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Research Article

Removal of Antibiotics by Algae: Elucidating the Removal Mechanisms, Treatment Systems and Post-Treatment Antibiotic Resistance

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Abstract:
Pharmaceuticals, particularly antibiotics, have been increasingly detected in surface and groundwater in recent years. Antibiotics are a contaminant of emerging concern (CEC) due to their role in inducing antibiotic resistance in several bacterial species. This analysis examines the effective elimination of antibiotics via algae-based technologies. The primary ways for eliminating antibiotics using microalgae are bioaccumulation, biodegradation, and bioadsorption. By optimizing the process and including other treatments like UV irradiation, enhanced oxidation, and co-cultivation with bacteria/fungi, a practical antibiotic elimination strategy can be developed. This article discusses the main factors that affect algal bioremediation of antibiotics and explores innovative methods to enhance removal effectiveness, such as hybrid systems combining microalgae-based technology with classic activated sludge and AOPs. Microalgae have shown the ability to biodegrade many classes of antibiotics. The review emphasizes the necessity for more research focused on enhancing microalgae-based technology, particularly in terms of performance improvement, capacity scaling, field implementation, environmental sustainability, and economic viability. This paper addresses the advanced microalgae-based technology for antibiotic elimination and suggests prospective areas for future research.

Keywords: antibiotics, algae, biodegradation, bioadsorption, antibiotic resistant gene

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Introduction

Ubiquitous antibiotic use in various mammalian pharmaceuticals, as well as for promoting aquaculture, has increased in recent years (W. hai Xu et al., 2007). Antibiotics may possibly represent a harm to aquatic environments owing to their long-term use and bioaccumulation (Araújo et al., 2021). Antibiotics are harmful to aquatic creatures (Polianciuc et al., 2020; Rodriguez-Mozaz et al., 2020). Antibiotics in the environment have led to antibiotic resistance in bacterial populations, which may harm human health. It is not possible to remove antibiotics from wastewater using conventional treatment methods. (Ashfaq et al., 2017; W. Sun et al., 2016; L. Wang et al., 2018).

Current activated sludge technologies in wastewater treatment facilities don't degrade or remove antibiotics efficiently (Kim & Aga, 2007; Park et al., 2020). Physical and chemical treatment techniques have large energy consumption, high operational costs, and secondary contamination (Jiao et al., 2008). According to the findings of several studies, the products of the Fenton oxidation reaction or ultraviolet light are often more hazardous than the precursor (Du, Zhang, et al., 2015; Elmolla & Chaudhuri, 2011; Y. Liu et al., 2017a; Yuan et al., 2011). Activated sludge methods have become increasingly popular among biological treatments (Gulkowska et al., 2008). Antibiotics can cut down on biological activity directly, which means that they may slow down the biodegradation of contaminants. Because of this, activated sludge technologies used in modern wastewater treatment facilities (WWTPs) are not intended to remove antibiotics. Antibiotic residues and other chemicals found in wastewater treatment plants (WWTPs) also have the potential to create antibiotic-resistant bacteria (ARB) and genes (ARG) (Galvin et al., 2010; Łuczkiewicz et al., 2010).

Microalgae are unicellular and common in most aquatic environments (Coogan et al., 2007). Microalgae may remove organic contaminants and heavy metals effectively (R. Guo & Chen, 2015; Usha et al., 2016; X. S. Wang et al., 2009). *Chlorella vulgaris* may remove Antibiotics like tetracycline and norfloxacin (de Godos et al., 2012a; J. Zhang et al., 2012) whereas *M. aeruginosa* can remove 30% of spiramycin (R. Liu et al., 2021). Algae cells that are left can be used to produce biofuels, fix carbon, and manufacture various biochemical products, therefore preventing further pollution (R. Guo & Chen, 2015; Nozzi et al., 2013; Rosgaard et al., 2012). Studies have shown that microalgae may eliminate third generation cephalosporins and amino penicillins (Du, Feng, et al., 2015; Du, Zhang, et al., 2015; R. Guo & Chen, 2015; H. Li et al., 2015a; Y. Liu et al., 2017a). In addition, the algal treatment did not increase the antibiotic's toxicity (Du et al., 2018; Yu et al., 2017).

This review focuses on microalgae-based antibiotics removal efficiency, processes, hybrid systems, and the influence on antibiotic resistance genes.

Mechanism of removal of antibiotics by microalgae-based treatment system

Microalgae remove antibiotics primarily by biosorption, (triggering bioaccumulation) followed by biodegradation mechanisms (Hena et al., 2021; Leng et al., 2020; J. Q. Xiong et al., 2018a). When there are microalgae present, several antibiotics are eliminated through photo-oxidation, which is followed by volatilization (Sutherland & Ralph, 2019a). Photodegradation and volatilization are uncommon and frequently considered insignificant (H. T. Nguyen et al., 2021). This review also investigates the mechanisms of the processes bioadsorption, bioaccumulation, and biodegradation (Fig. 1). The elimination steps are: 1) Rapid and passive adsorption through physicochemical interactions between contaminants and the cell surface. 2) Slow diffusion of chemicals through the cell membrane, 3) Cell membrane accumulation of substances through bioaccumulation and/or biotransformation (Yu et al., 2017).

