International Journal of Pharmaceutics, 53 (1989) 175–179
Elsevier

IJP 01807

In vitro adsorption of mepyramine maleate onto some adsorbents and antacids

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(Received 19 December 1988)
(Accepted 29 January 1989)

Key words: Adsorption; Antacid; Adsorbent; Mepyramine maleate; Cetrimide

Summary

The adsorption of mepyramine maleate on bentonite, charcoal, magnesium oxide, magnesium carbonate, magnesium trisilicate, bismuth carbonate and kaolin, was investigated. Maximum adsorption was found with charcoal followed by bentonite while kaolin and bismuth carbonate showed minimum adsorption. The results also showed that as the weight of the adsorbent increases the amount of drug adsorbed per gram decreased. Behaviour of charcoal and bismuth carbonate followed Langmuir and Freundlich isotherms. The present study also revealed that firstly, it is contraindicated to coadministrate mepyramine maleate with the tested adsorbents and antacids; secondly, cetrimide can be added to formulated antidotes for improving their adsorption efficiency.

Introduction

Adsorption onto finely divided solids, like charcoal, has been utilized beneficially for a long time to remove bacterial toxins and for treatment of intoxication by drugs or chemicals (Oppenheim and Miles, 1981). However, the uptake of many therapeutic agents by such solid particles could result in appreciable loss of their therapeutic value. Some reports have pointed out the adsorption of many drugs by antacids and mineral clays (e.g. Gokhale and Bhalla, 1981; Thoma and Lieb, 1985). Therefore, coadministration of drugs with these adsorbents by patients or during mixing of these particles with drugs during manufacture, must be studied to assure adequate drug availability.

Some creams contain hydrogel bases, like bentonite, so when some drugs are formulated with such bases, adsorption of drugs may have occurred before it has been used. So in the present study the in vitro adsorption of the antihistamine mepyramine maleate onto some antacids and adsorbents was investigated.

Furthermore, effects of weight of studied adsorbents, and different concentrations of cetrimide, on the extent of mepyramine maleate adsorption have also been studied.

Materials and Methods

Materials

Mepyramine maleate (MM) [1], bentonite [2], kaolin [3], bismuth carbonate (BC) [4], light magnesium

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[1] Hassco Trading House, Belgium.
[2] Hopkin and Williams, Essex, U.K.
[3] E. Merck, Darmstadt, F.R.G.
[4] Rhone-Poulenc, Paris, France.

carbonate (MC) [5], light magnesium oxide (MO) [5], magnesium trisilicate (MTS) [5], charcoal [6] and cetrimide [7].

Adsorption experiments

Volumes of 20 ml containing increasing initial concentrations of MM in distilled water (50–450 mg/100 ml) were prepared in tightly closed conical flasks. In each experiment 0.5 g from each adsorbent under investigation was added to the MM solutions of various concentrations. The suspensions were shaken horizontally in a thermostatically controlled water bath at 37 °C for 2 h. The time of maximum adsorption was predetermined till no further adsorption (after 30 min). Subsequently, flasks were set aside for a further 4 h, to attain equilibrium and then filtered. Aliquots from the filtrate were taken for determination of the amounts of free drug spectrophotometrically [8] at 230 nm.

The experiments were run in duplicate. The results obtained were appropriately treated to construct the adsorption isotherms and Langmuir and Freundlich plots.

Effect of weight of adsorbents

Charcoal MC, MTS and bentonite (0.5–1.5 g) were used in these experiments. The conditions of these experiments were the same as described above (*Adsorption experiments*) except that a constant initial concentration (200 mg/100 ml) of MM was added to the variable weights of each adsorbent.

Influence of surfactant on adsorption

Ascending concentrations of cetrimide (1–15 mg/100 ml) were equilibrated with either BC or MTS with a constant concentration of MM solution (200 mg/100 ml). The rest of procedures were run as adsorption experiments.

[5] Kyowa Chemical Industries Co. Ltd., Tokyo, Japan.
[6] Prolabo, France.
[7] Danochemo, Copenhagen, Denmark.
[8] Unicam Spectrophotometer SP 1500, U.K.

Results and Discussion

Adsorption isotherms

Amounts of MM in mg per gram adsorbent (x/m), were calculated for each adsorbent and plotted against the respective equilibrium concentrations (C_e). Different types of adsorption isotherms were obtained. Figs. 1 and 2 show adsorption of MM onto charcoal and BC. It can be seen that the adsorptions of both are type I isotherms whereas kaolin, MTS, MC and MO are of type III, but the adsorption of bentonite exhibited type V isotherms (Fig. 3), (Martin et al., 1983).

