Excessive use of antibiotics and their disposal into the environment poses a serious threat to public health (1). Penicillin G (PG) injection is used to treat and prevent a wide range of infections caused by bacteria, and pH-heat sensitivity has been reported for this beta-lactam antibiotic (2). It spontaneously dissolves in water, as well as isotonic sodium chloride and dextrose solutions (3, 4). Different methods, including electrolysis (5, 6), adsorption (7, 8), oxidation (9), biodegradation (10), and dissolved air flotation (1, 2), are used to remove PG from contaminated water. The adsorption process has an extensive application in industries for the elimination of organic pollutants (11). Granular activated carbons are widely utilized as adsorbing materials; nonetheless, they are hardly regenerated (12). Nanoparticles (NPs) are tiny materials sized within 1-100 nanometers (nm). Today NPs have a widespread application in various industries.
industries and professions, including textiles, paint, and diagnosis of diseases. Therefore, the research focus has now shifted towards nanotechnology and its development. NPs can be perfused into the polluted environment by pressure and/or under gravity owing to their very small size. Moreover, they remain in the solution as a suspension under certain conditions for a long time and flow through the water to have enough opportunity to decontaminate the pollutant (13).

Copper oxide nanoparticles (CuO-NPs) are used as a catalyst with high efficiency due to their high efficiency and quantum size effect (7). The present study aimed to assess the efficiency of CuO-NPs in the removal of PG from aqueous solution. To determine the optimum conditions, the effects of operational factors: the adsorbent (CuO-NPs) dosage, contact time, as well as pH and initial concentration of PG were examined. On a final note, the kinetic adsorption models were utilized to fit the experimental data.

Materials & Methods

The cupric oxide nanoparticles (CuO-NPs) obtained from Sigma Company has the following characteristics: size: 15-20 nm and purity: 99%. Penicillin G (PG) with a molecular weight of 372.48 g/mol, purity higher than 99%, and molecular formulae of C_{16}H_{17}KN_{2}O_{4}S was provided by Sigma-Aldrich. Different PG concentrations used for the study were prepared from a 1000 mg/L stock solution using distilled water. The structure of PG is displayed in Figure 1.

For the adsorption process experiments, the impact of various factors, namely pH (3, 5, 7, 9, 11), contact time (15, 30, 45, 60, 75, 90, 120 min), pollutant concentration (10, 25, 50, 100, 150, 200 mg/L) and adsorbent dose (0.1, 0.3, 0.5, 0.7, 0.9, 1 g/L) was assessed. A shaker of 150 rpm was used to create optimal conditions. The adsorbent was added to each 1 L of water sample containing PG at various concentrations. The solutions were agitated using an orbital shaker (with a speed of 150 rpm) for a specified time to reach equilibrium. Subsequently, the samples were eliminated, and the supernatant solution was filtered through Whatman filter paper no. 41. The pH adjustments of the water samples were performed by the addition of hydrochloric acid 0.1 N or 0.1 N sodium hydroxide solutions. A UV-visible recording spectrophotometer (Shimadzu Model: LUV-100A) was used to analyze the initial PG concentration and final PG concentration remaining in solutions. The concentrations of PG were determined at a wavelength of maximum absorbance (λ_{max}) of 248 nm (1, 14).

The PG removal efficiency (%R) of the studied parameters was calculated using the following formula (15):

\[ %R = \frac{(C_0 - C_f)}{C_0} \times 100 \]  \[ 1 \]

where \( C_0 \) and \( C_f \) are the initial and final PG concentrations, respectively.

The amount of PG adsorbed by CuO-NPs, \( q_e \) (mg/g) was calculated using the following mass balance relationship stated as Equation [2](16):

\[ q_e = \frac{(C_0 - C_e)V}{M} \]  \[ 2 \]

where \( M \) is the weight of CuO-NPs used (g), and \( V \) is the volume of the PG solution treated (L). \( C_0 \) and \( C_e \) are the initial and final equilibrium liquid-phase concentrations of PG.
(mg/g), respectively.

**Adsorption kinetics**

The rate of adsorption and the potential rate-controlling steps are assessed by kinetic models. The pseudo-first-order (PFO) rate equation is expressed as Equation [3](17):

\[
\log(q_e - q_t) = \log(q_e) - \frac{k_1}{2.303} t
\]

where \( q_e \) and \( q_t \) are the amounts of PG adsorbed (mg/g) at equilibrium and at time \( t \) (min), respectively, and \( k_1 \) is the PFO rate constant of adsorption (min\(^{-1}\)).

