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Translating wastewater reuse for irrigation from OECD Guidelines: Tramadol sorption and desorption in soil-water matrices.

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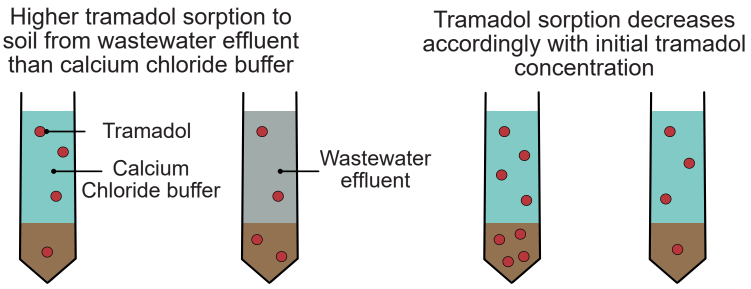
HIGHLIGHTS

- First study of tramadol soil/water partitioning at environmentally relevant conditions.
- Significantly ($p < 0.05$) higher tramadol sorption to soils with higher clay content.
- Tramadol sorption is mainly governed by cation exchange.
- Sorption-desorption hysteresis demonstrates potential tramadol soil accumulation.
- Higher tramadol sorption to soil from wastewater effluent than calcium chloride buffer.

GRAPHICAL ABSTRACT



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ABSTRACT

Treated and untreated wastewater is often used for agricultural irrigation and, despite the many benefits of this practice, it poses the risk of biologically active chemical pollutants (such as pharmaceuticals, like tramadol) entering the environment. The partitioning of tramadol between soil/water at environmentally relevant concentrations is important to understand its environmental toxicity. Kinetics and isotherm sorption studies based on the Organisation for Economic Cooperation and Development (OECD) 106 Guideline were undertaken, ensuring comparability to previous studies. Studies were undertaken in three soils of different characteristics using aqueous concentrations of tramadol from 500 ng L^{-1} (environmentally relevant) to 100 μg L^{-1} (comparable to previous studies). Two of the soils presented a significantly ($p < 0.05$) higher sorption at a lower initial tramadol concentration (5000 ng L^{-1}), compared to 20,000 ng L^{-1}. Hysteresis was observed in all studied soils, indicating the accumulation of tramadol. Higher sorption to soils correlated with higher clay content, with soil/water partitioning coefficients (K_d) of 5.5 ± 13.3, 2.5 ± 3.8 and 0.9 ± 3.0 L kg^1 for soils with clay contents of 41.9%, 24.5% and 7.4%, respectively. Cation exchange was proposed as the main sorption mechanism for tramadol to soils when the pH was below tramadol's pK_a values (9.41 and 13.08). A comparative kinetics study between tramadol in soil/calcium chloride buffer and soil/wastewater effluent demonstrated significantly higher ($p < 0.05$) tramadol sorption to soil from wastewater effluent. This has the environmental implication that clay

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soils will be able to retain tramadol from irrigation water, despite the organic content of the irrigation water. Therefore, our studies show that tramadol soil sorption is likely to be higher in agricultural environments reusing wastewater than that predicted from experiments using the OECD 106 Guideline calcium chloride buffer.

1. Introduction

Tramadol is an opiate widely used since 1995, that provides effective reduction of moderate to severe pain at relatively low risk, in terms of addiction and respiratory depression, compared with other opiates (Gong et al., 2014; Subedi et al., 2019). However, the presence of tramadol in the environment is of concern given its known persistence and effects in terms of acute toxicity (Petrie et al., 2015; Thiebault et al., 2015). About 30% of the tramadol dose is excreted in the urine as the parent drug and the rest is excreted as metabolites (Gong et al., 2014). The widespread use of this drug means that large quantities of unchanged tramadol can be found globally in municipal wastewater influent at concentrations of hundreds of ng L^{-1} (Du et al., 2021; Petrie et al., 2015; Silva et al., 2017) to tens μg L^{-1} (Petrie et al., 2015). Due to incomplete removal in conventional wastewater treatment processes (WWTPs), tramadol is present in effluents at similar concentrations as in the influent (Petrie et al., 2015, 2017; Silva et al., 2017). After wastewater effluents are released to receiving surface waters and undergo dilution and attenuation, tramadol remains at concentrations ranging from <10 ng L^{-1} to >100 μg L^{-1} (Campos-Mañas et al., 2019; Petrie et al., 2017).

Using raw untreated or treated wastewater for irrigation is a widespread global practice (Thebo et al., 2017), and a source for bioactive chemical pollutants (BACs), such as tramadol, to enter the agricultural environment (Carter et al., 2019). Transfer of tramadol from wastewater to soil has been observed, with tramadol having been quantified in Cameroonian soils at 21 ng g^{-1} in the wet season and 1470 ng g^{-1} in the dry season (Kusari et al., 2016). Once in contact with agricultural soil, the sorption of organic pollutants is a determinant factor in the potential for subsequent leaching to groundwater (Llamas et al., 2020; Paz et al., 2016), bioavailability (Goulas et al., 2018; Li et al., 2019) and uptake to plants, which can lead to pollutants entering the food network (Azanu et al., 2018; de Santiago-Martín et al., 2020; Kodesova et al., 2019; Singh, 2021). Sorption to soil is pollutant-dependent (Conde-Cid et al., 2020; Gregg et al., 2015; Kiecak et al., 2019; Li et al., 2020), therefore it is important to generate pollutant-specific data.

Tramadol sorption to soil has been barely studied (Barron et al., 2009; Filep et al., 2021; Stein et al., 2008; Wojsławski et al., 2019) and discrepancies between its behaviour in batch studies and packed column tests have been observed (Wojsławski et al., 2019). In batch tests, it was found to be highly mobile in soils, conversely in packed column studies tramadol was able to bind strongly to non-structured soil (Wojsławski et al., 2019). Discrepancies between batch and column tests can be due to the differing hydraulic conditions and the soil packing itself. However, one way to bridge these discrepancies is to better emulate environmental conditions in batch studies. Bench-scale studies done to date have been at concentration levels higher than those observed in the environment or only at the higher end of those observed in wastewater influent (equating to raw untreated) and effluent (concentration of tramadol in the liquid phase of batch sorption studies of 25–2500 μg L^{-1} (Stein et al., 2008), 125–1000 μg L^{-1} (Barron et al., 2009), 250–10,000 μg L^{-1} (Paz et al., 2016) and 100–5000 μg L^{-1} (Filep et al., 2021)). While the lower range of these concentrations are relevant for countries where raw (untreated) wastewater is used for irrigation (Thebo et al., 2017), they are not so relevant where treated wastewater effluents or surface waters are used for irrigation. Therefore, it is important to perform laboratory scale batch-sorption studies at environmentally relevant concentrations, since sorption is concentration dependent (Paz et al., 2016). This being due to specific interactions between the dissolved contaminants and the functional groups on the soil organic matter, which are dominant at lower sorbate concentrations (Paz et al., 2016).

