Chitosan-graft-poly(N-tert-buty lacrylamide) Copolymer: Synthesis, Characterization and Optimization of Tetracycline Removal Using RSM

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Abstract
In the present study, a graft copolymer was synthesized in accordance with the free radical method using N-tertiary butylacrylamide monomer on chitosan, which is an environmentally friendly polymer. The chemical structure and surface morphology of the newly synthesized graft copolymer were determined by Fourier transform infrared spectroscopy, scanning electron microscopy and X-ray diffraction. Moreover, the thermal behavior was analyzed by thermogravimetric analysis. The chitosan-graft-poly(N-tert-buty lacrylamide) graft copolymer was used as an adsorbent for the rapid removal of tetracycline from aqueous solutions in order to investigate its applicability. Response surface methodology (RSM) was employed for the optimization of the study conditions, namely adsorbent dosage (0.01–0.04 g 100 mL−1), reaction time (10–90 min) and initial tetracycline concentration (10–100 mg 100 mL−1). The effects of these conditions on tetracycline uptake capacity were examined and the results were statistically analyzed. The RSM results showed that the maximum tetracycline uptake capacity of 104.81 mg g−1 was achieved under the following conditions: adsorbent dose of 0.03 mg 100 mL−1, reaction time of 51.12 min and initial tetracycline concentration of 97.99 mg L−1. ANOVA based on central composite design combined with RSM showed a good agreement between the experimental values and quadratic model estimates, thus resulting in a coefficient (R2) of 0.9118 for tetracycline uptake. The kinetics, isotherms, and thermodynamics of adsorption were examined, and results showed that equilibrium data fitted the Freundlich isotherm model, and the adsorption kinetics of tetracycline followed pseudo-second-order model. Thermodynamic parameters like the enthalpy − 10.39 kJ mol−1 (ΔH°), entropy 0.044 kJ mol−1 K−1 (ΔS°) and Gibbs free energy − 23.26 kJ mol−1 (ΔG°) were evaluated and also, ΔG° shows a negative values indicating that the adsorption process was exothermic and spontaneous. The findings demonstrated that the chitosan-graft-poly(N-tert-buty lacrylamide) copolymer is an effective adsorbent for pharmaceutical wastewater treatment.

Keywords Chitosan · Graft copolymerization · Response surface methodology · Tetracycline · Uptake

Introduction
Recently, there has been an increasing interest in renewable natural polymers. Among these, chitosan has a special place due to its high adsorption capacity, biodegradability, non-toxicity, antimicrobial activity and biocompatibility [1]. Chitosan is a linear biopolymer that can be prepared by the alkaline deacetylation of chitin, which is the second most abundant biopolymer in nature after cellulose [2]. It is a cationic polysaccharide produced mainly from marine organisms such as shrimp and crab [1, 3]. It is utilized in pharmacology, medicine [4–6] wastewater treatment [7], food packaging [8], cosmetics [9], textiles [10], drug delivery systems and tissue engineering [11]. The high chemical reactivity and high complexing ability of the amine and hydroxyl groups in the structure of chitosan make it...
possible to synthesize derivatives containing different functional groups and modify the chitosan molecule, which significantly expands the application of the biopolymer. In addition, the amino and hydroxyl functional groups in the chitosan polymeric structure can serve as multifunctional active sites for the removal of phenolic compounds [12, 13], heavy metal ions [14] and dyes [15] from aqueous solutions. However, the high swelling and degradability of chitosan in aqueous and acidic solutions limit its use. Various modification methods such as monomer grafting [12, 16], crosslinking [17], and physical mixing with synthetic and natural polymers [18] can be applied to improve its physicochemical properties. In the literature, graft copolymers of chitosan have been prepared with many monomers such as acrylamide [19, 20], polyacrylonitrile [21, 22], acrylates [23] or methacrylates [22]. Thermoresponsive polymer-grafted polysaccharides, which possess the characteristics of the biological activity derived from polysaccharides and thermoresponsive units such as poly(N-tert-butylacrylamide), are biomaterials. They can be used in many fields such as sustained drug delivery, immobilization of enzymes and cells, and dewatering of protein solutions. Therefore, in the present study N-tert-butylacrylamide (NTBA) was selected as the thermoresponsive polymer-grafted polysaccharide. Additionally, there is no single graft copolymer of chitosan and N-tert-butylacrylamide (NTBA) used in the present study, and it was not used in the adsorption of tetracycline using RSM.

