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Adsorption of atropine and hyoscine on magnesium trisilicate

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The adsorption of atropine and hyoscine by magnesium trisilicate has been studied. At relatively low initial concentrations the adsorption data were shown to fit a Langmuir plot and values for monolayer adsorption were 14·9 and 3·8 mg g^{-1} for atropine and hyoscine respectively. The extent of adsorption was increased at higher initial concentrations due to multilayer formation. The presence of either sodium citrate or sodium phosphate suppressed the adsorption. Elution of the adsorbed alkaloid was dependent on the pH of medium used and followed the order: 0·05N HCl (pH 1·5) >0·01N HCl (pH 2·1) > water (pH 5·5). Due to the dissolution of magnesium trisilicate, at 37° in 0·05N HCl, neither the rate of acid uptake nor the acid absorption test of the adsorbent were significantly reduced by the adsorption of either alkaloid. In the B.P.C. mixture of magnesium trisilicate and belladonna, almost complete adsorption of hyoscyamine occurred and the elution of the adsorbed alkaloid depended on the level of hydrochloric acid in the elution medium used.

El-Masry & Khalil (1973) have described a colorimetric method for the microdetermination of atropine and hyoscine when present in belladonna tincture and in mixtures. During the application of the recommended method for the determination of atropine in some B.P.C. mixtures containing belladonna tincture, it was found that the supernatant of magnesium trisilicate and belladonna mixture was almost devoid of alkaloids. This was confirmed by t.l.c. testing. We have investigated the possible adsorption of tropane alkaloids by magnesium trisilicate which has been found previously to adsorb streptomycin sulphate (El-Nakeeb, Aggag & Yousef, 1969) and benzalkonium chloride (Yousef, El-Nakeeb & Labib, 1971).

We examined the uptake of atropine and hyoscine by magnesium trisilicate and the effect of citrate and phosphate ions on the adsorption. The influence of adsorption on both the acid absorption test and the rate of acid uptake by magnesium trisilicate was also studied. A correlation existed for the elution rate of the adsorbed alkaloid and the release of magnesium ions from the adsorbent in the different elution media. The release of atropine from the B.P.C. mixture of magnesium trisilicate and belladonna is discussed.

MATERIALS AND METHODS

Materials. Magnesium trisilicate (Evans Medical Ltd.) of mean volume-surface diameter 11·2 μm, atropine sulphate (Sandoz, Basle) and hyoscine hydrobromide (May & Baker) were all B.P. Hyoscyamine sulphate (BDH) was a sample crystallized from ethanol (m.p. 206°). Chloroform, sodium citrate and sodium phosphate were Analar (BDH). Bromocresol purple (BDH) and belladonna tincture B.P. (William Ransom & Son Ltd., Hitchen) were used.

Methods

Adsorption experiments. Aqueous solutions of the alkaloid (100 ml) of appropriate concentrations were added to each of a duplicated series of weighed quantities (1 g) of magnesium trisilicate in ground glass stoppered conical flasks. The flasks were shaken at 25 ± 0·1° till complete equilibration (30 min). The suspension was centrifuged for 3 min at 2000 rev min^{-1} and the concentration of the alkaloid in the supernatant was determined in an aliquot suitably diluted. The pH of the suspension at the commencement of the adsorption experiment was 9·7 and after equilibration the supernatant had a pH of 9·5.

Determination of atropine, hyoscyamine or hyoscine in the supernatant. A modification of the acid dye technique reported by El-Masry & Khalil (1973) was adopted.

For atropine and hyoscyamine. To an aliquot of the supernatant were added 10 ml of McIlvaine buffer solution (pH 6·6 ± 0·1) and 10 ml of solution of bromocresol purple in chloroform (4×10^{-4}M). After shaking for 1 min, the phases were left for complete separation (10 min). After separation of the chloroform phase, the aqueous layer was extracted with 3 × 10 ml of chloroform. The combined chloroform phase was extracted with 0·1N NaOH and the violet colour of the liberated dye was measured spectrophotometrically at 580 nm; a blank was similarly prepared.

For hyoscine. McIlvaine buffer solution pH 5·6 ± 0·1 was used instead of pH 6·6; the procedure adopted was essentially the same as under atropine. Beer's law was obeyed for the three alkaloid-dye complexes in the range of concentrations used. In calculating the percentages of adsorption, a run, using a standard solution of the alkaloid, was made under the same conditions.

