



Clarithromycin as soil and environmental pollutant: Adsorption-desorption processes and influence of pH

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ABSTRACT

Antibiotics pollution is a growing environmental issue, as high amounts of these compounds are found in soil, water and sediments. This work studies the adsorption/desorption of the macrolide antibiotic clarithromycin (CLA) for 17 agricultural soils with different edaphic characteristics. The research was carried out using batch-type experiments, with an additional assessment of the specific influence of pH for 6 of the soils. The results show that CLA adsorption reaches between 26 and 95%. In addition, the fit of the experimental data to adsorption models provided values between 1.9 and 19.7 Lⁿ μmol¹⁻ⁿ kg⁻¹ for the K_F , Freundlich affinity coefficient, and between 2.5 and 10.5 L kg⁻¹ for K_d , distribution constant of Linear model. Regarding the linearity index, n , it varied between 0.56 and 1.34. Desorption showed lower scores than adsorption, with an average of 20%, and with values of 3.1 and 93.0 Lⁿ μmol¹⁻ⁿ kg⁻¹ for $K_{F(des)}$ and 4.4 and 95.0 L kg⁻¹ for $K_{d(des)}$. The edaphic characteristics with the highest influence on adsorption were the silt fraction content and the exchangeable Ca content, while in the case of desorption, they were the total nitrogen, organic carbon, and exchangeable Ca and Mg contents. Regarding the pH, within the range studied (between 3 and 10), its value did not decisively affect the adsorption/desorption process. Overall, the set of these results could be of help to program appropriate measures leading to the retention/elimination of this antibiotic when it reaches the environment as a pollutant.

1. Introduction

Antibiotics, as emerging contaminants, represent a problem with increasing repercussion at the level of different environmental compartments (Aydin et al., 2022; Barreiro et al., 2022; Cela-Dablanca et al., 2022; Conde-Cid et al., 2020; Ghirardini et al., 2020; Mejías et al., 2021; Rodríguez-López et al., 2022). In fact, the use of antibiotics has increased considerably in recent years, and an increase of 200% is expected to be reached by 2030, compared to 2015 (Klein et al., 2018; Yang et al., 2021). Clarithromycin (CLA) is among the most widely consumed antibiotics used in both human and veterinary medicine. Relevant concentrations of this compound have been detected both in soils (Lyu et al., 2020; García-Valverde et al., 2023), and sediments (Yang et al., 2021), as well as in waterbodies (Anh et al., 2021; Lyu et al., 2020; Yi et al., 2019; Zainab et al., 2020; Castaño-Ortiz et al., 2023).

Its marked presence in the environment is due to the use of sludge and effluents from wastewater treatment plants as amendments and irrigation water, respectively. Most treatments applied to wastewater treatment cannot completely remove CLA and other pharmaceutical products; hence, represents a potential risk for water bodies and surrounding soils (Aydin et al., 2022; Castaño-Ortiz et al., 2023). Concentrations of this antibiotic have been reported in the range of 380–1854 ng L⁻¹ in effluents (Baumann et al., 2015; Gevao et al., 2022; Göbel et al., 2005; Tran et al., 2016), and reaching up to 1496 μg kg⁻¹ (dm) in sludge (Aydin et al., 2022; Göbel et al., 2005), due to being excreted in high percentages in faeces and urine. Specifically, in the case of CLA, up to 40% of the ingested dose is excreted in its original form, and 60% as metabolites (Baumann et al., 2015). Therefore, this question represents an environmental challenge due to the increased use of reclaimed waters on agricultural soils as a sustainable alternative for regions with water

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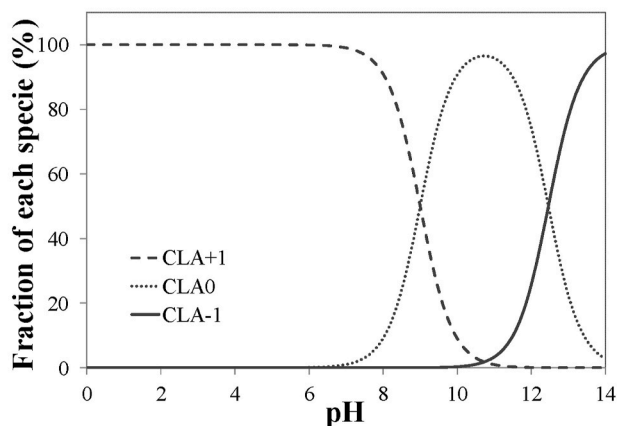
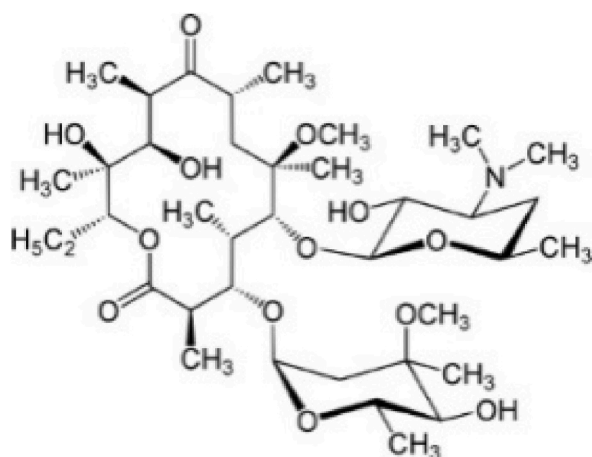


Fig. 1. Clarithromycin (CLA) molecule (on the left) and CLA speciation diagram (on the right) as a function of pH (CLA⁺¹ = cationic species; CLA⁰ = not charged species; CLA⁻¹ = anionic species) (Hosseini et al., 2018).

scarcity, such as the Mediterranean regions (Ben Mordechay et al., 2021; García-Valverde et al., 2023).

