

## SPECTROSCOPIC EVALUATION OF ACTIVATED CHARCOAL AS A POISON ANTIDOTE FOR GLICLAZIDE DRUG

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### ABSTRACT

**Objective:** The aim of the present study is to evaluate the ability of activated charcoal in adsorbing overdose of gliclazide drug, and to study the effects of pH, concentration and time on this process.

**Methods:** To evaluate the effect of pH, concentration and time; 50 ml of the drug solution (100 mg/L) were allowed to stand with the activated charcoal for 1 h at pH of 1.5, 4, 7, and 9 for pH study. 50 ml of the drug solution concentrations of 25, 50, 75, and 100 (mg/L) were allowed to stand with 1 g activated charcoal for 1 h for concentration study. 50 mg of the drug solution (100 mg/L) were allowed to stand with the activated charcoal for 15, 30, 45, and 60 min for time study. The concentrations of the adsorbed drug were determined spectrophotometrically.

**Results:** The adsorption of the gliclazide drug on activated charcoal was found to be pH, concentration, and time-dependent. The amounts of the drug adsorbed were 3, 0.75, 0.6, and 0.5 mg/g for pHs 1.5, 4, 7, and 9, respectively, for pH study. For concentration study, the amounts adsorbed were 0.15, 0.22, 0.33, and 0.58 mg/g for concentrations 25, 50, 75, and 100 mg/L, respectively. For time study, the amounts were 0.3, 0.4, 0.51, and 0.65 mg/g for reaction times 15, 30, 45, and 60 min, respectively.

**Conclusion:** The best adsorption circumstances of gliclazide drug on activated charcoal that were found; acidic pH, a high concentration of the drug and longtime of contact.

**Keywords:** Gliclazide, Activated charcoal, Adsorption, Elimination, Poisoning.

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### INTRODUCTION

Activated charcoal is a fine black odorless and tasteless powder, due to its high adsorptive capacity; it is used as an adsorbent for a large variety of compounds. It is used for removal of colors from solutions [1-3], in the adsorption of gases and vapors such as ammonia, carbon tetrachloride and methane [4], adsorption of nitrogen dioxide from combustion gases [5], and the adsorption of carbon dioxide and methane [6].

Activated charcoal is the most important adsorbent that is able to host many chemical compounds including drugs on its surface in relatively large amounts. This property encouraged scientists in the pharmaceutical field to use it as an antidote for a drug poisoning. It is used for flatulent treatment, and as a good treatment for reducing blood lipid concentrations in patients with uremia and diabetes [7]. It is also used for the adsorption of odors from wounds [8].

An adsorption study of the affinity of two different activated charcoal samples for paracetamol, and the effect of ethanol on the adsorptive properties of the charcoal showed that the use of 10% ethanol decrease the amount of the drug adsorbed on activated charcoal samples by an amount that might be clinically relevant in cases of intoxications by high-dose doses [9]. A 50 mg activated charcoal is able to adsorb 4802.692 mg from tramadol hydrochloride at the gastric condition and 8064.516 mg at the intestinal condition [10]. Activated charcoal has the ability to adsorb a sufficient amount of diazepam drug (200 mg/g-25 mg/g) with maximum adsorption at intestinal pH. The standard dose of 50 g of activated charcoal was found to be suitable to prevent diazepam intoxication with or without ethanol [11]. Activated charcoal found to be unable to prevent toxicity of some drugs such as acetaminophen, in the gastrointestinal if the administration was beyond 1 h after a drug overdose. The experiments conducted on fasting volunteers [12]. Super

activated charcoal of surface area 2000 m<sup>2</sup>/g was found to be beneficial for eliminating acetaminophen drug 3 h after overdose ingestion [13]. Increasing activated charcoal dosage and contact time enhance the removal of caffeine, acetaminophen, sulfamethoxazole, sulfamethazine, naproxen, diclofenac, 2, 4-D, triclocarban, and atrazine micropollutants from the water. The adsorption processes varied in dependence on pH from one drug to another. The decrease in adsorption removal was more significant for hydrophobic than hydrophilic compounds [14]. The adsorption of 2,4-dichlorophenoxyacetic acid (2,4-D) is influenced by the activated charcoal type, adsorbent concentration and solution characteristics. The adsorption process decreases with an increase in pH over the range 1.5-9. Maximum adsorption occurred at pH≈2.5 [15]. The existence of N-acetylcysteine turns down the ability of activated charcoal to adsorb acetaminophen. When salicylic acid was added to simulate a coingestants, N-acetylcysteine significantly decreased salicylate adsorption by activated charcoal [16]. The adsorption capability of activated charcoal measured in mg/g to adsorb 12 different drugs was: Aspirin, 262; glutethimide, 252; methaqualone, 179; chlordiazepoxide, 157; propoxyphene napsylate, 137; diazepam, 136; amitriptyline, 133; propoxyphene hydrochloride, 127; secobarbital, 124; pentobarbital, 103; phenobarbital, 70; and amobarbital, 51. They found that adsorption of the weak acids was most markedly decreased at pH 10.8 [17].

