

RECENT ADVANCES IN AZITHROMYCIN REMOVAL THROUGH THE BIOCHAR

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Review



ABSTRACT

Azithromycin contamination is one of the environmental concerns worldwide and it has been included in the EU's watch list for emerging contaminants in the aquatic environment. It is imperative to decrease azithromycin's environmental footprint from the environment in sustainable ways. Azithromycin remediation can be carried out either by adsorption through biochar or microbial degradation. Biochar-based adsorbents are produced using various feedstocks, including waste products. The use of biochar for contaminants removal is an economic and environmentally sustainable approach. Biochar adsorption mechanism involves surface complexation, weak van der Waals' forces, π - π bonding, electrostatic interactions, and H-bonding. Physico-chemical properties of biochar affect the adsorption and removal of azithromycin. Several chemical, thermal, electrochemical, and microwave-aided regeneration methods being used for recycling biochar those are essential for the cost-effectiveness of the process. This also fits with worldwide tendencies toward sustainable development and a circular economy. The latest research on the elimination of azithromycin by using biochars has been discussed in this review.

Keywords: Azithromycin, Adsorption, Engineered biochar, Emerging contaminant, Remediation

INTRODUCTION

Azithromycin is one of the most regularly prescribed medications for bacterial infections. The use of macrolides such as azithromycin is increasing (Hao *et al.*, 2020). Azithromycin contaminant is distributed worldwide. It is reported that the main sources of azithromycin pollutants are hospital wastewater, fish farms, human and animal feces, urine, and pharmaceutical industry. It is now easier to evaluate the risk of contaminants in water that are not yet regulated, with azithromycin included in the EU's watch list for emerging problems in the aquatic environment (Robert *et al.*, 2018). Velpandian *et al.* (2018) found that the level of azithromycin in surface water of NCR was $70 \pm 170 \text{ ng L}^{-1}$. The azithromycin concentration in cow milk samples has been found to be $9708.7 \mu\text{g kg}^{-1}$ (Kurjogi *et al.*, 2019). Azithromycin was found in municipal wastewater in the city of Zagreb, with concentrations ranging from 0.27 to $22.7 \mu\text{g L}^{-1}$ (Senta *et al.*, 2019).

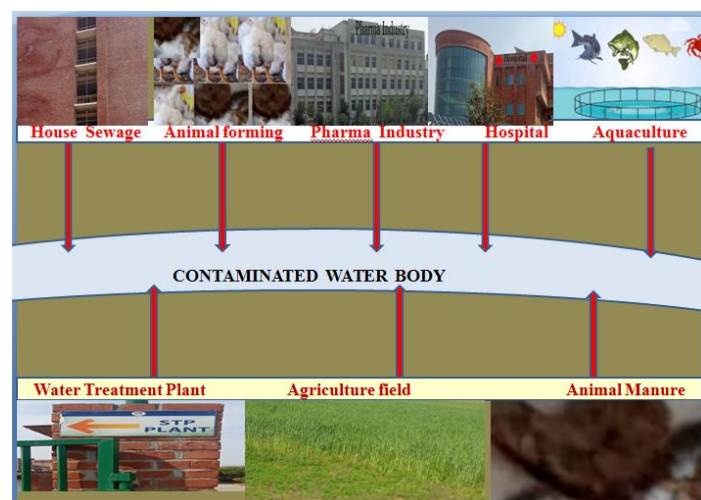


Figure 1 Sources of azithromycin contamination

Azithromycin has even been found across various water bodies, it include wastewater (Grela *et al.*, 2023), drinking water (Ślósarczyk *et al.*, 2021), surface water (Guardo *et al.*, 2024; Ilie *et al.*, 2023), cave water (Oppeltová *et al.*, 2024), groundwater (Arun *et al.*, 2022), seawater (Mirzaie *et al.*, 2022), sediments (Mirzaie *et al.*, 2022) and even soil and milk (Kurjogi *et al.*, 2019). Azithromycin

