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Detoxification of Chlordiazepoxide Using Activated Charcoal Prepared from Olive Seeds

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Abstract

The study concerns the adsorption of chlordiazepoxide on the olive seeds-activated charcoal (OS-AC). It is carried out to investigate the possible use of OS-AC in the management of chlordiazepoxide intoxication. UV-visible spectrophotometry is applied to measure the concentration, and then it is used to study the adsorption isotherm and the factors influencing it, such as contact time, pH, temperature, ionic strength, and adsorbent dose. The results show that the best contact time is 1 min and 0.1 g dose of adsorbent olive seeds - -activated charcoal with no or small change concerning pH. The study of the adsorbent weight shows an increase in adsorption with an increase in olive seeds-activated charcoal weight. The removal of chlordiazepoxide by using olive seeds-activated charcoal is studied at different temperatures (10C°, 25C°and 50C°) to determine the adsorption isotherms and the thermodynamic functions. The experimental isotherm data are analyzed using Freundlich and Langmuir isotherm models. It is found that Langmuir's isotherm model fits the data very well for the drug chlordiazepoxide on olive seeds activated charcoal. According to Gile's classification, the shapes of the isotherms obtained from experimental data are comparable to the (H - Curve) type. Add the meaning of the abbreviation

السيطرة على سمية دواء الكلورديازيبوكسيد باستخدام الفحم المنشط المحضر من بذور الزيتون

زينب عبد الامير السلطان، رجوان عبد الجبار غزاي، سرى لطيف سلمان عبد الباري مهدي ماهود ، حسن محمود موسى

الخلاصة

تتعلق الدراسة بامتزاز الكلورديازيبوكسيد على بذور الزيتون - الفحم المنشط. وقد أجريت هذه الدراسة للتحقيق في الاستخدام المحتمل لـ OS-AC في السيطرة على التسمم بالكلورديازيبوكسيد. يتم تطبيق مطيافية الأشعة فوق البنفسجية المرئية لقياس التركيز ومن ثم استخدامها لدراسة تساوي درجة حرارة الامتصاص والعوامل المؤثرة عليه مثل وقت التلامس والرقم الهيدروجيني ودرجة الحرارة والقوة الأيونية وجرعة المادة المازة. تظهر النتائج أن أفضل وقت تلامس هو 1 دقيقة وجرعة 0.1 جرام من المادة المازة لبذور الزيتون - الفحم المنشط مع عدم وجود تغيير أو تغيير بسيط للغاية فيما يتعلق بالرقم الهيدروجيني. تظهر دراسة وزن المادة المازة زيادة في الامتصاص مع زيادة وزن بذور الزيتون - الفحم المنشط. تتم دراسة إزالة الكلورديازيبوكسيد باستخدام بذور الزيتون - الفحم المنشط عند درجات حرارة مختلفة (10 درجة مئوية و25 درجة مئوية و50 درجة مئوية) لتحديد تساوي درجة حرارة الامتصاص والوظائف الديناميكية الحرارية. تم تحليل بيانات معادلة الحرارة التجريبية باستخدام نماذج معادلة الحرارة فراندلش ولانكَماير. وقد وجد أن نموذج معادلة الحرارة لانكَماير يناسب البيانات بشكل جيد للغاية لعقار الكلورديازيبوكسيد على الفحم المنشط لبذور الزيتون. وقد وجد أن أشكال معادلة الحرارة التي تم الحصول عليها من البيانات التجريبية قابلة للمقارنة بنوع (H-Curve) وفقًا لتصنيف جيلز.

1. Introduction

Chlordiazepoxide (CDPX) is 7-chloro-4-hydroxy-N-methyl-5-phenyl-3H1,4-benzodiazepine-2-imine Fig.1, having the molecular formula of $C_{16}H_{14}ClN_3O$ and a molecular weight of 299.758 g/mol, sold under the brand names of (Librium, Librax, Limbitrol) (Ford, 2015; Kang et al., 2011; M. Beale, 2011).