Elution experiments. The elution rate of the adsorbed alkaloid was determined by digesting the residue (0·3 g), obtained by centrifugation of the suspension after the adsorption run, in 100 ml of water (pH 5·5), 0·01N HCl (pH 2·1) or 0·05N HCl (pH 1·5). After the digested material had been shaken at 37 ± 0·1°, the amount of alkaloid eluted, as a function of time, was determined in an aliquot after centrifugation.

Acid absorption test. The B.P. procedure for the determination of acid absorption for magnesium trisilicate (B.P. 1968) was adopted. The test was carried out on magnesium trisilicate before and after absorbing varying amounts of either atropine or hyoscine.

Rate of acid uptake. This was determined by monitoring, as a function of time, the pH changes during the acid absorption test but using 60 ml of 0·05N HCl.

Determination of rate of magnesium release. The amounts of magnesium released during the elution experiments were determined by titrating an aliquot with 0·05M disodium edetate solution in the presence of strong ammonia—ammonium chloride mixture and using mordant black mixture as the indicator.

RESULTS

Preliminary experiments showed that the adsorption of either atropine or hyoscine by magnesium trisilicate was rapid since equilibrium was attained after 10 min. This time was found to be not appreciably different when both higher and lower concentrations of either alkaloid were used. An equilibrium time of 30 min was therefore adopted. Fig. 1 shows, as a function of the initial alkaloid concentration, the amount of alkaloid adsorbed per 1 g of magnesium trisilicate. The adsorption plots of both alkaloids showed a similar pattern, where after a 'short' plateau (corresponding to the

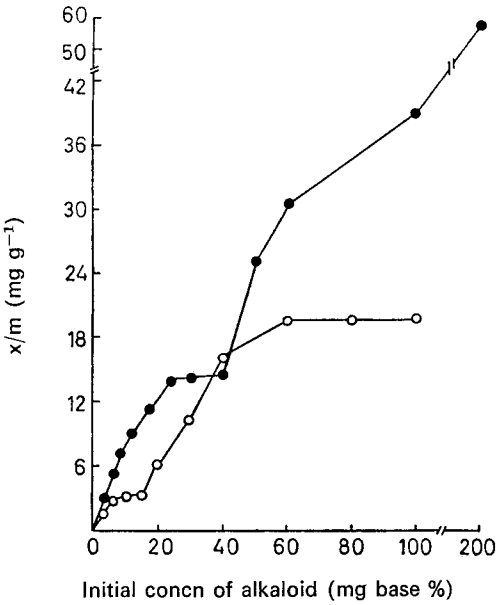

FIG. 1. Adsorption of atropine (●); and hyoscine (○) by magnesium trisilicate at 25 ± 0·1°.

completion of the monolayers) an increase in adsorption occurred due to multilayer formation. For hyoscine, the completion of the multilayers was attained at initial concentrations above 60 mg %. This was not the case for atropine where the formation of multilayers was not completed in systems containing up to 200 mg % (Fig. 1). The adsorption data were found to fit a Langmuir plot for systems containing up to 40 mg % atropine or 15 mg % hyoscine. The slopes of the linear plots, calculated by the method of least squares, were 0·067 and 0·263 for atropine and hyoscine, respectively. The values of monolayer adsorption (computed from 1/slopes) were 14·9 and 3·8 mg g^{-1} for atropine and hyoscine, respectively.

Results of elution of the adsorbed alkaloids (Fig. 2A) show that both atropine and hyoscine gave almost the same elution profile in a particular medium. Elution followed the sequence: 0·05N HCl (pH 1·5) > 0·01N HCl (pH2·1) > water (pH 5·5).

Determinations of the rate of magnesium release from magnesium trisilicate, under the conditions of the elution experiments, revealed that the release was dependent on the medium used in a similar way as found during the elution studies (Fig. 2B). By considering the amount of magnesium released as a measure of magnesium trisilicate dissolution, it is shown (Fig. 2B) that after 1 h the percentages dissolved were 25·6 and 84·3 in 0·01 and 0·05N HCl, respectively. Dissolution in water was insignificant. The adsorption of either atropine or hyoscine on magnesium trisilicate did not significantly affect the acid absorption capacity of the adsorbent. The volume of 0·05N HCl absorbed by 1 g of magnesium trisilicate was 276·8 ml. After atropine adsorption (14·9 and 39·1 mg g^{-1}) or hyoscine adsorption (3·8 and 19·9 mg g^{-1}), the volume of 0·05N HCl consumed ranged between 273 and 278 ml. It follows, therefore, that the monolayer or multilayer adsorption of either alkaloid did not significantly alter the acid absorption capacity of the adsorbent. The rate of acid uptake, as measured by changes in pH values, was not reduced due to the adsorption of either alkaloid. The presence of the adsorbed alkaloids enhanced slightly the rate of acid uptake

