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Review Article

Antacids: physiology versus pharmaceutics

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Introduction

Antacids are preparations which are primarily designed to neutralize gastric acid. Despite recent advances in the pharmacology of anti-secretory and cytoprotective agents, these materials still have a useful place in the treatment of a number of gastric complaints. Although dyspepsia is caused by a variety of disorders of gastric motility, and/or gastric secretory malfunction, the irritant property of hydrochloric acid is central to theories of the aetiology of dyspepsia. The capacity to neutralize gastric acid is, therefore, a prime factor in the efficacy of antacids. The objective in the design of many formulations is to achieve a prolonged period of neutralization by careful choice of ingredients. Unfortunately, the efficacy of a formulation is compromised by the physiological processes of removal of the antacid by gastric emptying and the rate of acid secretion.

The 'over-the-counter' (i.e. non-prescription) formulations are self-administered by the layman to relieve a variety of symptoms, for example, from the discomfort of overindulgence in food and alcohol, to dyspepsia and 'heartburn' (reflux oesophagitis). This breadth of indiscriminate use has led to antacids being regarded as trivial medicines. However, a study by Graham et al. (1983) revealed that a sample of the apparently healthy people who were regular antacid users often displayed some form of detectable organic disease, especially reflux oesophagitis. All believed that they had a physical basis for symptoms, but none would consult a physician. The same study reported that 50% of the American population have used an antacid at some point in their lives, and 27% take 2 or more doses a week. 75% of regular users take 6 or more doses weekly.

The compounds most frequently used in classical antacid formulations are weak bases and include sodium bicarbonate, calcium carbonate, magnesium carbonate, magnesium hydroxide, magnesium oxide, aluminium hydroxide, aluminium phosphate and magnesium trisilicate. Each compound has differences in chemical behaviour and pharmacology and they have been combined in various proportions in an attempt to produce an 'ideal' antacid. Other materials such as alginic acid, polydimethylsiloxane (dimethicone), and anticholinergic drugs may also be added for their complementary actions in the treatment of dyspepsia and suppression of reflux. The American Hospital Formulary lists over 120 antacid preparations composed of single ingredients or mixtures of materials in almost every conceivable combina-

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tion. In the United Kingdom and in other countries, attempts have been made to reduce the cost of health care by restriction in the choice of medicines. Much debate has been centred on the publication of the British Government's list of medicines prescribable within the National Health Service (the 'White List'). For antacids this has resulted in the reduction of the number of proprietary formulations containing mixtures of antacid materials. Although it is accepted that there is no 'ideal' antacid formulation, some of the materials remaining on the 'White List' are far from optimized in terms of both physiological and pharmaceutical considerations. However, in the present climate there is little incentive to invest in the design of better formulations.

Definitions of 'ideal' antacids vary enormously, but generally it is believed that a good antacid reacts rapidly with acid, buffers in the pH range of 3–6, has high acid neutralizing capacity and few or minimal side-effects. A buffer which elevates gastric pH from 1 to 3.5 eliminates over 99% of free hydrogen ions (Morrissey and Barreras, 1974) and since the pH scale is logarithmic, raising the pH further produces little additional effect on the hydrogen ion concentration. If the therapeutic objective is to inhibit the enzymatic activity of pepsin, then the pH must be raised to about 5.5 (Piper and Fenton, 1965). The optimum pH for maximum peptic activity is around pH 2; adjustment to pH 3–3.5 (the "target" pH for most formulations) increases the peptic activity to 3 times that in basal secretion at pH 1.3 (see Fig. 1).

Harvey (1980) has suggested that if the acid–pepsin combination is the attacking factor, it might be best to leave gastric acid output undisturbed rather than to try to neutralize it partially. Thus the long-held view that pH should be held between 3 and 5 to minimize proteolytic activity (Woolfson et al., 1985) should be questioned as within this pH range, the peptic activity is still 70% of its maximum (Fig. 1).

A sub-group of antacids contain alginates and a bicarbonate and these provide their therapeutic action by a different mechanism to the antacids which neutralize the gastric contents. These materials form a neutral, floating foamy layer or "raft" in the stomach, but do not significantly change the

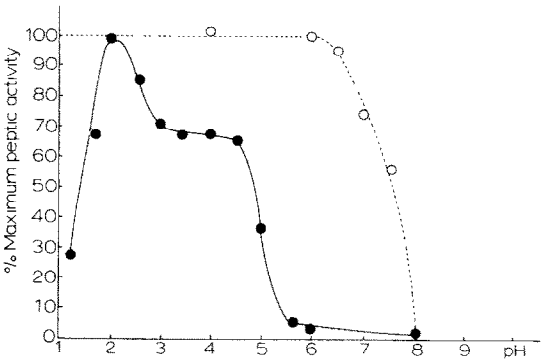

Fig. 1. Percentage maximum peptic activity versus pH (redrawn from Piper and Fenton, 1965). ·····, pH stability curve: ———, pH curve.

bulk pH. They are believed to act firstly as a mechanical barrier to suppress gastro-oesophageal reflux episodes, and secondly to be refluxed preferentially to the acidic gastric contents should a reflux event occur.

