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COMPRESSION BETWEEN KAOLIN AND CORN SEED AS ADSORBENTS ON THE ADSORPTION OF METFORMIN HYDROCHLORIC FROM AQUEOUS SOLUTION UNDER DIFFERENT CONDITIONS

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Abstract

Metformin is currently the medicine used to treat hypoglycemia most frequently. We used kaolin and corn seed surfaces to draw out the drug metformin hydrochloride from aqueous solutions. The medicine metformin, which is currently the most frequently prescribed oral hypoglycemic, has outstanding safety profiles and is only contraindicated in people with definite medical problems, particularly chronic renal failure, congestive heart failure, chronic obstructive pulmonary disease, and liver disease. The analysis demonstrates how many factors, such as equilibrium time (5–15 min), pH (8.5) as well as for pH of small intestine, temperature (32–37°C). It is discovered that when temperature and pH increase, the amount of adsorbate present decreases, with equilibrium requiring 15 minutes. The wavelength used for the analysis of metformin HCl was (260 nm). To discover the appropriate adsorption parameters, it was chosen to apply response surface methodology (RSM). Through thorough physical characterization using techniques including FTIR it was demonstrated that the primary driving forces behind the adsorption processes are H-bonding, electrostatic attraction, and so-called (electron donor-acceptor) EDA interactions. Modeling revealed that the best explanation for the MF adsorption involved an isotherm that depended on Giles categorization, was spontaneous (ΔG = -5.9 kJ/mole), and was endothermic (ΔH = +12.14 kJ/mole).

Keywords: *Adsorption, Kaolin, Thermodynamic, Metformin Hcl, Pharmacokinetics And Diabetic Type 2.*

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Introduction

The common disease known as diabetes affects up to 45 million individuals globally. It contributes to heart disease and chronic kidney illness. [1]

Around 150 million individuals have metformin prescriptions today, making it one of the most widely used medications in the world. Metformin HCl [2] is a biguanide anti-diabetic drug taken orally. It all started in 1918 when guanidine, a chemical contained in the European herbal medicine Galega officinalis, was identified to lower blood sugar levels. [3]

It has been suggested as the first-line oral medicine in all significant guidelines after lifestyle modifications for T2D have failed. [4], [5], [6] In other words, metformin lessens insulin resistance while increasing glucose absorption [7]. The mechanism of action of metformin may be associated with an increase in insulin sensitivity. Although it does not encourage the secretion of insulin, insulin must be present for it to have a hypoglycemic effect [8]. Additionally, activating the AMPK pathway to inhibit gluconeogenesis, or the production of glucose, in the liver [9], and by both EASD (European Association for the Study of Diabetes) and ADA (American Diabetes Association) since 2009. [10] The main anti-diabetic impact of metformin is assumed to be accomplished through reducing gluconeogenesis in the liver. Two main molecular targets of metformin have been identified, and both can be found in the mitochondria (Figure 1). Because of this, metformin reduces the activity of the mitochondrial respiratory complex I, which lowers the efficiency of ATP synthesis and raises the ratio of adenosine monophosphate (AMP) to adenosine triphosphate (ATP) in cells. AMP-activated protein kinase (AMPK) is activated by this increase in the AMP: ATP ratio which has a variety of effects on energy metabolism. [11]

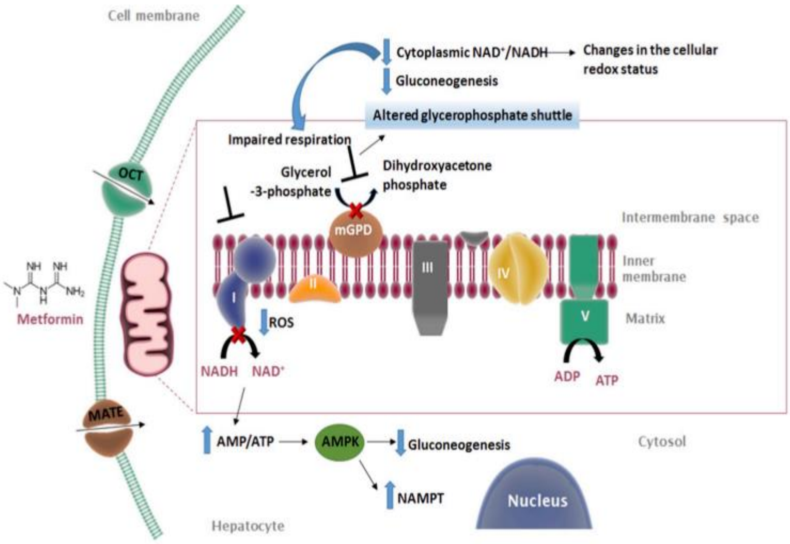

Figure- 1 Metformin's influence on the mitochondria is mediated through molecular processes. [10]

Metformin increases the absorption and anaerobic metabolism of glucose in the stomach, which helps to explain why using metformin results in a rise in lactate. [12], [13] figure (2).

