



Review

Antibiotic adsorption by natural and modified clay minerals as designer adsorbents for wastewater treatment: A comprehensive review

Gül Gülenay Haciosmanoğlu^{a,*}, Carmen Mejías^b, Julia Martín^b, Juan Luis Santos^b, Irene Aparicio^b, Esteban Alonso^b^a Environmental Engineering Department, Faculty of Engineering, Marmara University, Uyanık Cd. No:6, 34840, Istanbul, Turkey^b Departamento de Química Analítica, Escuela Politécnica Superior, Universidad de Sevilla, C/Virgen de África, 7, E-41011, Seville, Spain

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ABSTRACT

Increased antibiotic use worldwide has become a major concern because of their health and environmental impacts. Since most antibiotic residues can hardly be removed from wastewater using conventional treatments, alternative methods receive great attention. Adsorption is one of the most efficient and cost-effective treatment methods for antibiotics. Among the adsorbents, clay minerals have garnered increasing attention due to their unique properties including availability, high specific surface area, low cost, cation exchange capacity, and good removal efficiency. This paper reviews the recent progress made in the use of natural and modified clay minerals for the removal of antibiotics from water. First, the sources, occurrence, removal and health effects of the antibiotics commonly encountered in water bodies are described. Antibiotic concentration levels and average removal efficiencies measured in conventional activated sludge treatment systems worldwide are also provided to better address the problem. Second, the review explores the characteristics of clay minerals as adsorbent of antibiotics and the factors affecting the adsorption. The review identifies and discusses the future trends and strategies used to increase the adsorption capacity of clay minerals by modification and combination techniques (intercalation of novel functional groups such as organocations, biopolymers and metal pillared-clay minerals, combination with biochar or thermal activation). The quantitative comparisons of clay minerals' ability for antibiotic removal are given. Some natural clay minerals have good removal potential for antibiotics, with maximum adsorption capacities over 100 mg/g. For most other adsorbents, surface modifications and combination techniques resulted in improved adsorption properties (including higher surface area, enhanced adsorption capacity, increased stability and mechanical strength). Finally, the application of these adsorbents at pilot scale, using real wastewater samples, their reuse, economic analysis and life cycle assessment are other issues that have been considered.

1. Introduction

Antibiotics are widely used to prevent and treat microbial infections in both humans and animals. In most cases, antibiotics are non-biodegradable by nature and can be hardly removed from wastewater in conventional wastewater treatment plants (WWTPs) (Akhil et al., 2021; Langbehn et al., 2021; Ashiq et al., 2019a). It is estimated that more than 50% of the antibiotics used enter the environment (as parent compound or its metabolites) through hospital and industrial effluents and the use of animal manure as a fertilizer for farming (Dutta and Mala, 2020; Fukahori et al., 2011). In this regard, residues of quinolones, sulphonamides, tetracyclines or penicillins have been detected in

environmental compartments ranging from ppt to ppb levels (Langbehn et al., 2021). The occurrence of antibiotics in the environment is considered an emerging issue due to the adverse effects to the ecosystem (Ashiq et al., 2019a) related to the antibiotics entering the water supply system, where they promote the growth of resistant bacteria (Chaturvedi et al., 2021; Kalhori et al., 2017).

The continuous discharge of antibiotic residues into the aquatic environment has led the European Union to include some antibiotic compounds in the Watch List (WL) of emerging water pollutants under the Water Framework Directive (European Commission, 2020; 2018). The WL includes compounds with potential risk to or via the aquatic environment but that still need monitoring data to support their actual risk (Rodriguez-Mozaz et al., 2021; Carballa et al., 2017). In this regard,

* Corresponding author. Marmara University Environmental Engineering Department, Uyanık Cd. No:6, 34840, Istanbul, Turkey.

E-mail address: gulenay.haciosmanoglu@marmara.edu.tr (G.G. Haciosmanoğlu).

Nomenclature		KAOL	Kaolinite
<i>Acronyms</i>		LCA	Life-cycle analysis
B-2MTH	Stearildimethylbenzyl ammonium chloride	MIP	Molecularly imprinted polymers
BENT	Bentonite	MMT	Montmorillonite
BHDAP	1,3-bis(hexadecyldimethylammonio)-propane dibromide	MTA	Myristyltrimethylammonium
BS-12	Dodecyl dimethyl betaine	PAC	Powdered activated carbon
CNT	Carbon nanotube	PAL	Palygorskite
CTAB	Cetyltrimethylammonium bromide	PC	Phosphatidylcholine
DDBAC	Dodecyl dimethyl benzyl ammonium chloride	PSO	Pseudo-second order
DK1	Hexadecyl trimethyl ammonium	RECT	Rectorite
HALL	Halloysite	SDBS	Sodium dodecyl benzene sulfonate
HDAPS	3-(N,N-dimethylhexadecylammonio) propane sulfonate	SEP	Sepiolite
HDTMA	Hexadecyl trimethyl ammonium bromide	SM	Smectite
I	Illite	STV	Stevensite
K	Kaolin	VERM	Vermiculite
		WL	Watch List

the macrolide antibiotics erythromycin, clarithromycin and azithromycin were included in the first WL and it was recommended to continue their monitoring. Amoxicillin and ciprofloxacin were included in the second WL. The 2020 version of the WL still maintains the monitoring of amoxicillin and ciprofloxacin, and the sulphonamide sulfamethoxazole and the diaminopyrimidine trimethoprim have been added. Since the conventional treatment processes can not completely eliminate these substances, alternative technologies such as electrocoagulation (Tarpani and Azapagic, 2018), membrane filtration (Liao et al., 2020), advance oxidative process (Mehrjoui et al., 2014) or adsorption (Han et al., 2019; Guillosoy et al., 2019) have received great attention and proposed for treatment of antibiotic-containing effluents (Chauhan et al., 2020; Ashiq et al., 2019a; Tarpani and Azapagic, 2018). Adsorption is probably the most promising technology due to its unique properties regarding its effectiveness, simplicity in the design and operation, lower cost, environmental friendliness, and the absence of high toxicity by-products (Imanipoor et al., 2021). The development of adsorbents is crucial for a more efficient adsorption process. Adsorbents such as activated carbon, graphene oxide, zeolites, hydrogels, or metal-organic frameworks (Yao et al., 2020; Chen et al., 2019; Premarathna et al., 2019; Cao et al., 2018; de Sousa et al., 2018; Wang et al., 2016) have been proposed for antibiotic removal from aqueous media (Imanipoor et al., 2021), but their low adsorption efficiencies in some cases or the high cost or unfeasibility of recycling in others are some of the drawbacks for practical application. Clay minerals have received much attention as adsorbents for antibiotic removal from aqueous media (Chauhan et al., 2020) due to their low cost, availability, high specific surface area, cation exchange capacity (CEC), good removal efficiency and selectivity (Antonelli et al., 2020a,b; Ali and Ahmed, 2017). In addition, the fact that clay minerals are chemically and physically stable, have low toxicity and can be easily regenerated make them adequate adsorbents for large-scale applications (Bangari and Sinha, 2019).

Additionally, the modification of clay minerals has been found to increase the adsorption affinity of the modified clay minerals towards organic compounds (Buruga et al., 2019; Han et al., 2019). Physical and chemical modification processes such as the melt-blending method, which involves mixing the clay mineral with a (bio)polymer (Das et al., 2020; Perez et al., 2020; Ma et al., 2019), or surfactant-based exfoliation (Li et al., 2021; Wu et al., 2020; Lu et al., 2014) have been proposed. Hydrophilic clay mineral surfaces can be made hydrophobic by the intercalation of organic cations into the clay mineral interlayer space (Martín et al., 2018). The substitution of exchange inorganic cations in the clay by organic cations (e.g cationic surfactants) increases the interlayer distances and greatly enhances the sorption of organic contaminants (Ashiq et al., 2019a; Awad et al., 2019). Wang et al. (2018)

investigated the capacity of vermiculite (VERM) to adsorb sulfamethoxazole from aqueous solution and found that a combination of a thermal pre-treatment and surface modification of the clay mineral resulted in higher antibiotic removal (98%) than for surface modification alone (95%).

Different studies and reviews have focused on the use of natural and modified clay minerals for the separation of many classes of pollutants including heavy metals, dyes, phenols, ions (nitrate, ammonia.) as well as bacteria (Manna et al., 2021; Awad et al., 2019). The objective of this paper is to review the available literature published between 2000 and 2021 on the technical applications of clay minerals and modified clay minerals for the adsorption of antibiotics from water sources. The main topics that will be discussed are: (i) overview of antibiotic sources, occurrence, removal in conventional systems and health effects; (ii) use of clay minerals and modified clay minerals as adsorbent of antibiotics (including adsorption mechanisms, desorption and reuse, cost analysis and life cycle assessment aspects); and, (iii) future trends (modification with novel functional groups, thermal activation, combination of modification techniques, use of adsorbent mixtures, and studies that rely on actual wastewater and pilot-scale).

2. Search strategy

The review included the search in Scopus and Sciencedirect databases. The search was conducted separately using the base terms “antibiotics” and “adsorption” followed by: “clays”, “water”, “adsorbents”, “wastewater”, “modified-clays”, and “bionanocomposites”. The exclusion criteria were studies published before 2000 and in languages other than English.

