Use of graphene oxide for the removal of norfloxacin and ceftriaxone antibiotics from aqueous solution: process optimization using response surface approach

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In this research, graphene oxide (GO) as an adsorbent was used to remove norfloxacin and ceftriaxone antibiotics from aqueous solutions. All environmental factors affecting removal (e.g., pH, adsorbent mass, contact time, and concentration) were optimized in a discontinuous system. The design of experiments and the optimization of variables were carried out using the response surface method (RSM). The results of the analysis of variance (ANOVA) and the regression coefficients of the quadratic terms indicated that the responses were significantly affected by all the studied variables ($P < 0.05$). Also, the quadratic polynomial model results corresponded to empirical data with a high coefficient of determination (i.e., $R^2 > 0.99$ for both antibiotics). Besides, the adjusted R^2 (R^2-adj > 0.98 for both antibiotics) was close to R^2 values, indicating a good and acceptable statistical model. According to the results, the optimal removal of antibiotics by GO occurs in conditions of pH of 8, 0.034 g of the adsorbent mass, a sonication time of 20 min, and a concentration of 25 mg L^{-1}. In these conditions, the maximum removal efficiencies of ceftriaxone and norfloxacin were equal to 95.87% and 98.64%, respectively. GO was recovered in five adsorption/desorption processes, and the removal efficiency declined very slightly after using the adsorbent for five cycles. Therefore, it is concluded that GO is an efficient and acceptable adsorbent for removing ceftriaxone and norfloxacin from aqueous environments.

KEYWORDS

central composite design, norfloxacin, ceftriaxone, response surface method, ultrasound-assisted removal

1 Introduction

The presence of pollutants of organic origin in water resources is considered a serious threat to the environment and human health (Singh et al., 2022). Pharmaceutical compounds account for a type of these pollutants entering surface and underground water sources, mainly through sewage and urban/industrial effluents. Due to their high stability, the presence of pharmaceutical substances in the environment not only causes disturbances in the standard wastewater treatment processes in treatment systems but also

exerts toxic effects on humans and other living organisms; hence, their removal is of interest to researchers (Jäger et al., 2018; Farhat et al., 2022).

Among the wide range of pharmaceutical pollutants, antibiotics are widely used in medicine and veterinary medicine because of their antimicrobial effects (Bilal et al., 2023). These organic compounds enter the environment not only through effluent from the pharmaceutical industry but also due to an incomplete metabolism mechanism during the treatment period. In this respect, the persistent presence of antibiotics in the aquatic environment and their bioaccumulation leads to microbial and bacterial resistance (Wydro et al., 2023; Wysowska et al., 2024).

As an antibiotic of the third generation of cephalosporins, ceftriaxone ($C_{18}H_{18}N_8O_7S_3$) is used to kill many bacteria and to treat bacterial infections such as meningitis, gonorrhea-induced infections, pneumonia, and orthopedic surgeries (Nguyen et al., 2022). The main side effects of ceftriaxone include skin and digestive complications, dyspnea, increased blood platelet levels, anaphylactic shock, anaphylactoid reactions, and cardiac arrest. These effects have severe effects on patient's life-threatening in many cases. Unfortunately, the excessive use of ceftriaxone in unnecessary cases (e.g., colds) is an important factor for the increased occurrence of the drug's side effects. Ceftriaxone may also cause severe intestinal disorders such as diarrhea or abdominal cramps (Tao et al., 2024). Research has shown that some of these highly consumed antibiotics enter the wastewater treatment systems in their original form daily through the renal biliary excretion system of the patients under treatment (Noman et al., 2022).

As the second generation of fluoroquinolones, the antibiotic norfloxacin ($C_{16}H_{18}FN_3O_3$) is used to treat various infections, particularly urinary infections (Liu et al., 2022). This antibiotic prevents the function of a bacterial enzyme involved in DNA replication called DNA gyrase and topoisomerase II and inhibits the multiplication of bacterial DNA. The side effects of norfloxacin include nausea, headache, fatigue, arthritis, gastrointestinal bleeding, depression, and indigestion (Swidan and Rubin, 2020). This drug can cause severe side effects such as tendon irritation or rupture and nervous system problems. Tendon problems may appear a long time after treatment and can lead to lifelong disability in severe cases (Sharma et al., 2008). Multiple fluoroquinolone family antibiotics and their modified by-products in drinking water, surface and underground water, and wastewater have currently caused major concerns (Hiasa, 2018; Bhatt and Chatterjee, 2022).

These pollutants not only do not vanish in wastewater treatment systems but also kill effective microbes in biological treatment, leading to the ineffectiveness of wastewater treatment systems (Pei et al., 2019; Madhusoodanan, 2022). Due to their resistance to biological decomposition, these compounds enter the environment (particularly water sources) through wastewater treatment plants (Kim et al., 2023). Researchers have frequently addressed the entry of these antibiotics into the environment in the concentration range of ng L^{-1} to µg L^{-1} (Dorival-García et al., 2013). Therefore, it is necessary to adopt appropriate treatment methods to eliminate or reduce such antibiotics before entering the environmental resources.