Pharmaceutical antibiotics have been categorized under permanent contaminants as a class of newly-emerging pollutants [24, 25]. It has been noted that many drugs such as antibiotics, antidepressants and chemotherapy agents have been discharged into water systems during their production and use. Antibiotic residue in the environment causes the increase of resistant microbes, which threaten the ecosystem function and, thus, human health [26, 27]. Tetracycline is the second most commonly used antibiotic in the world due to its broad-spectrum activities, low cost, low toxicity, and suitability for oral absorption in both humans and animals [28–30]. Many studies have determined that tetracycline is poorly adsorbed in the digestive system of living organisms, with the majority being excreted through feces and urine [31]. Tetracycline is often detected in drinking water and wastewater, from which its complete removal is extremely difficult. The most common ways of entry of tetracyclines into the environment is through animal feces and their direct release into the environment. The presence of tetracyclines in soil can protect or develop antibiotic-resistant microbial populations. In addition, its presence in soil and underground and surface waters can destroy microorganisms and disrupt the microbial community in nature. Moreover, it can cause the evolution of antibiotic-resistant pathogenic microorganisms [32, 33]. Therefore, developing an efficient and sustainable method to remove tetracycline from water is a priority in improving water quality and reducing harm to public health and low-cost wastewater treatment technologies. For this purpose, several techniques have been used for the treatment of wastewaters including ozonation [34], microbial degradation [35], photocatalytic degradation [36], membrane filtration [37], and adsorption [38]. Among them, adsorption is the most applicable technique due to its advantages such as ease of use, affordable costs and high efficiency [39]. The adsorption process is the main factor for the retention of antibiotics on soil constituents, and can control the biological effects of antibiotics and their transport in the environment.

Various adsorbent types including activated carbon [40], polymers [28], metal-based adsorbents [41] and bioadsorbents [42] have been used to remove antibiotics from aqueous solutions. However, some of these adsorbents have various disadvantages such as poor adsorption capacity, long equilibrium time and no regeneration. Recently, natural polymers with different functional groups in their surface areas have been accepted as suitable adsorbents due to their ability to reduce environmental concerns [43]. Chitosan is a remarkable adsorbent alternative due to its unique physicochemical properties, hydrophilicity, stability to most chemicals and excellent adsorption capacity. In addition, its use as an adsorbent in removal studies requires low cost [44].

RSM is a statistical and mathematical optimization technique based on polynomial equations prepared on experimental data [45–47]. It is applied when a response is affected by several variables and the aim is to optimize the selected variables simultaneously to achieve the best performance. It helps researchers to develop new methods with the least number of experiments [48]. The solo and interactive effects of input variables such as adsorbent dose, solution pH, temperature and contact time on response efficiency can be evaluated by RSM [3, 34], which leads to a reduction in experimental error. The RSM empirical equation permits the estimation of the coefficients of each factor and replication of actual experiments at optimum predicted value giving information regarding the accuracy and applicability of the predicted models. Analysis of variance (ANOVA) is a very effective method used to analyze the importance of different variables [49]. With this method, the most important factors can be evaluated efficiently. Moreover, the compatibility between the predicted and experimental statistical values was examined with ANOVA [50].

In recent years, great attention has been paid to the use of biopolymers as adsorbents for the removal of antibiotics from aqueous media due to their exceptional properties such as biocompatibility and biodegradability. Within this context, the main objective of this study was to develop a graft copolymer of chitosan with NTBA and use it to optimize the removal of tetracycline, an antibiotic, from aqueous
solutions. The structural properties of the first synthesized graft copolymer were analyzed by Fourier transform infrared spectroscopy (FT-IR), scanning electron microscopy (SEM) and X-ray diffraction (XRD). The effects of various parameters, namely, dose of adsorbent, reaction time and initial concentration of tetracycline on the uptake capacity of tetracycline, were studied by using RSM. In addition, the adsorption kinetic, adsorption isotherms and adsorption thermodynamic were investigated. As far as we know chitosan-graft-poly(N-tert-butylacrylamide) copolymer has not been used for tetracycline removal. In addition, RSM has been rarely encountered before in tetracycline removal.

**Experimental**

**Materials**

In this study, chitosan (product of Russia) with a molecular weight between 100,000 and 300,000 was used without further purification. The tetracycline (CAS Number: 60-54-8, ≥ 98% pure, Molecular formula: C\text{22}H\text{24}N\text{2}O\text{8}, Molecular weight: 444.43 g mol\(^{-1}\)) was obtained from Sigma-Aldrich (Germany). The NTBA (Sigma-Aldrich, Germany), 2,2'-azobisisobutyronitrile (AIBN) (Sigma-Aldrich, Germany), acetic acid (Sigma-Aldrich, Germany), acetone (Labkon, Turkey), ethanol (Labkon, Turkey), and dioxane (Sigma-Aldrich, Germany) were used without any purification. All the chemicals used were of analytical grade.

**Equipment**

The copolymer was characterized by FT-IR (Jasco, USA) in the range of wave numbers from 4000 to 400 cm\(^{-1}\) using ATR. The morphology of the graft copolymer was evaluated by SEM, which was performed using a Hitachi SU-3500 (Japan) with an accelerating voltage of 15 kV. The XRD patterns were recorded on a powder X-ray diffractometer (Rigaku miniflex-600, Japan) at a voltage of 40 kV and a current of 15 mA. A thermogravimetric analysis (TGA) was conducted using a differential thermal analyzer (Shimadzu TGA-50, Japan) with nitrogen gas and heat from ambient temperature to 600 °C at a 10 °C min\(^{-1}\) heating rate. For the tetracycline sorption process, an orbital shaker (Zhicheng ZHWY-200B, China) was used at 200 rpm. The adsorption properties were examined by using a UV–Vis spectrophotometer (Shimadzu-1800, Japan).