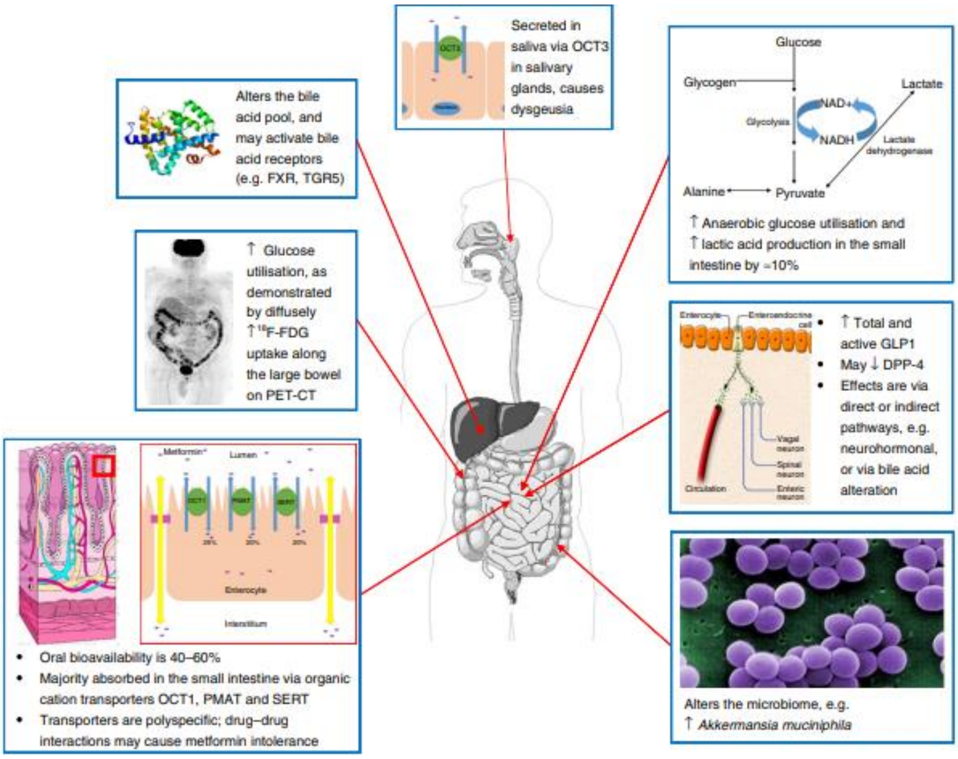

Figure- 2 Some of the actions of metformin within the GI tract [12].

The most well-known impact of metformin is its capacity to lower hyperglycemia's clinical symptoms and indicators. Due to its low cost, good therapeutic benefit in terms of glycemic management and safety, and minimal body weight reduction, it is currently one of the most commonly prescribed drugs on the market [14], [15].

Metformin occurs in a positively charged state under physiological conditions, indicating the need for a transporter to allow metformin to traverse plasma membranes [16].

Some methods for removing MF from wastewater include ozone, photolysis, photocatalysis, and adsorption. Due to its versatility, simplicity, efficiency, and selectivity, adsorption is suitable for eliminating MF [17].

One of the most significant isotherms is the Freundlich isotherm. In relation to solid-liquid adsorption interfaces. Since the majority of surfaces are diverse, which causes the potential energy to fluctuate often and the adsorption sites to have different energies, it is generally anticipated that many layers will form. Adsorption behavior for uncomplicated solutes is typically simple and may be accurately predicted based on interactions between the surface of the adsorbent and the adsorbing adsorbate. The Langmuir isotherm can also be used to explain the adsorption behavior down to the monolayer level [18].

In a process of Langmuir-type adsorption, the shape of an isotherm can be classified using a dimensionless constant separation factor known as RL [19].

2. Method

The equipment used included an Eppendorf 5804 R centrifuge, a pH meter from TDA Electronics Ltd. called the HM-73, a UV-VIS Spectrophotometer (UV-1800) from Shimadzu, a thermostatic Shaker bath from Germany (GFL (D-3006), a pH meter from TDA Electronics Ltd. called the UV-1800, and an electronic balance from Sartorius Lab. called the BP 3015. NaOH is the substance used (Emscope laboratories Ltd.). The medication was metformin HCL, which is available from Hopkins & Williams, Ltd. England.