Various methods, such as chemical precipitation, biological processes, ion exchange, membrane filtration, and electrochemical techniques, are available for antibiotic-containing wastewater treatment (Molinari et al., 2020; Uluseker et al., 2021; Spit et al., 2022; Li J. et al., 2023; Vinayagam et al., 2023; da Silva Júnior et al., 2024). The efficiency of these methods is limited due to the high cost, long treatment time, toxicity of chemicals, prohibition in wide applications, and limited access in developing countries, making it necessary to use alternative techniques (Ahmed et al., 2021). Adsorption is among the low-cost methods of high interest used for reducing some pollutants for various reasons such as low cost, flexibility, simplicity of design, ease of operation, insensitivity to toxic pollutants, and the availability of a wide range of inexpensive adsorbents compared to other treatment methods (Tony, 2022; Dutta et al., 2024).

Different adsorbents, including natural and synthetic adsorbents, are used in adsorption method. A group of synthetic adsorbents used for this purpose is graphene oxide (GO). The identified unique properties of this adsorbent (e.g., a high surface area, special functional groups on the surface, and high absorption capacity) have nowadays directed attention toward using this material as an adsorbent (Wang et al., 2018; Krishna et al., 2023).

Yang et al. (2022) used the GO adsorbent to remove enrofloxacin and rhodamine B. They obtained the optimum conditions as a pH of 7, optimal contact time of 23 min, and removal of ˃92.5% for both analytes. The GO adsorbent performed well in enrofloxacin and rhodamine B removal from an aqueous solution with maximum adsorption capacities of 45.035 and 107.230 mg g^{-1} for enrofloxacin and rhodamine B, respectively (Yang et al., 2022).

Kadhim et al. (2020) modified the polyether sulfone (PES) membrane using the GO adsorbent. They used the PES/GO adsorbent to remove Acid Black and Rose Bengal. They presented evidence that this adsorbent could efficiently remove the mentioned dyes. The performance of the PES/GO adsorbent showed a removal rate of >99% for both dyes (Kadhim et al., 2020).

Madadrang et al. (2012) removed Pb (II) through the silanization reaction between N-(trimethoxysilylpropyl) ethylenediamine triacetic acid (EDTA-silane) and hydroxyl groups on the GO surface to improve the removal technique. The results showed that the adsorption capacity of the adsorbent to remove Pb (II) was equal to 479 mg g^{-1} (Madadrang et al., 2012).

Yang et al. (2011) used GO to remove methylene blue from aqueous solutions. They reported that using the hematite powder adsorbent could remove more than 99% of methylene blue from aqueous solutions, with an adsorption capacity of 714 mg g^{-1} (Yang et al., 2011).

This study reports using GO as an adsorbent to remove ceftriaxone and norfloxacin from aqueous solutions. The surface characteristics of the adsorbent and operating variables in the adsorption process, including pH of the solution, concentration, time, and mass of the adsorbent, were investigated in this research.

2 Materials and methods

2.1 Chemicals, reagents, and instrumentation

The materials used in this study include laboratory-grade chemicals without the need for further purification. A stock

solution of the antibiotics (1,000 mg L^{-1}) was prepared in double distilled water (DDW). Working solutions were prepared by diluting the stock solution. In all experiments, DDW was used to prepare solutions and reagents. The pH of the solution was adjusted using 0.1 M HCl and 0.1 M NaOH. The pH was measured by a pH meter (Metrohm 632). The adsorbent was separated from the mixture with an Andreas Hettich D72 centrifuge. The residual concentration of antibiotics was quantified using a (DR6000) UV-VIS spectrophotometer. The GO adsorbent was characterized with a scanning electron microscope (SEM, Cambridge Stereoscan S360), a Fourier transform infrared spectrophotometer (FTIR, Thermo Nicolet Avatar 370), x-ray powder diffraction (XRD, Philips XPERT MPD), and Brunauer-Emmett-Teller (BET, NOVA 2000e) techniques.

2.2 Synthesis of GO

GO was synthesized using the Hummers method. According to this method, 23 mL of concentrated sulfuric acid was added to 1 g of graphite powder, and the resulting mixture was stirred at 5°C for 20 min. The color of the solution is black due to the presence of graphite. Then, 0.5 g of sodium nitrate was added to the solution and stirred at 20°C for 30 min. Next, 3 g of potassium permanganate was added to the mixture gradually during 1 h. The graphite oxidation process was completed by stirring the mixture on a stirrer for 3 h. At this stage, the color of the solution turned dark green. Afterward, 100 mL of DDW was added to the solution and stirred for some time, followed by adding about 5 mL of hydrogen peroxide to neutralize the excess permanganate. Finally, the GO obtained from the solution was separated using a centrifuge at 2,500 rpm. The separated GO was washed with DDW several times. Graphite oxide was converted to graphene oxide by heating it in an ultrasonic bath with a power of 400 W for 30 min. Next, the precipitate was separated from the liquid through centrifugation. Finally, GO powder was obtained by drying the resulting precipitate completely in an oven with a maximum temperature of 80°C for 24 h (Omar et al., 2023).

2.3 Experimental design

Using design methods in any research helps manage the order and number of required tests before starting the tests such that the least number of tests are needed in the shortest time. Using this method, in turn, saves time, reduces material consumption, and improves accuracy (Li X. et al., 2023).

