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Original Research

A comparative study of the *in vitro* adsorption of some drugs on activated charcoal

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In vitro adsorption of an antimalarial (chloroquine phosphate), an anti asthmatic (aminophylline) and a vitamin (ascorbic acid) on activated charcoal were evaluated in this study. Some factors which influence adsorption of drugs on adsorbents such as pH and ionic strength were investigated. Desorption studies were also carried out. Results obtained indicated that all the three drugs interacted with activated charcoal to varying degrees. While adsorption of chloroquine phosphate on activated charcoal showed a type 1 adsorption isotherm, the interaction of aminophyline and ascorbic acid did not result in any of the established adsorption isotherms. The extent of adsorption of the three drugs on activated charcoal dependent on ionic strength, pH and the concentration of the adsorbent. Drug desorption studies showed that with the exception of ascorbic acid, all the drugs were desorped to some extent with the degree of absorption varying directly with pH.

Keywords: adsorption isotherm, chloroquine phosphate, ascorbic acid, aminophylline, ionic strength, desorption studies

Introduction

Drug adsorption is an important phenomenon in drug availability hence pharmaceutical dosing and practice in general. Adsorbents such as activated charcoal are widely applied in medicine as gastrointestinal detoxicant. In fact charcoal is used as adsorbent for a variety of drugs and chemicals taken by mouth.

The use of activated charcoal as antidote in poison management has been the subject of many publications (1 – 5) in recent years. Ginoza *et al* (6) have observed that the administration of high surface area activated charcoal significantly increased the clearance of theophylline in low birth infants. They further observed that total body clearance of the drug is nearly twice that demonstrated without charcoal. They concluded that activated charcoal might be useful in the treatment of theophylline toxicity. Recent evidence indicates that activated charcoal not only inhibits drug absorption from the gastro-intestinal tract (GIT) but also increases the clearance of drugs that have already been absorbed and are in the systemic circulation (2).

The absorptive capacity of adsorbents used in the management of drug poisoning could be affected by pH, ionic strength, temperature, GIT motility, secretions and the presence of other drugs or substances.

In this study, we have investigated the absorption of these commonly used drugs (chloroquine phosphate, aminophylline and ascorbic acid) on activated charcoal.

Experimental

Materials

The following drugs and chemical were used as procured from their manufacturers: Chloroquine phosphate (May & Baker, England), aminophylline, ascorbic acid, hydrochloric acid (Merck, Germany), Potassium chloride (BDH Chemicals, England). Buffer solutions and activated charcoal were obtained from our Faculty chemical and drug store.

Method

Activation of Adsorbent

The charcoal was activated by drying in the hot air oven (B & T Unitemp) at 120°C for 5 h. The activated powder was stored in an air-tight container for further experiments.

Determination of Adsorption Isotherm

The solution media for the drugs were 0.01 N HCl for ascorbic acid and 0.1 N HCl for aminophylline and chloroquine phosphate. The concentration of the stock solution for the three drugs was maintained at 1 mg/ml. Varying quantities of the adsorbent (50, 100, 150, 200 and 250 mg) were weighed into different 250 ml volumetric flasks. A 100 ml portion of the stock

solution of each drug was added into each flask. The contents of the flask were shaken on a mechanical shaker (Gallenkamp, England) for 30 mins. The flasks and their contents were incubated at 37 ± 1 °C for 24 h. Two blanks, containing the least weight of the adsorbent in a 100 ml of either 0.01 N HCl or 0.1 N HCl but containing no drug, and one containing the drug but no adsorbent were similarly treated. Samples were withdrawn from each flask, filtered through a non-adsorbent filter paper and analysed at the appropriate wavelength for maximum absorption (chloroquine phosphate 257 nm, ascorbic acid 243 nm and aminophylline 272 nm). Equilibrium concentrations "c" were obtained from Beer's plot previously constructed for each of the drug. The quantities of drug absorbed "x" by "m" grams of adsorbent were calculated by subtracting the equilibrium concentration values from the quantity of drug initially added. The adsorption isotherms were then constructed by plotting x/m values against equilibrium concentration "c".

Effect of Ionic Strength on Adsorption

Varying concentrations of potassium chloride solution (0.0050, 0.0075, 0.010 and 0.125 M) were prepared from a stock of one molar solution. A 25 ml portion of each solution was added to a 250 ml volumetric flask containing the drug solution in each case. Two blanks, one containing no potassium chloride but the drug and the other containing only a 100 ml solution of 0.0050 M potassium chloride was similarly prepared. All the flasks contained the same weight of the adsorbent and were shaken on a mechanical shaker for 30 min, after which they were incubated for 24 h at 37 ± 1 °C. Samples were withdrawn and filtered and the content of the filtrates were analysed spectrophotometrically, at the wavelength of maximum absorption stated above.

