based biotechnology has received considerable interest in academia, and emerged as an economical, effective and green strategy for removing antibiotics from wastewater, with advantages such as effectively antibiotic and other contaminants removal, saving nutrients input, CO_2 fixation, and potential of developing algae-derived products (Leng et al., 2020). For example, a cephalosporin antibiotic (7-amino cephalosporanic acid) could be removed effectively from wastewater by three microalgae strains (i.e., *Chlorella* sp., *Chlamydomonas* sp., and *Mychonastes* sp.) (Guo et al., 2016). It is demonstrated that the prominent removal mechanism of erythromycin by *Chlorella pyrenoidosa* is biodegradation, and some intermediate products have significant effects on the removal efficiency (Li J. et al., 2022). Therefore, this biotechnology exhibits great application opportunity and prospect in the field of antibiotic removal from wastewater.

2.2 Main challenges in the removal of antibiotics using microalgae

Based on previous studies, microalgae-based biotechnology has been recognized as a promising strategy for removing antibiotics from wastewater, but there is still a long way to go for large-scale application of this biotechnology due to the following limiting factors.

(1) low removal efficiency of antibiotics by microalgae. Although this technology has various advantages relative to physicochemical techniques, its overall removal efficiency is only 62.3% (Lu et al., 2023). Influential factors on the removal efficiency are structure and characteristic of antibiotics, removal capacity of microalgae, and operational conditions (e.g.,

hydraulic retention time, temperature, and light intensity) (Leng et al., 2020; Lu et al., 2023). Thus, low removal efficiency is the first challenge, suggesting that more investigations should be carried out for enhancing the efficiency.

(2) toxicity of antibiotics and their intermediate transformation products (TPs). The algal growth is significantly inhibited by antibiotics because they could affect the synthesis of chemicals and the activities of enzymes in algal cells (Bashir and Cho, 2016). Moreover, intermediate TPs of antibiotics possess greater toxicity than themselves (Yu et al., 2022). For example, some TPs have been identified during the biodegradation of sulfamerazine, sulfamethoxazole, and sulfamonomethoxine by microalgae, and one of them (TP126) has been proved to have high acute and chronic toxicity to green algae concurrently (Kiki et al., 2020). Thus, the toxicity of antibiotics and TPs is the second challenge, which should be paid more attention in the future.

(3) undefined antibiotic removal mechanisms. Recently, several removal mechanisms (e.g., bioadsorption, bioaccumulation, and biodegradation) have been demonstrated when microalgae are used to remove antibiotics from wastewater (Leng et al., 2020; Xiong et al., 2021). However, an explicit mechanism has not been proposed in previous investigations because different mechanisms have different contributions to the removal of antibiotics even though the same microalgae strain is used (Kiki et al., 2020; Li J. et al., 2022). Thus, exact mechanisms of interaction between microalgae and antibiotics are also a challenge when microalgae are used to remove antibiotics from wastewater.

(4) effects of wastewater-born bacteria. Many pathogenic and antibiotic-resistant bacteria, such as *Enterobacteriaceae*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Acinetobacter* sp., are detected in wastewater (Li et al., 2022b). They could influence the removal efficiency of antibiotics because interactions between microalgae and bacteria cover a wide range of relationships from cooperation to competition (Xiong et al., 2021). It has been reported that both microalgae and bacteria can serve as biosorbents for the biosorption of antibiotics in wastewater (Li et al., 2022c); however, presence of these bacteria would make the algal biomass unable to become a high-quality raw material for producing food, feed, fertilizers, cosmetics, pharmaceuticals, and nutraceuticals. Thus, how to balance the relationships between microalgae and bacteria is a challenge when microalgae-based biotechnology is used for removing antibiotics from wastewater.

2.3 Opinions on the future directions

In order to overcome the above challenges, more investigations should be carried out in following opinions.