To address this knowledge gap, this study evaluated several concentrations, at 3 orders of magnitude lower than those previously studied, corresponding to tramadol concentrations reported in surface water (i.e., the lowest concentration studied was 500 ng L^{-1}) (Campos-Mañas et al., 2019; Petrie et al., 2017). Higher initial concentrations of tramadol (the highest was 100 μg L^{-1}) were also studied in order to have an order of magnitude in the range of tramadol concentrations observed in influent and effluent wastewaters (Barron et al., 2009; Filep et al., 2021) as well as in the range of tramadol batch sorption studies published to date. It is important to produce data that is comparable to previous published studies to support meta-analysis, hence obtaining a better understating of the sorption behaviour of tramadol across different studies. Another consideration is the reality that wastewater and surface waters contain many other constituents from BACs, including tramadol, to organic matter and mineral cations, each with the potential to compete for sorption sites in the receiving soil (Chefetz et al., 2008; Conde-Cid et al., 2019; Paz et al., 2016) or able to interact with the sorbate to form complexes with different sorption properties (Krogh et al., 2008). Therefore, the objectives of this paper were to:

i. Provide data on batch sorption of tramadol from water to soils which is comparable to published data for other organic pollutants based on the OECD 106 Guideline, allowing for a more comprehensive understanding of the fate of BACs found in wastewater irrigation systems.
ii. Compare the data obtained using calcium chloride buffer as the aqueous phase, to a more environmentally relevant aqueous phase (wastewater effluent) and an environmentally relevant concentration range of tramadol to better understand its behaviour in the environment.

2. Materials and method

2.1. Chemicals and reagents

Ammonium bicarbonate (≥99%), formic acid (≥99.5%), and HPLC grade methanol, water and acetonitrile were acquired from Fisher (Loughborough, UK). Tramadol analytical standard (>98%, purity) was bought from Sigma-Aldrich (Dorset, England). Anhydrous calcium chloride (>97%, purity) was bought from Sigma-Aldrich (Dorset, England). Tramadol stock solution was prepared by dissolving 4 mg in 4 mL of methanol, and stored at −20 °C. For each experiment an aliquot of this main stock was used to prepare a working stock in the tested aqueous phase at the necessary concentration, ensuring methanol content was below 5%.

2.2. Soils and wastewater effluent characterisation

Three characterised soils (Soil 1, Soil 2 and Soil 3, Table 1) were obtained from Lufa-Speyer (Speyer, Germany). Soil was autoclaved prior to the sorption experiments, and the moisture after autoclaving was determined gravimetrically (Table 1). Wastewater effluent was sampled from Stoke Bardolph WWTP (Nottinghamshire, UK) in July 2021. This process plant serves a population equivalent of ~650,000 and utilises a mixture of conventional and advanced activated sludge. Wastewater samples were filtered through a 1.2 μm microglass fibre filter paper (Fisher, Leicestershire, UK) and characterised (Table 1). Wastewater quality parameters were quantified as detailed in Section

Table 1
Characterised soils (Soil 1, Soil 2 and Soil 3) from Lufa-Speyer (Speyer, Germany) and wastewater effluent characterisation.

MATRIX CHARACTERISTIC	Soil 1	Soil 2	Soil 3	WASTEWATER EFFLUENT (ON DAY CA^{2+} WAS MEASURED)
PH	7.3 ± 0.1	6.2 ± 0.3	7.5 ± 0.1	6.75 (6.99)
CLAY (%)	41.9 ± 2.7	7.4 ± 0.9	24.5 ± 1.8	–
SILT (%)	54.9 ± 1.0	90.3 ± 0.9	73.9 ± 2.0	–
SAND (%)	2.2 ± 0.4	2.4 ± 0.2	1.5 ± 0.4	–
ORGANIC CARBON CONTENT (%)	1.55 ± 0.14	0.66 ± 0.09	1.83 ± 0.25	–
NITROGEN (%)	0.18 ± 0.01	0.08 ± 0.02	0.23 ± 0.02	–
CEC (MEQ/100G)	18.7 ± 1.2	6.0 ± 0.9	17.6 ± 0.9	–
MOISTURE CONTENT AFTER AUTOCLAVING (%)	7.0 ± 1.4	4.9 ± 2.7	9.6 ± 2.3	–
TEMPERATURE (°C)	–	–	–	19.0 (17.3)
TOTAL SUSPENDED SOLIDS (MG L^{-1})	–	–	–	5 (4)
CHEMICAL OXYGEN DEMAND (MG L^{-1})	–	–	–	34.58 (11.6)
TRAMADOL (N GL^{-1})	–	–	–	724.7 ± 20.9
NA (MG L^{-1})	–	–	–	67.4 ± 1.3
MG (MG L^{-1})	–	–	–	22.4 ± 0.4
S (MG L^{-1})	–	–	–	38.9 ± 1.0
K (MG L^{-1})	–	–	–	16.3 ± 0.4
CA (MG L^{-1})	–	–	–	62.9 ± 2.5

S1. The concentrations of BACs and minor cations (concentrations < mg L^{-1}) in wastewater can be found in Table S1.

2.3. Batch sorption experiments set up: kinetics and sorption isotherms

Preliminary work was undertaken to determine the adequate soil/liquid ratio for the sorption tests. In all assays, 1 g of soil and 10 mL of liquid phase (ratio 1/10) were contacted, in compliance with the OECD 106 Guideline recommendations (OECD Guideline for testing chemicals No. 106, 2000). Experiments were undertaken in 15 mL falcon tubes using a horizontal shaker and incubated at 20 °C.