The cost–benefit ratio of liquid antacids is generally considered to be better than tablet antacids (Brody and Bachrach, 1959; Piper and Fenton, 1964). The most effective liquid antacids, which are composed of either aluminium and magnesium hydroxide mixtures or calcium carbonates, vary in buffering capacity from 3 to 4.2 mEquiv. of antacid per ml (Drake and Hollander, 1981). Tablets are, of course, more convenient to carry about than liquids. Littman and Pine (1975) comment that as the tablets have lower neutralizing capacities, patients often complain that they do not get relief if their medication is switched from liquid to tablet form. Palatability may be an important factor in compliance and a recent study suggested that individuals requiring antacid therapy should be allowed to choose from a range of preparations (Jacyna et al., 1984). However, there are certain groups of antacid formulations, for example, the "raft-forming" antacids, which are more suited for specific diseases such as oesophagitis.

Measurements of Neutralization Capacity

The measurement of total neutralizing capacity is a widely used test of antacid performance, and

has been developed into a variety of more specific techniques. These vary from those which simply measure total available neutralizing capacity, i.e. the standard acid-consuming capacity test, through methods which provide varying amounts of kinetic (i.e. reaction rate) information, to those which attempt to measure performance under conditions which bear some resemblance to those occurring in vivo. Typical of the intermediate class of tests are the Reheis reaction velocity test, which measures the time taken for the antacid to neutralize a sample of acid to pH 3.5, thus attempting to describe the time-dependent reaction rate by a single figure. The Mutch reaction velocity test is similar in that it measures the time for 78% of the antacid to be consumed (Mutch, 1946). More sophisticated tests monitor the reaction rate as a function of time, e.g. pH stat methods, which measure the amount of acid required to hold the system pH at a given level, usually 3 or 3.5 (Steinberg et al., 1965). This test was popularized by Fordtran et al. (1973).

Further modifications of the testing procedures led finally to models showing some resemblance to the expected neutralization profile of an antacid in the stomach. In the method described by Holbert et al. (1947), 2 g of antacid were added to a fixed volume of acid (150 ml of 0.1 N hydrochloric acid), then the pH measured as reactants were alternately removed and replaced by aliquots of fresh acid. The Rossett and Rice test (1954), and the similar Fuchs test (1949), pump acid continuously into the acid/antacid mixture and measure the resultant pH. Finally, the Beekman process (1960) removes reactants at a constant rate; a method which has been further modified by Smyth et al. (1976) with the inclusion of a second pump to keep the volume of the reactants constant. A similar approach has been used in this laboratory to modify the Rossett and Rice (1954) test (Washington et al., 1984, 1985a). pH radiotelemetry has been employed to determine the pH–time profiles for antacid formulations in vivo. The mean pH–time profile for 10 ml 'Asilone Suspension' (Berk Pharmaceuticals, U.K.), given 1 h after food is shown in Fig. 2a. The effect of these modifications on the in vitro pH–time profile for 'Asilone', a typical proprietary liquid antacid is shown in Fig. 2b. It can be seen that the duration of action is altered, but not the peak pH reached (Washington et al., 1984, 1985a). The antacid neutralization profile in vitro then more closely correlates with the results obtained by pH telemetry. However, for a strict analogy with gastric emptying (see later section), the reactant volume should continually decrease. This poses practical problems and a more pragmatic approach is to keep the volume of the reactants constant.

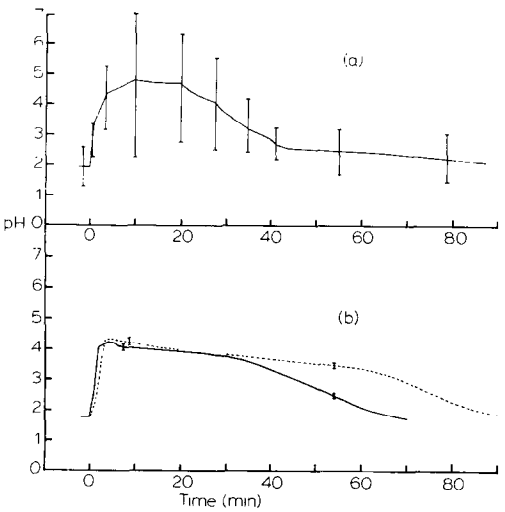

Fig. 2. Mean pH neutralization profiles for 10 ml dose of 'Asilone Suspension'. (a) In vivo (±S.D., n = 6). (b) In vitro: ·····, standard Rossett and Rice test (1954); ———, with modification as described by Washington et al. (1984, 1985a).