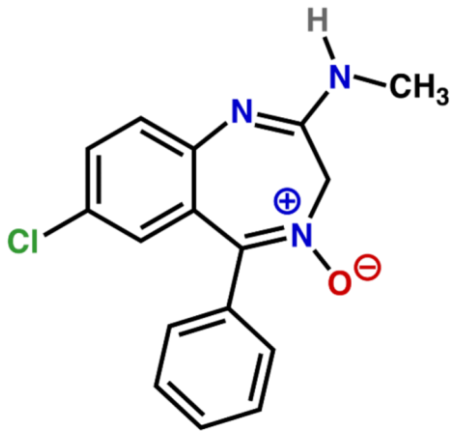

Figure1: Shows the Structure of Chlordiazepoxide

CDPX is used as an anticonvulsant and to treat symptoms of anxiety, another use is the treatment of irritable bowel syndrome (IBS) due to its muscular relaxing activity. The drug chlordiazepoxide (CDPX) has a complex metabolic pathway because it is biotransformed into several active metabolites (desmethylchlordiazepoxide, demoxepam, desmethyldiazepam, and oxazepam). Chlordiazepoxide (CDPX) clearance is reduced in the elderly and those with hepatic cirrhosis (Goodman & Gilman, 1966; Khonsary, 2023; Thompson Coon, 2002). Chlordiazepoxide is considered a safe drug because it is very rare to cause fatal effects when it is taken alone. However, in case of overdose, toxic effects appear like muscle weakness, CNS depression, ataxia and may cause respiratory depression, coma, which last for 24h, hypothermia and hypotension may occur. Chlordiazepoxide toxicity is increased if it is used in combination with other CNS-related drugs like tricyclic antidepressants or alcohol. In this study, the olive seeds activated charcoal is used to detoxification of Chlordiazepoxide. Detoxification can be defined as many interventions that manage acute intoxication, on the other hand clearing the body from acute accumulation of toxins and reduce the harmful or life-threatening effects that appear if the patient is left untreated (Goodman & Gilman, 1966; Khonsary, 2023; M. Beale, 2011; Thompson Coon, 2002). The toxic substances can be either as a byproduct from the normal human metabolic processes like carbon dioxide or urea and from the environment like pollutants, chemicals, which include drugs, and other harmful substances (M. A. Tadda et al., 2016, 2018). The activated charcoal adsorption process is one of the most commonly used techniques in the removal of trace organic compounds from the aqueous solution**.** One of the important properties of adsorbents is the high surface area to volume ratio and the activated charcoal is considered a good adsorbent for removal of organic compounds due to this ratio ranging from 500-1000 m^2/g (Adeniyi et al., 2023; M. Tadda et al., 2016). Activated charcoal is known as carbonic material with a wide internal surface area which has a highly developed porous structure that resulting from the processing of raw material at the high-temperature reaction. The appearance of activated charcoal is a fine, black powder that has no odor, no taste and it's nontoxic. It's produced through the slow combustion, or addition of acid, or addition of steam to a carbonic material like wood; peat; lignite, etc... The activated charcoal has a higher adsorption surface area due to a large number of pores.

The pores that are formed work through trapping liquid, solid or gaseous toxins and chemicals in GIT which prevent their absorption. These porous surfaces have negative electric charges and give rise to positive charges of chemicals and toxins in order to bond with them. So, they detoxify the system of the body and promote digestive functions by carrying the bounded toxins out of the body through feces (Abuelnoor et al., 2021; M. A. Tadda et al., 2018; Tan et al., 2017).

2. Materials & Methods

2.1. Materials

All the chemicals and instruments were presented in Table1 and Table2

Table1: Material Used in This Study

Materials / Instruments	Supplier/ Manufacture
Chlordiazepoxide	SDI
Hydrochloric acid HCl	HIMEDIA
Activated charcoal (olive seeds)	Prepared in lab
Potassium chloride KCl	HIMEDIA
sodium chloride NaCl	HIMEDIA
Magnesium chloride $MgCl_2$	HIMEDIA
Manganese(ll)chloride $MnCl_2$	HIMEDIA
Sodium hydroxide NaOH	HIMEDIA

Table2: The Instruments Used in This Study

Instruments	Manufacture
UV-1800 SHIMADZU with 1cm matched pair quartz cell and spectral bandwidth of 1nm.	SHIMADZU - Japan
Muffle oven	China
Sensitive balance.	Germany

2.2. Preparation of Olive Seeds Activated Charcoal

Previously collected, cleaned and dried olive seeds are placed in a closed crucible in a muffle oven, which its temperature is raised to 650 C^o and keep there for around 10 minutes. The resultant charcoal is left to be cooled and transferred to a mill to create a fine powder of activated charcoal.