2.3.1. Kinetics and isotherm studies for the three soils using a 0.01 M $CaCl_2$ buffer

For the kinetics experiments, two tramadol concentrations in the liquid phase were tested: 5000 and 20,000 ng L^{-1}. The contact time was set as 1, 2, 3, 7, 24, 48 and 72 h for the lower concentration level, and 0.25, 0.5, 1,3, 7, 24, 48 and 72 h for the higher concentration level. The parallel method was used as recommended by the OECD 106 Guideline (OECD Guideline for testing chemicals No. 106, 2000), consisting of triplicates for each time point prepared in separate falcon tubes and analysed separately.

To obtain the sorption isotherms, the tested concentrations were of 500, 1,000, 5,000, 20,000, 50,000, and 100,000 ng L^{-1}, with each concentration level tested in triplicate. Isotherm samples were analysed after 72 h contact time. Both the kinetics and isotherm studies were carried out for the three soils.

2.3.2. Kinetics study comparing 0.01 M $CaCl_2$ buffer to wastewater effluent as aqueous phase

Kinetics studies to compare sorption of tramadol to soil using 0.01 M $CaCl_2$ buffer solution against wastewater effluent were carried out using only Soil 1. Three different aqueous phases were used: wastewater effluent with the endogenous tramadol concentration of 724.7 ± 20.9 ng L^{-1}, 0.01 M $CaCl_2$ buffer solution with 20,000 ng L^{-1} tramadol, and wastewater effluent with the endogenous concentration of 724.7 ± 20.9 ng L^{-1} plus spiking at 20,000 ng L^{-1}. This study was also performed using the parallel method (in triplicate) and the time spans tested were 0.25, 0.5, 0.75, 1, 24, 48 and 72 h.

2.4. Sample preparation and tramadol quantification

Preliminary mass balances were undertaken to determine there was no tramadol sorption to the tubes and stability tests were carried out to test for tramadol degradation in the aqueous phase within 72 h. A mass balance was carried out to ensure accurate quantification of tramadol in the soil phase by difference, when measuring the tramadol only in the aqueous phase (Section S2). Control samples consisting of the aqueous phase with no soil, in triplicate were analysed for all and used in the calculations as the initial concentration of tramadol in the aqueous phase. After sorption tests, the samples were centrifuged for 8 min at 4000 rpm and 4 °C, then 1 mL aliquot was placed in LC vials and stored at 4 °C until analysis (carried out within 24 h) by LC-MS/MS (Section S3). Where the liquid phase was wastewater effluent, the 1 mL aliquot was filtered through 0.22 μm microglass fiber filter paper (Fisher, Leicestershire, UK) prior to analysis. Any losses of tramadol sorbed on the filter were accounted for by comparing to control samples. Analysis was carried out in a triple quadrupole 1290 Series HPLC-MS/MS, using an Agilent jet stream electrospray ioniser (Agilent Scientific, Cheshire, UK).

The LC-MS/MS method used a C18 Gemini column (3 μm particle size, 110 Å pore size, 100 × 3 mm, Phenomenex, Cheshire, UK) at 50 °C and an injection volume of 10 μL. Mobile phase A was made up of 0.1% formic acid in water and mobile phase B was 100% acetonitrile. The starting mobile phase composition was 95% A and it was ramped to 5% An over 6 min; this composition was kept for 1.6 min, then it was ramped back to 95% An over 0.8 min and then kept at 95% A for 1.4 min. The gradient lasted for a total of 10 min and the flowrate was 0.3 mL min^{-1}. The retention time for tramadol was 2.9 min, and a chromatogram and mass spectra can be seen in Figure S2. The drying gas flow was 7 L min^{-1}, sheath gas flow was 12 L min^{-1}, while the source temperature was 200 °C and the nebuliser pressure was 50 psi. Tramadol was monitored in positive ionisation mode, using multiple reaction monitoring (MRM) mode, with a precursor ion of $m/z = 264.2$ and quantifier and qualifier ions of $m/z = 246.0$ and 58.2, respectively. Fragmentor voltages were 90 and 100 V, collision energies were 4 and 28 eV and the cell accelerator voltages were 7 and 4, for the quantifier and qualifier ions, respectively. The instrumental limit of detection and linearity were 0.02 ng mL^{-1} and 0.9972, respectively. The intra-day and inter-day method precision were 0.6% and 0.1%, respectively. The intra-day accuracy was 99.9%.

2.5. Data analysis

The data from the batch-sorption experiments was analysed using the soil-liquid partitioning coefficient K_d (OECD Guideline for testing chemicals No. 106, 2000), with K_d calculated using Equation (1).

$$K_d = \frac{m}{(1-m)}\frac{v}{s} \tag{1}$$

where m is the fraction of tramadol sorbed onto soil particles, v is the volume of the liquid (mL) phase and s the amount of soil (g) (Durán–Álvarez et al., 2014). Data was fitted to the linearised form of the Freundlich and Langmuir models (Equations (2) and (3)).

$$\log(q_e) = \log K_f + \frac{1}{n}\log(C_e) \tag{2}$$

where K_f is the Freundlich constant or maximum adsorption capacity, $\frac{1}{n}$ is the slope obtained from plotting $\log(q_e)$ against $\log(C_e)$ in the linear range (Singh, 2016), q_e is the equilibrium concentration of the adsorbate in the soil (mg g^{-1}), and C_e is the equilibrium aqueous phase concentration of the adsorbate (mg L^{-1}),

$$\frac{1}{q_e} = \frac{1}{K_L C_{max}} \times \frac{1}{C_e} + \frac{1}{C_{max}} \tag{3}$$

For the Langmuir linearised model, C_{max} is the maximum adsorption capacity and K_L is the Langmuir's isotherm constant showing the sorbate's affinity for the soil.

The apparent hysteresis index (HI) was calculated as detailed in Equation (4):

$$HI = \frac{{q_e}^d}{{q_e}^s} \tag{4}$$

where ${q_e}^d$ and ${q_e}^s$ are the concentration of tramadol in the soil for the desorption and sorption experiments, respectively.

