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Mechanistic insights into metformin sorption onto natural, sodium-exchanged, HDTMA-modified, and cerium-loaded clinoptilolite zeolites

Estudio mecanístico de la sorción de metformina sobre clinoptilolita natural, sódica, modificada con HDTMA y cargada con cerio

A.M. Dávila-Estrada*, J.J. Ramírez-García

Laboratorio de Química Analítica, Facultad de Química, Universidad Autónoma del Estado de México, Paseo Colón S/N, Residencial Colón, Toluca, Estado de México, C.P. 50120.

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Abstract

Metformin is a persistent antidiabetic drug frequently detected in aquatic environments due to its incomplete removal in conventional wastewater treatment plants. In this study, the dominant sorption mechanisms of metformin onto natural clinoptilolite (ZN), sodium-conditioned zeolite (ZNa), hexadecyltrimethylammonium bromide-modified zeolite (ZMS), and cerium-loaded zeolite (ZCe) were investigated. Experiments were conducted at intrinsic pH (5–6), where metformin is predominantly present in its protonated form. The materials were characterized by Fourier Transform Infrared Spectroscopy (FT-IR), Scanning Electron Microscopy coupled with Energy Dispersive X-ray Spectroscopy (SEM–EDS), Thermogravimetric Analysis (TGA), CHNS elemental analysis, and point of zero charge (pH_{pzc}).

Kinetic assays performed at 100 mg L^{-1} and 25 °C showed that ZNa exhibited the highest sorption capacity (2.42 mg g^{-1}), followed by ZMS (1.90 mg g^{-1}), ZN (1.62 mg g^{-1}), and ZCe (1.23 mg g^{-1}). The Elovich model provided the best fit ($R^2 > 0.90$), indicating heterogeneous, activation-controlled sorption. The release of Na^+ provided qualitative evidence supporting cation exchange as the predominant sorption mechanism under the evaluated conditions.

Overall, sodium conditioning enhanced metformin sorption by increasing the availability of exchangeable Na^+ sites.

Keywords: Clinoptilolite, cation exchange, metformin, pharmaceutical pollution, sorption mechanism.

Resumen

La metformina es un fármaco antidiabético persistente frecuentemente detectado en ambientes acuáticos debido a su eliminación incompleta en plantas de tratamiento de aguas residuales. En este estudio se investigaron los mecanismos dominantes de sorción de metformina sobre clinoptilolita natural (ZN), zeolita acondicionada con sodio (ZNa), modificada con bromuro de hexadeciltrimetilamonio (ZMS) y cargada con cerio (ZCe). Los experimentos se realizaron a pH intrínseco (5–6), donde la metformina se encuentra predominantemente en forma protonada. Los materiales fueron caracterizados mediante: Espectroscopía infrarroja por transformada de Fourier (FT-IR), microscopía electrónica de barrido acoplada a espectroscopía de dispersión de energía de rayos X (SEM–EDS), análisis termogravimétrico (TGA), análisis elemental CHNS y punto de carga cero (pH_{pzc}).

Los ensayos cinéticos realizados a 100 mg L^{-1} y 25 °C mostraron que ZNa presentó la mayor capacidad de sorción (2.42 mg g^{-1}), seguida por ZMS (1.90 mg g^{-1}), ZN (1.62 mg g^{-1}) y ZCe (1.23 mg g^{-1}). El modelo de Elovich mostró el mejor ajuste ($R^2 > 0.90$), indicando sorción heterogénea controlada por activación. La liberación de Na^+ aportó evidencia cualitativa que respalda al intercambio catiónico como el mecanismo predominante de sorción bajo las condiciones evaluadas.

En conjunto, el acondicionamiento con sodio mejoró la sorción de metformina al incrementar la disponibilidad de sitios intercambiables de Na^+.

Palabras clave: Clinoptilolita, intercambio catiónico, metformina, contaminación farmacéutica, mecanismo de sorción.

*Corresponding author. *E-mail*: mich.vica8617@gmail.com ;
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1 Introduction

Due to its low cost and high therapeutic effectiveness, metformin is one of the most widely prescribed antidiabetic drugs worldwide. The global prevalence of diabetes continues to rise, with approximately 463 million people affected in 2019 and projections estimating an increase to nearly 700 million by 2045, suggesting that metformin consumption will continue growing in the coming decades (Saeedi *et al*., 2019). However, the widespread use of metformin has raised increasing concern regarding its environmental impact.

Approximately 70% of the administered dose of metformin is excreted unmetabolized through urine and feces, allowing this compound to enter wastewater treatment plants, which are generally not designed for its effective removal. Consequently, metformin and its main transformation product, guanylurea, have been detected in surface waters, groundwater, and even drinking water sources at concentrations ranging from ng L^{-1} to μg L^{-1}, posing potential risks to aquatic ecosystems and biodiversity (Godoy *et al*., 2018).

Several studies have demonstrated that metformin exposure in aquatic environments may induce endocrine disrupting effects, including the feminization of male fish, leading to reproductive impairment and population imbalance. Moreover, the persistence of metformin raises concerns about its potential transfer through the food chain, increasing long term ecological risks and possible human exposure (Shearer *et al*., 2022; Zorita *et al*., 2008).

In response to this emerging environmental issue, various treatment technologies have been investigated, including sorption, photocatalysis, biodegradation, and electrochemical processes. Among these, sorption using low cost and environmentally friendly materials has attracted considerable attention. In particular, functionalized zeolites have emerged as promising sorbents for the removal of pharmaceutical contaminants from aqueous media (Bajda *et al*., 2024; Momeni *et al*., 2016). However, beyond removal efficiency, understanding the fundamental sorption mechanisms governing pharmaceutical uptake is essential for the rational design of effective and selective materials.

Zeolites are crystalline aluminosilicates characterized by a three-dimensional framework composed of $[SiO_4]^{4-}$ and $[AlO_4]^{5-}$ tetrahedra. The isomorphic substitution of Si^{4+} by Al^{3+} generates a permanent negative charge in the framework, which is balanced by exchangeable cations such as Na^+, K^+, Ca^{2+}, and Mg^{2+} located within the channels and cavities of the structure, along with water molecules (Jiang *et al*., 2018; Mijailović et al., 2022; Moshoeshoe *et al*., 2017; Wang & Peng, 2010).

Clinoptilolite is one of the most abundant natural zeolites and is widely studied due to its high cation exchange capacity, structural stability, and availability. Its chemical composition and porous structure make it suitable for the removal of inorganic and organic contaminants, including pharmaceutical compounds, from water systems (Biblioteca *et al*. 2023; Helmi *et al*. 2024). Furthermore, surface modification strategies, such as ion exchange and functionalization with cationic surfactants or metal species, have been extensively explored to enhance its sorption performance and selectivity (Flores-Alamo *et al*., 2025; Leal-Perez *et al*., 2024; Martucci *et al*., 2012; Misaelides, 2011; Pérez Cordoves *et al*., 2008)

Although numerous studies have addressed the sorption of metformin using carbonaceous materials, metal oxides, and advanced oxidation processes, comparative studies conducted under identical experimental conditions remain scarce. Nevertheless, adsorption capacity alone does not provide sufficient information to explain the performance of modified zeolitic materials, since understanding the dominant sorption mechanisms is essential for the rational development and optimization of these systems. However, the combined influence of different modification strategies (Na^+, HDTMA, and Ce^{3+}) on the sorption and mechanistic pathways of metformin under equivalent experimental conditions has not yet been fully elucidated (Ferri *et al*., 2024; Król *et al*., 2024; Li *et al*., 2008; Wingenfelder *et al*., 2006).

In aqueous environments, metformin predominantly exists in its protonated cationic form under mildly acidic conditions, favoring electrostatic interactions and cation exchange processes during sorption onto aluminosilicate materials. Given the permanent negative charge of the clinoptilolite framework, cation exchange is expected to play a dominant role in the uptake of positively charged pharmaceutical compounds. In particular, sodium modification increases the availability of exchangeable Na^+ ions, potentially enhancing metformin sorption through ion exchange mechanisms (Li *et al*., 2008; Wingenfelder *et al*., 2006). Therefore, investigating sodium release and surface charge properties provides direct experimental evidence to clarify whether cation exchange constitutes the dominant sorption pathway.