Adsorbate the almost uniform use of supra-pharmacological dosages of metformin in older studies, which are 10-100 times higher than the greatest therapeutic concentrations reported in individuals with type 2 diabetes, may be a key contributing factor. [20]

The process of heating 2-cyanoguanidine (dicyandiamide), first described in a 1922 journal and reproduced in multiple subsequent patents and publications, is typically used to produce metformin. [21] Metformin (C4H11N5) [22] is a (N, N-dimethyl imidodicarbonimidic diamide monohydrochloride) [23], [24] in figure (3) is a hygroscopic, white, crystalline powder that is freely soluble in water. [25] as well as the figure (4) of the scanning electron microscopy for metformin HCl.

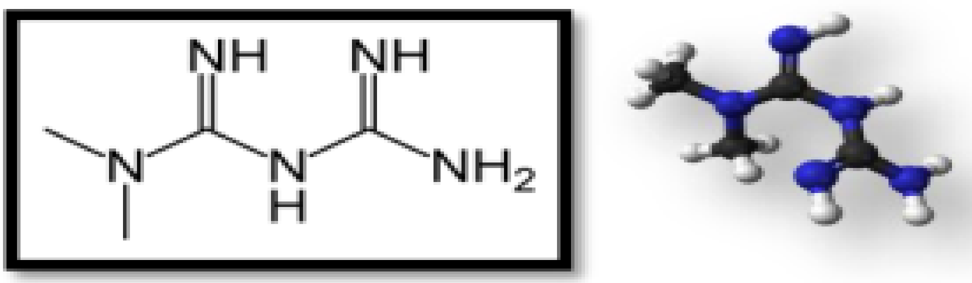

Figure -3 Chemical structure of metformin [21], [26].

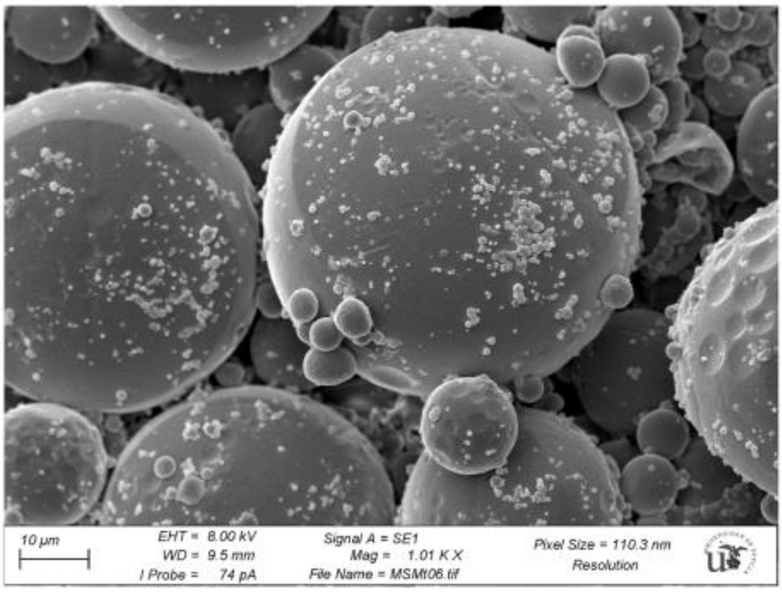

Figure- 4 images taken using a scanning electron microscope (SEM) after lyophilization of the surfaces of the PLA microparticles being studied that were loaded with metformin [27].

4. Adsorbents

1- Iraqi kaolin as powder for adsorption of metformin HCl (Fig. 5) was supplied by the "General Company for Geological Survey and Mining," Baghdad, Iraq, and was obtained from Dwaikhla) opened mine (north of Rutba) in the western desert of Iraq.

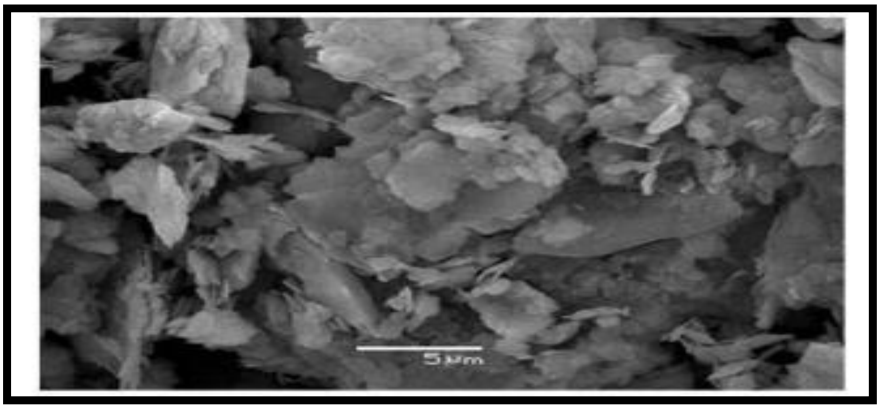

Figure- 5 the shape characterization of kaolin [28].