3. Results and discussion

3.1. Mass balance

Stability tests demonstrated no tramadol sorption to the falcon tubes and no tramadol degradation in the liquid phase within 72 h. Control samples (containing no soil) were used to corroborate the initial concentration for all sorption experiments. The results from mass balance experiments (Table S2) demonstrated that it was possible to accurately quantify tramadol in the soil and liquid phases by difference between the tramadol concentration measured in the supernatants obtained throughout the sorption experiment and the initial concentration measured in the control samples.

3.2. Tramadol sorption kinetics using calcium chloride buffer as liquid phase

No significant difference ($p < 0.05$) was observed in the sorption rate at 1 or 0.25 h compared to the tramadol sorption at 72 h for any of the three soils at either concentration level (5000 and 20,000 ng L^{-1}). Thus, the sorption of tramadol was deemed to be fast in the tested soils. However, since variability was observed across the time scale for the sorption at each point (Fig. 1), a 72 h equilibration time was chosen for further work. For Soil 1, sorption equilibrium was observed from 7 h for the lowest initial concentration, and from 24 h for the highest initial concertation (Fig. 1a). In Soil 2, sorption reached equilibrium from 24 h, at both initial concentrations (Fig. 1b). For Soil 3, at the lowest initial concentration, equilibrium was achieved from 24 h, while equilibrium was observed from 48 h for the highest starting concentration (Fig. 1c). Previous results have reported equilibrium of tramadol on soils is achieved after 24 h using 0.01 M $CaCl_2$ as liquid phase (Barron et al., 2009; Stein et al., 2008; Wojsławski et al., 2019).

For Soil 2 and Soil 3 there was a significant difference in the sorption percentage depending on the initial tramadol concentration, with significantly ($p < 0.05$) higher sorption for the lowest initial concentration (5000 ng L^{-1}), compared to that observed when 20,000 ng L^{-1} was the initial concentration (Fig. 1b and c, respectively); this is consistent with that previously reported (Paz et al., 2016). Conversely, sorption of tramadol was not significantly different as a function of the initial concentration in Soil 1 (Fig. 1a). These results indicate high affinity of tramadol to Soil 1, which can be attributed to its high clay and organic carbon contents, resulting in more sorption sites than in Soils 2 and 3. In fact, comparing the sorption kinetics of Soils 1 and 3 (both with similar content of organic carbon), equilibrium was faster in the former, suggesting that clay has a more relevant role in the sorption kinetics than the organic carbon content, while other soil components, such as

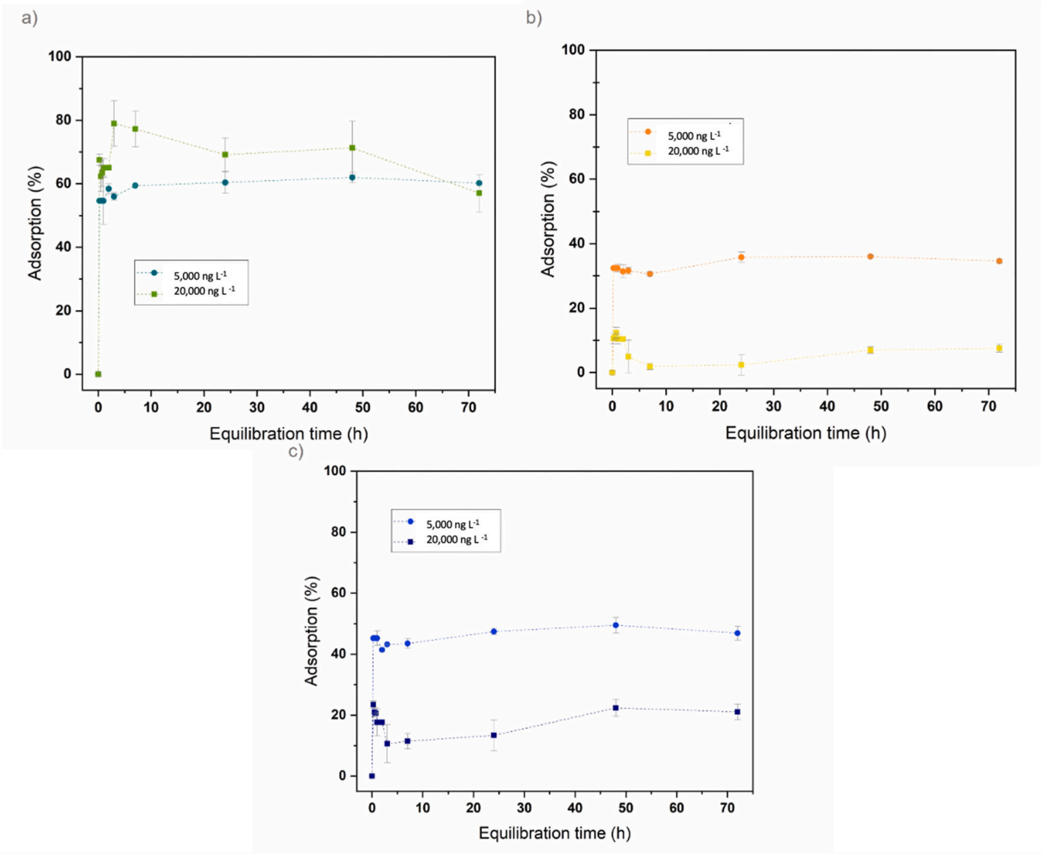

Fig. 1. Kinetics of percentage sorption of tramadol at two initial concentrations: 20,000 ng L^{-1} and 5000 ng L^{-1} to the three soils studied; a) Soil 1, b) Soil 2, c) Soil 3.

sand and silt, have little to no effect in the sorption process.

