International Journal of Pharmaceutics, 34 (1986) 105–109
Elsevier

IJP 01143

What is "Liquid Gaviscon"? A comparison of four international formulations

N. Washington [1], C. Washington [2], C.G. Wilson [1] and S.S. Davis [2]

[1] *Department of Physiology and Pharmacology, Queen's Medical Centre, Nottingham (U.K.)* and [2] *Department of Pharmacy, University of Nottingham, Nottingham (U.K.)*

(Received 6 May 1986)
(Accepted 6 July 1986)

Key words: Alginate; 'Raft-forming antacid; Antacid; "Liquid Gaviscon"

Summary

Four international formulations of "Liquid Gaviscon" have been assessed for the strength of the alginate raft formed on reaction with acid and neutralization properties in a modified Rossett and Rice (1954) test. The results from this investigation show that each formulation of "Liquid Gaviscon" possesses markedly different raft strength and neutralization profiles. The inclusion of antacid materials into "Liquid Gaviscon" formulations increases the neutralization capacity within the raft, but decreases the breaking strength and hence the ability of the raft to form a viscous 'plug' in the opening of the oesophagus as a barrier to reflux. This suggests that the modes of action may be different even though the trade names of the formulations are the same. This may have clinical consequences when dispensing parallel imports bearing the 'Gaviscon' name.

Introduction

"Liquid Gaviscon" is used to suppress gastro-oesophageal reflux and alleviate the symptoms of "heartburn". The formulation contains alginate, which forms a gel of alginic acid, and a carbonate or bicarbonate component, which evolves carbon dioxide bubbles, on reaction with gastric acid. The gel becomes buoyant by entrapping the gas bubbles, and consequently floats on the stomach contents as a viscous layer which has a higher pH than the gastric contents. Only the British formulation of "Liquid Gaviscon" (Reckitt and Colman, U.K) does not contain any antacids in addition to the bicarbonate required to elevate the raft.

It has been postulated that the raft acts by forming a physical barrier on top of the stomach contents, preventing contact of the acid with the squamous epithelium of the oesophagus which is vulnerable to acid damage (Amdrup and Jakobsen, 1969). In the event of the raft being ruptured, neutral raft material is refluxed into the oesophagus in preference to the acidic gastric contents (Malmud et al., 1979). This may constitute a second possible mode of action of raft-forming antacids.

Although "Liquid Gaviscon" is available in many countries, it is manufactured under licence by different pharmaceutical companies and the formulations vary greatly in composition. Previous communications from our laboratories have de-

Correspondence: N. Washington, Department of Physiology and Pharmacology, Queen's Medical Centre, Clifton Boulevard, Nottingham NG7 2UH, U.K.

scribed a technique for measuring the in vitro strength of the raft as an indicator of possible barrier action in vivo (Washington et al., 1985a and b, 1986). In the present study, the in vitro behaviour of a selection of the "Liquid Gaviscon" formulations from different countries has been assessed for raft strength and neutralization capacity.

Materials and Methods

The "Liquid Gaviscon" formulations from England (Reckitt and Colman; batch no. E06544), U.S.A. (Marion Laboratories; batch no. H5881), Canada (Sterling Winthrop; batch no. L061AD) and Sweden (Ferring; batch no. LK6127) were studied. These formulations were used without modification.

The total in vitro pH–neutralization profiles for 10 ml of each formulation were measured as described by Rossett and Rice (1954). The neutralization profiles in and below the alginate raft were measured using modifications of the above test (Washington et al., 1985a).

The strength of the rafts was measured using a purpose-built apparatus described previously (Washington et al., 1985a and b). The raft was formed by adding the antacid to 125 ml of 0.03 M hydrochloric acid at 38°C. A microcomputer-controlled force balance was used to apply a force to the underside of the raft via a wire probe. The microcomputer measured the raft deflection and collected the data. The formulations varied in composition, and it was considered that a comparison of equal fractions of a recommended dose was the most clinically relevant. The alginate concentrations of all the formulations were the same (5%) except for the U.S. formulation. In order to compare the formulations on an equi-alginate basis, the volume of the U.S. formulation was doubled while equal volumes of the other formulations were used. The raft strengths were measured 10 min, 30 min and 2 h after formation at 37°C to determine the time required for the raft to attain full strength.

Results

The total neutralization profiles obtained when the raft was destroyed are shown in Fig. 1 for all the formulations studied.

