Effect of Chloroquine Adsorption on Acid Reactivity of Magnesium Trisilicate

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Abstract □ Due to the adsorption of chloroquine by magnesium trisilicate, both the BP acid absorption test and the rate of hydrochloric acid uptake, as monitored by pH measurements, were significantly reduced. This reduction was dependent on the amount of chloroquine adsorbed, since multilayer adsorption produced relatively more suppressive effects than did monolayer adsorption. The presence of adsorbed chloroquine also decreased the amounts of magnesium released in an acid medium. The inhibition of the antacid property due to chloroquine adsorption may be attributed to the occupation of the reactive sites of the antacid surface by chloroquine and to a reduction of the surface area of the antacid due to flocculation of the particles.

Keyphrases □ Chloroquine—adsorption by magnesium trisilicate, effect on acid reactivity □ Magnesium trisilicate—adsorption of chloroquine, effect on acid reactivity □ Adsorption, drug—chloroquine by magnesium trisilicate, effect on acid reactivity □ Acid reactivity—magnesium trisilicate, effect of adsorption of chloroquine □ Antacids—magnesium trisilicate, adsorption of chloroquine, effect on acid reactivity □ Antimalarial agents—chloroquine, adsorption by magnesium trisilicate, effect on acid reactivity

Few reports have appeared on the effects of drug adsorption on the surface properties of the adsorbents. However, protective colloids and surfactants adsorbed at liquid–solid interfaces are known to inhibit crystal growth (1, 2) and polymorphic conversion of drugs (3). The adsorption of some certified dyes resulted in the inhibition of single crystal dissolution of a number of pharmaceuticals (4, 5). In recent years, the adsorption of some drugs by magnesium trisilicate was reported (6, 7), but no detailed studies appear to have been made concerning the effect of drug adsorption on the antacid efficacy.

The present work examines the influence of chloroquine adsorption on the acid reactivity of magnesium trisilicate as measured by both the BP acid absorption test and the rate of hydrochloric acid uptake. Measurements of flocculation and determination of the amounts of magnesium released were also made before and after chloroquine adsorption by magnesium trisilicate.

EXPERIMENTAL

Materials—Magnesium trisilicate powder BP[1] of 11.2-nm mean surface–volume diameter and chloroquine phosphate powder BP[2] were used.

Methods—*Adsorption Experiments*—These experiments were carried out at 37 ± 0.2° by adding aqueous solutions of chloroquine phosphate (100 ml) of appropriate concentrations to a series of weighed quantities (1 g) of magnesium trisilicate. The glass-stoppered flasks were shaken in an oscillating water bath (25 ± 2 strokes/min) until completely equilibrated (6 hr). After centrifugation at 2000 rpm for 3 min, the supernate was suitably diluted with 0.01 *N* HCl and the chloroquine concentration was determined spectrophotometrically[3] at 329 nm.

Acid Absorption Test—The BP procedure (8) was adopted using magnesium trisilicate before and after chloroquine adsorption. The results were expressed as the volume of 0.05 *N* HCl absorbed by 1 g of magnesium trisilicate. To study the effect of chloroquine adsorption on the acid absorption test, the antacid after the adsorption experiment was centrifuged and the residue, equivalent to 0.3 g of magnesium trisilicate, was tested.

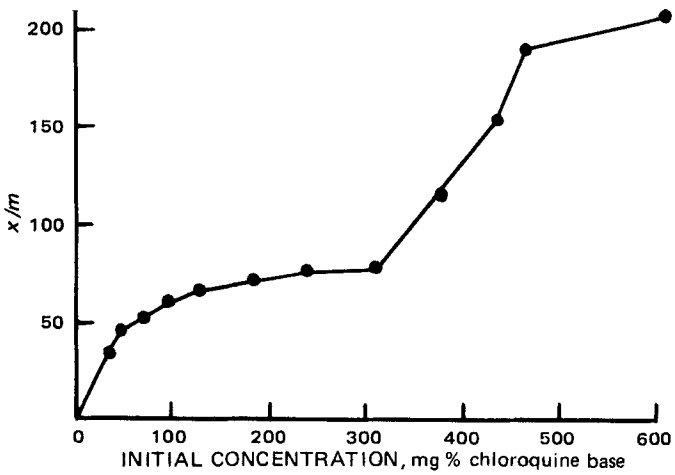

Figure 1—*Adsorption of chloroquine by 1% (w/v) magnesium trisilicate at 37 ± 0.2° (pH of the medium was 9.6).*

Rate of Hydrochloric Acid Uptake—The rate was determined at 37 ± 0.2° by monitoring the pH changes produced after the addition of 340 ml of 0.02 *N* HCl to 1 g of magnesium trisilicate. The apparatus and procedure adopted were as reported previously (9). To study the effect of chloroquine adsorption on the rate of hydrochloric acid uptake, the residue, equivalent to 1 g of the antacid remaining after the adsorption run, was used.