Total neutralization capacity is largely irrelevant in the therapeutic care of the patient since the amount of unreacted antacid remaining in the stomach is a dynamic balance between rate of reaction and rate of gastric emptying. Much of the confusion in the literature has been due to inappropriate in vitro tests and misinterpretation of the data. Berchtold et al. (1985) have claimed that in vitro tests overestimate in vivo neutralizing capacity of antacids in the presence of a meal. The group concluded that the loss of antacid activity in vivo is due to an interaction between aluminium hydroxide and food. The in vitro test which was used is the pH-Stat method described by Fordtran et al. (1973). This provides a measure of reaction rate and total neutralization capacity; it is a chem-

ical test and has no claim to be a physiological model for antacid activity. It is not surprising, therefore, that the antacid potencies are much higher in vitro. A test which simulates loss by gastric emptying would have provided a more appropriate in vivo/in vitro correlation.

Some workers have attempted to describe the total neutralization capacity of an antacid by integration of the area under the pH–time curve, in a manner analogous to that used in pharmacokinetics. However, the pH scale is logarithmic and this approach is mathematically incorrect; the area under the H^+ concentration–time curve gives a more rigorous measure of the total neutralization.

The in vitro tests cannot, of course, take into account the variations in antacid activity resulting from changes in gastric secretions, motility and interactions of antacids with the gastric mucosa. For example, Malagelada and Carlson (1979) reported that one ounce of liquid 'Maalox' (aluminium and magnesium hydroxides) increases gastric acid output by 16%. Similarly, there have been no satisfactory tests which model the behaviour of the raft-forming antacids (see later), used in the treatment of gastro-oesophageal reflux.

Recent work has been directed towards modifications of the Rossett and Rice test to correlate in vitro and in vivo performance of 'raft-forming' antacids (Washington et al., 1984, 1985a). There are two critical factors which need to be controlled in order to mimic the neutralization curve obtained in vivo. The first factor is to avoid a large increase in the volume of reactants during the neutralization as mentioned previously. The second factor is to avoid destruction of the raft. A collar placed around the stirrer shaft avoids vortex mixing whilst acid is pumped in at the bottom of the reaction vessel. The pH probe may then be positioned either in or under the raft. In vivo radiotelemetry data (Fig. 3a) suggests that a better correlation between in vivo and in vitro tests in the alginate raft is achieved when the acid input rate is reduced to 2 ml/min (representing conditions in the top of the stomach), a reflection of the distribution of parietal cells whose number decreases towards the top of the stomach. A comparison of the neutralization profiles for "Liquid Gaviscon" (Reckitt and Colman, U.K.) in the unmodified

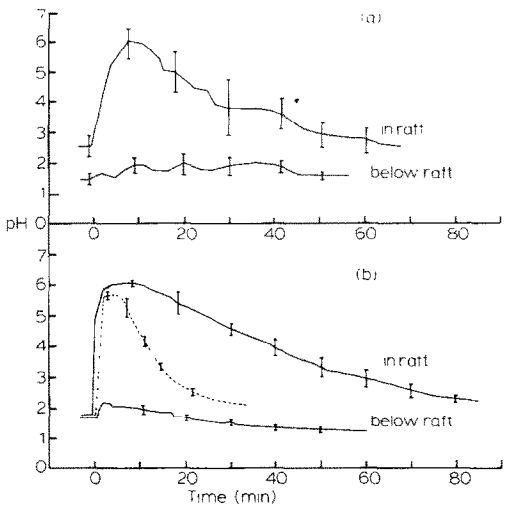

Fig. 3. Mean pH neutralization profiles for 10 ml dose of 'Liquid Gaviscon'. (a) In vivo (±S.D., n = 6). (b) In vitro: ·····, standard Rossett and Rice test (1954); ——— with modification as described by Washington et al. (1984, 1985a).

Rossett and Rice test and with the modifications described by Washington et al. (1984, 1985a) is shown in Fig. 3b.