**Grafting Poly(N-tert-butylacrylamide) onto Chitosan**

The NTBA monomer was grafted onto chitosan by free radical polymerization using AIBN as an initiator at 65 °C under constant stirring. The chitosan (0.5 g) was dissolved in 50 mL of a 1% v/v (0.23 mol L\(^{-1}\)) acetic acid solution. The NTBA (1 g) and AIBN (0.015 g) were dissolved in a small amount of dioxane (5 mL) and mixed with the aqueous acetic acid solution of chitosan. The mixture was passed through nitrogen to provide an inert environment. The polymerization was continued for approximately 6 h. After the polymerization was completed, the chitosan-graft-poly(N-tert-butylacrylamide) was separated from the reaction mixture by precipitation in a 50:50 acetone/ethanol at room temperature. The obtained copolymer was washed with distilled water a few times and then with ethanol to remove any homopolymers or unreacted monomers present in the mixture. The insoluble graft copolymer was removed by filtration and dried in a vacuum oven at 50 °C for at least 24 h. The synthesis of the copolymer was carried out as shown in Scheme 1. The grafting percentage was calculated according to Eq. (1):

\[
\%\text{Grafting} = \left( \frac{W_1 - W_2}{W_2} \right) \times 100
\]

where \(W_1\) (g) is the mass of the dried graft copolymer and \(W_2\) (g) is the weight of the chitosan.

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Scheme 1  Graft copolymerization of the NTBA onto chitosan
Tetracycline Adsorption Experiments

As tetracycline solutions are unstable, the required amount of tetracycline for each experiment was prepared by dissolving in distilled water. Batch tetracycline adsorption experiments were performed at room temperature (25 ± 2 °C), the natural pH of the solutions, and a stirring speed of 200 rpm, in 250 mL capacity glass capped bottles wrapped with aluminum foil containing 100 mL of tetracycline. The experiments were carried out in duplicate and averaged.

A total of 20 experiments designed with central composite design are carried out to investigate the effect of initial tetracycline concentration (10–100 mg L⁻¹), adsorbent dose (0.01–0.04 g 100 mL⁻¹) and reaction time (10–90 min). The tetracycline uptake capacity \( q_t \) (mg g⁻¹) was calculated using Eq. (2) as given below [51]:

\[
q_t = \frac{(C_e - C_i) V}{m}
\]

where \( C_e \) and \( C_i \) (mg L⁻¹) are the initial and at \( t \) time concentrations of tetracycline, respectively; \( V \) (L) is the volume of the solution, and \( m \) (g): is the weight of adsorbent.

The adsorption isotherm and kinetic experiments for tetracycline were investigated at different concentrations of tetracycline (10–100 mg L⁻¹): A 0.03 g of chitosan-graft-poly(N-tert-butylacrylamide) was mixed with 100 mL of 10, 25, 55, 80 and 100 mg L⁻¹ of tetracycline with shaken for different periods of time (between 5 and 90 min). Langmuir and Freundlich isotherm models were used to express the adsorption of tetracycline by chitosan-graft-poly(N-tert-butylacrylamide). The linear forms of the Langmuir and Freundlich isotherms are given in Eqs. (3) and (4), respectively [52]:

\[
\frac{C_e}{q_e} = \frac{C_0}{Q_{max}} + \frac{1}{bQ_{max}}
\]

\[
\ln q_e = \ln K_f + \frac{1}{n} \ln C_e
\]

where \( C_e \) (mg L⁻¹) is the equilibrium concentration of the remaining tetracycline in solution, \( q_e \) (mg g⁻¹) is the amount of tetracycline adsorbed at equilibrium concentration, \( Q_{max} \) (mg g⁻¹) is the maximum amount of tetracycline to form a monolayer coverage, and \( b \) (L mg⁻¹) is the Langmuir constant.

The kinetics of tetracycline adsorption by chitosan-graft-poly(N-tert-butylacrylamide) were analyzed by pseudo-first order, pseudo second-order and intraparticle diffusion models and their formulas given in Eqs. (5)–(7), respectively [53]:

\[
\ln(q_e - q_t) = \ln q_e - k_1 t
\]

\[
\frac{t}{q_1} = \frac{1}{k_2 q_e^2} + \frac{1}{q_e}
\]

\[
q_t = k_i t^{0.5} + C
\]

where \( q_e \) (mg g⁻¹) is the adsorption capacity at time \( t \) (min), \( k_1 \) (min⁻¹) is the rate constant of pseudo-first-order model, \( k_2 \) (g mg⁻¹ min⁻¹) is the rate constant of pseudo second-order model, \( k_i \) (mg⁻¹ min⁻0.5) is the rate constant of intraparticle diffusion model and \( C \) is the intercept related to the thickness of the boundary layer.