2.3. Preparation of standard solutions

Standard solution of 100 µg/ml chlordiazepoxide is prepared by dissolving 0.010 gm of chlordiazepoxide in a 100 ml volumetric flask with 0.100 N HCl. Further working solutions are prepared by dilution (Ioannidou & Zabaniotou, 2007; Yogin Soodesh et al., 2024).

The solution of 0.100 N HCl is prepared by measuring 2.18 ml of concentrated HCl and completing the volume in a 250 ml volumetric flask to the mark with distilled water. The salts solutions *(0.02, 0.05, 0.07 M)* of NaCl, KCl, $MnCl_2$ and $MgCl_2$ are prepared by dissolving (0.058 - 0.204) g, (0.074 – 0.260) g, (0.120 – 0.440) g and (0.095 – 0.330) g of the compounds respectively in distilled water and the volume is completed to 50 ml in volumetric flasks.

2.4. Equilibrium time of adsorption system

To a series of 25 ml, volumetric flasks (1 ml) of the drug was transferred and completed with 0.1 N HCl to the mark. Olive seeds activated charcoal 0.1 gm are added to solutions and shaken for different times, which are filtered after that. The absorbance of these solutions are measured and recorded (Deng et al., 2011).

2.5. Adsorption isotherm

To determine the adsorption isotherm for the drug with olive seeds activated charcoal, different concentrations ranged from (4 - 8) ppm of CDPX are used and mixed with 0.1 g of adsorbents for 1 min, which are filtered then and their absorbance are measured and recorded.

3. Results & Discussion

3.1. Study of UV - Visible Spectrum

The UV – Visible spectrum of chlordiazepoxide in Fig.2 shows that high absorbance of the drug is at λ_{max} = 245 nm (Lennard, 2004; Sari et al., 2023).

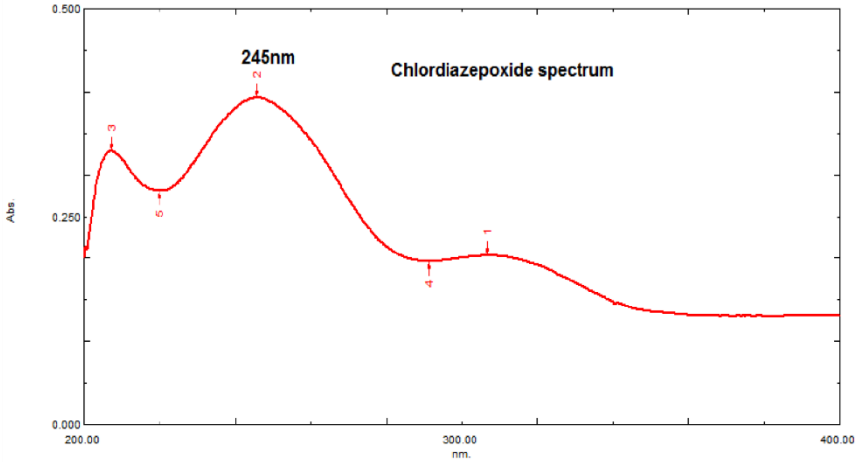

Figure2: UV-Visible Absorption Spectrum of Chlordiazepoxide, showing a prominent absorption peak at 245 nm, indicating the λmax (maximum absorbance wavelength) used for subsequent spectrophotometric measurements. The spectrum was recorded in the range of 200–400 nm using 0.1 N HCl as the solvent medium.

3.2. CDPX Calibration Curve

The calibration curve of CDPX is determined. Fig.3 shows a linear calibration curve at 245 nm in the range (0.5-15) ppm (Hegazy & Kabiel, 2010) .