Statistical and multivariate engineering techniques such as the response surface method (RSM) are among the widely used design methods in wastewater treatment. Studies employ RSM to build models free from problems existing in the method of changing one factor at a time (OFAT) and can simultaneously examine and optimize the effect of multiple factors (Maldonado al., 2023). Compared to OFAT, the advantages of RSM include prioritizing the importance of factors, reducing the number of tests, determining the interaction between factors, providing a mathematical relationship between factors to reach the response, and predicting new answers by changing the factors (Shojaei et al., 2021a; He et al., 2023).

TABLE 1 The CCD of independent variables.

Variables	Unit	Symbols	Level of variables				
			−α	−1	0	+1	+α
Concentration	mg L^{-1}	A	20	40	60	80	100
pH of solution	—	B	3	5	7	9	11
Adsorbent mass	g	C	0.01	0.02	0.03	0.04	0.05
Sonication time	min	D	5	10	15	20	25

The built models may also be applied to access the linear or quadratic effects of the tested factors and various graphs, including the interaction graphs between the factors. RSM includes factors, levels, and responses (Veza et al., 2023).

Factors are actually the variables affecting the results of tests, namely environmental factors such as pH, contact time, adsorbent mass, and adsorbent concentration in adsorption processes. The levels refer to the range of factor changes, including the minimum, maximum, and average values of the factors. The responses deal with the necessary values for the outputs.

Among the RSM design methods, the central composite design (CCD) method was chosen in the present study due to the greater number of levels. In this design, the factors have five levels defined as -α, −1, 0, +1, and +α. Here, +α and -α are the maximum and minimum values of each factor, respectively (Amin et al., 2023). In this method, four important and influential factors (i.e., pH, adsorbent mass, contact time, and concentration) were simultaneously optimized using Design-Expert V.12 software. This design allows the responses to be modeled by fitting a second-order polynomial, which can be expressed as (Equation 1).

$$Y = \beta_0 + \sum_{i=1}^{k} \beta_i X_i + \sum_{i=1}^{k} \beta_{ii} X_i^2 + \sum_{i \le j}^{k} \sum_{j}^{k} \beta ij X_i X_j + e \quad (1)$$

where β0, βi, βii, and βij are the constant, linear, square, and interaction coefficients of the factors, respectively. Xi and Xj are independent variables, and e is the unpredicted error. Y (R%) is the response. In the CCD design, the number of tests is calculated using Equation 2.

$$N = 2^k + 2K + nc \quad (2)$$

where k is the number of independent variables, and nc is the number of central points. According to the mentioned inputs, the model determined 30 tests for each antibiotic. Table 1 shows the test design matrix of CCD to remove antibiotics. The number of responses defined for the Design-Expert software included the removal percentages of ceftriaxone and norfloxacin (Table 2).

2.4 Removal of ceftriaxone and norfloxacin from aqueous solution by GO

This empirical study was conducted discontinuously on a laboratory scale in 250-mL Erlenmeyer flasks. Operating factors, including pH (3–11), contact time (5–25 min), concentration

TABLE 2 The CCD with their corresponding experimental and predicted removal.

	Variables				Ceftriaxone		Norfloxacin	
Run	A	B	C	D	Observed	Predicted	Observed	Predicted
1	−2	0	0	0	82.57	82.13	92.25	90.32
2	1	−1	−1	1	40.43	41.22	40.06	40.70
3	1	1	−1	−1	36.39	38.22	35.87	36.78
4	1	−1	1	−1	37.62	38.39	41.41	41.20
5	0	0	0	0	71.5	71.71	78.05	75.47
6	2	0	0	0	42.69	40.60	37.49	36.63
7	0	2	0	0	58.79	56.92	61.5	59.52
8	−1	1	−1	1	71.06	71.55	76.64	78.17
9	1	1	1	−1	47.65	48.53	49.29	51.40
10	−1	−1	1	1	80.85	80.28	79.11	79.52
11	−1	1	−1	−1	54.8	54.85	61.57	61.45
12	−1	−1	1	−1	58.29	59.14	66.73	67.64
13	0	0	−2	0	44.37	43.46	45.54	44.64
14	0	0	0	0	69.62	71.71	75.48	75.47
15	0	0	0	2	76.43	75.28	79.77	78.58
16	0	0	0	0	74.22	71.71	73.02	75.47
17	1	−1	1	1	54.17	55.38	48.91	50.50
18	−1	1	1	−1	68.94	69.41	75.4	76.08
19	0	0	0	0	72.37	71.71	76.47	75.47
20	−1	1	1	1	89.01	90.30	89.16	90.99
21	1	1	−1	1	50.36	50.77	50.35	50.92
22	0	−2	0	0	37.75	37.10	41.67	40.86
23	0	0	0	−2	42.97	41.60	54.16	52.56
24	1	1	1	1	64.43	65.27	64.48	63.73
25	1	−1	−1	−1	28.46	28.43	29.95	29.59
26	−1	−1	−1	1	61.47	61.86	70.35	69.71
27	−1	−1	−1	−1	44.5	44.92	53.96	56.02
28	0	0	0	0	70.19	71.71	73.19	75.47
29	0	0	2	0	73.79	72.18	70.95	69.07
30	0	0	0	0	72.38	71.71	76.62	75.47