A total of 6208 articles were identified (Table S1) when the two based terms were used. To identify the articles of interest the ‘two base terms’ were combined with the rest of ‘keywords’ (see Table S1). After including “clays” as third keyword the search was reduced to 250 articles in the whole period 2000– present, and the increase in the number of papers published per year is displayed in Figure S1. Subsequently, 90 potentially eligible articles were selected for title and abstract screening. After this, the potentially relevant studies were read full text and critically appraised on the relevance. A total of 82 articles, including experimental and observational studies, were finally selected to identify and discuss the strategies related to the use of clay minerals for antibiotic removal. Almost half of them (45%) were focus on the used of natural clay minerals as adsorbent materials, while the remaining 55% were based on the development of new designed adsorbents by modification and combination techniques applied on clay minerals (intercalation of novel functional groups (organocations (17%), biopolymers (16%), metal pillared-clay minerals (11%)), combination with biochar

(5%) or other modification techniques such as thermal activation (7%) (Figure S2).

3. Sources, occurrence and environmental impact of antibiotics in wastewater treatment plants

Antibiotics are biologically active compounds widely used to treat or prevent microbial infections in humans and animals. Antibiotics are classified according to their biological activity, chemical structure, and mechanism of action (Akhil et al., 2021; Ahmed et al., 2015). Table S2 shows the classification class and physiochemical properties of the most commonly detected antibiotics in wastewater and water sources (Akhil et al., 2021).

The global consumption of antibiotics has increased disproportionately in recent years. A recent study reported that in 2030 the global use of antibiotics will increase by 200% in comparison to 2015, if adequate policy measures are not taken (Klein et al., 2018). Antibiotics are broadly used in humans and they are also an integral part of intensive animal agriculture and aquaculture. Moreover, during the COVID-19 pandemic, the increased use of antibiotics was noted as a concern (Chen et al., 2021). Although antibiotics are not recommended in SARS-CoV-2 therapy (if there is no bacterial co-infection), injudicious use of them for the treatment and prevention of the disease was highlighted (Usman et al., 2020). Hospital effluents are the main source of antibiotics in the environment and the main source in terms of generated pharmaceutical load (Bhattacharyya et al., 2021; Dutta et al., 2020). Household pharmaceuticals enter municipal wastewaters through human and household waste. Animal antibiotics used in livestock farms are used to increase livestock productivity suppress parasites and prevent microbial diseases. They enter the environment via animal waste, wastewater discharge, and manure application to aquaculture (Dutta et al., 2020). Antibiotics have been found in concentrations from $\mu\text{g/L}$ to ng/L in wastewater and their presence is a matter of concern worldwide. Antibiotic concentrations (in ng/L) found in influent and effluent wastewater in different countries is shown in Table S3. Fluoroquinolones (ciprofloxacin, norfloxacin and ofloxacin), sulphonamides (sulfamethoxazole, sulfadiazine and sulfamethazine) and trimethoprim were detected at highest concentrations, with ciprofloxacin and sulfamethoxazole being the dominant compounds (concentrations >7910 and 7220 ng/L in influent wastewaters, respectively). Langbehn et al. (2021) investigated the type and occurrence of antibiotics on wastewater samples from different human activities. Overall, sulfonamides, tetracyclines, macrolides, quinolones, and β -lactams are the most commonly investigated antibiotics in the processes of water treatment. The most commonly detected antibiotics in urban and hospital wastewater are sulfamethoxazole, ciprofloxacin, and trimethoprim (Langbehn et al., 2021). For example, concentrations up to 54.83 $\mu\text{g/L}$ and 72.85 $\mu\text{g/L}$ for sulfamethoxazol and trimethoprim, respectively, have been found in urban wastewater from Kenya (K'oreje et al., 2016). In hospital wastewater concentrations reached 40.90 $\mu\text{g/L}$ for ciprofloxacin and 30.38 $\mu\text{g/L}$ for trimethoprim in Romanian (Szekeress et al., 2017) and Vietnam (Thai et al., 2018), respectively. Antibiotic concentrations found in wastewater from livestock farming is high (Zhu et al., 2020), particularly in wastewater from piggeries where ciprofloxacin (up to 16 $\mu\text{g/L}$) and sulfamethoxazole (up to 9.748 $\mu\text{g/L}$) are the antibiotics found at the highest concentrations (Leon-Aguirre et al., 2019; Parpounas et al., 2017).

Evidence has shown that antibiotics are not efficiently removed in conventional WWTPs and require special degradation treatments of effluents (Table S3) (Akhil et al., 2021). There is a wide variation in antibiotic removal in conventional WWTPs. In this regard, some antibiotics like penicillin can be easily removed, while others like fluoroquinolones, tetracyclines or lincomycins are more recalcitrant to conventional treatments and require specific degradation treatments. These differences in antibiotic removal using Conventional Activated Sludge (CAS) treatments have been reported even for the same

compound and in some cases within the same study (Bhattacharyya et al., 2021; Rodriguez-Mozaz et al., 2021). For instance, removal rates from -65% to 100% (Samaraweera et al., 2019) were reported for sulfamethoxazole, from 6% to 100% (Aydin et al., 2019) for doxycycline, and from -60% to 72% (Nieto-Juárez et al., 2021) for erythromycin.

Over the last two decades, the overuse of antibiotics has had an impact on the food chain and on the development of antibiotic resistance, which have in turn resulted in harmful health effects on the health of humans and animals and ecological issues (Shejale et al., 2020). According to Santos et al. (2010) antibiotics could be classified as extremely toxic to microorganisms (EC_{50} below 0.1 mg/L). Several studies have investigated the effect of antibiotics on the environment and found that even low concentration levels (from 0.78 $\mu\text{g/L}$ (Andreozzi et al., 2004) to 3597 mg/L of amoxicillin (Park and Choi, 2008) can disrupt the normal growth and reproductive function of certain animals like birds and fish, and of plants and bacteria (Santos et al., 2010). Moreover, it has been found that trace levels of antibiotics in soil and water can also have an impact on human health through the food chain (Chaturvedi et al., 2021). Some antibiotic residues found in the environment have a particular relevance because long-term exposure at relatively low concentrations has the capacity to activate antibiotic resistant genes (ARGs) (Langbehn et al., 2021; Ahmed et al., 2015). In this regard, Hernandez et al. (2019), who studied the presence of antibiotics in samples of sea water and treated wastewater from King George Island (Antarctica), an area with high anthropogenic presence, found that the most commonly detected antibiotics were ciprofloxacin and norfloxacin in wastewater effluents. The authors found ARGs in WWTP bacteria and, as reported in previous studies, they also found *Escherichia coli* strains resistant to antibiotics (Langbehn et al., 2021). Certain bacterial strains are becoming antibiotic resistant increasingly fast; for instance, after treatment with erythromycin $>70\%$ of *Staphylococcus aureus* isolates were found to be resistant to this macrolide (Chaturvedi et al., 2021).

Antibiotic resistance is already a major public health issue worldwide that, if left uncontrolled, will result in the inability to treat common infections or perform routine treatments. For this reason, the development of affordable and efficient wastewater remediation methods for antibiotic wastewater removal is paramount. Some advanced technologies like advanced oxidation, which can completely degrade or even mineralize antibiotic molecules, are already available but have very high cost (Mehrajouei et al., 2014) and are difficult to maintain at large scale. In contrast, physicochemical technologies are becoming a feasible way to remove organic compounds from wastewater (Homem and Santos, 2011). From the recent technologies, adsorption seems the most effective method as it is fast, relatively inexpensive, simple to design and operate, and has low toxicity compared to biological processes (Ahmed et al., 2015).

4. Clay-based adsorbents

Adsorption is a well-known process, but its application for antibiotic removal has not been extensively explored. The most common adsorbents used for antibiotic removal are active carbon, carbon nanotubes, ion exchange resins and biochar. Clay-based adsorbents are widely used for the removal of organic contaminants from contaminated water bodies (Han et al., 2019; Homem and Santos, 2011), but regarding antibiotic removal, these adsorbents have been reported for the removal of only about 25 compounds, most of them including in the tetracyclin, sulphonamide and fluoroquinolone groups. Overviews of published articles for antibiotic removal by adsorbents are shown in Table S4 (natural clays) and Table S5 (modified/composite materials based on clays).

The clay-based adsorbents evaluated for the removal of antibiotics are illite (I), rectorite (RECT), bentonite (BENT), montmorillonite (MMT), halloysite (HALL), kaolinite (KAOL), sepiolite (SEP), smectite (SM), stevensite (STV) and vermiculite (VERM) (with or without surface

modification) and the composite materials derived from these minerals. Fig. 1 shows the schematic diagram of commonly used clay minerals in adsorption studies and their important features related to adsorption.

4.1. Montmorillonite

MMT is a 2:1 layered phyllosilicate that has one central alumina octahedral layer and two tetrahedral silicate layers. It is a member of the SM clay minerals group with the formula $Al_4Si_8(OH)_4O_{20}$. As indicated in Table S4, MMT is the most common clay mineral evaluated for the adsorptive removal of antibiotics from aqueous solutions. Wang et al. (2010) obtained an adsorption capacity as high as 330 mg/g for ciprofloxacin, with initial concentrations (C_i) between 500 and 4000 mg/L, by using MMT in acidic and neutral aqueous solutions (Wang et al., 2010). In another study, the maximum monolayer adsorption capacity of MMT for ciprofloxacin ($C_i = 500\text{--}2500$ mg/L) was reported as 400 and 520 mg/g at pH 3 and 11, respectively (Wu et al., 2010). Gulen and Demircivi (2020) also studied ciprofloxacin adsorption ($C_i = 250$ mg/L) by MMT and they indicated that the maximum adsorption capacity was 128 mg/g at pH 7 (Gulen and Demircivi, 2020). The reason of these differences can be explained by diverse origins of the MMT minerals, as well as different experimental conditions.

