Hydroxychloroquine Adsorption in Aqueous Medium Using Clinoptilolite Zeolite

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Received: 28 March 2022 / Accepted: 13 July 2022 / Published online: 18 July 2022
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Abstract The presence of drugs on a large scale in aquatic matrices raises concern and requires the study of efficient technologies to remove these compounds. This study investigated the adsorption capacity of the natural zeolite clinoptilolite (CP) in removing the drug hydroxychloroquine (HCQ). Zeolite was characterized by BET, XRD, FT-IR, SEM, and pH\text{pzc} techniques. The kinetic model that best fits the experimental data was the pseudo-first-order and the SIPS isotherm provided the best fit. The Langmuir isotherm RL separation factor (>0.01) indicated that the adsorption process was favorable and the Freundlich isotherm (n>1) suggested that the adsorption mechanism occurred mainly by physisorption, with intraparticle diffusion as the step limiting the process. The process was spontaneous (ΔG\text{ads}<0), endothermic (ΔH\text{ads}>0), and with increased randomness at the solid-solution interface (ΔS\text{ads}>0). The initial pH variation of the effluent was not favorable for the adsorption process and the zeolite was easily regenerated for later use. The ecotoxicological tests with Artemia salina and Lactuca Sativa proved that the final effluent did not show toxicity after the adsorption treatment. Based on the results obtained in this work, clinoptilolite zeolite is a potential adsorbent for reducing HCQ toxicity in aquatic matrices.

Keywords Pandemic · Kinetics · Isotherm · Bioindicators · Emerging pollutant · Water treatment

1 Introduction

The presence of pollutants in environmental matrices is a reason for constant concern in the scientific community (Besha et al., 2017), in particular, the compounds known as emerging persistent pollutants, which encompass a range of compounds such as herbicides, hormones, and drugs and are considered a threat to the environment (Daughton, 2004).

Among these compounds, hydroxychloroquine (HCQ) attracts significant attention since it is widely used for treating diseases such as malaria, rheumatoid arthritis, and systemic lupus (Haque et al., 2008; Lee et al., 2011; Price et al., 2014). In addition, due to the negative impacts generated by the global pandemic caused by COVID-19 and the search for a cheap and efficient treatment for the disease, HCQ was tested in the treatment of COVID-19, and its use was allowed by medical organizations in the treatment of illness for certain hospitalized patients (Cortegiani et al., 2020; Gao et al., 2020). However, the use of HCQ for...
the treatment of COVID-19 is hypothesized, and its effectiveness against SARS-CoV-2 infection has been questioned by several studies (da Luz et al., 2021; Ghazy et al., 2020).

Once HCQ has a high potential to persist, bioaccumulate, and transfer to living organisms, even in small quantities, the concern becomes greater, given the large amount of wastewater contaminated with hydroxychloroquine, which can reach aquatic matrices, persisting in the environment and causing damage to living beings (Dabić et al., 2019; Gosu et al., 2016; Howard and Muir, 2011; Ramesh et al., 2018). This perspective leads to studying efficient and low-cost processes that can eliminate these compounds (Nippes et al., 2021).

In this context, the adsorption process is a promising alternative, recognized by the Environmental Protection Agency as one of the best technologies available for removing organic and inorganic pollutants from water as it is a process with high efficiency and smooth operation (Serna-Carrizales et al., 2021). However, to achieve adequate efficiency, it is necessary to use a low-cost adsorbent with an affinity for removing the contaminant. Considering this scenario, natural clinoptilolite zeolite is a prominent alternative for application in adsorption processes, such as for HCQ removal, due to its appreciable characteristics, such as textural properties with large internal surface, and due to its crystalline structure and promising adsorption capacity, in addition to its high availability and therefore low cost. In addition, it can be applied naturally without needing treatments (Davaranah et al., 2020; Pandey et al., 2020).

Therefore, given the problem presented concerning water contamination by HCQ, and the urgency of seeking efficient alternatives for its removal, it is essential to investigate the HCQ adsorption process on the natural zeolite clinoptilolite evaluating the main aspects of the process. In addition, studies related to the removal and destination of HCQ in water are still scarce. Da Silva et al. (2021) studied the photocatalytic degradation of HCQ in aqueous solution, while the authors Bensalah et al. (2020) evaluated the electrochemical oxidation of HCQ and Bendjeffal et al. (2021) assessed the adsorption processes with different adsorbents to eliminate HCQ from water. Inspired by these studies, this work aimed to contribute to removing HCQ and reducing its toxicity in aqueous media, applying clinoptilolite zeolite as an adsorbent. To evaluate the toxicity of the effluent containing HCQ, bioindicators widely disseminated in the literature, *Artemia Salina* and *Lactuca Sativa*, were used.

