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Preliminary investigations into the in-vitro interaction of folic acid with magnesium trisilicate and edible clay

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Summary

The in vitro interaction between folic acid and magnesium trisilicate as well as edible clay was studied. Folic acid was significantly adsorbed onto the absorbents from both water and 0.01 M HCl at 37 °C. The adsorption of the drug onto magnesium trisilicate from distilled water obeyed the Langmuir relationship while that from 0.01 M HCl was biphasic. The adsorption of folic acid onto the clay was affected by the inclusion of sodium chloride (NaCl) and followed the rank order: edible clay + 7.5% w/w NaCl > edible clay + 5.0% w/w NaCl > edible clay + 10.0% w/w NaCl > unsalted edible clay. Complete desorption of folic acid from the adsorbents by digestion in water, 0.01 M HCl or 0.1 M HCl was not achieved. This is an indication that adsorption was facilitated by the presence of strong chemical bonds. Dissolution of folic acid from tablets in the presence of the adsorbents was retarded due to the adsorption of the drug onto the adsorbents.

Introduction

Folic acid is commonly used during pregnancy in the prevention and treatment of anaemia (WHO Report, 1972) and neural tube defects (Milunsky et al., 1989). Magnesium trisilicate is a known adsorbent which has antacid properties.

Edible clay is consumed in relatively large amounts by many pregnant women in Nigeria to reduce gastric irritation, nausea and vomiting. The anti-irritant property of the clay could be as a result of its adsorptive property. The mineral content of the clay preparation is also believed to be nutritious. Some amounts of salt may be added to enhance the otherwise bland taste of the clay. The clay has been shown in previous experiments in our laboratory to be a potent adsorbent (Iwuagwu and Anidu, 1987). The classification of edible clay has been carried out previously (Drover and Borrell, 1980).

The literature is replete with reports of drug-drug interactions involving adsorbents used as antacids and antidiarrhoeals (Khalil and Iwuagwu, 1978; Remon et al., 1979; Naggar, 1981; Thoma and Lieb, 1983; Gibaldi, 1984). Such interactions may decrease the bioavailability of drugs (Huruwitz, 1977; Bucci et al., 1981; Gouda et al., 1984; Takahashi et al., 1985; Moustafa et al., 1986, 1987).

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The present work describes an investigation of the possible interaction of folic acid with magnesium trisilicate and edible clay which may be consumed concomitantly. The effect of salt on the interaction between the drug and the clay was also studied.

Materials and Methods

Magnesium trisilicate (mean surface volume diameter = 11.4×10^{-6} m) and sodium chloride crystals (analytical grade) were obtained from Merck (Darmstadt, F.R.G.). The edible clay was purchased from a local market; it was milled and finely sifted; mean surface volume diameter = 14.4×10^{-6} m. Folic acid B.P. powder (courtesy of Rambaxy Montari, Nigeria) and folic acid B.P. (5 mg) tablets (Glaxo, Nigeria) were used without any further treatment. All the chemicals used were of analytical reagent grade.

Adsorption study

A 1% w/v suspension of the clay was prepared in distilled water and placed in various flasks which were protected from light by wrapping with aluminium foil. The flasks were allowed to attain 37 °C in a shaking incubator (Gallenkamp, U.K.) at the same temperature. Folic acid was then fed into the flasks in graduated quantities until the desired concentration was reached. The flasks were equilibrated with constant shaking for at least 2 h. A previous study had shown that complete equilibration occurred within 1 h. After equilibration, the suspension was centrifuged (Gallenkamp, U.K.) and the concentration of folic acid in the supernatant was determined spectrophotometrically at 283 nm (Unicam SP 500) against a blank which was similarly treated but without the drug. The procedure was repeated after known amounts of salt were added to the clay suspension. Magnesium trisilicate was also used as the adsorbent. Similar experiments were carried out using 0.01 M HCl (pH 2.0) as the adsorption medium. The adsorption studies were carried out in duplicate.