Bioadsorption and bioaccumulation of antibiotics by microalgae

Bioadsorption occurs when antibiotics attach to microalgae cell walls or extracellular polymeric substances (EPS) (Sutherland & Ralph, 2019b; J. Q. Xiong et al., 2018a). EPS are biopolymers produced by bacteria with up to 90% organic content, including polysaccharides, enzymes, proteins, lipids, and other substituents. Microalgal biomass adsorbs antibiotics through hydrogen bonding, electrostatic interaction, distribution/partitioning, and hydrophobic effect (Tan et al., 2015). The elimination of 7-ACA by three microalgae, *Chlorella* sp. Cha-01, *Chlamydomonas* sp. Tai-03, and *Mychonastes* sp. YL-02, involved adsorption as one of the primary processes (W. Q. Guo et al., 2016). After 24 hours of incubation, the residual concentrations of 7-ACA were 23.8 mg L^{-1}, 35.1 mg L^{-1}, and 30.7 mg L^{-1}, about 30% lower than the abiotic control (initial concentration = 100 mg L^{-1}). In the first 10 minutes, the adsorption was relatively quick, 4.74 mg g^{-1}, 3.09 mg g^{-1}, and 2.95 mg g^{-1} for the dried *Chlorella* sp. Cha-01, *Chlamydomonas* sp. Tai-03, and *Mychonastes* sp. YL-02 biomass, respectively (W. Q. Guo et al., 2016). According to researchers, the kinetics of biosorption of 7-ACA fitted the Langmuir adsorption isotherm better than the Freundlich isotherm. The Langmuir model suggests monolayer adsorption happens at uniform locations on the adsorbent's surface, but this is not entirely accurate (Balarak & Chandrika, 2019; W. C. Li & Wong, 2015; Wu et al., 2015; Xie et al., 2020a).

Adsorption is also a major TC removal mechanism in High Rate Algal Ponds (de Godos et al., 2012b; Norvill et al., 2017). Lipid-depleted *Chlorella sp.* biomass has the potential to be a bioadsorbent for Cephalexin (Angulo et al., 2018). Equilibrium needed 2 hours of interaction time. Findings fit the Freundlich model (q_{max} = 63.29 mg/g of bioadsorbent) (Angulo et al., 2018). *Scenedesmus quadricauda* and *Tetraselmis suecica* can remove 295 mg g^{-1} and 56.25 mg g^{-1} of tetracycline from water, respectively (Daneshvar et al., 2018). These results showed that the surface chemistry and effective surface area, greatly influenced their bioadsorption capacities. (Norvill et al., 2016). Presence of functional groups such as hydroxyl, carboxyl, and phosphoryl, impart negative charge on the EPA and microalgal cell walls. (Sheng et al., 2010; J. Q. Xiong et al., 2019).

Microalgae's ability to adsorb substances depends greatly on the species' structure and the surrounding environment (Norvill et al., 2016). Hydrophilic compounds are more durable in growth medium and have low affinity for bioadsorption (Sutherland and Ralph, 2019; Xiong et al., 2019). Log K_{ow} may be used to measure the lipophilicity or hydrophobicity of a material, with a larger log K_{ow} value suggesting increased adsorption of antibiotics on the microorganism surface/solid phase (Avdeef, 1996). Higher log K_{ow} values (>5) also suggest that these antibiotics are more readily absorbed than low log K_{ow} values (<2.5) antibiotics (Tiwari et al., 2017). The antibiotic removal efficiency of *Chlorella vulgaris* and *Chlorella ovalisporum* followed this pattern: enrofloxacin (ENR) > sulfamethazine (SM2) > sulfadiazine (SD) > norfloxacin (NOR). For *C. vulgaris* and *C. ovalisporum*, the efficacy of ENR removal was the highest, around 53%-73% and 58%-79%, respectively (S. Chen et al., 2020).

Factors affecting bioadsorption

Process parameters influencing the bioadsorption process are bioadsorbent loading, initial concentration of adsorbate, time span of adsorption, pH, temperature, and excretions of extracellular polymeric substances (Sutherland and Ralph, 2019). Cephalexin removal underwent a reduction when initial antibiotic concentration was increased to 482.92 mg L^{-1} from 49.17 mg L^{-1} for both live *Chlorella* sp. (82.8% to 45.6%) and lipid extracted *Chlorella* sp. (71.2% to 24.7%) (Angulo et al., 2018). Chlorella vulgaris's efficacy in removing metronidazole decreased as the initial concentration of antibiotics rose (Hena et al., 2020). Daneshvar et al. (2018) studied the influence of initial substrate concentration (tertracycline) on the bioadsorption of both *Scenedesmus quadricauda* and *Tetraselmis suecica* biomass (Daneshvar et al., 2018). Linear increase in bioadsorption efficacy was observed when the initial TC concentration was increased from 2.5 mg L^{-1} to 80 mg L^{-1} for both algal biomasses, but decreased for *T. suecica* biomass as initial TC concentration increased from 80 mg L^{-1} to 300 mg L^{-1}. The elimination efficiency of TC increases as the initial concentration rises (till 80 mg L^{-1}) which may be connected to the concentration gradient's driving force (Crini & Badot, 2008).