Antacids and Food

The schedule of administration with regard to food is very important in the efficacy of antacid action. The presence of a meal in the stomach, not surprisingly, influences the behaviour of antacids, as demonstrated by Fordtran and Collyns (1966) and Deering and Malagelada (1977) who reported that various antacids elevated the gastric pH for longer periods when given 1 h after a meal than when administered 3–4 h after the meal. This is primarily due to the decrease in gastric emptying rate of the antacid in the presence of food. The delivery rate of calories to the duodenum is constant (Hunt and Stubbs, 1975) and the food remaining at 1 h delays the delivery of the antacid to the duodenum. Malagelada and Carlson (1979) estimated that a total of 20% of an antacid (Maalox) was emptied from the stomach unused, when two doses are given 1 and 3 h after a meal. The amount of antacid which is emptied unreacted is dependent upon the reaction rate of the neutral-

izing components. Magnesium trisilicate, for example, reacts very slowly and thus the majority of the dose leaves the stomach before it can have a useful effect (Harvey, 1980). Magnesium trisilicate alone fails the current U.S. Pharmacopaeia tests for non-prescription antacids as its rate of reaction is too slow and it cannot raise the pH to an acceptable range when acid is added to it at physiological rates (Washington et al., 1986a). Magnesium Trisilicate Mixture BP is used extensively in the pre-operative procedure for the prevention of Mendelson's syndrome (Crawford and Potter, 1984; O'Sullivan and Bullingham, 1984). However, the formulation owes all of its buffering power to other antacids present in the formulation (Washington et al., 1986a).

It has long been recognized that antacids given on an empty stomach are used very inefficiently (Grossman, 1956). In fasted volunteers 8 g of calcium carbonate has no more effect than 4 g on gastric pH, but 1 h after food the 8 g has a significantly more prolonged action than the 4 g dose (Fordtran and Collyns, 1966).

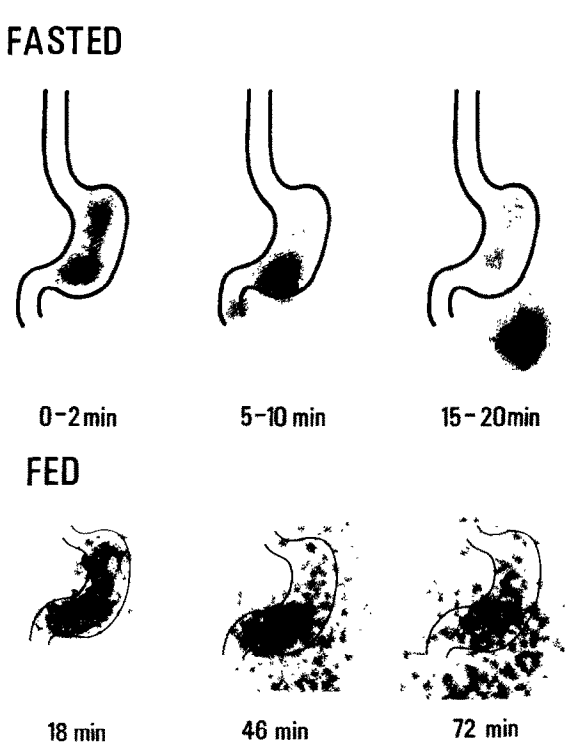

Fig. 4. Radionuclide images of ^{113m}In-labelled 'Asilone Suspension' given to: (a) fasted subjects; and (b) 30 min after a meal.

The volume of a liquid antacid remaining in the stomach has been measured directly by gamma scintigraphy. Jenkins et al. (1983) and May et al. (1984) found that a 10 ml dose of 'Asilone' (aluminium and magnesium hydroxide) emptied completely from a fasted stomach within 20 min, but persisted for over an hour if administered 30 min after a liquid meal (Fig. 4).

The pH of the gastric contents is elevated from a basal level of between 1 and 2, to between 5 and 7 by the diluting and buffering effect of a meal. The length of time that the meal elevates gastric pH depends upon the nature of the meal, but an antacid taken during the time that the gastric pH is still high will not have any measurable effect. After 1 h, a considerable proportion of a meal would have emptied, the remaining food being insufficient to maintain the high gastric pH, especially as the gastric secretion rate is increased by the meal. The interval between the meal and antacid dose is, therefore, critical both in terms of gastric emptying and pH.

How Much Antacid is Required?