The thermodynamic parameters such as enthalpy change (\( \Delta H^0 \)), Gibb’s free energy change (\( \Delta G^0 \)), and entropy change (\( \Delta S^0 \)) were analyzed by the temperature dependence adsorption process performed at different temperatures of 25 °C, 35 °C and 45 °C, using the following equations [54].

\[
\Delta G^0 = \Delta H^0 - T \Delta S^0
\]

\[
K_L = \frac{q_e}{C_e}
\]

\[
\ln K_L = \frac{\Delta S^0}{R} - \frac{\Delta H^0}{RT}
\]

where \( R \) (8.314 J mol⁻¹ K⁻¹) is the universal gas constant, \( T \) (K) is the absolute temperature and \( K_L \) (L mol⁻¹) is the adsorption equilibrium constant.

After each experiment, the samples were filtered through 0.45 μm polyvinylidene fluoride (PVDF) filters and the residual concentration of the tetracycline was analyzed using a UV–Vis spectrophotometer at a wavelength of \( \lambda = 350 \) nm.

Experimental Design for Tetracycline Adsorption and Statistical Analysis

Experimental design allows simultaneous optimization of factors, minimizes error with the minimum number of runs and improves performance characteristics [55]. In this study, the experiments for tetracycline removal were designed using an RSM-based central composite design with three independent factors, namely initial tetracycline concentration (A), adsorbent dose (B), and reaction time (C), at five levels \((-\alpha, -1, 0, +1, +\alpha)\) using Design-Expert 7.0 with 20 runs. The experimental design points with the coded values of the factors utilized in the matrix of the experiments consisted of eight factorial points, six axial points and six replicates at the center points (Table 1). The data obtained
from the central composite design were analyzed by multiple regressions to fit the second-degree polynomial equation given below [56]:

\[ Y = b_0 + \sum_{i=1}^{k} b_i A_i + \sum_{i=1}^{k} b_{ii} A_i^2 + \sum_{j=i+1}^{k} \sum_{j=i+1}^{k} b_{ij} A_i A_j + e \]  

(11)

where \( Y \) is the tetracycline uptake capacity (predicted response); \( b_0, b_i, b_{ii}, \) and \( b_{ij} \) are the constant, linear, quadratic, and interaction coefficients, respectively; and \( A_i \) and \( A_j \) are the coded variables affecting response \( Y \).

Values of the regression variables such as \( p \)-value, Fisher test value (\( F \)-value), regression coefficient (\( R^2 \)), and adjusted \( R^2 \) were calculated using ANOVA and utilized to determine the suitability and relevance of the predicted model. Design-Expert 7.0 software was used for the ANOVA.

**Regeneration Studies**

Regeneration experiments were performed under the optimum conditions achieved with the central composite design. At the end of each adsorption cycle, 0.1 M NaOH was used to regenerate the tetracycline loaded chitosan-graft-poly(N-tert-butylacrylamide). The adsorbent was washed with distilled water until it reached the natural pH of the wash solution and then dried at 60 °C for 24 h for use in the next cycle.

**Results and Discussion**

**Characterization**

The free radical initiated graft copolymerization onto chitosan was carried out with the NTBA monomer using an AIBN initiator at 65 °C. The grafting yield (%G) value was calculated using gravimetric data. Accordingly, %G was experimentally reported as 80.8%.

The FT-IR spectra of chitosan-graft-poly(N-tert-butylacrylamide) is presented in Fig. 1. The characteristic absorption bands of NTBA were observed at approximately 3400 cm\(^{-1}\) secondary amide (–NH), at 2867 cm\(^{-1}\) C–H stretching of \( CH_2 \) and \( CH_3 \) groups, 1654 cm\(^{-1}\) amide carbonyl stretching (–HN=C=O) and 1564 cm\(^{-1}\) amide II (–NH), and the band at 1222 cm\(^{-1}\) may belong to the tertiary butyl groups [–C(CH\(_3\)\(_3\)] [57, 58]. In addition, the characteristic bands of chitosan were observed in the FT-IR spectrum, with many observed at 1655 cm\(^{-1}\), 1638 cm\(^{-1}\), 1561 cm\(^{-1}\) and 1320 cm\(^{-1}\) [59]. A peak at 1068 cm\(^{-1}\) was observed due to the O–H bending vibration of a primary alcoholic group of chitosan [19, 41]. These observations showed that the grafting of NTBA onto chitosan had taken place successfully. As can be seen from Fig. 1 no significant change occurred in the chemical structure of the graft copolymer after the adsorption process. This can be explained by the Van der Waals interaction between the tetracycline molecules and the chitosan-graft-poly(N-tert-butylacrylamide) molecules and shows that the adsorption process was carried out on the surface of the adsorbent. The main functional groups responsible for adsorption were the OH and NH groups in the chitosan and the C = O and N units in the poly(N-tert-butylacrylamide).