(20–100 mg L^{-1}), and the adsorbent mass (0.01–0.05 g), were investigated in this research. The removal process of antibiotics was implemented with GO in an ultrasonic bath. For each test, 150 mL of the sample with an antibiotic concentration of 25 mg L^{-1} was first poured into the Erlenmeyer flask. If needed, 0.1 M NaOH or 0.1 M HCl solutions were used to adjust the pH of the samples. Next, a determined volume of the GO adsorbent was weighed and added to the sample in an Erlenmeyer flask, and the suspension was heated in an ultrasonic bath for a defined period. After the determined

contact time, centrifugation was applied to separate adsorbent particles from the sample. The antibiotic concentration in the final solution was measured by a spectrophotometer. The antibiotic removal percentage was calculated using Equation 3.

$$\%Removal = \frac{C_0 - C_e}{C_0} \times 100 \qquad (3)$$

where C_0 and C_e are the initial and final concentrations of the antibiotic (after the adsorption process), respectively.

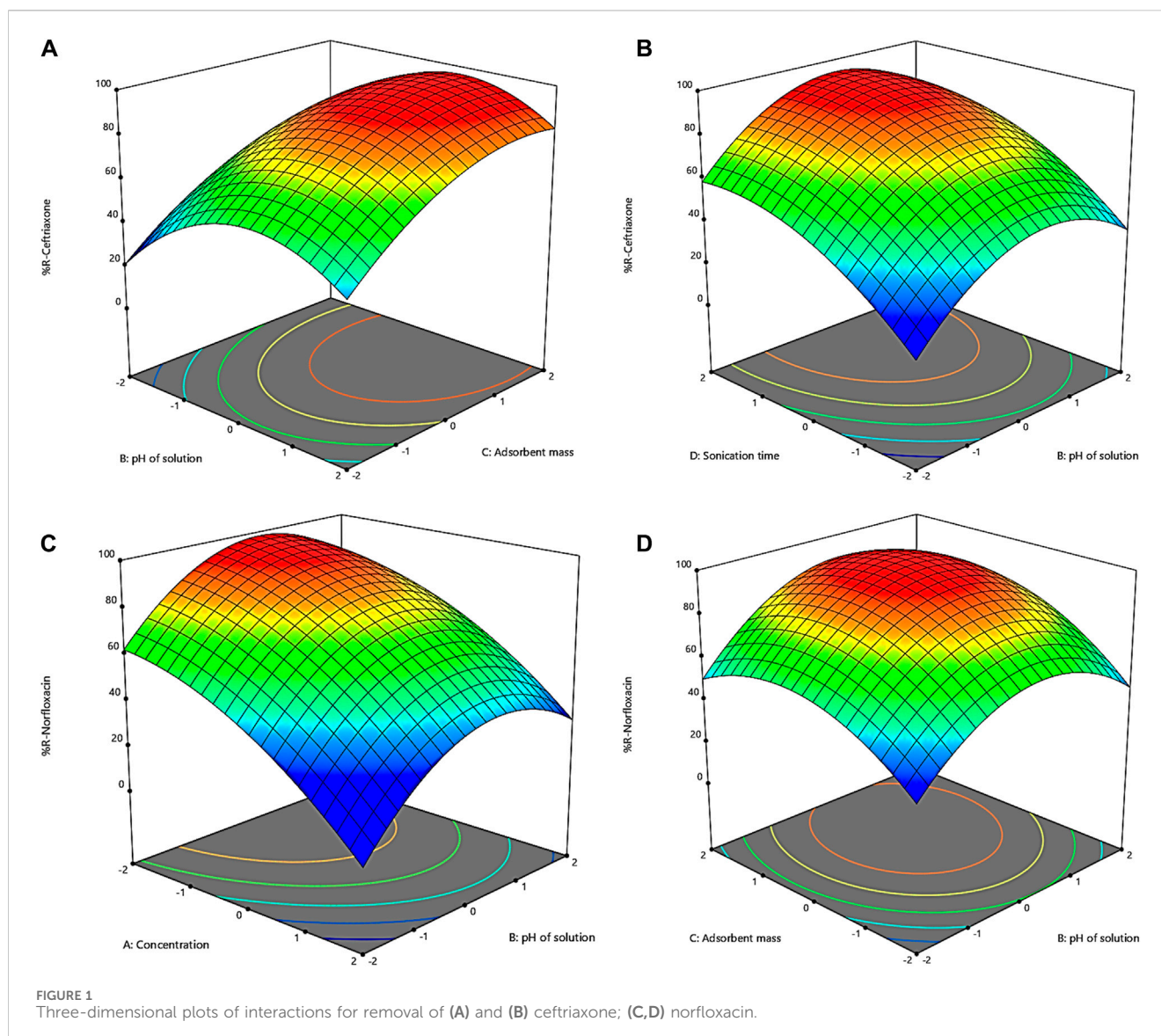**TABLE 3** The ANOVA of remove ceftriaxone and norfloxacin.