The Iraqi kaolin clay's weight percentages were: SiO_2 (54.68%), Al_2O_3 (30.19%), Fe_2O_3 (1.02%), TiO_2 (1.00%) and loss on ignition (10.94%).

2- corn seeds powder

The Nano Center at the University of Technology provided the function groups for corn seed powder used as adsorption of metformin HCl in this method because have large surface aera by using Molecular sieve 75µm. As seen in figure (6).

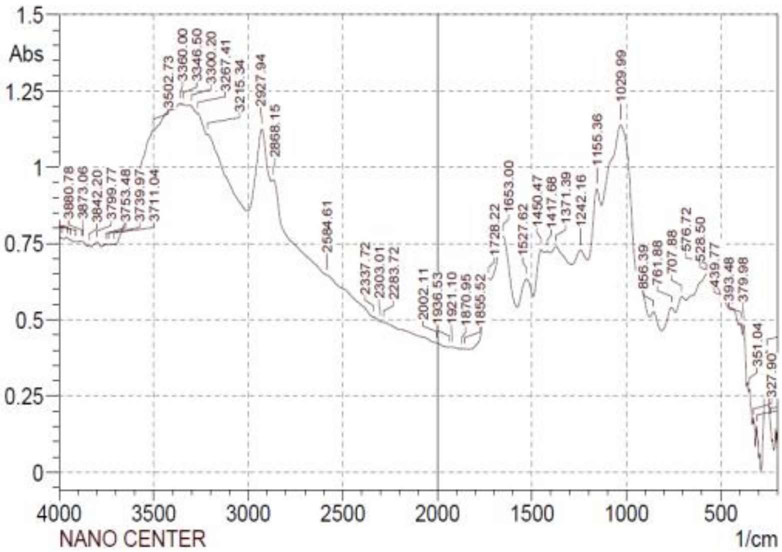

Figure -6 FT-IR spectrum for corn seeds powder.

Stretching and deformation vibrations generate the functional groups for the metformin HCl absorption bands. The size, relative intensity, and shape of the infrared absorption bands are used to determine the typical vibrational modes in a manner similar to band assignments. [29] (In figure 7).

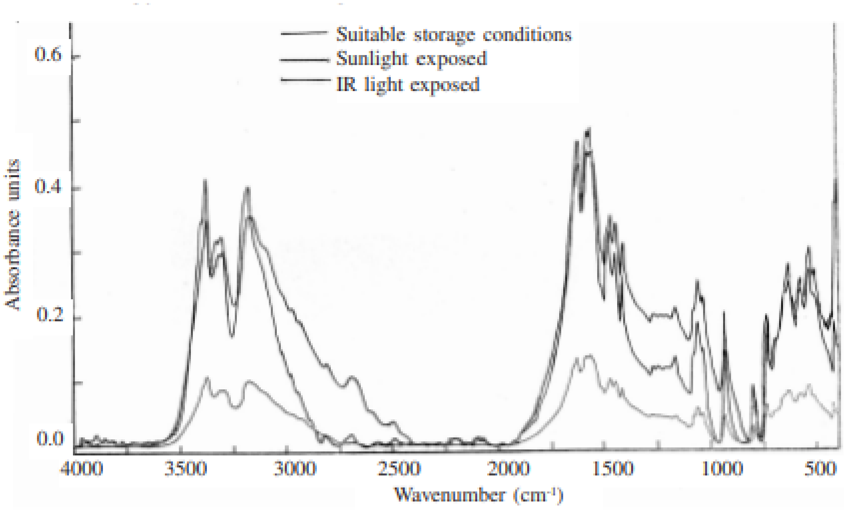

Figure- 7 FT-IR spectra of metformin hydrochloride [29].

They were each repeatedly rinsed in copious volumes of distilled water before being dried at 150 c^{o}, three hours in the oven, then stored in sealed jars. The Retch test sieve 150m was used to grind and sift each adsorbent. The process described below has been used to calculate the amount of time needed to attain equilibrium in order for the adsorbate to fully saturate the adsorbent surface at 37^{o} C it considers normal temperature for human health: Adsorbate solution with an initial concentration of (0.003 mg/L) in 500 ml was mixed with (0.5 g) of each adsorbent. The absorbance of adsorbate solutions was measured using a UV/Visible spectrophotometer at varied intervals of 10, 20, 30, and 60 minutes until equilibrium was established (no more adsorbate was being taken up by the adsorbent as the time passed). There are two adsorbent-adsorbate systems for each pair, an organized process was used to determine the adsorption isotherms. A mixture of five distinct medication strengths in a 50 ml volume maximum absorbance (λ_{max}) was (260nm) (Fig. 8).