Many factors could affect the adsorption process on activated charcoal such as temperature, pore size, particle, and surface area of charcoal, the solubility of the poison, ionization state of the poison, pH, presence of inorganic salts, and gastric contents [18-20].

Single-dose activated charcoal treatment now becomes the most common method of gastrointestinal decontamination for the poisoned patient [18,19]. The method includes oral administration of a single-

dose activated charcoal or installation by a nasogastric tube of an aqueous mixture of the charcoal after the ingestion of a poison [21]. In general, if the time interval between drug ingestion and activated charcoal administration is increased, the ability of activated charcoal to reduce drug absorption decreases [22].

The aim of this study is to assess the ability of activated charcoal in adsorbing overdose of gliclazide drug from diabetic patients that may mistakenly ingest overdose from the drug and to study the effects of pH, concentration and time, in order to reach the best conditions for disposal of the drug in case of poisoning.

## METHODS

The activated charcoal used in the present study was obtained from Sigma-Aldrich after repeatedly washed with distilled water; the activated charcoal was dried to constant weight at 105°C for over 24 h. All chemicals used in this work were of analytical grade obtained from Sigma-Aldrich. The drug sample of gliclazide was obtained from Servier Company.

The electronic spectra were recorded on PG instruments T80 ultraviolet (UV)/VIS double beam spectrophotometer. The pH was monitored using a Philips (PW-9409) digital pH meter.

The wavelength at which maximum absorbance occurs ( $\lambda_{max}$ ) was recorded for the aqueous solutions of the drug and found to be 232 nm.

An exact weight of 50 mg of gliclazide was dissolved in 100 ml of methanol in a 500 ml volumetric flask, and the volume was adjusted up to the mark of the flask with distilled water to obtain a stock solution of 100 mg/L. The solution was filtered through Whatman filter paper No. 41.

The flask containing 50 ml of gliclazide solution (100 mg/L) and 1 g of activated charcoal was shaken at room temperature for 1 h and pH of 1.5, 4, 7, and 9 for pH dependence study. For the concentration dependence study, 50 ml of the drug solution of concentrations 25, 50, 75, and 100 mg/L were shaken with 1 g activated charcoal for 1 h. For time dependence study, 50 ml of drug solution (100 mg/L) were shaken with 1 g activated charcoal for 15, 30, 45, and 60 min. The mixtures were shaken vigorously at room temperature using magnetic stirrer after which filtered through filter paper, and the filtrate assayed spectrophotometrically in the ultraviolet region at  $\lambda=232$  for residual drug concentration. The process was repeated under different equilibrium conditions of pH, concentration, and time. The pH was adjusted using 0.1 N solution of HCl and NaOH.

The amount of the drug adsorbed was calculated spectrophotometrically using the equation:

$$Q_e = (C_o - C_e) V / m$$

Where  $Q_e$  is the maximum quantity of the drug in mg/g adsorbed on the activated charcoal,  $C_o$  is the initial concentration (mg/L) of the drug solution,  $C_e$  is the concentration of the drug (mg/L) in the supernatant at the equilibrium stage, V is the volume of the drug solution in liter, and m is the mass of adsorbent employed in grams.

The calibration curve was accomplished by measuring the absorbance of solutions for each experiment, thereafter plotting of absorbance versus PH, concentrations, and time.

## RESULTS AND DISCUSSIONS

Gliclazide belongs to the sulfonylurea class; it is an anti-diabetic medication used to treat diabetes mellitus. It is a white crystalline powder, relatively insoluble in water, sold under the brand name Diamicon. The chemical formula is  $C_{15}H_{21}N_3O_3S$ , and the chemical name is [1-(3-azabicyclo (3,3,0) oct- 3-yl)-3-p-tolylsulfonylurea] [23]. The chemical structure of the drug is shown in Fig. 1.