Determination of Magnesium Release—The amounts of magnesium

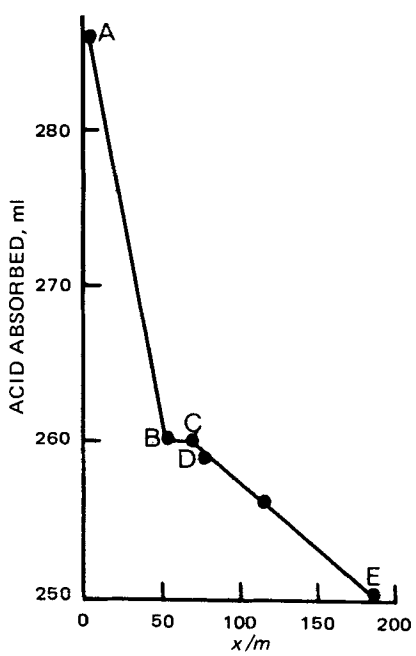

Figure 2—*Effect of amount of chloroquine adsorbed on the volume of 0.05 N HCl absorbed by 1 g of magnesium trisilicate (x/m) as measured by the BP acid absorption test.*

[1] Evans Medical Ltd., England.
[2] May & Baker, England.
[3] Unicam SP 500 Series 2.

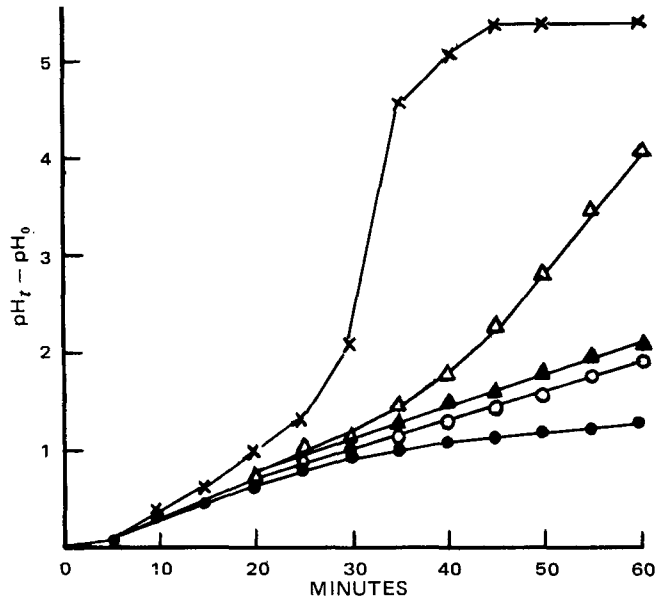

Figure 3—*The pH change* versus *time curves for magnesium trisilicate before chloroquine adsorption* (×) *and after adsorption of the following amounts of chloroquine (in milligrams per gram):* △, *68.2;* ▲, *75.9;* ○, *112.0; and* ●, *183.5.*

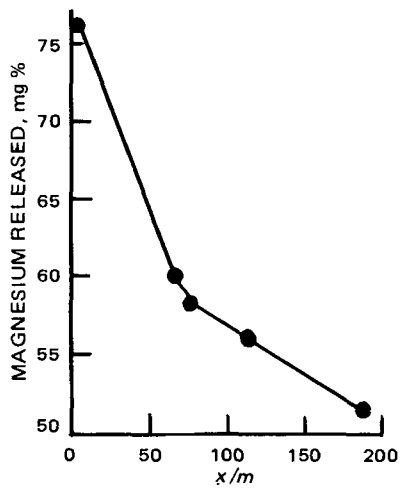

Figure 4—*Effect of amount of chloroquine adsorbed on the amount of magnesium released after 1 hr under the conditions of the BP acid absorption test.*

released after 1 hr under the conditions of the rate of hydrochloric acid uptake were determined by titrating an aliquot of the supernate with 0.05 *M* disodium ethylenediaminetetraacetate. A mordant black mixture was used as the indicator. Interference due to the released chloroquine was negligible.