In this context, the primary objective of the present study was to elucidate the dominant sorption mechanisms governing metformin uptake onto natural and modified clinoptilolite zeolites, rather than optimizing adsorption capacity or operational conditions, with particular emphasis on the role of cation exchange processes in sodium-modified clinoptilolite. Natural clinoptilolite, HDTMA-modified zeolite, and cerium-loaded zeolite were systematically evaluated under identical experimental conditions to enable a meaningful

comparison of their sorption performance and interaction pathways. Special attention was given to surface charge properties (pH_{pzc}), sodium release behavior, and structural and chemical modifications, as these parameters are directly linked to the sorption mechanism of cationic pharmaceuticals such as metformin. Comprehensive physicochemical characterization and sorption studies were conducted to support the proposed mechanistic interpretation.

The findings of this study are intended to contribute to a mechanistic understanding of pharmaceutical–zeolite interactions, which is fundamental for future optimization and scale-up studies. Although adsorption capacity was not the primary objective of this work, the mechanistic insights obtained provide a scientific basis for the rational design and future optimization of zeolite-based sorbents for pharmaceutical removal.

2 Materials and methods

2.1 Zeolitic materials and reagents

A natural clinoptilolite-type zeolite from San Luis Potosí, Mexico, was used in this study. The material was ground using an agate mortar and sieved to obtain particle sizes in the range of 0.420–0.841 mm. Sodium chloride (NaCl) was obtained from Fermont, while hexadecyltrimethylammonium bromide (HDTMA-Br), cerium(III) nitrate hexahydrate ($Ce(NO_3)_3{\cdot}6H_2O$), and metformin ($C_4H_{11}N_5$) were purchased from Sigma-Aldrich. All reagents were of analytical grade (≥ 99%).

Four zeolitic materials were evaluated: natural clinoptilolite (ZN), sodium-conditioned clinoptilolite (ZNa), HDTMA-modified clinoptilolite (ZMS), and cerium-loaded clinoptilolite (ZCe).

2.2 Preparation of modified materials

2.2.1 Sodium conditioning

A total of 100 g of natural clinoptilolite (ZN) was contacted with 1 L of a 0.1 mol L^{-1} NaCl solution under reflux for 3 h. This procedure was repeated twice to ensure effective sodium exchange. The solid was washed thoroughly with distilled water until the absence of chloride ions was confirmed using $AgNO_3$ and then dried at room temperature. The resulting material was designated ZNa.

2.2.2 Modification with HDTMA

Sodium-conditioned clinoptilolite (ZNa) was contacted with 30 mmol L^{-1} HDTMA-Br solution at 30 °C for 48 h under constant agitation (100 rpm). After modification, the solid was washed repeatedly with distilled water to remove excess surfactant and dried at room temperature. This material was designated ZMS.

2.2.3 Cerium loading

Natural clinoptilolite (ZN) was treated with 90 mL of a 1 mol L^{-1} nitric acid (HNO_3) solution under constant stirring for 4 h at room temperature. The solid was washed several times with deionized water and dried at 60 °C overnight; this acid-treated material was designated HZ.

HZ was subsequently contacted with an aqueous solution of cerium (III) nitrate hexahydrate ($Ce(NO_3)_3{\cdot}6H_2O$) and stirred continuously for 6 h at room temperature. The pH was adjusted to 7–8 by gradual addition of 2 mol L^{-1} ammonium hydroxide ($NH_3{\cdot}H_2O$). The resulting cerium-loaded clinoptilolite (ZCe) was dried at 60 °C overnight and calcined at 480 °C for 4 h.

2.3 Materials characterization

2.3.1 FT-IR spectroscopy

Fourier transform infrared (FT-IR) spectra were recorded in the range of 4000–400 cm^{-1} using a Vertex 70 spectrometer. Samples were prepared as KBr pellets.

2.3.2 SEM/EDS analysis

Platinum-coated samples were analyzed using a JEOL JSM-6510LV scanning electron microscope operating at 20 kV and equipped with a backscattered electron detector. Elemental composition was determined by energy-dispersive X-ray spectroscopy (EDS) using an Oxford PentaFETx5 detector.

2.3.3 Thermogravimetric analysis (TGA)

Thermogravimetric analysis was performed using a TA SDT Q600 analyzer under a nitrogen atmosphere. Samples were heated from room temperature to 950 °C at a heating rate of 10 °C min^{-1}.

2.3.4 CHNS elemental analysis

Elemental CHNS analysis was carried out using a Vario Micro Cube analyzer. Samples were encapsulated in tin and combusted at 1150 °C using oxygen, with helium as the carrier gas.

2.4 Point of zero charge determination (pH_{pzc})

The point of zero charge (pH_{pzc}) of ZN, ZNa, ZMS, and ZCe was determined by contacting 100 mg of each

material with 10 mL of a 0.1 mol L^{-1} $NaNO_3$ solution with initial pH values ranging from 2 to 11, adjusted using HCl or NaOH. Experiments were conducted at 25 °C and 100 rpm. After 24 h of equilibration, the final pH was measured. All experiments were performed in triplicate.

2.5 *Sorption experiments*

Sorption experiments were carried out by contacting 100 mg of each sorbent (ZN, ZNa, ZMS, and ZCe) with 10 mL of a 100 mg L^{-1} metformin solution at 25 °C and 100 rpm. Aliquots were collected at contact times ranging from 0.25 to 72 h, filtered, and analyzed by HPLC using an Eclipse XDB-C18 column with a mobile phase consisting of 0.1% formic acid/acetonitrile (60:40, v/v) at a flow rate of 1.0 mL min^{-1}, with UV detection at 232 nm.

The amount of metformin sorbed at time t (q_t) was calculated as:

$$q_t = \frac{(C_0 - C_t)V}{m} \tag{1}$$

where C_0 and C_t are the initial and time-dependent metformin concentrations (mg L^{-1}), V is the solution volume (L), and m is the adsorbent mass (g) (González-Ortiz *et al*., 2018).

After completion of the sorption experiments, the recovered zeolite samples were designated according to the contact time. Thus, the suffix "-72" refers to materials collected after 72 h of contact with metformin, namely ZN-72, ZNa-72, ZMS-72, and ZCe-72 for the natural, sodium-conditioned, HDTMA-modified, and cerium-loaded clinoptilolite samples, respectively. These designations are used throughout the characterization and discussion sections.

2.6 *Kinetic modeling*

Sorption kinetic data were fitted using the nonlinear forms of the pseudo first order (Lagergren), pseudo second order (Ho and McKay), and Elovich models. The quality of fit was evaluated using the coefficient of determination (R^2), the agreement between the experimental and calculated equilibrium sorption capacities (q_e,exp and q_e,cal) (Wang *et al*. 2006). The kinetic parameters were estimated by nonlinear regression using OriginPro 2024, and parameter uncertainties are reported as standard errors obtained directly from the nonlinear regression analysis.

2.6.1 *Pseudo First Order Model (Lagergren)*

This model assumes that the rate is proportional to the difference between the equilibrium sorption capacity and the amount adsorbed at time (t) (Chenet *et al*. 2024; Ho and Mckay 1999; Serna-Galvis *et al*. 2024):

$$q_t = q_e\left(1 - e^{-K_1 t}\right) \tag{2}$$

Where:

- q_t = Sorption capacity at time t (mg g^{-1})
- q_e= Equilibrium sorption capacity (mg g^{-1})
- K_1 = Pseudo first order rate constant (h^{-1})

2.6.2 *Pseudo Second Order Model (Ho)*

This model assumes that the sorption rate is proportional to the square of the number of available sorption sites and is commonly applied to describe adsorption systems involving surface interactions (Chenet *et al*., 2024; Ho & Mckay, 1999):

$$q_t = \frac{q_e^2 K_2 t}{1 + q_e K_2 t} \tag{3}$$

Where:

- q_t = Sorption capacity at time t (mg g^{-1})
- q_e= Equilibrium sorption capacity (mg g^{-1})
- K_2= Pseudo second order rate constant (g mg^{-1} h^{-1})

2.6.3 *Elovich model*

This model is suitable for heterogeneous surfaces and assumes a logarithmic relationship between sorption capacity and time (Chenet *et al*., 2024; Kuleyin, 2007):

$$q_t = \beta \ln(\alpha) + \beta \ln(t) \tag{4}$$

Where:

- q_t = Sorption capacity at time t (mg g^{-1})
- α = Initial sorption rate constant (mg g^{-1} h^{-1})
- β = Constant related to surface coverage (g mg^{-1}).