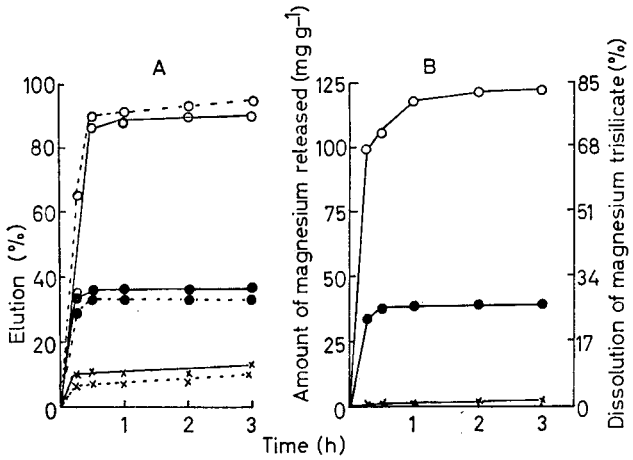

FIG. 2A. Elution rates of atropine (——) and hyoscine (- - -) adsorbed by magnesium trisilicate in (×) water, (●) 0·01N HCl; (○) 0·05N HCl at 37 ± 0·1°.

B. Release rates of magnesium from magnesium trisilicate at 37 ± 0·1° in (×) water; (●) 0·01N HCl; (○) 0·05N HCl and the corresponding percentage dissolution of the adsorbent.

after 30 min. The addition of either sodium citrate or sodium phosphate to the suspension before the addition of the alkaloid resulted in suppression of adsorption; the effect was dependent on the time of contact of the electrolyte with the adsorbent and the concentration of magnesium trisilicate. In a system containing magnesium trisilicate (1% w/v) and sodium citrate (0·1M), a minimum contact time of 30 min was essential to suppress the adsorption of atropine sulphate from 93·6 to 37·8%. At a fixed sodium citrate concentration (0·1M) and a contact time of 30 min, the percentages of atropine adsorption depended on the magnesium trisilicate content. The percentages adsorbed were 0, 37·3, 55·0 and 80·9% in the presence of 0·5, 1·0, 2·5 and 5·0% w/v magnesium trisilicate respectively.

The effect of sodium citrate and sodium phosphate concentration is shown in Table 1. Complete suppression of the adsorption occurred in the presence of 0·25M of either electrolyte.

Table 1. *Effect of sodium citrate and sodium phosphate on the adsorption of atropine and hyoscine by magnesium trisilicate.*

Concentration of the salt (M)	Adsorption (%)	
sodium citrate	atropine	hyoscine
0	93·4	49·9
0·05	52·0	31·1
0·075	47·1	23·0
0·10	38·3	11·3
0·20	15·2	0
0·25	0	0
0·50	0	0
Sodium phosphate		
0·05	48·8	25·7
0·10	32·4	18·8
0·15	8·8	7·6
0·20	1·1	0
0·25	0	0

Concentration of magnesium trisilicate 1% w/v, concentration of either alkaloid: 3 mg % of the base, contact time of the salt: 30 min.

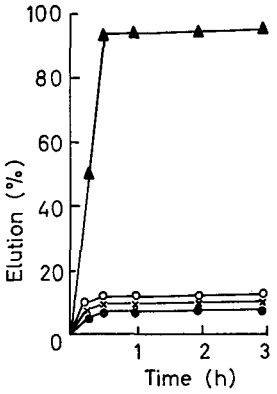

FIG. 3. Elution rate at 37° of hyoscyamine from magnesium trisilicate and belladonna mixture B.P.C. in (×) water; (●) 0·01N HCl; (○) 0·05N HCl; (▲) 0·5N HCl, at 37 ± 0·1°.

Adsorption of hyoscyamine in magnesium trisilicate and belladonna mixture, B.P.C. Analyses of the supernatant of the B.P.C. mixture revealed that about 93% of the hyoscyamine content of belladonna tincture added was adsorbed. Adsorption was completed in 30 min after the addition of the tincture and is solely attributable to magnesium trisilicate since light magnesium carbonate (an ingredient of the B.P.C. mixture) was found to possess no adsorptive effect.