The British formulation showed only a small amount of total neutralization, rapidly reaching a peak pH of 4.6, and falling below pH 3 within 7 min. The U.S. formulation also rose rapidly to a peak pH of 6.1, and fell below pH 3 within 10 min. The Canadian and Swedish formulations behaved similarly, both taking 4 min to reach a peak pH of 4.8 and 4.6, respectively and nearly 20 min to fall below a pH of 3.

The in vitro pH profiles for the materials measured in and below the raft are shown in Fig. 2a to d. None of the formulations produced any detectable neutralization below the raft. The raft, however, maintained a pH elevated to above 3 for 60 min for the British formulation, 78 min for the U.S. formulation, 88 min for the Swedish formulation and 170 min for the Canadian formulation. The strengths of the rafts from each formulation are shown in Fig. 3. Comparisons were made between formulations using an unpaired Student's *t*-test.

The strongest raft is formed by the British formulation (2.7, S.D. $\pm$ 0.2 g), followed by the Canadian formulation (1.1, S.D. $\pm$ 0.3 g), Swedish (0.8, S.D. $\pm$ 0.2 g), and the U.S. formulation (0.4, S.D. $\pm$ 0.1 g). These results were obtained with 5 ml of antacid, except for the U.S. formulation,

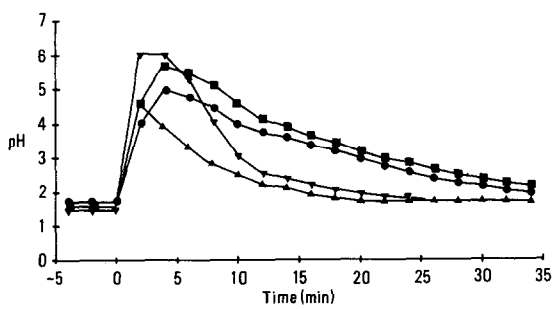

Fig. 1. Neutralization profiles of "Liquid Gaviscon" formulations. Conventional Rossett and Rice test raft is destroyed ($n = 5$, S.E.M < 0.2 pH unit). ▲, U.K. formulation; ▼, U.S. formulation; ●, Canadian formulation; and ■, Swedish formulation.

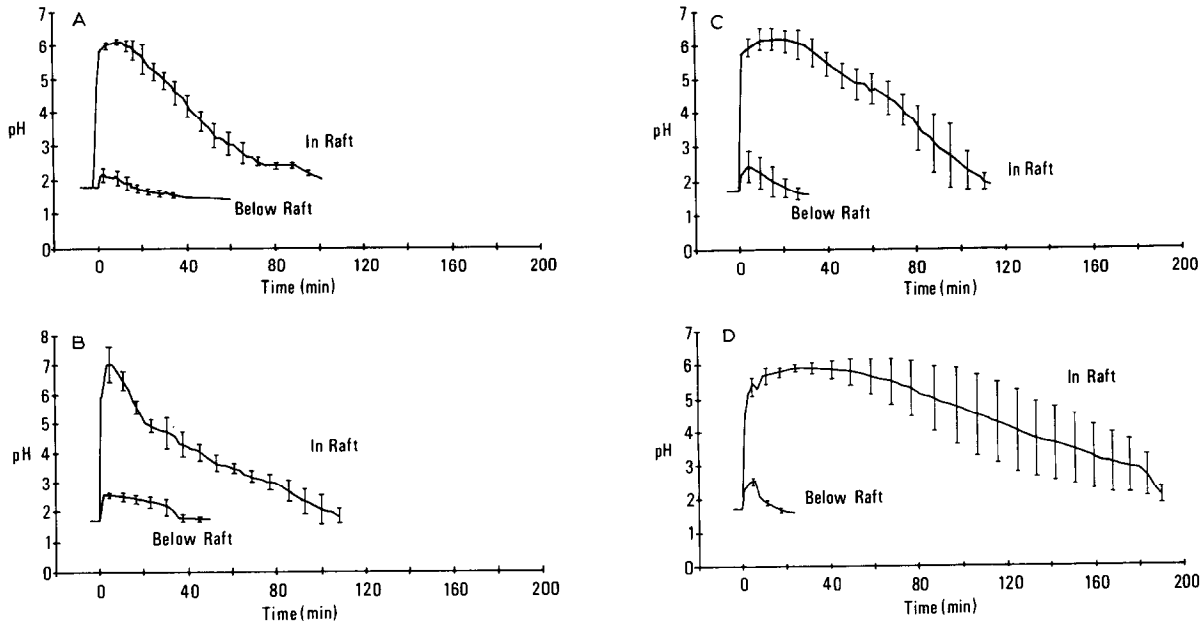

Fig. 2. Neutralization profile of "Liquid Gaviscon" in and below raft (modified Rossett and Rice test; $n = 5$, $\pm$S.E.M.). A: U.K. formulation (Reckitt and Colman). B: U.S. formulation (Marion Laboratories). C: Swedish formulation (Ferring). D: Canadian formulation (Winthrop Laboratories).