Figueroa et al. (2004) used Na-MMT for the adsorption of three tetracycline antibiotics (oxytetracycline, chlortetracycline, and tetracycline). The maximum Langmuir adsorption capacities of Na-MMT for chlortetracycline, oxytetracycline and tetracycline were determined as 79.97, 33.15 and 49.78 mg/g, respectively (at pH 5.5) (Figueroa et al., 2004). In this study the initial concentrations were 3.8–110.1, 3.7–105.9 and 3.6–102.2 mg/L for chlortetracycline, oxytetracycline and tetracycline, respectively. In another study, Chang et al. (2009) compared the adsorption capacity of different clay based materials (SWy-2: a low charge Na-MMT, SAz-1: a high charge Ca-MMT, and a rectorite) for the removal of tetracycline ($C_i = 100\text{--}3000$ mg/L) and found significant differences between them (the maximum adsorption were 355, 460, and

140 mg/g for SWy-2, SAz-1, and RECT, respectively) (Chang et al., 2009).

4.2. Kaolinite

KAOL with the formula of $Al_2Si_2O_5(OH)_4$ is a 1:1 layered phyllosilicate mineral, where each layer has one silica tetrahedral sheet and one alumina octahedral sheet. It is the second common clay mineral used in antibiotic adsorption studies. However, the reported adsorption capacities of KAOL for antibiotics were relatively low when compared to other clay minerals based adsorbents like MMT. Rivagli et al. (2014) studied marbofloxacin and enrofloxacin removal by KAOL and found that the maximum adsorption capacities of KAOL were 21.2 and 25.1 mg/g for marbofloxacin and enrofloxacin, respectively (Rivagli et al., 2014). (The initial concentrations of marbofloxacin and enrofloxacin were 10–1600 and 10–1500 mg/L, respectively). KAOL was also evaluated for tetracycline and ciprofloxacin adsorption. The maximum adsorption capacities of KAOL for tetracycline ($C_i = 0.1\text{--}1$ mM) and ciprofloxacin ($C_i = 0.1\text{--}2$ mM) were 4 mg/g (Li et al., 2010a, 2010b) and 6.3 mg/g (Li et al., 2011), respectively.

4.3. Bentonite

BENT is a composite material mainly containing MMT, as well as other minerals (i.e., quartz, feldspar, and calcite). It is the third commonly used clay minerals based material for antibiotic adsorption. Putra et al. (2009) evaluated BENT for the removal of amoxicillin from aqueous solutions. Based on Langmuir model, the maximum adsorption capacity of BENT for amoxicillin with an initial concentration of 300 mg/L, was 47.37 mg/g (Putra et al., 2009). In another study, Genç et al. (2015) used BENT for the adsorption of ciprofloxacin. The maximum Langmuir adsorption capacity of BENT was determined as 147.06 mg/g for ciprofloxacin with initial concentration of 50–500 mg/L (Genç et al., 2013). BENT was also found to be effective for tetracycline ($C_i = 5\text{--}200$

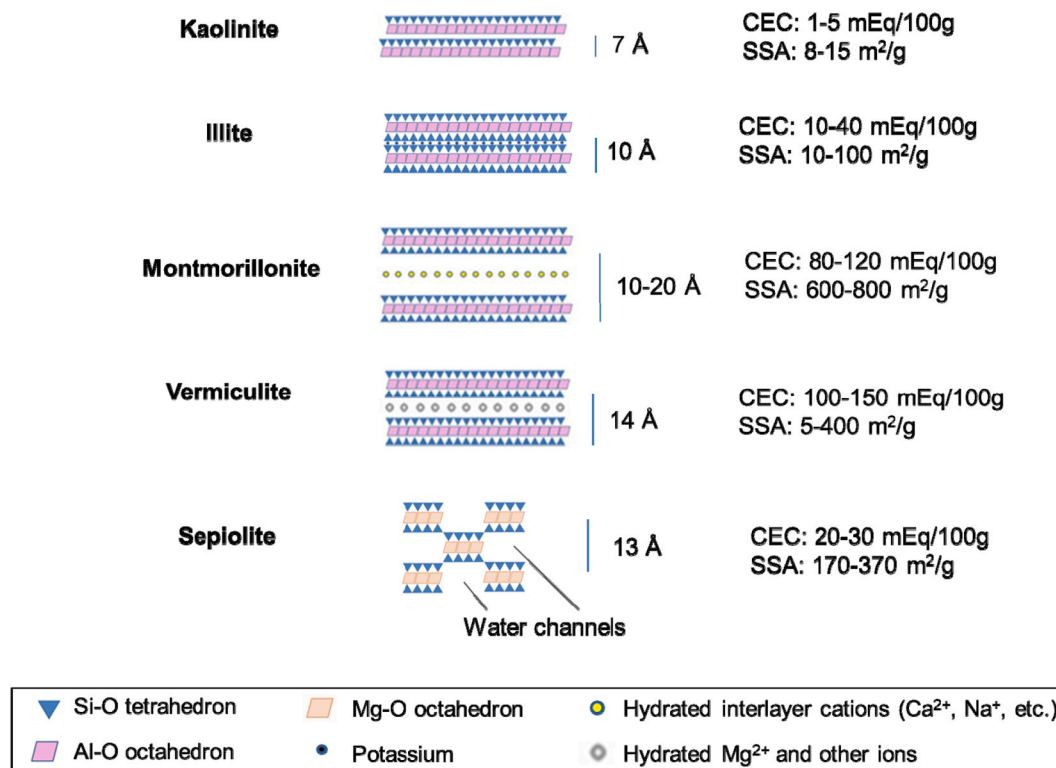


Fig. 1. Main features of commonly used clay minerals in adsorption studies (Data from Murray (2006); Mohamed and Paleologos (2018); Kumari and Mohan (2021)).

mg/L) with a maximum adsorption capacity of 156.7 mg/g (Maged et al., 2020). When these results are compared, the adsorption capacity of BENT is much lower for amoxicillin, compared to ciprofloxacin and tetracycline. This observation can be explained by pH dependent speciation of the target antibiotics and the differences in their pK_a values (Githinji et al., 2011). As indicated in Table S2, pK_{a1} of amoxicillin is relatively lower than that of ciprofloxacin and tetracycline. Thus amoxicillin dissociate more readily than ciprofloxacin and tetracycline. Under neutral (and close to neutral) pH conditions, the anionic form of amoxicillin has relatively higher percent, compared to the other two compounds, which leads to less sorption of amoxicillin by negatively charged BENT surface. For the design of novel adsorbents with surface modifications, such differences in the chemical properties of the target pollutants need to be considered, as a future perspective.

4.4. Sepiolite

SEP is a trioctahedral phyllosilicate with theoretical formula of $Si_{12}O_{30}Mg_8(OH)_4(OH_2)_4 \cdot 8H_2O$. SEP is structurally different from laminar clay minerals with its microfibrillar morphology. Sturini et al. (2016) used SEP for the adsorptive removal of marbofloxacin and enrofloxacin. The adsorption capacities obtained from the S-logistic 1 model were high, i.e., 132 mg/g and 112 mg/g, for marbofloxacin and enrofloxacin, respectively, while the initial antibiotic concentrations were between 20 and 1800 mg/L (Sturini et al., 2016).

4.5. Illite

It is a dioctahedral 2:1 phyllosilicate. It has a similar structure to MMT with some replacements in silica for alumina in tetrahedral sheet. Wan et al. (2013) studied the adsorption of enrofloxacin by I. They showed that I has a high adsorption capacity (81.9 mg/g) for enrofloxacin ($C_i = 103.1$ – 1998.3 mg/L) (Wan et al., 2013). In another study, Chang et al. (2012) evaluated the adsorption of tetracycline on I (IMt-2). The adsorption capacity of IMt-2 for tetracycline ($C_i = 50$ – 1000 mg/L) was reported as 32 mg/g (Chang et al., 2012). This result was lower than tetracycline ($C_i = 100$ – 3000 mg/L) adsorption capacity of MMT (460 mg/g) (Chang et al., 2009). However, it was higher than 4 mg/g obtained for tetracycline ($C_i = 33.1$ – 662.7 mg/L) adsorption by KAOL (Li et al., 2010a, 2010b). These results give valuable information to make comparison between different adsorbent materials. However, different experimental conditions might also influence the results, which will be further discussed in the next sections.

4.6. Other clay minerals

As indicated in Table S4, there are other studies evaluating different types of clay minerals (i.e. HALL, RECT, SM, STV and VERM) for the adsorptive removal of antibiotics from aqueous solutions. STV showed high adsorption capacities for tetracycline, oxytetracycline and chlortetracycline corresponding to 127.1, 126.1 and 139.9 mg/g, respectively, with the initial adsorbate concentrations of 50–1000 mg/L (Antón-Herrero et al., 2018). On the other hand, VERM (without modification) gave lower removal results for the adsorption tetracycline ($C_i = 10$ – 180 mg/L) with the maximum monolayer adsorption capacity of 16.03 mg/g (Yang et al., 2020).

