Alginate rafts and their characterisation

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Abstract

Alginate/antacid anti-reflux preparations are designed to provide symptom relief by forming a physical barrier on top of the stomach contents in the form of a neutral floating gel or raft. This study tested the in vitro effectiveness of a range of liquid products in forming rafts that were cohesive, buoyant, voluminous, resistant to reflux and durable under conditions of movement (resilient). The products tested had a wide range of acid neutralising capacities (ANCs). It was found that products with a high ANC and no calcium ion source formed rafts of low strength, weight and volume, which appeared more as floating precipitates than coherent gels. Products with a high ANC and a calcium ion source formed medium strength, weight and volume rafts. Products with a low ANC formed strong coherent rafts with medium to large weight and volume, and those with low ANC and a calcium ion source formed the strongest rafts. Products with stronger rafts were found to be more resilient and more resistant to reflux in an in vitro reflux model. Significant overall differences in raft buoyancy were found between products forming coherent rafts but these could not be related to the product formulation or amount of available carbon dioxide.

Keywords: Alginate; Gastro-oesophageal reflux; Raft; Formulation

1. Introduction

One of the primary treatments for gastro-oesophageal reflux disease (GORD) is the administration of alginate/antacid anti-reflux preparations. These provide a physical barrier on contact with the stomach contents in the form of a neutral floating gel or raft. This physical mode of action is quite distinct from the chemical neutralisation of the bulk gastric contents provided by antacids alone, although alginate raft forming preparations have often, mistakenly, been classified as antacids. The advantage of alginate/antacid combinations over antacids alone is that they provide longer lasting symptom relief, even though relief is rapid in both cases (Chevrel, 1980; Lindow et al., 2003). Their rapid onset of action makes them more suitable for self-medication than pharmacologically acting acid suppressants such as H2-receptor antagonists or proton pump inhibitors (Washington et al., 1999). This has also led to their successful use as a well tolerated,
non-systemic treatment for prevention of relapse in healed reflux oesophagitis (Poynard et al., 1993) and for the treatment of heartburn in pregnancy (Bryan et al., 2001; Lindow et al., 2003).

Alginate rafts may be formed in liquid products by the action of gastric fluid on a soluble alginate to form an insoluble gel of alginic acid. They may also be formed by the interaction of soluble alginate with metal ions released by acid from an insoluble antacid such as calcium carbonate. The simultaneous action of gastric acid on a bicarbonate salt produces carbon dioxide, which should ideally be trapped inside the alginate gel to aid buoyancy of the raft.

Several features of rafts formed by alginate/antacid anti-reflux preparations are useful in forming an effective long lasting barrier between corrosive gastric fluid and the oesophageal mucosa. Such rafts would be expected to be cohesive, buoyant, voluminous, resistant to reflux into the oesophagus and not easily broken up by movement in the stomach.

It would be expected that formulation factors such as the amounts and types of antacids used, their ratio to the alginate dose, the acid neutralising capacity, the concentration and the viscosity of each formulation should have an effect on the formation of the raft. There are a number of alginate/antacid formulations sold in the major healthcare markets of the world (e.g. Europe, USA and Australia) for this type of product. Some products are intended primarily as antacids and therefore have been formulated to have a high acid neutralising capacity, whereas others are intended to have raft formation as their main mechanism of action and include antacids only to assist in this physical action.

Alginate rafts may be formed in liquid products marketed at that time and showed that there was a wide range of raft strengths according to seaweed species, part of the plant (stem or leaf), sea conditions and age (Haug et al., 1974; Moe et al., 1995). The most effective alginates for rapid strong gel formation in liquid alginate/antacid products are generally those with a high GG content and a low molecular weight. This is because the high alginate concentration needed in liquid products demands a low molecular weight, low viscosity polymer and high GG alginates form stronger gels with divalent cations. Low molecular weight alginate extracted from the stipe (stem) of Laminaria hyperborea, a species of brown seaweed which grows in rough seas along the western coast of Norway, has one of the highest naturally occurring guluronate contents (up to 70%) and is commonly used in alginate/antacid anti-reflux preparations.