3.2.1. Tramadol soil affinity depending on soil properties

Higher affinity of tramadol to soil was observed in the order, Soil 1 (pH 7.3) > Soil 3 (pH 7.5) > Soil 2 (pH 6.2) (Table 2). This is to be expected, as tramadol is ionised at the soil pH, given it has a tertiary amide moiety which can gain a positive charge at pH < pK_a (9.41 and 13.08 (Wishart et al., 2017)) (speciation diagram is presented in Figure S3). The pH of the aqueous phase was below tramadol's pK_a and did not vary significantly ($p < 0.05$) during the experiment (Soil 1: 6.9 ± 0.3, Soil 2: 6.7 ± 0.3, Soil 3: 6.8 ± 0.2). As a positively ionised molecule, tramadol can be attracted to the negatively charged organic matter and clay particles, as has been previously reported (Stein et al., 2008; Wojsławski et al., 2019). Higher affinity of tramadol was observed as the clay content increased, as follows: Soil 1 (41.9%) > Soil 3 (24.5%) > Soil 2 (7.4%). The cation exchange capacity of the soils was in the order of Soil 1 (18.7 ± 1.2 meq 100^{-1}) > Soil 3 (17.6 ± 0.9 meq 100^{-1}) > Soil 2 (6.0 ± 0.9 meq 100^{-1}), which also accounted for the order observed for tramadol's sorption affinity to the soils, and is in line with that reported elsewhere (Jolin et al., 2017). Tramadol has been observed to present higher sorption to soils with high organic matter content (Filep et al., 2021; Szabó et al., 2020), due to the capacity of organic matter to retain positively charged molecules via bonding with the –CO. O^- moieties (Filep et al., 2021). Another sorption mechanism for tramadol is partitioning to organic matter, given the organic nature of tramadol (LogP = 1.39 at neutral pH). The benzene ring can readily anchor with the soil organic matter, as occurs with other organic pollutants (Hiller and Šebesta, 2017). In the case of the studied soils, clay content and cation exchange capacity likely have a higher influence on tramadol sorption, whereas the role of organic carbon remains uncertain given that the range of the organic carbon content between the soils is rather narrow (Soil 3: 1.83% > Soil 1: 1.55%, and Soil 2: 0.66%).

3.3. Tramadol sorption-desorption isotherms

3.3.1. Soil-liquid partitioning (K_d values)

The K_d value provides a snap-shot of the ratio of the pollutant in the aqueous phase when equilibrium has been achieved (OECD Guideline for testing chemicals No. 106, 2000). In line with that observed in kinetics studies, the K_d values were in the order Soil 1 > Soil 3 > Soil 2 (Table 2). For Soil 1, K_d were between 5.1 ± 0.4 and 13.3 ± 6.3 L kg^{-1}, whereas for Soil 3 it was between 2.5 ± 0.0–6.0 ± 3.9 L kg^{-1}, and for Soil 2 between 0.9 ± 0.0–3.0 ± 2.1 L kg^{-1}. For Soil 1 and Soil 3, the sorption behaviour was linear, presenting R^2 values above 0.99, indicating that the adsorption sites on the surface of the soil particles were not fully occupied in the range of the initial concentrations tested. On the other hand, a non-linear isotherm was obtained for Soil 2, indicating saturation of adsorption sites. For this soil, the linear range of the sorption isotherm was found when initial concentrations below 20,000 ng L^{-1} were used.

High variability (higher standard deviation between the replicates) in the sorption kinetics and the K_d values were observed for Soil 1, which may be attributed to its higher clay content, compared to Soil 2 and Soil 3. It is known that sorption-desorption equilibrium of pharmaceuticals may be readily achieved with the organic components (presumably occurring through partition), while cation exchange with clay and other mineral components leads to a reversible equilibrium (Strawn, 2021). The K_d values obtained herein are in a similar range to a previous report on a sandy soil, despite the initial tramadol concentration range in this reference being up to four orders of magnitude higher (Wojsławski et al., 2019). However, in the referred study the liquid phase was made up of 0.01 M $CaCl_2$ plus 0.1 g L^{-1} sodium azide and the soil:liquid ratio used was not the same for all soils (Wojsławski et al., 2019), which is not directly comparable to the 0.01 M $CaCl_2$ solution used in the present study. On the other hand, The K_d values obtained herein were an order of magnitude lower than those reported by another study using a silt soil (Barron et al., 2009). The experimental set-up of (Barron et al., 2009) was the same as the present study, so the difference in K_d values highlight the importance of the soil texture on the sorption behaviour of tramadol besides the content of organic matter.

Out of the three soils studied, the desorption of tramadol was the highest for Soil 2 at K_d values of 3.3–9.9 (Table 2), being consistent with the low sorption rate. Considering the low organic carbon and clay contents in Soil 2, tramadol may be sorbed on slit and sand particles through weak interactions, which were rapidly broken when fresh $CaCl_2$ solution was added in the desorption step. For all three soils, higher ($p < 0.05$) desorption K_d values were observed as the initial concentration was increased (Table 2). In the case of Soil 2, the desorption K_d values of tramadol were significantly ($p < 0.05$) higher at concentrations of 20,000 and 50,000 ng L^{-1} compared to those obtained when initial

Table 2

Linear sorption and desorption partitioning coefficient (K_d) and hysteresis index (HI) at 72 h equilibrium in the three different soils tested (Soil 1, Soil 2 and Soil 3).

Initial tramadol concentration in aqueous phase for the sorption experiments (ng L^{-1})	K_d sorption Soil 1	*K_d desorption Soil 1 (Initial concentration in soil phase ng g^{-1})*	K_d sorption Soil 2	*K_d desorption Soil 2 (Initial concentration in soil phase ng g^{-1})*	K_d sorption Soil 3	*K_d desorption Soil 3 (Initial concentration in soil phase ng g^{-1})*	*HI Soil 1*	*HI Soil 2*	*HI Soil 3*
500	6.8 ± 0.3	*2.7 ± 0.2 (1.6 ± 0.0)*	1.8 ± 0.0	*3.3 ± 0.3 (0.6 ± 0.0)*	3.8 ± 0.1	*2.6 ± 0.2 (1.1 ± 0.0)*	*1.03 ± 0.07*	*1.30 ± 0.07*	*1.13 ± 0.06*
1000	9.4 ± 3.7	*2.4 ± 0.1 (2.7 ± 0.1)*	1.0 ± 0.0	*4.1 ± 0.3 (0.7 ± 0.0)*	2.6 ± 0.2	*2.1 ± 0.3 (1.7 ± 0.0)*	*1.15 ± 0.05*	*1.74 ± 0.09*	*1.37 ± 0.12*
5000	13.3 ± 6.3	*2.4 ± 0.2 (16.1 ± 0.1)*	3.0 ± 2.1	*3.4 ± 0.1 (4.4 ± 0.0)*	6.0 ± 3.9	*3.0 ± 0.1 (10.6 ± 0.1)*	*1.11 ± 0.04*	*1.66 ± 0.03*	*1.18 ± 0.02*
10,000	9.8 ± 5.6	-	–	-	–	-	-	-	-
20,000	9.0 ± 6.1	*3.3 ± 0.3 (85.2 ± 0.2)*	1.1 ± 0.4	*11.2 ± 1.0 (25.3 ± 0.1)*	2.8 ± 0.3	*3.2 ± 0.1 (49.5 ± 0.1)*	*0.77 ± 0.05*	*0.45 ± 0.04*	*0.76 ± 0.02*
50,000	5.1 ± 0.4	*3.6 ± 0.5 (176.7 ± 2.0)*	1.4 ± 0.4	*9.9 ± 0.7 (63.2 ± 0.7)*	2.5 ± 0.0	*4.1 ± 0.1 (106.3 ± 1.2)*	*0.73 ± 0.07*	*0.44 ± 0.03*	*0.67 ± 0.01*
100,000	5.5 ± 0.17	*4.7 ± 0.3 (341.6 ± 3.1)*	0.9 ± 0.0	-	2.7 ± 0.0	*6.2 ± 0.3 (207.6 ± 1.9)*	*0.62 ± 0.03*	-	*0.50 ± 0.02*