In addition, pH of the medium regulates antibiotic bioadsorption onto the biomass (Daneshvar et al., 2018). pH affects antibiotics' aggregation, hydrophobicity, electrostatic attraction, and repulsion (Zambrano et al., 2021). As log K_{ow} increases, lipophilicity also increases. pK_a influences the lipophilicity and protein-binding capacity of a substance, and in turn, increasing lipophilicity reduces pK_a (Besha et al., 2020; S. Chen et al., 2020; Manallack, 2007). Temperature fluctuations impact the speed at which antibiotics are absorbed by microalgal cells in bioadsorption (Zeraatkar et al., 2016,.Sheng et al., 2010).

Unlike bioadsorption, bioaccumulation is an intracellular, active, energy-intensive process (Bai & Acharya, 2017; Davis et al., 2003). Algal cell membranes may absorb some drugs. Sonication and dichloromethane/methanol extraction may remove intracellular antibiotics (Kiki et al., 2020; J. Q. Xiong et al., 2016). Algae allegedly eliminates drugs including trimethoprim, sulfamethoxazole, and doxycycline (Bai & Acharya, 2017; Prata et al., 2018). Reactive oxygen species (ROS), crucial for controlling cellular metabolism, can lead to significant cell damage or death when present in excess, and may be triggered by specific antibiotics (J. Q. Xiong et al., 2018a). Sulfamethazine antibiotic bioaccumulated in *C. pyrenoidosa* and was subsequently removed. (M. Sun et al., 2017). *C. vulgaris* also eliminated levofloxacin by accumulation, followed by a further process of intracellular biodegradation (J. Q. Xiong, Kurade, & Jeon, 2017a).

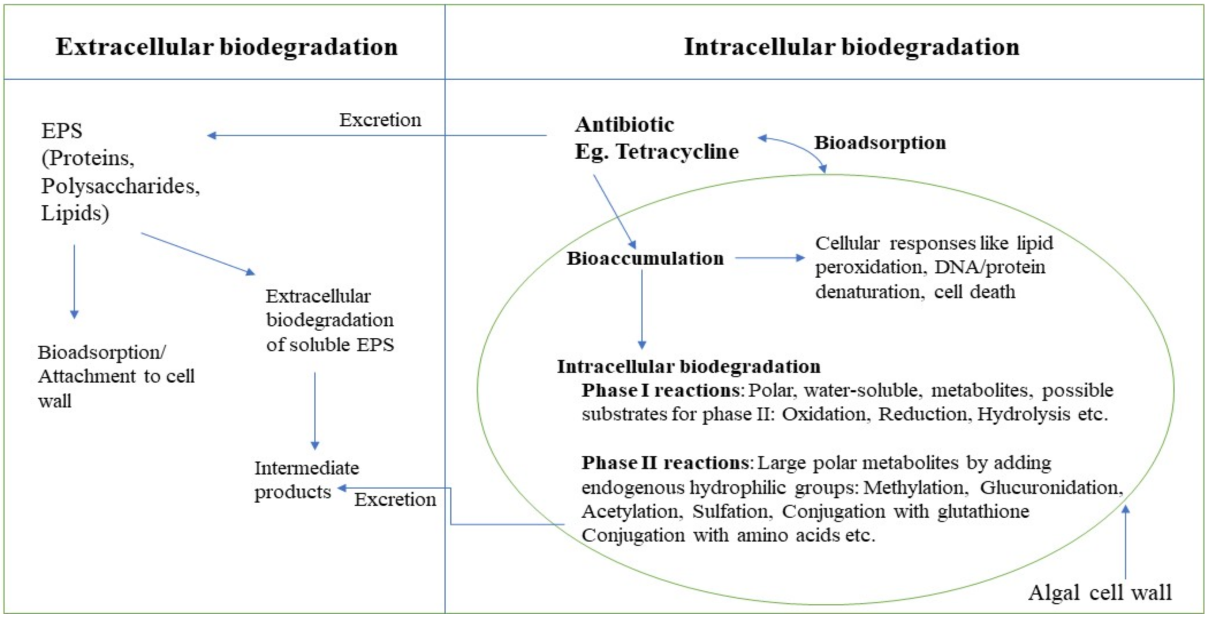

Fig. 1: Removal mechanism of antibiotics by algae

Biodegradation of antibiotics by microalgae

Biotransformation was identified as the primary step in the elimination of florfenicol by *Chlorella* sp. L38, as opposed to bioaccumulation and bioadsorption, (Song et al., 2019). As initial amoxicillin concentrations varied from 10 mg L^{-1}, 50 mg L^{-1}, and 150 mg L^{-1}, Amoxicillin (AMX) removal efficiencies of greater than 99.9%, 99.9±0.006% and 99.4±0.01% respectively were observed (Shi et al., 2018). *Chlorella* sp showed considerable AMX removal activity during the first 2 hours for all three doses of AMX, resulting in maximal degradation. Moreover, Xie et al. (2020) revealed that *Chlamydomonas sp*. was 100% effective in removing ciprofloxacin (Xie et al., 2020a). Biodegradation contributed 65.05% of the elimination of Tai-03. Similar observation was reported by X. Li et al., 2020 (X. Li et al., 2020). Between 18.81% and 27.16% of the initial substrate (ROX) was removed through photolysis after 21 days of exposure. In contrast, biodegradation destroyed 45.99% to 53.30% of ROX at concentrations ranging from 0.1 mg L^{-1} to 1.0 mg L^{-1}. Kiki et al. (2020) studied the capacity of *Haematococcus pluvialis, Selenastrum capricornutum, Scenedesmus quadricauda, and Chlorella vulgaris*, and concluded that between 23% and 99% of the removal efficacy of ten antibiotics came from biodegradation (Kiki et al., 2020).