## 2 Material and Methods

### 2.1 Material and Used Chemicals

Clinoptilolite (CP) natural zeolite was provided by the company Celta Brazil located in Vila Jovina—Cotia/SP, 06,705–150. CP is mainly composed of SiO$_2$ and Al$_2$O$_3$. Before the experimental tests, the zeolite was washed with deionized water, dried in an oven, and sieved (0.4–1.0 mm). Hydroxychloroquine (HCQ) (>98%) was obtained from Sigma-Aldrich. Reverse osmosis water was used to prepare the solutions.

### 2.2 Adsorbent Characterization

The CP was characterized by textural analysis through N$_2$ physisorption at 77 K, using Micromeritics, model: ASAP 2020. X-ray diffraction was performed on a Bruker diffractometer, with CuKa radiation, 40 kV, 30 mA; a step size of 0.01° 2θ; and a scanning speed of 2.0° 2θ/min, in the range 5–65°. Infrared spectroscopy (FTIR) analysis was performed in a Bruker–Vertex 70 spectrophotometer in the range of 4000 to 400 cm$^{-1}$ with 100 scans and 4 cm$^{-1}$ resolution with KBr as reference. CP morphology was observed using a Shimadzu SS-550, Superscan, Superscan SS-550 software scanning electron microscope. The pH$_{pzc}$ was determined by the potentiometric method in which 0.20 g of material is added in solutions with pH ranging from 2 to 12 and kept under stirring for 24 h at 25 °C. After 24 h, the samples were filtered and their final pH was analyzed with a pHmeter. The initial versus final pH is plotted and pH$_{pzc}$ corresponds to the range in which the final pH remains constant.

### 2.3 Adsorption Experiments

The adsorption experiments were carried out in batch mode, using a shaking table (Shaker Cientec CT/712R) with a stirring speed of 200 rpm; temperatures of 298, 303, and 308 K; 50 mL of hydroxychloroquine synthetic solution as adsorbate at a

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concentration of 20 mg L\(^{-1}\); and 0.1 g of CP zeolite as adsorbent. The aliquots of each experiment were filtered using a stainless-steel holder support, holder type, and 0.22 µm membranes supplied by Millipore. The spectrophotometric analyses were performed on a Shimadzu UV–VIS spectrophotometer, model UV-1800, using the calibration curve obtained at different concentrations of HCQ and read through the absorbance at the maximum wavelength of 343 nm (Kargar et al., 2021) and determined by its respective calibration curve. The adsorbed amount was determined by the difference between the final and initial concentration of HCQ using Eq. 1.

\[
q_t = \frac{(C_0 - C_e) \cdot V}{m_a}
\]  

where \(q_t\) is the amount adsorbed per gram of adsorbent at equilibrium (mg g\(^{-1}\)), \(C_0\) is the initial concentration of adsorbate (mg L\(^{-1}\)), \(C_e\) is the concentration of adsorbate at equilibrium (mg L\(^{-1}\)), \(V\) is the volume of solution (L), and \(m_a\) is the mass of adsorbent (g).

2.4 Adsorption Kinetics

The adsorption kinetics was determined using a volume of 50 mL of solution with a concentration of 20 mg L\(^{-1}\) of HCQ and a mass of 0.1 g of zeolite, with the removal of aliquots at time intervals (0, 15, 30, 45, 60, 90, 120, 150, 180, 210, 240 min) until the process is reached equilibrium. To calculate the thermodynamic parameters, the temperature used was 298, 303, and 308 K. The experimental data were applied to the adsorption kinetic models in Table S1. Based on these models, the kinetics that best fits the HCQ adsorption process on CP was defined.

2.5 Adsorption Isotherms

The adsorption isotherms were determined using 50 mL of HCQ solution at 1, 3, 5, 7, 10, 13, 15, 17, and 20 mg L\(^{-1}\); mass of 0.1 g of zeolite CP; and temperatures of 298, 303, and 308 K to obtain thermodynamic parameters. The contact time was determined by adsorption kinetics, in which the equilibrium was reached in 240 min. The results obtained were fitted to the isotherm models present in Table S2.