Source	DF	Ceftriaxone				Norfloxacin			
		Sum of squares	Mean square	F-value	*P*-value	Sum of squares	Mean square	F-value	*P*-value
Model	14	7566.90	540.49	201.55	<0.0001	8376.49	598.32	153.20	<0.0001
A	1	2586.90	2586.90	964.64	<0.0001	4323.39	4323.39	1107.03	<0.0001
B	1	589.35	589.35	219.76	<0.0001	522.11	522.11	133.68	<0.0001
C	1	1237.40	1237.40	461.42	<0.0001	894.99	894.99	229.17	<0.0001
D	1	1701.01	1701.01	634.30	<0.0001	1,015.30	1,015.30	259.97	<0.0001
AB	1	0.0189	0.0189	0.0071	0.9342	3.10	3.10	0.79	0.3872
AC	1	18.13	18.13	6.76	0.0201	0.0000	0.0000	6.40	0.9980
AD	1	17.20	17.20	6.41	0.0230	6.66	6.66	1.70	0.2114
BC	1	0.1139	0.1139	0.0425	0.8395	9.09	9.09	2.32	0.1479
BD	1	0.0588	0.0588	0.0219	0.8842	9.18	9.18	2.35	0.1460
CD	1	17.62	17.62	6.57	0.0216	3.26	3.26	0.83	0.3755
A^2	1	183.48	183.48	68.42	<0.0001	246.62	246.62	63.14	<0.0001
B^2	1	1046.33	1,046.33	390.17	<0.0001	1095.49	1095.49	280.50	<0.0001
C^2	1	331.00	331.00	123.43	<0.0001	594.30	594.30	152.17	<0.0001
D^2	1	302.12	302.12	112.66	<0.0001	167.99	167.99	43.01	<0.0001
Residual	15	40.23	2.68			58.58	3.91		
Lack of Fit	10	26.32	2.63	0.9462	0.5622	38.40	3.84	0.9515	0.5595
Pure Error	5	13.91	2.78			20.18	4.04		
Cor Total	29	7607.13				8435.07			

Model Summary Statistics								
		Ceftriaxone			Norfloxacin			
Precision		R^2	R^2-Adj	R^2-Pred	R^2	R^2-Adj	R^2-Pred	
		0.9947	0.9898	0.9774	0.9931	0.9866	0.9703	

3 Results and discussion

3.1 Characterization of the GO adsorbent

The FT-IR technique is a powerful characterization method used to determine functional groups in a substance. Supplementary Figure S1 A shows the FT-IR spectrum of GO. The FT-IR pattern recorded at room temperature was measured in the range of 4,000–500 cm^{-1}. The peak at 3,400 cm^{-1} belongs to the presence of the hydroxyl group, 1730 cm^{-1} corresponds to carboxyl groups, 1,650 cm^{-1} is assigned to the carbon-carbon double bond (C = C), and 1,220 cm^{-1} refers to epoxy rings on the surface of GO. The carbon-oxygen bond also creates the 1,050 cm^{-1} peak. SEM was applied to determine the morphology of the GO adsorbent. According to the SEM image of GO (Supplementary Figure S1 B), the adsorbent surface is layered with the layers overlapped on each other. Due to the π-π bond between the benzene rings on the surface of GO, bonding is possible between different adsorbent layers, forming multilayer GO in this case. Supplementary Figure S1 C represents the N$_2$ adsorption and desorption isotherm for GO. The surface area of GO and the total volume of its cavities were measured using the BET method. The obtained surface area of GO, the holes' total volume, and the holes' average diameter were equal to 260.8 m^2 g^{-1}, 0.254 cm^3 g^{-1}, and 3.85 nm, respectively. According to the IOPAC, adsorbents with pore sizes between 2 and 50 nm are called mesoporous. Therefore, GO falls under the mesoporous adsorbents. The structure of GO was identified using the XRD analysis. The obtained results of the XRD pattern of GO (Supplementary Figure S1 D) show that the main peak at 2θ = 11.3° belongs to the GO (002) plane, and a weak peak at 2θ = 43° results from the un-laminated graphite.

FIGURE 1
Three-dimensional plots of interactions for removal of **(A)** and **(B)** ceftriaxone; **(C,D)** norfloxacin.

3.2 Statistical analysis

Table 3 represents the ANOVA data for ceftriaxone and norfloxacin removal. After entering the required information into the software and running the model, the usefulness and appropriateness of the model should be evaluated in terms of application in the removal process of antibiotics. These assessments can be done using the ANOVA table data provided by the model. In this table, the *P*-value shows the effect of the factors on the response; the higher its value, the lower the effect of the factor. Therefore, if the *P*-value is >0.05 in a model, it means a very low impact of the factors on the obtained response, thereby rendering the model inappropriate. On the other hand, when the *P*-value is <0.05, the confidence level of the model is >95%, meaning favorable conditions (Di Leo and Sardanelli, 2020; Li Z. et al., 2023). According to Table 3, the *P*-value of the model is <0.0001 for both antibiotics, suggesting that the model is acceptable. The F-value represents a measure of the significance or validity of the model, and a higher value indicates more

significance of the model. The F-value was high for both models, suggesting that the model is generally significant and acceptable.