Clarithromycin belongs to the group of macrolides, one of the most widely used families of antibiotics, together with penicillins (ECDC, 2021), due to its broad spectrum and efficacy, but in the case of macrolides, and specifically CLA, studies on their behaviour once they reach soils and water bodies as pollutants are scarce. Given that the presence of these compounds in the environment can favour the appearance of resistant genes, which can reach humans through the food chain, it is important to study their evolution once they are released into environmental compartments (Tian et al., 2019; Wang et al., 2023). In addition, as the consumption of antibiotics is also progressively increasing, and is expected to continue to do so due to continued population growth, increasing demand for animal protein and greater access to medicines (Yang et al., 2021), the presence of resistant genes and bacteria is likely to continue to grow, posing a much greater problem in the near future (Wang et al., 2023).

The appearance of resistance genes is partly due to the permanence of antibiotics and their metabolites in the environment, since many antibiotics are not sufficiently altered by degradation and sorption processes. If some of them later reach water and plants, they would enter the food chain.

The processes of adsorption, biodegradation, photo-degradation and/or hydrolysis of antibiotics taking place in soils and water, affect the evolution and fate of these contaminants. Previous studies have shown that the half-life of CLA in water varies between 2 h (Hanamoto et al., 2018; Rodríguez-López et al., 2021) and 10 days (Yi et al., 2019). Once in the water bodies, adsorption-desorption is the main process conditioning the mobility of the antibiotic towards other environmental compartments, because if antibiotics are present in water, they can be retained in the soil, and if this process is strong, they do not move to groundwater (Liu et al., 2019). The adsorption/desorption is affected by edaphic characteristics, as well as by the properties of the antibiotic, such as its degree of hydrophobicity, the electrostatic interactions it establishes with soil particles, and the soil microbial activity (Gworek et al., 2021). In the case of wastewater treatment plants, adsorption processes may also be considered, together with biodegradation, as some of the key factors to control the retention and removal of these organic pollutants (Carballa et al., 2008; Tran et al., 2016).

Specifically, for clarithromycin, all previous adsorption-desorption experiments do not include desorption or the pH variation in the process (Kodesová et al., 2015; Stylianou et al., 2021), so taking into account the above considerations, the main objective of this study is to determine the characteristics of CLA adsorption-desorption processes in agricultural soils with different characteristics, as well as, specifically, to

study the influence of pH in the case of representative soils with variable organic matter content. Overall, the research could contribute to increase the knowledge on the evolution and fate of this antibiotic once it reaches the environment as a pollutant.

2. Materials and methods

2.1. Chemicals

The antibiotic used was clarithromycin (CLA, C₃₈H₆₉NO₁₃, Sigma Aldrich, Barcelona, Spain), with 98% purity. Its molecular weight is 748 g mol⁻¹, and the logarithm of its octanol-water partition coefficient (K_{OW}) is 3.16. It has a relatively low solubility in water (2 mg L⁻¹) and two dissociation constants (pK_a), with values of 9 and 12.46 (Ghirardini et al., 2020; Baumann et al., 2015; Hosseini et al., 2018), being an amphoteric molecule. As it has two pK_a, it exists as a cation, zwitterion, and anion, depending on the pH (Fig. 1). Most CLA molecules have a positive charge under acidic conditions, a neutral charge between pH values of 9 and 12.5, and a negative charge under extreme alkalinity conditions (pH higher than 12.5).

2.2. Soil samples

For this study, 17 agricultural soils were used, devoted to corn and vineyard production. Soil samples were collected at different points in Galicia (NW Spain), at a depth of 0–20 cm, with an Edelman probe. Subsequently, once in the laboratory, they were air-dried, sieved through a 2 mm mesh and stored in polyethylene containers until further analysis.

To determine the particle size content, wet sieving was followed by the Robinson Pipette procedure to separate sand (2–0.05 mm), silt (0.05–0.002 mm) and clay (<0.002 mm). The determination of pH was carried out in water and in 0.1 M KCl (soil:liquid ratio 1:2.5) using a pH meter (Crison, Barcelona, Spain). Total organic carbon and total organic nitrogen were determined using an elemental analyser (Thermo Finnigan 1112 Series NC, Thermo Finnigan, The Netherlands). The effective cation exchange capacity (eCEC) was determined by measuring exchangeable basic cations (Na_e, K_e, Ca_e, Mg_e) and exchangeable Al (Al_e), with the sum of all five being eCEC; to do that, 0.2 M NH₄Cl was used for the extraction of the basic cations (Sumner and Miller, 1996), while 1M KCl was used for Al (Bertsch and Bloom, 1996).