2.6 Temperature Effect

To evaluate the effect of temperature on the adsorption process of HCQ on zeolite CP, adsorption tests were carried out at three temperatures (298, 303, and 308 K) and thus the thermodynamic parameters of adsorption enthalpy (\(\Delta H_{\text{ads}}^o\)), adsorption free energy (\(\Delta G_{\text{ads}}^o\)), and adsorption entropy (\(\Delta S_{\text{ads}}^o\)) were determined. These parameters allow the understanding of some characteristics relevant to the final state of the system, if the process is favorable or not from the thermodynamic point of view and the spontaneity of the system and if the adsorption occurs with absorption or release of energy. Thermodynamic parameters were calculated according to Eq. (2).

\[
\ln K_d = -\frac{\Delta H_{\text{ads}}^o}{R} \frac{1}{T} + \frac{\Delta S_{\text{ads}}^o}{R}
\]  

where \(K_d\) is the adsorbate distribution coefficient (L/g). A graph (ln \(K_d\)) versus (1/T) gives a linear relationship, with slope equal to (−\(\Delta H_{\text{ads}}^o\)/R) and linear coefficient (\(\Delta S_{\text{ads}}^o\)/R). When the enthalpy or heat of adsorption value (\(\Delta H_{\text{ads}}^o\)) and entropy variation (\(\Delta S_{\text{ads}}^o\)) is known, the free energy (\(\Delta G_{\text{ads}}^o\)) is calculated using the thermodynamic relationship shown in Eq. (3).

\[
\Delta G_{\text{ads}}^o = \Delta H_{\text{ads}}^o - T \Delta S_{\text{ads}}^o
\]  

The activation energy was estimated by the Arrhenius equation that relates the dependence of the speed constant as a function of temperature, as described in the linear form of Eq. (4).

\[
\ln(k_c) = \ln(A) - \frac{E_a}{RT}
\]

where \(k_c\) is the kinetic constant, which the best order represents the experimental data; \(A\) is a pre-exponential factor (min\(^{-1}\)); \(E_a\) is the activation energy (J mol\(^{-1}\)); \(R\) is the universal gas constant (8.31441 J K\(^{-1}\) mol\(^{-1}\)); and \(T\) is the temperature (K).

2.7 pH Effect

To evaluate the influence of pH on the adsorption process of HCQ on zeolite CP, 50 mL solutions were prepared with a concentration of 20 mg L\(^{-1}\) of HCQ with a mass of 0.1 g of CP, pH ranging from 2, 4, 6, natural, 8, and 10 to 12, with a contact time of
240 min and a temperature of 298, 303, and 308 K. The pH was obtained in a pH meter of the Bel brand and the pH of the solution was adjusted to the desired value using HCl (0.1 M) or NaOH (0.1 M).

2.8 Reuse of CP Zeolite

To evaluate the efficiency of zeolite CP in successive adsorption cycles, reuse tests were performed. After the adsorption experiments, the CP zeolite samples were filtered and washed with deionized water and then dried in an oven at 100 °C for 16 h. The CP zeolite was then reused in the adsorption process without adding adsorbent to repair losses during the process. The reuse was repeated ten times.

2.9 Toxicity Test

The guideline for hatching Artemia salina cysts followed the precursor methodology of Meyer et al. (1982), in which the cysts were incubated in synthetic seawater (35 g L\(^{-1}\)) for 48 h at 28 °C with constant light exposure and aeration. After hatching, the most active organisms were separated from the cysts that did not hatch using a light beam directed at these organisms for over 24 h. For toxicity tests, ten larvae of Artemia salina were transferred using a pipette to a multi-well plate containing 35 g L\(^{-1}\) saline solution and 1 g L\(^{-1}\) of potassium dichromate in five different concentrations (0, 10, 20, 40, and 60 mL), which correspond to the control plate, and ten more larvae which were added to another multi-well plate containing 35 g L\(^{-1}\) saline solution prepared with a sample to be tested in six different concentrations (0, 0.1, 0.3, 0.7, 1, and 2 mL), which correspond to the sample plate. The plates were kept for 24 h in the dark and the tests were performed in triplicate. The mortality of the nauplii was assessed and when the rate was greater than 50%, it was possible to determine the LC\(_{50}\) from the Reed-Muench graph (Fig. S2. and Fig. S3. in Supplementary Materials). The test was considered valid if mortality in control did not exceed 10%.