2.6.4 *Statistical analysis*

For statistical analysis, all sorption experiments were performed in duplicate, and the results are reported as mean ± standard deviation (n=2). Statistical differences among the sorption capacities obtained for the evaluated zeolite systems were assessed using one-way analysis of variance (ANOVA), followed by Tukey's multiple comparison test. Differences were considered statistically significant at $p < 0.05$. Statistical analyses were performed using OriginPro 2024.

2.6.5 *Intraparticle Diffusion Model (Weber-Morris)*

The Weber–Morris intraparticle diffusion model was applied to evaluate the possible contribution of pore diffusion to the overall sorption process (Chenet *et al*., 2024; Tran *et al*., 2017; Weber & Morris, 1963):

$$q_t = K_D t^{\frac{1}{2}} + C \quad (5)$$

Where:

- q_t = Sorption capacity at time t (mg g^{-1})
- K_D = Intraparticle diffusion rate constant (mg g^{-1} $h^{-1/2}$)
- C = Intercept related to the boundary layer thickness (mg g^{-1})

If the regression line passes through the origin (C=0), intraparticle diffusion is considered the sole rate-controlling step. Otherwise, additional transport mechanisms contribute to the overall sorption process.

3 Results and discussion

3.1 *Surface charge properties and metformin speciation*

3.1.1 *pH_{pzc}*

Figure 1 shows the variation of ΔpH as a function of the initial pH for the evaluated zeolitic materials. Under acidic conditions (initial pH ≈ 3), positive ΔpH values are associated with the protonation of surface hydroxyl groups, whereas under alkaline conditions (initial pH ≈ 11), negative ΔpH values are attributed to deprotonation reactions occurring on the zeolite surface. These acid-base equilibria are characteristic of aluminosilicate materials and explain the opposite trends observed at both ends of the pH range. The pH_{pzc} values were determined by linear regression of the approximately linear region around ΔpH=0. The corresponding regression equations and coefficients of determination (R^2) are summarized in Table 1.

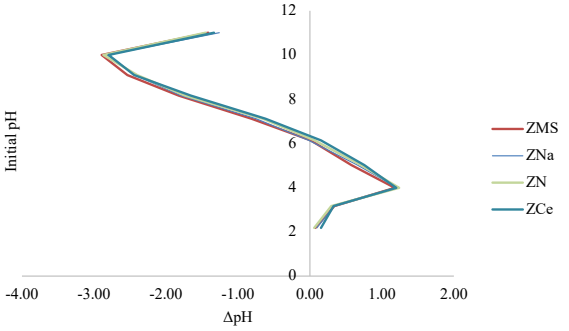

Fig. 1. pH_{pzc} values for zeolite samples: ZN, ZNa, ZMS and ZCe.

The pH_{pzc} values of the evaluated zeolitic materials ranged from 5.84 to 6.02, indicating that under the natural pH of the metformin solution (pH 5-6), the external surface of the zeolites remains close to its point of zero charge (Table 1). Therefore, the contribution of surface electrostatic interactions is expected to be limited under the evaluated experimental conditions.

At pH values between 5 and 6, metformin predominantly exists in its monocationic form ($HMet^+$), which enables its uptake through cation exchange with framework-compensating cations such as Na^+, Ca^{2+}, and K^+ present within the clinoptilolite structure. This process remains thermodynamically favorable despite the limited contribution of surface electrostatic interactions (Momeni *et al*., 2016).

Minor differences in pH_{pzc} were observed among the materials. The HDTMA-modified zeolite exhibited a slightly lower pH_{pzc} (5.84), likely due to changes in surface charge distribution induced by the organic surfactant layer, whereas the cerium-loaded zeolite showed the highest pH_{pzc} value (6.02), consistent with partial surface charge neutralization by cerium species anchored to the zeolite framework (Inglezakis *et al*., 2010). However, the narrow pH_{pzc} range observed for both natural (5.97) and sodium-conditioned clinoptilolite (5.90) indicates that variations in surface charge alone cannot account for the markedly different sorption performances, thereby emphasizing the dominant role of ion exchange mechanisms (Fig. 1).

Although the pH_{pzc} reflects the pH-dependent charge of the external surface, clinoptilolite possesses a permanent negative framework charge arising from the isomorphic substitution of Si^{4+} by Al^{3+} within the aluminosilicate structure.

Table 1. pH_{pzc} values and linear regression equations used for their determination.

Material	Linear regression equation	R^2	pH_{pzc}
ZN	y = -1.3721x + 5.9723	0.9903	5.97 ± 0.22
ZNa	y = -1.3930x + 5.9004	0.9913	5.90 ± 0.23
ZMS	y = -1.3749x + 5.8404	0.9895	5.84 ± 0.18
ZCe	y = -1.3757x + 6.0159	0.9848	6.02 ± 0.24

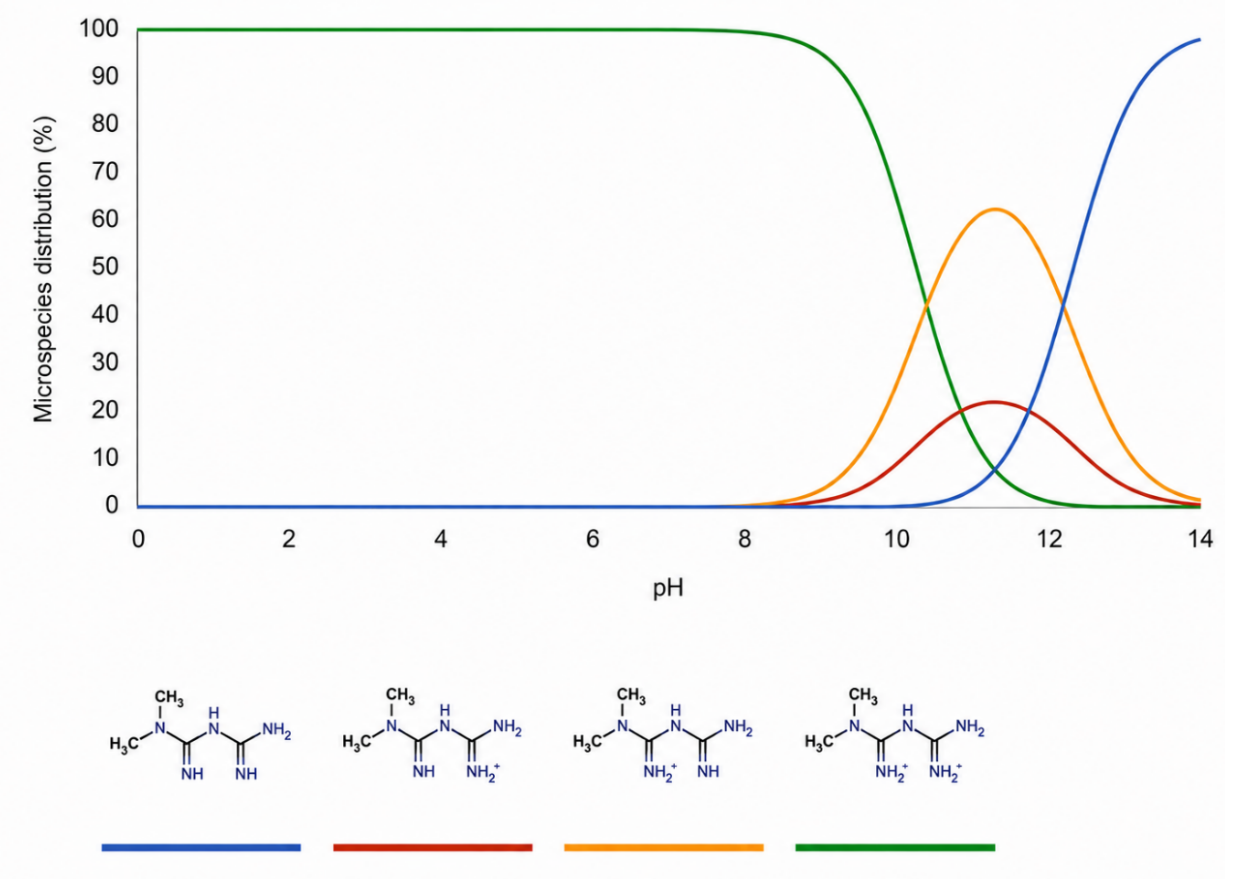

Fig. 2. Speciation diagram of metformin as a function of pH generated using Chemicalize software (ChemAxon).