2.3. Adsorption/desorption experiments

Sorption experiments were conducted according to previous

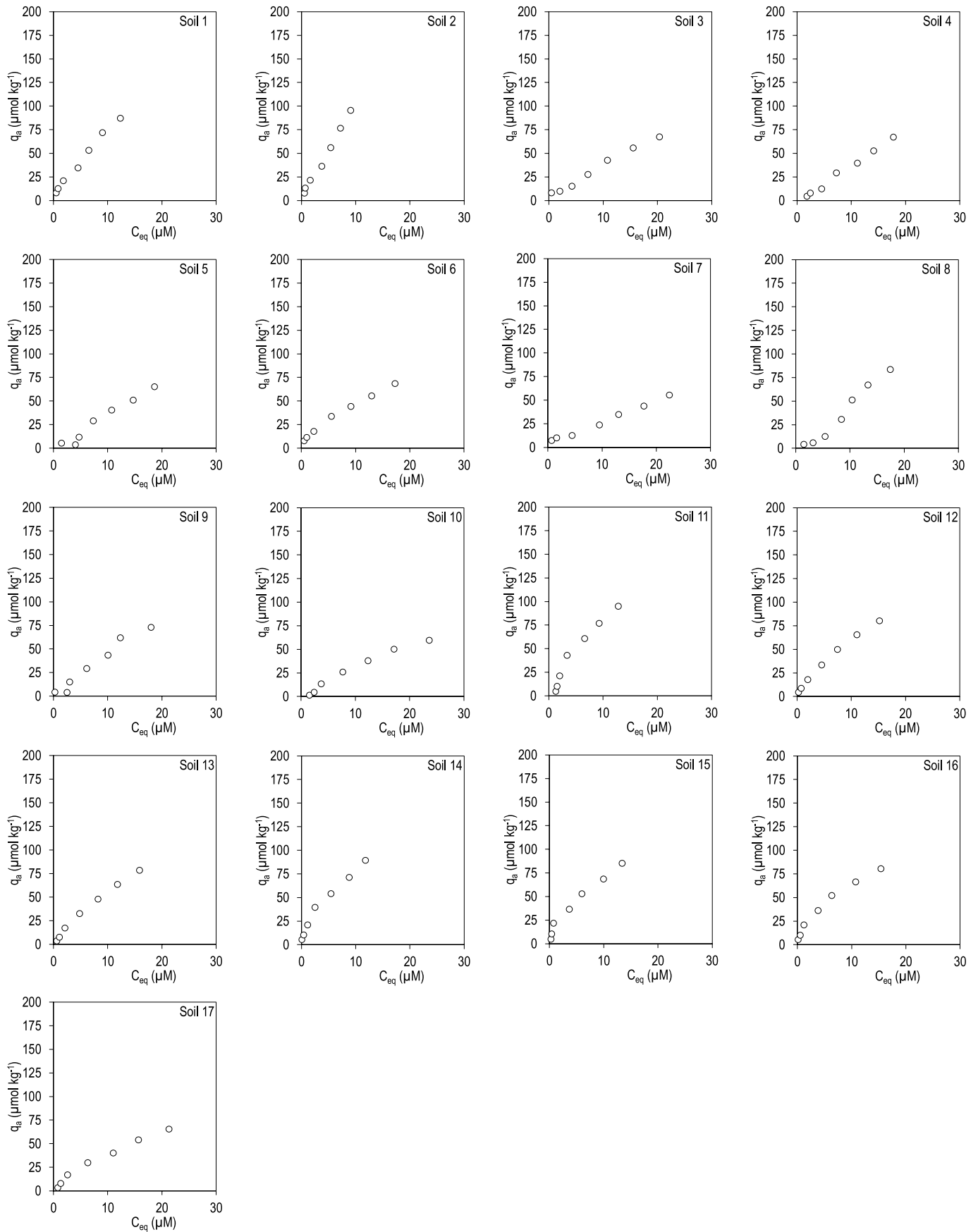


Fig. 2. CLA adsorption curves for the 17 soils studied. C_{eq} (μM): concentration of antibiotic in the equilibrium solution, q_a ($\mu\text{mol kg}^{-1}$): amount adsorbed in the soil. Average values ($n = 3$), with coefficients of variation always lower than 10%.

experiments (Conde-Cid et al., 2019; Álvarez-Esmorís et al., 2020). To carry out the batch-type adsorption experiments, 2 g of soil were weighed in 15 mL centrifuge tubes (Labbox, Spain) and suspended in 5 mL of solutions containing the antibiotic, using 7 different concentrations (2.5, 5, 10, 20, 30, 40, and 50 μM), with 0.005 M CaCl_2 as ionic background electrolyte. These suspensions were shaken at room temperature (25 ± 1 °C) for 48 h in the dark, on a rotary shaker, at 50 rpm. Forty-eight h was selected as stirring time after carrying out studies of the adsorption kinetics and determining that equilibrium was always reached before that time.

At the end of the 48 h of agitation, the samples were centrifuged for 15 min at 4000 rpm in a Rotina 35R centrifuge (Hettich Zentrifugen, Germany), and subsequently filtered through nylon syringe filters (0.45 μm pore size). The filtered samples were transferred to 2 mL Eppendorf propylene vials (Fidherbrand, Spain), and the pH was then measured using a combined glass micro-electrode (Crison, Barcelona, Spain). The antibiotic concentration was quantified in a HPLC chromatographic equipment, also using 2 mL capacity vials.

For studying the desorption process, the remaining samples derived from those previously used in the adsorption experiments were weighed to determine the amount of antibiotic solution contained in the soil, and then these soil materials were re-suspended in 5 mL of 0.005 M CaCl_2 . These samples were shaken for 48 h and later centrifuged and filtered, and then the antibiotic concentration was quantified as in the adsorption phase.

To study the influence of pH on the adsorption/desorption processes, six soils (among the initial 17) were selected, specifically soils 1, 5, 9, 12, 15 and 16. They were selected based on total organic carbon content, as they show a high variability from 1% to 7.67%. The experiment was carried out at different pH values, between 3 and 10, adjusting it with different amounts of 0.5 M HCl and 0.5 M NaOH. The concentration of antibiotic added was 50 μM , with the soil:solution ratio being 2:5 (as in the adsorption/desorption experiment detailed above) and adding 0.005 M CaCl_2 as the background electrolyte. The suspensions were shaken at 50 rpm for 48 h, in the dark, and centrifuged at 4000 rpm for 15 min. Next, the samples were filtered with nylon syringe filters, separating the supernatant, and the remaining solid phase (soil material) being used for studying desorption. In the samples, pH was measured using a combined glass micro-electrode, and the antibiotic concentration was determined by HPLC. Regarding desorption, the remaining soil samples derived from the adsorption process were weighed and re-suspended in 5 mL of 0.005 M CaCl_2 , using the appropriate amounts of HCl or NaOH to maintain the pH conditions of the adsorption step. The samples were shaken, centrifuged, filtered and analyzed as in the adsorption phase.

2.4. Quantification of the antibiotic

To determine the concentration of CLA, a liquid chromatography equipment (Ultimate 3000 HPLC, Thermo Fisher Scientific, Madrid, Spain) was used. The equipment consists of a quaternary pump, an autosampler, a thermostatted column compartment and an Ultimate 3000 series UV detector. Attached to this equipment is a computer with Chromeleon software version 7 (Thermo Fisher Scientific, Madrid, Spain). Chromatographic separations were carried out with a C18 analytical column (150 mm long; 4.6 mm internal diameter; 5 μm particle size) from Phenomenex (Madrid, Spain) and a safety column (4 mm long; 3 mm internal diameter; 5 μm particle size), packed with the same material as the column.

