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In vitro and *in vivo* defoaming action of three antacid preparations

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The defoaming activity of three tablet antacids (hydrotalcite, hydrotalcite/dimethicone and aluminium hydroxide/dimethicone) powdered to 60 mesh was measured *in vitro* using a new static/dynamic technique. Their antacid actions and that of aluminium hydroxide gel B.P.C. were also measured using a modified Fuch's test. Combination of dimethicone with hydrotalcite conferred good defoaming activity with little effect on pH profile whilst combination of aluminium hydroxide with dimethicone markedly altered both. Additionally, the defoaming actions of the three commercial antacids were assessed *in vivo*. Radiographs were taken after administration of antacid, a foaming mixture and a normal barium meal. The radiographs were then ranked blind by 5 radiologists. The rankings assigned the significantly greatest (Mann-Whitney U-test) defoaming effect to the hydrotalcite/dimethicone combination, there being no difference between the other two preparations. The *in vitro* results were thus confirmed.

The use of activated dimethicone with antacid therapy is widely accepted for the alleviation of distress caused by gas formation (Rider, 1968). The foam destroying activity of antacid-defoamer tablets is commonly measured *in vitro*, the methods used having been classified by Carless, Stenlake & Williams (1973) as either static or dynamic. The static tests are generally based on the method of Rezak (1966) where a volume of foam is produced by agitation of a surfactant solution and the rate of foam destruction is measured. Dynamic methods involve measurement of the rate at which foam, formed by passing air through a sintered glass disc immersed in surfactant solution, is destroyed. For this study a test was devised which may be regarded as a combination of the static and dynamic types. The assessment of anti-foaming action *in vivo* has been studied only rarely (Garry, 1956; Rider & Moeller, 1960; Hoon, 1966; Birtley, Burton & others, 1973) and the correlation between *in vitro* and *in vivo* results not at all. The following report is of a study comparing the effects of three prescription antacids.

IN VITRO MATERIALS AND METHODS

The foaming medium comprised a solution containing hydroxyethylcellulose (Natrosol 250 HR–Hercules) 0·25% and sodium laurylsulphate 0·1% w/v dissolved in water with the pH adjusted to 1·2 with hydrochloric acid. 200 ml of the foaming medium was introduced into a 500 ml graduated measuring cylinder and compressed air introduced into the bottom of the test medium through a sintered glass disc. The foam was allowed to build up to the 500 ml mark and 1 ml of test suspension (tablets ground to a 60 mesh powder and a weight equivalent to two tablets suspended in 10 ml of water) was added, the cylinder was then inverted five times, observed for 15 s and inverted once more; the foam height 30 s after the addition of the sample was recorded. The test was continued by building up the foam again to the mark, adding a further 1 ml dose and repeating the procedure until the foam height was reduced to about 270 ml.

Antacid activity was evaluated using a modified Fuch's Test (Playle, Gunning & Llewellyn, 1974). Here 1 g of antacid was added to 150 ml simulated gastric juice U.S.P., maintained at 37·5 ± 1° and stirred at 600 rev min^{-1}. After 10 min simulated gastric juice was added at the rate of 2 ml min^{-1} for a further 90 min. The pH profile was recorded.

The formulations tested were tablets, each containing: 500 mg hydrotalcite (Altacite, Roussel Laboratories). 500 mg hydrotalcite + 250 mg activated dimethicone (Altacite Plus, Roussel Laboratories). 500 mg aluminium hydroxide + 250 mg dimethicone (Asilone—Berk Pharmaceuticals). Additionally, the antacid effect of aluminium hydroxide dried gel B.P. was studied.

IN VITRO RESULTS

It can be seen from the results of the defoaming test (Fig. 1) that the hydrotalcite/dimethicone tablets

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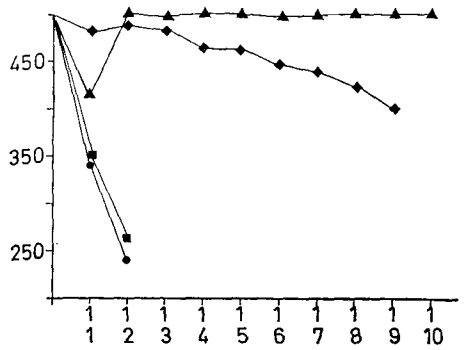

FIG. 1. The foam destroying action of three antacids *in vitro*. Foam volume was measured 30 s after addition of aliquots of antacid: between each addition foam height was returned to 500 ml by bubbling air through the foaming medium. Each aliquot of antacid corresponded to 20% of a tablet ground and suspended in water (i.e. 100 mg hydrotalcite; 100 mg hydrotalcite + 50 mg dimethicone; 100 mg aluminium hydroxide + 50 mg dimethicone). ▲ Hydrotalcite; ◆ aluminium hydroxide/dimethicone; ■ hydrotalcite/dimethicone (1 year at 37°); ● hydrotalcite/dimethicone. Ordinate: Total test volume (foam and medium) (ml). Abscissa: Volume of test sample added (ml).