4.7. Modification and combination techniques

The need for improved adsorbent performance (i.e., high adsorption capacity and reusability, fast kinetics and low cost) led researchers to develop specifically designed adsorbents. As shown in Table S5, the modification and combination techniques applied on clay minerals for improved antibiotic adsorption properties include the synthesis of new clay-based nanocomposites using organocations and biopolymers, metal pillared-clay minerals, combination with biochar or two different clay

minerals and other modification techniques such as thermal activation. These modifications help to increase the specific surface area and tune the pore dimensions of the adsorbent materials, as well as to obtain diverse surface functional groups.

Bionanocomposites based on the combination of clay minerals and biopolymers have emerged as promising materials for the removal of pollutants from contaminated water due to their improved properties regarding the biocompatibility and biodegradability of biopolymers together with the excellent sorption capacity of clay minerals. The natural polysaccharides (chitosan, cellulose or alginate) incorporating to layered silicates of the smectite group constitute the bionanocomposites most studied for environmental applications. Ma et al. (2019) modified MMT with carboxymethyl-chitosan. (In this study, carboxymethyl-chitosan was used instead of chitosan because of its higher solubility.) Using the synthesized material, high adsorption capacities were obtained as 178.57 and 271.74 mg/g for tetracycline and chlortetracycline, respectively (where the initial adsorbate concentrations were in the range of 5–400 mg/L). These results were explained by the advantages of both MMT with high ion exchange capacity and large specific surface area, and chitosan with different functional groups (i.e., amine and hydroxyl groups) resulting in strong interactions with chemical molecules and ions. Moreover, the intercalation of carboxymethyl-chitosan molecules with MMT structure increased the interlayer spaces resulting in a bigger specific surface area of the adsorbent material (Ma et al., 2019).

The resulting properties of bionanocomposites will be determined by the modification method and the agent used for clay functionalization. Overall, there are three main methods for the clay incorporation into the polymer matrix: (i) solution blending; (ii) polymer melt blending; and (iii) in situ polymerization method. Solution blending seems to adequately enhance the dispersion of the clay within the matrix. In addition, the presence of magnetic nanoparticles in the polymer matrix can also optimize the functionality of bionanocomposites. Arya and Philip (2016) prepared magnetic polymer clay composite using BENT, chitosan, powdered activated carbon (PAC) and Fe_3O_4 magnetic nanoparticles. The optimum ratio of constituents was found to be 1:0.5:0.3:0.3 for BENT: chitosan: PAC: Fe_3O_4 . In addition to the new functional groups due to chitosan (i.e., amino and hydroxyl groups), magnetic separation ability due to Fe_3O_4 is another advantage of the synthesized material. The equilibrium adsorption of ciprofloxacin using the composite material followed Freundlich isotherm with K_F and $1/n$ values estimated to be $15.45 \text{ mg}^{1-1/n} \text{ L}^{1/n} \text{ g}^{-1}$ and 0.84, respectively (Arya and Philip, 2016).

Synthetic polymers and surfactants are also widely used for clay modification. The most common examples include quaternary ammonium surfactants, polyamides and polyaniline. In recent years, molecularly imprinted polymers (MIP) have been introduced as a novel approach for clay modification. MIP is produced around a target molecule (template). After the template is removed, some binding cavities with affinity and selectivity for the template molecule are obtained in the imprinted polymer. Li et al. (2018) fabricated magnetic HALL nanotubes combined with molecularly imprinted polymer. Using this material, high adsorption capacity (312.08 mg/g) was obtained for norfloxacin with initial concentration of 50–550 mg/L (Li et al., 2018). The high selectivity and stability of the molecularly imprinted polymer-clay composites are especially useful for the separation technologies and sensor devices.

Another commonly applied practice to improve clay properties (i.e., specific surface area, porosity, surface acidity and CEC) is acid activation. For this purpose, clay minerals are usually treated with mineral acid solutions causing partial dissolution of cations and leading to increased porous structure, higher specific surface area, and surface acidity (de Andrade et al., 2018). Many studies use commercially available acid activated clay minerals (without further treatment) for the application in adsorption experiments. For example, MMT KSF (acid activated MMT) showed good adsorption potential for trimethoprim

removal with the maximum adsorption capacity of 129.51 mg/g (Bekçi et al., 2006).

Biochar is a low-cost, porous and carbon-rich material that exhibits excellent potential as adsorbent in the immobilization and removal of environmental contaminants from water and soil. To enhance the surface area, functionalities and adsorption efficiency of biochar various biochar-clay composites have been proposed. In this sense, Zhang et al. (2018) prepared montmorillonite-biochar (MMT-BC) composite derived from wheat straw for the adsorptive removal of norfloxacin. According to the obtained results, the maximum Langmuir adsorption capacity of biochar was 10.58 mg/g and that of MMT-BC composite was 25.53 mg/g, for norfloxacin ($C_i = 0.4\text{--}15$ mg/L). This improved adsorption was explained by the fact that the oxygen-containing functional groups on the biochar increased after the introduction of MMT (Zhang et al., 2018).

Besides, clay pillaring is another important process for modification and improvement of clay structure. This technique is presented to open up the space between clay layers by adding stable columns in these areas and increase in this way the permanent porosity of the material. Pillared interlayered clay minerals are two-dimensional materials similar to zeolites, which are produced through cation exchange between clay layers and some voluminous cations, and/or large mineral cations. These cations are polymers or oligomers of metal hydroxyl cations, which are formed by hydrolysis of metal oxides or their salts. When these agents are exposed to heat treatment for dehydration and dehydroxylation processes, they are converted into stable metal oxide clusters (as columns) which separate silicate layers and create interstitial spaces with molecular dimensions (Najafi et al., 2021). The smectite group is often very effective in the pillaring process. The pillaring process consists of two steps: 1) the interlayer space is increased significantly due to the replacement of pillaring agents between host clay layers. 2), these pillaring precursors are transformed into stable pillars through calcination, and the interlayer space is also slightly reduced compared to the previous step. In a recent study, four pillared clay minerals using BENT and different oligocations (Al, Fe, Si, and Zr) were synthesized. The synthesized materials were evaluated for the adsorptive removal of ciprofloxacin. Among different pillared clay minerals, Si- and Fe-pillared clay minerals showed the highest ciprofloxacin adsorption capacities of 100.6 and 122.1 mg/g, respectively ($C_i = 18\text{--}500$ mg/L). These results were attributed to the higher access of the ciprofloxacin species to the porous structure when compared to the other pillared clay minerals, favoring its interaction with the different adsorption sites within the interlamellar region (Roca Jalil et al., 2017).

Another effective treatment technique to enhance the adsorption properties of the clay minerals is heating at high temperature. Antonelli et al. (2020a, b) applied calcination for Verde-Iodo BENT at 500 °C. Using calcined Verde-Iodo (CVL) BENT, the maximum Langmuir adsorption capacity obtained for ciprofloxacin was 114.4 mg/g (Antonelli et al., 2020a) and it was 116.72 mg/g for ofloxacin (Antonelli et al., 2020b), with the initial concentrations between 0.01 and 4 mM. Heat treatment eliminates impurities in the clay and causes to hydroxyl loss in the clay structure which supply increased stability and reduced expansion in water. The increased stability is especially important for the application of clays in fixed-bed adsorption systems (Almeida Neto et al., 2012).

Tian et al. (2016) synthesized a functionalized hybrid silicate adsorbent derived from low-grade palygorskite (PAL) clay as the initial material via a hydrothermal process in the presence of sodium silicate, magnesium sulphate, and monochloroacetic acid. The hybrid silicate adsorbent showed high adsorption capacities for chlortetracycline (329.84 mg/g) and oxytetracycline (207.47 mg/g), where the initial concentrations were 50–800 mg/L. The results indicated that the adsorption capacities of the hybrid silicate adsorbent were enhanced by 218.9% and 107.9%, for chlortetracycline and oxytetracycline, respectively, when compared to that of raw PAL. These changes were attributed to the large surface area and abundant pores of the hybrid silicate

adsorbent which provided a significant amount of adsorptive sites for the antibiotics. Moreover, the active surface groups and negative charges promoted the attraction and capture for these antibiotics (Tian et al., 2016).

Layered double hydroxides (LDH) also called as anionic clays, have brucite-like structure with the general formula of $Mg_6Al_2(OH)_{16}CO_3 \cdot 4H_2O$ and can be easily synthesized by co-precipitation process. LDH can be used for antibiotic adsorption and their adsorption capacity can be improved by combination and modification techniques. For example, Li et al. (2015) used MgAl LDH for minocycline adsorption ($C_i = 200$ mg/L) and they obtained maximum adsorption capacity of 200.5 mg/g. When the adsorption studies were conducted with MgAl LDH/ γ -AlO(OH)/carbon composite the maximum adsorption capacity for minocycline was increased to 302.5 mg/g. This improvement was explained by the presence of the hierarchically porous structure leading to higher surface area and pore volume of the composite material, thus providing more active adsorption sites (Li et al., 2015).