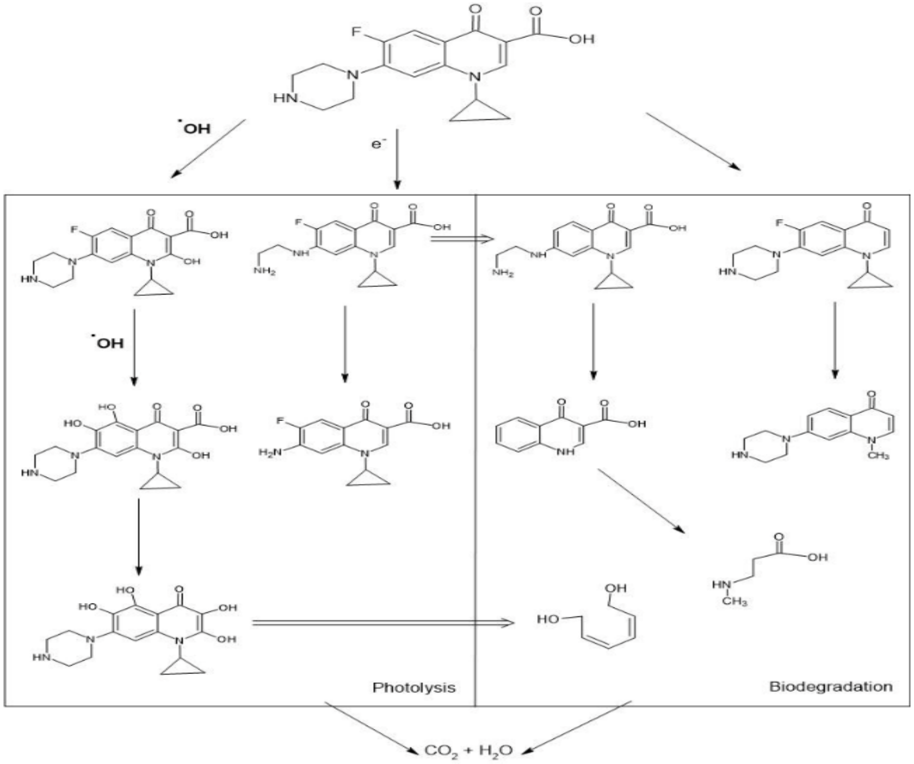

Fig. 2a. Pathway of degradation of Ciprofloxacin (Xie et al., 2020b)

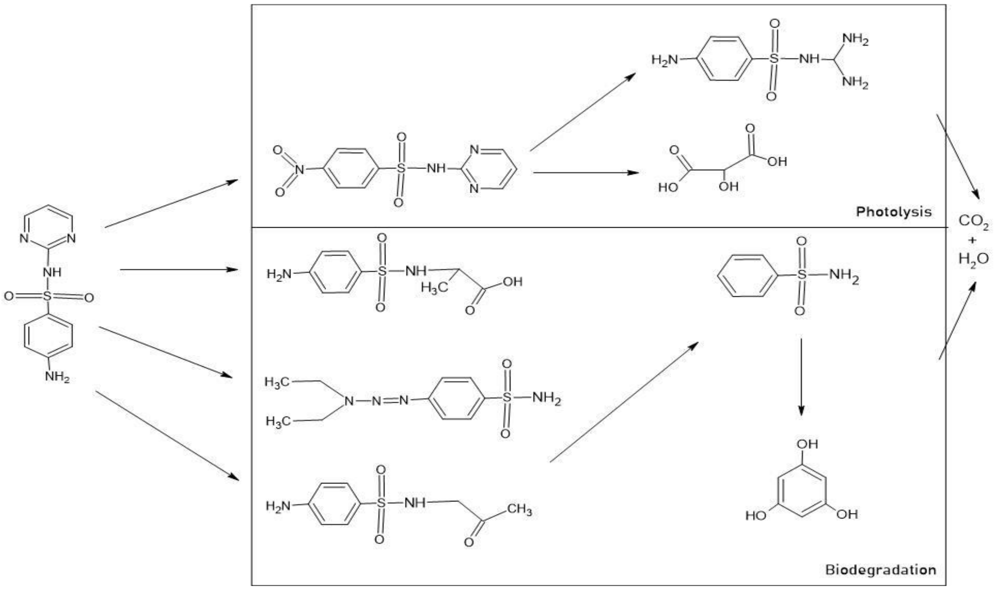

Fig. 2b. Pathway of degradation of Sulfadiazine (Xie et al., 2020b)