*Initial concentrations for the desorption experiments are not the same for all three soils, given that the soil which was used for the desorption experiments was the one used for the corresponding initial liquid phase tramadol concentration.

concentrations were in the range of 500 to 5000 ng L^{-1}. For Soil 3, desorption K_d values were significantly ($p < 0.05$) different at the three levels, with the highest values observed at initial concentrations of 50,000 and 100,000 ng L^{-1}, mid-range values for initial concentrations of 5000 and 20,000 ng L^{-1}, and the lowest K_d values for initial concentrations of 1000 and 500 ng L^{-1}. A similar pattern was observed for Soil 1, with higher desorption K_d values at initial concentrations of 20,000–100,000 ng L^{-1}, compared to lower values obtained for initial concentrations of 500–5000 ng L^{-1}. This behaviour could be explained by two phenomena occurring simultaneously: On one hand, the sorption active sites on the soil particles are readily occupied by tramadol molecules, then the remaining molecules form successive layers that are desorbed when fresh $CaCl_2$ solution is added in the desorption step. On the other hand, tramadol molecules can be rapidly sorbed on the organic matter and clay, while the remaining molecules, when initial concentration is high, are weakly adsorbed on sand and silt particles with further desorption (Rytwo, 2004).

Hysteresis indices (HI) of <1 were obtained for the three highest initial concentration levels (20,000–100,000 ng L^{-1}), indicating more sorption than desorption (Table 2). The sorption-desorption hysteresis effect can also be observed in Fig. 2 for all three soils**.** Soil 2 presented the highest desorption rate (Table 2), as expected from its lower clay and organic carbon content. Tramadol displayed higher desorption from Soil 3 compared to Soil 1 for most concentration levels, but this difference was not significant for all the initial concentration levels (Table 2). The hysteresis has an environmental implication regarding the accumulation of tramadol in the studied soils, which can result in higher bioavailability in Soil 2. Considering the low biodegradability of tramadol (Bergheim et al., 2012), along with its moderate water solubility (0.75 g L^{-1}), entering the food network through soil biota or plant uptake could be a plausible environmental fate.

3.3.2. Freundlich and Langmuir isotherms

Sorption data was fitted to the Freundlich model, and the values obtained (Table 3) were consistent with that described in Section 3.3. According to this model, the sorption rate was in the following order: Soil 1 ($K_F = 5.23$ ng g^{-1}) > Soil 3 ($K_F = 2.42$ ng g^{-1}) > Soil 2 ($K_F = 1.00$ ng g^{-1}). Both, Soil 1 and Soil 3, presented R^2 values above 0.99, as opposed to Soil 2 displaying $R^2 < 0.99$ (Fig. 2). The higher correlation indicates that tramadol is adsorbed to soils as a multilayer, achieving the maximum adsorption capacity when high initial concentration levels were tested. The high content of clay of these soils (>20%) favours the Freundlich type adsorption, as has been previously reported for the sorption of cationic organic molecules on clay soils (Stein et al., 2008). For Soil 2, the sorption isotherm reached equilibrium (Fig. 2), indicating the saturation of the active sorption sites, a similar trend was observed for concentrations of up to 4 orders of magnitude above those studied

Table 3
Freundlich and Langmuir isotherm sorption and desorption parameters for initial concentrations of 500–100,000 ngL^{-1} for the three soils studied (Soil 1, Soil 2 and Soil 3) K_F and K_L are the Freundlich and Langmuir sorption coefficients, respectively. 1/n is the non-linearity parameter for the Freundlich isotherm and C_{max} is the maximum sorption capacity in the Langmuir model.

Soil type	Freundlich isotherm parameters			Langmuir isotherm sorption parameters		
	K_F	1/n	R^2	K_L	C_{max} (μg g^{-1})	R^2
Soil 1 sorption	5.23	0.98	0.9974	28.15	5.55	0.9977
Soil 1 desorption	15.26	0.90	0.9956	–	–	–
Soil 2 sorption	1.00	0.96	0.9892	15.40	6.93	0.9988
Soil 2 desorption	2.14	0.74	0.9639		–	
Soil 3 sorption	2.42	0.96	0.9971	20.99	6.03	0.9982
Soil 3 desorption	8.91	0.84	0.9923	–	–	–