Lack of fit (LOF) means the degree of compatibility of the model with real data, which should not be significant. The most ideal model is the one in which the model's fit with the laboratory data is statistically significant, and its incompatibility is not significant. Since such an ideal state can be seen for both antibiotics, it can be concluded that the models produced for both antibiotics and the responses provided by these models are in good agreement with the laboratory data. The coefficient of determination (R^2) should also be controlled in addition to examining the *P*-value and F-value. The closer R^2 is to 1, the better the model corresponds to the laboratory data. In addition to the R^2, this software provides two other coefficients of determination: 1) one belonging to the laboratory data, known as the adjusted R^2 (R^2-Adj) and 2) the prediction of the model responses, called the prediction R^2 (R^2-Pred). The difference between these two values should be less than 0.2 for the model to be acceptable (Yin et al., 2023). It can also be seen that this agreement is established in Table 3.
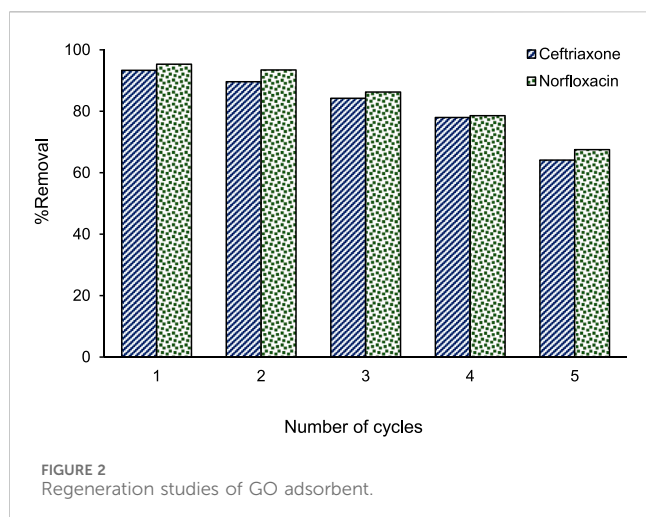
FIGURE 2
Regeneration studies of GO adsorbent.

In addition to examining the numbers in the ANOVA table, the obtained graphs should also be verified to visually evaluate the appropriate agreement of the model results with the laboratory data. Supplementary Figure S2 shows the real and predicted values for the response of the removal percentage of norfloxacin and ceftriaxone. Obviously, a good agreement exists between the predicted values of the model and the laboratory data because the laboratory-obtained points are distributed near the normal line. Among the useful outputs provided by the software is a mathematical equation between the factors affecting the removal (i.e., pH, contact time, adsorbent mass, and concentration) to reach the response. Equations 4, 5 are polynomial functions illustrating significant relationships between experimental variables and responses in the experimental design.

$$\begin{aligned} \text{Removal of ceftriaxone} = &+ 71.71 - 10.38A + 4.95B + 7.18C \\ &+ 8.41D - 0.03AB - 1.06AC - 1.03AD \\ &+ 0.08BC - 0.06BD + 1.04CD - 2.58A^2 \\ &- 6.17B^2 - 3.47C^2 - 3.31D^2 \end{aligned}$$

$$(4)$$

$$\begin{aligned} \text{Removal of norfloxacin} = &+ 75.47 - 13.42A + 4.66B + 6.10C \\ &+ 6.50D + 0.44AB - 0.01AC - 0.64AD \\ &+ 0.75BC + 0.75BD - 0.45CD \\ &- 2.99A^2 - 6.31B^2 - 4.65C^2 - 2.47D^2 \end{aligned}$$

$$(5)$$

where A, B, C, and D were concentration, pH, adsorbent mass, and sonication time, respectively.

3.3 Three-dimensional plots

Design-Expert software can also provide three-dimensional levels of the influence of factors on the response and exhibit the influence level of each factor on the response in colored forms. Figures 1A–D present the three-dimensional response surface for the effect of two factors simultaneously on the antibiotic removal rate. Accordingly, all four factors have a maximum area, indicating the influence of each factor on the response.

Figure 1A shows the effect of pH changes on ceftriaxone removal by the GO adsorbent. The range of pH changes was chosen to be from 3 to 11. Figure 1A shows that ceftriaxone has a low removal percentage in the acidic range. In other words, the reactions between the adsorbent and the adsorbate are low in these conditions. The removal percentage increases with rising pH toward neutral; however, the removal percentage declines with the continued ascending trend of pH. These observations can be attributed to the type of bond between ceftriaxone and the adsorbent, which is related to the surface charge of the adsorbent because this bond is electrostatic. The lowest negative charge for the GO adsorbent exists at acidic pHs. Therefore, an increase in both pH and the negative charge of the adsorbent allows for more bonds between the cationic molecule and GO, leading to increased adsorption (Zhang et al., 2016). The decrease in adsorption at pHs >7 is due to water ionization in the basic environment. Since the adsorbent is a hydrophilic substance, it shows a greater reaction affinity to water than ceftriaxone molecules. Indeed, water molecules and ceftriaxone molecules compete to seize the negative charges of the adsorbent surface in basic conditions, and the presence of this competitor lowers antibiotic adsorption (Olusegun et al., 2023).

To investigate the effect of the adsorbent mass on the removal of ceftriaxone, values of 0.01 to 0.05 g were chosen for the adsorbent. Figure 1A illustrates the effect of changes in the adsorbent mass on the ceftriaxone removal rate by the GO adsorbent. According to Figure 1A, the removal efficiency of ceftriaxone increased with increasing the adsorbent from 0.01 g to 0.05 g. The elevated efficiency with increasing the adsorbent mass can be attributed to the expanded surface of the adsorbent in contact with GO. This increased surface, in turn, amplifies the number of available adsorption sites for pollutant adsorption (Shojaei et al., 2021b). As can be inferred from Figure 1A, an amount of 0.034 g was optimal for the GO adsorbent. Moreover, this part of the study showed that the removal efficiency was not significantly affected by increasing the GO mass by more than 0.034 g.