Clarithromycin was quantified as previously indicated (Rodríguez-López et al., 2021). Briefly, the injection volume used for the measurement was 200 μL , and the selected flow rate was 1 mL min^{-1} . The mobile phases used were acetonitrile (Phase A) and 0.025 M potassium monophosphate (Phase B). The dilution gradient was from 5% to 70% for phase A and from 95% to 30% for phase B, over a period of 18 min. The initial conditions were resumed after 2 min and maintained

for 3 min. The total analysis time was 25 min, with a retention time for the antibiotic of 13.6 min. The wavelength used was 210 nm.

2.5. Statistical treatment and data analyses

The data obtained in the adsorption and desorption experiments for the 17 soils were described with the Freundlich and Linear models, which correspond to the following equations:

$$q_a = K_F C_{eq}^n \quad (1)$$

$$q_a = K_d C_{eq} \quad (2)$$

where q_a ($\mu\text{mol kg}^{-1}$) is the amount of antibiotic adsorbed at equilibrium; C_{eq} ($\mu\text{mol L}^{-1}$) is the concentration of antibiotic that remains in the equilibrium solution; K_F ($\text{L}^n \mu\text{mol}^{1-n} \text{kg}^{-1}$) is the Freundlich affinity coefficient; n (dimensionless) is the Freundlich linearity index; and K_d (L kg^{-1}) is the distribution coefficient in the Linear model.

The adjustment of the different models to the experimental data was carried out using the SPSS 15.0 software. In addition, Pearson's bivariate correlations among the adsorption and desorption parameters and the different soil properties were calculated using the SPSS software.

3. Results and discussion

3.1. Soil characteristics

The physicochemical characteristics of the 17 soils under study are shown in Table S1 (Supplementary Material). The pH values in water were between 5.0 and 8.0, being slightly lower in the case of the pH in KCl (between 4.2 and 7.8), which indicates the predominance of negative charges in the soil. Regarding the cation exchange capacity (eCEC), the values were between 5.43 and 42.81 $\text{cmol}_c \text{kg}^{-1}$, with Ca_e cation being dominant in the exchange complex in most cases. Both the organic carbon and the total nitrogen contents showed very variable values, going from 1.0% to 7.7% for carbon, and from 0.11% to 0.63% for nitrogen. Regarding the soil particle sizes, sand was the predominant fraction in all cases, with percentages between 50% and 77%, followed by silt (between 14 and 40%), and finally, clay, which varied between 3% and 8%. The texture of these soils was sandy loam, with the exception of soil 2, which was loam.

3.2. CLA adsorption

Fig. 2 shows the adsorption curves for the 17 soils studied. The curves are type L (Giles et al., 1974), not linear, as pointed out in previous studies on CLA adsorption (Sibley and Pedersen, 2008). In this type of curve, it is shown that at low concentrations of clarithromycin added, the antibiotic/soil interactions are higher than when higher concentrations are added, as indicated by the concave shape of the curves, as well as by the decrease in the percentages of adsorption as the initial concentration added increases. These greater adsorption values at low initial concentrations of the antibiotic indicate the existence of higher affinity for the soil at these low concentrations added (Table S2). The adsorption percentages vary between 26 and 95%, presenting an average of around 69% considering all soils (Table S2).

The adsorption of this antibiotic in the soil can be conditioned by coulombic attractions, that is, electrostatic between soil surface charges and those of the antibiotic (Hanamoto et al., 2018). At the pH values of the soils included in the study (between 5.0 and 8.0), CLA is in cationic form (Fig. 1), with the $\text{NH}(\text{CH}_3)_2$ group being positively charged in the molecule. Tetracycline antibiotics present the same group (Wang and Wang, 2015), although these antibiotics experience higher adsorption on soils. The greater adsorption of tetracyclines compared to macrolides is due to the fact that the latter generally have a lower amount of $-\text{OH}$, $-\text{C}$ and $=\text{O}$ functional groups per unit mass (Wang and Wang, 2015).

Table 1

Parameters resulting from the adjustment of the experimental adsorption data to the Freundlich and Linear models. K_F ($L^n \mu\text{mol}^{1-n} \text{kg}^{-1}$) is the Freundlich affinity coefficient; n (dimensionless) is the Freundlich linearity index; K_d ($L \text{kg}^{-1}$) is the distribution constant in the Linear model; R^2 is the coefficient of determination.

Soil	Freundlich			Linear	
	K_F	n	R^2	K_d	R^2
1	11.7 ± 1.3	0.80 ± 0.05	0.992	7.5 ± 0.3	0.971
2	11.3 ± 1.3	0.96 ± 0.06	0.993	10.5 ± 0.2	0.992
3	5.4 ± 1.0	0.84 ± 0.07	0.985	3.5 ± 0.1	0.972
4	2.9 ± 0.5	1.10 ± 0.07	0.992	3.7 ± 0.1	0.988
5	2.5 ± 1.0	1.12 ± 0.14	0.962	3.5 ± 0.2	0.956
6	10.9 ± 0.4	0.64 ± 0.02	0.999	4.3 ± 0.3	0.907
7	4.1 ± 1.0	0.83 ± 0.09	0.978	2.5 ± 0.1	0.966
8	11.8 ± 2.8	0.83 ± 0.10	0.960	8.1 ± 0.5	0.940
9	1.9 ± 0.8	1.34 ± 0.15	0.974	4.6 ± 0.3	0.938
10	11.1 ± 0.5	0.73 ± 0.02	0.999	5.8 ± 0.3	0.958
11	9.0 ± 0.7	0.79 ± 0.03	0.997	5.3 ± 0.2	0.973
12	5.1 ± 1.6	0.94 ± 0.12	0.966	4.4 ± 0.2	0.965
13	4.1 ± 1.0	0.86 ± 0.09	0.979	2.8 ± 0.1	0.968
14	19.7 ± 1.4	0.60 ± 0.03	0.994	8.2 ± 0.7	0.890
15	17.7 ± 1.8	0.60 ± 0.04	0.989	6.9 ± 0.6	0.887
16	17.6 ± 0.9	0.56 ± 0.02	0.997	6.0 ± 0.6	0.844
17	7.5 ± 0.8	0.71 ± 0.04	0.993	3.4 ± 0.2	0.940

Other authors relate CLA adsorption to different interactions. Specifically, Stylianou et al. (2021) studied the adsorption of this antibiotic on biochar, and the results obtained showed that, in addition to electrostatic interactions, van der Waals forces may be responsible for adsorption. In addition, Wang and Wang (2015) indicated that CLA adsorption was affected by the hydrogen bonds that the antibiotic forms with the polar portion of humic acids.