(1) isolation, selection and breeding of microalgae strains. Except for the most common techniques (e.g., chemical mutagenesis, physical mutagenesis, and adaptive laboratory evolution), molecular-based approaches (e.g., heterologous transformation, homologous recombination, and gene editing
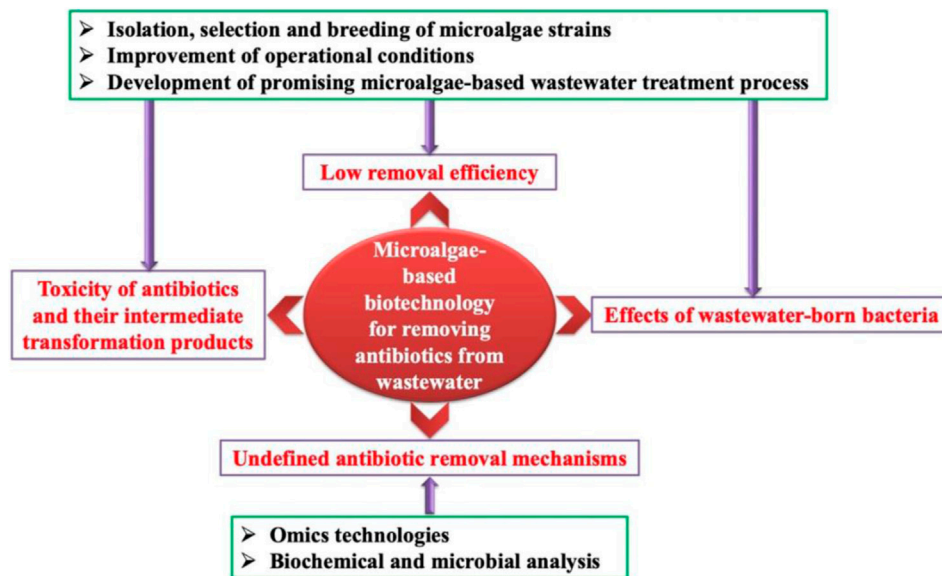
FIGURE 1
Challenges and potential solutions of using microalgae-based biotechnology to remove antibiotics from wastewater.

tools) should also be employed individually or combined with the common techniques for generating microalgae strains with high removal efficiency and stress resilience of antibiotics (Sproles et al., 2021; Jebali et al., 2022).

(2) improvement of operational conditions of the removal strategy. In order to enhance removal efficiency of antibiotics by microalgae, concentrations and classes of antibiotics should be analyzed firstly, and then environmental and operational parameters (e.g., light conditions, hydraulic retention time, temperature, and culture's pH) need to be optimized and improved (Bhatt et al., 2022; Wang et al., 2022). It will be always a research topic in the future due to unique properties of algal species and enormous kinds of antibiotics.

(3) deciphering antibiotic removal mechanisms by microalgae *via* omics technologies. Understanding the precise antibiotic removal mechanisms could help to develop some novel antibiotic removal techniques, and obtain more information about their toxicity (Kiki et al., 2020; Wang et al., 2022). Besides of biochemical and microbial analysis, omics technologies have been recognized as promising tools for deciphering antibiotic removal mechanisms, which would be the hotspots of future studies (Xiong et al., 2021).

(4) development of promising microalgae-based wastewater treatment process. To avoid the influences of wastewater-born bacteria, wastewater should be treated with ultraviolet irradiation, H_2O_2, and/or NaClO before applying the microalgae-based biotechnology to remove antibiotics from wastewater (Yu et al., 2022). In addition, novel antibiotics removal systems and promising advanced techniques will be a research topic in the future. For example, this removal strategy could be synergized with other technologies, such as advanced oxidation processes, activated sludge, and membrane filtration (Yu et al., 2022; Lu et al., 2023). Thus, promising microalgae-

based wastewater treatment process should be developed further.

3 Summary and recommendations

Nowadays, microalgae-based biotechnology has been considered as a promising strategy, and shows great potential applications in the field of antibiotic removal from wastewater. On the basis of published literatures, there are some challenges that hinder the rapid development of this biotechnology (Figure 1). Firstly, overall removal efficiency of antibiotics by microalgae is not very high, which should be enhanced further by using different techniques, such as selection of microalgae strains, optimization of operational parameters, and design of novel removal systems. Secondly, toxicity of antibiotics and the intermediate products should be paid more attention in future studies because it plays an important role during the removal of antibiotics by microalgae. Thirdly, limited information is known about antibiotic removal mechanisms by microalgae, which should be further investigated by using biochemical and microbial analysis combined with omics technologies. Finally, effects of wastewater-born bacteria should be taken seriously, and eliminated with some promising microalgae-based wastewater treatment process. Therefore, microalgae-based removal of antibiotics from wastewater has not been applied widely because of the above challenges, which should be paid more attention in the future.

Author contributions

MZ contributed to data collection and analysis, and writing-original draft preparation; RN contributed to data collection and analysis; QZ contributed to writing-original draft preparation; KG contributed to

writing-review and editing, and manuscript revision. All authors contributed to the article and approved the submitted version.

Funding

Conflict of interest

Author KG was employed by Zhenjiang Zhongnong Biotechnology Co., Ltd.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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