The pseudo-second-order (PSO) rate equation is stated as Equation [4](18, 19):

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

where \( k_2 \) is the PSO rate constant (g mg\(^{-1}\)min\(^{-1}\)), \( q_t \) and \( q_e \) are the amounts of PG adsorbed on the CuO-NPs (mg/g) at equilibrium and at time \( t \), respectively.

The adsorption of PG on CuO-NPs may be controlled by intraparticle diffusion or penetration process. Its mathematical model is expressed as Equation [5](20, 21):

\[
q_t = K_{pi}t^{0.5}+c
\]

where \( c \) is a constant, \( K_{pi} \) is the intraparticle diffusion rate constant (mg/g min\(^{1/2}\)), and \( q_t \) is the amount adsorbed (mg/g) at time \( t \) (min).

Bhattacharya and Venkobachar kinetic equation is stated as Equation [6](22):

\[
\log(1 - U_{tr}) = \frac{K_1}{2.303} t
\]

where \( C_i \) and \( C_t \) = concentration of PG at time zero and time \( t \), respectively (mg/L). Moreover, \( q_e \) and \( q_t \) = amount of PG adsorbed at equilibrium time and time \( t \), respectively (mg/g).

where \( C_e \) = equilibrium dye concentration (mg/L), and \( k_1 \) = first-order adsorption rate constant (min\(^{-1}\)).

**Results**

**Scanning electron microscopy (SEM) image of Copper oxide nanoparticles**

The scanning electron microscopy (SEM) method was applied to measure the specific surface area of the nanoparticles. SEM has been extensively used to characterize the surface morphology and major physical advantage of the adsorbent surface. The specific surface area of CuO-NPs was measured as 20 m\(^2\)/g. Figure 2 (SEM image of 300x and 800x) demonstrates that the CuO-NPs appear spongy in nature.

**Influence of initial pH**

The effect of different pH (2 to 12) on the adsorption of PG on CuO-NPs is displayed in Figure 3. The removal efficiency of PG was elevated by increasing the pH values from 2 to 6, while a pH higher than 6 reduced the removal efficiency. The removal efficiency increased
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Figure 3) Effect of pH on the removal of penicillin G onto cupric oxide nanoparticles (Time: 60 min, CuO-NPs dosage: 0.9 g/L, PG concentration: 50 mg/L)

from 51 to 75 % when pH was increased from 2 to 6. The optimal pH for the adsorption of PG on CuO-NPs was obtained at 6.

Influence of contact time and initial penicillin concentration

To assess the impact of contact time and initial PG concentration on the adsorption process, the initial concentration of PG varied from 25 to 100 mg/L at the optimum pH, the contact time of 60 min, and the CuO-NPs dose of 0.1 g/L. As illustrated in Figure 4, the initial concentration of 25 mg/L resulted in optimum efficiency removal.

The impact of contact time on percentage removal of PG onto CuO-NPs at a constant initial concentration of 25 mg/L, optimum pH, and the optimum CuO-NPs dosage is demonstrated in Figure 4. The adsorption of PG on CuO-NPs was rapid in the first 60 min.

Effect of cupric oxide nanoparticles dosage

As indicated in Figure 5, the adsorbent dose exerts a significant impact on the amount of adsorbed adsorbate. The impact of CuO-NPs dose on the elimination of PG was investigated by varying the dose of CuO-NPs from 0.1-1 g/L. The removal efficiency increased from 65-83% when the CuO-NPs dosage was raised from 0.1 to 1 g/L at the PG concentration of 25 mg/L. On the other hand, the biosorption capacity (qe) of PG on CuO-NPs decreased from 15 to 4.15 mg/g when CuO-NPs dosage increased from 0.1 to 1 g/L.
Adsorption kinetics

The results and correlation coefficients for Kinetic Model are presented in Table 1, and Figure 6-9.

Values of \( k_1 \) (depicted in Table 1) were evaluated from the slopes of the log plots of \((q_\text{e} - q_t)\) versus \(t\) for 25, 50, and 100 mg/L concentrations (Figure 6).