Consequently, the cation-exchange behavior of clinoptilolite is primarily governed by this permanent structural negative charge rather than by the pH-dependent charge of the external surface. Therefore, the pH_{pzc} alone does not fully explain metformin uptake. Instead, the Na^+ release observed during the sorption experiments provides strong qualitative evidence supporting cation exchange as the predominant sorption mechanism under the evaluated conditions.

3.1.2 Metformin speciation as a function of pH

Metformin possesses two protonation sites with reported pKa values of approximately 2.8 and 11.5. Within the pH range investigated in this study (5–6), metformin predominantly exists in its protonated, positively charged monocationic form ($HMet^+$), as shown in Fig. 2 (Momeni *et al*., 2016).

Under these pH conditions, the chemical speciation of metformin favors interaction pathways primarily involving cation exchange, with a possible contribution from electrostatic interactions. Consequently, ion exchange with exchangeable cations, particularly Na^+, is expected to play a major role in the sorption process. In contrast, although HDTMA modification can provide additional organic domains and alternative interaction sites, the incorporation of bulky quaternary ammonium molecules may partially occupy exchange sites and reduce the accessibility of negatively charged sites within the zeolite framework, making Na^+-mediated ion exchange the most favorable pathway.

As the pH increases toward alkaline values, the fraction of less protonated metformin species increases, reducing the thermodynamic driving force for cation exchange processes. Therefore, the operational pH range employed in this study provides favorable conditions for evaluating sorption mechanisms dominated by ion exchange.

3.2 Structural and chemical characterization

3.2.1 FT-IR

Fig. 3 shows the FT-IR spectra of the studied zeolites, with ZN used as the reference material. The broad absorption band centered around 3400-3600 cm^{-1} (1) is attributed to the stretching vibration of O-H groups associated with adsorbed water and surface silanol (Si-OH) groups. The band at approximately 1635 cm^{-1} (2) corresponds to the H-O-H bending vibration of molecular water. The intense absorption band located between 1000 and 1200 cm^{-1} (3) is

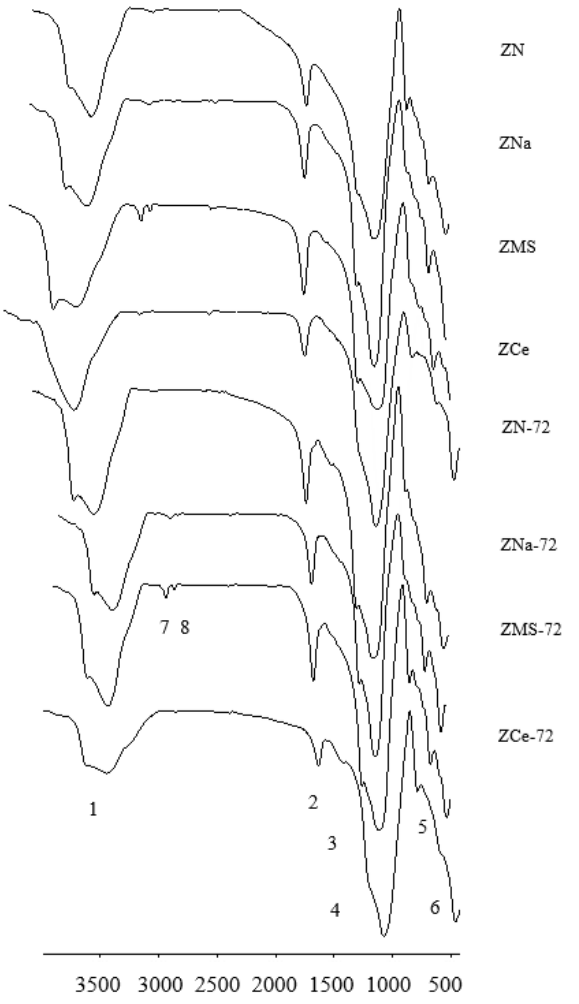

Fig. 3. FT-IR spectra of ZN, ZNa, ZMS and ZCe at different modification stages and after metformin sorption. Numbers indicate the principal absorption bands.

assigned to the asymmetric stretching vibrations of Si-O-Si and Si-O-Al linkages, whereas the bands near 790 cm^{-1} (4), 605 cm^{-1} (5), and 460-470 cm^{-1} (6) are attributed to the symmetric stretching, internal double-ring vibrations, and Si-O-Si bending vibrations of the aluminosilicate framework, respectively. These observations are consistent with reports describing the structure of natural zeolites (Doula, 2007; Helmi *et al*., 2024; Król *et al*., 2021; Naghash & Nezamzadeh-Ejhieh, 2015).

When comparing ZNa with ZN, slight variations in the intensity of the O–H bands can be observed. This suggests that cation exchange with sodium alters the hydration of the zeolite surface. The persistence of the framework band (3-6) indicates that the primary structure of the zeolite remains essentially unchanged during ion exchange (Alcantara-Cobos *et al*., 2019).

In the case of ZMS, more pronounced spectral changes are evident. New absorption bands (7 and 8) appear in the 2800–3000 cm^{-1} region, corresponding to the stretching vibrations of C–H bonds.

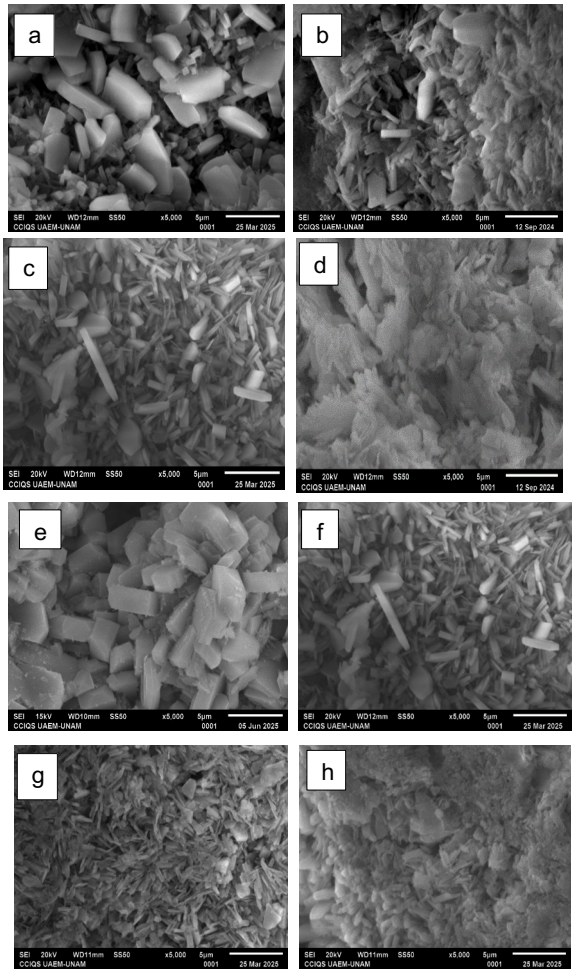

Fig. 4. SEM micrographs of zeolite samples at different modification stages: a) ZN b) ZNa treated with 0.1 mol L^{-1} NaCl c) ZMS treated with 30 mmol L^{-1} HDTMA d) ZCe e) ZN after 72 h of contact with metformin f) ZNa after 72 h of contact with metformin g) ZMS after 72 h of contact with metformin h) ZCe after 72 h of contact with metformin. All micrographs were acquired at the same magnification (x5,000) using a 5 μm scale bar.

These bands are assigned to the asymmetric and symmetric stretching vibrations of CH_2 groups from the long alkyl chain of HDTMA, confirming the successful incorporation of the surfactant onto the zeolite surface (Alcantara-Cobos *et al*., 2019; Naghash & Nezamzadeh-Ejhieh, 2015; Nezamzadeh-Ejhieh & Tavakoli-Ghinani, 2014; Rožić *et al*., 2009).