The values of (x/m) and (C_e) were subsequently treated to construct the Langmuir and Freundlich plots according to Eqns. 1 and 2, respectively:

$$\frac{C_e}{x/m} = \frac{1}{k_1 k_2} + \frac{C_e}{k_2} \quad (1)$$

$$\log(x/m) = \log K + P \log C_e \quad (2)$$

where k_1, k_2, K and P are constants characteristic for each pair of adsorbent and adsorbate. Only

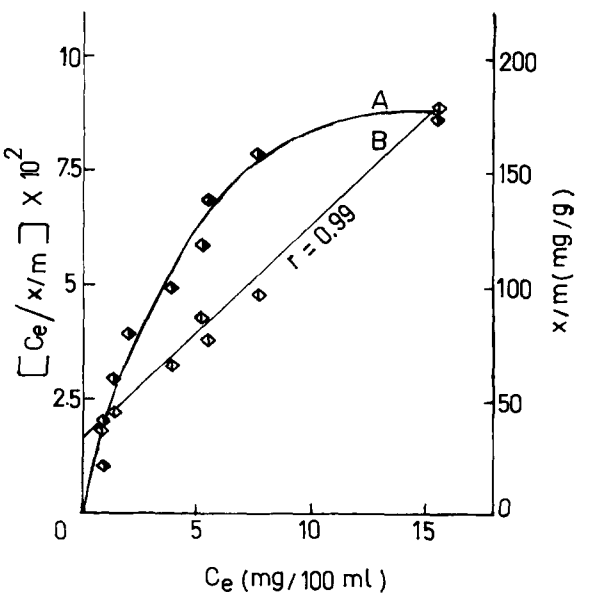

Fig. 1. Adsorption of mepyramine maleate on charcoal. A: adsorption isotherm. B: Langmuir plot, $y = 0.017 + 0.0046\,x$.

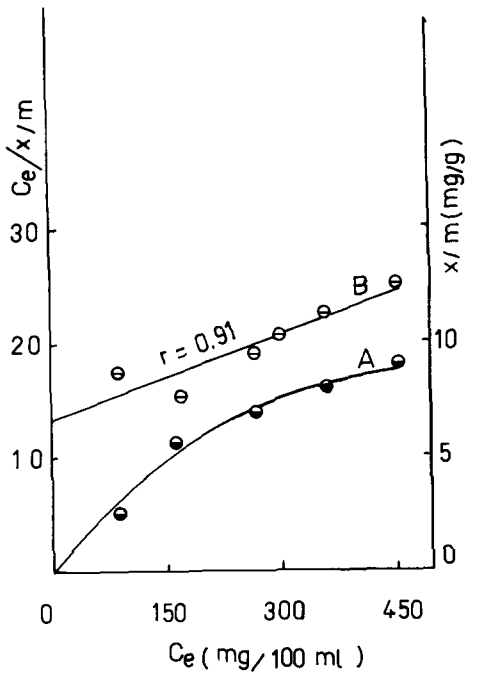

Fig. 2. Adsorption of mepyramine maleate on bismuth carbonate. A: adsorption isotherm. B: Langmuir plot, $y = 13.36 + 0.024\ x$.

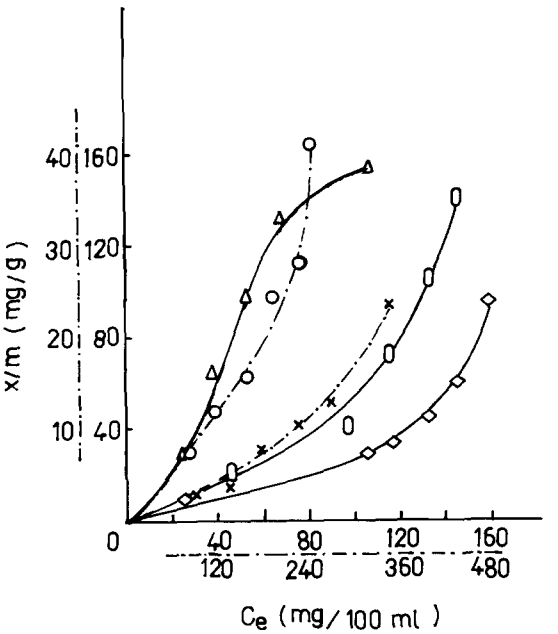

Fig. 3. Adsorption isotherms for mepyramine maleate onto different adsorbents, (△), Bentonite; (○), magnesium trisilicate; (×), kaolin; (0), magnesium oxide; (◇), magnesium carbonate.