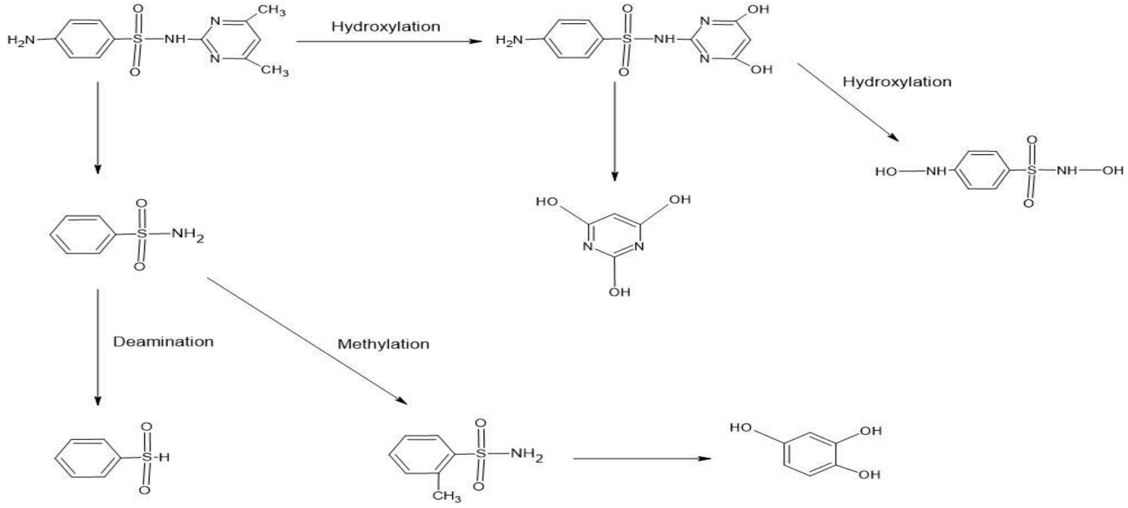

Fig. 2c. Pathway of degradation of Sulfamethazine (J. Q. Xiong et al., 2018b)

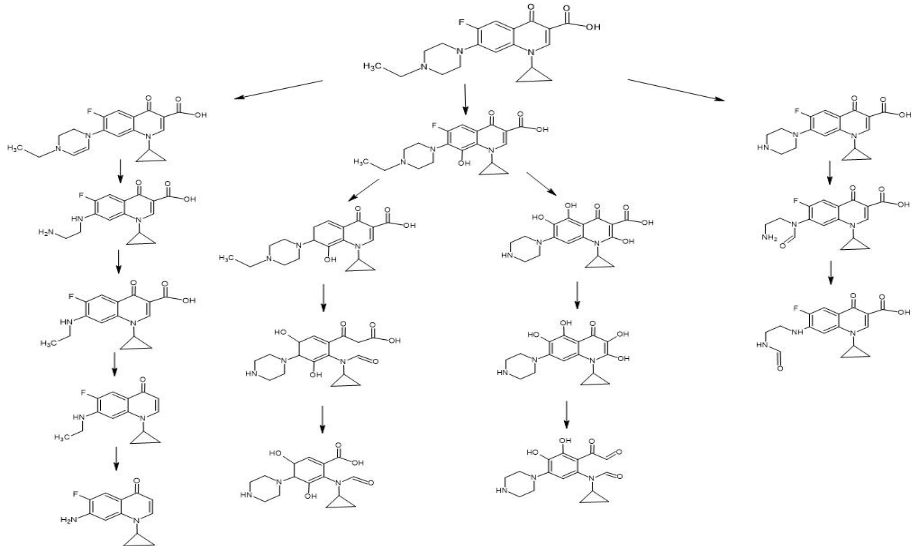

Fig. 2d. Pathway of degradation of Enrofloxacin (R. Liu et al., 2021)

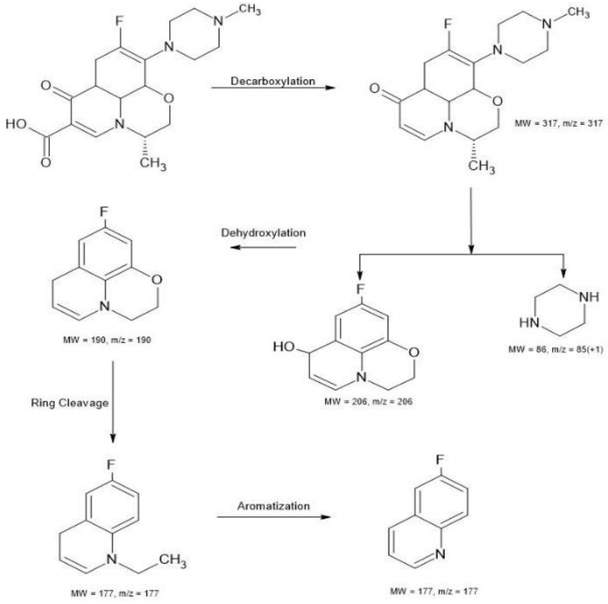

Fig. 2e. Pathway of degradation of Levofloxacin(J. Q. Xiong, Kurade, & Jeon, 2017b)

Biodegradation is defines as the breakdown of organic compounds through biotransformation, yielding metabolic intermediates,(Achermann et al., 2018; J. Q. Xiong et al., 2019; Q. Xiong et al., 2020), or using either pure or mixed microbial cultures for full conversion into CO_2 and H_2O (Alvarino et al., 2016; Helene et al., 2012). There are two biodegradation pathways: (1) where the antibiotic is the only source of carbon or a redox reactant for microalgae during biotransformation; and (2) Co-metabolism involves metabolism of more than one substrates simultaneously, where several substrates initiate synthesis of algal biomass because they are serving as the electron donor (Leng et al., 2020; Tiwari et al., 2017; Tran et al., 2016). Microalgae often engage in antibiotic biodegradation through both extracellular and intracellular biotransformation, or through both the processes (Tiwari et al., 2017; J. Q. Xiong et al., 2018a). EPS may operate as a surfactant, emulsifier, or external digestion system to improve antibiotic bioavailability (Xiao & Zheng, 2016).