The actual dose used and frequency of administration is a compromise, since frequent small doses are more effective than a smaller number of larger doses of antacid (Grossman, 1956). However, this may result in poor compliance which is reported to be a frequent problem with antacid therapy (Roth and Berger, 1960). It has been reported that patients take on average only half the prescribed dose of liquid antacid (Roth et al., 1970). One approach to this problem is to improve the low efficacy and not increase the dose of antacid. A typical dose sequence was suggested by Malagelada and Carlson (1979) to be about 80 mEquiv., 1 and 3 h after a meal (480 mEquiv. daily). Using this regimen, approximately 20% of the antacid was emptied unused, leaving 380 mEquiv. performing useful neutralization. The study by Kumar et al. (1984) suggests that a total neutralizing capacity of 207 mEquiv. daily was sufficient to provide maximum symptomatic and asymptomatic relief in

27 duodenal ulcer patients, and further dosage led to unwanted side-effects. The authors, however, gave no indication of when the patients were instructed to take the antacid in relation to meals. The major problem still to be overcome with antacid therapy is nighttime dosage, since the basal gastric acid secretion continues unchecked for longer periods than during the day.

Inclusion of Anticholinergic Drugs into Antacid Therapy

The time over which the last dose of antacid taken in the day can persist in the stomach is relatively short, the maximum being typically 2–3 h. This poses a problem for anti-ulcer therapy which has been approached in a number of ways, for example, the use of anticholinergics and H_2 receptor antagonists. Anticholinergic drugs are used as antispasmodic agents and also to reduce basal gastric acid output in the treatment of peptic ulcer. They decrease gastric motility at high doses, but at these concentrations produce debilitating side-effects such as a dry mouth, tachycardia and ocular disturbances. Furthermore, anticholinergics reduce the volume of gastric secretion but not necessarily the concentration of acid (Weiner, 1980) or the output of pepsin and mucus (Piper and Stiel, 1962; Piper, 1966). Anticholinergic drugs, therefore, do not reduce the peptic digestive capacity of gastric juice, but facilitate the neutralization of gastric juice by food and antacids (Piper, 1967). The literature on the efficacy of anticholinergics is divided, but the studies which report that the drugs are ineffective in treating ulceration, frequently attempt to use the anticholinergic alone to decrease basal gastric acid secretion (Trevino et al., 1967; Kay et al., 1970). Baume et al. (1972) found that an anticholinergic agent used with an antacid improved the healing rates of gastric ulcer compared to the use of antacid alone. Preparations containing anticholinergics should be avoided by patients with gastro-oesophageal reflux as they decrease lower oesophageal sphincter pressure and worsen symptoms (Lind et al., 1968). Antacids have been shown to decrease the absorption of anticholinergics, possibly to sub-therapeutic levels and it has been recommended that the anticholinergic drug should be administered before the antacid to avoid this occurrence (Barger, 1975). This does, however, complicate the dosage regimen, which would probably decrease compliance. A sustained release form of hyoscyamine given 2 h before an antacid material has been shown to increase the duration of action (time of gastric pH above 3) of the antacid from 30 to 70 min (Dotevall and Walan, 1967); in part this is likely to be due to the decrease in gastric acid secretion produced by the anticholinergic. The success of anticholinergic therapy is clearly dependent upon dosage regimen with respect to meals and antacid intake.

Effects of Aluminium and Calcium Ions on Gastric Emptying

It interesting to note that aluminium and calcium ions released from antacid formulations have a direct influence on the rate of gastric emptying. Calcium chloride and ethylenediaminetetraacetic acid each significantly prolonged the gastric emptying time of a test meal, but when the two materials were administered in combination, there was no change from the control (Shafer et al., 1985). Both increasing and decreasing luminal gastric calcium content prolongs gastric emptying. The role of calcium in the control of gastric emptying appears complex and not yet understood. Hurwitz et al. (1976) showed that increasing concentrations of free aluminium ions changed the half-time of gastric emptying of water from 13.1 min to 48 min. Increasing pH raises the hydroxyl ion concentration, decreasing the concentration of free aluminium ions (the solubility product of aluminium hydroxide is a constant). Consequently an aluminium hydroxide-based antacid, which buffers at a pH which is at the lower end of the therapeutic range, will produce a high concentration of free aluminium ions in the stomach and thus delay its emptying compared to an aluminium hydroxide-containing mixture buffering at a higher pH.

Functional cytoprotection has been demonstrated in rats for Al^{3+} antacids which is indepen-

dent of acid neutralization (Szelenyi and Postius, 1985). At various times before inducing ulceration with ethanol the animals were pre-treated with aluminium-containing antacids. They all inhibited gastric ulceration in a dose-dependent manner, and were all equally effective when considered by aluminium ion content. The luminal prostaglandin E_2 was found to be increased. Pre-treatment with indomethacin decreased, but did not abolish the ulcer-protective effect of the antacids. It is speculated that the ulcer-protective effects of aluminium-containing antacids may be mediated through a direct action on prostaglandin release.