Desorption study

The residue obtained after the centrifugation of 12.5 ml of adsorbent/adsorbate in 0.01 M HCl was digested with 12.5 ml water (pH 6.5), 0.01 M HCl (pH 2.0) or 0.1 M HCl (pH 1.2). The suspension was equilibrated at 37 °C in the shaking incubator for 2 h. At suitable time intervals the amount of desorbed folic acid was determined in the supernatant obtained by centrifugation of aliquots of the desorption system.

Dissolution study

Eight tablets (equivalent to 40 mg) of folic acid were placed in 800 ml of a 1% w/v suspension of some of the adsorbents in 0.01 M HCl contained in a modified B.P. dissolution testing apparatus. The dissolution medium was maintained at 37 °C. At various time intervals samples were withdrawn and centrifuged. The amount of folic acid in the clear supernatant was estimated spectrophotometrically. This experiment was carried out in duplicate. After a sample was withdrawn for analysis a fresh aliquot of the dissolution medium containing the adsorbent was added to maintain a constant volume and concentration of the adsorbent.

Results and Discussion

The adsorption isotherms of folic acid onto the various edible clay systems as well as magnesium trisilicate are illustrated in Figs 1–3. The adsorption of folic acid onto the clay from distilled water (see Fig. 1) exhibits a steep slope. This is indicative of the spontaneity of adsorption of the drug, perhaps due to a large number of adsorption sites being available (Bornstein and Lach, 1966). The adsorption isotherm illustrates that the folic acid is almost completely adsorbed from the adsorption medium by the salted and unsalted edible clay. Giles et al. (1960) referred to this type of isotherm as the H-type isotherm.

The adsorption of folic acid onto the clays from 0.01 M HCl followed a pattern (H-type isotherm) similar to that of its adsorption from distilled water (see Fig. 2). The adsorption of folic acid by the clays in both distilled water and 0.01 M HCl followed the rank order: edible clay + 7.5% w/w NaCl > edible clay + 5.0% w/w NaCl > edible clay + 10.0% w/w NaCl > edible clay (unsalted). The foregoing may be explained thus: with the

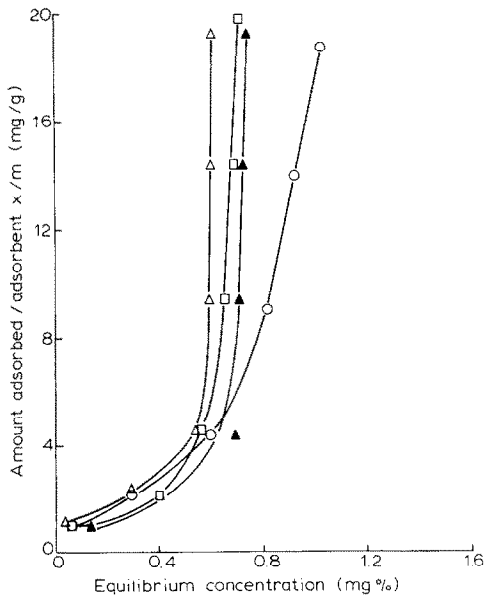

Fig. 1. Adsorption isotherms of folic acid onto various adsorbents in distilled water. (○———○) Unsalted edible clay; (□———□) edible clay+5% w/w NaCl; (△———△) edible clay+7.5% w/w NaCl; (▲———▲) edible clay+10% w/w NaCl.

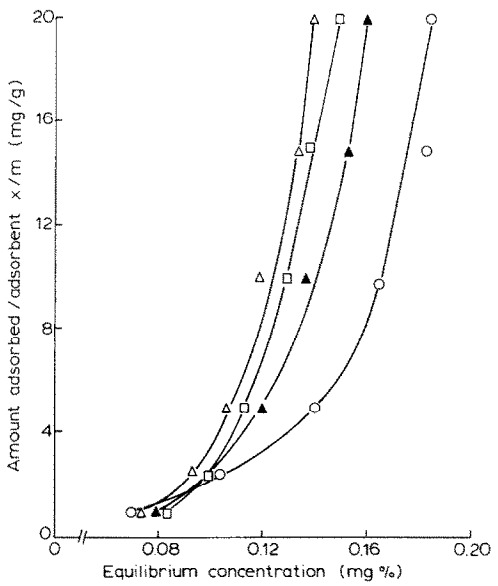

Fig. 2. Adsorption isotherms of folic acid onto various adsorbents in 0.01 M HCl (pH 2.0). Symbols as in Fig. 1.