Effect of pH on absorption

Buffer solutions of pH range 2 – 6 were prepared according to BP (1980) specifications. Activated charcoal (300 mg) was added to each of the five volumetric flasks containing 30 ml of the pH solutions. The volumes were made up to 100 ml using the drug solution. A sixth flask serving as the blank contained no buffer solution. The flasks were shaken on a mechanical shake for 30 min and incubated at 37 ± 1 °C for 24 h. Samples were withdrawn, filtered and analysed spectrophotometrically. Two replicate determinations were made in each case.

Desorption studies

Desorption studies were carried out through variation in pH. Buffer solutions of pH range 2 – 6 were employed. Normal adsorption studies were initially carried out for each drug using 100 ml of stock solution of each drug in the presence of 300 mg of activated charcoal. Each content of the flask was filtered and the filtrate analysed spectrophotometrically. In each case, a 100 ml portion of a buffer solution of known pH was used to wash the adsorbent complex from the filter paper into the flasks. The flasks and their contents were shaken on a mechanical shaker, filtered and analysed spectrophotometrically to determine the quantity of drug desorped. This procedure was repeated for the different buffer solutions.

RESULTS AND DISCUSSION

The interaction of the drugs with activated charcoal is shown in Figure 1. The interaction of the drugs differed markedly. There was a gradual increase in the quantity of ascorbic acid that interacted with the absorbent as the concentration of the adsorbent was increased from 50 to 250 mg. The quantity of aminophylline interacting with the adsorbents decreased as the adsorbent was increased from 50 to 150 mg, but increased at 200 to 250 mg. The interaction with chloroquine phosphate did not follow any pattern with a sharp decrease occurring at 100 and 200 mg adsorbent concentrations. The adsorption of chloroquine phosphate on activated charcoal followed the type I adsorption isotherm (Fig. 2), while the interactions between activated charcoal and aminophylline and ascorbic acid did not yield any isotherm of the established types, hence may be indicative of another mechanism other than adsorption. Type I isotherms indicate monolayer formation and probably chemisorptions resulting in a chemical interaction, which is irreversible.

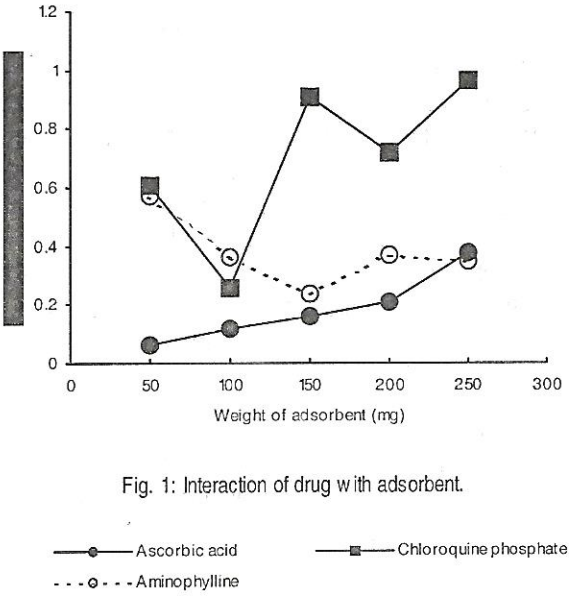


Fig. 1: Interaction of drug with adsorbent.

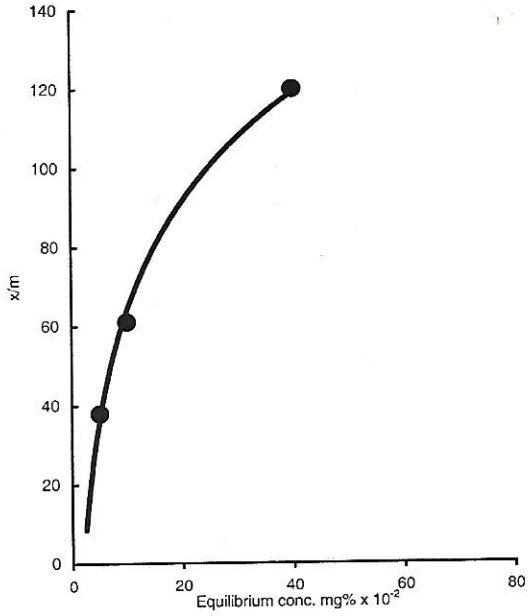


Fig. 2: Adsorption isotherm of chloroquine on activated charcoal.