levels in water and wastewater exceed recommended limits. The availability of azithromycin in the environment has been reported to be 0 – 500 ng L^{-1} (Cruz *et al.*, 2021; Mariano *et al.*, 2023), but in some cases up to 10000 ng L^{-1} (Wu *et al.*, 2021). Azithromycin contaminates water bodies that have adverse effects on aquatic organisms. Fish and other aquatic life may experience toxicity, reproductive problems, and behavioral changes (Li *et al.*, 2020). It can disrupt the balance of microbial communities in water ecosystems, affecting overall ecological health (Huang *et al.*, 2021b; Pinto *et al.*, 2022). Pollution of environmental systems with antibiotics such as azithromycin leads to enrichment of antibiotic resistance genes (ARGs) in bacterial populations (Konopka *et al.*, 2022). The enrichment of ARGs in bacteria is caused by selective pressure of antibiotics on bacterial population. It favors the survival and spreading of antibiotic resistant bacterial strains (Green, 2022). Ammonia-oxidizing bacteria (AOB) are essential for the nitrogen cycle, converting ammonia to nitrite. Exposure to antibiotics affects the abundance and activity of AOB (Beduk, 2023; Liu *et al.*, 2019; Zhou *et al.*, 2024). The enrichment of resistant genes disrupts their ecological function and imbalances nitrogen cycling processes (Beduk, 2023). This has widespread impacts on the ecosystem, affecting plant growth, water quality, and overall ecosystem health (Sidhu *et al.*, 2019). These resistance genes can be transferred horizontally between bacterial species, leading to the spread of antibiotic resistance among microbial communities (Tao *et al.*, 2022). Azithromycin has also been found to accumulate in some plant species. The extent of bioaccumulation azithromycin is depending on factors such as soil composition, plant species, and exposure duration (Carballo, *et al.*, 2021; Sidhu, *et al.*, 2019; Zhang, *et al.*, 2023). The accumulation of azithromycin was reported in both roots and shoots of lettuce (*Lactuca sativa*) (Almeida *et al.*, 2021). Several other studies have reported bioaccumulation of azithromycin in various plant species, including grasses. Bioaccumulation in plants does not directly harm them, it mainly concerns about the potential transfer of azithromycin through the food chain (Sidhu *et al.*, 2019). Azithromycin is an antibiotic that targets bacteria, so it is not inherently toxic to plants. However, like many pharmaceuticals, it has unintended effects on non-target organisms (Almeida *et al.*, 2021; Mao *et al.*, 2021). The exposure of azithromycin to plants causes minor stress responses and changes in physiological processes but is unlikely to cause serious toxicity at normal environmental concentrations (Krupka *et al.*, 2021).

Azithromycin, like many drugs, may have effects on human health, particularly during pregnancy and in individuals with certain sensitivities (Kong *et al.*, 2024; Lu *et al.*, 2023). Studies on the teratogenic risk of azithromycin have produced mixed results, with some finding a small increase in the risk of some birth defects, while others found no significant association. While serious toxicity is rare, azithromycin has also been associated with potential hepatic toxicity,

cardiovascular effects (such as QT prolongation), and gastrointestinal disturbances (Almeida, et al., 2021; Choi et al., 2018; Mao et al., 2021; Ribeiro et al., 2024).

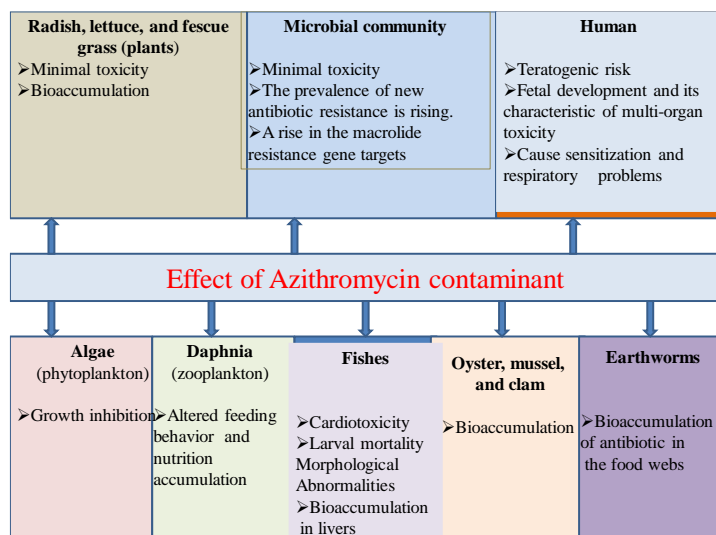


Figure 2 Effect of azithromycin on different biota (Almeida et al., 2021; Mao et al., 2021; Ribeiro et al., 2024; Shearer et al., 2022).

There are lot other methods used for remediation of azithromycin e.g. biodegradation, adsorption, advanced oxidation processes, coagulation and electrocoagulation etc. (El et al., 2023; Imwene et al., 2022; Gopalakrishnan et al., 2023; Hübner et al., 2024; Jalali et al., 2023; Mao et al., 2021; Padmaja et al., 2020; Shokri et al., 2019). Biodegradation processes are effective against low-concentration of azithromycin. Biodegradation organism are inhibited at higher concentrations of azithromycin (El et al., 2023; Mao et al., 2021). Advanced oxidation agents have poor solubility in water, require more energy, and produce more toxic products than the parent compounds (Gopalakrishnan et al., 2023; Hübner et al., 2024). Coagulation and electrocoagulation produce a large amount of sludge that needs to be treated and disposed. Electrocoagulation (EC) is a process that involves supplying electric current through sacrificial electrodes to remove pollutants from wastewater (Padmaja et al., 2020). The remediation of azithromycin with biochar can be an environmentally friendly alternative. One of the most obvious reason is its biodegradability, as it usually comes from organic wastes (Awah and Hendricks, 2024). The high adsorption capacity of biochar is particularly useful for antibiotics removal (Ighalo et al., 2022; Lee et al., 2021). It has a large surface area and a porous structure that significantly improves adsorption capacity (Mane et al. 2024; Satyam and Patra, 2024). The stable activity of biochar makes it a versatile and effective material for various applications (Ighalo et al., 2022). Biochar as a cost-effective and environmental-

friendly. The modified biochar obtained at higher pyrolysis temperature have large specific surface area, high pore volume and abundant functional groups favorable for the adsorption process.