To germinate the seeds of Lactuca sativa, the USEPA (1996) guideline was followed. Ten seeds were placed under filter paper prepared in Petri dishes. Three milliliters of treated effluent, without dilution, was added to the plate. Negative control was performed with distilled water and positive control with three different concentrations of sodium chloride (2 M, 1 M, 0.5 M). The plates were left in the dark for 120 h at 25 °C. The tests were considered valid when the germination of the seeds of the negative control is equal to or greater than 65% and the roots reach at least 5 mm. After 120 h of exposure, the number of germinated seeds was counted and the length of the roots was measured with the aid of a scale. The relative germination rate (RGR) was calculated using Eq. (5), taking into account the ratio of the number of germinated seeds to the total number of seeds and the relative length rate (RLR) was calculated using Eq. (6), considering the ratio of the average root length of the samples to the average root length of the control plate.

\[
RGR = \frac{n^\circ of \text{germinatedseeds}}{n^\circ \text{totalseeds}} \times 100
\]

\[
RLR = \frac{\text{averagerootlength}}{\text{meanrootlengthinthecontrol}} \times 100
\]

3 Results and Discussion

3.1 Adsorbent Characterization

The morphology of the natural zeolite sample CP, raw and after the adsorption process, can be seen in Fig. 1 (a) and (b), respectively. The results show that the natural zeolite CP has an irregular and heterogeneous surface with a rocky appearance and an apparently rough texture. The presence of pores on the zeolite surface is noticeable, which is desirable for the adsorption process. Furthermore, the images indicate that the natural zeolite CP is highly crystalline, confirmed by XRD analysis. The micrograph after the adsorptive process did not show significant changes, which corroborates the result of the mechanism proposed by the work.

The physical properties of the zeolite sample were determined by nitrogen adsorption equipment and the results are set out in Table 1, along with pH\(_{\text{pzc}}\) results. The values of the textural parameters suggest that the adsorbent in question is a material with a predominance of mesopores (d > 2 nm), although the presence of micropores cannot be disregarded, as reported in other studies that used clinoptilolite.
zeolite (Hernández et al., 2000; Kennedy et al., 2019a, 2019b; Kennedy, Mujčin, et al., 2019). The specific area of clinoptilolite is a significant parameter for adsorption because it denotes the accessibility of the pores to this material. The specific area obtained for the CP zeolite sample was 131.17 m² g⁻¹. This value differs from other studies but is acceptable, as the characteristics of natural clinoptilolite zeolite vary according to the extraction region (Diógenes et al., 2022). The pHₚzc value obtained from the CP natural zeolite sample was 7.2, indicating that for pH values below the PZC value, the adsorbent surface will be positively charged and for values above, the surface will be negatively charged (Batistela et al., 2017).

Figure 2 shows the diffractogram of the natural zeolite sample CP, raw and after the adsorption process. It was possible to observe that the natural zeolite sample CP has a crystalline structure, and its pattern is identified with the characteristic peaks of clinoptilolite. The peaks identified in the XRD spectrum located at 2θ = 9.8, 11.1, 22.3, 26.0, 28.1, and 30.0 are associated with the monocyclical crystal phase according to JCPDS catalog number 22–1236. The crystallinity of the sample was calculated through the ratio of the area of the crystalline peaks of the sample by the area of the crystalline peaks of the reference standard and a crystallinity close to 63% was obtained, which corroborates the proposition that the adsorbent has a crystalline structure. The diffractogram of the sample after the adsorption process indicates no significant changes in the lamellar layers of the crystal structure of the adsorbent, strongly suggesting a physisorption process.

Figure 3 shows the infrared spectrum of the CP natural zeolite sample and HCQ-contaminated CP. The swept wavelength region is between 4000 and 400 cm⁻¹. The bands indicated at 3450 and 1636 cm⁻¹ correspond to the O–H bonds related to the water molecule (Dehghan et al., 2019). The peak at 1043 cm⁻¹ is related to asymmetric stretching vibrations of the Si–O–Si and Al–O–Al bonds (Rouhani et al., 2022). The characteristic absorption bands of the material, such as the symmetric tetrahedral elongation and the connections between the SiO₄ tetrahedrons, are found at 460 cm⁻¹ and 609 cm⁻¹, respectively (Trujillo et al., 2013). After the adsorption process, it was possible to verify that the spectrum of contaminated CP zeolite is similar to that of the unmodified adsorbent, indicating a physisorption mechanism (Gümüş and Gümüş, 2022), being possible to observe significant changes only in the region
corresponding to 3450 cm$^{-1}$ of the infrared spectrum, as highlighted in the figure, referring to absorption band of hydroxyl groups. A band shift to 3634 cm$^{-1}$ was observed for higher energies, indicating the difficulty of vibration (Nezamzadeh-Ejhieh and Shirzadi, 2014), which may be associated with the appearance of molecules of HCQ functional groups adsorbed on the surface of CP zeolite, such as -OH and -NH functional groups (Bendjeffal et al., 2021).