For ZCe, the introduction of cerium induces subtle changes in the O-H band (1) and in the framework region (3-6). Slight increases in intensity and broadening of the band suggest interactions between cerium species and surface hydroxyl groups, potentially through ion exchange or coordination bonding. Modifications in the low-frequency region may indicate the formation of metal–oxygen bonds (Ce–O) (Barczyk *et al*., 2014; Moshoeshoe *et al*., 2017).

Table 2. Elemental composition determined by EDS for zeolite samples.

Element	ZN	ZNa	ZMS	ZCe	ZN-72	ZNa-72	ZMS-72	ZCe-72
N	0	0	7.39 ± 0.47	0	0	0	0	0
O	---	---	**---**	---	----	----	----	----
Na	1.15 ± 0.30	2.51 ± 0.73	2.74 ± 0.39	0.05 ± 0.10	4.21 ± 1.37	1.91 ± 1.28	2.85 ± 0.49	0
Mg	0.33 ± 0.08	0.86 ± 0.18	0.70 ± 0.09	0.09 ± 0.08	0.53 ± 0.40	0.52 ± 0.23	0.47 ± 0.27	0.08 ± 0.07
Al	14.85 ± 0.30	16.12 ± 0.55	13.13 ± 0.71	11.94 ± 0.88	17.49 ± 1.66	17.21 ± 0.97	18.11 ± 1.26	18.22 ± 1.20
Si	73.26 ± 0.52	70.75 ± 0.01	75.22 ± 0.95	67.97 ± 1.62	69.30 ± 1.06	67.20 ± 1.55	68.46 ± 1.94	66.66 ± 3.54
K	3.73 ± 0.22	3.52 ± 0.55	3.51 ± 0.24	1.86 ± 0.23	3.45 ± 0.58	3.59 ± 0.28	3.26 ± 0.10	2.01 ± 0.40
Ca	5.79 ± 0.45	4.67 ± 0.82	3.85 ± 0.29	2.70 ± 0.47	5.84 ± 0.26	4.53 ± 0.16	4.58 ± 0.21	3.90 ± 0.54
Ti	0	0	0.01 ± 0.01	0	0.14 ± 0.10	0.17 ± 0.23	0.14 ± 0.19	0
Fe	0.91 ± 0.19	1.39 ± 0.22	0.83 ± 0.27	1.54 ± 0.63	1.36 ± 1.29	2.58 ± 0.84	2.13 ± 1.38	0.75 ± 0.73
Ce	--	---	---	13.86 ± 2.22	----	----	----	8.37 ± 3.00

Despite these changes, the FT-IR spectra recorded before and after contact with metformin did not show significant variations in the characteristic aluminosilicate framework bands (3-6). These observations suggest that no major alterations occurred in the characteristic functional groups of the zeolite framework during metformin sorption. Therefore, metformin is inferred to interact predominantly through surface cation-exchange sites and electrostatic interactions, while preserving the characteristic FT-IR features of the clinoptilolite framework.

3.2.2 SEM/EDS

Fig. 4a shows the ZN crystals, which exhibit the typical morphology of clinoptilolite: a laminar or sheet-like crystal structure with a columnar arrangement consistent with previous reports.

Treatment with NaCl (Fig. 4b) enhances the definition of crystal edges, likely due to the removal of amorphous surface phases during ion exchange an effect commonly reported in alkaline activation of zeolites (González-Ortiz *et al*., 2018; Helmi *et al*., 2024; Moshoeshoe *et al*., 2017; Nezamzadeh-Ejhieh & Tavakoli-Ghinani, 2014; Rožić *et al*., 2009; Salazar-Gil *et al*., 2016).

Modification with HDTMA (Fig. 4c) preserves the basal structure but increases surface roughness, attributed to surfactant micelle formation consistent with studies on zeolite functionalization for removal of organic contaminants (Alvarez-García *et al*., 2020; Helmi *et al*., 2024). In contrast, cerium loading (Fig. 4d) results in substantial agglomeration and loss of crystalline texture, likely caused by preferential nucleation of cerium oxide/hydroxide clusters on acidic surface sites (He *et al*., 2022) inducing pore blocking and local structural tension, as documented in metal-doped zeolite catalysts.

SEM micrographs of ZN, ZNa, ZMS, and ZCe after 72 h of contact with metformin (Fig. 4e–4h) show well-preserved crystalline morphology, with defined edges and irregular surfaces exhibiting thin surface coating, likely associated with adsorbed metformin (Biblioteca *et al*., 2023; Díaz-Nava *et al*., 2005; Ferri *et al*., 2024; Perić *et al*., 2004).

EDS results (Table 2) reveal a clear increase in sodium content in ZN and ZNa (1.15% → 2.51%), confirming successful NaCl conditioning, where sodium replaces native cations (Al Abri *et al*., 2024; Alcantara-Cobos *et al*., 2019; Hosseini *et al*., 2017; Torabian *et al*., 2010).

For ZNa, EDS analysis shows a marked decrease in sodium content after contact with metformin (2.51% → 1.91%), indicating the release of Na^+ from exchangeable positions within the zeolite framework. Variations in the relative proportions of Si and Al, together with reductions in K and Ca, are consistent with the displacement of exchangeable cations during metformin sorption, although EDS alone cannot directly identify the exchanged species (Biblioteca *et al*., 2023; Kukwa & Dann, 2019). Following 72 h of contact with metformin, only minor variations were observed in the relative contents of Si and Al, indicating that the aluminosilicate framework remained essentially unchanged during sorption, whereas the most significant compositional variations involved the exchangeable cations.

Nitrogen is detected only in ZMS, indicating the incorporation of the HDTMA surfactant. The absence of nitrogen in ZN, ZNa, and ZCe reinforces its use as a marker for ZMS functionalization (Alcantara-Cobos *et al*., 2019).

A general decrease in native cations (K, Ca, and in some cases Al and Si) is observed in ZMS compared with ZN and ZNa, consistent with ion-exchange processes where HDTMA replaces native clinoptilolite cations, modifying surface chemistry and affinity for organic molecules (Nannu Shankar *et al*., 2023). These compositional changes are consistent with the formation of an organic surfactant layer that partially modifies the accessibility of exchangeable cation sites.

The presence of cerium in ZCe confirms successful loading with cerium nitrate, introducing distinct physicochemical properties compared with HDTMA modification. The incorporation of cerium was accompanied by a marked decrease in Na, K, and Ca contents, suggesting that cerium species partially occupied or covered exchangeable cation sites on the

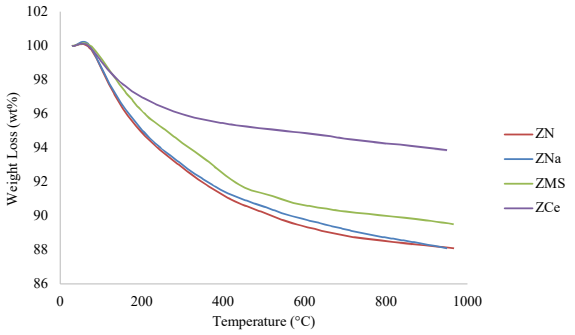

Fig. 5. TGA curves for ZN, ZNa, ZMS and ZCe.

external surface of the zeolite.

These results (Table 2) reflect the high cation exchange capacity of clinoptilolite and highlight how its composition changes following NaCl conditioning, cerium loading, and HDTMA modification, as well as after subsequent contact with metformin.

3.2.3 TGA

Fig. 5 presents the TGA curves for ZN, ZNa, ZMS and ZCe, exhibiting three main stages of weight loss associated with dehydration and dehydroxylation, with no evidence of framework degradation:

1. Surface dehydration (20–200 °C)

Weight loss is more pronounced in ZN (~3%) compared with ZNa and ZMS, indicating a greater amount of physically adsorbed water. The lower loss in ZNa suggests removal of impurities during sodium conditioning.

2. Zeolitic water (200–400 °C)

ZNa and ZCe show continuous weight loss associated with the removal of water coordinated to Na^+ and Ce^{3+}. ZMS exhibits reduced loss, likely due to pore occupation by HDTMA, decreasing water retention.