In this section, modified clay minerals applied for antibiotic adsorption was reviewed. However, for the wastewaters containing complex mixture of pollutants, even more advanced solutions than single-modification of clays might be necessary. For example, Barakan and Aghazadeh (2021) indicated that multifunctional-modified clays such as porous clay heterostructure (PCH) exhibited significant advantages in comparison with single-modified clays (Barakan and Aghazadeh, 2021). These advantages include improved material characteristics (e.g., high specific surface areas, high ion exchange capacity, and large mesoporous structure with a narrow pore size distribution, high thermal stability and mechanical strength), high pollutant removal efficiency and high reusability. Similarly clay/graphene oxide (Chang et al., 2020) and clay-carbon nanotube (CNT) composites (Marszałek et al., 2022) are shown to be effective adsorbents toward different contaminants. Regarding their high removal capacities these novel materials can be applied for the removal of antibiotics as a future perspective. However, CNTs have the drawbacks of high production cost (as will be discussed in the economic analysis part) and this is among the most important challenges that researchers in the field should overcome.

Among 82 articles reviewed, experiments with real wastewater were missing, except 15 articles (Anggraini et al., 2014; Antón-Herrero et al., 2018; Das et al., 2020; Jin et al., 2014; Li et al., 2018; Martín et al., 2018; Peng et al., 2019; Putra et al., 2009; Rahardjo et al., 2011; Rivagli et al., 2014; Sturini et al., 2016; Wang et al., 2018; Xing Zha et al., 2013; Zhang et al., 2018; Zhao et al., 2020). However, wastewater characteristics are very different than that of the synthetic model solutions used in the adsorption experiments and the adsorption performance of the clay-based materials can be affected by the real wastewater components. Therefore, experiments with real wastewater and pilot-scale applications are necessary for scale-up of adsorption systems. For example, Rahardjo et al. (2011) conducted the adsorption experiments using BENT and CTAB-BENT for the removal of ampicillin from synthetic wastewater and a pharmaceutical company wastewater. When real wastewater was used instead of synthetic wastewater, the adsorption capacities for ampicillin were decreased from 89.9 to 59.3% (for BENT) and from 100 to 90.6% (for CTAB-BENT). This change was explained by the competition in the adsorption with other substances in the real wastewater (Rahardjo et al., 2011). In another study, Antón-Herrero et al. (2018) used STV for the adsorption of tetracyclines by applying both batch adsorption experiments and a pressurized continuous system. They indicated that a continuous wastewater flow through a system composed by STV leaved this system with no tetracyclines, indicating water purification by tetracyclines adsorption in clay (Antón-Herrero et al., 2018).

Another important criterion for the selection of adsorbent materials is the applicability at large scale and continuous systems. As indicated previously, heat treatment of clays is especially beneficial for the applications in continuous systems due to the increased stability and mechanical strength of clays after heat treatment at high temperature.

Among the articles reviewed for antibiotic removal by clay-based adsorbents, there are only seven studies evaluating the application in continuous flow systems (Antón-Herrero et al., 2018; Antonelli et al., 2020b; Das et al., 2020; Lawal and Moodley, 2018; Maged et al., 2020; Zelaya Soulé et al., 2020; Nguyen et al., 2020) and no study for pilot scale applications. However, pilot scale studies are necessary to demonstrate the applicability of laboratory results to field scale conditions. Another future direction is the combined/hybrid application of different advanced technologies (e.g., adsorption, advanced oxidation, membrane filtration and biological processes) to obtain maximum efficiency. Using the combination of membrane filtration and clay-based adsorbents, effective removal of ciprofloxacin (Das et al., 2020) and tetracycline (Nguyen et al., 2020) were demonstrated. In these studies, membranes containing montmorillonite, i.e., montmorillonite-impregnated cellulose acetate nanofiber and poly (vinylidene fluoride)/polyaniline/MMT membranes were synthesized and successfully applied in batch and continuous scale adsorption of antibiotics. In another study, catalytic ozonation process was coupled to NH₄Cl-activated carbon (NAC) fixed-bed columns for the removal of amoxicillin. The results indicated that the saturated NAC bed could be efficiently regenerated through a catalytic ozone-regeneration process (Yaghmaeian et al., 2014). More studies are needed to develop novel and efficient solutions for antibiotic removal by combined applications of advanced technologies.

4.8. Tools to determine the adsorption mechanism

Material characterization is an essential part of the adsorption studies. Before the assays, to obtain information on the morphological and structural characteristics of the adsorbent, and, after the adsorption assay, to elucidate the type of interaction between the clay minerals and the contaminant. Commonly used material characterization techniques include nitrogen adsorption-desorption isotherms, scanning electron microscopy (SEM), transmission electron microscopy (TEM), infrared (IR) or Fourier transform infrared (FTIR) spectroscopy, X-ray photoelectron spectroscopy (XPS) and X-ray diffraction (XRD), isoelectric point (IEP) and point of zero charge (PZC) analyses. Solid state nuclear magnetic resonance (SS-NMR) and density functional techniques (DFT) were also used in determination of the adsorption mechanism, albeit to a lesser extent.

Nitrogen adsorption-desorption isotherms analysis is used to obtain the structural data including the average pore size, pore volume, pore size distribution and surface area of the adsorbent material. SEM and TEM analyses help to examine the morphological characteristics of the adsorbent including the shape and size of individual pores on the adsorbent surface. FTIR spectroscopy is usually used to identify the functional groups present on the material surface. In order to study the crystalline structure of the adsorbent, X-ray diffraction (XRD) analysis is performed. XPS analysis is used to investigate the surface chemical composition and chemical states on the adsorbent material. Both IEP and PZC analyses are used to determine the electrical state of the adsorbent's surface in solution; however, they are often misused interchangeably. The IEP indicates the solution conditions at which the electrokinetic potential at the shear plane is zero and PZC occurs when the surface charge density equals zero (Tran et al., 2017).

The results of the above analyses should be interpreted together with the results of adsorption experiments. For the kinetic studies, different contact times are applied while keeping the other variables constant. Then, kinetic models are applied to the obtained data to evaluate the rate of the adsorption process and to determine the potential rate limiting step. As shown in Tables S4 and S5, for the adsorptive removal of antibiotics by clay-based materials usually follow pseudo-second order (PSO) kinetic model, though Avrami, Elovich and intra-particle diffusion models are also reported. For these studies, the equilibrium times are relatively low, usually less than 2 h (Tables S4 and S5).

The adsorption isotherm studies are important to obtain useful

information related to the surface properties, adsorbate-adsorbent affinity, adsorption capacity and favorability of the sorption process. For antibiotic adsorption by clay-based materials, the most common isotherm model fit is Langmuir model, while the other isotherm models (i.e., Freundlich, Sips, Hills, Redlich–Peterson, Dubinin–Radushkevich, Temkin and Toth) are also applied (Tables S4 and S5).

Caution must be taken with any description of the adsorption mechanism without enough supporting evidence. In many adsorption studies, the adsorption process was classified as chemisorption (or physisorption) according to the kinetic data fit to the PSO model (or PFO model). However, this approach was criticized by different authors (Kumar, 2006; Lima et al., 2015; Tran et al., 2017) because the mechanism of adsorption cannot be directly determined according to the results of kinetic experiments and kinetic model fit. To determine the adsorption mechanism, evidence based on the analytical techniques such as FTIR, SEM, IEP, PZC, Raman spectroscopy, NMR, XRD, and XPS are necessary. The results of these analyses should be evaluated together with the results of the adsorption experiments while taking into account the chemical nature of the adsorbate and adsorbent to elucidate the adsorption mechanism (Lima et al., 2015; Tran et al., 2017).

4.9. Mechanism of antibiotics adsorption

Adsorption mechanism is used to describe the types of molecular interactions taking place during the adsorption process. Revealing the adsorption mechanism is important for understanding, controlling and improving the adsorption systems. Once the adsorption mechanism is understood, it is possible to:

- * deeply understand the factors affecting the adsorption;
- * extrapolate the laboratory findings to the larger scale;
- * design more efficient adsorption systems.

The mechanism of antibiotics adsorption by clay based materials depends on the type antibiotic and clay mineral used, pre-treatments or surface modifications applied on the adsorbent material, and the adsorption conditions (mainly pH, co-existing ions, salinity etc.). The possible driving forces in the adsorption mechanism include electrostatic attractions which can be subdivided into covalent bonding, coulombic attraction, and dipole interactions (e.g., hydrogen bonding, π -interactions, London forces), as well as non-specific interactions such as hydrophobic interactions (Tong et al., 2019). In this section, the adsorption mechanism of specific antibiotics by clay based materials will be discussed.

Wang et al. (2010) studied the properties of ciprofloxacin adsorption by Ca-MMT. The authors interpreted the adsorption mechanism based on the results of adsorption and desorption experiments together with XRD and FTIR analyses (Wang et al., 2010). The obtained data demonstrated that cation exchange was the principal mechanism for ciprofloxacin adsorption on MMT. For ciprofloxacin, the adsorption mechanism is highly pH dependent due to its speciation as the pH of the solution changes. On the other hand, the surface charge of MMT remains negative over pH range studied (pH 2.8–11). When the solution pH is lower than 6.1, the ciprofloxacin molecules are in the cationic and zwitterionic forms. In this case, cation exchange occurs between the positively charged amine group and the cations in the interlayer sites of MMT. Between pH 6.1 and 8.7, zwitterionic form is dominant. Under this condition, the positive charge of the amine group of zwitterionic ciprofloxacin may still contribute to the adsorption mechanism. When the solution pH is higher than 8.7, the anionic form of ciprofloxacin dominates, inducing repulsion to negatively charged MMT surface and thus, reducing the amount adsorbed (Wang et al., 2010).