The effect of pH on the adsorption of the drugs on activated charcoal is presented on Figure 3. The three drugs showed decrease in adsorption as pH was increased with minimum adsorption occurring at pH 3 for chloroquine phosphate, pH 4 and 6 for ascorbic acid and aminophylline. Aminophylline and ascorbic acid exhibited maximum adsorption at pH 2 and 5 while chloroquine showed maximum adsorption at pH 2 and 4 – 6. pH influences adsorption by changing solubility and extent of ionization. Particularly it has a marked effect on the adsorption properties of charcoal because it changes the charge distribution on the surface of the adsorbent. For simple molecules, adsorption increases as ionization of the drug is suppressed. An equation relating solubility, pKa and pH is given by

$$S_T = K_s \frac{(1 + K_a)}{H^+} \ldots \ldots \ldots (1)$$

This equation has been modified to give

$$[H^+] = \frac{K_s K_a}{S_T - K_s} \ldots \ldots \ldots (2)$$

Where S_T represents solubility of the drug, K_a dissociation constant of the drug, K_s solubility constant. The equation shows that as hydrogen ion concentration increases, pH decreases and the solubility of the drug decreases. Hydrogen ion concentration and solubility effects are similar since the unionized form of most drugs has low solubility in aqueous solution (3). As the pH increased from 2 to 6, the hydrogen ion concentration decresed and therefore a large quantity of ionized forms of the drugs in solution is expected. These ionized forms cause increase in solubility of adsorbate play a significant role in the adsorption of these drugs on activated charcoal. Weak acids and bases are better adsorbed on activated charcoal when they are in non-ionized from (4). The three drugs – chloroquine phosphate (weakly basic), aminophylline (weakly basic) and ascorbic acid (slightly acidic) have these characteristics with respect to their pKa and solubility. This accounts for variation in the extent of their adsorption with variation in pH.

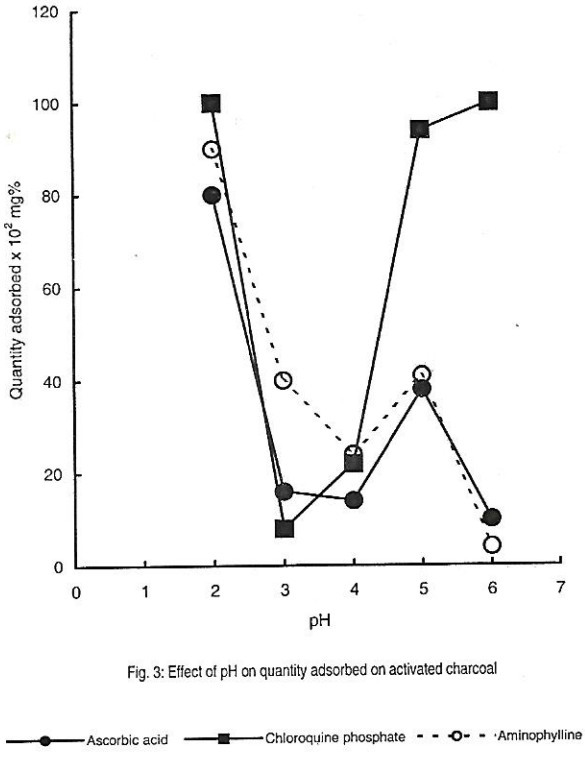


Fig. 3: Effect of pH on quantity adsorbed on activated charcoal

Increase in the concentration of potassium chloride led to decrease in adsorption of chloroquine phosphate and aminophylline on activated charcoal, while increased adsorption occurred with ascorbic acid (Fig. 4). Ionic strength has marked effect on the extent of adsorption of drugs as it affects pH, ionization and the solubility of drugs. It has been shown that ionic strength also alters the surface charges on the adsorbent and the dielectric constant of the suspension (5). Charcoal consists of hexagonal rings of carbon atoms joined together to form very small crystals. During destructive distillation of coal which gives rise to charcoal, many of the carbon hexagons inevitably left broken at the surface and are used in binding adsorbates (6). In systems containing chloroquine phosphate or anionic materials such as chloride ion, there is competition for the available sites on adsorbents.

This competition is between the ionic portion of the drug and chloride ions. Ordinarily, considering the fact that activated charcoal has affinity for anions, the anionic portion of the drug could get adsorbed thereby increasing adsorption. However there is the cationic portion of the drug to contend with and the fact that there is increase in quantity of electrolyte present which will increase the quantity of chloride ion present and favour its adsorption onto the adsorbent in preference to the drug. This will reduce the likelihood of vacant sites on the surface of the adsorbent, and consequently decrease the adsorption of these drugs. Ginoza *et al* (6) observed that the mechanism of adsorption process of theophylline on charcoal involves the chemical bonding of the drug to the walls of the pores of each charcoal particle. This results in limitation of adsorption to the number of these pores or internal surface area. From these results obtained, it is suggested that increase in ionic strength represented by increase in quantity of potassium chloride decreases quantity of drug adsorbed by the adsorbent. This could result from the chloride ion getting adsorbed by charcoal, which has affinity for anions, thereby filling up pores of the charcoal. This could then reduce the internal surface area and subsequently decrease adsorption. Another possible mechanism may be at work. The electrostatic binding of the drug to the anionic site on the charcoal may be inhibited by increasing ionic strength due to the restriction of the electric double layer around the cationic and/or anionic center.

