

## ***In vitro* buffering capacity of Alka Seltzer Effervescent**

**A comparison with magnesium trisilicate mixture B.P. and sodium citrate 0.3 M**

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### **Summary**

*The variety of antacids used as a prophylaxis for acid aspiration syndrome reflects dissatisfaction with each agent. Alka Seltzer Effervescent is a proprietary product without aspirin. We have shown that it can easily be dissolved in a small volume, readily mixes with hydrous fluids, and has a satisfactory neutralising capacity. Its non-particulate nature, storage in individual packages and palatability, indicated by commercial acceptance overseas, show that further trials in vivo as a method of raising gastric pH may be useful.*

### **Key words**

*Complications; aspiration, prophylaxis.*

Antacids are used to raise intragastric pH above 2.5 as a prophylactic for acid aspiration syndrome.<sup>1</sup> However, each agent has some problem. Magnesium trisilicate mixture (MMT) is particulate, which may have been a cause of pneumonitis,<sup>2</sup> mixes poorly with gastric contents so that gastric pH is not uniformly raised, contains peppermint oil which reduces lower oesophageal sphincter pressure and settles concreting in storage.<sup>3</sup> Sodium citrate (0.3M) only has a shelf life of about 8 weeks,<sup>4</sup> which introduces problems with manufacturing. It is not palatable and is slightly more expensive than MMT.

Alka Seltzer Effervescent is a commercial 'over-the-counter' preparation in the United States, where there is a demand for antacids without aspirin. A previous study<sup>5</sup> has shown that intragastric pH before emergency general surgery was satisfactorily increased by use of two

tablets dissolved in 20 ml of water. In dogs, no change occurred in oxygenation, intrapulmonary shunting, or pulmonary vascular resistance after instillation of Alka Seltzer solution into the lungs. One tablet of Alka Seltzer Effervescent contains sodium bicarbonate, potassium bicarbonate, and citric acid, which is converted to citrate with loss of carbon dioxide when the tablet is dissolved in water. Thus, the solution mainly contains sodium and potassium citrates.

This study compares the buffering capacity and miscibility of Alka Seltzer Effervescent with magnesium trisilicate mixture (B.P.) and 0.3M sodium citrate.

### **Method**

The pH measurements were made with a Phillips digital pH meter PW 9409, with the slope set between 95 and 100%, after calibration with

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universal phosphate buffer pH 7.4 and acid phosphate buffer pH 1.0 before each test period. Initial tests showed that the calibration was satisfactory for at least 20 individual measurements with a standard variation of 0.006 around the pH 7.40 reference. Recalibration was carried out after two titrations.

Titration was carried out with 1M hydrochloric acid added rapidly in 2 ml aliquots from the burette, during continuous stirring of the mixture. This acid solution is ten times stronger than normal gastric acid, but the volumes were more convenient and it provided a severe test of buffering capacity for each antacid.

#### *The effect of timed exposure to air*

Two Alka Seltzer tablets dissolved in 20 ml of water, 30 ml of 0.3M sodium citrate and 20 ml of MMT were tested for buffering capacity at intervals of 0, 2, 5, 10, 15 and 30 minutes after exposure to air, to determine loss of potency by carbon dioxide emission. At 1 minute, Alka Seltzer tablets were still effervescent, so 2 minutes was used as the starting point.

#### *The buffering capacity of antacid solutions*

The buffering capacities of the 20 ml solutions of Alka Seltzer containing 1, 2, 3 or 5 tablets, 30 ml of 0.3M sodium citrate and MMT 20ml were tested by titration. In a non-particulate mixture, the new pH was reached within seconds, but MMT was much less consistent as, even with stirring, the pH reading 'wandered'. However, if it had not settled by 3 minutes, the reading was recorded and the titration proceeded.

#### *Mixing of antacid solutions*

The ability of an antacid solution to mix with an acid was tested by slowly adding the antacid to the surface of 100 ml of 0.1M hydrochloric acid (pH 1) via a narrow stemmed funnel. Addition was completed in 60 seconds. The mixture was not stirred initially and the pH measured at two marked levels (by gently raising and lowering the pH electrode) at 5-minute intervals for 30 minutes. The upper level was set with the electrode just sufficiently covered for consistent readings, as shown by a prior test with buffer. The lower level was just above a point at which a prior test showed an interface. After 30 minutes the mixture

was stirred, once initially, then if no change occurred after 5 minutes, one stir was applied again and if still little or no change occurred, the mixture was stirred vigorously.