In another study, MMT, I and KAOL were evaluated for the adsorption of enrofloxacin (Wan et al., 2013). To determine the adsorption mechanisms, XRD and FTIR analyses were evaluated together with the adsorbent and adsorbate characteristics. The pH dependent speciation of

enrofloxacin has an important role in the adsorption mechanism. The pK_{a1} and pK_{a2} values of enrofloxacin are 5.94 and 8.70. Thus, the acidic cation and zwitterionic form of enrofloxacin are dominant in acidic and neutral pH, respectively, which are attracted to the permanently negative surface of MMT and I. As a result, under acidic and neutral conditions, the major enrofloxacin adsorption mechanism for MMT and I was cation exchange. When the pH value was above 7, the amounts adsorbed were significantly lowered however, enrofloxacin could still be removed under basic conditions. These results were attributed to the presence of non-electrostatic interaction such as cation bridging, for the enrofloxacin sorption at high pH. The enrofloxacin adsorption capacity of KAOL was much smaller than that of MMT and I, which is in accordance with its lower CEC. As a result, in addition to cation exchange, cation bridging was expected to contribute significantly to enrofloxacin adsorption by KAOL. It was also indicated that enrofloxacin adsorption on MMT (swelling clay) was on both external surface and in the inter-layer spaces. However, it was limited to the external surfaces for non-swelling clays, I and KAOL (Wan et al., 2013).

Putra et al. (2009) examined the adsorption properties of BENT towards amoxicillin. PZC analysis, FTIR measurements and elemental analysis (by atomic absorption spectrophotometer) were carried out for BENT (pristine and after adsorption). Based on the obtained results, the possible adsorption mechanisms included cation exchange, interactions of protonated aluminol groups in BENT with deprotonated carboxyl groups in amoxicillin, interactions of unprotonated aluminol with silanol groups in BENT and carboxyl groups in amoxicillin, and the attraction of positively charged amoxicillin by the negatively charged isomorphous BENT (Putra et al., 2009).

Ashiq et al. (2019a) used a composite material prepared from municipal solid waste biochar and MMT for ciprofloxacin adsorption. The composite material showed an improved ciprofloxacin adsorption when compared to the pristine adsorbents. Based on FTIR and powder XRD analysis results, the major adsorption mechanism of ciprofloxacin by the composite material was explained by the cumulative effect from the parent materials: biochar and MMT. The major mechanisms of ciprofloxacin adsorption by the evaluated materials were pi-pi electron donor interactions, electrophilic interactions, and hydrophobic interactions. The higher adsorption of the composite material was due to the enhanced active sites on the composite adsorbent which improved its interaction with ionisable ciprofloxacin molecules (Ashiq et al., 2019a). The main adsorption mechanisms involved in antibiotic adsorption with clay and biochar components of the composite material are shown in Figure S3.

For the adsorptive removal of doxycycline hydrochloride from aqueous solutions, Kong et al. (2019) synthesized lignin xanthate resin intercalated BENT composite. The synthesized material was characterized by SEM, FTIR, XRD, XPS and zeta potential analyses and the adsorption mechanism was discussed. The predominant adsorption mechanism of doxycycline by lignin xanthate resin intercalated BENT was explained by the conjugated pi-pi interaction of benzene ring in the doxycycline molecules and lignin moieties, as well as the hydrogen bonds between doxycycline and the composite material (Kong et al., 2019).

Wang et al. (2019) evaluated the use of magnetic attapulgite clay-biochar composite (MABC) for the adsorption of oxytetracycline. Material characterization was conducted by SEM, XRD, FTIR spectroscopy. The specific surface area of the composite material was determined by Brunauer–Emmett–Teller (BET) method and its magnetic property was observed by vibrating sample magnetometer (VSM). The adsorption mechanism was explained based on the physicochemical properties of the synthesized material components, and by the comparison of FTIR analyses of MABC before and after adsorption. According to the obtained results, the adsorption mechanism was explained by the well-developed pore structure, large specific surface area, and abundant surface oxygen-containing functional groups of the composite material (Wang et al., 2019). As shown in a previous study,

biochar can interact with organic molecules through hydrogen bonding, acid–base interaction and π - π stacking (Liu et al., 2011). In addition to these interactions, ion exchange with attapulgite clay in the composite material (MABC) also contributes to the higher adsorption capacity (Wang et al., 2019).

Laabd et al. (2021) prepared a mesoporous hydroxyapatite@montmorillonite hybrid composite for ciprofloxacin adsorption from aqueous solutions. The composite material showed higher ciprofloxacin adsorption performance (95.41%) when compared to that of hydroxyapatite (81.43%) and MMT (34.81%). The improved removal efficiency of the composite material was explained by the fact that coating of hydroxyapatite on the MMT surface results to an increase in the exposed functional moieties of hydroxyapatite which include the hydroxyl (-OH) and phosphate (\equiv POH) groups. The ciprofloxacin adsorption mechanism was explained by the electrostatic interactions, hydrophobic interactions, hydrogen bonding and n-p electron donor/-acceptor interactions (Laabd et al., 2021).

4.10. Factors affecting adsorption mechanism

Selection and/or design of efficient clay based adsorbents for antibiotic removal requires the understanding of possible adsorption mechanism and factors affecting it. These factors include the antibiotic properties, clay characteristics and solution conditions which are summarized in Figure S4.

Important antibiotic properties related to the adsorption mechanism are the molecular weight and size, $pK_{a,acid}$, $pK_{a,base}$, and polarity of the compound. The impacts of these factors on the adsorption mechanism are strongly interdependent with the other factors related to the adsorbent properties and solution characteristics. Usually, polar compounds can be adsorbed via coulombic attraction (depending on the properties of solution pH and the adsorbent characteristics) while non-polar molecules are expected to be adsorbed mainly by non-coulombic interactions, i.e., dipole interactions (hydrogen bonding, π -interactions, london forces), hydrophobic interactions. However, the adsorption mechanism may also be a combination of these forces for the adsorbents and adsorbates possessing different functional groups.

Main clay properties determining the adsorption mechanism include surface chemistry of the material such as surface functional groups, CEC, IEP and PZC. Textural characteristics of the material are also essential, which include pore size distribution, specific surface area and pore volume. The surface modifications and combination techniques usually improve the adsorption properties of clay minerals by increased specific surface area and introduction of new surface active groups. For example, thermally activated BENT showed higher adsorption capacity (388.1 mg/g) for tetracycline removal than that of raw BENT (156.7 mg/g). This improvement was attributed to the loss of water and hydroxyl in bentonite structure, which could uncover the binding sites with negative potential and enhance its activity (Maged et al., 2020). Another example is VERM modified with surfactant of phosphatidylcholine (PC) showing significantly increased adsorption capacities from 36.80 to 36.87 mg/g to 66.44 and 93.72 mg/g, for oxytetracycline and ciprofloxacin, respectively. The higher adsorption capacities after modification were explained by the fact that loaded PC surfactants on VERM made the surface more hydrophobic and enhanced the adsorption capacity towards oxytetracycline and ciprofloxacin, which was mainly ascribed to the hydrophobic interaction, electrostatic attraction and hydrogen bond between PC-VERM and antibiotics (Liu et al., 2017). Zhu et al. (2016) indicated that for the cationic contaminants, modified MMTs (by different methods) may have better adsorption capacities than raw MMT, however, the enhancement is generally not quite significant. In this case, regarding the higher price of the modification methods, modified MMTs can be less suitable than original MMT (Zhu et al., 2016). As a result, selection and/or design of clay-based adsorbents should take into account the cost-benefit approach which will be discussed in the next section.

Another factor influencing the adsorption mechanism is the solution properties, which include pH, temperature, and ions and molecules present in the solution. pH of the solution both affects the surface charge of the adsorbent material and the speciation of the antibiotic molecules. pH dependent speciation of antibiotics can be determined by their pK_a values and this information can be used to estimate the adsorption mechanism. For example, if the solution pH is lower than $pK_{a,acid}$ of the antibiotic, the cationic form dominates. Meanwhile, if the solution pH is greater than the isoelectric point of the adsorbent material, the surface is negatively charged which can lead to coulombic attraction between the cationic form of the antibiotic molecule and adsorbent surface. This mechanism is summarized in Fig. 2. For the compounds with more than one pK_a value, the case might be more complicated, where zwitterionic or neutral forms of the compounds might dominate. An interesting point about this topic was indicated by Thiebault (2019). Though misinterpretations can be found in the literature, it is important to determine whether zwitterionic or neutral form of a specific compounds occur at solution pH between pK_{a1} and pK_{a2} . If $pK_{a,base} < pK_{a,acid}$ for the target compound, the neutral state of the compound can be observed between pK_{a1} and pK_{a2} . On the other hand, zwitterionic charge state can be observed if $pK_{a,acid} < pK_{a,base}$ (Schaffer and Licha, 2014). In summary, to elucidate the adsorption mechanism, solution pH conditions and clay surface properties under these conditions should be considered carefully with the pH dependent speciation of the antibiotics.