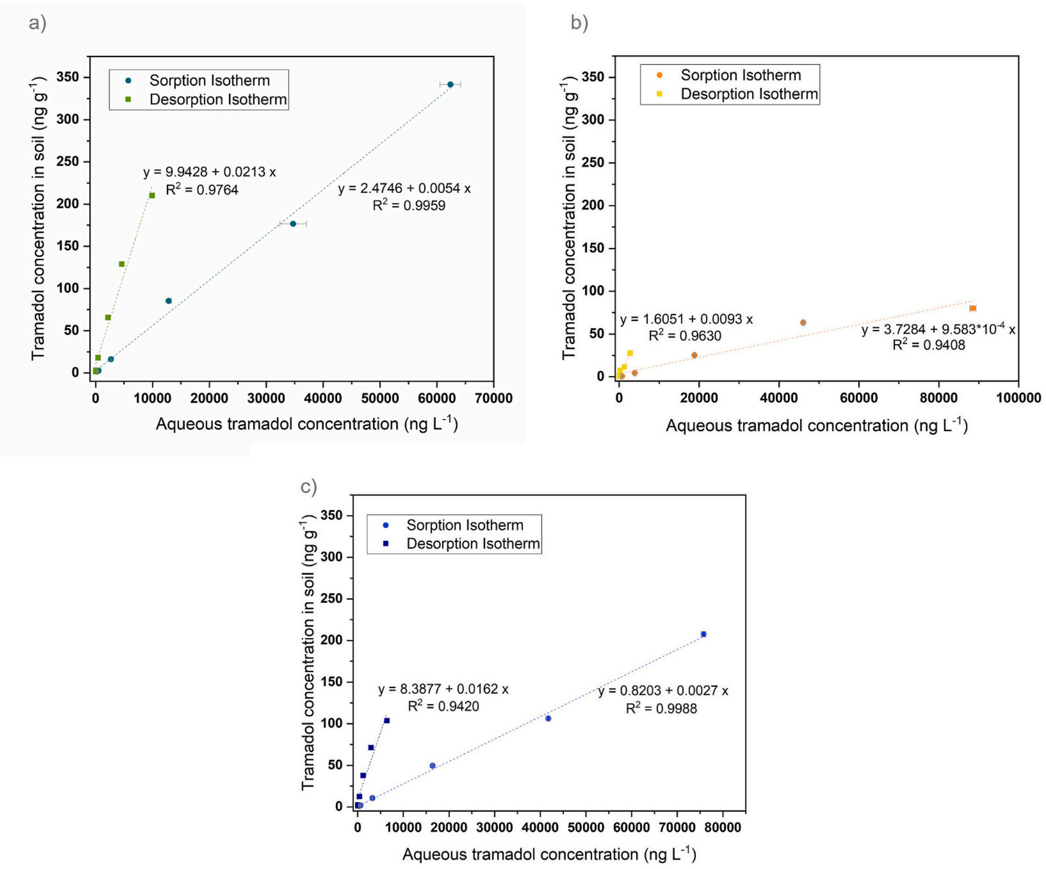

Fig. 2. Sorption and desorption isotherms of tramadol in the three soils studied; a) Soil 1, b) Soil 2, c) Soil 3.

here (Wojsławski et al., 2019).

The Langmuir sorption model presented similar R^2 values to the Freundlich model (Table 3), indicating tramadol's sorption mechanism, in the conditions studied, is also well described by the monolayer adsorption model. Conversely, the Langmuir model did not fit for the tramadol sorption ($R^2 < 0.96$) in a previous study using initial concentrations of at least 3 orders of magnitude above those used herein (Wojsławski et al., 2019), highlighting the importance of studies at environmentally relevant concentrations to identify models that will best describe environmental behaviour.

3.4. Sorption of tramadol using different liquid matrices

Significantly higher ($p < 0.05$) tramadol sorption was observed using treated wastewater spiked with 20,000 ng L^{-1} (52.7 ± 2.2%), compared to that observed using 0.01 M $CaCl_2$ (42.8 ± 2.5%) (Fig. 3). This equates to linear K_d values of 9.2 ± 0.4 L kg^{-1} and 7.5 ± 0.4 L kg^{-1} for spiked effluent and 0.01 M $CaCl_2$, respectively. Competition of Ca^{2+} for sorption sites on clay particles (Jolin, 2016) might be a determinant factor in the sorption of ionised tramadol. The use of 0.01 M of $CaCl_2$ as the aqueous phase, following the OECD 106 Guideline, is equivalent to 400.78 mg L^{-1} of dissolved Ca^{+2}, whereas in the wastewater used in these experiments, the concentration of calcium was 63.86 mg L^{-1} (and in a similar range to previously reported Ca^{2+} concentration in other secondary treated effluent of 74.1 mg L^{-1}) (Chefetz et al., 2008). Even considering the potential competition for sorption sites from the sum of all the major cations in the wastewater, such as sodium and magnesium, these are still lower than the Ca^{2+} concentration in the buffer solution (Table 1). Considering the high load of dissolved organic matter (DOM) in treated wastewater, a decrease in the sorption of tramadol was expected, either through the formation of highly polar tramadol-DOM complexes or because both organic species compete for the active sorption sites. However, the opposite effect was observed, providing evidence on the cationic exchange as the dominant adsorption mechanism. It is likely that in the wastewater/soil system the DOM is adsorbed on the organic domain of soil through partition, while tramadol is adsorbed mainly through cation exchange in the clay and organic matter surfaces. Therefore, in the wastewater/soil system, tramadol has lower competition with dissolved cations than in the $CaCl_2$ solution and thus higher tramadol sorption was observed. This result highlights the value added by comparing the sorption of organic pollutant's under environmentally relevant conditions (i.e., wastewater as the aqueous phase) to standard conditions following the OECD 106 Guideline. Results following the OECD Guidelines have great value in terms of comparison across the literature (allowing for meta-analysis) and acting as a standardised benchmark. Adding environmentally relevant studies for comparison can more accurately explain environmental fate.

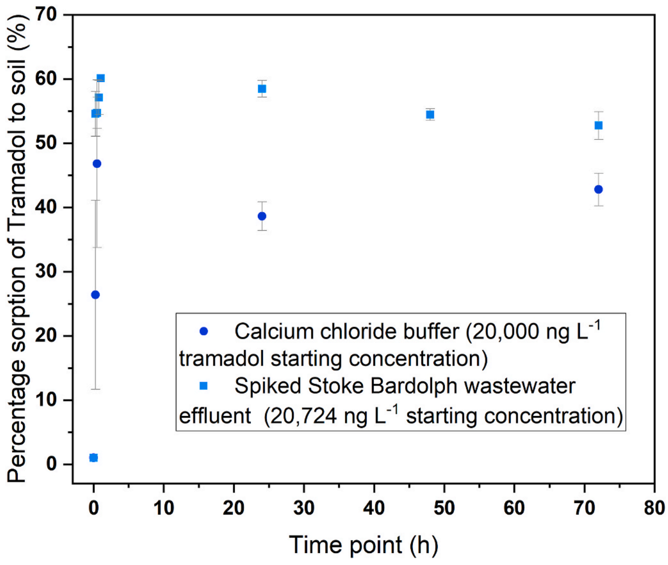

Fig. 3. Comparison of percentage sorption kinetics using two different aqueous phases: wastewater effluent with endogenous tramadol concentration plus spiked concentration equating to 20,724 ng L^{-1} and 20,000 ng L^{-1} tramadol in 0.01 M $CaCl_2$.