3.2 Adsorption Kinetics

The kinetic parameters provide information to select the optimal conditions for a future application of the contaminant removal process on an industrial scale. The pseudo-first-order model considers that the adsorption occurs in a monolayer, without interaction between the adsorbed molecules and at specific sites, governed by a first-order equation. The pseudo-second-order kinetic model follows the same precepts as the pseudo-first-order but is governed by a second-order equation (Sato et al., 2019).

Figure 4 (a) and (b) show the experimental data of the adsorption of HCQ on zeolite CP by process time at the three temperatures studied, with the non-linear fits of the pseudo-first-order, pseudo-second-order kinetic models, and intraparticle diffusion. Table 2 presents the calculated parameters of each kinetic model and the static parameters of the adjustments ($R^2$, $R^2_{adj}$ e $\chi^2$).

Assessing the experimental data, it is possible to observe that the process reached an equilibrium level around 240 min, with more effective adsorption in the first 60 min. This result showed the greater availability of sites on the surface of the CP zeolite at the beginning of the process, reaching the stabilization and equilibrium plateau. The increase in temperature caused a slight increase in the adsorbed amount, characteristic of an endothermic process. However, the effect of temperature can be considered to have little influence on the process.

As for the adjustments of the kinetic models, it is possible to categorically state, evaluating the values of the correlation coefficients ($R^2$), adjusted correlation coefficient ($R^2_{adj}$), and the Chi-square statistical function ($\chi^2$), that the pseudo-first-order was the model that best fits the experimental data. The first-order model is based on a simple reversible reaction with an equilibrium between two phases, in which the HCQ molecule reacts with an active site of the CP zeolite and the step controlling the reaction rate is the transition between the free state of the molecule in solution to the condition adsorbed on the surface of the solid. Based on the assumptions of this model, adsorption occurred exclusively due to the concentration gradient between the solution and the surface of
the adsorbent without considering secondary effects (Charaabi et al., 2021).

The intraparticle diffusion model helps to understand the HCQ adsorption process on the CP zeolite. This model considers the diffusion of the liquid film negligible, while the internal diffusion inside the adsorbent controls the steps of the adsorption process. Figure 4 (b) depicts the fit of the intraparticle diffusion model to the results obtained by adsorption kinetics. It is possible to observe the presence of multilinearity, which strongly indicates the presence of more than one effect influencing the adsorption rate. The first region of $t^{1/2}$ between 0 and 8 (min$^{1/2}$) influences the time of the adsorption process through the external transport of the contaminant to the particle surface. The second region indicates the contribution of the surface diffusion process, which reduces the adsorption rate. Finally, the last stage refers to the dynamic balance, with intraparticle diffusion reducing due to the lower concentrations of adsorbate in the solution.

**Table 2** Results of the kinetic adsorption models studied

| Model                  | Parameter          | Temperature (K) |
|------------------------|--------------------|-----------------|
|                        |                    | 298  | 303  | 308  |
| Pseudo-first-order     | $k_1$ (min$^{-1}$) | 0.0352| 0.0192| 0.0218|
|                        | $q_e$ (mg g$^{-1}$)| 5.8158| 6.4241| 6.4258|
|                        | $R^2$              | 0.9992| 0.9983| 0.9885|
|                        | $R^2_{adj}$        | 0.9991| 0.9980| 0.9869|
|                        | $\chi^2$          | 0.0033| 0.0087| 0.0615|
| Pseudo-second-order    | $k_2$ (g mg$^{-1}$ min$^{-1}$) | 0.0840| 0.0027| 0.0032|
|                        | $q_e$ (mg g$^{-1}$) | 6.4602| 7.8286| 7.7060|
|                        | $R^2$              | 0.9954| 0.9939| 0.9837|
|                        | $R^2_{adj}$        | 0.9948| 0.9931| 0.9813|
|                        | $\chi^2$          | 0.0190| 0.0314| 0.0876|
| Intraparticle diffusion | $K_D$ (mg g$^{-1}$ min$^{-0.5}$) | 0.3591| 0.4202| 0.4017|
|                        | $C$ (mg g$^{-1}$)  | 1.2532| 0.6303| 1.0422|
|                        | $R^2$              | 0.8424| 0.9359| 0.8974|
|                        | $R^2_{adj}$        | 0.8198| 0.9267| 0.8828|
|                        | $\chi^2$          | 0.6678| 0.3347| 0.5102|

**Fig. 4** Kinetic curves for HCQ adsorption on CP zeolite at temperatures of 298, 303, and 308 K and fit to a pseudo-first-order, pseudo-second-order, and b intraparticle diffusion models.
3.3 Adsorption Isotherms

Figure 5 shows the equilibrium isotherms obtained during the 60-min contact time for the temperatures of 298, 303, and 308 K, as well as the non-linear fits for the Langmuir, Freundlich, and SIPS models. The isotherms obtained experimentally are classified as L2 type, belonging to Langmuir’s L class and to subgroup 2, which indicates that the adsorption affinity increases with increasing adsorbate concentration until saturation (Giles et al., 1960).