Azithromycin is used in humans and animals for skin ulcers, respiratory tract, acute sinus, ear infections, tonsillitis, acute exacerbation of chronic bronchitis, community-acquired pneumonia, throat infections, pelvic floor inflammation, cervical and urinary tract infections (Firth and Prathapan, 2020; Abruzzo et al., 2022). They are often used in combination with other drugs to treat various infectious disorders. Macrolides are natural compounds that contain a large lactone ring containing a deoxy sugar (Patel and Hashmi, 2023). Azithromycin is a macrolide antibiotic that is very effective in treating bacterial infections (Oliver and Hinks, 2020). Due to its broad spectrum of immunomodulatory, antibacterial, antiviral, and anti-inflammatory capabilities, it is administered to patients with coronavirus SARS-CoV or MERS-CoV (Choi et al., 2018; Dejeni et al., 2021; Oliver and Hinks, 2020).

Challenges associated with azithromycin removal

Azithromycin is often present in environmental matrices at low concentrations, particularly in surface water and wastewater (Arun et al., 2022; Cela-Dablanca et al., 2022, 2024). Sensitive analytical methods and efficient treatment technologies are required to detect and effectively remove azithromycin at these trace levels (Cestaroli 2021; Guerra and Kabir, 2021; Montone et al., 2024). Azithromycin is commonly found in municipal wastewater, hospital effluents, and agricultural runoff, which contain a diverse range of organic and inorganic compounds. The emergence of other contaminants can interfere removal processes as well as affect the efficiency of treatment methods (Martinez-Polanco et al., 2022; Samal et al., 2022; Cela-Dablanca et al., 2022; Löffler et al., 2023). Understanding the fate, behavior of azithromycin and its transformation products is valuable to developing effective removal strategies (Harrower et al., 2021). To ensuring effective adsorption on biochar surfaces is challenging due to factors such as competition with other organic and inorganic compounds present in the environment (Kurniawan et al., 2023). Azithromycin is challenging to remove due to its physicochemical properties. A molecule is considered sufficiently volatile if its K_H value is greater than $3 \times 10^{-3} \text{ mol}/\text{dm}^3/\text{Pa}$. Volatility is an important factor determined by this constant. However, antibiotics have very low K_H values making their extraction by evaporation difficult (Bubonja-Šonje, et al., 2020; Epps and Blaney, 2016; Huang et al., 2021a). Excessive amounts of suspended particles in wastewater increase turbidity that prevents sunlight from reaching the upper layer and prevents the photodegradation of azithromycin (Wu et al., 2020). The concentration of azithromycin in wastewater can vary depending on factors such as population demographics, healthcare practices, and seasonal variations in antibiotic use (Giebutowicz et al., 2020; Mirzaie et al., 2022). This variability complicates the design and operation of wastewater treatment systems to effectively target and remove azithromycin (Al-Wasify et al., 2023; Phoon et al., 2020).

Table 1 Removal of azithromycin by different biochars

Adsorbent	Azithromycin removal efficiency	Reference
Microalgae-derived nitrogen-doped porous activated carbon	98.5%	(Ameen et al., 2023)
Pines Cons	87.8	(Aziz et al., 2024)
Rice husk, impregnated with montmorillonite	33.4 mg g ⁻¹ and 44.73 mg g ⁻¹	(Arif et al., 2023)
ZIF-8/Zeolite composite	85% in 10 cycles	(Liu et al., 2023)
Molecularly imprinted polymer	Over 80%	(Xie et al., 2023)
Rice husk	95%	(Herrera et al., 2022)
Azolla filiculoides based activatedporous carbon	87% and 98%	(Balarak et al., 2021)
Raw saponin-modified nano diatomite	68 mg g ⁻¹ and 91.7 mg g ⁻¹	(Davoodi et al., 2019)
Pines Cons based Fe modified	88%	(Aziz et al., 2024)
Pines Cons based Fe modified	85 % mixture of Azithromycin and Ciprofloxacin	(Aziz et al., 2024)
Oak ash	9600 μmol kg ⁻¹ , meaning >80% retention	(Cela-Dablanca et al.,2024)
Pine bark	8280 μmol kg ⁻¹ , 69%	Cela-Dablanca et al., 2024)
Mussel shell	between 3000 and 6000 μmol kg ⁻¹ , 25–50% retention	Cela-Dablanca et al., 2024)