Clinical evidence has shown that alginate products form rafts on top of the stomach contents after a meal and that they are effective in controlling GORD symptoms. Studies using a variety of techniques such as combined pH and X-rays (Goodall et al., 1977), γ scintigraphy (Knight et al., 1988; May et al., 1984; Washington et al., 1993, 1998, Lambert et al., 1990) and magnetic resonance imaging (Paterson et al., 2000; Marciani et al., 2002) have been used to visualise rafts in vivo and highlight characteristic differences between the some of the products available.

Previously reported in vitro raft characterisation studies have been based on measurement of pH in and below the raft or on measurement of raft strength. Those reporting on pH (Washington et al., 1985; Vatier et al., 1998) showed that alginate products such as Gaviscon Liquid do not neutralise the bulk of the acid but maintain a high pH inside the raft for an extended period. Several studies by Washington et al. (1985, 1986a, b, 1987) report the use of an early raft strength method, based on the same principles as the current method described here. These studies showed that there was a wide range of raft strengths for liquid alginate products marketed at that time and that the raft strength was reduced by the inclusion of antacids such as aluminium hydroxide. There have been no published papers covering the quantitative
determination of other important parameters such as
raft buoyancy, reflux resistance or resilience.

The aims of this research were to develop in vitro
methods to measure all characteristics (strength or
coherence, volume, buoyancy, reflux resistance and
resilience) useful as indicators for good in vivo raft per-
formance and to draw conclusions about the formula-
tion ingredients necessary to achieve this, from testing
a wide range of marketed liquid alginate products.

2. Materials and methods

2.1. Materials

Liquid alginate products investigated were: Algi-
con (Rhone-Poulenc Rorer, UK), Gastrocote (Seton
Healthcare, UK), Gaviscon Advance and Gaviscon
Liquid (Reckitt Benckiser Healthcare, UK), Gaviscon
Liquid Antacid, Regular Strength and Gaviscon Liq-
uid Antacid, Extra Strength (Glaxo SmithKline Con-
sumer Healthcare, USA), Mylanta Heartburn Relief
(Warner Lambert, Australia), Peptac Liquid (Baker
Norton, UK) and Rennie Duo (Roche Products, UK).

Low viscosity sodium alginates extracted from sev-
eral species were obtained from FMC Biopolymer,
Drammen, Norway, and were used to prepare sam-
pies of Gaviscon Liquid for comparative raft formation
studies.

2.2. Methods

2.2.1. Raft strength

Rafts were formed by adding a maximum dose of
liquid product to 150 ml of 0.1 M HCl, maintained at
37 °C in a 250 ml low-form glass beaker. Each raft was
formed around an L-shaped stainless steel wire probe
held upright in the beaker throughout the whole period
(30 min) of raft development. After 30 min of raft de-
velopment, the beaker was placed on the table of a TA-
XT2 Texture Analyser (Stable Micro Systems, UK),
the wire probe was hooked onto the Texture Analyser
arm and pulled vertically up through the raft at a rate of
5 mm/s. The force (g) required to pull the wire probe up
through the raft, was recorded by the Texture Analyser.
A diagram of the raft strength measurement apparatus
is shown in Fig. 1.

2.2.2. Raft volume and raft weight

Rafts were formed and developed for 30 min in glass
beakers, as above, but without the inclusion of a wire
probe. Each beaker used for raft formation was pre-
weighed (W1). The position to which the top of each raft
reached was marked on the outside of the beaker. The

Fig. 1. Raft strength measurement.
total weight of the beaker and contents was obtained after raft development ($W_2$). The raft was then removed from the beaker by carefully decanting off the subnatant liquid and tipping the raft into a pre-tared plastic weighing boat. This was left to stand for 30 s, excess subnatant liquid was drained off and the raft was weighed ($W_3$). Remaining liquid was removed from the inside of the beaker with a paper towel and it was then refilled with water to the marked position and weighed ($W_4$).

The volume of each raft was then calculated from the formula: 

$$\text{raft volume} = (W_4 - W_1) - (W_2 - W_1 - W_3),$$

where raft volume is measured in ml. and all weights are measured in g. The formula assumes that the density of the subnatant liquid is the same as that of water.

### 2.2.3. Reflux resistance

In this method rafts were forced to either extrude or rupture through an orifice similar in cross sectional area to the relaxed lower oesophageal sphincter and resistance to this simulated reflux was measured using the TA-XT2 Texture Analyser. This required the Texture Analyser to be fitted with a HDP90 heavy duty platform accessory and the use of a HDPFPE forward extrusion accessory in which to form the rafts. A diagram of this apparatus for raft formation and reflux resistance testing is shown in Fig. 2.