The parameters, \( k_2 \), and \( q_\text{e} \) (illustrated in Table 1) were determined from the intercepts and slopes of the plots of \( t/q_t \) versus \( t \), respectively, for 25, 50, and 100 mg/L.
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Figure 7) PSO plot of penicillin G sorption onto cupric oxide nanoparticles

Figure 8) Intraparticle diffusion plot of penicillin G adsorption onto cupric oxide nanoparticles

Figure 9) Bhattacharya-Venkobachar plot of penicillin G adsorption onto cupric oxide nanoparticles
concentrations (Figure 7).

The Kpi and c values (illustrated in Table 1) were estimated from the slopes and intercepts of linear plots of qt against t0.5, respectively for 25, 50, and 100 mg/L concentrations (Figure 8).

The linear plots of In (1-U(T)) versus t (Figure 9) were used to obtain the constant KB at different temperatures (Table 1).

By comparing the correlation coefficients R2, it can be seen that the experimental equilibrium sorption data are better described by the pseudo second-order model than by the other models.

**Discussion**

Large pores can be detected on the NPs pointing to the presence of adsorption sites on the adsorbent for PG removal. This will also lead to a high level of contact with the adsorbate (23, 24).

Solution pH is a key controlling parameter affecting the adsorption process. The anionic and cationic nature of the solution due to the competition between the ions of OH\(^{-}\) and H\(^{+}\) with the adsorbate exerts a significant impact on the process of adsorbate removal on an adsorbent (24).

The increased rate of removal efficiency at pH of 6 is related to the point of zero charge and pKa of the CuO-NPs and PG, respectively. The point of zero charge is defined as the pH at which the net charge of the total particle surface is equal to zero (25). The PG pKa was reported as 2.75, and the pHzpc of CuO-NPs was equal to 9.4. The adsorbent had a positive charge at pH less than the pHzpc value. PG took a carboxylic agent (-COOH) in acidic pH, and in pKa less than 2.75, the carboxyl group transformed to carboxylate charge; therefore, the removal efficiency increased (26). At pH within 7-11, the OH- ions decreased resulting in a marked increase in competition between them and anions. The removal efficiency decreased as the result of the repulsive force of negative charges of adsorbent and COO- anions (27).

The PG reduction decreased with an increase in initial PG concentration. As the adsorption process progressed with higher dye concentration, the adsorbent surface was easily saturated by PG particles (28).

By increasing the time to 60 min, as the optimum time, the collision of the nanoparticles and PG increased and resulted in enhanced adsorption cross-section and efficiency (29-31). The reduction efficiency of PG on CuO-NPs was decreased by increasing the contact time above the optimum time (60 min) to 120 min. It can result from the existence of the desensitization (reversible) phenomenon (31, 32).

This can be attributed to the increase in adsorption sites with more nanoparticles resulting in a marked increase in adsorption capacity (33). The decrease in the adsorption capacity is also ascribed to active adsorption sites which are unsaturated during the process of PG removal on CuO-NPs (25, 34).

The kinetic results and the correlation coefficients (R2) for the kinetic models are listed in Table 1. Based on the obtained results (Table 1 and Figures 6-9), the present study (the adsorption of PG on CuO-NPs) fitted well with the PSO model. R2 is the rationale for choosing the PSO kinetic adsorption model as the appropriate model (R2>0.99) since this parameter is higher for this model, compared to other adsorption kinetic models. This is indicative of the predominance of the PSO model mechanism suggesting that R2 values for the PSO kinetic model are greater than 0.99 which is followed by the uptake process. This also denotes that the adsorption of PG on CuO-NPs is controlled by chemisorptions (22). The intraparticle diffusion is not a suitable controlling factor in determining the kinetics of the adsorption process since the c values were not close to the
origin and the values of R2 (Table) were not high (35, 36). A similar observation was made by Nourmoradi et al. (37) for PG removal on modified montmorillonite.

The adsorption capacities (qe) and removal efficiencies (%R) of PG removal using various adsorbents are listed in Table 2. Table 2 shows that CuO-NPs can be efficiently be used for the removal of PG from water containing PG, in comparison with other materials.