Table 3 summarizes the parameter values of the studied isotherms, their coefficients of determination ($R^2$), and the chi-square error-related parameter ($\chi^2$). The model represented by the SIPS isotherm was that best fit the studied temperatures as it assumed the highest correlation values (>0.99) and the most negligible chi-square errors ($\chi^2$). From Fig. 5, it is possible to observe that the curves of the SIPS and Langmuir models overlap, showing that the two models can define the studied adsorption process well and that they have higher values of maximum adsorption capacity ($Q_{\text{max}}$) when compared to the Freundlich model.

The SIPS isotherm model is considered a combination of the Langmuir and Freundlich models since at low concentrations of adsorbate, it simplifies the Freundlich isotherm while at high concentrations, it assumes monolayer adsorption, characteristic of the Langmuir model (Tzabar and ter Brake, 2016). The parameter $n$ of the SIPS isotherm represents the heterogeneity of the solid and if the result of $1/n$ is equal to 1, the model falls into the Langmuir isotherm for homogeneous solids (de Araújo et al., 2020). For the

| Model  | Parameters | Temperature (K) | 298 | 303 | 308 |
|--------|------------|----------------|-----|-----|-----|
| **Langmuir** | $Q_{\text{max}}$ (mg g$^{-1}$) | 6.3879 | 9.5106 | 9.8801 |
|        | $K_L$ (L mg$^{-1}$) | 1.0534 | 0.7913 | 0.8175 |
|        | $R_L$ | 0.0453 | 0.0594 | 0.0576 |
|        | $R^2$ | 0.9977 | 0.9954 | 0.9982 |
|        | $\chi^2$ | 0.0104 | 0.0357 | 0.0152 |
| **Freundlich** | $k_f$ (mg g$^{-1}$) | 3.0949 | 3.9803 | 4.2004 |
|        | $n$ | 2.7924 | 2.2655 | 2.2868 |
|        | $R^2$ | 0.9800 | 0.9931 | 0.9935 |
|        | $\chi^2$ | 0.0826 | 0.0543 | 0.0551 |
| **SIPS** | $Q_{\text{max}}$ (mg g$^{-1}$) | 6.5041 | 12.0032 | 11.4403 |
|        | $K_s$ (L mg$^{-1}$) | 1.0106 | 0.4344 | 0.5662 |
|        | $n$ | 1.0634 | 1.0749 | 1.0834 |
|        | $R^2$ | 0.9987 | 0.9970 | 0.9990 |
|        | $\chi^2$ | 0.0093 | 0.0263 | 0.0090 |

**Table 3** Results of the adsorption isotherm models studied

![Fig. 5 Adsorption isotherms of HCQ on zeolite CP for temperatures of 298, 303, and 308 K and fit to Langmuir, Freundlich, and SIPS models](image-url)
present study, the results at the three temperatures studied were close to 1, proving that the best fit is the Langmuir model. Corroborating the result of the SIPS parameter, the parameter of the Langmuir isotherm results in a value between 1 and 0.01 for all tested temperatures, indicating that the isotherms are favorable in the evaluated concentration range (Vargas et al., 2011). Although the Freundlich model is not the most adequate, the values presented for the parameter \( n \) are more significant than 1, indicating that the adsorption refers to physical adsorption (Wibowo et al., 2017).

3.4 Adsorption Thermodynamics

The thermodynamic values of adsorption enthalpy and entropy change were calculated from the \( \ln (k_d) \times 1 / T (K^{-1}) \) graph (Fig.S1a) and the activation energy from the \( \ln (k_c) \times 1 / T (K^{-1}) \) graph (Fig.S1b). The values of the linear and angular coefficients were obtained through Eqs. (02) and (04) to determine the thermodynamic properties of the process. Table 4 shows the obtained values of \( \Delta G^\circ_{ads}, \Delta H^\circ_{ads}, \) and \( \Delta S^\circ_{ads} \) as thermodynamic parameters that are used to identify the characteristic of the adsorption process.