### Results

Alka Seltzer acted as a buffer, preventing change in pH as acid is added, much more effectively than the same volume of water (Fig. 1). The vertical

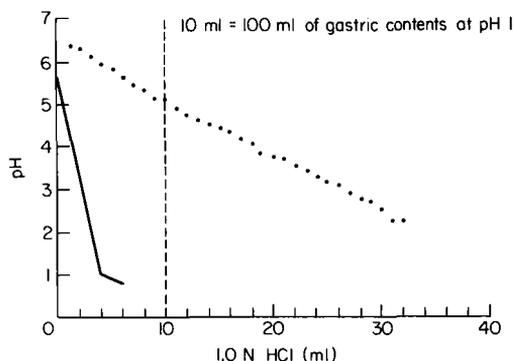


Fig. 1. Comparison of pH change on adding acid to 20 ml of water or Alka Seltzer solution. The dotted line illustrates the usual maximum hydrogen ion load found in the gastric contents. (—), water; (....), Alka Seltzer.

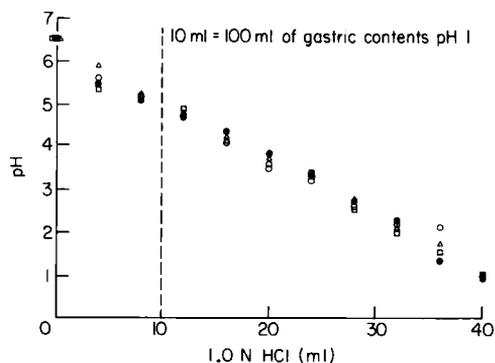
line on this figure and all other figures, corresponds to the volume of acid containing the same number of hydrogen ions as would be found in 100 ml of gastric juice at pH 1. The intercept of this line allows a comparison between antacids of their efficacy in raising the pH of gastric juice. As a buffer curve intercepts at a pH of 5.3 it is reasonable to expect it to raise the gastric pH to above the safety margin of 2.5–3.5 after ingestion.

#### *Effect of exposure to air*

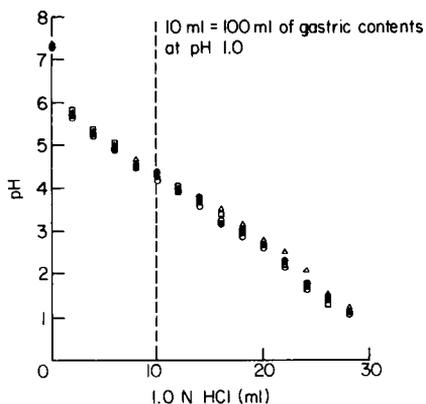
Figures 2 and 3 show that standing open to atmosphere has little effect on the buffering capacity of 0.3M sodium citrate or Alka Seltzer in the short term. MMT showed no consistent change with time, and the differences in Fig. 4 are probably due to inadequate mixing.

#### *Buffering by different solutions*

The buffering capacity of one tablet of Alka Seltzer is markedly less than that of two tablets, but even so one tablet is still able to raise the pH



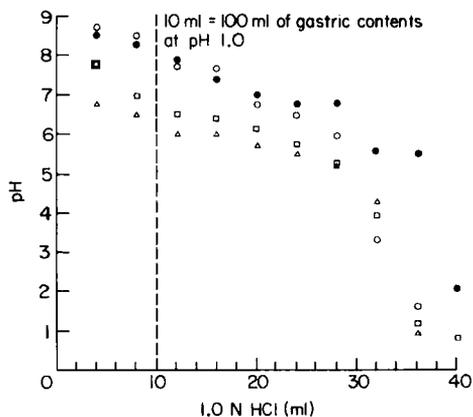
**Fig. 2.** Buffering capacity of Alka Seltzer after exposure to air when initial effervescence has ceased. Two tablets in 20 ml, titration commencing at (●), 2 minutes; (▲), 5 minutes; (□), 15 minutes; (○), 30 minutes.