Rafts were formed by adding a maximum dose of liquid product to 150 ml of 0.1 M HCl, previously equilibrated at 37 °C, inside a cylindrical forward extrusion cell fitted with a base disc giving an extrusion orifice of 10, 15, or 20 mm diameter, in a beaker. After raft development for 30 min, the beaker and extrusion cell were carefully inverted, allowing excess liquid to decant off and leaving the formed raft in the bottom of the cell. The cell was then placed on the raised platform of the TA-XT2 Texture Analyser as shown in Fig. 2.

Resistance to reflux by extrusion was measured by the Texture Analyser as the maximum force required to drive the raft through the orifice with a plunger fitted to the arm. Resistance to reflux by rupture was measured by the Texture Analyser as the maximum force required to break the raft, through a 10 mm diameter orifice only, with a 9 mm diameter cylindrical rod fitted to the arm.

### 2.2.4. Raft resilience

The objective of this test was to give an indication of the durability of product rafts under more vigorous movement conditions than those of the foregoing
methods. Rafts were formed in 200 ml glass jars by adding a maximum dose of liquid product to 150 ml of 0.1 M HCl, previously equilibrated at 37 °C. Rafts were developed for 30 min, then the jars were capped and placed in a tumble mixer (Turbula T2C, W.A. Bachofen AG, Basle), set to rotate at 20 rpm, to simulate gastric agitation. The rafts were assessed visually for gel size and coherence after total periods of agitation of 2, 5, 10, 20, 30, 45, and to a maximum of 60 min, or until such time that a raft could no longer be detected. A raft was defined, for visual assessment, as two or more floating gels at least 15 mm in diameter. Raft resilience was defined as the last time point at which a raft was observed.

3. Results

Nine products were tested at least 10 times for raft strength, weight, volume and resilience. Observations of the speed and character of raft formation in the beaker were made and are presented in Table 1. The speed of formation was assessed as immediate if a floating raft was formed within a few seconds of addition of product to acid, and slow if not. Flotation was assessed as complete if all insoluble material rose to the liquid surface. Some products formed some insoluble material which sank to the bottom of the beaker and remained there for the full 30 min raft development time. This was assessed as partial flotation. In two products most of the insoluble material remained on the bottom of the beaker and this was assessed as very low flotation. The coherence of rafts was observed when removed from the beaker for weighing. Coherence was assessed as good if the rafts held together in a single mass during removal, but poor if they broke up into small particles.

It was obvious from these initial observations that those products forming only a small amount of floating (mostly particulate) material would be unlikely to give consistent raft weight and volume results. Table 2 presents the mean raft strength, weight and volume results for the nine products tested.

The errors inherent in each result are shown as coefficient of variation (CV%), which is the standard deviation expressed as a percentage of the mean result.

The small amount of floating material formed by the Gaviscon Regular Strength (USA), Gaviscon Extra Strength (USA) and Algicon products did not give consistent weight or volume results as the large errors for these three products show.

Table 3 shows the medians and ranges of the raft resilience measurements for each product.

Two products only (Gaviscon Advance and Gaviscon Liquid) were assessed for reflux resistance. These were chosen because they formed alginate rafts with very different strength, weight, volume and resilience, but both contained the same amount of sodium alginate per dose.

Six rafts were tested for each product, through each orifice size. Fig. 3 shows the variation of extrusion force with orifice size for the two products. The mean force required to extrude Gaviscon Advance through the 10 mm diameter orifice, at 3.0 kg, was significantly greater than that required for Gaviscon Liquid, at 2.3 kg. The mean force required to extrude both products decreased with orifice size, but at the largest orifice diameter of 20 mm there was no significant difference between the products. Resistance to reflux by rupture was measured for the two products through