the results of charcoal and BC fitted both equations. The regression lines for BC and charcoal are presented in Figs. 1 and 2. These results are in agreement with the statement that Eqns. 1 and 2 are adequate for the description of type I isotherms only (Martin et al., 1983). It is well documented that the application of these two equations give a better quantitative evaluation of the adsorption process. We therefore applied these equations to our results. Table 1 shows the calculated specific adsorption parameters, where k_2 describes the maximum amount of MM which could be adsorbed by 1 g of adsorbent and form a monolayer; K_1 represents the force of interaction between the MM molecules and binding sites. It may be concluded from Table 1 that the adsorption capacity of charcoal as well as the force of interaction with MM are more profound and strong, since k_1 and k_2 have higher values for charcoal in comparison with BC under the same experimental conditions.

With respect to the Freundlich constant, K, (amount of adsorption at unit conc.), it is obvious from Table 1 that the amount of MM adsorbed on charcoal was larger than the corresponding value of BC. Regarding the constant P, (the factor by which adsorption is increased as C_e is raised by one order of magnitude), Table 1 and Fig. 4 show that with decreasing concentration of MM (C_e), the adsorption of it became ever more efficient on charcoal, since the P-value recorded for adsorption on charcoal is smaller than that of BC (Table 1). This was in the agreement with some of the results obtained by Gessner and Hasan (1987) on

TABLE 1

Langmuir and Freundlich parameters for adsorption of mepyramine maleate on charcoal and BC

Adsorbent	Langmuir constants		Freundlich constants	
	k_2	k_1	K	P
Charcoal	216.0	0.28	56.2	0.454
Bismuth carbonate	40.9	0.0018	0.186	0.761

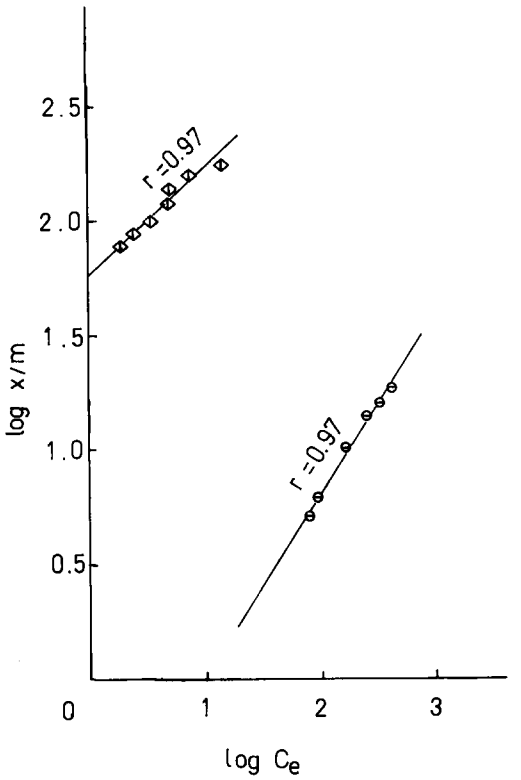

Fig. 4. Freundlich isotherms for the adsorption of mepyramine maleate on (◇), bismuth carbonate, $y = -0.73 + 0.76\ x$; (○), charcoal, $y = 1.75 + 0.45$ x.

adsorption of some drugs onto charcoal. Furthermore, to allow better comparison between all tested adsorbents and antacids, the values of (x/m) for each adsorbent at the following initial concentrations, 200, 300 and 400 mg MM/100 ml for each adsorbent were calculated and are presented in Table 2. The decrease in (x/m) values determined at the three conc. levels used could be arranged in the following sequence, charcoal > bentonite > MO > MC > MTS > BC > kaolin. It can also be seen from Table 2 that the calculated mean of MM loss (%) due to adsorption at the above mentioned concentration, the minimum loss was in the case of kaolin and BC (10%), whereas the maximum (98%) was detected with charcoal.

According to the results obtained in the present study, it is obvious that the mixing of MM with one or more of the studied adsorbents during preparation of pharmaceuticals or during coadministration of these materials with MM or similar drugs, could dramatically decrease their bioavailability. On the other hand, charcoal appeared to be a superior agent for use in the treatment of MM intoxication.