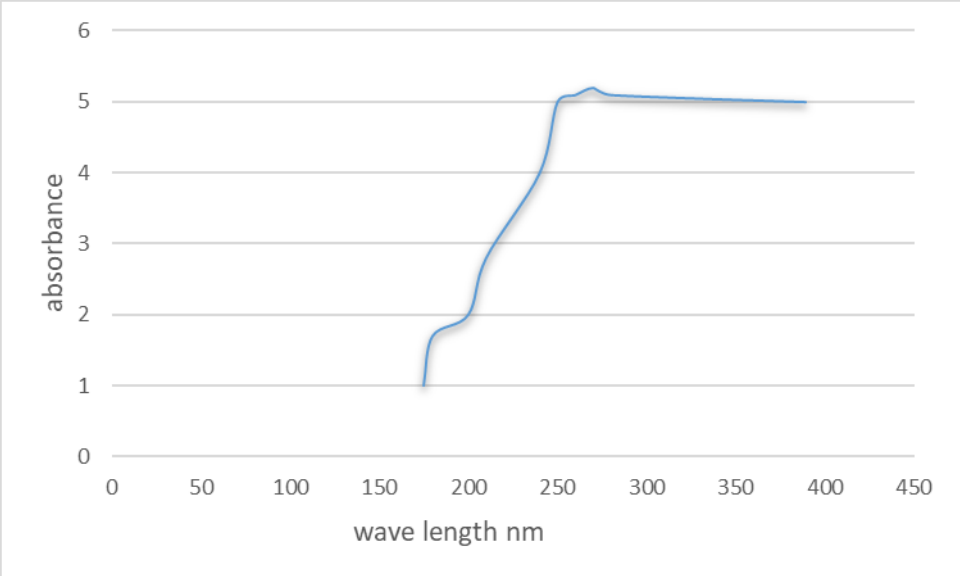

Figure- 8 UV Spectra of aqueous solution of (λ_{max}) of metformin HCl between absorbance and wave length at pH=8.5 and temperature 37℃.

The stock solution was diluted with distilled water to create several drug solutions with varied concentrations (0.001, 0.0008, 0.0006, 0.0004, 0.0002 mgL1). Using a UV-Vis double beam spectrophotometer. The values of these medication solutions' absorbance were determined at a particular (max) and plotted against the concentrations of these drug solutions in order to create the calibration curve for aqueous solutions of these medications, for metformin HCL at pH = 8.5 similar to pH of small intestine. (In figure 9).

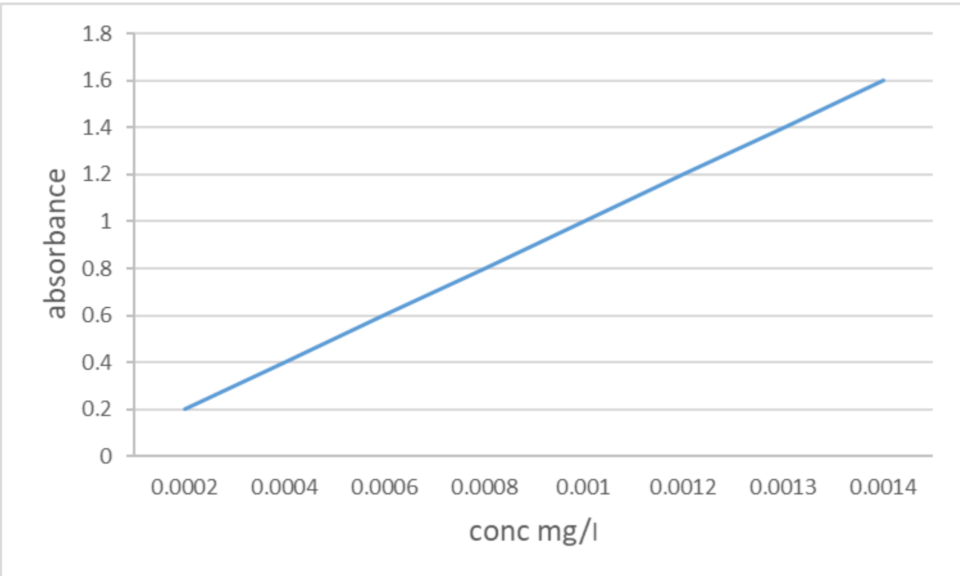

Figure -9 at 37° C, the calibration curve for aqueous solutions of metformin HCL.