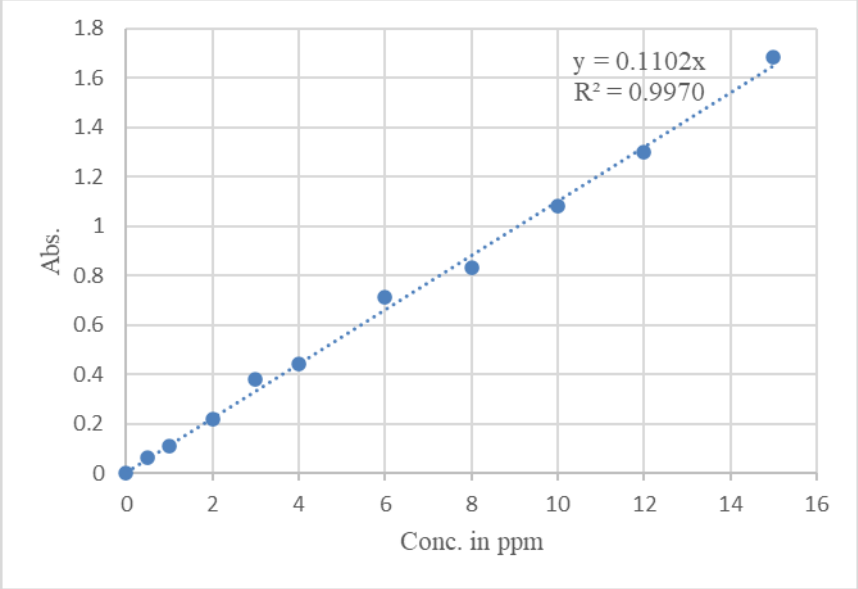

Figure3: Calibration Curve of Chlordiazepoxide Showing the Linear Relationship Between Absorbance and Concentration (Ppm) At 245 Nm. The regression equation is $y = 0.1102x$ with a high correlation coefficient ($R^2 = 0.9970$), indicating excellent linearity within the tested concentration range.

3.3. Effect of Charcoal Weight

The olive seeds activated charcoal (OS –AC) shows increased adsorption (a decrease in absorbance values with increased weight) with an increase in its amount (weight), and this is attributed to an increase in its adsorption capacity (its total effective surface area), with an increase in active sites that lead to increase in removal percentage (Re%) as shown in Fig.4 (Olalekan et al., 2013).

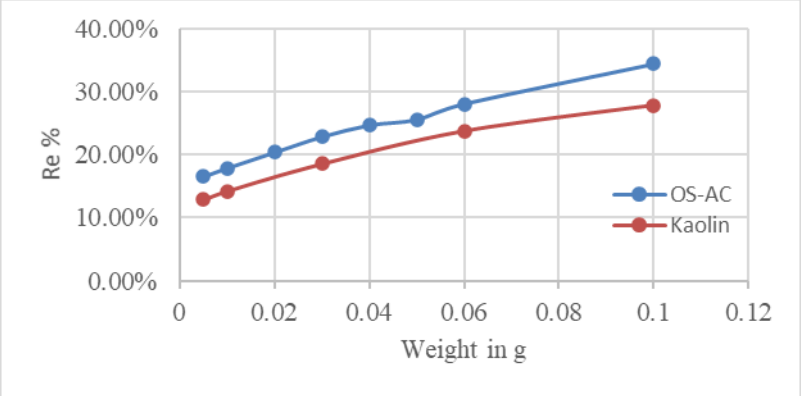

Figure4: Effect of Adsorbent Weight on The Removal Efficiency (Re%) of Chlordiazepoxide Using Olive Seed Activated Charcoal (OS-AC) And Kaolin.

As the weight of adsorbent increases, the removal efficiency also increases for both adsorbents, with OS-AC showing consistently higher performance compared to kaolin.

3.4. Effect of Time

The olive seeds activated charcoal shows the highest adsorption (drug removal) amount rapidly (at the 1 min. mark) which shows that it can be used for rapid drugs detoxification. The decline in the adsorption amount can be attributed to the breakage of weak physical bonds and only the chemical ones remain and observed with the constant removal amount after 13 min (Gale et al., 2021; Hassan et al., 2023).

3.5. Effect of Concentration of the Drug

Table3 refers to 0.1 gm of olive seeds activated charcoal shows the best and highest efficacy at a CDPX concentration of 4 ppm. (2 ppm is not used because it is too low for practical use) (Ehiomogue et al., 2022; Foo & Hameed, 2010).

Table3: Concentration of CDPX with and without OS-AC

Conc. in ppm	Abs. without charcoal	Abs. with charcoal	Re.%
2	0.260	0.119	45 %
4	0.472	0.266	40.65 %
6	0.703	0.531	19.69 %
2	0.840	0.764	14.3 %

3.6. Effect of Temperature

The adsorption amount increases with a decrease in a solution temperature and vice versa, which was expected as the adsorption process is an exothermic one and is improved by lowering the temperature of the solution as presented in Table4.