TABLE 2

Amount of meypyramine maleate adsorbed (x/m, in mg/g)

Adsorbent	Initial Conc. of MM (mg/100 ml)		
	200	300	400
Charcoal	79.2	118.0	157.0
Bentonite	64.7	98.6	132.9
MO	41.4	73.8	107.2
MC	32.2	61.6	96.8
MTS	16.3	28.4	49.1
BC	11.2	13.9	16.1
Kaolin	8.7	13.1	23.4

Effect of adsorbent weight

An initial constant concentration of MM (200 mg/100 ml) was used during the effect of adsorbent weight. Fig. 5 depicts the effect of varia-

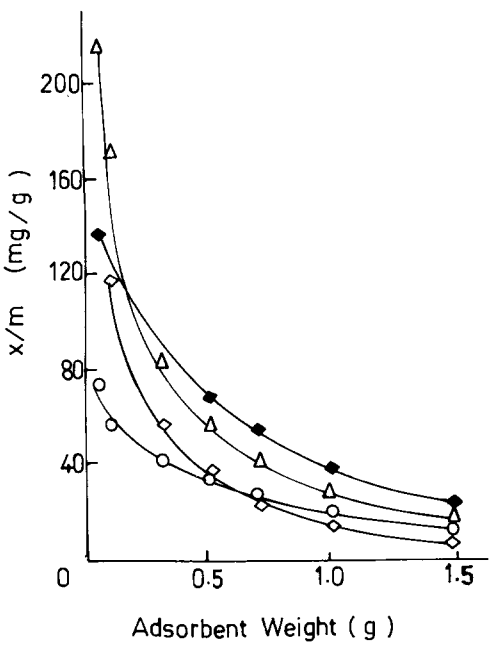

Fig. 5. The relationship between adsorbent weight and adsorption of mepyramine maleate. (△), Bentonite; (◆), charcoal; (○), magnesium trisilicate; (◇) magnesium carbonate.

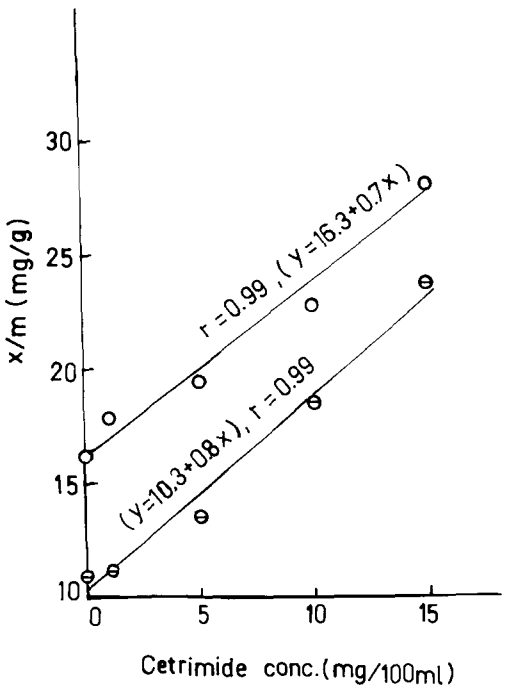

Fig. 6. Relationship between cetrimide and adsorption of mepyramine maleate. (○), Magnesium trisilicate; (⊖), bismuth carbonate.

tion in (x/m) values with amounts of each adsorbent. The values of (x/m) decreased sharply by increasing the weight of adsorbent in the lower range (0.05–0.5 g). This stage was followed by a moderate drop in (x/m) values at the higher weight range (0.5–1 g). So it is clear that even a small amount of adsorbent (< 0.5 g) affected the adsorption of MM.

Influence of cetrimide on adsorption

The effect of addition of increasing amounts of cetrimide to the MM solution (200 mg/100 ml) before adsorption onto BC and MTS is illustrated in Fig. 6. The relationship between (x/m) values and cetrimide concentration is linear, i.e., increased cetrimide concentration leads to an increase in (x/m) values. This could be explained by improved wettability of the adsorbents due to the presence of such concentrations of cetrimide. Higher surfactant concentration, above its CMC, might cause a decrease in drug availability due to micellar entrapment rather than adsorption onto adsorbents. Therefore, it is advantageous to include a low concentration of cetrimide in various formulations for treatment of drug intoxication. In addition it would be advisable not to incorporate MM with MO and/or bentonite in the formulation of topical antihistaminic preparations, specially in the presence of cetrimide, to avoid appreciable loss of drug through adsorption.

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