### Table 2) Comparison of cupric oxide nanoparticles with other materials for the adsorptive removal of penicillin G

<table>
<thead>
<tr>
<th>Sorbent material</th>
<th>Maximum qe or %R</th>
<th>Conditions</th>
<th>Kinetic model tested</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-walled nanotubes (SWCNT)</td>
<td>qe = 141 mg/g, %R = 68.25%</td>
<td>pH: 5&lt;br&gt;SWCNT dosage: 0.8 g/L&lt;br&gt;Reaction time: 105 min&lt;br&gt;PG concentration: 50 mg/L&lt;br&gt;Working temperature: 10±2°C&lt;br&gt;Agitation speed: 300 rpm&lt;br&gt;Volume of solution: 100 mL</td>
<td>-PFO (R²=0.9991)&lt;br&gt;-PSO (R²= 0.988)</td>
<td>(38)</td>
</tr>
<tr>
<td>Magnesium oxide nanoparticles (MgO)</td>
<td>qe = 25.66 mg/g, %R = 74.97%</td>
<td>pH: 3&lt;br&gt;MgO nanoparticles dose: 1.5 g/L&lt;br&gt;Reaction time: 60 min&lt;br&gt;PG concentration:50 mg/L&lt;br&gt;Working temperature: 298±2 K&lt;br&gt;Agitation speed: 180 rpm&lt;br&gt;Volume of solution:100 mL</td>
<td>-</td>
<td>(39)</td>
</tr>
<tr>
<td>Cationic surfactant modified montmorillonite</td>
<td>qe = 88.5 mg/g</td>
<td>pH: 9&lt;br&gt;Adsorbent mass: 0.1 g&lt;br&gt;Reaction time: 60 min&lt;br&gt;PG concentration: 150 mg/L&lt;br&gt;Working temperature: 35±2°C&lt;br&gt;Agitation speed: 250 rpm&lt;br&gt;Volume of solution: 100 mL&lt;br&gt;Surfactant loading = 150%</td>
<td>-PFO (R²= 0.489)&lt;br&gt;-PSO (R² = 0.999)&lt;br&gt;-Intraparticle diffusion (R²=0.491)</td>
<td>(37)</td>
</tr>
<tr>
<td>Multi-walled carbon nanotubes (MWCNT)</td>
<td>qe = 119 mg/g, %R = 56.37%</td>
<td>pH: 5&lt;br&gt;MWCNT dosage: 0.8 g/L&lt;br&gt;Reaction time: 105 min&lt;br&gt;PG concentration: 50 mg/L&lt;br&gt;Working temperature: 10±2°C&lt;br&gt;Agitation speed: 300 rpm&lt;br&gt;Volume of solution: 100 mL</td>
<td>-PFO (R² = 0.156)&lt;br&gt;-PSO (R²=0.994)</td>
<td>(38)</td>
</tr>
<tr>
<td>Cupric oxide nanoparticles (CuO NPs)</td>
<td>qe = 15 mg/g, %R = 83%</td>
<td>pH: 6&lt;br&gt;CuO-NPs dosage: 1 g/L&lt;br&gt;Reaction time: 60 min&lt;br&gt;PG concentration: 25 mg/L&lt;br&gt;Working temperature: 30±2°C&lt;br&gt;Agitation speed: 150 rpm&lt;br&gt;Volume of solution treated: 1 L</td>
<td>-PFO (R²=0.68-0.99)&lt;br&gt;-PSO (R²=0.9963-0.9977)&lt;br&gt;-Intraparticle diffusion (R²=0.664-0.821)&lt;br&gt;-Bhattacharya–Venkobachar (R²=0.9107-0.9925)</td>
<td>This study</td>
</tr>
</tbody>
</table>
**Conclusion**

The present study assessed the adsorption of PG onto CuO-NPs. Based on the obtained results, CuO-NPs can be used as an alternative adsorbent for the removal of PG from its aqueous solution; with the CuO-NPs dosage of 1 g/L, PG concentration of 25 mg/L pH of 6 and contact time of 60 min, the optimum removal of 83% and adsorption capacity of 15 mg/g were attained. Consequently, PG adsorption by CuO-NPs fitted the pseudo-second-order model (suggesting chemical adsorption process) with a higher correlation coefficient ($R^2 > 0.99$), compared to that of pseudo-first-order, intraparticle diffusion, and Bhattacharya-Venkobachar models. Moreover, the best fit model for the experimental data was the Bhattacharya-Venkobachar and pseudo-first-order models.

**Footnotes**

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**Conflict of Interest**

The authors state that they do not have any competing financial interests or personal connections that might have influenced the work presented in the paper.

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