Temperature is also an important factor affecting the adsorption. In order to evaluate the effects of temperature, the adsorption experiments (with complete isotherm studies) are repeated at different temperatures and thermodynamic parameters i.e., Gibbs free energy change (ΔG), enthalpy change (ΔH) and entropy change (ΔS) of adsorption are calculated. The negative value of ΔG shows the spontaneous nature of the adsorption process, while its positive value shows non-spontaneous nature. Moreover, if ΔG value decreases with increasing temperature, it can be concluded that the adsorption process is favourable at higher

temperatures (and vice-versa). The positive value of ΔH indicates that the adsorption process is endothermic and its negative value indicates exothermic process. The positive value of ΔS suggests the increased randomness at the solid-liquid interface (while the opposite is suggested for the negative value of ΔS). When Tables S4 and S5 are examined, it can be concluded that for most of the studies on the antibiotic adsorption by clay based materials, ΔS is positive (indicating the increased randomness at the solid-liquid interface) while ΔG is negative (spontaneous adsorption) and ΔH is positive (endothermic process).

Depending on the adsorption mechanism and solution chemistry, different ions and molecules present in the solution might show competing effect for the adsorption sites leading to a reduced adsorption capacity or they may lead to an increased amount of adsorption via bridging and complex formation mechanisms, and salting out effects. For example, the presence of Cu (II) ions increased the adsorption of tetracycline by MMT in a wide pH range (Wang et al., 2008). This observation was explained with the complex formation between tetracycline species and Cu (II) which have higher sorption coefficients and potentially lower mobility compared to tetracycline species alone. In another study, different effects of monovalent cations (Li^+ , Na^+ , K^+) and divalent cations (Mg^{2+} , Ca^{2+} , Cu^{2+}) on tetracycline adsorption by MMT was elucidated (Zhao et al., 2012). The adsorption was enhanced by the presence of divalent cations compared to monovalent cations. The increased adsorption amounts were attributed to the capability of bridge formation of divalent cations. Humic acid (at high concentration) also promoted tetracycline adsorption by MMT, especially under acidic and neutral pH conditions, which was explained by the complexation mechanism (Zhao et al., 2012).

The operational conditions such as mixing speed, contact time, adsorbent dose and adsorbate concentration do not affect the adsorption mechanism but these are important considerations for the design of adsorption experiments, as well as for process optimization. For example, for the studies reported in this review, making comparison

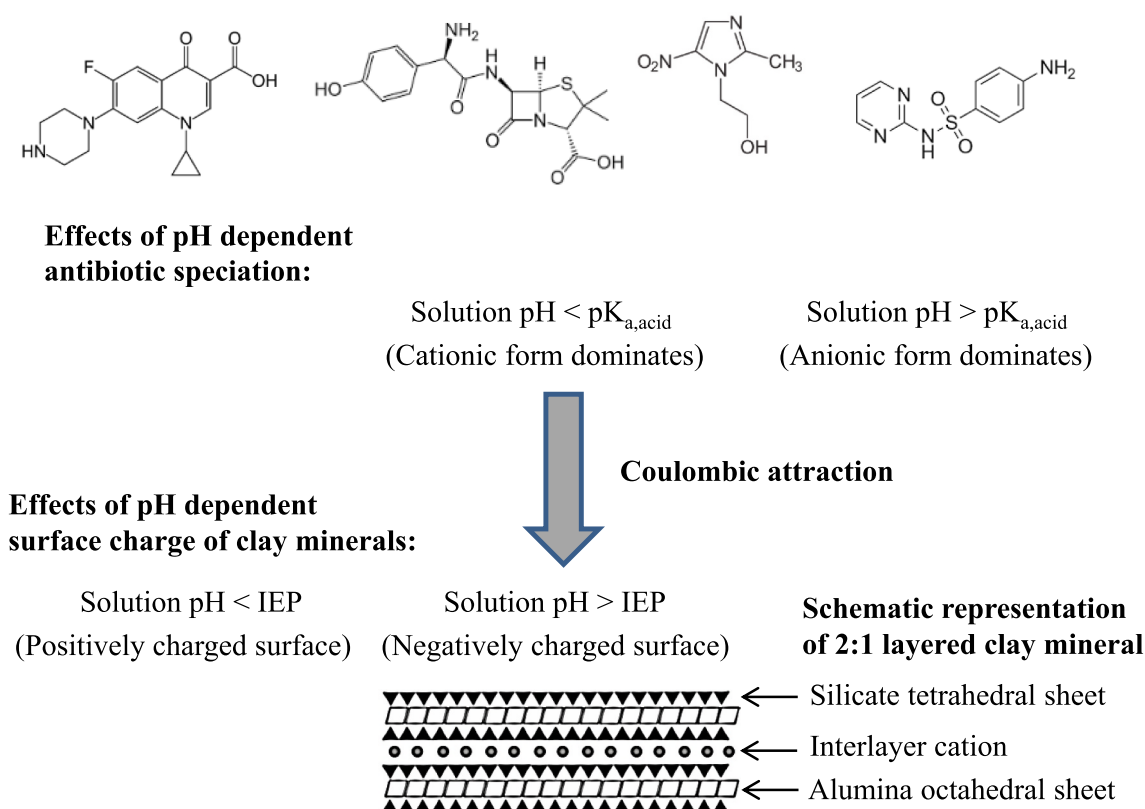


Fig. 2. Adsorption mechanism involving coulombic attraction and the effects of solution pH.

between different results is difficult because of the different experimental conditions. Especially, for the isotherm studies, it is important to present a complete adsorption isotherm to identify the regions (e.g., linear, saturation etc.) in which the experimental data of adsorption equilibrium are located (Kumar, 2006; Tran et al., 2017). In summary, in order to make comparison between different adsorbent materials, similar experimental conditions and presentation of complete adsorption isotherms need to be established.

4.11. Desorption and reuse

Reusability of an adsorbent is important for its economic viability and applicability at large scale. Unfortunately, most studies in the literature didn't report the reusability of the evaluated adsorbents. Moreover, some adsorbent materials are not reusable. For example, the reusability of surfactant modified zeolite in fixed bed column was tested by using NaOH solution at pH 12.2 as the eluent (Masukume et al., 2011). Although elution process was successful, the reuse studies indicated that the adsorption capacity of surfactant modified zeolite was reduced from 7.82 mg/g to 2.97 mg/g. Another non-reusable material was indicated as zero-valent iron (Li et al., 2019). This material is non-reusable because of its instability in water and low particle size. As a result, in addition to the efficiency of a material for the adsorption process, its reusability should be considered for long-term applications. In this section, the available results for the regeneration and reuse studies on clay based materials after antibiotic adsorption are reviewed.

Antonelli et al. (2020a) applied heat treatment at 500 °C for the regeneration of calcined Verde-Iodo BENT (CVL) clay after ciprofloxacin adsorption. The authors suggested that regeneration by heat treatment had the advantages of low cost and not residue generation. After three adsorption/desorption cycles, the ciprofloxacin removal percent by CVL clay (regenerated at 500 °C) was reduced by 13.3% (Antonelli et al., 2020a). Similarly, CVL clay was regenerated after ofloxacin adsorption by heat treatment at 500 °C (Antonelli et al., 2020b). At the end of three cycles, the percent removal of ofloxacin decreased by only 6.23% compared to the original adsorption capacity of the clay. This change was explained by the loss of a few active adsorption sites due the heat treatment. In conclusion, the CVL clay exhibited a high level of reusability after heat treatment.

Laabd et al. (2021) investigated the elution of adsorbed ciprofloxacin from the hydroxyapatite@montmorillonite hybrid (HAP@Mt) surface by applying different solutions (methanol, methanol + 0.1 M NaOH equi-volume solution, 0.1 M NaOH, 0.5 M NaOH, 1.0 M NaOH and 1.5 M NaOH). Among the evaluated solutions, 1.0 M NaOH solution exhibited high desorption performance and resulted in the nearly complete (99.1%) recovery of ciprofloxacin. This result was explained by the electrostatic repulsions between the negatively charged HAP@Mt surface sites and the anionic form of ciprofloxacin. Moreover, the large amount of hydroxide ions interacting with HAP@Mt disrupted the adsorption bonds and competed with ciprofloxacin for binding sites. After four adsorption-desorption cycles, the ciprofloxacin adsorption efficiency remained higher than 78.5% (Laabd et al., 2021).

Chauhan et al. (2020) evaluated different eluents for desorption of pharmaceutical compounds from the surface of MMT clay pillared with titanium oxide (Ti-PILC). The authors used HCl, HNO₃, NaOH, NaCl, and H₃PO₄ (each with 0.1 N) as desorbing solutions and indicated that NaOH showed the maximum yield for amoxicillin desorption from Ti-PILC. At the end of three successive adsorption/desorption cycles, the reusability efficiency of Ti-PILC for amoxicillin was attained up to 65.2% using 0.1 N NaOH for desorption (Chauhan et al., 2020).

Similarly, NaOH solution (0.1 M) was used for desorption of tetracycline from the surface of raw and thermally activated BENT (Maged et al., 2020). Reuse studies demonstrated that the removal efficiency of tetracycline onto raw BENT was decreased from 50% to 30% after five consecutive adsorption-desorption cycles. This result was explained by the loss of some active adsorption sites after washing with solvent. On

the other hand, percent removal of tetracycline onto thermally activated BENT was slightly decreased from 95% to 83% at the end of five cycles, indicating that thermally activated BENT was successfully regenerated by NaOH application.

Another commonly used desorption reagent is methanol. Zhang et al. (2018) carried out five adsorption-desorption cycles to evaluate the reusability of MMT-biochar (MT-BC) composite after norfloxacin adsorption. For desorption process, methanol solution was selected since the strong H-bond between norfloxacin and methanol facilitated the desorption of norfloxacin. The percent removal of norfloxacin by MT-BC were 86.8%, 88.1%, 87.2%, 87.9%, and 86.5% for the number of regeneration cycle from one to five, respectively (Zhang et al., 2018).