The values of \( \Delta G^\circ_{ads} \) obtained are negative and decrease with increasing temperature, indicating that the HCQ adsorption process on CP zeolite is spontaneous. The positive value of \( \Delta H^\circ_{ads} \) suggests that this is an endothermic process favored by the increase in temperature. There was a slight increase in the adsorbed amount in the process in question. This can be attributed to the rise in the number of active sites available for adsorption and in the decreasing thickness of the boundary layer around the adsorbent, which can reduce the mass transfer resistance of the adsorbate in the boundary layer.

The positive value of \( \Delta S^\circ_{ads} \) shows an increase in randomness at the solid-solution interface in the HCQ adsorption process. This can be attributed to the extra translational entropy acquired by the water molecules, which were previously adsorbed or located in the surrounding multilayers of the surface of CP zeolite (Anastopoulos and Kyzas, 2016). In the literature, studies report negative values of \( \Delta G^\circ, \Delta H^\circ, \) and \( \Delta S^\circ \) for adsorption of different contaminants with clinoptilolite zeolite (Güney et al., 2007; Wibowo et al., 2017), while other researchers reported the adsorption process with positive values of \( \Delta H^\circ \) and \( \Delta S^\circ \) (Chakraborty et al., 2005; Huo et al., 2012; Romero-González et al., 2005). This demonstrates that the parameters are dependent on the species involved in the process.

Regarding the activation energy of the process, the value found was 4.96 kJ mol\(^{-1}\). What is known is that lower activation energy values, as found in this study, indicate that the adsorption rate is controlled by the intraparticle diffusion mechanism, which is a physical step in the adsorption (Doğan and Alkan, 2003). As stated in item 3.2, intraparticle diffusion is a limiting step in the HCQ adsorption process on CP zeolite. This leads us to understand that a physisorption process predominantly governs the HCQ adsorption process on CP.

3.5 pH Effect

Figure 6 shows the results of the adsorption tests carried out with the variation of the initial pH of the solution at temperatures of 298, 303, and 308 K. Through the results presented, it is possible to verify that the removal of HCQ increases gradually from the pH 2 to 7.5, and at pH above 7.5, the adsorption process is unfavorable, resulting in lower amounts of adsorbed HCQ. Optimum removal occurs at 7.5, that is, at the natural pH of the solution. The favoring of removal at pH close to neutrality is justified by the absence of the influence of the forces of hydrogen and hydroxyl ions that can be strongly adsorbed on the surface of the adsorbent and generate competition for

| Temperature (K) | 1/T (K\(^{-1}\)) | Kd (L g\(^{-1}\)) | \( \Delta G^\circ_{ads} \) (kJ mol\(^{-1}\)) | \( \Delta H^\circ_{ads} \) (kJ mol\(^{-1}\)) | \( \Delta S^\circ_{ads} \) (kJ mol\(^{-1}\) K\(^{-1}\)) | E\(_a\) (kJ mol\(^{-1}\)) |
|----------------|-----------------|-----------------|---------------------------------|-------------------------------|---------------------------------|-----------------|
| 298            | 0.00332         | 1.0242          | -0.2636 ± 0.19                  | 46.6714 ± 0.22                | 0.1575 ± 0.11                   | 4.9676          |
| 303            | 0.00322         | 1.7371          | -1.0511 ± 0.17                  |                               |                                 |                 |
| 308            | 0.00312         | 1.8847          | -1.8386 ± 0.21                  |                               |                                 |                 |
the active sites of these species with the HCQ molecule (Titchou et al., 2021). Furthermore, this value is also very close to the pH<sub>pzc</sub> value of the clinoptilolite zeolite, which reinforces that the absence of charges on the surface of the adsorbent can contribute to the efficiency of the adsorption process (Mall et al., 2006). Bendjefal et al. (2021) found similar pH optimum values for HCQ removal using Algerian kaolin as an adsorbent.

### 3.6 Reuse of CP Zeolite

The CP zeolite reuse test was performed for eleven uses, the first use referring to the removal of the drug HCQ and the other consecutive tests referring to the reuses. The results are shown in Fig. 7. It is possible to observe a slight reduction in the adsorbed amount between the first use and the subsequent reuses and also the difference in the adsorbed amount between the first use and the tenth reuse, which was approximately 16%. This evidenced that the adsorption process in the removal of HCQ using CP zeolite occurred predominantly through physisorption, which involves weaker interactions between the adsorbent and the surface of the adsorbent. Thus, a simple regeneration process carried out with water could recover the adsorbent for its subsequent reuse and keep the adsorbed quantity rates high.