Turbidity Measurements—A nephelometer[4] was used to measure, at 25°, the turbidity of the supernate sampled from the suspension after 10 min from a depth of 5 cm. The suspension was prepared by dispersing the residue (equivalent to 0.3 g of magnesium trisilicate) obtained after the adsorption experiment in 100 ml of water in a stoppered glass measure.

RESULTS AND DISCUSSION

Figure 1 shows the adsorption plot of chloroquine (where *x/m* is milligrams of chloroquine adsorbed per gram) on magnesium trisilicate (1% w/v) at pH 9.6[5]. At initial chloroquine concentrations below 300 mg %, the adsorption data fitted a Langmuir plot within the monolayer adsorption region; at higher drug concentrations, multilayer adsorption occurred. In the present study, the acid reactivity of magnesium trisilicate was tested before and after adsorbing varying amounts of chloroquine. Figure 2 shows the results of the BP acid absorption test. The adsorption of chloroquine on magnesium trisilicate resulted in a reduction of the volume of 0.05 *N* HCl absorbed by 1 g of the antacid. After an initial decrease from 282.2 to 260.1 ml (line AB, Fig. 2), an increase in the amount of chloroquine adsorbed within the region of monolayer adsorption (BCD) did not produce any significant reduction in the volume of the acid. Multilayer adsorption of chloroquine, however, produced a further decrease (line DE).

Measurements of the rate of hydrochloric acid uptake were made by monitoring the pH changes over 1 hr. The results shown in Fig. 3 illustrate a gradual suppression of the rate of acid uptake as the amount of chloroquine adsorbed was increased. At an *x/m* value of 183.5 mg/g, the acid reactivity decreased to 24.1%, calculated by comparing the pH changes 1 hr before and after adsorption. Determinations of the amounts of magnesium released under acidic conditions showed a gradual decrease due to chloroquine adsorption (Fig. 4). As a result of the adsorption, the antacid particles flocculated. Consequently, the turbidity percentages of the supernate decreased to 53.1, 41.6, and 40.3 for *x/m* values of 68.2, 75.9, and 112.0 mg/g, respectively.

The results suggest that the acid reactivity of magnesium trisilicate was suppressed due to chloroquine adsorption. This finding was evidenced by the acid absorption test where the volume of 0.05 *N* HCl consumed by 1 g of the antacid decreased from 282.2 ml to between 260.1 and 250.3 ml (Fig. 2). The suppressive effect of chloroquine adsorption of the acid reactivity was also reflected in the rate of hydrochloric acid uptake (Fig. 3). In the absence of adsorption, the pH change recorded after 1 hr was 5.4 units. Due to the adsorption of 183.5 mg of chloroquine, however, the pH value did not change by more than 1.3 units.

Since chloroquine has pKa values of 8.4 and 10.8, the ionization percentages at pH 9.6 (of the adsorption medium) would be 5.9 and 94.1, respectively. Therefore, the monoprotonated form probably is mainly involved in the adsorption. The mechanism suggested is probably electrostatic attraction between the negatively charged silicate surface and the monoprotonated form of chloroquine. As a result, neutralization of the charges occurred, as evidenced by the flocculation of the system. Since the reactive sites on the antacid were occupied by chloroquine, both the volume of the acid absorbed by 1 g of the antacid and the rate of acid uptake were reduced. Also, the amounts of magnesium released decreased as the amount of chloroquine adsorbed was increased, probably due to the "blocking" of the dissolution sites on the surface. The suppression of the acid reactivity may have been due to the decreased surface area of the flocculated antacid. The latter was, however, a direct effect of chloroquine adsorption.

In conclusion, the interaction between chloroquine and magnesium trisilicate not only resulted in the adsorption of the antimalarial drug (possibly altering its bioavailability) but also reduced the acid reactivity of magnesium trisilicate.

[4] Corning EEL, Evans Electroselenium Ltd., Essex, England.

[5] At this pH, no precipitation of chloroquine occurs since it is monoprotonated (pKa values of 8.4 and 10.8).

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