Table 1 shows the parameters obtained from the adjustments of the experimental data of the current study, indicating that the Freundlich and Linear models satisfactorily describe it, with values for the coefficient of determination (R^2) between 0.960 and 0.999 in the case of Freundlich, and between 0.844 and 0.992 in the Linear model. The Freundlich affinity coefficient (K_F) values vary between 1.9 and 19.7 $L^n \mu\text{mol}^{1-n} \text{kg}^{-1}$, with the highest scores corresponding to soils 14, 15 and 16. In the case of the distribution constant of the Linear model (K_d), the range is between 2.5 and 10.5 $L \text{kg}^{-1}$, with the highest values corresponding to soils 1, 2, 8 and 14 (Table 1). The values obtained for K_d are similar to those previously reported for other macrolides, such as erythromycin, specifically reaching levels of 8.3–0.8 $L \text{kg}^{-1}$ (Deng et al., 2022).

Comparing the values obtained for the Freundlich parameters (K_F , n) with those of other antibiotics, the affinity of CLA is similar to that of trimethoprim (a diaminopyrimidine) or clindamycin (a lincosamide), as reflected in the study by Kodesová et al. (2015). Comparing the K_d values with those of other antibiotics, tetracycline (a tetracycline antibiotic) shows a value of 1093 $L \text{kg}^{-1}$, and it is 591 $L \text{kg}^{-1}$ for norfloxacin (a fluoroquinolone), both indicative of higher adsorption than clarithromycin, while the with value for sulfamethazine (a sulfonamide) is 1.37 $L \text{kg}^{-1}$, indicative of lower adsorption (Pan and Chu, 2016). Therefore, following an order from lower to higher adsorption for different families of antibiotics, the sequence observed is SAs (sulfonamides) < MAs (macrolides) < FQs (fluoroquinolones) < TCs (tetracyclines) (Yang et al., 2021).

Relating the parameters of the models with the edaphic characteristics of the soils, there is a positive and significant correlation between the adsorption constants (K_F and K_d) and the silt fraction, being $r = 0.700$ ($p < 0.01$) for K_F and $r = 0.821$ ($p < 0.01$) for K_d . Both adsorption parameters show a negative and significant correlation with the sand content, with $r = 0.681$ ($p < 0.01$) and $r = 0.762$ ($p < 0.01$), respectively. On the other hand, K_F presents a positive and significant correlation with Ca_e ($r = 0.674$, $p < 0.01$), with soil 14 showing the highest adsorption and highest Ca_e content, results similar to those obtained in another

Table 2

The amount of CLA desorbed at equilibrium ($\mu\text{mol kg}^{-1}$) and desorption percentage (in brackets) for each of the initial concentrations (C_0) used and for each of the 17 soils. Mean values ($n = 3$), with coefficients of variation always less than 10%.

Soil	C_0 ($\mu\text{mol L}^{-1}$)						
	2.5	5	10	20	30	40	50
1	0.3 (3.9)	0.8 (6.2)	2.6 (12.3)	7.5 (21.8)	9.8 (18.4)	12.3 (17.2)	14.4 (16.5)
2	0.1 (1.8)	0.7 (5.3)	1.8 (8.4)	5.7 (15.9)	8.6 (15.5)	10.8 (14.2)	13.4 (14.0)
3	0.2 (1.9)	0.5 (5.2)	2.0 (13.5)	6.7 (24.3)	9.2 (21.5)	11.1 (20.0)	13.2 (19.7)
4	0.2 (4.0)	0.9 (11.1)	2.0 (16.2)	6.5 (22.3)	11.4 (28.8)	16.4 (31.2)	24.5 (36.6)
5	0.2 (4.9)	0.2 (4.6)	1.2 (10.7)	7.9 (27.1)	10.6 (26.3)	13.1 (25.7)	15.89 (24.4)
6	0.3 (3.9)	0.7 (6.1)	1.2 (6.6)	3.2 (9.6)	5.9 (13.3)	12.7 (23.0)	19.1 (28.0)
7	0.0 (0.3)	0.5 (4.8)	1.2 (10.0)	3.8 (16.1)	10.0 (29.0)	15.3 (35.1)	22.6 (40.9)
8	2.9 (72.4)	3.9 (68.3)	5.3 (42.7)	8.9 (29.2)	12.9 (25.3)	16.6 (24.9)	20.0 (24.0)
9	0.3 (6.4)	0.0 (0.2)	1.4 (9.4)	4.0 (13.6)	5.7 (13.2)	8.7 (14.1)	10.9 (15.0)
10	0.2 (14.1)	0.3 (6.3)	2.5 (18.5)	3.8 (14.8)	5.5 (14.7)	8.1 (16.1)	9.5 (16.0)
11	2.1 (45.1)	2.5 (25.0)	3.3 (15.9)	4.7 (11.0)	10.6 (17.5)	13.4 (17.5)	15.1 (15.9)
12	0.9 (19.9)	1.2 (14.6)	2.3 (13.3)	5.8 (17.4)	7.8 (15.6)	10.7 (16.4)	11.7 (14.7)
13	0.4 (11.1)	0.9 (11.9)	2.4 (14.0)	4.9 (15.1)	8.1 (16.8)	10.6 (16.7)	12.9 (16.4)
14	0.1 (1.8)	0.2 (1.9)	0.8 (3.6)	1.6 (4.1)	6.3 (11.7)	12.3 (17.3)	20.3 (22.8)
15	0.3 (5.9)	0.5 (4.5)	0.6 (2.9)	0.8 (2.1)	1.0 (1.8)	2.0 (2.9)	2.1 (2.5)
16	0.2 (4.1)	0.5 (4.8)	0.6 (2.8)	1.7 (4.7)	2.1 (4.1)	2.9 (4.4)	3.1 (3.9)
17	0.8 (25.1)	1.1 (13.5)	2.0 (11.6)	2.0 (6.7)	3.3 (8.2)	4.5 (8.3)	6.4 (9.8)

study on CLA (Kodesová et al., 2015), in which a positive correlation was detected between the adsorption of the antibiotic and the CaCO_3 content of the soil.