Wang et al. (2019) also used methanol as the desorption reagent for regeneration of magnetic attapulgite-biochar composite (MABC) after oxytetracycline adsorption. Initially, the adsorption capacity of MABC for oxytetracycline was 4.69 mg/g. After five adsorption-desorption cycles it was slightly reduced to around 3.90 mg/g. As a result, MABC exhibited good reusability (Wang et al., 2019).

For the desorption of azithromycin from L-methionine modified MMT K10 (LMP) and aminopropyltriethoxysilane functionalized magnesium phyllosilicate organoclay (AMP), Imanipoor et al. (2021) washed the adsorbents using deionized water, acetone and methanol. Four adsorption-desorption cycles were applied to assess the removal efficiency of azithromycin with regenerated materials. The results showed that azithromycin removal efficiency onto organoclay minerals was still above 92% for the first removal after four cycles. Thus, it was concluded that the organoclay minerals had excellent reusability (Imanipoor et al., 2021).

In summary, different regeneration/reuse methods were evaluated for desorption of antibiotics after their adsorption onto clay based materials. The results of reuse studies are summarized in Fig. 3. The most commonly applied desorption methods include the use of NaOH solution or methanol to wash the adsorbent material. Another effective method is high temperature heat treatment (at 500 °C). However this method should be used with caution since it might alter the structure of the adsorbent (especially composite materials). For example, poly (methyl methacrylate) (PMMA) grafted Na-MMT started to decompose at 345 °C resulting from the thermal degradation of grafted PMMA. On the other hand, Na-MMT degradation occurs at 500 °C due to the dehydroxylation of the clay structure (Bunhu et al., 2017). In another case, cellulose-BENT composite hydrogels were reported to start to decompose at around 200 °C because of the thermal degradation of cellulose in the composite material (Santoso et al., 2019).

4.12. Economic analysis and life cycle assessment

Economic analysis is a crucial element for the implementation of any new technology, including water and wastewater treatment by clay based adsorbents. For full scale applications, cost analysis includes both capital cost (equipment and installation costs), and operational costs (material cost, energy consumption, labor and maintenance costs). For comparative purposes, the material cost for clay based adsorbents are given in Table S6, along with the cost of other common adsorbents.

As can be seen in Table S6, raw clay minerals have usually lower cost than that of the other materials used in the adsorption studies. For MMT the unit price was reported as 40–120 US\$/ton (Khalilzadeh Shirazi et al., 2020), while that of BENT was 74 US\$/ton (Kelly Vargas and Qi, 2019). On the other hand, granular activated carbon (1000 US\$/ton) and CNTs (12,000–90,000) have substantially higher costs depending on the type, quality and grade of the material (Zinicovscaia et al., 2020). For modified and composite materials, the costs related to the modifications (i.e., chemicals and energy consumption) should also be included in addition to the raw material costs. For example the unit price of Ti-PILC was estimated to be 9500 US\$/ton (Chauhan et al., 2020). Unfortunately, the cost analysis for clay based adsorbents used for antibiotic removal is missing in most of the studies. In addition to the

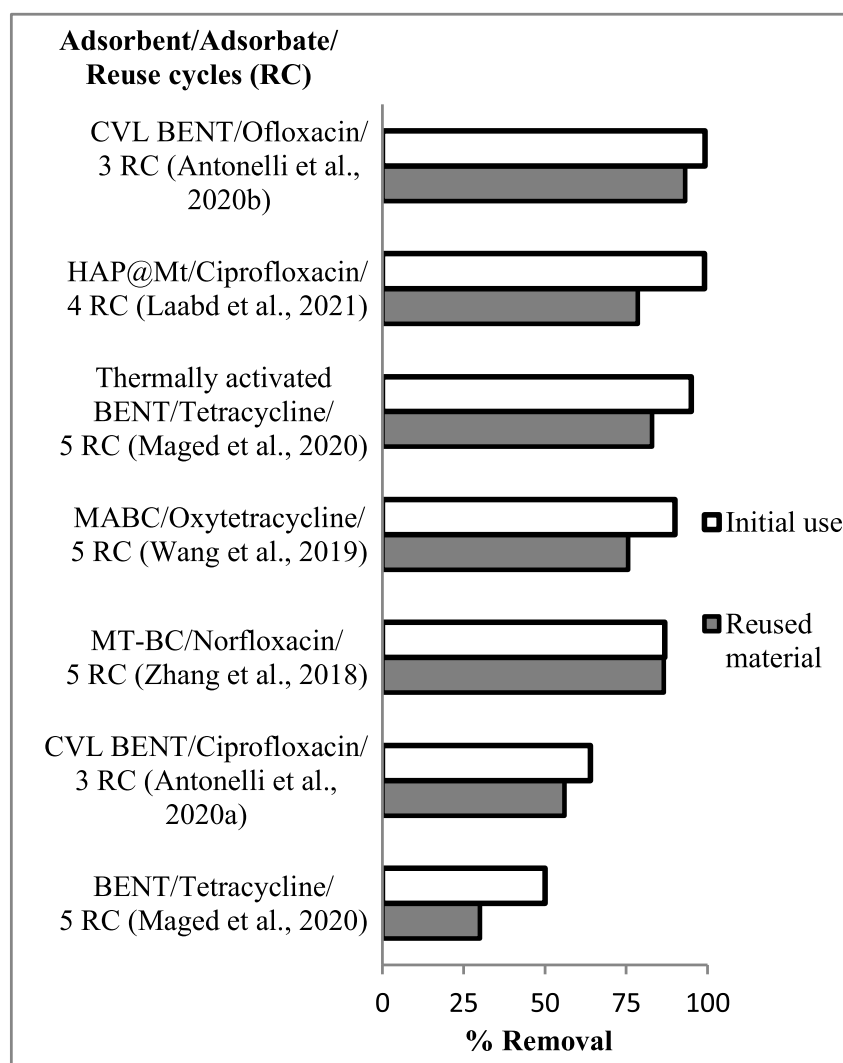


Fig. 3. The results of reuse studies.

direct cost of the material, the reusability of the material, as well as costs related to regeneration and reuse applications including the use of the chemical agents and energy consumption (for example high temperature heating) should also be accounted for the cost analysis.

When compared to the other advanced treatment methods used for antibiotic removal, clay based adsorbents are very promising in terms of high removal efficiency and economic benefits. For example, high antibiotic removal rates (>99%) were reported for clay based adsorbents (Sturini et al., 2016). In a cost efficiency perspective also, the adsorption process with clay based materials is advantageous due to their high availability, low unit price and simplicity in operation. The other alternative processes, such as oxidation and advanced oxidation processes have the drawbacks of high energy cost, chemical requirement and possible formation of toxic by-products, while the membrane filtration requires high pressure application which is expensive and it has difficulties in treating large volumes (Crini, 2006).

Although high removal efficiency and economic analysis are important considerations for selection of treatment alternatives, a complete life-cycle analysis (LCA) is necessary to develop sustainable solutions. Such an analysis is missing in the studies using clays for the removal of pharmaceutical products from aqueous solutions (Thiebault, 2020). As a result, in addition to economic analysis, conducting a complete LCA is recommended for future researches. This will allow the researchers and decision makers to make more comprehensive comparison between different process alternatives and different adsorbent

materials towards the treatment of antibiotic containing wastewater.

5. Concluding remarks and future perspectives

The use of advanced technologies for wastewater treatment is key to reduce the antibiotic load and to protect the environment and human health by reducing antibiotic resistance. In this regard, the use of clay-based materials as adsorbents seems promising for antibiotic removal from water sources, due to their availability, affordability, and the fact that they can be easily modified.

- 1) On the one hand, the synthesis of new clay-based nanocomposites using organocations, biopolymers and metal pillared-clay minerals has shown to highly increase the maximum adsorption capacity due to the introduction of novel additional sites for the binding of antibiotics. The adsorption capacity of clay minerals, both raw and modified, is highly related to the clay mineral properties, the type, size and shape of the contaminant molecules, as well as the operating conditions.
- 2) Other recent studies have proved that the combination of surface-modified clay minerals and thermal treatment, as well as the combining of different adsorbent mixtures such as biochar increase the adsorption capacity. Moreover, composite clay materials with magnetic properties exhibited good separation property and reusability due to their magnetic separation ability. Thermal treatment

can be used to improve the structural properties of clay by reducing expansion in water, increasing mechanical strength, dihydroxylation, and eliminating some impurities in the clay mineral.

- 3) Another future direction of research is the use of hybrid process, where clay adsorption can be used in combination with other technologies including advanced oxidation, membrane filtration and biological processes.

However, there are yet main questions that would need to be answered and conducted in future research:

- 1) Studies at continuous and pilot scale using clay-based materials as well as experiments using real wastewater samples and multisolite systems,
- 2) To include cost-benefit analysis of the use of these adsorbents, including their production and regeneration steps,
- 3) To improve reusability performance of the adsorbents and to develop sustainable waste management strategies for the exhausted materials,
- 4) To conduct a complete life cycle assessment enabling the researchers to understand the environmental impact of proposed adsorbent materials (and related treatment systems) across their life cycles.

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.

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Appendix A. Supplementary data

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