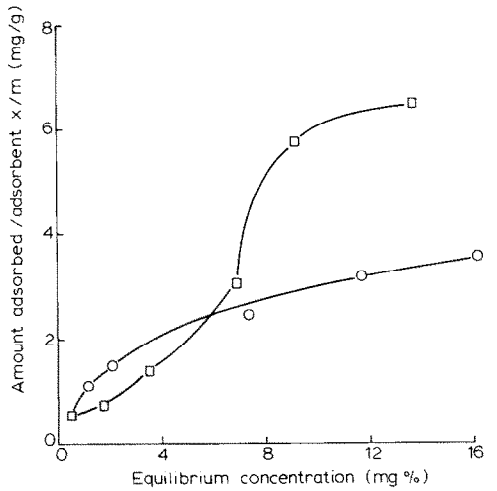

Fig. 3. Adsorption isotherms of folic acid onto magnesium trisilicate in distilled water (○———○) and in 0.01 M HCl (□———□).

inclusion of sodium chloride in the clay adsorbent in increasing quantities the polarity of the adsorbent was increased. Consequently, edible clay + 7.5% w/w NaCl had a greater adsorptive capacity than that of edible clay + 5.0% w/w NaCl. The ability of edible clay + 10.0% w/w NaCl to adsorb folic acid was considerably decreased, probably due to the fact that as the concentration of sodium chloride increased a layer of the salt which is not an adsorbent formed over the clay particles and prevented further adsorption of folic acid.

The adsorption isotherms of folic acid onto magnesium trisilicate from distilled water and 0.01 M HCl are shown in Fig. 3. The adsorption of the drug from distilled water is characteristic of Langmuir adsorption. A linear curve was obtained when a plot of $C_e(x/m)$ vs C_e was constructed (see Fig. 4). The limiting adsorptive capacity of magnesium trisilicate for folic acid in distilled water was computed to be 4.54 mg/g. The adsorption isotherm of folic acid onto magnesium trisilicate from 0.01 M HCl was biphasic. This may have resulted because in acid magnesium trisilicate forms silica gel which also has significant adsorptive properties. The initial phase of the adsorption may be attributed to mono-layer adsorption, while the later phase could be due to multi-layer adsorption. This isotherm is characteristic of the Type II iso-

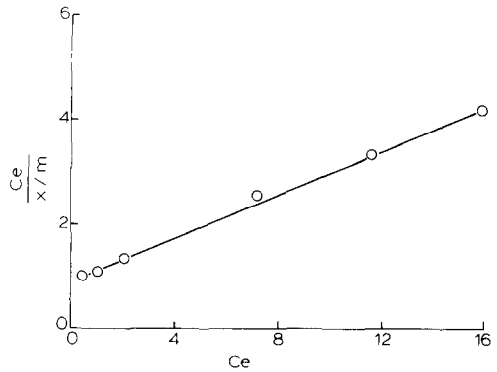

Fig. 4. Langmuir adsorption isotherm for the adsorption of folic acid onto magnesium trisilicate in distilled water.

therm in the classification of isotherms by Giles et al. (1960).

The results of desorption studies of folic acid from magnesium trisilicate, edible clay and edible clay + 7.5% w/w NaCl are illustrated in Fig. 5. The degree of desorption depended on the acidity of the elution medium. Water caused the desorption of insignificant amounts of folic acid from all the adsorbents studied. In 0.01 M HCl and 0.1 M HCl, the desorption of folic acid was significant due to the dissolution of folic acid in the solvents. In all cases 0.1 M HCl desorbed more folic acid than 0.01 M HCl. This result is indicative of chemisorption of folic acid onto the adsorbents.