Anti-Foaming Agents

Antacid formulations may contain other materials in addition to the basic compounds which perform neutralization, for example, dimethicone (polydimethylsiloxane) or simethicone (dimethicone and silica; also known as activated dimethicone). Dimethicone is added as an anti-foaming and deflatulent agent, the silica-activated form being the more effective (Birtley et al., 1973). It is believed to change the surface tension of the smaller bubbles so that they coalesce, forming larger bubbles which are easier to eliminate (Rider and Moeller, 1960). The original rationale for including dimethicone in antacids appears to be that this material alleviated bloat in ruminants (Quin et al., 1949). There is evidence that activated dimethicone alleviates foaming in rat models and provides symptomatic relief of gaseous discomfort in humans (Rider and Moeller, 1960; Bernstein and Kasich, 1974). The X-ray contrast techniques used to detect the presence of foam do not, however, provide quantitative information. The addition of dimethicone to aluminium hydroxide-containing antacids is somewhat questionable as the aluminium hydroxide interferes with the defoaming action of the dimethicone, and the dimethicone decreases the neutralization power of aluminium hydroxide (Stead et al., 1978).

It is also claimed that dimethicone has a mucosal protective action, but there is little published evidence that dimethicone provides much protection against acid or stress-induced ulcers. It has, however, been shown to protect against aspirin-induced ulceration (Birtley et al., 1973). Peptic ulcers of the stomach and duodenum only develop in the presence of hydrochloric acid and pepsin since ulceration of this type is unknown in achlorhydrics (Dotevall and Walan, 1967). The aspirin-induced ulceration models do not provide conclusive evidence for a mucosal protective action of dimethicone against peptic ulceration, but rather suggest that dimethicone may have a role in alleviating gastrointestinal upset from prolonged aspirin or other non-steroidal anti-inflammatory drug therapy, e.g. in arthritic patients. There have been many clinical trials which have established that dimethicone is of value in the symptomatic relief of dyspepsia and "gas". However, the data available are based mainly on analysis of questionnaires and have not contributed to knowledge of the mechanism of action of the dimethicone component. In a typical study, for example that reported by Cobden et al. (1981), a magnesium hydroxide/aluminium hydroxide suspension produced a significant benefit over a dimethicone/hydrotalcite antacid in the treatment of symptomatic gastritis. Unfortunately, the number of variables in this trial do not allow for firm conclusions to be drawn. A basic study in humans showing an increased mucosal protective action of an antacid containing dimethicone against the same antacid without dimethicone has not been found by the authors despite an extensive search.

Floating Antacids

The group of alginate-containing preparations is also classed with the antacids, e.g. 'Gaviscon' (Reckitt and Colman Pharmaceuticals, U.K.). This preparation is a raft-forming antacid; the sodium bicarbonate which it contains is not used for its neutralization properties, but rather to produce carbon dioxide bubbles by reaction with the gastric acid (Harcus, 1978; Beckloff et al., 1972; Beeley and Warner, 1972). The gas bubbles become entrapped in the gel structure of the alginate and produce a floating layer on the gastric contents. May et al. (1984) demonstrated raft formation in vivo and delayed gastric emptying of an alginate

preparation compared to a liquid antacid when taken 30 min after food (Fig. 5). It is interesting to note that patients with gastro-oesophageal reflux have a slower than normal gastric emptying (Valanzuela et al., 1981).

Raft antacids are believed to act by the neutral raft material being refluxed preferentially to acidic gastric contents (Malmud et al., 1979; May et al., 1984). Some alginate preparations also contain antacid materials in addition to that required to raise the raft. The gastric contents beneath the raft remain acid and the only acid consumed is a small amount used to elevate the raft.

"Liquid Gaviscon" (Reckitt and Colman, Hull) as manufactured in the U.K. does not contain any additional antacid material, but other "Gaviscon" formulations by Marion Laboratories (U.S.A.) and Winthrop Laboratories (Canada) both contain aluminium hydroxide. Inclusion of aluminium hydroxide into "Liquid Gaviscon" (U.K.) has been shown to alter the raft-forming properties of the alginate, decreasing its strength and its barrier function (Fig. 6) (Washington et al., 1985c, 1986b). The pharmacodynamic action of the "Gaviscon" formulations may vary according to the country of origin which poses an interesting problem in the standardization of medications, especially as the same trade-name is used in each case.