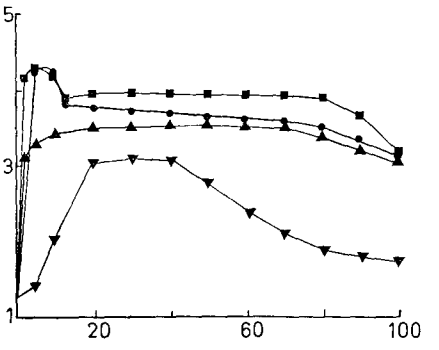

FIG. 2. The effects of antacids on pH of simulated gastric juice (modified Fuch's test). pH was monitored following addition of 1 g antacid to 150 ml simulated gastric juice U.S.P. maintained at 37·5° and stirred continuously, 10 min later further simulated gastric juice was added at the rate of 2 ml min^{-1} for 90 min. ● Hydrotalcite; ▲ aluminium hydroxide dried gel B.P.; ■ hydrotalcite/dimethicone; ▼ aluminium hydroxide/dimethicone.

possessed a markedly higher defoaming activity than either plain hydrotalcite tablets or aluminium hydroxide/dimethicone tablets. As the defoaming activity of antacid-defoamer tablets may decrease with ageing (Rezak, 1966), the defoaming activity of hydrotalcite/dimethicone tablets that had been stored for 1·8 years at 37° was measured. There was no change, indicating a high stability for the defoaming activity.

Hydrotalcite, hydrotalcite/dimethicone and aluminium hydroxide gave similar results in the modified Fuch's test (Fig. 2), the pH being maintained above 3 for the whole experiment. Aluminium hydroxide in combination with dimethicone, however, only maintained the pH above 3 for 22 min.

IN VIVO EVALUATION

Twelve patients (3 males, 9 females, aged 27–70 mean 49 years) attending hospital for routine barium meal examinations and presenting with vague symptoms of indigestion were selected with their active consent. In none was there any radiographic demonstration of abnormality in the oesophagus, stomach or duodenum.

Method

Each subject chewed and swallowed two tablets of one of the three antacids. Six subjects took hydrotalcite/dimethicone tablets, three took hydrotalcite tablets and three took aluminium hydroxide/dimethicone tablets. Five min later gas distension of the stomach was obtained by 4 g sodium bicarbonate followed by 3 g tartaric acid and a further 5 min later a barium sulphate preparation (100 ml Baritop 100, Concept Pharmaceuticals) was taken and 0·1 mg glucagon (Novo) administered intravenously as a muscle relaxant. The standard upper gastrointestinal series of radiographs were taken. From these radiographs, one of the erect and the other of a supine right anterior oblique position were selected for assessment of defoaming. The pairs were ranked blind by five experienced radiologists in order of efficacy of the defoaming agent.

IN VIVO RESULTS

The rankings (Fig. 3) were analysed statistically and significant association of drug with defoaming action was found ($P < 0{\cdot}001$, χ^2 test, two degrees of freedom). The defoaming activity of hydrotalcite/dimethicone was significantly greater than that of either plain hydrotalcite ($P = 0{\cdot}012$) or aluminium hydroxide/dimethicone ($P = 0{\cdot}024$). There was no statistically significant difference between hydrotalcite and aluminium hydroxide/dimethicone (all tested using the Mann-Whitney U-test).

DISCUSSION

Preparations containing antacids in combination with a defoaming agent possess significant defoaming activity both *in vitro* (Rezak, 1966; Carless & others, 1973; Rigby, Bisknell & Smith, 1974) and *in vivo*

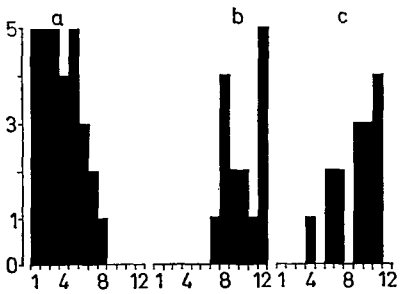

FIG. 3. The defoaming effect of antacids *in vivo*. Radiographs of 12 patients taken after intake of antacid (two tablets)/foaming mixture/barium meal were ranked blind by five radiologists according to the amount of foam present in the stomach (rank 1 = least foam rank 12 = most foam). The histograms show the distribution of ranks assigned to each antacid treatment. a: Hydrotalcite/dimethicone; b: hydrotalcite; c: aluminium hydroxide/dimethicone.

(Garry, 1956; Rider & Moeller, 1960; Hoon, 1966; Birtley & others, 1973) and are able to relieve symptoms of gaseousness (Weiss, 1969; Bernstein & Schwartz, 1974). We have found differences between formulations containing the same defoaming agent, i.e. between hydrotalcite/dimethicone and aluminium hydroxide/dimethicone. It is possible that the arbitarily fixed time interval between dosing and X-ray in the *in vivo* study could have masked the defoaming activity of aluminium hydroxide/dimethicone by not allowing for difference in rates of dissolution. This seems unlikely on the basis of the results of the *in vitro* work where little defoaming effect was evident over the test period.

The observed low activity of the aluminium hydroxide/dimethicone combination suggests that the defoaming agent has been adsorbed onto the antacid rendering both materials less available. Evidence in favour of this is provided by the *in vitro* antacid activity of the formulation which was much lower than that of an equivalent quantity of aluminium hydroxide dried gel (Fig. 2). In contrast, hydrotalcite + dimethicone has a similar antacid activity to hydrotalcite alone. Careful formulation is obviously essential in such combination preparations if chemical and/or physical interaction between the components is to be minimized.

In vitro tests are almost always more convenient to use in studies such as those described but their validity to the *in vivo* situation is open to question, however, the tests used show that good correlation can be obtained with the procedures used.

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