Using their absorbencies, the calibration curve can be used to calculate the equilibrium concentrations of the produced solutions. Equation (1) was used to determine the amount of medication that had been adsorbed under specific circumstances based on the concentration of the solution prior to and following adsorption:

$$Xm = (Co - Ce)\, V / m \qquad (1)$$

where Co and Ce represent, respectively, the initial and equilibrium drug concentrations. Alternative (mg/L) A fixed value of Ce for all study temperatures, *Xm* is the maximum quantity of adsorbate (in mg) that may be adsorbed on the adsorbent, and (m) is the weight of the adsorbent in grams. Xm can be determined from equation (2):

$$Qe = Xm / m \qquad (2)$$

where Qe= is the amount of adsorbate (measured in mg) that (0.5 g) of adsorbent can hold.

$$K = (Qe)\,(0.5\, g)/(Ce)\,(0.05\, L) \qquad (3)$$

where (0.05 liter) denotes the amount of medication solution utilized during adsorptions procedure and (0.5 g) denotes the weight of the clay that was employed. Equation (4) could be used to compute the free energy change (ΔG):

$$\Delta G = -R\, T \ln k \qquad (4)$$

where T is the absolute temperature and R is the gas constant (8.314 J/mol deg).

Equation (5) can be used to determine the heat of adsorption (ΔH):

$$In\, Xm = -\Delta H / RT + constant \qquad (5)$$

Equation (6) can be used to determine the entropy change (ΔS):

$$\Delta G = \Delta H - T\Delta S \qquad (6)$$

5. Results

Effects of temperature and thermodynamic variables: -

Figures (10 and 11) show the overall morphologies of metformin HCL adsorption on kaolin and corn seeds at various temperatures (37 and 32 C °). Figures (10 and 11), which also demonstrate that the shapes isotherm is dependent on the Giles classification, show the adsorption isotherms of metformin HCl on kaolin and corn seeds at pH=8.5 and various temperatures.

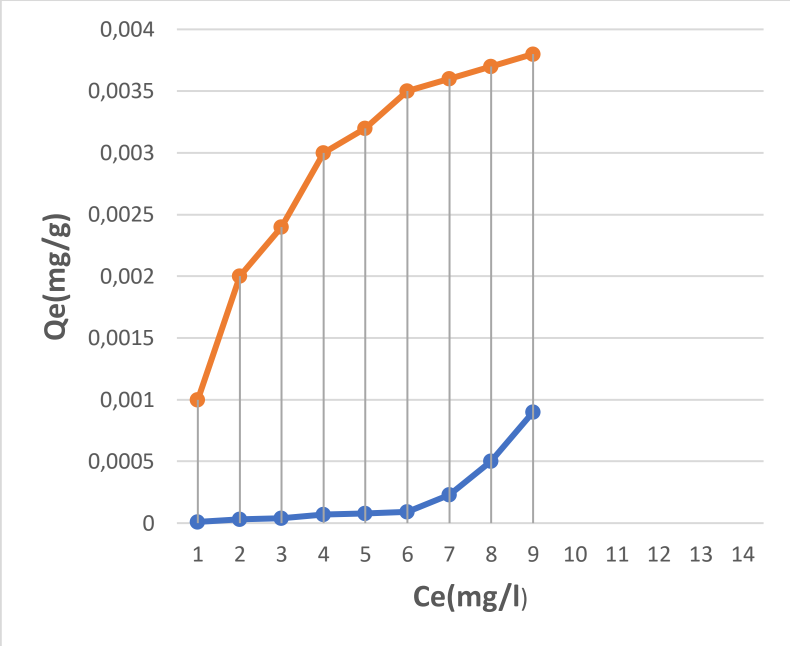

Figure-10 Metformin HCL adsorption isotherm on kaolin at different temperatures (37 and 32°c) and at pH=8.5