which formed a raft which was too weak to be measured, and the quoted strength refers to a raft formed by 10 ml of the preparation. It should be noted that the strengths are dependent on the measurement probe used, and should be regarded as a relative index of performance.

The British and Canadian formulations of "Liquid Gaviscon" appeared to attain full strength within 10 min, and ageing had no significant effect (Table 1) ($P > 0.95$).

The Swedish formulation showed a marked increase in strength on standing at 37°C, (t-test,

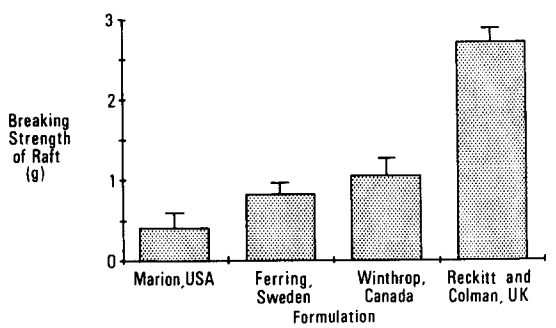

Fig. 3. Raft strengths of "Liquid Gaviscon" formulations. 5 ml of U.K., Swedish and Canadian formulations, 10 ml of U.S. formulation ($n = 6$, $\pm$ S.D.).

TABLE 1

EFFECT OF AGEING ON RAFT STRENGTH (MEAN $\pm$ S.E.M.)

Time	Formulations			
	U.K.	Sweden	U.S.A.	Canada
10 min	2.5 $\pm$ 0.2	0.83 $\pm$ 0.18	0.4 $\pm$ 0.34	1.05 $\pm$ 0.27
30 min	2.25 $\pm$ 0.19	1.55 $\pm$ 0.1	0.21 $\pm$ 0.23	1.46 $\pm$ 0.23
2 h	2.31 $\pm$ 0.24	1.60 $\pm$ 0.13	0.16 $\pm$ 0.02	1.29 $\pm$ 0.12

$P < 0.001$) whereas the raft formed by the U.S. formulation appeared to get weaker with time ($P < 0.02$).

Discussion

The test for antacid activity described by Rossett and Rice destroys the alginate raft due to the disruptive effect of the stirring, and the pH of the mixture is measured. The full neutralization capacity of the antacid component is not released because although the raft is destroyed, the alginate structure is fragmented and can still entrap the antacid material within the smaller pieces (Washington et al., 1985b, 1986).

The British formulation of "Liquid Gaviscon" contains only sufficient sodium bicarbonate to elevate the raft and so demonstrated only a small transient neutralization. The other three formulations contain additional antacid materials and hence produced prolonged neutralization profiles. The components of the various formulations are shown in Table 2.

Beckloff et al. (1972) and Hasan (1980) have reported that the alginate-antacid tablets do not affect the pH of the bulk of the gastric contents in vivo. Our results confirm that no change in pH occurs in the acid phase below the raft even in liquid formulations containing a large proportion of antacid. However, the incorporated antacid materials increased the time for which the raft pH remained above 3 and the rate of reaction of the antacid is reduced because it is trapped within the alginate gel. Aluminium hydroxide, when added to the British formulation of "Liquid Gaviscon" increased the time for which the raft pH remained above 3, but did not alter the pH below the raft (Washington et al., 1986).

To accommodate for the fact that the alginate content of the American formulation was approximately half of that of the others, the volume of this preparation used in the experiments was doubled. The differences in raft strength between the formulations thus cannot be due to the quantity of alginate present. The physicochemical properties of the alginic acid gel are primarily determined by the chain length and block structure, since alginic acid is composed of blocks of D-mannuronic acid (M-blocks), L-guluronic acid (G-blocks) in various proportions. The alginate chains are bonded together by calcium ions, predominantly at the G-blocks. As the amount of calcium is increased, the gel becomes strong, more shear force is required to liquefy it, and it reforms more quickly after disruption (McDowell, 1977). The addition of antacid materials can reduce the raft strength since aluminium or magnesium may display the calcium ions. Alteration of the size and charge of the ion may disrupt the ordered "egg-box" structure of the alginic acid gel.