3. Structural dehydroxylation (400–800 °C)

This stage corresponds to elimination of structural –OH groups. Although weight loss is more prominent in ZCe, the overall stability of all samples up to 800 °C indicates a robust aluminosilicate framework (Helmi *et al*., 2024; Król *et al*., 2024; Montalvo *et al*., 2012).

These results confirm good thermal stability for all zeolites, with cerium incorporation not compromising structural integrity.

3.2.4 CHNS Analysis

Elemental CHNS results (Table 3) provide quantitative information about the chemical modifications introduced into the zeolite samples. ZN and ZNa exhibited negligible nitrogen contents and very low carbon percentages (0.08–0.09%), confirming the mineral nature of the aluminosilicate framework. Hydrogen contents of 1.34% and 1.22%, respectively, are mainly associated with adsorbed water and structural hydroxyl groups.

Table 3. Elemental composition determined by CHNS analysis for zeolite samples.

Sample	Weight	%N	%C	%H	%S
ZN	3.18	0	0.08	1.34	0
ZNa	3.14	0	0.09	1.22	0
ZMS	3.17	0.08	1.41	1.25	0
ZCe	3.12	0	0.07	0.3	0
ZN-72	2.71	0.22	0.25	1.29	0
ZNa-72	2.84	0.35	0.35	1.38	0
ZMS-72	3.09	0.33	1.59	1.53	0
ZCe-72	2.92	0.11	0.20	0.91	0

After HDTMA functionalization (ZMS), carbon increased markedly from 0.09% to 1.41%, while nitrogen rose to 0.08%, providing clear evidence of successful surfactant incorporation onto the zeolite surface. In contrast, as expected, ZCe did not introduce nitrogen; however, a significant decrease in hydrogen content (0.30%) was observed, suggesting that cerium loading altered the hydration environment of the zeolite surface through interaction with surface hydroxyl groups.

Following contact with metformin after 72 h, all materials showed increases in both carbon and nitrogen contents, confirming uptake of the pharmaceutical. For instance, nitrogen increased from 0 to 0.22% in ZN-72 and from 0 to 0.35% in ZNa-72, while carbon rose from 0.08% to 0.25% and from 0.09% to 0.35%, respectively. These increments are consistent with incorporation of an organic nitrogen-containing molecule within the zeolite structure.

Although ZMS-72 exhibited the highest carbon percentage (1.59%), this value is largely influenced by the intrinsic carbon contribution of the HDTMA layer rather than exclusively by metformin sorption. Therefore, CHNS results support the occurrence of ion exchange and surface interactions in all materials, with particularly clear evidence in ZNa, where nitrogen incorporation correlates with the pronounced sodium release observed during sorption.

3.3 Sodium release and implications for the sorption mechanism

Atomic flame emission analysis revealed a markedly higher release of Na^+ from sodium-modified clinoptilolite (ZNa), reaching 32.79 mg L^{-1} after 72 h of contact with metformin (Table 4). This result provides strong experimental evidence that cation exchange plays a dominant role in the sorption of metformin onto ZNa, consistent with previous reports for cationic pharmaceutical compounds interacting

Table 4. Sodium release during metformin sorption in zeolite samples.

Sample	Emission intensity	Na content (mg L^{-1})	Average Na content (mg L^{-1})
Control ZN 72 h	4	0	0
ZN-1	27	21.51	22.03
ZN-2	28	22.54	
Control ZNa 72 h	4	0	0
ZNa-1	40	34.84	32.79
ZNa-2	36	30.74	
Control ZMS 72 h	6	0	0
ZMS-1	30	24.59	23.56
ZMS-2	28	22.54	
Control ZCe 72 h	5	0	0
ZCe-1	6	0	0
ZCe-2	5	0	

with sodium-rich zeolitic materials (Biblioteca *et al.*, 2023).

The ion exchange process can be represented by the following reaction:

$$\text{Z-Na} + \text{HMet}^{+}_{(aq)} \rightleftharpoons \text{Z-HMet} + \text{Na}^{+}_{(aq)}$$

In contrast, ZN, ZMS, and ZCe exhibited substantially lower Na^+ release, indicating a reduced contribution of cation exchange mechanisms. For ZMS, the presence of the HDTMA surfactant layer likely limits access to exchangeable sites and restricts cation mobility within the zeolite channels. In the case of ZCe, the incorporation of cerium species appears to reduce the availability of exchangeable sodium ions within the framework, thereby diminishing ion exchange capacity.

The pronounced Na^+ release observed for ZNa correlates with its higher metformin sorption performance, suggesting that the uptake process is primarily governed by ion exchange between framework-associated Na^+ ions and protonated metformin species.

3.4 Sorption kinetics

The sorption kinetics were evaluated to identify the dominant rate-controlling mechanisms governing metformin uptake onto the different zeolitic materials and to determine the influence of each modification strategy under identical experimental conditions.

The sorption kinetics of metformin onto natural and modified clinoptilolite materials exhibited a two-stage uptake behavior (Fig. 6). An initial rapid sorption phase, occurring within the first approximately 15 h, was observed and can be attributed to interactions with readily accessible exchange sites. This stage was followed by a slower uptake period, suggesting the participation of additional mass-transfer processes, including intraparticle diffusion and the gradual occupation of

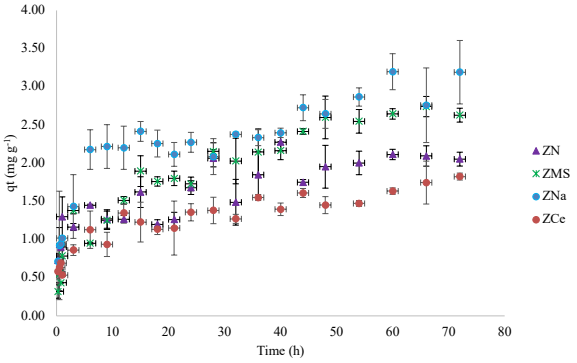

Fig. 6. Sorption kinetics of metformin (100 mg L^{-1}) on ZN, ZNa, ZMS and ZCe. Error bars represent the standard deviation of duplicate experiments.

internal exchange sites. After approximately 15 h, only minor fluctuations in sorption capacity were observed, remaining within the experimental variability of the measurements. Therefore, this contact time was considered representative of equilibrium conditions for kinetic model evaluation.

Sodium-modified clinoptilolite (ZNa) reached equilibrium within approximately 15 h and exhibited a sorption capacity (2.42 mg g^{-1}) at an initial metformin concentration of 100 mg L^{-1}, followed by ZMS (1.90 mg g^{-1}), ZN (1.62 mg g^{-1}), and ZCe (1.23 mg g^{-1}). These values fall within the range reported for natural clinoptilolite (1.5–2.0 mg g^{-1}) and clearly demonstrate the enhanced sorption performance achieved through sodium exchange (Ferri *et al.*, 2024).

A one-way analysis of variance (ANOVA) revealed statistically significant differences among the sorption capacities of the evaluated zeolite materials ($p<0.001$). Tukey´s multiple-comparison test further indicated statistically significant differences among the evaluated materials ($p<0.05$), yielding the following order of sorption performance: ZNa > ZMS > ZN > ZCe (Table 5).

Table 5. Sorption capacity of metformin on the evaluated zeolite systems and statistical comparison by one-way ANOVA and Tukey´s multiple-comparison test.

Zeolite system	qt (mg g^{-1})	Tukey grouping
ZNa	2.42 ± 0.01	a
ZMS	1.90 ± 0.01	b
ZN	1.62 ± 0.02	c
ZCe	1.23 ± 0.03	d

Values are expressed as mean ± standard deviation of duplicate experiments (n=2). Different lowercase letters indicate statistically significant differences according to Tukey's multiple-comparison test ($p < 0.05$).