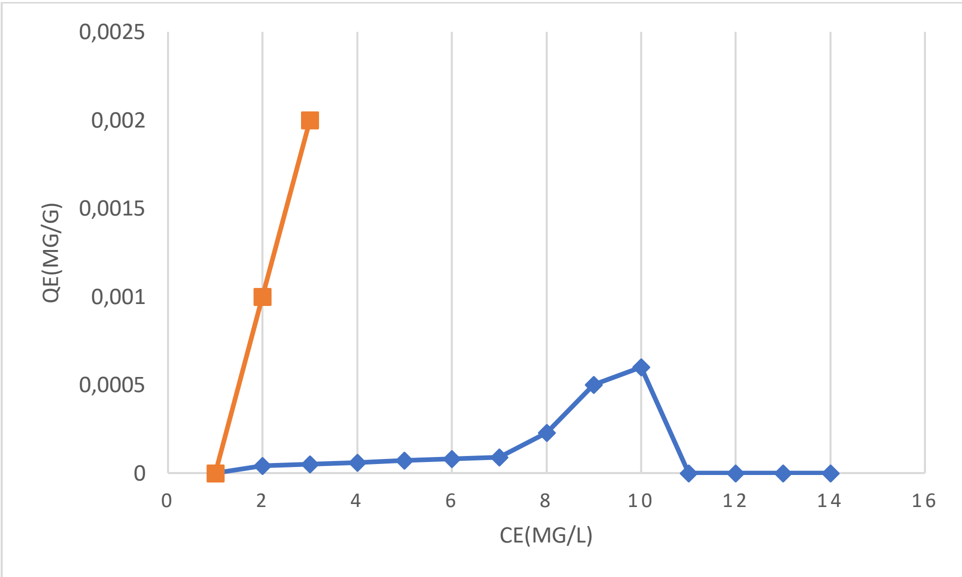

Figure-11 at 37 and 32° C and pH=8.5, the adsorption isotherm of metformin HCl on corn seeds is shown.

The examination of the effects of temperature on adsorption leads to the discovery of the fundamental thermodynamic functions (ΔH, ΔG, and ΔS) of the adsorption processes. The values for Xm at various temperatures and at a pH of 8.5 are shown in table (1). The effect of temperature on the highest concentrations of metformin HCL adsorbed on kaolin and maize seeds is shown in Table 1. Where, at a given (Ce) value, Xm is the maximum quantity of adsorbate that can be absorbed at all temperatures.

Table 1 The effect of temperature on the highest concentrations of metformin HCL.

Adsorbent	T.c°	T.k°	1000/T. °k-1	Xm(mg)	In Xm
kaolin	37				
	32	310	3.22	0.009	-4.71
		305	3.27	0.008	-4.82
Corn seed					
	37	310	3.22	0.0025	-5.99
	32	305	3.27	0.0015	-6.5

Figures (12, 13) illustrate the result of plotting (In Xm) versus 1000/T. k^{-1} as a straight line with a slope of - ΔH/R.

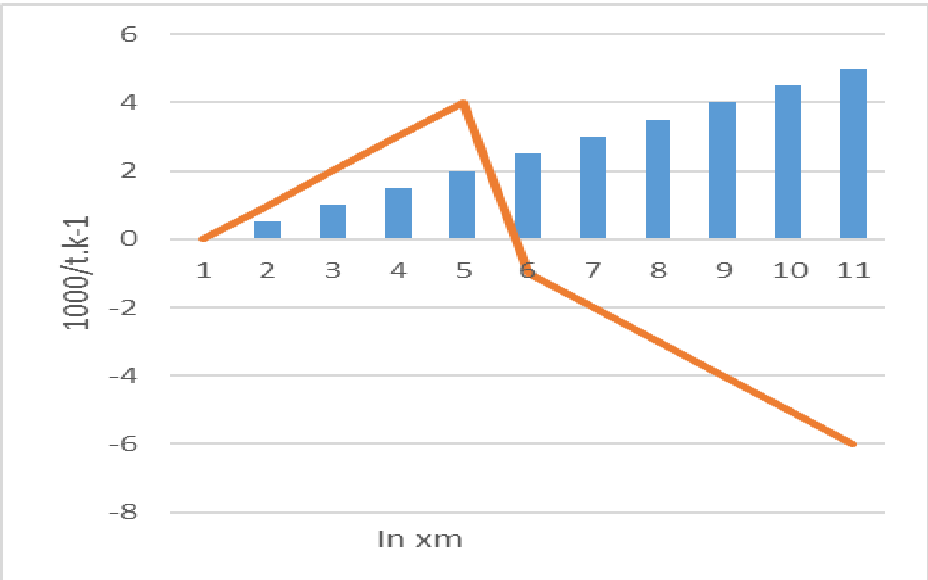

Figure-12 for the adsorption of metformin HCl on kaolin at pH=8.5, the temperature in Xm is displayed against the reciprocal absolute temperature.