The drug exhibits slow gastrointestinal absorption rate and inter-individual variations of its bioavailability. Oral bioavailability of the drug is in the range of 79–81%. The half-life of the drug is about 10 h. The UV spectrum of the gliclazide solution is shown in Fig. 2.

The results of pH dependence study are presented in Table 1. The amount of the drug adsorbed increasing with decreasing pH. The mg/g values seem to be small. At pH 4, 7 and 9 the values are almost identical, but a noticeable jump is clear at pH 1.5.

Fig. 3 shows a plot of absorbance versus pH. The jump in the amount of the drug adsorbed at pH 1.5 is very clear.

An increase in adsorption was observed with an increase in the concentration of the drug as shown in Table 2. The maximum adsorption was attained at 100 mg/L. Here again, the amounts of gliclazide drug adsorbed are small.

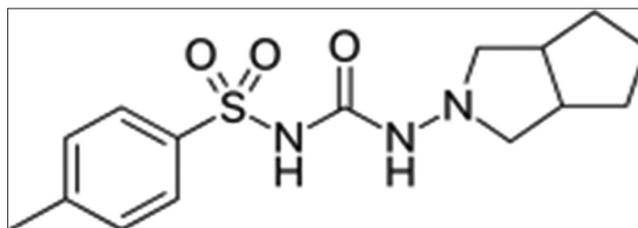


Fig. 1: The chemical structure of gliclazide

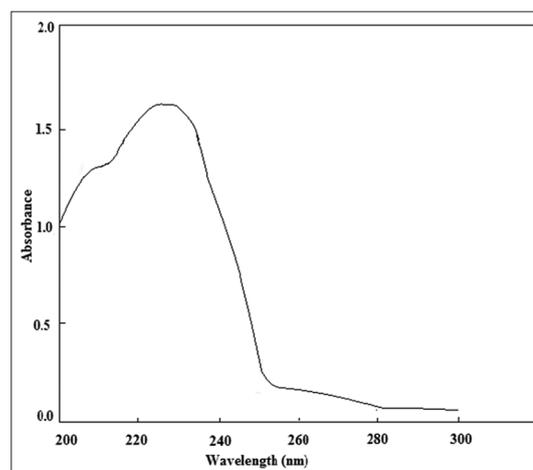


Fig. 2: The ultraviolet spectrum of gliclazide

Table 1: Parameters of pH dependence study

pH	Concentration of adsorbate mg/L	Gliclazide adsorbed mg/g
1.5	40	3
4	85	0.75
7	88	0.6
9	90	0.5

Table 2: Parameters of concentration dependence study

Concentration mg/L	Concentration of adsorbate mg/L	Gliclazide adsorbed mg/g
25	22	0.15
50	45.5	0.22
75	68.5	0.33
100	85.8	0.58

Table 3: Parameters of time dependence study

Time (min.)	Concentration of adsorbate mg/L	Gliclazide adsorbed mg/g
15	94	0.3
30	92	0.4
45	89.8	0.51
60	87	0.65

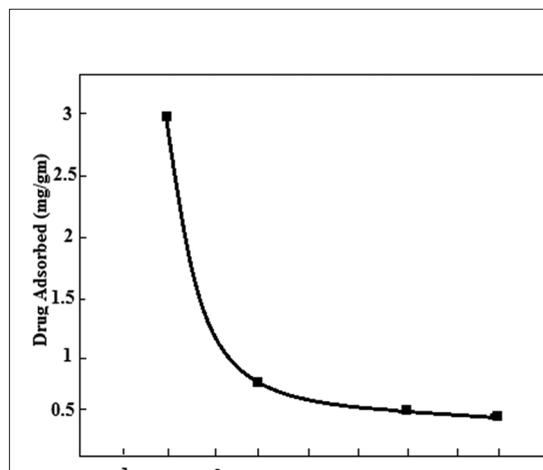


Fig 3: Plot of adsorbed drug (mg/g) versus pH for pH dependence study

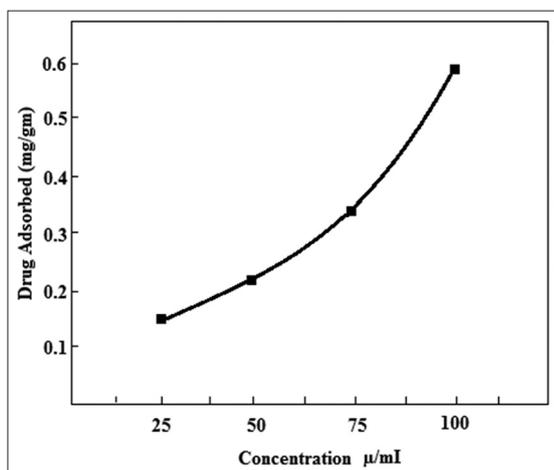


Fig. 4: Plot of adsorbed drug (mg/g) versus concentration for concentration dependence study