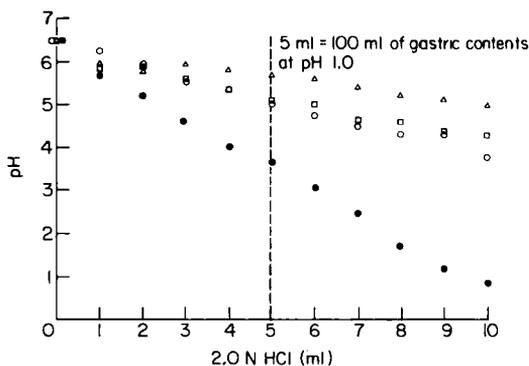
**Fig. 3.** Buffering capacity of 20 ml sodium citrate 0.3M after exposure to air. Titration commencing at (●), 2 minutes; (○), 5 minutes; (△), 15 minutes; (□), 30 minutes.

of the equivalent of 100 ml of gastric fluid to above 3.5 (Fig. 5). It can also be seen from this figure that three and five tablets are little better than two tablets. There is a small amount of precipitate after dissolving two tablets, but this is more obvious after five are dissolved in 20 ml. This precipitate completely disappears after addition of a few millimetres of acid. Thus, there are not likely to be any particles after mixing with gastric contents.

Comparison of antacids by means of titration revealed them all as satisfactory. Sodium citrate 0.3M had the lowest intercept, with a line representing the hydrogen ion content of 100 ml of gastric juice, Alka Seltzer seems slightly better, and MMT, despite wider variation, was able to



**Fig. 4.** Buffering capacity of magnesium trisilicate mixture B.P. after exposure to air and with agitation during titration. Titrations commencing at (●), 2 minutes; (△), 5 minutes; (□), 15 minutes; (○), 30 minutes.



**Fig. 5.** Buffering capacity of different numbers of Alka Seltzer tablets dissolved in 20 ml of water with titration commenced at 2 minutes. (●), 1 tablet; (○), 2 tablets; (□), 3 tablets; (△), 5 tablets.

maintain a high pH in the face of an acid challenge.

#### Mixing with acids

Table 1 shows that it was easy to make a separate layer with each antacid. MMT initially sat on the surface of the acid but, as the full amount was added, sank as a mass, leaving an oily appearance on the surface. Sodium citrate and Alka Seltzer slightly raised the pH of the solution close to the interface even without agitation, Alka Seltzer slightly more so. After the second stir, Alka Seltzer had raised the pH slightly more than

**Table 1.** Change of pH in acid-antacid mixture with an without stirring

Time of measurement	Magnesium trisilicate		0.3 sodium citrate		20 ml solution of 2 tablets of Alka Seltzer	
	pH at		pH at		pH at	
	Upper level	Lower level	Lower level	Upper level	Lower level	Upper level
Before addition of antacid	1.05	—	0.98	—	0.97	—
5 minutes	1.75	1.00	4.69	.98	5.51	1.09
10 minutes	2.23	0.98	4.59	.95	5.44	1.01
15 minutes	2.69	1.00	4.56	.98	5.52	1.01
20 minutes	2.61	0.97	4.60	.96	5.52	1.01
25 minutes	2.99	0.96	4.60	.96	5.49	1.04
30 minutes	2.74	0.98	4.56	.96	5.55	1.18
After one stir	2.4	2.00	4.83	1.08	5.50	1.49
After second stir	1.79	1.00	5.22	1.50	5.46	2.71
After vigorous stir + 5 minutes	5.70	5.00	4.79	4.78	5.01	5.01
	6.46	5.46	4.80	4.79	—	—

sodium citrate, but vigorous stirring was necessary to provide a substantial rise in pH.

MMT behaved differently, with no neutralisation of acid without vigorous stirring, even after 30 minutes. It took 5 minutes longer for pH changes to be complete.

