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ADSORPTION CHARACTERISTICS OF NORFLOXACIN TO PHARMACEUTICAL ADDITIVES

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ABSTRACT

Norfloxacin is a very potent drug, adsorption of even a few milligrams of this drug may account for a significant fraction of total dose, hence, adsorption effect might be of great significance. The results of in vitro adsorption studies of norfloxacin to different pharmaceutical additives are plotted on the basis of Langmuir Equation. The linear nature of the adsorption isotherms shows that the adsorption process is due to monomolecular layer. Adsorption constants were calculated to determine the binding capacity of this drug to various additives. The adsorbents with their decreasing binding capacity are as follows:

Activated charcoal (33.0×10^{-3}) > Bentonite (17.0×10^{-3}) > Kaolin (9.5×10^{-3}) > Methyl cellulose (8.6×10^{-3}) > Potato starch (7.4×10^{-3}) > Talc (6.0×10^{-3})

The mechanism of adsorption has been discussed in light of physical characteristics of the adsorbents.

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INTRODUCTION

Norfloxacin (MK-0366, AM 715) has a very broad spectrum of antibacterial activity against gram-positive and gram-negative, primarily aerobic pathogens (1). The antibacterial potency of norfloxacin exceeds that of every known compound of this type presently available or under investigation. In addition, the compound was shown to be more potent *in vitro* than amoxicillin, carbenicillin, cefaclor, erythromycin, penicillin G, tetracycline, trimethoprim and clotrimoxazole when tested against fresh clinical isolates of the family *Enterobacteriaceae*, *Staphylococcus aureus*, *Pseudomonas aeroginosa*, *Acinetobactor sp.*, *Neisseria gonorrhoeae*, and *Hemophilus influenzae* (2,3). Little information is available concerning the adsorption interactions of this drug to different pharmaceutical adsorbents.

The objectives of the prsent study were to determine if any adsorption interaction occurs with some commonly employed pharmaceutical ingredients including talc, kaolin, potato starch, bentonite, methyl cellulose and activated charcoal with norfloxacin.

MATERIALS

Norfloxacin (Merck Sharp and Dohme, New Jersey), activated charcoal, talc, kaolin, potato starch, bentonite and methyl cellulose were used as received. All other reagents and chemicals were used without further purification.

METHODS

The adsorbents used *viz.* activated charcoal, potato starch, talc, bentonite and kaolin were washed repeatedly with distilled water followed by analytical grade methanol until the washed solution exhibited no absorbance at 270 nm (the wavelength of maximum norfloxacin absorption). The adsorbents were passed

through a 20-mesh sieve while still moist and permitted to dry in an oven at approximately 45°C. The dried materials were then passed through a 100-mesh sieve to ensure that the particle size of all the adsorbents were 100 mesh or smaller.

In order to make an intimate contact between solid liquid interfaces for the measurement of the uptake, various experimental arrangements have been generally employed by a number of scientists (4-6). The simplest experimental set up is of shaking a definite weight of adsorbent with a solution of known concentration for an appropriate length of time to obtain adsorption equilibrium.

Fifty mg of activated charcoal and 1 g of other adsorbents were weighed accurately and transferred to 200 ml glass-stoppered bottles. Standard solutions of norfloxacin in concentrations of 0.2, 0.3, 0.4, --- 1 mg/ml, in water (pH 5.5), were prepared. One hundred ml of each concentration was added to each bottle. The bottles were placed in a mechanical shaker and shaken for 10 hr at room temperature, then left for 24 hr at 5°C. Each experiment was performed in triplicate. It was found by preinvestigative experiments that equilibrium was attained within the above mentioned period. The solutions were then centrifuged for 15 minutes. Four ml of supernatent liquid was put into separating funnel and extracted three times with chloroform (5+3+3 ml). The combined chloroform extract was evaporated at room temperature. The dried material was dissolved in distilled water and determined by spectrophotometer at 270 nm. The quantities of norfloxacin adsorbed by adsorbents were determined by subtracting the equilibrium concentration from the initial concentration. For every set of experiments a control bottle was prepared which differed from the other bottles in that it contained no adsorbent. Drug concentrations in each control bottle remained constant. This indicates that no degradation of norfloxacin occured at the conditions employed in the present study.

RESULTS

The results of *in vitro* adsorption studies of norfloxacin to different pharmaceutical additives are interpreted and discussed on the basis of Langmuir Equation (9).

$$\frac{C}{Y} = \frac{C}{K_2} + \frac{1}{K_1 K_2} \quad (1)$$

where C is the concentration of free drug in the solution at equilibrium (mg/100 ml). Y is amount of solute per mg adsorbent, K_2 is the maximal adsorbing capacity and K_1 is the constant called 'the adsorption coefficient'. It indicates the affinity of the drug to the adsorbent used. The applicability of the Langmuir equation to the isotherms can be indicated by the linear curves obtained on plotting C/Y against C.