Microalgae can degrade antibiotics by a two-phase enzymatic catalysis method (Leng et al., 2020; Y. Wang et al., 2017). First, oxidation, reduction, or hydrolysis introduce reactive functional groups (phase I). Microsomal monooxygenases, such as cytochrome P-450, catalyze these processes (Torres et al., 2008). Phase I activities include hydroxylation, dihydroxylation, methylation, demethylation, carboxylation, decarboxylation, oxidation, and ring breakage (Stravs et al., 2017; S. Wang et al., 2018; Xie et al., 2020a; J. Q. Xiong et al., 2017, 2019; Q. Xiong et al., 2020). Phase I metabolites enhance the polarity, which in turn increases the hydrophilic nature of the converted products, which increases the possibility of excretion as aqueous solution (Torres et al., 2008). Phase II processes involve combining xenobiotics (or phase I metabolites) with bulky, polar compounds like sugars and amino acids (Dudley et al., 2018; Pflugmacher et al., 1999; Torres et al., 2008).

Table 1 :

Antibiotic Group	**Antibiotic Name**	**Algal Species**	**%Removal of antibiotic, Initial concentration and incubation time**	**Mechanisms**	**Reference**
Beta lactum	Amoxicillin	*Microcystis aeruginosa*	30.5-33.6%, 50 ng L^{-1} - 500 ng L^{-1}, 7d	Biodegradation	(Y. Liu et al., 2012)
		Microcystis aeruginosa	18.5-30.5%, 200-500 ng L^{-1}, 7d	Biodegradation	(Y. Liu et al., 2015)
	Cefalexin	*Chlorella sp.* (lipid extracted dry biomass)	71.2 ± 38.9%, 49.17 ± 0.20 mg L^{-1}, 20d	Biosorption	(Angulo et al., 2018)
	7-amino cephalosporanic acid	*Chlorella pyrenoidosa*	96.07%, 40 mg L^{-1}, 6h	Bioadsorption and biodegradation	(Yu et al., 2017)
		Chlorella sp. Cha-01	4.74 mg g^{-1} of biomass	Bioadsorption	(R. Guo & Chen, 2015)
		Chlamydomonas sp. Tai-03	3.09 mg g^{-1} of biomass	Bioadsorption	
		Mychonastes sp. YL-02	2.95 mg g^{-1} of biomass	Bioadsorption	
Tetracyclines	Tetracycline	*Chlamydomonas sp.* Tai-03	10 mg L^{-1}, 100%, 8d	Biodegradation, photolysis and hydrolysis	(Xie et al., 2020a)
		Scenedesmus quadricauda (lipid extracted dry biomass)	48.84 ± 1.4%, 400 mg L^{-1}, pH 8	Biosorption	(Daneshvar et al., 2018)
		Tetraselmis suecica (lipid extracted dry biomass)	36.71 ± 2.1%, 400 mg L^{-1}, pH 8, 12d	Biosorption	(Daneshvar et al., 2018)
		Spirogyra sp.	89±2%, 200 µg L^{-1}, 20d	Photodegradation	(Garcia-Rodríguez et al., 2013)

	Oxytetracycline	*Spirogyra sp.*	93±2%, 200 µg L^{-1}, 20d	photodegradation, biodegradation and hydrolysis	(Garcia-Rodríguez et al., 2013)
Sulphonamides	sulfadiazine	*Chlorella vulgaris*	11-24%, 1- 50 mg L^{-1}, 16d	Not discussed	(S. Chen et al., 2020)
		Chlorella ovalisporum	10-20%, 1- 50 mg L^{-1}, 16d	Not discussed	(S. Chen et al., 2020)
		Chlamydomonas sp. Tai-03	35.6% , 80 mg L^{-1}, 9d	Photolysis and biodegradation	(Xie et al., 2020a)
	sulfamethazine	*Scenedesmus obliquus*	0.025-0.25 mg L^{-1}, 31.4- 62.3%, 12 d	Not discussed	(J. Q. Xiong et al., 2019)
	sulfamethoxazole	*Chlamydomonas sp.* Tai-03	20%, 1 mg L^{-1}, 8d	Biodegradation	(Xie et al., 2019)
		Scenedesmus obliquus	27.7- 46.8%, 0.025-0.25 mg L^{-1}, 12 d	Not discussed	(J. Q. Xiong et al., 2019)
		Nannochloris sp.	32%, 10 µg L^{-1}, 14d	Algae-mediated photolysis	(Bai & Acharya, 2016)
		Nannochloris sp.	11%, 360 ng L^{-1}, 14d	Algae-mediated photolysis	(Bai & Acharya, 2017)
		Chlorella pyrenoidosa	48.5-69.9%, 2-8 mg L^{-1}, 13d	Accumulation and biodegradation	(P. Sun et al., 2018)
Macrolides	Erythromycin	*Scenedesmus obliquus*	94.18%, 80.59%, and 49.60% for 1, 10, 100 µg L^{-1} respectively, 5 d	Biodegradation, hydrolysis, and photolysis	(X. Wang et al., 2021)
	Roxithromycin	*Chlorella pyrenoidosa*	80.45%, 76.35% and 64.81%, 0.1, 0.25 and 1.0 mg L^{-1} respectively, 21d	Photodegradation and biodegradation	(J. Li et al., 2020)
Quinolones	Ciprofloxacin	*Scenedesmus dimorphus*	93%, 25 µg L^{-1}, 144 h	Bioadsorption and biotransformation	(Grimes et al., 2019)
		Chlamydomonas mexicana	13%, 2 mg L^{-1}, 11d	Biodegradation, bioaccumulation and bioadsorption	(J. Q. Xiong et al., 2017)
		Chlamydomonas sp. Tai-03	65.05%, 10 mg L^{-1}, 9d	Biodegradation	(Xie et al., 2019)
	Enrofloxacin	*Scenedesmus obliquus*	23%, 1 mg L^{-1}, 11d	Biodegradation, bioaccumulation and bioadsorption	(J. Q. Xiong, Kurade, & Jeon, 2017a)
		Chlamydomonas mexicana	25%, 1 mg L^{-1}, 11d		
		Cholera vulgaris	26%, 1 mg L^{-1}, 11 d		
		Ourococcus multisporus	18%, 1 mg L^{-1}, 11d		