Fig. 4 is a plot of absorbance versus concentration for concentration dependence study.

Table 3 summarizes the parameters for time dependence study. It was found that the adsorption of the drug increases at the time of reaction increases. The relation between the time of reaction and absorbance is shown in Fig. 5.

It is obvious from the parameters in Tables 1-3 that the amounts of the gliclazide drug sample adsorbed on activated charcoal are low in all the experiment factors used (pH, concentration and time). That might be due to the poor solubility of the drug in water. Water is the only solution that has preferred ability to penetrate the pore structure of activated charcoal and many other adsorbents including clays. The bioavailability of a drug is an important factor that is connected with solubility. For any

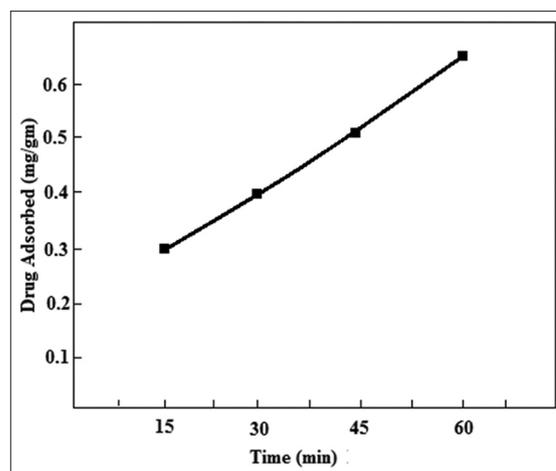


Fig. 5: Plot of adsorbed drug (mg/g) versus time for time dependence

drug to be absorbed in the gastrointestinal tract it must be dissolve first.

The enhancement of the solubility of insoluble or poorly soluble drugs in the water now become a major challenge for researchers [24]. Different techniques have been developed for this purpose, of which is the low-surfactant microemulsion gels [25], Liquisolid technique [26], and micronization through pH change [27].

The amounts of the gliclazide taken by the surface of activated charcoal increase with increase the time of contact and concentration of the drug and decrease the pH.

From the three factors studied it is of interest to note that the biggest amount of the drug adsorbed was 3 mg/g found at low pH (1.5). Although this amount is also small compared to the amounts of drugs adsorbed on activated charcoal that is mentioned in the literature, nevertheless it remains a good result. The 1.5 pH is similar to the pH of the gastric fluid which makes activated charcoal a good antidote for gliclazide poisoning since the gastric fluid is also acidic which enhance the elimination of the drug through adsorption on activated charcoal and help in gastrointestinal decontamination.

Multiple-dosage of activated charcoal in acidic pH can be suitable for elimination the gliclazide drug from the human body. Since the quantities adsorbed is small, the repeated dose is recommended.

## CONCLUSIONS

The adsorption of gliclazide drug on activated charcoal found to be very low at different pH, concentrations, and time. That might be due to the poor solubility of the drug in water. Water has preferred ability to penetrate the pore structure of activated charcoal. The greatest amount adsorbed was found at 1.5 pH which makes activated charcoal antidote of choice for elimination gliclazide drug since the pH of the gastric fluid is similar to this value. An increase in adsorption was observed with an increase in the drug solution concentration and contact time. An increase in the adsorption was also observed with decreasing the pH of the gliclazide drug solutions.

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**CONFLICT OF INTEREST**

The authors do not have any conflict of interest.

**AUTHORS CONTRIBUTIONS**

The idea of the research was suggested by Dr. Jasim H. Hassen, along with literature collection, manuscript writing, editing and data calculations. The materials preparation and laboratory experiments work were carried out by Abdalkareem H. Ayfan and Yasir M. Farhan with the participation of Dr. Jasim H. Hassen. Manuscript revision was done by Yasir M. Farhan.

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