Remediation of azithromycin

Azithromycin contamination can be reduced in the future by using precautionary measures such as reducing the number of prescriptions and preventing excessive use of azithromycin (Konopka et al., 2022; Pavlinac et al., 2017). Removal rates of azithromycin have been less than 55% in conventional wastewater treatment facilities (Cela-Dablanca et al., 2022; Talaiekhosani et al., 2020). Existing

methods to eliminate azithromycin from aquatic ecosystems have shown no effectiveness, therefore development of new strategies is required (Amalina et al., 2022a). Biochar is a type of char produced through the pyrolysis of biomass, such as agricultural waste, wood chips, and manure (Amalina et al., 2022a; Khater et al., 2024). Biochar is produced through a pyrolysis process. In this process, organic materials are heated in the absence of oxygen. Pyrolysis causes the decomposition of the material and produces a solid residue with high carbon content (Kalina et

al., 2022; Yaashikaa et al., 2020). There are hydroxyl (-OH) and carboxyl (-COOH) groups on the surface of biochar. Because these groups biochar participates in hydrogen bonding and other interactions with azithromycin, its adsorption makes it more potent (Murtaza et al., 2022; Kainth et al., 2024). The use of pine-based biochar to remediate azithromycin contamination is a simple, cost-effective, and beneficial approach to reduce the impact of antibiotic contamination on soil and water (Ameen et al., 2023; Monisha et al., 2021). Rice husk soaked with montmorillonite biochar is an attractive concept for azithromycin treatment (Song et al., 2020). Rice husk biochar impregnating with montmorillonite and activated by carbon dioxide was reported as an economical and sustainable adsorbent for the azithromycin removal (Arif et al., 2023). The porous structure of biochar provides a large surface area for azithromycin adsorption. In biochar montmorillonite composite and saponin-modified nanodiatomite provide additional binding sites (Arif et al., 2023; Davoodi et al., 2019). This combination potentially increases the efficiency of removal of azithromycin from water, thereby contributing to environmental cleanup efforts. Rice bran is a renewable and low-cost material for azithromycin removal. Biochar prepared from rice bran has the capability to remediate 33.4 mg g⁻¹ and 44.73 mg g⁻¹ azithromycin under specific environmental conditions. It showed the azithromycin removal efficiency by 95% (Herrera et al., 2022; Li et al., 2023; González-Hourcade et al., 2022; Shi et al., 2019). Montmorillonite clay has a layered structure with high cation exchange capacity, which enables it to remediate azithromycin through various interactions such as electrostatic forces, hydrogen bonding, and van der Waals forces (Perelomov et al., 2021; Uddin 2018). Thus this enhances adsorption capacity of the composite material. *Azolla filiculoides* based biochar is another interesting material that could be applied in various fields (Kimani et al., 2020). *Azolla filiculoides* biomass as feedstock for biochar production provides a sustainable and environmentally friendly approach to remediate azithromycin. (Olugbenga et al., 2024).

Process optimization

It is important to optimize parametric conditions for effective removal of higher concentrations of azithromycin from a sample solution, (Mojahedimotlagh et al., 2024). Several variables including temperature, pH, initial concentration, dosage of biochar, and contact time determine the maximum amount of azithromycin adsorbed (Balarak et al., 2021). It is necessary to predict the ideal parameters for the efficient removal of azithromycin using biochar in batch condition. Using a central composite design to maximize the efficiency of azithromycin release from mesoporous silica is more effectual approach than performing exhaustive 'one-at-a-time' optimization for each process variable affecting the SBA-15 adsorption process (Shen et al., 2021). This method allows more streamlined optimization process for azithromycin removal (Ibham et al., 2023). Azithromycin remediation is most effective in acidic pH, when the pH increases to the alkaline range, effectiveness declines. Response Surface Methodology (RSM) is a statistical technique that combines modeling to optimize variables. RMS is using for reducing costs, saving time, minimizing errors, and reducing the number of runs required (Ibham et al., 2023; Stylianou et al., 2021). This methodology has proven to be very effective in various sectors. It can be applied to raise the standard of research, development, and production processes (Gholamian et al., 2021). The use of RSM offers significant benefits, particularly in identifying variables critical to a process in a single activity. RSM is using for reducing the number of trials required for optimization. However, RSM is not commonly used for macrolides such as azithromycin, for which further work is required in the field to improve the capacity (mg/g) and adsorption effectiveness. RSM was employed for optimization of parameters such as temperature, concentration, and duration to remove macrolides (Madondo et al., 2022).