<table>
<thead>
<tr>
<th>Product</th>
<th>Formation speed</th>
<th>Flotation</th>
<th>Coherence</th>
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<tbody>
<tr>
<td>Algicon</td>
<td>Immediate</td>
<td>Partial</td>
<td>Poor</td>
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<tr>
<td>Gastrocote</td>
<td>Slow</td>
<td>Partial</td>
<td>Good</td>
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<tr>
<td>Gaviscon Advance</td>
<td>Immediate</td>
<td>Complete</td>
<td>Good</td>
</tr>
<tr>
<td>Gaviscon Liquid</td>
<td>Immediate</td>
<td>Complete</td>
<td>Good</td>
</tr>
<tr>
<td>Gaviscon Regular Strength (USA)</td>
<td>Slow</td>
<td>Very low</td>
<td>Poor</td>
</tr>
<tr>
<td>Gaviscon Extra Strength (USA)</td>
<td>Slow</td>
<td>Complete</td>
<td>Good</td>
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<tr>
<td>Mylanta Heartburn Relief</td>
<td>Immediate</td>
<td>Complete</td>
<td>Good</td>
</tr>
<tr>
<td>Pepcid</td>
<td>Slow</td>
<td>Partial</td>
<td>Good</td>
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<tr>
<td>Rennie Duo</td>
<td>Immediate</td>
<td>Complete</td>
<td>Good</td>
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only the 10 mm diameter orifice. The mean force required to rupture Gaviscon Advance rafts, 47.4 g, was statistically significantly greater (p < 0.001) than that for Gaviscon Liquid, 25.2 g. The results indicate that rafts of Gaviscon Advance are more resistant to simulated reflux than those of Gaviscon Liquid, either by an extrusion or a rupture mechanism.

Table 4 shows the rafting performance of batches of Gaviscon Liquid prepared with low molecular weight sodium alginates conforming to the Ph. Eur monograph but derived from different sources of seaweed. Rafts were formed and strength measured by the method described in Section 2.2.1 and the visual form and buoyancy of the rafts was observed. It can be seen from the results in Table 4 that product manufactured with alginate derived from L. hyperborea stem formed high strength (12.1 g) rafts with a coherent structure, large volume and good buoyancy. Product

- Gaviscon Liquid
- Gaviscon Advano

** Values significantly different at these orifice diameters (p < 0.001)

Fig. 3. Variation of extrusion force with orifice size for two products: (■) Gaviscon Liquid; (♦) Gaviscon Advance; (**) values significantly different at these orifice diameters (p < 0.001).
manufactured with alginate derived from the leaf of *L. hyperborea* formed similar rafts but with a statistically significantly lower raft strength (4.3 g, \( p < 0.001 \)). Leaf alginate has a more flexible chain structure with less GG blocks than stem alginate, resulting in less ability to cross-link with calcium and consequently a weaker gel structure.

Alginates derived from other species such as *Durvilia antarctica* and *Lessonia nigrescens* have less GG blocks in their chain structure and these are seen to form rafts with low buoyancy and low raft strength. Product manufactured with alginate derived from a mixture of *D. Antarctica* (80%) and *L. nigrescens* (20%) had raft strength (4.0 g) that was statistically significantly lower (\( p < 0.001 \)) than product made with alginate derived from *L. hyperborea* stem. Product manufactured with alginate derived from *L. nigrescens* only had raft strength (6.7 g) that was also statistically significantly lower (\( p < 0.001 \)) than product made with alginate derived from *L. hyperborea* stem. In the case of product made from alginate extracted from *Ascophyllum nodosum* no raft is formed at all: only a cloudy precipitate.

The type of alginate used is therefore very important in determining the performance characteristics of a rafting product, particularly in the case of a product in which the raft is strengthened by calcium.

### 4. Discussion

In each of the raft characterisation methods described above, identical conditions for raft formation and development were purposely chosen so that the different raft characteristics could be compared with each other and across a range of liquid alginate/antacid products. The maximum dose of each product was chosen

<table>
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<th>Table 5 Product active ingredients and ANCs</th>
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<td><strong>Product</strong></td>
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<tr>
<td>Algicon</td>
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<td>Gastrocote</td>
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<td>Gaviscon Advance</td>
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<td>Gaviscon Liquid, Peptac</td>
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<tr>
<td>Gaviscon Regular Strength (USA)</td>
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<td>Gaviscon Extra Strength (USA)</td>
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<td>Mylanta Heartburn Relief</td>
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<tr>
<td>Rennie Duo</td>
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to maximise the measurements of the various raft characteristics. An acid concentration of 0.1 M was chosen because it was known that some products do not reliably form rafts at lower concentrations.