The surface morphology of the chitosan-graft-poly(N-tert-butylacrylamide) copolymer before and after tetracycline adsorption was examined by SEM. As can be observed from Figs. 1a and b the graft copolymer had a rough, porous surface and contained cracks and crevices, a sign that the poly(N-tert-butylacrylamide) had been successfully incorporated into the chitosan. After the tetracycline was adsorbed onto the chitosan-graft-poly(N-tert-butylacrylamide) surface, it is clear to see from Fig. 2c that the surface roughness of the copolymer significantly

| Table 1 | Levels of the factors for the central composite design experiments |
|---|---|
| Factor | Ranges and level |
| Initial tetracycline concentration (mg L\(^{-1}\)) (A) | \(-\alpha\) | 10.00 | 28.24 | 55.00 | 81.76 | 100 |
| Adsorbent dose (mg 100 mL\(^{-1}\)) (B) | 0.01 | 0.016 | 0.025 | 0.034 | 0.04 |
| Reaction time (min) (C) | 10.00 | 26.22 | 50.00 | 73.78 | 90.00 |
reduced. Moreover, the morphology of the chitosan-graft-poly(N-tert-butylacrylamide) appeared to be more compact with attenuated porosity. This suggested that the antibiotic had been removed from the wastewater.

In order to confirm the crystal structures of the chitosan-graft-poly(N-tert-butylacrylamide) graft copolymer, XRD was conducted and the patterns before and after adsorption are shown Fig. 3. In previous studies in the literature, pure chitosan has been characterized by a scattering angle of $2\theta = 20^\circ$. This peak indicates that chitosan is an anhydrous crystal. Moreover, typical fingerprints of semi-crystalline chitosan have been reported to appear at $2\theta = 25^\circ$ [60, 61]. In the present study, these peaks for the chitosan-graft-poly(N-tert-butylacrylamide) graft copolymer were observed at $19.9^\circ$ and $27.5^\circ$ (Fig. 3a). This shows that the amorphous character increased with grafting. On the other hand, for the XRD spectra of the chitosan-graft-poly(N-tert-butylacrylamide) graft copolymer (Fig. 3b) a decrease was observed in the intensity of the peak at $2\theta = 15^\circ$ after tetracycline removal.

The heat stability and weight loss (%) of the chitosan-graft-poly(N-tert-butylacrylamide) were determined by TGA before and after tetracycline adsorption. As can be seen from Fig. 4a, thermal degradation occurred in three stages. Before adsorption, degradation occurred at 100 °C, 280 °C, and 320 °C and with weight losses of 15%, 40%, and 23%, respectively. Compared to before the adsorption process, degradation took place in two steps for graft copolymer after tetracycline adsorption (Fig. 4b). The significant weight loss step of up to approximately 20% observed at
280 °C can be attributed to the loss of H₂O molecules [62, 63]. The weight loss starting at approximately 320 °C may have occurred due to the degradation of the poly N-tert-butylacrylamide groups [64]. Moreover, the other weight loss in the 450–600 °C range implies the rest of the chitosan mass in the graft copolymer.

**Analysis of Variance and Response Surface Plots for Tetracycline Adsorption**

The impact of operation factors on the tetracycline uptake capacity onto chitosan-graft-poly(N-tert-butylacrylamide) was investigated and the experiments were carried out based on central composite design. Table 2 shows the design matrix and response values.

For the adsorption process, a quadratic model equation was obtained as shown in Eq. (12):

\[
\text{Tetracycline uptake capacity (mg g}^{-1}) = +39.96 + 21.50A + 9.59B - 8.48C + 13.44AB - 5.15AC + 1.85BC + 3.29A^2 - 8.71B^2 + 4.79C^2
\]  \hspace{1cm} (12)

The sufficiency of the model equation in defining the experimental data was confirmed from the plot of the predicted values of the model against the actual values (Fig. 5). Therefore, this plot clearly visualized the performance of the model.

The regression coefficients and statistical significance of the model and its adequacy were evaluated using ANOVA (Table 3). The larger the F-value of the model and the smaller the p-value, the more significant the applied model. The fact that the F-value and p-value of the model, which is 11.49, is lower than 0.0500, shows that the model is significant at the 95% confidence level (Table 3) [65, 66]. There is only a 0.03% chance that a "model F-value" this large could occur due to noise. Similarly, p-values less than 0.0500 for A (initial tetracycline concentration), B (adsorbent dose), C (reaction time), AB (initial tetracycline concentration and adsorbent dose) large could occur due to noise. Similarly, p-values less than 0.0500 for A (initial tetracycline concentration), B (adsorbent dose), C (reaction time), AB (initial tetracycline concentration and adsorbent dose) would have a significant effect on the predicted tetracycline uptake capacity.