The Langmuir adsorption isotherms of norfloxacin to different adsorbents in aqueous medium are shown in Fig.1. The K_2 values, for different systems have been calculated from the slopes of the isotherms and K_1 values computed accordingly. The values of these constants are presented in table 1.

Linear adsorption isotherms are obtained on plotting C/Y versus C as shown in fig.1 which denotes monomolecular adsorption pattern. The adsorption of norfloxacin to different adsorbates may be correlated with the adsorption constants as they are related to the forces involved in the binding process.

Findings of Table 1 indicate that activated charcoal in water is having highest adsorption coefficient and retained the largest amount of norfloxacin (33.0×10^{-3} mg/g). The other adsorbents with their decreasing binding capacity are as follows: Bentonite (17.0×10^{-3}) > Kaolin (9.5×10^{-3}) > Methyl cellulose (8.6×10^{-3}) > Potato starch (7.4×10^{-3}) > Talc (6.0×10^{-3})

Fig.2 and 3 reveal that the adsorption of norfloxacin to various adsorbents increases with increase in the drug concen-

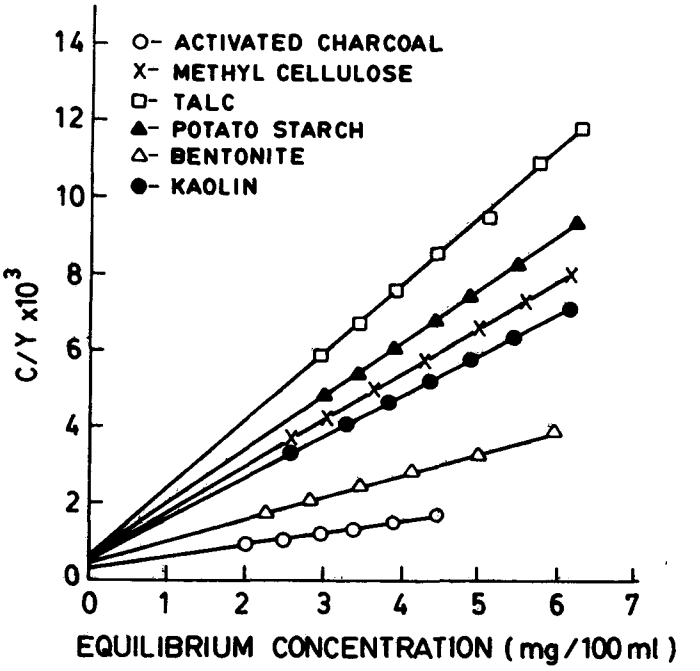

FIGURE -1

Linear Form of the Adsorption Isotherms for Norfloxacin.

TABLE 1

Langmuir Constants for Norfloxacin at 37°C

S.No.	Adsorbent	$K_2 x10^4$	$K_1K_2 x10^4$	K_1
1.	Activated charcoal	32.544	7.143	0.2222
2.	Bentonite	17.027	2.985	0.1753
3.	Kaolin	9.538	1.538	0.1608
4.	Methyl cellulose	8.649	1.370	0.1584
5.	Potato starch	7.428	1.163	0.1565
6.	Talc	6.032	0.893	0.1480

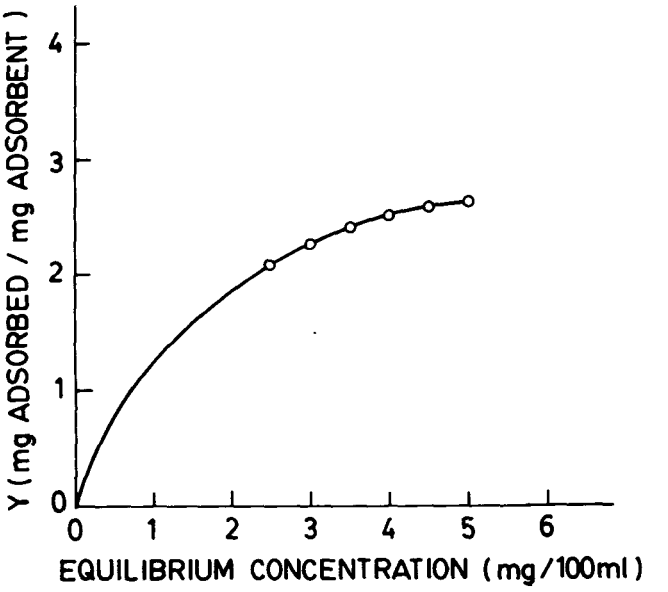

FIGURE-2

Adsorption Isotherms for Norfloxacin by Activated Charcoal.

tration until it reaches a plateu where no further increase in the adsorption of norfloxacin is being noticed.