The products tested represent a wide range of alginate/antacid formulations with different acid neutralising capacities (ANCs). Table 5 shows the named active ingredients and theoretical ANC of each product. ANC have been calculated only from the known antacid ingredients of each product, disregarding any small effect that the alginate ingredient may have on the ANC. They have also been calculated for the maximum recommended dose of each product, instead of the more usually quoted minimum dose, to make them relevant to the raft characterisation studies described here. Table 5 also illustrates the marked differences between Gaviscon liquid products marketed in the UK and the USA, a fact highlighted (Washington et al., 1986a) in a paper comparing their raft strength and neutralisation profiles.

Sodium alginate is listed as an inactive ingredient in the two products from the USA. These products are classified only as liquid antacids although they are also described as barrier products. Alginate are accepted as active ingredients in the British and European pharmacopoeias. The products from the UK and Australia therefore all quote alginate as an active ingredient. A polymer, such as alginate, which can gel to form a floating mass or raft in the stomach is an essential ingredient of anti-reflux products intended to work by a barrier action. All of the products also contain an antacid (sodium bicarbonate, potassium bicarbonate or magnesium carbonate), which may cross-link the alginate polymer chains to form a gel or precipitate in acid conditions. Gaviscon Advance also contains calcium carbonate although this is not listed as an active ingredient and therefore does not appear in Table 5. This interaction would be essential to form a strong, coherent raft in the weakly acidic conditions of the post-prandial stomach.

A complex set of chemical and physical interactions must occur at the same time after addition of liquid product to the gastric contents for a strong, buoyant and voluminous raft to be formed. A small amount of alginate (not more than 1 g) must take up a large amount of water (over 50 g in the case of one product) and form a gel. The alginate gel is formed by interaction of a cross-linking metal ion (e.g. Ca$^{2+}$) which is itself released by acid degradation of an antacid. Carbon dioxide gas must also be released by acid degradation of bicarbonate or carbonate antacid and this should occur inside the alginate gel.

The effects on raft formation of variation in the amounts and ratios of these three ingredients were reported in an early patent relating to alginate compositions for use in the suppression of gastric reflux (Withington, 1978). Here it was shown that rafts were formed from product without calcium carbonate but they were less rigid and cohesive than those formed from product with calcium carbonate. There is also evidence in the literature that the addition of a source of aluminium to an alginate/bicarbonate/calcium carbonate based product may not strengthen but weaken the raft (Washington et al., 1986b). The effects of calcium and aluminium on coherence of the raft need to be considered in conjunction with the ANC of the product dose used for raft formation. It can be seen from Table 5 that four of the products tested had ANC that was less than the 15 mequiv. of hydrochloric acid used in raft formation whereas the other five products had ANC up to three times the mequiv. of acid used. It might be expected therefore that alginate precipitation and raft formation would be more limited in those products of high ANC than those of low ANC.

The products may be classified into several groups based upon their raft performance and on the above considerations. Products with a high ANC and no calcium source (Algicon, and the USA products Gaviscon Regular Strength and Gaviscon Extra Strength) form rafts of low strength (<2 g), weight and volume, which appear more as floating precipitates than coherent gels. Products with a high ANC and a calcium source (Mylanta and Rennie Duo) form medium strength (4–5 g), weight and volume rafts. Products with a low ANC (Gastrocote, Gaviscon Advance, Gaviscon Liquid and Peptac) form strong coherent rafts (strength >7 g) with medium to large weight and volume. Products with low ANC and a calcium source (Gaviscon Advance, Gaviscon Liquid and Peptac) form the strongest rafts. The most important factor in determining strong coherent rafts seems therefore to be low ANC, with the presence of available calcium...
as a cross-linker being a strong secondary factor. This is illustrated in Fig. 4, in which the theoretical ANC is plotted against mean raft strength for each product. The products clearly fall into two groups: those with ANC higher than 15 mequiv. and those with ANC lower than 15 mequiv. In each group the calcium containing products (■) have the highest raft strength.