**Table 2** Central composite design matrix and the response for the tetracycline uptake capacity

| Run no | Actual factors | Tetracycline uptake capacity (mg g\textsuperscript{-1}) |
|--------|----------------|------------------------------------------------------|
|        | X\textsubscript{1} | X\textsubscript{2} | X\textsubscript{3} |                                  |
| 1      | 55.00          | 0.03           | 50.00          | 38.43                            |
| 2      | 55.00          | 0.03           | 50.00          | 42.35                            |
| 3      | 55.00          | 0.03           | 50.00          | 34.50                            |
| 4      | 10.00          | 0.03           | 50.00          | 3.34                             |
| 5      | 28.24          | 0.03           | 73.78          | 20.78                            |
| 6      | 28.24          | 0.02           | 26.22          | 27.71                            |
| 7      | 28.24          | 0.02           | 73.78          | 13.07                            |
| 8      | 81.76          | 0.03           | 73.78          | 73.72                            |
| 9      | 55.00          | 0.01           | 50.00          | 11.50                            |
| 10     | 55.00          | 0.03           | 50.00          | 48.23                            |
| 11     | 100.00         | 0.03           | 50.00          | 91.72                            |
| 12     | 81.76          | 0.02           | 73.78          | 12.02                            |
| 13     | 55.00          | 0.03           | 10.00          | 60.78                            |
| 14     | 55.00          | 0.03           | 50.00          | 42.35                            |
| 15     | 28.24          | 0.03           | 26.22          | 28.23                            |
| 16     | 55.00          | 0.04           | 50.00          | 15.68                            |
| 17     | 81.76          | 0.03           | 26.22          | 101.56                           |
| 18     | 81.76          | 0.02           | 26.22          | 47.50                            |
| 19     | 55.00          | 0.03           | 50.00          | 34.50                            |
| 20     | 55.00          | 0.03           | 90.00          | 42.74                            |

**Fig. 4** TGA curves of the chitosan-graft-poly(N-tert-butylacrylamide) a before tetracycline adsorption and b after tetracycline adsorption.

**Fig. 5** Plot of the predicted versus experimental values for the tetracycline uptake capacity of the chitosan-graft-poly(N-tert-butylacrylamide).
concentration-adsorbent dose), and $B^2$ (adsorbent dose-adsorbent dose) indicated that these model terms were statistically significant for tetracycline adsorption with the adsorbent. In this study, the coefficient of determination ($R^2$) value, which was calculated as 0.9118, showed that the model could explain 91.18% of the changes in adsorption. This demonstrated that the applied model could be reliable in predicting uptake efficiency. The adjusted $R^2$ value was found to be 0.9123. This is an important factor that proved a good fit between the experimental and predicted uptake efficiency for tetracycline adsorption of the model [67].

Adequation precision measures the signal-to-noise ratio and is desired to be greater than 4.0. As can be seen in Table 3, the adequation precision value was 12.668, indicating that there was enough signal. The coefficient of variation (CV) is a measure that expresses the standard deviation as a percentage of the mean and explains the extent to which the data is distributed [68]. The acceptable values of CV, namely 27.24%, for tetracycline uptake capacity proved that the performed experiments were credible.

The tetracycline uptake capacity of the adsorbent over different combinations of independent factors was visualized with the 3D response surfaces curves (Figs. 6a–c). Adsorbent dosage provides the required surface area and binding sites for the adsorption of tetracycline. Therefore, it is important to choose the appropriate amount of adsorbent. The plot in Fig. 6a illustrates the main and interaction effects of initial tetracycline concentration and adsorbent dose on the tetracycline uptake capacity when the reaction time was fixed at 50 min. The tetracycline uptake capacity appeared to increase up to approximately at an adsorbent dosage of 0.03 g and then decrease. This phenomenon can be explained in two ways: firstly, at a constant concentration and volume of tetracycline, increasing the amount of adsorbent will cause the adsorption sites to be unsaturated during the adsorption process, and secondly, particle aggregation due to the higher mass of the adsorbent can lead to a decrease in adsorbent capacity [69]. The plot in Fig. 6b illustrates the main and interaction effects of initial tetracycline concentration and reaction time on the tetracycline uptake capacity when the adsorbent dose was fixed at 0.03 g 100 mL$^{-1}$. It can be observed that with the increase of initial tetracycline concentration, the tetracycline uptake capacity increased. This is probably because the adsorbent was surrounded by more tetracycline ions due to the increased likelihood of contact between the tetracycline molecules and adsorbent active sites. In other words, the higher the concentration of tetracycline, the more diffusion consisted from the polymer surface to the pores [70]. Similar behavior for the impact of tetracycline concentrations on the uptake capacity of tetracycline was observed and discussed in regards to different adsorbents in the literature [69, 71, 72]. The plot in Fig. 6c illustrates the main and interaction effects of adsorbent dose and reaction time on the tetracycline uptake capacity when the initial tetracycline concentration was fixed at 55 mg L$^{-1}$. It can be seen that the increase in the surface area required