		Micractinium resseri	20%, 1 mg L^{-1}, 11d		
		Chlorella vulgaris	53-73%, 1-50 mg L^{-1}, 16 d	Bioadsorption and biodegrdaation	(S. Chen et al., 2020)
		Chlorella ovalisporum	58-79%, 1-50 mg L^{-1}, 16 d	Bioadsorption and biodegrdaation	
	Norfloaxacin	*Chlorella vulgaris*	36.9%, 30 min	Algae-mediated photodegradation	(J. Zhang et al., 2012)

Algae-based treatment system for removal of antibiotics from wastewater

Conventional treatment systems using microalgae: open and closed systems with suspended or immobilized cultures

For the large-scale development of microalgae, open systems such as circular ponds, tanks, and high-rate algal ponds (HRAPs) are commonly used. Prior studies have shown that HRAPs are just as efficient at getting rid of antibiotics as activated sludge (H. T. Nguyen et al., 2021; Villar-Navarro et al., 2018). The elimination of ciprofloxacin and tetracycline from HRAP was successfully accomplished by algal cells (de Godos et al., 2012b; Hom-Diaz et al., 2017). An efficient use of time and energy is immobilized microalgae culture as an alternative to suspended culture (He & Xue, 2010; Pires et al., 2013).

Algae based composite treatment systems for removal of antibiotics

Microalgae have stronger tolerance to contaminants, including antibiotics, than bacteria. Antibiotics are toxic to microalgae, inhibiting their growth (Carusso et al., 2018; R. X. Guo & Chen, 2012; Halling-Sørensen, 2000; Kolar et al., 2014).

Combination of microalgae with activated sludge system

Microalgae and bacteria collaborate to remove nutrients, heavy metals, and other micropollutants (Gonçalves et al., 2017; Perera et al., 2019; Quijano et al., 2017; B. Zhang et al., 2020). Guo and Chen (2015) eliminated cephalosporins with a combined method of both activated sludge and microalgae (R. Guo & Chen, 2015). Ji et al. (2020) developed an experiment using a novel microalgae/bacteria granular sludge system to remediate urban sewage. Analysing the parameters like stoichiometry, microbial diversity, and functional genes has demonstrated the effectiveness of these systems (Ji et al., 2020). Bioaccumulation, covalent bonding, physisorption, and biodegradation are the processes behind removal of micropollutants (B. Zhang et al., 2020). The efficiency of eliminating micropollutants in the hybrid microalgae-activated sludge system depends on different factors, including the inoculum ratio of the activated sludge (T. T. D. Nguyen et al., 2020), cultivation practices, the concentration and physicochemical characteristics of contaminants, and the inoculum dose of microalgae (B. Zhang et al., 2020).

Combination of microalgae with advanced oxidation system

Advanced Oxidation Processes (AOPs) include photocatalysis, ultrasonication, ozonation, and Fenton/photo-Fenton/sono-Fenton reactions (Y. di Chen et al., 2021). AOP systems are expensive and energy-intensive, especially when mineralizing organic pollutants (S. Li et al., 2021). AOP technologies create hydroxyl radicals, which attack target compounds (Anjali & Shanthakumar, 2019). Recently, AOPs have been used to enhance the biodegradability (algal) of antibiotic effluent, especially when the resultant intermediates are readily eliminated by later biological treatments (Almaguer et al., 2021). Although the overall effectiveness of removing the target antibiotic increased, reducing the loading of oxidant i.e. Fenton's reagent (H_2O_2 and Fe(II)) did not impact the contribution of the Fenton treatment (H. Li et al., 2015). UV radiation can be simultaneously employed with biological degradation processes (Y. Liu et al., 2017b). Researchers found a potential increase in the breakdown of contaminants in a UV-irradiated media due to algae, suggesting that rapid degradation could be caused by the production of hydroxyl radicals by the algae (Peng et al., 2006). Algae breakdown was suggested to play a vital function in decreasing the effluent's overall toxicity (Du et al., 2015). With *S. obliquus* and UV-irradiation at 365 nm, Yang et al. successfully achieved a 99.84% removal efficacy (Yang et al., 2017). UV radiation at 185 nm removed antibiotic substrate by 97.26%, at wavelengths over 280 nm the removal effectiveness was up to 97.15%, and at wavelengths exceeding 365 nm, the removal efficiency was just 8.52% (Y. Liu et al., 2017a). Despite the common use of UV irradiation in biological wastewater treatment, limited research has been done on the ability of algae and UV radiation to break down antibiotics (Tamer et al., 2006).