Table4: Effect of Temperature on Removal Percentage Re.%

Temp. in C°	Conc. in ppm	Abs.	Re.%
10	4	0.204	53.72 %
	6	0.496	24.98 %
	2	0.721	18.21 %
25	4	0.237	46.23 %
	6	0.532	19.54 %
	2	0.761	14.67 %
50	4	0.284	35.57 %
	6	0.559	15.45 %
	2	0.788	10.61 %

3.7. Effect of pH

The olive seeds activated charcoal shows constant adsorption amounts with different pH values ranging from 1 to 8, and this can be considered an excellent property because it means the olive seeds activated charcoal has a predictable and consistent adsorption amount regardless of the solution pH, so the stomach acidity will not affect the removal percent of OS- AC (Babel & Kurniawan, 2003; Ehiomogue et al., 2022; Mishra, 2022).

3.8. Effect Ionic Strength

Table5 refers to various univalent and bivalent salts in table (5) show very low adsorption amounts, which indicates that HCl is the best solution, in addition to the HCl found in the stomach, where the olive seed-activated charcoal is supposed to act (Kumar & Jena, 2016b, 2016a).

Table5: Effect of Ionic Strength in Removal Percentage Re.%

The concentration of salt	The removal percentage (Re.%)			
	NaCl	KCl	$MnCl_2$	$MgCl_2$
8	%9.7	%9.44	%4.4	%9.7
4	%6.384	%2.6	%4.294	%2.289
9	%9	%7.74	%6.44	%5..684

3.9. The Adsorption Isotherms

The experimental isotherms data were analyzed using Freundlich and Langmuir isotherm models as presented in Fig.5. and Fig.6 and Table6. The experimental isotherms data were analyzed by using Freundlich and Langmuir isotherm models. The data in the Table6 assert that Langmuir's isotherm model fits the data very well for the drug (CDPX) on olive seeds activated charcoal. The shapes of the isotherms obtained from experimental data that are found to be comparable to the (H-Curve) type according to Giles classification (Giles et al., 1960; Kumar & Jena, 2016b, 2016a; Mellouk et al., 2009).

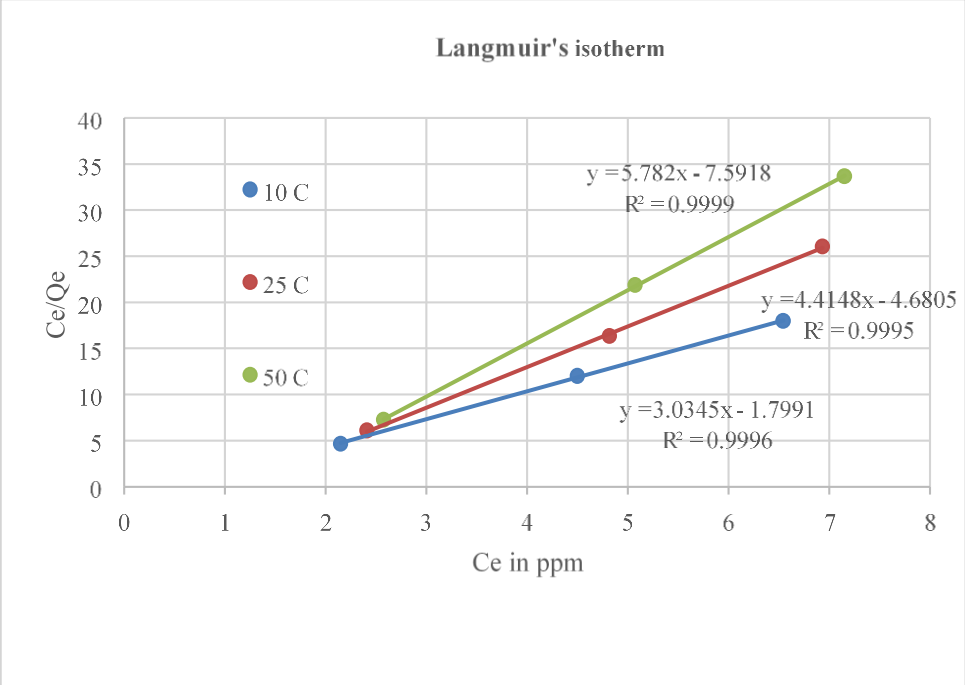

Figure5: Langmuir Isotherm Plots for The Adsorption of Chlordiazepoxide Onto Olive Seed Activated Charcoal (OS-AC) At Different Temperatures (10 °C, 25 °C, And 50 °C).