Kinetic modeling results (Table 6) indicated that the Elovich model provided the best fit to the experimental data (R^2>0.90), followed by the pseudo-second-order model, whereas the pseudo-first-order model generally exhibited lower fitting performance. In addition to the coefficient of determination, the experimental equilibrium sorption capacities (q_e,exp) were compared with the equilibrium sorption capacities predicted by the pseudo-first order and pseudo-second-order models (q_e,cal). The pseudo-first-order model predicted equilibrium sorption capacities closer to the experimental values for ZN, ZNa, and ZCe than the pseudo-second-order model, whereas both models overestimated the sorption capacity of ZMS. The superior performance of the Elovich model suggests that metformin sorption occurs on energetically heterogeneous exchange sites, where the sorption rate progressively decreases as surface coverage increases. In zeolitic systems, this behavior is consistent with cation exchange processes involving variable-energy exchange sites rather than irreversible chemisorption.

The kinetic parameters also provide valuable information regarding the sorption process. For the pseudo-first-order and pseudo-second-order models, the model-calculated equilibrium sorption capacities (q_e,cal) increased after sodium modification, reflecting the enhanced cation-exchange capacity of ZNa compared with the natural zeolite. Likewise, the rate constants (k_1 and k_2) varied among the zeolitic materials, indicating that the different surface modifications influenced the sorption rate. Unlike the pseudo-first-order and pseudo-second-order models, the Elovich model does not include an equilibrium sorption capacity parameter; instead, its parameters provide additional mechanistic insight into the heterogeneous nature of the sorption process.

The parameter α represents the initial sorption rate, whereas β is associated with the progressive decrease in sorption rate as surface coverage increases on energetically heterogeneous surfaces. The relatively higher α value obtained for ZNa indicates a faster initial sorption rate, which is consistent with the greater availability of readily exchangeable Na^+ ions following sodium conditioning. Conversely, lower β values indicate a less pronounced decrease in sorption rate as surface coverage increases, suggesting more sustained occupation of available exchange sites. Together with the higher coefficients of determination, these findings further support the conclusion that the Elovich model provides the most appropriate description of metformin sorption onto the evaluated zeolitic materials.

The Weber-Morris intraparticle diffusion model (Table 7) was applied to evaluate the possible contribution of intraparticle diffusion during metformin sorption (Tran *et al*., 2017; Weber & Morris, 1963). The multilinear behavior observed for all materials indicates that metformin sorption proceeds through successive stages involving external film diffusion followed by intraparticle diffusion before equilibrium is attained. All regression lines exhibited positive intercept values (C>0), indicating that intraparticle diffusion was not the sole rate-controlling step (Weber and Morris 1963; Tran *et al*. 2017). Therefore, additional transport processes, including external mass transfer and surface interactions, also contributed to metformin uptake. These observations are consistent with the Elovich kinetic model and with the sodium release experiments, suggesting that cation exchange between exchangeable Na^+ ions and protonated metformin species ($HMet^+$) contributes predominantly to metformin sorption under the evaluated experimental conditions, while external mass transfer and surface interactions also participate in the overall sorption process.

In this context, the substitution of Na^+ by protonated metformin species ($HMet^+$) is facilitated through electrostatic interactions and ion exchange within the zeolite framework, accompanied by minor structural rearrangements. The superior kinetic performance observed for ZNa reflects the combined effect of high pore accessibility, a high density of exchangeable sodium ions, and the greater availability of readily exchangeable cationic sites following sodium conditioning. In contrast, HDTMA and cerium modifications partially restrict cation mobility within the zeolite channels, resulting in slower uptake rates.

Overall, the kinetic analyses, together with the sodium release experiments and complementary characterization techniques, consistently indicate that sodium conditioning enhances metformin uptake by increasing the availability of exchangeable cationic sites, whereas HDTMA functionalization and cerium loading partially restrict access to these sites. Collectively, these results support the interpretation that cation exchange is the predominant sorption mechanism under the evaluated experimental

Table 6. Nonlinear kinetic models used to describe metformin sorption on zeolite samples.

Zeolite system	Experimental qe, exp (mg g^{-1})	Pseudo First Order Model (Lagergren)			Pseudo Second Order Model (Ho)			Elovich Model		
		qe (mg g^{-1})	K_1 (h^{-1})	R^2	qe (mg g^{-1})	K_2 (g mg^{-1} h^{-1})	R^2	α (mg g^{-1} h^{-1})	β (g mg^{-1})	R^2
ZN	1.62	1.70 ± 0.08	1.36 ± 0.43	0.74	1.78 ± 0.08	0.90 ± 0.37	0.54	24.69 ± 19.20	4.16 ± 0.6	0.84
ZNa	2.42	2.49 ± 0.09	0.46 ± 0.11	0.77	2.67 ± 0.09	0.22 ± 0.06	0.84	5.85 ± 2.15	2.41 ± 0.19	0.92
ZMS	1.9	2.48 ± 0.13	0.08 ± 0.01	0.84	2.82 ± 0.18	0.04 ± 0.01	0.88	0.97 ± 0.28	1.89 ± 0.18	0.94
ZCe	1.23	1.38 ± 0.06	0.65 ± 0.20	0.59	1.48 ± 0.06	0.49 ± 0.17	0.72	5.01 ± 2.24	4.645 ± 0.41	0.89

Values are reported as fitted parameter estimates ± standard error obtained from nonlinear regression.

Table 7. Weber-Morris intraparticle diffusion model parameters for metformin sorption.

Zeolite system	KD (mg g^{-1} $h^{-1/2}$)	C (mg g^{-1})	R^2
ZN	0.1567	0.8526	0.7957
ZNa	0.2590	0.9727	0.8582
ZMS	0.2895	0.4332	0.9444
ZCe	0.1413	0.5823	0.9096

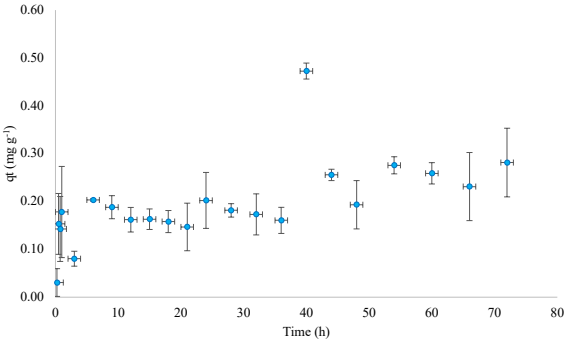

Fig. 7. Effect of contact time on metformin sorption by zeolitic materials (10 mg L^{-1}). Error bars represent the standard deviation of duplicate experiments.

conditions, while external mass transfer and surface interactions also contribute to the overall uptake process.

3.5 *Effect of the initial metformin concentration on sorption kinetics*

The effect of reducing initial metformin concentration from 100 to 10 mg L^{-1} on sorption kinetics was evaluated under otherwise identical experimental conditions. This reduction in concentration did not result in a proportional increase in sorption capacity, with a maximum uptake of approximately 0.28 mg g^{-1} after 72 h. The lower sorption capacity observed at 10 mg L^{-1} is consistent with the lower mass-transfer driving force and the lower amount of metformin available per unit mass of sorbent.

Similar behavior has been reported for microporous ion-exchange materials, where competition between inorganic cations (e.g., H^+ and Na^+) and organic cationic molecules constrains the total uptake capacity (Serna-Galvis *et al.*, 2024).

Across the investigated concentration range, ZNa consistently exhibited the highest sorption efficiency, suggesting that sodium conditioning enhances metformin uptake by increasing the availability of exchangeable Na^+ sites under the evaluated experimental conditions.

3.6 *Sorption mechanism*

Based on the combined structural, spectroscopic, and kinetic evidence, metformin sorption onto ZNa is predominantly governed by exchange between framework Na^+ ions and protonated metformin species ($HMet^+$), as schematically illustrated in Fig. 8. This process may also be stabilized by hydrogen bonding interactions between the amino groups of metformin and surface oxygen atoms of the aluminosilicate framework.

In the case of HDTMA-modified zeolite (ZMS), the presence of an organic surfactant layer introduces hydrophobic domains that may promote additional non-electrostatic interactions with metformin molecules. However, this modification simultaneously leads to partial blockage of internal channels and exchange sites, thereby limiting overall uptake capacity. For cerium-loaded zeolite (ZCe), the incorporation of Ce^{+3} species likely promotes partial pore obstruction and partial neutralization of active sites, significantly reducing the accessibility of exchangeable cations and, consequently, metformin sorption efficiency.