Figure 1B shows the effect of contact time on the ceftriaxone removal rate by the GO adsorbent. The contact time was examined in the range of 5–25 min. According to Figure 1B, the contact time changes have two slopes in times <20 min and >20 min. The first part has a high slope, indicating the rapid adsorption process in this period. From the beginning to the first 20 min, the surface sites of the adsorbent are filled with ceftriaxone, and a rapid connection is established between ceftriaxone molecules and the GO adsorbent. After 20 min, the removal rate decreases because the sites are occupied on the adsorbent surface, making it necessary for ceftriaxone molecules to penetrate the adsorbent and fill the internal sites and pores (Anjum et al., 2019). Since GO is a mesoporous adsorbent with a pore diameter of about 3.8 nm and relatively large ceftriaxone molecules, penetration into the pores may be difficult. Therefore, a very low slope of the graphs can be seen in the second part. This slope suggests that a contact time of more than 20 min does not significantly affect removal, and it is not economical to use longer times. As mentioned above, an optimal contact time of 20 min was estimated for ceftriaxone.

Figure 1C represents the effect of norfloxacin concentrations on the GO adsorbent's removal efficiency. The impact of concentration on the removal efficiency of norfloxacin was investigated in the range of 20–100 mg L^{-1}. According to Figure 1C, the removal

TABLE 4 Effects of influence substances on the removal of ceftriaxone and norfloxacin (N = 3).

Foreign ions	Added as	Tolerable concentration (w/w)	Ceftriaxone	Norfloxacin
Cl^-	KCl	1,000	98.24 ± 1.6	98.09 ± 2.2
Ba^{2+}	$BaCl_2$	800	98.15 ± 1.7	98.54 ± 1.1
Ca^{2+}	$CaCl_2$	600	96.68 ± 2.1	97.04 ± 1.8
Ag^+	$AgNO_3$	100	97.06 ± 1.3	97.35 ± 1.4
Ni^{2+}	$Ni(NO_3)_2$	50	97.16 ± 2.0	96.56 ± 1.5

TABLE 5 Removal of ceftriaxone and norfloxacin from the environmental samples (N = 3).

Samples	Ceftriaxone	Norfloxacin
Tap water	93.89 ± 1.5	95.88 ± 1.2
Wastewater	89.95 ± 2.1	98.55 ± 1.0
Groundwater	91.65 ± 1.3	94.43 ± 2.2

efficiency decreased due to insufficient surface to adsorb higher concentrations of norfloxacin by increasing the norfloxacin concentration from 20 to 100 mg L⁻¹. Based on the results, norfloxacin molecules at low concentrations interacted with the adsorption sites on the surface of the adsorbent, resulting in a higher removal percentage. At higher concentrations, the removal efficiency decreases due to the saturation of the active sites of the adsorbent (Ali et al., 2016). As shown in Figures 1A, C concentration of 25 mg L⁻¹ was determined as the optimal dose for norfloxacin.

3.4 Optimal conditions of removal

In addition to modeling the removal process, the removal conditions can be optimized using the RSM. The optimal removal conditions were assessed using the numerical software optimization technique in RSM. If the goal is to maximize the removal rate, the presented model with a utility of 1 will reach this goal. In this case, the removal efficiencies of ceftriaxone and norfloxacin will be 93.50% and 97.44%, respectively, with the adsorbent mass, contact time, concentration, and pH values of 0.034 g, 20 min, 25 mg L⁻¹, and 8, respectively (Supplementary Table S1). The prediction of the model was validated by conducting the experimental tests under optimal conditions. The experimental results of ceftriaxone and norfloxacin removal were 95.87% and 98.64%, respectively, confirming the model's accuracy.

3.5 Regeneration of GO adsorbent

A major aspect of an ideal adsorbent is that it can be used frequently. In fact, the reuse ability of an adsorbent in the adsorption process is valuable when a significant decrease is not observed in its efficiency. In this respect, an adsorbent with the possibility of recovery can significantly reduce the total costs of the removal process. In this research, the reusability of the GO adsorbent was examined by preparing some solutions containing ceftriaxone and

norfloxacin. After using the GO adsorbent to remove antibiotics, it was separated from the solutions by centrifugation. The separated adsorbent was washed with 2 mL of methanol and finally dried in an oven at 85°C. This reuse cycle of GO in adsorption/desorption processes was repeated 5 times. Figure 2 presents the changes in the removal percentages of ceftriaxone and norfloxacin using recovered GO. In the first reuse cycle of the GO adsorbent, the removal efficiency decreased very slightly for both antibiotics. Although the removal efficiency declined by about 30% in the fifth reuse cycle of adsorbent, a significant removal rate with removal percentages of >64% was obtained for both antibiotics. Therefore, this adsorbent could well remove ceftriaxone and norfloxacin in five cycles of use.