The values of the n parameter (the linearity index), are between 0.56

Table 3

Parameters resulting from the adjustment of the experimental desorption data to the Freundlich and Linear models. $K_{F(des)}$ ($L^n \mu\text{mol}^{1-n} \text{kg}^{-1}$) is the Freundlich affinity coefficient; $n_{(des)}$ (dimensionless) is the Freundlich linearity index; $K_{d(des)}$ ($L \text{kg}^{-1}$): distribution constant in the Linear model; R^2 : coefficient of determination.

Soil	Freundlich			Linear	
	$K_{F(des)}$	$n_{(des)}$	R^2	$K_{d(des)}$	R^2
1	11.7 ± 4.2	1.01 ± 0.23	0.932	11.9 ± 0.7	0.932
2	17.7 ± 4.1	0.88 ± 0.16	0.955	14.9 ± 0.8	0.952
3	11.1 ± 3.8	0.91 ± 0.23	0.915	9.8 ± 0.6	0.914
4	13.0 ± 0.7	0.52 ± 0.03	0.994	5.1 ± 0.5	0.808
5	9.1 ± 2.9	0.87 ± 0.19	0.953	7.4 ± 0.4	0.951
6	23.7 ± 1.9	0.38 ± 0.5	0.949	8.0 ± 1.5	0.259
7	16.5 ± 0.9	0.30 ± 0.03	0.972	4.4 ± 0.8	0.203
8	13.0 ± 3.7	0.98 ± 0.18	0.934	12.6 ± 0.8	0.934
9	3.1 ± 0.8	1.47 ± 0.13	0.986	7.3 ± 0.5	0.929
10	12.5 ± 1.7	1.06 ± 0.10	0.986	13.5 ± 0.4	0.985
11	14.6 ± 0.7	0.90 ± 0.03	0.998	12.7 ± 0.24	0.994
12	19.3 ± 1.4	0.79 ± 0.06	0.993	15.0 ± 0.6	0.977
13	14.1 ± 1.2	0.95 ± 0.07	0.991	13.3 ± 0.3	0.990
14	33.6 ± 2.4	0.35 ± 0.04	0.964	10.3 ± 1.9	0.421
15	93.0 ± 10.1	0.95 ± 0.18	0.909	95.0 ± 6.9	0.907
16	57.6 ± 2.5	1.00 ± 0.13	0.972	57.6 ± 2.2	0.972
17	25.4 ± 2.9	0.97 ± 0.15	0.931	24.9 ± 1.6	0.931

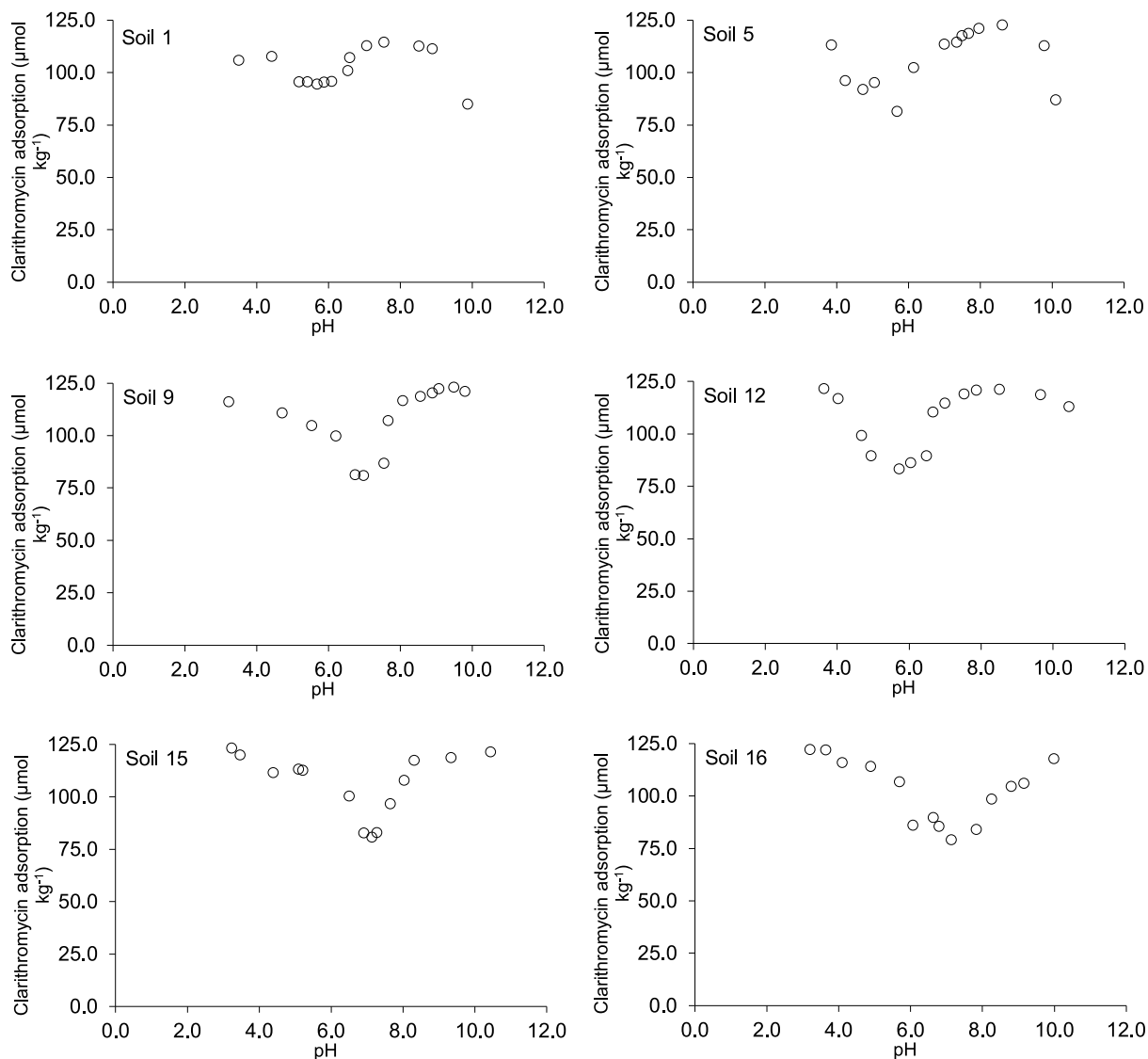


Fig. 3. CLA adsorption in different soils as a function of pH. Average values ($n = 3$), with coefficients of variation always lower than 10%.

and 1.34 (and in most cases are below 1), which indicates the non-linearity and certain concavity of the adsorption curves, as mentioned above, being these n values similar to those obtained Stylianou et al. (2021), with values ranging between 0.9 and 1.29.