Hasan (1980) reported that the aluminium hydroxide and magnesium trisilicate in a proprietary alginate-containing antacid remained associated with the alginate foam and did not affect the gastric pH. This has been confirmed in vitro (Washington et al., 1984, 1985a).

This type of preparation appears to be most useful in the treatment of gastro-oesophageal reflux rather than gastric or duodenal ulceration, since the antacid component remains associated with the raft material. A study by Graham and Patterson (1983) reported that 'Maalox' (Rorer Pharmaceuticals) was not found to produce significant improvement over a placebo in a double-blind endoscopic trial in the treatment of chronic heartburn patients. However, the alginate containing formulations have been reported to be significantly more useful than conventional antacids and

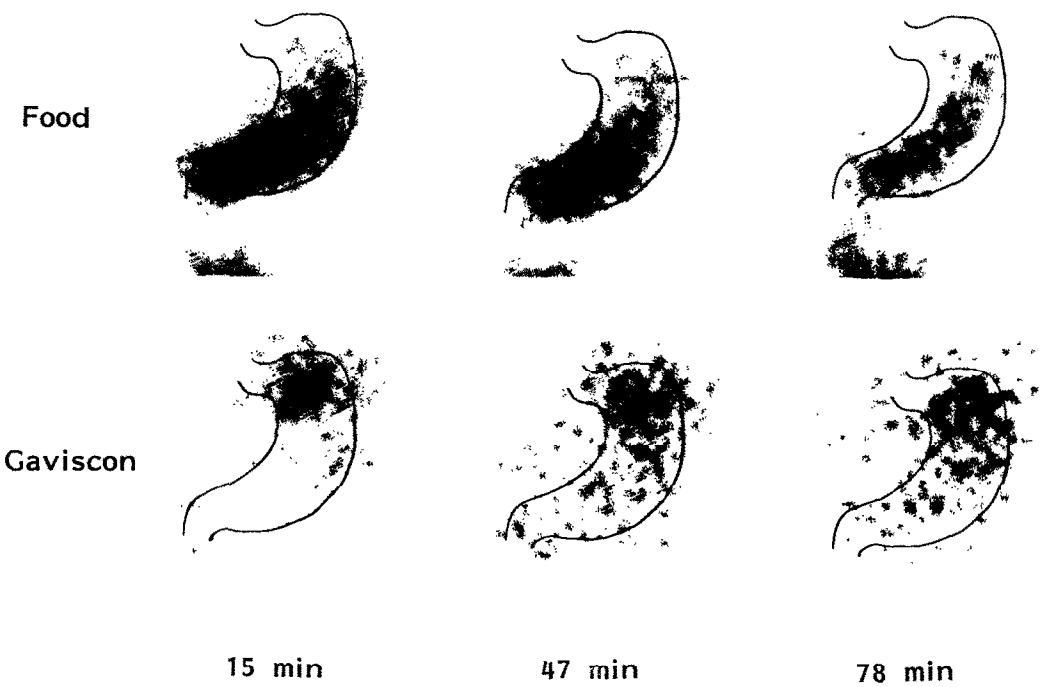

Fig. 5. Radionuclide images of ^{99m}Tc-labelled 'Clinifeed' and ^{113m}In-labelled 'Liquid Gaviscon' in the stomach at 15, 47 and 78 min after administration (May et al., 1984).