Following the B.P.C. (1968) procedure for testing the presence of belladonna alkaloids in the mixture, the supernatant (obtained after the centrifugation of 10 ml of the mixture) gave no spots upon t.l.c. testing. After extracting the residue with acetone—dilute ammonia solution mixture, the combined extracts yielded only about 45% of the hyoscyamine content originally present in belladonna tincture used.

Elution of hyoscyamine from the B.P.C. mixture. Fig. 3 shows the elution rates of hyoscyamine from the B.P.C. mixture when 10 ml aliquots were digested at 37° with 40 ml of water, or 0·01, 0·05 or 0·5N HCl. A significant release occurred in the presence of 0·5N HCl which amounted to about 92%. Elution in other media did not exceed 15% (Fig. 3).

DISCUSSION

The results show that both atropine and hyoscine are adsorbed by magnesium trisilicate, the adsorption data following a Langmuir plot over a limited concentration range (Fig. 1). Adsorption data reported for atropine on kaolin (Ridout, 1968) showed the absence of multilayer formation and the adsorption results were expressed, therefore, by a Langmuir plot over a much wider concentration range. In the present work, initial concentrations above 40 mg % (for atropine) and 15 mg % (for hyoscine) resulted in multilayer adsorption. The variation in the extents of adsorption of atropine and hyoscine may be attributable to the difference in ionization at pH 9·6 (of the system). The percentage ionization at this pH will be about 50 for atropine (pKa 9·65) and zero for hyoscine (pKa 7·6). It follows, therefore, that, during the adsorption experiment, hyoscine existed in the unionized form, nevertheless, this alkaloid was relatively less adsorbed than atropine. This appears to be

inconsistent with the findings of Phelps & Peters (1929) and Andersen (1947) that unchanged bases are adsorbed more readily than ionized molecules. However, the observed decrease in the adsorption of hyoscine may be interpreted in the light of the work of Patrick & Eberman (1925) who investigated the relation between solubility and adsorption. These authors concluded that, for a given solvent, the more soluble solutes are generally less strongly adsorbed than the less soluble solutes. Owing to the presence of the ether oxygen, hyoscine base is freely soluble in water (1 in 9·5 parts at 15° compared with 1 in 400 at 20° for atropine base). Hyoscine would therefore be expected to be less adsorbed than atropine.

The suppressive effect of both citrate and phosphate ions, found in the present work and previously reported (El-Nakeeb & others, 1969), may be attributed to possible adsorption of these ions on the adsorbent. Goldsztaub, Henin & Wey (1954) found that phosphate ions are adsorbed on kaolin. The 'insulating' or 'shielding' effect due to the adsorption of the electrolyte would diminish the extent of adsorption of the alkaloid.

Elution of the adsorbed alkaloids from magnesium trisilicate depended on the extent of dissolution of the adsorbent in the medium used. In 0·05N HCl (at 37°) about 92% elution of both alkaloids resulted since about 84% dissolution occurred to the adsorbent (Fig. 2). Due to the weaker effect of both water and 0·01N HCl on the solubility of magnesium trisilicate, elution was consequently low.

Because some surface properties may be affected as the result of adsorption of solutes onto surfaces, the effects of adsorption on both the acid absorption capacity and rate of acid uptake were examined. Owing to the dissolving effect of the acid used (0·05N HCl at 37°), both properties were not significantly reduced. In the B.P.C. mixture of magnesium trisilicate and belladonna, it was found that about 93% of the hyoscyamine content was adsorbed by magnesium trisilicate. Because of the presence of both sodium bicarbonate and magnesium carbonate in the mixture, a higher concentration of hydrochloric acid was required to effect elution of the adsorbed hyoscyamine. Water, 0·01 and 0·05N HCl (Fig. 3), in the quantities used, eluted only about 15% due to the partial neutralization of the components, the final pH being 8·6. In the presence of 0·5N HCl, however, complete neutralization occurred and the residual acidity was sufficient to yield about 92% of the adsorbed hyoscyamine.

From the foregoing discussion, it appears that the *in vivo* release of the adsorbed hyoscyamine from the B.P.C. mixture would depend on the level of hydrochloric acid present. Release can only occur when the pH value is lower than 2, a condition which is unlikely to be fulfilled after the administration of the B.P.C. mixture.

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