3.3. CLA desorption

Fig. S1 shows the desorption curves for the 17 soils studied. These curves represent the amount of CLA that remained adsorbed onto the soil after a desorption cycle ($q_{a(des)}$, $\mu\text{mol kg}^{-1}$) versus the CLA concentration in the equilibrium solution ($C_{eq(des)}$, $\mu\text{mol L}^{-1}$). The slope of these desorption curves is greater than those of the adsorption phase, which indicates that a part of CLA remains adsorbed onto the soil after a desorption cycle. It is observed that, in general, increasing the initial amount of CLA added, the desorption is slightly higher (Table 2). The desorption percentages are below 45% except for soil 8, which presents two values of 72% and 68% in the initial concentrations of 2.5 and 5 $\mu\text{mol L}^{-1}$ added. In general, considering all concentrations and all soils, the average desorption was less than 20%, being similar to that obtained by Wang and Wang (2015) for antibiotics of the same family, such as tylosin (13%).

Table 3 shows the values of the desorption parameters obtained from the adjustment of the experimental data to the Freundlich and Linear

models. In general, both models describe the experimental results satisfactorily since the R^2 values are above 0.909 in the case of Freundlich, and above 0.808 in the case of the Linear model, except for soils 6, 7 and 14, with a very low coefficient of determination. $K_{F(des)}$ shows values between 3.1 and 93.0 $\text{L}^n \mu\text{mol}^{1-n} \text{kg}^{-1}$, and always below 34 $\text{L}^n \mu\text{mol}^{1-n} \text{kg}^{-1}$, except for soil 15 and 16, which have the highest scores. This parameter is positively and significantly correlated with the total nitrogen content (TSN) ($r = 0.704$, $p < 0.01$), with the organic carbon (SOC) content ($r = 0.588$, $p < 0.05$) and with the Ca_e ($r = 0.587$, $p < 0.05$) and Mg_e contents ($r = 0.495$, $p < 0.05$). This indicates that both the organic carbon and nitrogen contents may condition the desorption of the antibiotic, and in the case of soil 8 (with higher percentages of desorption), it may be related to the low level of both soil parameters. In the case of the organic carbon content, the deprotonated superficial carboxyl and hydroxyl functional groups of the organic matter can make it easier for the positively charged antibiotic to be retained and, therefore, the higher the organic matter content, the lower the desorption (Hanamoto et al., 2018).

The $n_{(des)}$ values are in the range of 0.30–1.47, similar to those obtained in the adsorption phase. $K_{d(des)}$ varies between 4.4 and 95.0 L kg^{-1} , at levels higher than those of the adsorption phase and numerically similar to those of $K_{F(des)}$. Furthermore, as occurs with $K_{F(des)}$, $K_{d(des)}$ is positively and significantly correlated with TSN $r = 0.598$ ($p <$