DISCUSSION

The clays have been used in pharmaceuticals for both therapeutic effects and excipient action. The structure of clays plays important role in predicting their behaviour in pharmaceutical systems (10). The Kaolin group of minerals consists of sheets of silica tetrahedra and alumina octahedra shared in a 1:1 ratio. These minerals have little or no isomorphous substitution, further they do not swell in aqueous solutions. Since Kaolin is a nonexpanding type material, the edge surface

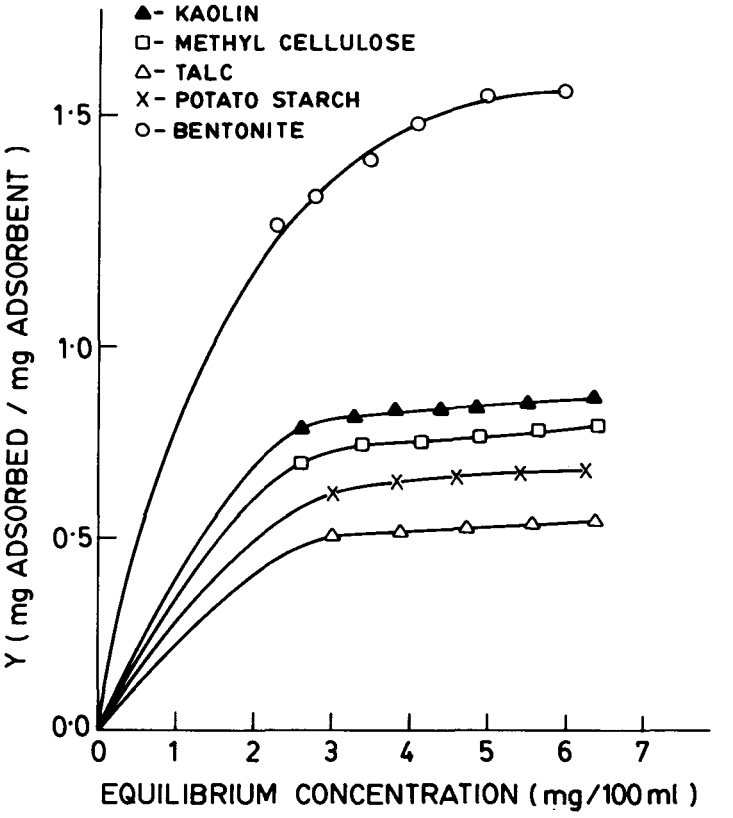

FIGURE-3

Adsorption Isotherms for Norfloxacin by other Adsorbents .

comprises a substantial portion (10-20%) of the total surface area. The broken bond of tetrahedral sheet at the edges normally give rise to a small permanent positive charge, which may be responsible for the adsorption of norfloxacin.

As adsorption mainly depends on the physical state and chemical nature of the adsorbent. In clays, it depends upon their residual valencies due to edges, corners, and cracks pre-

sent on their surface. These surface defects are responsible for enhanced adsorption. The pretreatment of the surface like etching, grinding, and washing also affect the adsorption. The higher surface area and exchange capacity of bentonite is probably responsible for enhanced adsorption of norfloxacin than kaolin since above properties are related directly to clay adsorption mechanism. The present investigation revealed that adsorption of norfloxacin to bentonite and kaolin followed Langmuir type of adsorption isotherms. The mechanism of adsorption may be by their cation exchange capacities and adsorption of unionised molecules in the interlamellar spaces of the adsorbents.

Talc is a nonadsorbent type of material made up of hydrous magnesium silicate. Some times containing a small portion of aluminium silicate. Its binding capacity for norfloxacin may be due to weak van der Waals forces. In the adsorbents under study, it adsorbed least quantity of the drug. Hence, it can be presumed that the use of talc in the formulation of norfloxacin will not affect its bioavailability.

The adsorption of different drugs onto activated charcoal in vitro has been studied by several scientists (5,11-15). The reason for its maximum adsorption capacity is its availability in a fine state of subdivision. Among the adsorbents studied it was observed that charcoal had highest adsorptive capacity even when used in small quantity. Thus, it can be administered in overdosing cases due to its high binding capacity for norfloxacin.

The adsorption of norfloxacin on methyl cellulose may be due to ionization of carboxyl groups on cellulose surface. These carboxyl groups are supposed to be formed by oxidation of hydroxy groups on individual anhydroglucose units (16). The pK_a of these carboxyl groups was found to be about 4. At the pH of study, the number of negatively charged carboxylate groups on the sur-

face of the cellulose particles will be significant. The increased number of anionic surface sites may have lead to increased adsorption of the positively charged drug (due to quaternary nitrogen) at the surface of the particles.

The adsorption of norfloxacin on to potato starch followed Langmuir Adsorption Isotherms. The binding capacity for potato starch was found to be 7.4×10^{-3}. The adsorption in this case may be due to penetration and diffusion of the drug solution into the starch grains. The structure and porosity of the starch grains are important factors to be considered in the study of adsorption, as external and internal surfaces of the grains participate when adsorption is taking place in solution. Thus the actual area available for adsorption will be much greater than the outer grain surface. The increased adsorption value of norfloxation to potato starch is in close agreement with the observations of Thakkar et al. (17).

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