Photodegradation of antibiotics caused by algae

Photodegradation is a crucial mechanism for decomposing residual antibiotics in natural water settings, particularly in surface layers (Dabić et al., 2019; Doll & Frimmel, 2003). Several antibiotics are extremely light-sensitive (Baena-Nogueras et al., 2017; Bonvin et al., 2013; Tian, Zou, et al., 2019). Antibiotics can rapidly break down or fragment upon exposure to light; this is referred to as direct photodegradation (Tian, Zou, et al., 2019; Wammer et al., 2013; Zepp & Cline, 1977). Chemical species mediated photodegradation depends on the particular reactive oxidizing species (e.g., hydroxyl radicals (·OH), singlet oxygen ($^1O_2$), superoxide ($O_2^{-}\cdot$), hydrogen peroxide (H_2O_2), peroxyl radicals (·OOR)) which are produced when added photosensitizers are irradiated with UV light (S. Li & Hu, 2016; Tian, Zou, et al., 2019). Indirect photolysis has a significantly higher reaction rate compared to direct photolysis, making it a crucial factor in the organic micropollutants degradation (Tian, Zou, et al., 2019; H. Xu et al., 2011). Algae in naturally occurring bodies of water are good photosensitizers and may produce reactive oxygen species when irradiated (Zepp & Schlotzhauer, 1983). Tian et al. (2018) discovered that *Chlorella vulgaris* when irradiated resulted in an over 96% chlortetracycline clearance rate, which is likely due to algae-induced photodegradation, as no further chemicals were used (Tian, Zou, et al., 2019). To complement these, Tian et al. (2019) reported that the algae *C. vulgaris*, *Microcystis aeruginosa*, and *Scenedesmus sp*. increase the rate of photodegradation of chlortetracycline, whereas Zhang et al. (2012) reported that the rate of degradation of norfloxacin in a suspension of *C. vulgaris* under UV irradiation is thrice than in the absence of algae (Tian, Wei, et al., 2019; J. Zhang et al., 2012). Guo and Chen (2015) have achieved exceptional results in the elimination of residual antibiotics and sludge inactivation using the alga-activated sludge combination method. (R. Guo & Chen, 2015). Microalgae treatment of pharmaceuticals outperformed activated sludge (>70%). Wastewater treatment with algae is feasible. (Villar-Navarro et al., 2018).

Extracellular organic matter containing proteins, polysaccharides, and humic-like compounds is the main contributor to photodegradation by producing active species upon exposure to light (L. Li et al., 2012; Tenorio et al., 2017; Tian, Wei, et al., 2019; Tian, Zou, et al., 2019). Algal EOMs produce ROS to photodegrade antibiotics. Several investigators have studied the photodegradation of two fluoroquinolone medications by *Platymonas subcordiformis* and *Isochrysis galbana*, specifically ciprofloxacin hydrochloride and enrofloxacin (Ge & Deng, 2015). Both algae contributed to the photodegradation of the two medicines. *P. subcordiformis*, however, increased the average rate of photolysis to 76.1%, but in case of *I. galbana*, it was only 68.7%. Tian et al. (2019) examined the efficacy of three distinct algal species' indirect photolysis on CTC: *M. aeruginosa*, *Scenedesmus meyen*, and *C. vulgaris*. All retrieved photosensitizers encouraged the decomposition of CTC to differing degrees, the highest being for *C. vulgaris* (Tian, Wei, et al., 2019). Under UV light, *Chlamydomonas reinhardtii* had a removal rate of 100% for cefradine (CED), whereas *Chlorella pyrenoidosa* had a rate of 77.99% (Du, Feng, et al., 2015; Jiang et al., 2019).

Antibiotic resistance genes after algae-based treatment for antibiotic removal

The gathered biomass should be thermochemically treated to eliminate any antibiotics (Leng & Huang, 2018; Zhuang et al., 2019). A microalgae-bacteria consortium successfully removed sulfamethoxazole (~54%), according to Rodrigues et al (da Silva Rodrigues et al., 2020).

This collaboration effectively removed (>90%) the antibiotics cephalexin and erythromycin. These findings demonstrate that even low concentrations of antibiotics in water, results in the spread of ARBs and ARGs. Cheng et al. (2020) showed that the use of *Galdieria sulphuraria* in an algae-based wastewater treatment system reduced the amount of ARBs and the relative abundance of ARGs (qnrA, qnrS, and tetW) in bacterial strains that survived the process (Cheng et al., 2020).

Conclusion:

This review focuses on the use of algae-based technologies for efficient antibiotic elimination. Bioaccumulation, biodegradation, and bioadsorption have been identified as the primary microalgal antibiotic elimination strategies (Hena et al., 2021; Leng et al., 2020; J. Q. Xiong et al., 2018a). This study investigated the involvement of bacteriophages in the transmission of antibiotic resistance genes (ARGs) by identifying ARGs in phages and comparing them to the quantity of ARGs in bacteria that survived. Four out of the five genes identified in the bacteriophage algal system exhibited a notable drop, indicating that the transmission of antibiotic resistance genes by phages in algal therapy is infrequent. This study identified numerous advantages of the algal wastewater treatment system over secondary wastewater treatment for managing ARG and ARB.

Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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