The Marion formulation produced a very weak raft under the conditions of these experiments. This may be partly due to the aluminium hydroxide content which competes for acid with the carbonate component and so the formation of the carbon dioxide bubbles required to elevate the raft is slower. The magnesium carbonate reacts with acid more slowly than sodium bicarbonate, because it is insoluble in water. Preliminary data suggest that the formulation may form a slightly stronger raft in more concentrated acids.

TABLE 2

COMPOSITION OF "LIQUID GAVISCON" FORMULATIONS (10 ml)

Formulation	Alginate (mg)	Sodium bicarbonate (mg)	Aluminium hydroxide (mg)	Magnesium carbonate (mg)	Calcium carbonate (mg)
U.K.	500	267	–	–	–
Canada	500	*	200	–	–
U.S.A.	267	–	63.33	274.66 mg	–
Sweden	500	170	1 g	–	150 mg

* Quoted as 60 mg of sodium/10 ml which is equivalent to 219 mg of sodium bicarbonate in 10 ml.

The different "Liquid Gaviscon" formulation may produce their therapeutic benefits by different mechanisms, depending on their physical properties. Thus the preparations with the highest raft strengths, such as the British formulation, may act as a mechanical barrier reducing the number of reflux episodes. Evidence for the clinical reduction of reflux episodes following treatment with Gaviscon tablets (U.K.) has been obtained by Stanciu and Bennett (1974); however, these conclusions were based on the measurements of pH in the oesophagus which would not detect neutral reflux.

Those formulations which form weaker rafts may be refluxed preferentially to the gastric contents, without reduction of the number of reflux episodes (Malmud et al., 1979). Since the refluxed material is almost neutral, it is potentially much less damaging to the oesophagus. None of the "Gaviscon" formulations produce significant neutralization of the gastric contents. In practice any or all formulations may act by a combination of modes, and more detailed in vivo studies are required to evaluate their relative importance.

The literature concerning alginate-containing antacids is extensive, but often it is not clear whether the formulations referred to are administered in liquid or tablet form nor are the sources of the formulations stated. The present research highlights the extreme differences in raft strength and neutralization properties of medications bearing the same trade name and this may have clinical implications when dispensing parallel imports bearing the name "Gaviscon".

References

Amdrup, E. and Jakobsen B.M., Reflux esophagitis treated with Gaviscon. *Acta Chir. Scand.*, Suppl. 396 (1969) 16–17.

Beckloff, G.L., Chapman, J.H. and Shiverdecker P., Objective evaluation of an antacid with unusual properties. *J. Clin. Pharmacol.*, 12 (1972) 11–21.

Hasan, S.S., Treatment of moderate to severe gastro-oesophageal reflux with alginate/antacid combination. *Curr. Med. Res. Opin.*, 6 (1980) 645–648.

Malmud, L.S., Littlefield, J., Reilly, J., Stern, H., Rosenburg, R. and Fisher R.S., The mode of action of alginic acid compound in the reduction of gastro-oesophageal reflux. *J. Nucl. Med.*, 20 (1979) 1023–1028.

McDowell R.H., *Properties of Alginates*, Alginate Industries Ltd., Lithofox Ltd., London, 1977.

Rossett, N.E. and Rice, M.L., An in vitro evaluation of the efficacy of the more frequently used antacids with particular attention to tablets. *Gastroenterology*, 26 (1954) 490–495.

Stanciu, C. and Bennett, J.R., Alginate/antacid in the reduction of gastro-oesophageal reflux. *Lancet*, 1 (1974) 109–111.

Washington, N., Washington, C., Wilson C.G. and Davis S.S., Apparatus for measuring the strength of "raft-forming" antacids. *Proc. 45th Int. Congress of Pharm. Sci.*, Montreal, 1985a, p. 29 (Abstr.).

Washington, N., Washington, C., Wilson C.G. and Davis S.S., Effect of aluminium hydroxide on "raft-forming" antacids. *J. Pharm. Pharmacol.*, Suppl. 37 (1985b) 13P.

Washington, N., Washington, C., Wilson C.G. and Davis S.S., The effect of inclusion of aluminium hydroxide in alginate containing "raft-forming" antacids. *Int. J. Pharm.*, 28 (1986) 139–143.