The relationships between raft strength and other parameters (raft weight, raft volume, theoretical ANC, theoretical ANC higher than 15 mequiv. and presence of calcium) were statistically investigated using univariate, product moment correlation analysis, and linear and bivariate regression analysis (assessment of partial correlation effects). All hypothesis tests were undertaken using the 5% significance level. There was a positive correlation of raft strength with both raft weight (correlation factor 0.641, \( p = 0.063 \)) and raft volume (correlation factor 0.608, \( p = 0.082 \)) but this was not statistically significant in either case. There was a highly significant negative relationship with theoretical ANC (correlation factor –0.818, \( p = 0.007 \)) and with the binary assessment ANC higher/lower than 15 mequiv. (correlation factor –0.893, \( p = 0.001 \)). The presence of calcium in the product formulation had a large positive correlation with raft strength but this did not achieve statistical significance (correlation factor 0.637, \( p = 0.065 \)). Failure to achieve formal statistical significance (defined as \( p < 0.05 \)) when only nine formulations are available for comparison is not surprising.

Raft strength is also related to raft resilience. As expected, the resistance to break-up under the conditions of movement in the raft resilience test is improved with increase in raft strength. Thus, Gaviscon Advance, with the highest raft strength, resists break-up for the longest period of time whereas products with low raft strength (<5 g) have little or no resistance to raft break-up in the resilience test.

The buoyancy of an alginate raft might be expected to contribute to the effectiveness of the product in resisting reflux since a more buoyant raft would be more likely to displace corrosive gastric contents in the upper part of the stomach and it would also be less likely to be emptied along with the meal. Raft buoyancy is most effectively obtained by trapping carbon dioxide gas in the raft as it is formed. A buoyancy index was computed for those products which formed a structured raft as opposed to a precipitate, as: raft buoyancy = (volume – weight)/weight.

Table 6 shows the computed means, standard deviations and pairwise product comparisons.

<table>
<thead>
<tr>
<th>Product</th>
<th>Mean raft buoyancy</th>
<th>Standard deviation</th>
<th>Groups of products which are not significantly different</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gaviscon Liquid</td>
<td>0.652</td>
<td>0.161</td>
<td>*</td>
</tr>
<tr>
<td>Rennie Duo</td>
<td>0.627</td>
<td>0.358</td>
<td>*</td>
</tr>
<tr>
<td>Gaviscon Advance</td>
<td>0.384</td>
<td>0.277</td>
<td>*</td>
</tr>
<tr>
<td>Peptic</td>
<td>0.256</td>
<td>0.206</td>
<td>*</td>
</tr>
<tr>
<td>Mylanta Heartburn Relief</td>
<td>0.232</td>
<td>0.161</td>
<td>*</td>
</tr>
<tr>
<td>Gastrocote</td>
<td>0.099</td>
<td>0.084</td>
<td>*</td>
</tr>
</tbody>
</table>
parisons of all the products in Table 6 were made using an adjusted comparison-wise significance level (α = 0.001) to make allowance for the large number of comparisons made. Products linked by a vertical line of (*) are not statistically significantly different from each other. Gaviscon Liquid and Rennie Duo had the highest buoyancy measures and had significantly higher mean buoyancy than the other products tested, except for Gaviscon Advance (p < 0.0001 in all cases). No relationship between raft buoyancy and product formulation, or between raft buoyancy and amount of available carbon dioxide, could be found, however. This is not surprising considering the small number of products involved. The statistically significant difference between the raft buoyancy of Gaviscon Liquid and Peptac, which have nominally the same active ingredients, indicates that other factors such as raw material specification or manufacturing process may have an effect upon the amount of carbon dioxide trapped in the raft.

The reflux resistance studies, which have been briefly reported, previously (Jolliffe et al., 2001) were an attempt to assess the performance of rafts under reflux during transient lower oesophageal sphincter relaxations (TLOSR). It is known from studies of the mechanisms of gastro-oesophageal reflux that it is most likely to occur during TLOSR in both upright and supine positions, in both healthy volunteers and GORD patients (Dodds et al., 1982; Mittal et al., 1995). Forced supine positions, in both healthy volunteers and GORD patients, indicates that other factors such as raw material formulation, or between raft buoyancy and amount of available carbon dioxide, could be found, however. This is not surprising considering the small number of products involved. The statistically significant difference between the raft buoyancy of Gaviscon Liquid and Peptac, which have nominally the same active ingredients, indicates that other factors such as raw material specification or manufacturing process may have an effect upon the amount of carbon dioxide trapped in the raft.

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The determination of a products rafting characterisation becomes an important factor when determining which liquid alginate product to prescribe or recommend to a consumer. Two factors which have been shown to have a large influence on the type of alginate raft formed are firstly the type of alginate raw material used and secondly how the liquid alginate product is formulated and manufactured.

References