3.6 Interference studies

The effect of possible interferences of various cations and anions in the removal of antibiotics was investigated to evaluate the method's applicability in removing norfloxacin and ceftriaxone in the presence of external ions. For this purpose, the signal of the sample solution was first measured in the absence of interfering species under optimal conditions. The obtained analytical signal was measured three times to calculate the average of the signals and the standard deviation. The possible interfering effect of each species was assessed by adding the target ion to the initial solution with a w/w ratio of 1,000 times compared to the antibiotics. Next, the corresponding analytical signal was obtained by performing the removal process on this solution. If the decomposition signal obtained in the presence of interfering species was not in the range of ±5%, it meant that the target ion was interfering with the existing ratio. Otherwise, the weight ratio of the interfering species would be reduced to the extent that the decomposition signal would be in the range of ±5%. The results (Table 4) show that when the species are present in the sample as much as 1,000 times of antibiotics, they do not interfere seriously in removing antibiotics.

3.7 Application to real samples

A synthetic sample was used to evaluate the proposed method's efficiency in removing ceftriaxone and norfloxacin. These samples were prepared using tap water, wastewater, and groundwater as fixed textures. In this procedure, specific doses of the antibiotics were added to a fixed volume of water samples to prepare synthetic samples. The resulting samples were examined using the proposed

TABLE 6 Literature comparison of removal for ceftriaxone and norfloxacin.

Analyte	Adsorbent	Amount	pH	Time	Removal/Adsorption	Ref.
Ceftriaxone	EC/AD process	0.75 g	7.5	12.5 min	100%	Noudeh et al. (2023)
	nZVI/SrFe$_{12}$O$_{19}$	0.15 g	5	8 min	98%	Amiri et al. (2020)
	O$_3$/UV/Fe$_3$O$_4$@TiO$_2$	2 g	9	30 min	92.40%	Hashemi et al. (2022)
	NBent-NTiO$_2$-Chit	0.2 g	5	10 min	93.5%	Mahmoud et al. (2020)
	GO	0.034 g	8	20 min	95.87%	This study
Norfloxacin	CoFe$_2$O$_4$@TiO$_2$_MMIP	0.4 g	7	60 min	91.1%	Fang et al. (2021)
	MgO/Chit/GO	0.01 g	7	360 min	1,000 mg g^{-1}	Nazraz et al. (2019)
	PDMPs	0.01 g	6.6	97 min	317 mg g^{-1}	Wan et al. (2018)
	HAP@CT	0.5 g	7	120 min	92%	Nayak et al. (2022)
	GO	0.034 g	8	20 min	98.64%	This study

method under optimal conditions. Each measurement was performed in triplicate. The standard increase method was used in the measurements. The results in Table 5 indicate the ability of GO to remove ceftriaxone and norfloxacin from water samples.

3.8 Comparison with other adsorbents

Table 6 compares the performance of the GO adsorbent with other adsorbents for ceftriaxone and norfloxacin removal. The experimental results revealed that the GO adsorbent was comparable with the other adsorbents for ceftriaxone and norfloxacin removal. The adsorbent consumption rate of the proposed method was considerably lower than that of other studies. Moreover, the duration of the current study on antibiotic removal was shorter than the other ones because the sonication process significantly increases the process efficiency. Additionally, using the RSM method dramatically reduces the number of tests, thereby saving time and the adsorbent amount. Therefore, the GO adsorbent performed well in ceftriaxone and norfloxacin removal from water samples.

4 Conclusion

In this research, the effectiveness of GO adsorbent in removing ceftriaxone and norfloxacin was investigated in laboratory conditions. The CCD-based RSM was used to model and optimize ceftriaxone and norfloxacin removal. The effects of adsorbent mass (0.01, 0.02, 0.03, 0.04, and 0.005 g), pH (3, 5, 7, 9, and 11), concentration (20, 40, 60, 80, and 100 mg L^{-1}), and sonication time (5, 10, 15, 20, and 25 min) were evaluated as independent variables and the removal rate as the dependent variable (response). Significant process variables were obtained as quadratic regression models for the response ($p < 0.0001$). An R^2 >0.99 was calculated for removal modeling by the CCD method for ceftriaxone and norfloxacin. The results showed that the antibiotic concentration and the adsorbent mass in the removal process had the most negative and positive effects. The best process conditions were obtained as a pH of 8, an adsorbent mass of 0.034 g, a sonication time of 20 min, and a concentration of

25 mg L^{-1}. The removal efficiencies were equal to 95.87% and 98.64% for ceftriaxone and norfloxacin, respectively, under optimal conditions. The interference studies revealed that external ions did not seriously interfere with antibiotics removal when they were present in the sample as much as 1,000 times the antibiotics. The removal rates of ceftriaxone and norfloxacin were in the range of 89.95% to 98.55% for environmental samples under optimum conditions. The results of this study demonstrated that the GO adsorbent has a good ability to remove ceftriaxone and norfloxacin from aqueous solutions. Moreover, CCD and RSM proved a good ability in modeling, predicting, and optimizing the behavior of parameters affecting the process.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Author contributions

ZL: Data curation, Formal Analysis, Writing–original draft. SZ: Supervision, Writing–review and editing. GZ: Conceptualization, Data curation, Formal Analysis, Writing–original draft. JX: Data curation, Formal Analysis, Writing–original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fenvs.2024.1436848/full#supplementary-material

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