The linear relationship between Ce/Qe and Ce indicates the applicability of the Langmuir model. Increasing temperature leads to higher Ce/Qe values, suggesting reduced adsorption capacity at elevated temperatures. Each line corresponds to a different temperature with its respective regression equation and R^2 value indicating a good fit.

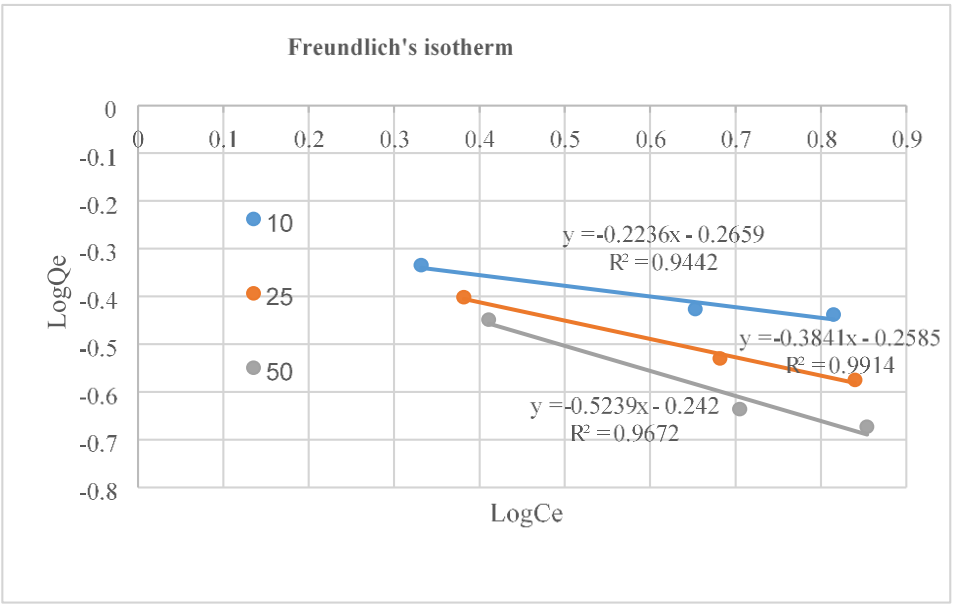

Figure6: Freundlich Isotherm Plots for The Adsorption of Chlordiazepoxide Onto Olive Seed Activated Charcoal (OS-AC) At Temperatures Of 10 °C, 25 °C, And 50 °C. The Linear Relationship Between Logce And Logqe Supports the Applicability of The Freundlich Model, Indicating Multilayer Adsorption on A Heterogeneous Surface.

The negative slopes represent the adsorption intensity (1/n), while the intercepts correspond to adsorption capacity (Kf). The correlation coefficients (R^2) indicate a good model fit across all tested temperatures, with adsorption intensity increasing slightly with temperature.

Table6: Results of Langmuir's and Freundlich's Equations

Temp. C^o	Langmuir isotherm				Freundlich's isotherm		
	a(mg/g)	b(mg/g)	(r^2)	RL	(kf)	Slope(n)	(r^2)
10	0.329	-1.623	0.9996	-0.182	-..8647	-4.4988	..7448
25	0.229	-0.348	0.9995	-0.348	-..8424	-8.6.34	..7754
50	0.173	-0.761	0.9999	-0.489	-..848	-5.7.29	..7698

4. Conclusion

This study demonstrates the potential of activated charcoal made from olive seeds (OS-AC) in effectively detoxifying chlordiazepoxide. The identified ideal adsorption parameters of neutral pH, 0.1g adsorbent dosage, and a one-minute contact duration, along with the accurate description of the adsorption process by Langmuir's isotherm model, inspire and motivate the future application of OS-AC in treating chlordiazepoxide intoxication, providing a new direction for professionals in the field of toxicology and pharmacology.

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