### Table 3 ANOVA for tetracycline uptake capacity onto chitosan-graft-poly(N-tert-butylacrylamide)

| Source | Sum of squares | Df | Mean square | $F$-value | $P$-value Prob $> F$ |
|--------|---------------|----|-------------|-----------|---------------------|
| Model  | 11,989.99     | 9  | 1332.22     | 11.49     | <0.0001             |
| $X_1$  | 6313.93       | 1  | 6313.93     | 54.46     | 0.0001              |
| $X_2$  | 1256.97       | 1  | 1256.97     | 10.84     | 0.0081              |
| $X_3$  | 981.04        | 1  | 981.04      | 8.46      | 0.0156              |
| $X_1X_2$ | 1445.34       | 1  | 1445.34     | 12.47     | 0.0054              |
| $X_1X_3$ | 212.49        | 1  | 212.49      | 1.83      | 0.2056              |
| $X_2X_3$ | 27.49         | 1  | 27.49       | 0.24      | 0.6368              |
| $X_1^2$ | 156.38        | 1  | 156.38      | 1.35      | 0.2725              |
| $X_2^2$ | 1092.17       | 1  | 1092.17     | 9.42      | 0.0119              |
| $X_3^2$ | 330.60        | 1  | 330.60      | 2.85      | 0.1222              |
| Residual | 1159.40       | 10 | 115.94      |           |                     |
| Pure error | 141.72      | 5  | 28.34       |           |                     |
| Cor total | 13,149.38     | 19 |             |           |                     |

*Degree of freedom

**CV%: coefficient of variation
for adsorption together with the increasing adsorbent dosage led to a decrease in the adsorption time.

In this study, the experimental results were optimized by the numeric optimization program in the Design-Expert software. The optimum values of the factors studied for tetracycline removal and the maximum tetracycline uptake capacity are shown in Table 4. By utilizing the highest uptake capacity as the optimization target, the optimized conditions were determined as follows: an initial tetracycline concentration of 97.99 mg L$^{-1}$, an adsorbent dose of 0.03 mg 100 mL$^{-1}$ and a reaction time of 51.12 min. Under these conditions an uptake capacity of 104.81 mg g$^{-1}$ was obtained.

The maximum tetracycline uptake capacities ($q_m$) obtained with the different adsorbents in previous studies were compared in Table 5. In the present study, it was observed that the chitosan-raft-poly(N-tert-butylacrylamide) used for tetracycline adsorption had one of the highest uptake capacities among the adsorbents used to date.

**Adsorption Isotherms**

Adsorption isotherms explain the relationship between the adsorbent and the adsorbate at equilibrium. In this study, two linear classical isotherm models known as Langmuir and Freundlich are used. The Langmuir model successfully explains that the adsorption process takes place in a monolayer on a homogeneous surface [39]. The Freundlich isotherm is an empirical model and explains the adsorption that occurs heterogeneous surface in multilayer [77]. As indicated in Table 6, the Freundlich models yields a somewhat better than Langmuir model on adsorption of tetracycline on chitosan-graft-poly(N-tert-butylacrylamide) as reflected with correlation coefficients ($R^2$).

**Adsorption Kinetics**

The kinetics of the tetracycline removal process were studied by using pseudo-first-order, pseudo-second-order, and intraparticle diffusion kinetic models. The slope and intercept of the graph of $\ln (q_e - q_t)$ versus $t$ were used to calculated the $k_1$ and $q_e$, respectively for pseudo-first-order. For pseudo-second-order, the rate parameters $q_e$ and $k_2$ can be defined from slope and intercept by the plotting $t/q_t$ versus $t$. Also the slope of the linear portion characterized the rate parameter $k_i$ corresponding to the intraparticle diffusion by the plotting $q_t$ versus $t^{0.5}$. The values summarized in Table 7 for
three kinetic methods. The experimental results indicated that adsorption process followed the pseudo-second-order model as correlation coefficients higher than 0.991. Also in this kinetic model the $q_{e,\text{cal}}$ (68.49 mg g$^{-1}$) and the $q_{e,\text{exp}}$ (65.46 mg g$^{-1}$) values were very close to each other.

**Adsorption Thermodynamics**

Thermodynamic parameters obtained are shown in Table 8. The value of $\Delta H^\circ$ for tetracycline is less than 40 kJ mol$^{-1}$ so it was suggested system is physical in nature [78]. The exothermic nature of process is well explained by negative value of the enthalpy change. The negative value of free energy suggests that the adsorption process is spontaneous and the affinity of the adsorbent for the tetracycline is indicated by the positive value of entropy.

**Reusability of Chitosan-graft-poly($N$-tert-buty lacrylamide)**

Regeneration studies are required to determine the reusability of adsorbents in practical applications due to economic and ecological requirements for sustainability [79]. In the present study, the reusability of chitosan-graft-poly($N$-tert-buty lacrylamide) was investigated by applying adsorption–desorption process with four cycles for tetracycline. It can be seen from Fig. 7 that the uptake capacity of chitosan-graft-poly($N$-tert-buty lacrylamide) decreases for each new cycle after desorption with four cycles. Initially, the uptake capacity of chitosan-graft-poly($N$-tert-buty lacrylamide) from 104.81 mg g$^{-1}$ for tetracycline decreased to 58.65 mg g$^{-1}$ after four cycles. The results showed that chitosan-graft-poly($N$-tert-buty lacrylamide) could be reused for removal of tetracycline in wastewater treatment.