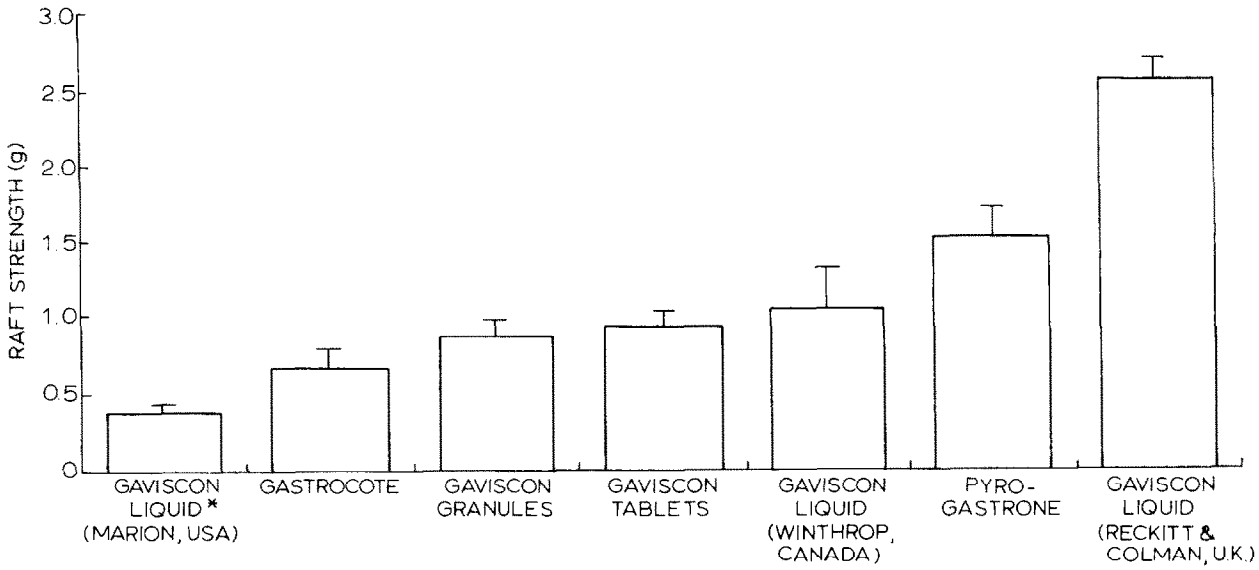

Fig. 6. Breaking strength of the rafts formed by a number of proprietary alginate-containing formulations ($\pm$S.D., n = 5) (after Washington et al., 1986b).

placebos in the relief of heartburn and epigastric pain in patients with gastro-oesophageal reflux (Williams et al., 1979; Chevrel, 1980). It is also more effective than a preparation containing the matched antacid without the alginate (Barnardo et al., 1975; Chaput De Saintonge et al., 1978; Stanciu and Bennett, 1974) or just the alginate alone (Beeley and Warner, 1972). Laitinen et al. (1985) reported that sucralfate and 'Gaviscon' powder produced healing of oesophagitis in 53% and 34% of patients, respectively. The patients were instructed to take the preparations half-an-hour before meals, at bed-time and also whenever necessary to relieve symptoms. The data obtained are not necessarily relevant as the optimum dosage schedule for 'Gaviscon' was not followed. It is recommended that 'Gaviscon' should be taken after meals, to enable it to form a raft on the gastric contents.

Bennett et al. (1984) reported an effect of posture on the gastric emptying of a raft-forming alginate preparation; it was found to empty faster than food in subjects lying on their left side, and slower in subjects lying on their right. This will, of course, influence the emptying of the dose of antacid taken immediately before retiring. It is interesting to note that even though the alginate raft is emptied more slowly when the subject is lying on the right side, the preparation would no longer provide protection to the oesophagus from the stomach contents. Posture is an important factor in the nighttime treatment of this condition as patients with reflux oesophagitis suffer symptoms more frequently when lying on their right side (Pattrick, 1970).

The use of alginate-containing antacids should be restricted to incidences of gastro-oesophageal reflux since their mode of action makes them inappropriate for treating cases of dyspepsia or just gastric or duodenal ulceration. Heartburn is more likely to be related to the presence of certain conditions e.g. gastritis (100%) and oesophagitis (76%) but not duodenitis (52%) (Earlam et al., 1985).

Competition From New Agents

Antacids are generally considered to be superceded by the new anti-ulcer agents, e.g. H_2 receptor antagonists, sucralfate, K^+,H^+-ATPase inhibitors or gastric muscarinic receptor antagonists. The intervention at receptor level is considered to

be a more elegant and effective method of reducing hydrogen ion concentration in the stomach. The recent trend in therapy appears to attempt to elevate gastric pH for the longest possible period of time (e.g. Sharma et al., 1984). It should be remembered that gastric acid is also produced by the body as a defence mechanism to the ingestion of harmful micro-organisms. Lack of this protection has been postulated as a possible cause of gastric cancer in patients whose stomach pH has been elevated for long periods. H_2 antagonists reduce the sensation of heartburn, but do not reduce regurgitation or dysphagia (Berstad, 1981) and thus they would not protect the oesophagus from injury from bile salts.

It appears that antacids, which have provided symptomatic relief for many years, are being overlooked in favour of more sophisticated treatments. The rationale for the use of more potent drugs is not always certain. Ippoliti et al. (1983) reported that cimetidine produced no advantage over antacids in the rate of healing of duodenal ulcer or the frequency of recurrence of the ulcer. Cimetidine has also been reported to occasionally fail in the treatment of Zollinger-Ellison Syndrome (Ziemniak et al., 1983). Antacid therapy, therefore, still remains a viable alternative to merely increasing the dose of H_2 receptor antagonist, or looking for more potent drugs.

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