Mechanisms of azithromycin removal by biochar

Azithromycin remediation by biochar is mainly driven by adsorption on biochar surface, with contributions from surface complexation, pore entrapment, and potential ion exchange processes (Sen et al., 2023). Mechanisms of biochar and azithromycin interactions is essential to optimize the performance of biochar-based treatment systems for azithromycin removal. It has been reported that H-bonding, O=C, -OH, and -NH₂ functional groups reside on the biochar and azithromycin surface (Arif et al., 2023; Gholamian et al., 2021; Ribeiro et al., 2024; Upoma et al., 2022). Azithromycin is primarily absorbed through π-π, electron donor acceptor interactions, involving the lactam ring on the macrolide and the ring on the adsorbent (Shearer et al., 2022). The absorption process involves ion exchange, hydrogen bonding, electrostatic interactions, and π-π electron-donor-acceptor interactions (Hassan et al., 2020). Electrostatic interactions occur between the cationic form of the macrolide and anionic surface of the adsorbent (Jia et al., 2024; Upoma et al., 2022). Figure 3 shows that a carbon dioxide-activated biochar montmorillonite composite is an effective, long-lasting, and reasonably priced adsorbent for removing azithromycin from contaminated water. Rice husk-based biochar, with its highly porous structure and large surface area, provides sufficient space for the physical adsorption of azithromycin molecules (Herrera et al., 2022; Shi & Liu 2021). Azithromycin has been adsorbed on the surface of rice husk biochar through weak van der Waals forces and other physical

interactions. Surface complexation involves the formation of adsorbents on the surface of rice husk biochar depending on the number of chemical complexes between azithromycin molecules and specific functional groups (Kanth et al., 2024). The mechanism involves the exchange of ions between the biochar surface and the azithromycin molecules in solution. All biochars generally follow similar mechanisms for the removal of azithromycin pollutants (Arif et al., 2023; Kainth et al., 2024)

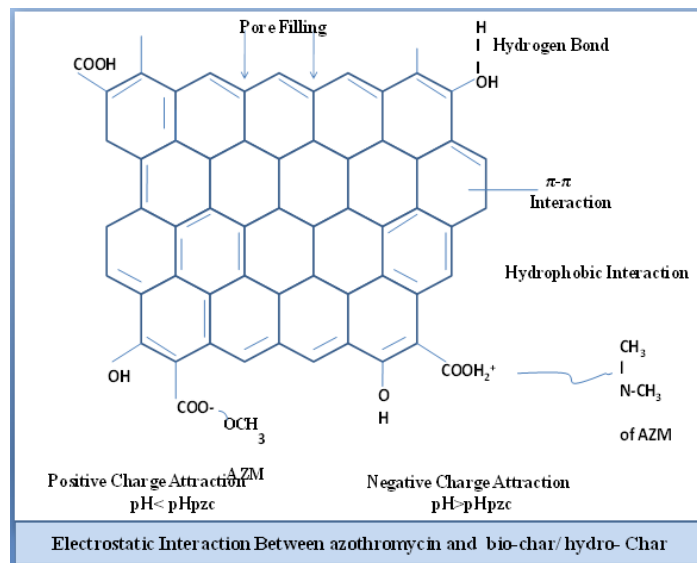


Figure 3 Mechanism of azithromycin adsorption on biochar

Physico-chemical properties of medium affecting the adsorption of azithromycin

The physicochemical properties of the medium play an important role in influencing the adsorption of azithromycin on adsorbents such as biochar. The batch experiment focused on the removal of azithromycin from liquid systems via adsorption on the surface of granular activated carbon prepared with non-reactive adsorbent (Stylianou et al., 2021; Upoma et al., 2022). The adsorption process involves the adsorption of azithromycin on activated carbon, and is highly dependent on various physical parameters. The treatment of pharmaceuticals involves several operational factors such as azithromycin using agarose-based adsorbents. Effect of pH, initial pharmaceutical concentration, adsorbent dose, temperature and contact time are some of these variables shown in Figure 4 (Arif et al., 2023; Davoodi et al., 2019; Dong et al., 2024; Ribeiro et al., 2024; Wahab et al., 2021).