**Table 4** Numerical values of the optimized process factors for maximum tetracycline uptake capacity (desirability $= 1.000$)

| Initial tetracycline concentration (mg L$^{-1}$) | Adsorbent dose (mg 100 mL$^{-1}$) | Reaction time (min) | Uptake capacity (mg g$^{-1}$) |
|-----------------------------------------------|----------------------------------|---------------------|-------------------------------|
| Optimum value                                 | 97.99                            | 0.03                | 51.12                         | 104.81                         |

**Table 7** The values of kinetic constants for tetracycline adsorption on chitosan-graft-poly($N$-tert-buty lacrylamide) ($T$=25 °C, $C_0$=55 mg/L, $m=0.03$ g/100 mL)

| KineticParameters | Value |
|-------------------|-------|
| Pseudo-first-order | $k_1$ (min$^{-1}$) | 0.043 |
| $q_{e,\text{cal}}$ (mg g$^{-1}$) | 51.60 |
| $q_{e,\text{exp}}$ (mg g$^{-1}$) | 65.46 |
| $R^2$ | 0.953 |
| Pseudo-second-order | $k_2$ (g mg$^{-1}$ min$^{-1}$) | 0.00047 |
| $q_{e,\text{cal}}$ (mg g$^{-1}$) | 68.49 |
| $q_{e,\text{exp}}$ (mg g$^{-1}$) | 65.46 |
| $R^2$ | 0.991 |
| Intraparticle diffusion | $k_i$ (mg g$^{-1}$ min$^{-0.5}$) | 2.386 |

**Table 5** Comparison of the maximum tetracycline uptake ($q_m$) with different adsorbents reported in the literature

| Adsorbent | $q_m$ (mg g$^{-1}$) | Reference |
|-----------|---------------------|-----------|
| Ceramsite substrate from bentonite/red mud/pine sawdust | 2.56 | [73] |
| Magnetic polyurethane polymer nanocomposite | 19.27 | [74] |
| Commercial granulated activated carbon | 29.58 | [75] |
| Cu-immobilized alginate | 53.26 | [41] |
| Chitosan-based nanoparticles loaded with Fe$_3$O$_4$ nanoparticles | 78.11 | [76] |
| Pistachio shell coated with ZnO nanoparticles | 95.06 | [72] |
| Graphene oxide/calcium alginate composite fibers | 131.60 | [71] |
| This work | 104.81 | |

**Table 6** Constant of Langmuir and Freundlich isotherms

| $T$ (°C) | Langmuir | Freundlich |
|----------|----------|------------|
| $Q_{\text{max}}$ (mg g$^{-1}$) | $b$ (L g$^{-1}$) | $R^2$ | $K_f$ (L g$^{-1}$) | $1/n$ | $R^2$ |
| 25 | 108.75 | 0.032 | 0.9390 | 4.014 | 0.532 | 0.9889 |
Fig. 7 Tetracycline uptake capacity of chitosan-graft-poly(N-tert-butyacrylamide) after regeneration (T=25 °C, tetracycline concentration = 97.99 mg L⁻¹, adsorbent dose = 0.03 mg 100 mL⁻¹, time = 51.12 min)

Conclusions

In this study, the effect of three factors, namely dose of chitosan-graft-poly(N-tert-butyacrylamide), reaction time and initial tetracycline concentration, on the uptake capacity of tetracycline from wastewater were investigated. For this purpose, firstly the graft copolymer of NTBA and chitosan was successfully prepared according to the free radical copolymerization method and characterized. The effects of the adsorption parameters on the adsorption process were evaluated using RSM. The modeling and optimization of tetracycline removal were examined using Stat-Ease Design-Expert software version 7.0 in accordance with central composite design. The ANOVA results showed that the applied model was statistically significant as the F-value of the model and the corresponding p-value were 11.49 and < 0.0001, respectively. The best conditions for tetracycline removal were recorded as follows: tetracycline concentration of 97.99 mg L⁻¹, adsorbent dose of 0.03 mg 100 mL⁻¹, and reaction time of 51.12 min. These findings show the feasibility of chitosan-graft-poly(N-tert-butyacrylamide) as an efficient bio-adsorbent for the removal of tetracycline. The design of the experiment revealed that the three parameters chosen were dependent and had significant effects on tetracycline uptake. A high correlation was found between the experimental and predicted results ($R^2 = 0.9118$). Langmuir and Freundlich isotherms were used to describe the adsorption equilibriums. Freundlich isotherm is better fit than Langmuir. Thermodynamic parameters were evaluated. It was observed that the pseudo-second order model best described the adsorption kinetics. Gibbs free energy shows negative values indicating that the adsorption process was spontaneous in nature.

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Data Availability All relevant data are within the manuscript.

Declarations

Conflict of interest The authors declare that there are no conflict of interest.

Consent to Participate All authors participated in this work.

Consent for Publication All authors agree to publish.

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