### Discussion

Many antacids have been used to raise intragastric pH as prophylaxis against acid aspiration syndrome. The work of Vandam<sup>6</sup> Teabeut<sup>7</sup> and Roberts and Shirley<sup>1</sup> established guidelines to reduce the risks, and recommended that a pH of greater than 2.5 and a gastric volume of less than 25 ml be aimed at; these figures were established by experiments on rabbits and monkeys. Taylor<sup>9</sup> later suggested a minimum pH of 3.5, after he recorded an incident of pulmonary aspiration syndrome with a gastric pH less than 3.5, but more than 2.5.

Magnesium trisilicate mixture has remained the most common antacid used, probably because it was the first to be widely introduced. Sodium citrate solution is now gaining popularity because of concern about MMT. Sodium citrate and Alka Seltzer, non-particulate antacids, both mixed much more easily than MMT and, thus, mixing started even before agitation. This confirms the findings of Holdsworth and his colleagues,<sup>9</sup> who showed that MMT mixed poorly and that all antacids require that the patient move around to ensure adequate mixing in the stomach.

MMT was able to neutralise gastric acid contents, perhaps with a larger capacity than other antacids, but there remains a question regarding its effects in the lungs. Aspirated, unchanged, particulate antacids have greater adverse effects than non-particulate antacids, but it is difficult to be categorical about MMT. Heaney and Jones<sup>10</sup> reported two cases of aspiration pneumonitis, one of whom definitely regurgitated MMT and may have aspirated gastric contents, but eventually recovered. Gibbs and Wynne<sup>11</sup> claim that MMT would behave in a similar fashion to other particulate antacids, which increase physiological shunting and pulmonary vascular resistance. Peppermint oil in MMT has undesirable pharmacological actions, in that it lowers the lower oesophageal sphincter tone, thus increasing the chances of reflux.<sup>12</sup> This alone would cast a shadow on its use for the prophylaxis of acid aspiration. Also, many patients find MMT distasteful; it may cause nausea and vomiting, resulting in poor compliance, even in the labour ward.<sup>13</sup>

Sodium citrate is certainly more miscible, but is slightly more expensive than MMT, and requires aniseed or syrup to disguise its flavour.<sup>14</sup> Many pharmacies place a short time limit on the expiry date for sodium citrate, which may be because of interaction with the atmosphere, crystallising of the syrup, or interaction with silica in the glass of the container. Sodium citrate can be sealed in glass containers which ensure storage for 8 weeks.<sup>4</sup>

Alka Seltzer tablets contain 958 mg of sodium bicarbonate (approximately 11.4 mM), 312 mg potassium bicarbonate (3.1 mM), and 832 mg of citric acid (4.3 mM). Our measurements show the solution consistently has a pH of 6.5. At 20°C, the pKa of the three proton donor sites of citric acid are respectively 3.14, 4.77, and 6.34,<sup>15</sup> so that the first two sites are ionised and most of the third at the pH of Alka Seltzer solution. Thus, the citric acid is in solution as citrate, a potent buffering ion. Examination of the molar quantities also shows that there is sufficient bicarbonate to 'neutralise any hydrogen ions present in the citric acid.

Sodium citrate contains 18 mM sodium/20 ml dose,<sup>16</sup> MMT 18.9 mM/30 ml dose<sup>17</sup> and Alka Seltzer 23 mM/two tablet dose, so the difference in sodium content is small. Palatability of Alka Seltzer solution in pregnant mothers has not been assessed, but as it already sells directly to the consumer in the USA, it is likely to be acceptable. Theoretical expectations have been confirmed in the dog lung that Alka Seltzer Effervescent has little effect on the lung,<sup>5</sup> and so may be an improvement. Alka Seltzer has adequate neutralising ability, provided two tablets are used, and it is unimportant how long the solution stands (up to 30 minutes), as long as effervescence has ceased. This would also prevent carbon dioxide being generated in the stomach which, theoretically at least, might increase intragastric pressure. Individual packaging means a higher initial outlay (2.00 US dollars per box of 36 tablets USA or 11p a dose), but since it has a long shelf life there should be little waste. If it were administered immediately before Caesarean section, then its palatability, and rapid mixing would bestow definite advantages over MMT.

Further investigation is justified to assess the palatability of Alka Seltzer to pregnant mothers and its efficacy compared to other antacids prior to Caesarean section.

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