Wastewater effluent with and without additional spiking of tramadol to the liquid phase was investigated, equating to low (724.7 ± 20.9 ng L^{-1}) and high (20,724.7 ng L^{-1}) initial concentrations. The higher sorption rate (64.9% ± 1.8, $K_d = 11.3 \pm 0.3$ L kg^{-1}) of tramadol to soil when using treated wastewater effluent with an endogenous tramadol concentration (no additional spiking), compared to the sorption rates determined in spiked wastewater effluent is consistent with that observed using $CaCl_2$ buffer; lower initial concentration of tramadol means more adsorption sites available on the soil surface (Figs. 3 and 4). For the $CaCl_2$ buffer system, higher coefficients of variation (CVs) were observed at the initial 0.25 and 0.5 h times (55.7 and 27.9%, respectively), compared to the CVs at the same time points in the wastewater/soil system (<6.5%). The higher CVs observed in the $CaCl_2$/soil system at time points <1 h may be due to the competition taking place between Ca^{+2} and the positively charged tramadol, further supporting the stronger role of cation exchange as the main sorption mechanism for tramadol when it is at a pH lower than the pK_a (see Figure S3 for speciation diagram).

The pH of the 0.01 M $CaCl_2$ buffer did not vary significantly ($p < 0.05$) over the 72 h sorption tests, with an average of 7.20 ± 0.05. Conversely, the pH of the wastewater effluent increased from 6.75 at time 0 h to 7.40 ± 0.10 at 72 h for samples contacted with soil, and to 7.65 ± 0.10 for control samples where no soil was added. The increase of pH in the soil/wastewater systems could be attributed to degradation and partitioning of the DOM to the soil (Wang et al., 1998). This increase of pH in the wastewater leads to the deprotonation of some tramadol molecules, even when the pK_a value was not surpassed, more neutral tramadol molecules occurred in the soil/wastewater system when compared with the soil/$CaCl_2$. In this scenario, at pH values close to 7, partitioning to the soil organic matter would be happening, along with cation exchange, which is supported by the higher K_d value observed in the soil/wastewater system.

4. Conclusion

The results from this work demonstrate that the dominant sorption mechanism for tramadol to loam soils is ionic interactions with negatively charged particles when the pH of the soils and aqueous phase is below the pK_a value of tramadol. Increased affinity of tramadol was found in soils with higher clay content (which is negatively charged), and tramadol also presented a fast <1 h sorption equilibrium under the conditions studied. Furthermore, higher tramadol sorption to soil was observed from wastewater effluent than from calcium chloride buffer (as per OCED 106 Guideline), demonstrating higher competition from calcium ions in the buffer than from dissolved organic matter in wastewater. This observation demonstrates tramadol's sorption to soil is predominantly due to cation exchange rather than hydrophobic partitioning. This has the environmental implication that clay soils will be able to retain tramadol from irrigation water despite the organic content of the irrigation water. The lower hysteresis observed for clay soils reinforces this observation in that high retention of tramadol will be achieved in clay soils. This work demonstrates the importance of environmentally relevant conditions in batch sorption studies for bioactive chemical pollutants to better understand their sorption mechanism and their environmental fate.

When error bars cannot be seen it is because the marker is larger than the bars.

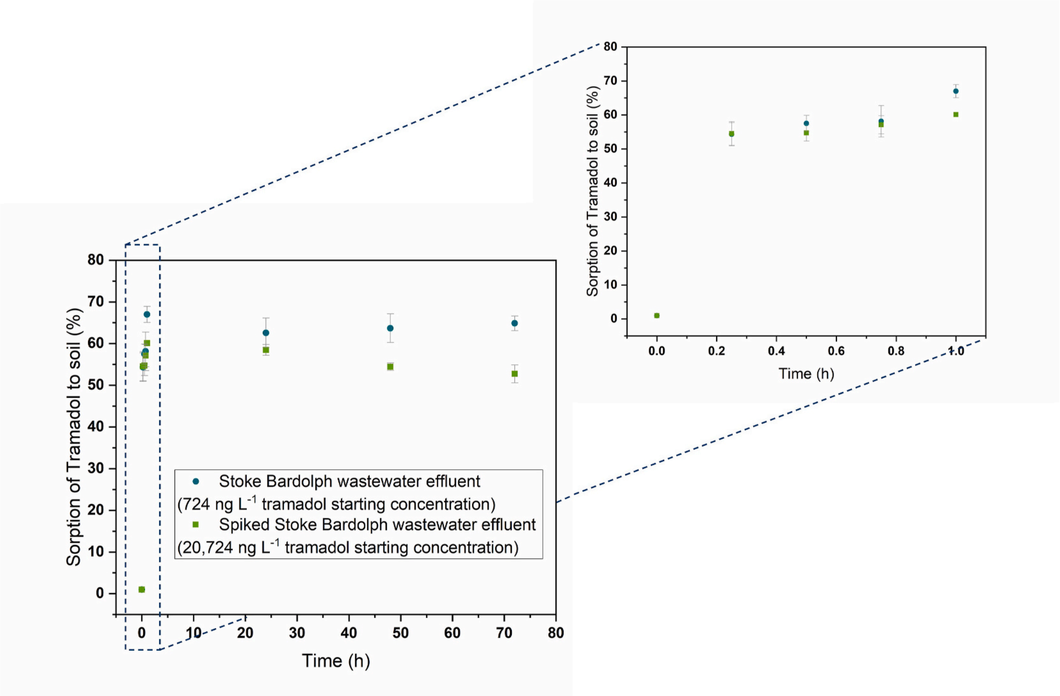

Fig. 4. Comparison of percentage sorption kinetics with two different aqueous phases: wastewater effluent endogenously containing 724 ng L^{-1} tramadol and wastewater effluent with endogenous tramadol concentration plus spiked concentration equating to 20,724 ng L^{-1} of tramadol.

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Credit author statement

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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

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2022.135031.

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