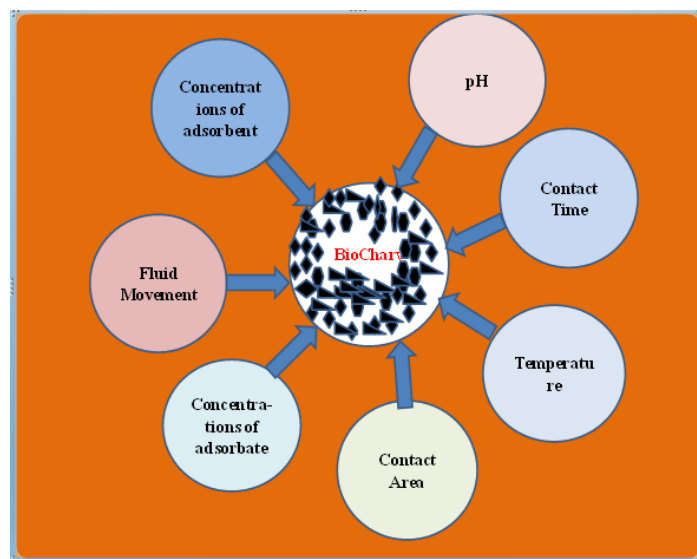


Figure 4 Physico-chemical properties affect adsorption

The results of the adsorption process showed that the R-ND and M-ND methods achieved maximum elimination of azithromycin at a concentration of 20 ppm and a contact time of 60 min. The removal percentages are 99.5% and 98.5% respectively (Davoodi et al., 2019). The removal of azithromycin by α-HNPs had a significant effect on the adsorbent mass effect, which showed that increasing the dosage of adsorbent α-HNPs to 150 mg increases the azithromycin adsorption capacity. This results in an increase in αHNPs. The removal efficiency increased

to some extent with each mass increase of adsorbent (Amin et al., 2023). The findings indicate that increasing the dosage of adsorbent enhances azithromycin removal. As the biochar penetrates and the total surface area expands, the elimination of azithromycin also increases (Arif et al., 2023). *Azolla filiculoides* based biochar has been used to study the effects of adsorption time and temperature. *Azolla filiculoides* based biochar has high capacity and efficiency to eliminate azithromycin. The adsorption procedure proceeds rapidly in the initial stage due to the large pore volume and high surface area of the adsorbent. This first stage is followed by a slower stage. The final stage is an equilibrium stage (Balark et al., 2021). The solubility of the adsorbent in water and the degree of dissociation are directly and indirectly affected by temperature, which has a significant impact on the adsorption process (Al-Ghouti & Al-Absi 2020; Wahab et al., 2021).

The efficiency of azithromycin removal is affected by pH level of the solution due to the inherent characteristics of azithromycin (Upoma et al., 2022; Saita et al., 2018). The azithromycin molecule assumes different conformations depending on the pH of the solution. As a result of the antibiotic and dissociation constant, changes in pH level can affect the electrostatic interactions between the sludge and azithromycin, which in turn affects the removal efficiency of azithromycin (Petropoulos, et al., 2009; Saita, et al., 2018). The pH value exceeds 9.0 and ranges up to 11.0. It is also confirmed that azithromycin has a pKa of 8.7, which has higher adsorption capacity than the unmodified saponin molecule. It may be important to note that this change may also result in the addition of more hydroxyl groups which may further increase the adsorption capacity. Diatomite has a pH of about 2.5 and its surface is negatively charged above that point. Azithromycin and diatomite have opposite charge at the pH range of 2.5 to 8.7, resultant that the electrostatic attraction take place. A pH of 11 is considered an ideal pH due to high electrostatic interactions that enhance the interaction between raw diatomite and azithromycin molecules (Shearer et al., 2022). Mechanisms such as H-bonding may also be responsible for the increased negative surface charge of the adsorbent, since pH 11 is higher than the pKa of azithromycin (Davoodi et al., 2019). According to de Sousa, electrostatic interactions and H-bonding generate negative charges on the zeolite surface at acidic pH levels. While it was previously believed that adsorption occurred mostly along the surface groups of the zeolite, the azithromycin molecules may be blocked by acidic sites present in the internal channels of the zeolite due to steric hindrance. However, the ideal pH for azithromycin adsorption is 6.5 if it becomes prorogated (Aguar et al., 2018). The main mechanism of action appears to be electrostatic attraction, as seen from reduced adsorption at pH 7. Therefore, pH plays an important role in electrostatic interactions and adsorption. The surface charges of the composites revealed how pH affected the adsorption loading (Liu et al., 2019, 2023). Maximum adsorption occurred at a neutral pH of 8. The adsorption capacity is reduced when both the contaminant and adsorbent surfaces have the same positive charge at pH values below 7. Azithromycin surface charge and dissociation constant (pKa) explain, how pH of the solution affects the adsorption capacity of AFAC (*Azolla filiculoides* activated carbon) (Balarak et al., 2021). The pH of the solution is affected by the oxygen functional groups which are available on the surface of the adsorbent that affect the ability of the adsorbent to remove antibiotics from the solution. The surface charge of the adsorbent changes as a result of the presence of H⁺ or OH⁻ ions in the solution, which ultimately affects its effectiveness in removing antibiotics (Zhang et al., 2023). The presence of OH⁻ ions in solution causes deprotonation of surface functional groups at pH values lower than pH 7. The functional groups will be precipitated when the pH value becomes higher than the pH_{pzc} of the point of zero charge, due to the presence of H⁺ ions in the solution (Balarak et al., 2021). The surface of AFAC is more positively charged than pH_{pzc} at a lower pH, i.e. 8.45 (Balarak, et al., 2021; Zhang, et al., 2023). The pH level also affects the solubility and dissociation of the adsorbent, leading to better interaction with the adsorbent. The pKa value of azithromycin is approximately 8.5, which means that at pH 8.543, 50% of azithromycin is unionized (not charged) and 50% ionized (Herrera et al., 2022). When it comes to the removal of azithromycin through adsorption, this process is less effective in solutions with lower pH levels (2.0-4.0). Starting at 20.8%, the removal rate of azithromycin increases only marginally to 22.2%. It was observed that the surface electrostatic attraction force between the drug azithromycin and α-HNPs (hematite nanoparticles) gradually increases up to pH adsorption levels higher than 8.0 (Al-Hakkani et al., 2022). This behavior is particularly noticeable at pH 10.0, where the elimination percentage reaches approximately 79% (Ameen et al., 2023). The effect of pH on the degradation ability of phytate-modified biochar depends on the pyrolysis temperature of the biochar; However, it had no obvious effect on non-amended biochar (Hua et al., 2022). The solubility of the adsorptive in water and the degree of dissociation are both directly and indirectly affected by temperature, which usually has a significant effect on the adsorption process (Robinson et al., 2022).