### 3.7 Adsorption Mechanism of HCQ on Zeolite CP

Therefore, through the kinetic and equilibrium study, it can be stated that the HCQ adsorption process on zeolite CP results from a physisorption process due to the difference in attraction forces, widely known...
as Van der Waals forces. Due to the induced dipole moment, these forces make the HCQ molecule physically attached to CP zeolite, a consequence of the greater apolarity of the HCQ molecule. These interactions have a long range but are weak, which would justify the easy regeneration of zeolite (item 3.4). In addition, another process to consider is that HCQ is a basic substance with measured pKa values of 8.27 and 9.67 and in a neutral solution, HCQ is mainly protonated as H2HCQ2+ (95%) and partially as HHCQ+ (5%) (Dabić et al., 2019). In this case, the protonated species can interact with exchangeable clinoptilolite cations (Sprynskyy et al., 2009).

3.8 Toxicity Test

After conducting the adsorbent tests, the effluent generated by the best condition ([Zeolite CP] = 0.1 g, 308 K and pH free) was subjected to toxicity tests against the bioindicators Lactuca sativa and Artemia salina.

Tests with Artemia salina confirm that the toxicity of hydroxychloroquine was reduced after treatment, as shown in Table 5. The higher the LC50 concentration, the less toxic the effluent and, therefore, it is possible to state that the final effluent was non-toxic after removal of hydroxychloroquine using CP zeolite as adsorbent, as it presented a LC50 greater than 200 mg L−1 and a mortality rate of 3%. This result is valuable because, as mentioned in the introduction, HCQ is considered a drug with a high potential for pollution due to its persistence for several days in the environment, so it can bioaccumulate and be transferred to other organisms in a toxic manner.

The tests with Lactuca sativa comprised triplicate series with negative control, positive control, samples of untreated synthetic effluent, and samples of treated synthetic effluent. The results expressed in Table 6 show that 100% relative germination was achieved for the treated samples, while in the untreated, it was 70%. The relative root growth for the treated sample was 90%, showing that the adsorptive process was effective in reducing the toxicity of the effluent.

4 Conclusion

This study indicated that it was possible to characterize the natural clinoptilolite zeolite and evaluate its potential as an adsorbent for the removal and reduction of the toxicity of HCQ in aqueous solution. From the results obtained, it was possible to state that the characterization techniques employed were adequate and important to know the physical and chemical characteristics of the adsorbent. Regarding the kinetic data, the kinetic model that best fits the experimental data was the pseudo-first-order model. The SIPS model better described isotherm data. The thermodynamic study indicated that the adsorption of HCQ on zeolite CP is spontaneous and endothermic and increases the solid-solution interface. The adsorption mechanism of HCQ on zeolite CP occurred mainly by physisorption through Van der Waals forces and intraparticle diffusion was a limiting step in the process. Adsorption was favored without changing the initial pH of the solution. The CP zeolite was easily regenerated using water as eluent and can be used in ten reuses, showing the occurrence of the physisorption process. The ecotoxicological tests carried out

| Table 5 | Toxicity assessment against Artemia salina |
|----------|------------------------------------------|
|          | LC50 | Concentration (mg L−1) | Mortality (%) |
| Control  | 1.45 | 29.51                  | 100           |
| Effluent non-treated | 2.15 | 141.25                 | 48            |
| Effluent treated     | -    | > 200.00               | 3             |

| Table 6 | Toxicity assessment against Lactuca sativa |
|----------|------------------------------------------|
|          | Germinated seed | Mean root length (cm) | Relative seed germination (%) | Relative root elongation (%) |
| Negative control | 0 | 0 | 0 | 0 |
| Positive control  | 10 | 2.36 ± 0.20 | 100 | 100 |
| Initial effluent  | 7 | 1.33 ± 0.15 | 70 | 56 |
| Treated effluent   | 9 | 2.14 ± 0.25 | 90 | 90 |
with the bioindicators proved that the application of CP zeolite as an adsorbent reduced the toxicity of the effluent containing HCQ after the process. With this, it can be said that CP zeolite can potentially reduce the toxicity of HCQ in aqueous media and can drive new studies outside the laboratory scale with real effluents.

Acknowledgements The authors would like to thank the Fundação Araucária (FA-PR) for the RENEWABLE HYDROCARBONET (NAPI-HCR) project for granting a scholarship.

Author Contribution Ramiro Picoli Nippes: conceptualization, methodology, investigation, and writing – original draft. Paula Derksen Macruz: investigation, writing – original draft, review, and editing. Luiza Carla Augusto Molina: adsorption experiments. Mara Heloisa Neves Olsen Scaliente: supervision and writing – review and editing.

Data Availability All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Code Availability Not applicable.

Declarations

Ethics Approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication Not applicable.

Competing Interests The authors declare no competing interests.

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