Fig. 6 illustrates the dissolution profiles of folic acid tablets in 0.01 M HCl in the absence and presence of various adsorbents. All the adsorbents used in this investigation retarded the dissolution of folic acid. The retardation of dissolution of folic acid from the tablets by the various adsorbents followed the rank order: magnesium trisilicate > edible clay + 7.5% w/w NaCl > edible clay (unsalted). The implication of the result of this dissolution study in relation to the bioavailability of folic acid when consumed concomitantly with any of these adsorbents needs to be confirmed by in-vivo studies.

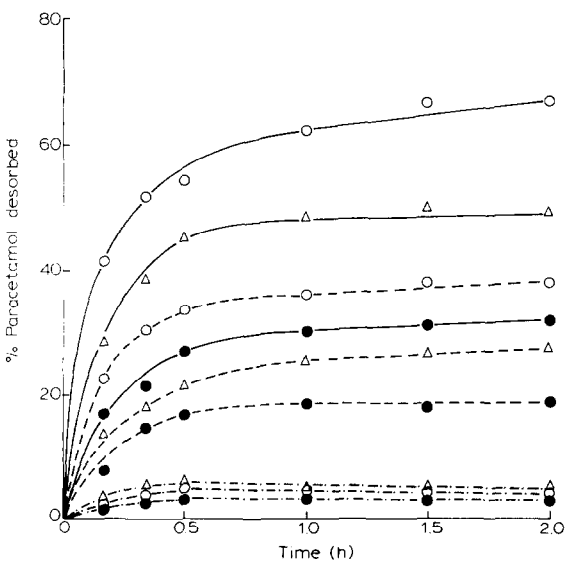

Fig. 5. Desorption of folic acid from magnesium trisilicate (●), unsalted edible clay (○) and edible clay + 7.5% w/w NaCl (△) by water (–·–·–), 0.01 M HCl (- - - - - -) and 0.1 M HCl (———).

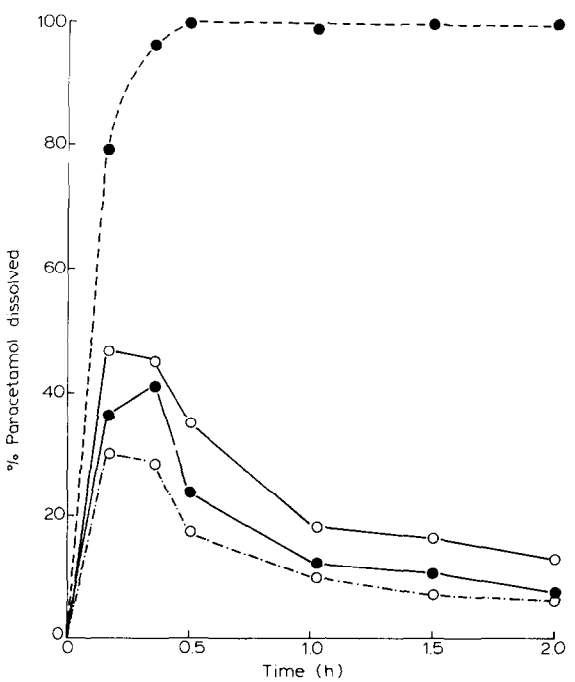

Fig. 6. The effect of adsorbents on the dissolution of folic acid from tablets in 0.01 M HCl. (●- - - - -●). No adsorbent, (○–·–○) magnesium trisilicate, (○———○) unsalted edible clay, (●———●) edible clay + 7.5% w/w NaCl.

Conclusions

This study has demonstrated that edible clay (salted and unsalted) and magnesium trisilicate adsorb folic acid significantly. The inclusion of sodium chloride in the edible clay up to an optimal value increased the adsorptive capacity of the clay. The dissolution of folic acid from tablets was significantly retarded by all the adsorbents studied. Consequently, concomitant consumption of folic acid and salted edible clay, unsalted edible clay or magnesium trisilicate should be discouraged since the bioavailability of the drug may be impaired.

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