Regeneration of biochar

Regeneration of biochar involves restoring its adsorption capacity and effectiveness after it has been used to remove contaminants from water or other media (Alsawy et al., 2022; Jagadeesh and Sundaram, 2023). One of the key factors in assessing the feasibility and cost-benefit ratio of a material is its regeneration capacity. Operating, purchasing, and preparation costs of adsorbent

are reduced through the reuse process. The percentage of regeneration varies for deionized water, NaOH, HCl, and ethyl alcohol (Januario et al., 2021). The ideal regeneration conditions not only created excellent structure effect relationships between physical and chemical properties but also successfully controlled the competition. There is a close connection between the deep carbonization process and the adsorption/oxidation site repair process (Jay et al., 2023). Direct thermal regeneration involves heating biochar to high temperatures, typically between 400°C and 800°C, in an inert atmosphere such as nitrogen or argon (Zhan et al., 2023). Steam regeneration involves heating biochar in the presence of steam at temperatures ranging from 300°C to 700°C. Biochar derived from rice husk and subjected to thermal treatment at temperatures between 450°C and 600°C has shown significant removal efficiencies for azithromycin, achieving over 95% removal from pharmaceutical effluents (Ajala et al., 2023; Kang, et al., 2022). The electrochemical regeneration of biochar impregnated with azithromycin is an innovative approach that combines the principles of electrochemistry and sustainable remediation. This method involves using an electric current to induce redox reaction. It can regenerate the adsorption capacity of biochar. It allow reutilization of the biochar-azithromycin composite (Li et al., 2019; Zhou et al., 2021). A new technology is used for recycling spent activated biochar based on hydrothermal treatment at a temperature of 160–320 °C. Treatment at 280°C is sufficient to completely decompose azithromycin (Nouioua et al., 2023; Wurzer et al., 2023). Biological regeneration of biochar impregnated with azithromycin involves utilizing microbial activity. Microbes having capability to degrade or metabolize the adsorbed antibiotic on the biochar surface.

This process harnesses the natural capabilities of microorganisms and enzymes to break down organic compounds, such as azithromycin, into simpler, less harmful substances (Amalina et al., 2022b; Jayakumar et al., 2021). Magnetically active biochar-zeolite composites are washed with methanol, ultrasonicated in distilled water, and coated with polymers for their regeneration. Biochar and hydrochar are regenerated using different techniques. Each regeneration technique has some advantages and disadvantages as shown in Table 2 (Amalina et al., 2022b; Hassan et al., 2020; Mishra et al., 2023; Nouioua et al., 2023; Wurzer et al., 2023).

Table 2 Advantage and disadvantage of different regeneration methods

Type of method	Advantages	Disadvantages
Biological	-Natural and Sustainable -Low cost -Long effectiveness	-Slow Treatment rates -Site specific requirement -Risk of incomplete remediation
Hydrothermal	-Mild condition -Effective desorption -Environmental friendly -Versatile	-Energy intensive -Long treatment time -Complex operation -Limited effectiveness
Chemical	-Easy - Reduction of carbon loss - Higher recovery of the adsorbents & regeneration	- Referring to both the effectiveness of regeneration and the structural characteristics. - Less recoveries
Electrochemical	- In-situ operation - Lowe energy consumption - Moderate temperatures - Chemicals are not use	Generation of strongly bound compounds - At low pollutant concentrations, the efficiency of current for organic decomposition is diminished
Microwave-aided Regeneration	-Short treatment time - Energy consumption Lower - High restoration of carbon porosity	-The effectiveness of the regenerated samples in adsorbing various pollutants cannot be assured
Thermal	- Easy -Widely used	-Harmful products generation - High carbon loss