Overall, the proposed sorption mechanism, summarized in Fig. 8, describes a heterogeneous, activation-controlled pathway predominantly governed by electrostatic interactions and cation exchange phenomena. The sodium release experiments provide strong experimental evidence supporting cation exchange as the predominant sorption mechanism. Nevertheless, minor contributions from electrostatic interactions and hydrogen bonding cannot be completely excluded under the evaluated experimental conditions. Furthermore, direct spectroscopic evidence confirming the exchanged metformin species

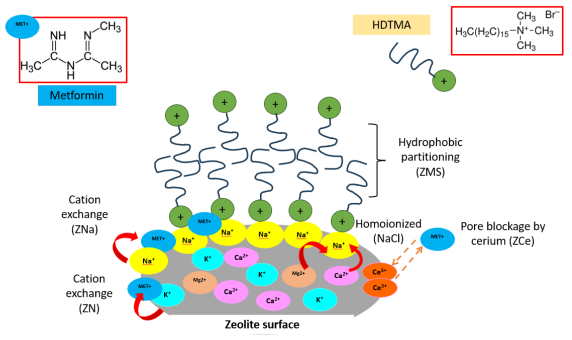

Fig. 8. Proposed sorption mechanism of metformin on natural and modified clinoptilolite systems. Schematic illustration of the proposed interactions between metformin and the four zeolitic materials (ZN, ZNa, ZMS, and ZCe), highlighting the predominant cation-exchange pathway in sodium-conditioned clinoptilolite and the reduced accessibility of exchange sites after HDTMA and Ce^{3+} modification.

was not obtained in the present study; therefore, additional spectroscopic investigations would be valuable to further verify the proposed mechanism.

3.7 Comparison of sorption performance with materials reported in the literature

To contextualize the performance of the materials evaluated in this study, Table 8 summarizes reported sorption capacities for metformin removal using different zeolite-based and aluminosilicate materials. The reported values reveal a strong dependence of sorption capacity on surface chemistry, initial solute concentration, operating temperature, solid-to liquid-ratio, contact time and material pretreatment, providing a relevant framework for comparison. Therefore, direct comparison of sorption capacities should be made with caution because differences in experimental design can substantially influence the reported adsorption performance.

The sodium exchanged clinoptilolite (ZNa) investigated in this work exhibited a sorption capacity of 2.42 mg g^{-1} under ambient conditions (25 °C, pH 5–6, C_0 = 100 mg L^{-1}), which is comparable to other aluminosilicate-based materials evaluated under controlled experimental conditions. Natural clinoptilolite evaluated by Ferri et al. (2024) exhibited an experimental sorption capacity of 6.8 mg g^{-1} under kinetic conditions (25 °C, pH 7, C_0 = 10 mg L^{-1}). The difference between the capacities obtained in both studies may be associated with variations in the initial metformin concentration, pH conditions, adsorbent dosage, contact time, and intrinsic properties of the zeolitic materials, including exchangeable cation content and accessibility of sorption sites. In addition, differences in adsorption methodologies, such as equilibrium criteria and experimental protocols, also contribute to the variability of the reported sorption capacities.

Considerably lower sorption capacities were reported for pumice derived zeolite (0.196 mg g^{-1}), likely due to differences in its physicochemical characteristics and the availability of active sorption sites (Prajaputra & Isnaini, 2023). Fe modified zeolites exhibited moderate performance (2.30 mg g^{-1}), attributed to changes in surface charge distribution and the presence of additional active sites (Helmi *et al*., 2024). Likewise, recent studies have demonstrated that surfactant-modified zeolites have been proposed as an effective strategy for improving adsorption properties, although the final performance depends on the nature of the target contaminant and the interaction mechanism involved (Flores-Alamo *et al*., 2025). These results indicate that chemical modification can influence metformin sorption; however, the effectiveness of each modification depends on the interaction between the introduced species and the dominant sorption mechanism (He *et al*., 2022).

Although the sorption capacities obtained in the present study are moderate compared with those reported for some modified adsorbents, direct comparisons should be made with caution because adsorption performance is strongly influenced by experimental conditions, including the initial metformin concentration, adsorbent dosage, contact time, pH, specific surface area, and the physicochemical properties of the sorbent. Furthermore, the primary objective of this work was not to maximize adsorption capacity but to elucidate the dominant sorption mechanism governing metformin uptake under controlled experimental conditions.

From a practical perspective, the moderate sorption capacities obtained suggest that additional optimization of the adsorbent or operating conditions would be required before large-scale application. Nevertheless, the mechanistic insights obtained in this study provide valuable information for the rational design and future optimization of zeolite-based sorbents for pharmaceutical removal.

In this context, the enhanced performance of ZNa compared with the untreated and other modified clinoptilolite materials highlights the importance of exchangeable sodium ions and cation exchange processes in metformin sorption. The results obtained under controlled laboratory conditions demonstrate how different chemical modifications influence the sorption mechanism, thereby providing a mechanistic basis for the future development of more efficient zeolitic materials for water treatment applications (Khader *et al*., 2022). Future studies including equilibrium isotherms over a wider concentration range will complement the mechanistic findings reported herein by enabling determination of the

Table 8. Comparison of reported sorption capacities for metformin removal using zeolitic materials.

Adsorbent	Conditions	Sorption capacity (mg g^{-1})	Reference
ZNa	25 °C, pH 5–6, C_0 = 100 mg L^{-1}	2.42	This work
Natural clinoptilolite	25–35 °C, C_0= 10 mg L^{-1}	6.80	(Ferri *et al*., 2024)
Fe–zeolite	25 °C, pH 7, C_0 = 50 mg L^{-1}	2.30	(Helmi *et al*., 2024)
Pumice–zeolite	pH 6–10, 14–40 °C, C_0 = 10 mg L^{-1}	0.196	(Prajaputra & Isnaini, 2023)

maximum sorption capacity and equilibrium behavior of these materials.

Conclusions

This study demonstrates that sodium-exchanged clinoptilolite (ZNa) showed the most effective sorption performance for metformin among the evaluated materials, achieving 2.42 mg g^{-1} at an initial concentration of 100 mg L^{-1} and pH 5-6, which is attributed primarily to the abundance and accessibility of exchangeable Na^+ sites. The consistent release of Na^+ ions during sorption, together with the kinetic modeling, Weber–Morris intraparticle diffusion analysis, and statistical evaluation, supports the interpretation that cation exchange between framework sodium and protonated metformin species ($HMet^+$) is the predominant sorption mechanism under the evaluated experimental conditions.

In contrast, HDTMA-modified (ZMS) and cerium-loaded (ZCe) zeolites showed reduced sorption capacities, suggesting that surface functionalization may partially block exchange sites or alter surface chemistry, thereby limiting ion-exchange efficiency. Structural characterization (FT-IR, SEM–EDS, TGA, and CHNS) did not reveal major alterations in the aluminosilicate framework after modification, suggesting that the observed differences in sorption performance arise mainly from variations in surface accessibility and the distribution of exchangeable active sites.

The pH_{pzc} values (5.84–6.02) and the good fit to the Elovich kinetic model (R^2>0.90), the statistically significant differences among the evaluated zeolite systems confirmed by one-way ANOVA and Tukey's multiple comparison test, and the positive intercepts obtained from the Weber–Morris intraparticle diffusion model collectively support a heterogeneous, activation-controlled sorption process in which exchangeable Na^+ sites play a predominant role. These findings indicate that intraparticle diffusion was not the sole rate-controlling step and are consistent with the proposed contribution of cation exchange during metformin sorption.

The primary objective of this study was to elucidate the dominant sorption mechanism of metformin on natural and chemically modified clinoptilolite rather than to optimize adsorption capacity or operational conditions. Although the sorption capacities obtained were lower than those reported in some studies under different experimental conditions, the results provide mechanistic evidence of the predominant role of cation exchange in metformin sorption. These findings contribute to a better understanding of pharmaceutical-zeolite interactions and provide a scientific basis for the rational design and future optimization of zeolite-based sorbents.

Future studies including equilibrium isotherms over a wider concentration range, regeneration and reusability assessments, a more detailed evaluation of the cation-exchange stoichiometry, and validation under practical operating conditions will complement the mechanistic findings reported herein by enabling determination of the maximum sorption capacity, equilibrium behavior, and long-term applicability of these materials.

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