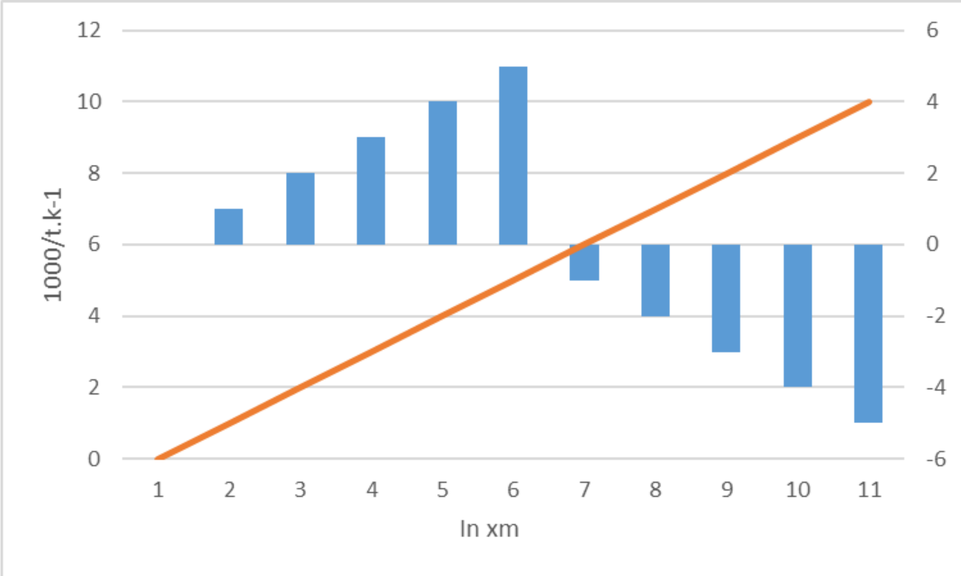

Figure- 13 For the adsorption of metformin HCl on corn seeds at pH=8.5, in Xm plotted against reciprocal absolute temperature.

The metformin HCl adsorption on kaolin and corn seeds had negative ΔG values.

Showed that folic acid adsorption occurs spontaneously. The positive readings of ΔH at different temperatures served as evidence for the endothermic reaction. The positive values of ΔS demonstrated the enhanced level of freedom of the adsorbed species (metformin HCl). As shown in table (2)

Table (2) shows the basic thermodynamically values of adsorption of metformin HCl on kaolin and corn seeds.

Adsorbent	**ΔH**	**ΔG**	**ΔS**	**pH**	**Temperature (c◦)**
kaolin	+12.14				
	+12.22	-5.9	+0.05	8.5	37
		-3.8	+0.05	8.5	32
Corn seed					
	+15.91	-15.7	+0.1	8.5	37
	+16.72	-13.6	+0.09	8.5	32

6. Discussion

HCl metformin at physiological pHs, it is a hydrophilic cation [30]. A daily dose of 2 grams of metformin is recommended for many diabetics. Metformin is quickly distributed to multiple tissues after partial small intestine absorption following a single oral dose, but the luminal concentration in the gastrointestinal tract is still high. [31] The functional groups of heterogeneous surfaces analysis for corn seeds surface were found with the use of the FT-IR spectrum. It was shown that the O-H band, peptide bonds, phenolic O-H and C-O stretching bonds, aliphatic C-O bands, as well as CH_2, CH_2 and COO vibrations, are all present at 3400 cm1 in these surface compounds. The "1000 cm 1" The phosphate was in the finger print zone and sulfur groups. [32]

The SiO_2 structure on the surface of corn seeds vibrates both stretching and bending can be used to explain two bands at 1022 cm^{-1} and 465 cm^{-1}. Additionally, a band related to the carboxylic group's C=O could be discovered at 1720 cm^{-1}, whereas the aliphatic chains' C-H band stretching might be linked at 2900 cm-1. [33][34]. at pH=8.5, on the surface of the corn seed, the carboxylic group interacts with the NH group of the MF [35]. The elevated pH in this investigation illustrates the adsorbents' negatively charged surfaces. which enhance the Figure 1 illustrates the surface's electrostatic forces of attraction of the adsorbent causing positively charged functional groups of the adsorbate to bind to it. In general, at high pH, the adsorbent has a zero-point charge and its surface becomes negatively charged. [36]

In this study, it was found that the effect of temperature on the adsorption process increased as the temperature increased. The endothermic nature of the adsorption may be caused by the formation of stronger bonds at higher temperatures. [37] and the model as Freundlich and Langmuir models depend on Giles classifications this is as agree with the reference [38]

The effect of adsorbent geometry, shape, and generating atoms on the physicochemical reactivity of the MF molecule. [22] Drug particles cover the surface when the surface pores are filled with them, indicating that adsorption has occurred when a coating of drug particles formed on the surface. As a result, the surface was smoother and less porous or nonporous. [39].

7. Conclusion

The in vivo bioavailability of the majority of oral drugs must be forecast because in vitro disintegration studies do not always show a good link. Dissolution testing of drug products is a vital quality assurance technique for monitoring the consistency of drug release from a dosage form from batch to batch. To assess a solid oral dosage form's potential in vivo performance and as a quality control test to show that drug products are performing as intended, in vitro dissolving procedures have been developed. Particularly with regard to neurodegenerative conditions like MDD and AD that are linked to depression in both T2DM patients and populations at risk of diabetes, metformin may operate as a possible drug to slow down aging. It concludes the kaolin surfaces showed at pH=8.5 and various temperatures, the capacity to adsorb metformin HCl from its aqueous solution is higher than corn seed surface. As a result, these adsorbents can be utilized as countermeasures to reduce the concentration of metformin HCl.

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