Effect of biochar properties on azithromycin adsorption

Biochars undergo an extensive characterization process to determine their adsorption capacity (Muhammad et al., 2024). The assessment takes into account several important elements, including surface area, micropore volume, total number, and total pore volume. The properties of biochar significantly influence its adsorption capacity and the plant's ability to remove azithromycin (Castiglioni et al., 2021; Jagadeesh and Sundaram, 2023). As the temperature in the pyrolysis increases, the surface area and structure of the char improves. Much attention has been paid to the creation of engineered biochar with a large porous structure and large surface area. Chemical activation is most popular and efficient means to increase the surface area and porosity of biochar (Alsawy et al., 2022; Li et al., 2022). The functional groups including -C=O and -C-O are generally associated with organic agricultural products that cover a significant part of the total pore volume (Yuan et al., 2021). It contains several surface functional groups for adsorption, including amino (-NH₂), hydroxyl (-OH), and carboxyl (-COOH) (Hassan et al., 2023).

Azithromycin bio-adsorption and sustainability

Azithromycin removal using biochar technology under line with several sustainability goals. It addresses the environmental impact of azithromycin, promotes clean water, supports responsible production practices and contributes to climate action. Biochar technology is an important step toward achieving a more sustainable and healthy future. It effectively removing azithromycin from water supplies, this way it prevents the spread of azithromycin-resistant bacteria and protects human health thereby contributing to UN Sustainability Goal 3. Biochar also improves water quality by removing azithromycin contaminants thereby contributing to safe and clean drinking water and meets UN Sustainability Goal 6. Producing biochar from agricultural waste promotes responsible resource use and reduces waste and meets UN Sustainability Goal 12. Biochar production and its use would achieve carbon sequestration leading into a possible contribution to climate change mitigation and meets UN sustainability Goal-13.

FUTURE PERSPECTIVE AND CHALLENGES

The future of biochar-based extradiation of azithromycin holds great promise as a sustainable and effective solution. It holds the capability to address pharmaceuticals pollutants in wastewater. Optimized biochar materials may have the potential to extradiate azithromycin from complex water matrices by providing improved selectivity, efficiency, and recyclability. The overall removal efficiency can be raised by integrating biochar-based adsorption with other technologies on treatment, such as membrane filtration, advanced oxidation processes, and biological treatment. The challenges linked to azithromycin removal, such as recurrent contaminants and low concentration values, can be approached easily by biochar. Moreover, it will allow tracking and control of the total biochar-based adsorption process in real time during removal of azithromycin. However, non-conventional pyrolysis processes produce numerous by-products that include polycyclic aromatic hydrocarbons and volatile organic compounds; these may threaten the growth of microbes (Bus et al., 2022; Jose et al., 2019; Yemele et al., 2024). Biochar is difficult to recycle and leads to secondary pollution and increase costs (Kosar et al., 2024; Sarougi and Routray, 2024). The release of azithromycin from biochar depends on the type of biochar, the interaction between biochar and azithromycin, and the conditions (Ngigi et al., 2020; Patel et al., 2022). Biochar's low density and small particle size make it challenging to remove from water after dissolving. Biochar may not be effective at immobilizing metals, hazardous substances and it might allow them to migrate through the soil (Bus et al., 2022). Biochar stability affects the mobility of metals and metalloids in contaminated soils. The production and application of nano-biochar is costly, and there is little information on its widespread use. In some cases it has been reported that nano-biochar has toxic effects on plants, mammals and soil microflora (Rajput et al., 2022). Interaction of nano-biochar with pollutants in the rhizosphere and their effect on plant-soil dynamics (Sarma et al., 2024).

CONCLUSION

Ecosystems are in a great risk because of widespread presence of azithromycin contaminants in the environment. Microbial communities, bioaccumulation in food chains are disrupted by these contaminants and contribute to increasing antibiotic resistance. To address this issue strict regulations are necessary. Biochars are innovative solutions that are needed for improved waste management, protection of health and minimizing environmental impact. Selection of appropriate biomass feedstock, thermal treatment methods where biomass is treated at high temperatures are the steps for the preparation and activation of biochar. Carbon content, stability and porosity are properties of the resulting biochar influenced by factors such as feedstock type, particle size, residence time and post-treatment processes of biochar. Biochar is an environmentally and sustainable resource for

removal of antibiotics because of high surface area and adsorption capacity. Adsorbents based on biochar have varying adsorption and removal capacities for organic pollutants such as azithromycin, depending on the biomass source and the amendments applied. While common biochars achieve moderate to high efficiencies. Engineered -biochars with tailored properties exhibit improved adsorption, which is essential for achieving high removal rates. Therefore, biochar is a promising material for wastewater treatment, particularly for the removal of pharmaceuticals and other organic contaminants because this versatility.

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