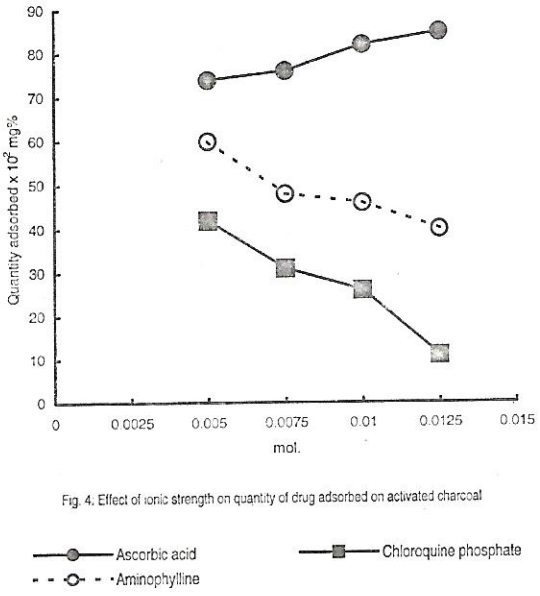
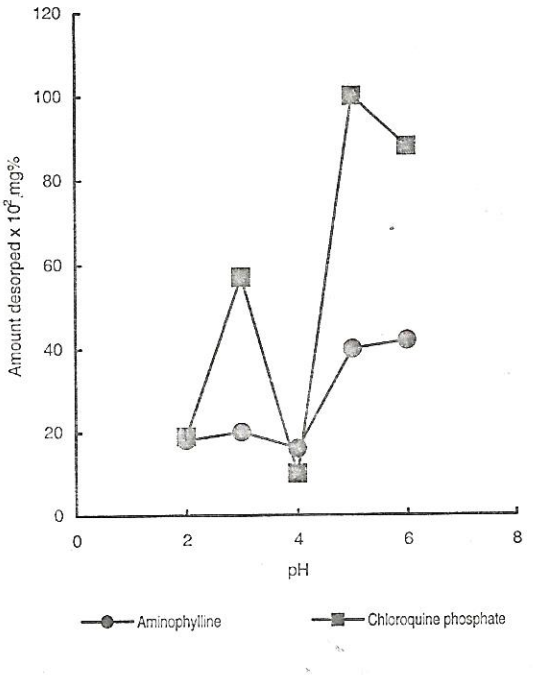


Fig. 4. Effect of ionic strength on quantity of drug adsorbed on activated charcoal

The increase in adsorptive capacity of activated charcoal for ascorbic acid as the ionic strength was increased tends to contradict the fact that simple ion-exchange is a major mechanism of adsorption. The failure of the electrolyte to depress adsorption in this case might suggest that adsorption of ascorbic acid by activated charcoal *in vitro* is mediated other than through ion-exchange mechanism. Even in considerably large quantity, the electrolyte could not displace the drug from the adsorptive sites. Even though the process involved here is not fully understood, Sorby *et al* (7) have suggested that increase in adsorption by sodium chloride may be due to the effect of various physical properties of the solute. This is said to increase the tendency of the solute to accumulate at the solution-solute interface. Potassium chloride or any other electrolyte may be exerting its action on the solubility of the drug or on other physical properties of the drug and those of the adsorbent too.

The results obtained in desorption studies are presented in Figure 5. Adsorbed drugs may be eluted from the adsorbent by a change in one or more factors that affect adsorption in solution. For aminophylline there was increase in the quantities desorbed with increase in pH. Aminophylline (theophylline ethyldiamine) is adsorbed on charcoal by chemical interaction which involves ion-exchange mechanisms. It is expected that there should be low level of desorption when compared to the level of adsorption. This is in agreement with the general concept that the more strongly adsorbed a drug is the less it is easily desorped.



Davies (8) reported that elution generally occurs better in solution from which little adsorption occurs. The results obtained in this study for aminophylline

are therefore expected. These indicate that as adsorbent-adsorbate complex of aminophylline and adsorbent get into GIT compartments of higher pH, the drug is more likely to be desorbed. Similar results were obtained for chloroquine, except that the magnitude of desorption was more. Adsorption of chloroquine phosphate by activated charcoal is known to be by chemical interaction, and thus with increase in pH, it is expected that there should be increase in amount of drug desorbed. Ascorbic acid showed no significant desorption after repeated treatment.

Conclusion

The results obtained in this study are consistent with suggestion of many workers on the use of activated charcoal in the treatment of drug over-dose.

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