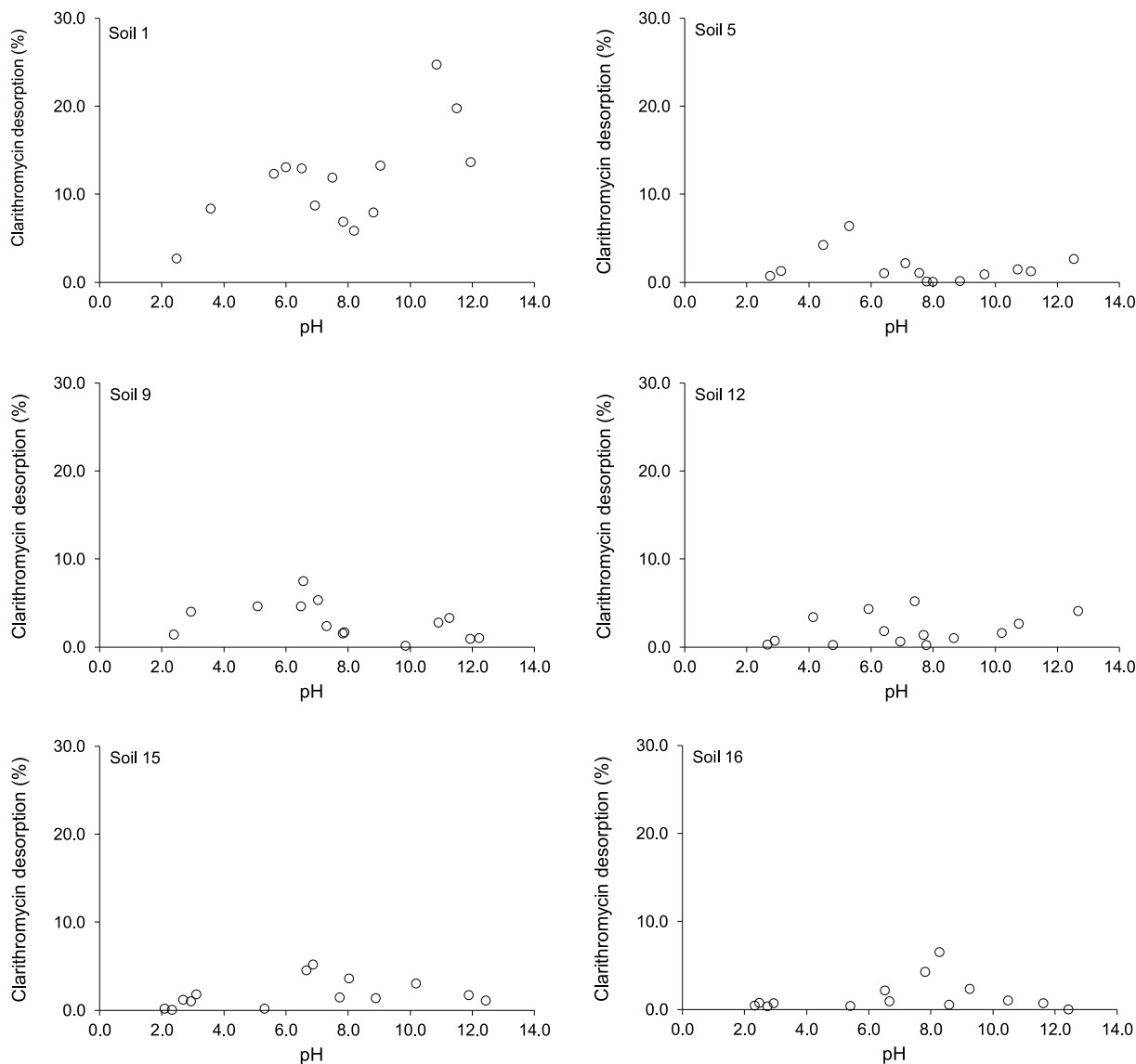


Fig. 4. CLA desorption percentages as a function of pH for the six selected soils. Average values ($n = 3$), with coefficients of variation always lower than 10%.

0.05).

3.4. Influence of pH on CLA adsorption and desorption

Fig. 3 shows the CLA adsorption results as a function of pH. The maximum adsorption is above $120 \mu\text{mol kg}^{-1}$ (except for soil 1, which is $114.5 \mu\text{mol kg}^{-1}$) and the minimum values are between 79 and $85 \mu\text{mol kg}^{-1}$. In general, the adsorption of the antibiotic is low and is not clearly influenced by the pH variation, since, in the pH range studied (between 3 and 10), the molecule is mainly in the cationic form (Fig. 1). A minimum of adsorption is observed between pH 5.0 and 7.0 for all soils, and a maximum of adsorption coincides with the pK_a value at pH 9.0, approximately, except for soils 15 and 16, which is displaced at pH 10. These two soils (15 and 16) have organic carbon concentrations higher than the rest, with levels of 5.56% and 7.67%, respectively. The fact of finding higher adsorption values at that pH may be due to the presence of the zwitterion form of CLA, that is, the antibiotic presents simultaneously positive and negative charges (Fig. 1), facilitating polar interactions with the soil organic matter (Laak et al., 2006).

Compared with other macrolides with different pK_a , the behaviour is different. In the case of tylosin, Wegst-Uhrich et al. (2014) observed that despite having a high molecular weight (as CLA), its behaviour varies,

presenting a maximum of adsorption at pH 5 and later, as the pH increases, the adsorption is lower. This is due to the fact that its dissociation constant (pK_a) is lower (specifically 7.2) than in the case of CLA.

Since CLA has high pK_a values (9.0 and 12.46), under most common environmental conditions, the influence of pH can be ruled out, similar to what occurs with other organic molecules, such as iopromide (a non-ionic iodinated compound) and carbamazepine (an antiepileptic), which also present high pK_a (9.9 and 13.9, respectively) (Carballa et al., 2008).

Regarding CLA desorption, Fig. 4 shows that it presents values below 25% in soil 1, and in the case of the other soils, all values are below 8%. The highest desorption values are situated around pH corresponding to neutrality, between 6 and 8, except in soil 1, which corresponds to pH 10.9.

The desorption values are similar to those obtained with other types of antibiotics, such as doxycycline (a tetracycline) or enrofloxacin (a fluoroquinolone), which present desorption percentages below 10% as pH conditions vary (Álvarez-Esmorís et al., 2022).

The results obtained show that CLA is susceptible to a non-negligible degree of mobility in the soil, since its adsorption presents mean values of around 70% at pH around 6–7, common in a large number of soils. It should be noted that for this antibiotic, it is not foreseeable that eventual pH changes due to agricultural practices will substantially reduce its

transport to different environmental compartments. It is, therefore, necessary to establish measures to increase its adsorption in soils, and minimize its desorption, avoiding their transport to other compartments such as water bodies, where it was found to be one of the antibiotics with the highest ecological risks (Li et al., 2018). However, these measures should take account of soil organisms, such as bacterial communities, since potential changes in soil properties can increase antibiotic toxicity and impact them (Rodríguez-González et al., 2023).

4. Conclusions

The results of this research indicate that the adsorption of the antibiotic clarithromycin in the 17 soils studied varies between percentages of 26 and 95%, with average values of around 70%. The adsorption curves obtained are type L, non-linear, indicating that adsorption is higher at low concentrations added of the antibiotic than at high concentrations. Regarding the parameters derived from the adjustments of the experimental data to the Freundlich and Linear models, both models satisfactorily described the results obtained. The edaphic variables that influence the adsorption are the silt mineral fraction and the Ca_e content. Desorption values are low with respect to adsorption, with mean desorption percentages around 20%. Finally, at the usual ranges in most soils, pH is not a factor that significantly influences clarithromycin adsorption, since the values oscillate in a small interval as the pH increases, possibly because the antibiotic has high pK_a values. These results increase the scarce knowledge regarding the behavior of the antibiotic clarithromycin in different soils, especially about the edaphic variables that influence to a greater extent, the adsorption/desorption processes, and specifically the effect of pH. The overall set of data obtained, together with those that may eventually be derived from future studies including other types of soils, as well as additional details of various kinds affecting the process, could help to predict to what extent the application of different agricultural techniques or specific management practices would affect the mobility and global evolution/fate of the antibiotic and its transport to other environmental compartments. Besides, these data could also help to develop appropriate (bio-)adsorbents for reducing antibiotic mobility in soils, reducing a possible risk to the food web and human health.

Credit author statement

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Statements & declarations

Ethical Approval, Consent to Participate and consent to publish.

Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within the article.

Declaration of competing interest

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

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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