Evaluation of the buffering capacity of powdered cow's, goat's and soy milk and non-prescription antacids in the treatment of non-ulcer dyspepsia

D Lutchman, S Pillay, R Naidoo, N Shangase, R Nayak, A Rughoobeer

Background. Non-ulcer dyspepsia (NUD) is the term most commonly used to describe a heterogeneous and often ill-defined group of dyspepsia patients whose symptoms of upper abdominal pain, discomfort or nausea persist in the absence of identifiable cause. Treatment choice commonly includes over-the-counter medicines and home remedies, e.g. milk.

Objective. To determine the relative buffering capacity of goat's, cow's and soy milk, non-prescription antacid drugs and combinations thereof.

Methods. The buffering capacities of 25 ml aliquots of each of the powdered milk products, the antacids alone and the combination of antacid and milk were determined. Statistical analysis was used to determine any significant differences in buffering capacity.

Results. When the antacids were examined alone, significant differences in buffering capacity were observed. When powdered milk products were examined alone, cow's milk had a significantly higher buffering capacity than either goat's or soy milk. There was no significant difference between goat's and soy milk. In the combination of cow's milk with each of the antacids, brand A and B had a similar buffering capacity, significantly higher than that observed with brand C.

Conclusions. The combination with best observed buffering capacity was brand A with cow's milk, and the weakest buffering capacity was observed with brand C with soy milk. The results obtained can be attributed to the chemical constituents of the antacids and the milk products.

S Afr Med J 2006; **96:** 57-61.

Dyspepsia is a pain or discomfort in the upper abdomen or chest. It is often described as a feeling of having gas, of fullness, or a gnawing or burning pain. Dyspepsia patients with no peptic ulceration are collectively labelled as having non-ulcer dyspepsia (NUD). It is a common gastrointestinal symptom experienced by 20 - 40% of the adult population in the Western world.[1] Often a person with dyspepsia is treated without having laboratory tests done. However, when tests are done, in about 50% of cases no abnormalities are identified.[1]

Patients with NUD are usually healthy, eat regularly and live with their symptoms for months or years without suffering from adverse health problems.[2]

Treating NUD can be difficult for sufferers as they face an array of over-the-counter (OTC) and prescription remedies. The objectives of OTC treatment are to reduce acidity by raising the pH level, to enhance mucosal protection, and to expel excess gas.[1] Antacids are the best medication for fast and effective relief from NUD because of their rapid acid-neutralising properties.[1]

School of Pharmacy and Pharmacology, University of KwaZulu-Natal, Durban

D Lutchman, MPharm
S Pillay, BPharm
R Naidoo, BPharm
N Shangase, BPharm
R Nayak, BPharm
A Rughoobeer, BPharm

Corresponding author: *D Lutchman (lutchmand@ukzn.ac.za)*

All antacids are basic compounds that react with gastric acid to form water and a salt. There are 4 primary neutralising compounds found in OTC antacid products: sodium bicarbonate, calcium carbonate, aluminum salts and magnesium salts. All antacids contain at least one of these ingredients, which differ significantly in potency, gastrointestinal side-effects, systemic complications, and drug interactions. Most of these properties are determined by the metal cation of the antacid and the degree of its systemic absorption.[3] It is documented that the buffering capacity of magnesium salts is greater than that of aluminum hydroxide but less than that of sodium bicarbonate and calcium carbonate.[3]

Non-drug home remedies such as commercially available milk are frequently used to relieve dyspepsia. Other remedies include goat's milk and soy milk.

The concentrations of phosphates, calcium and caseins in milk have a major effect on its buffering capacity.[4] The buffering capacity is the ability of a solution to withstand a drop in pH, even following an input of lactic acid, resulting from activity of lactic acid bacteria. Therefore, in a weakly buffered milk, the pH will drop rapidly, e.g. from 6.6 to 6.0, following the addition of a little lactic acid. In strongly buffered milk the pH will decline only slightly, e.g. from 6.6 to 6.4, even if a lot of lactic acid is added. The good buffering capacity of milk is therefore ideal in the treatment of NUD. The principal buffering components of goat's milk are proteins and phosphates, while the major buffering components of cow's milk are the casein protein, calcium and the phosphates. Goat's milk is slightly on the acid side, with a pH range of 6.4 - 6.7.[5] Soy milk is an excellent substitute for cow's milk and is far more digestible and compatible with human nutritional requirements than cow's milk. Soy milk reduces many digestive disorders because of its high fibre content. This aids in healthy digestion, and it has been shown to reduce the risk of colon and rectal cancer. Soy milk is also dairy-free and can be used as a substitute in cases of lactose intolerance and milk allergy.[6]

Objectives

Powdered cow's, soy and goat's milk have not been assessed adequately or compared with regard to their buffering capacity, so the aim of the study was to determine the relative buffering capacity of these powdered milks and commercial non-prescription antacid drugs. The primary objectives were to determine the buffering capacity of each product, and by using appropriate statistics, to determine whether the milk products and antacid preparations differed from each other with regard to buffering capacity individually and in combination. The secondary objectives were to identify synergistic buffering mechanisms, and to determine the most cost-effective treatment with regard to buffering capacity.

Materials

Milk

Commercially available powdered cow's, goat's and soy milks were selected for this study. The primary selection criteria for these products were based on availability and cost. The powdered milk formulas of all three products were more available commercially than the natural (liquid) preparations, as evidenced by the availability of the products in major retail stores. Various brands were available for each individual milk product, and in each case the most affordable was selected for the study. The approximate costs of the milk products are reflected in Table I.

Table I. Cost of powdered milk products

Milk	Cost (R/200 ml)
Goat	3.30
Soy	1.44
Cow	1.20

Non-prescription antacid drugs

Three different brands were selected for the study (Table II). The selection criteria were again based on availability and cost. However, brand popularity was also considered by enquiring at local retail and hospital pharmacies. This was done to establish which brands were popular among consumers, and based on this the most affordable brands were selected.

Table II. Constituents of the antacid preparations

Brand	Constituent	Quantity (mg)	Cost (R/tablet)
A	Calcium carbonate	680	0.41
	Magnesium carbonate	80	
B	Alginic acid	500	1.80
	Magnesium trisilicate	25	
	Aluminium hydroxide gel	100	
	Sodium bicarbonate	170	
C	Aluminium hydroxide gel	250	1.04
	Magnesium trisilicate	500	

Other chemicals

Hydrochloric acid 0.5M (BDH Laboratory Supplies, Poole, UK) was used as supplied. HCl 0.1M was not selected because it produced insufficient responses as a titrant.

Equipment

The Hanna pH 211 Microprocessor pH meter (Hanna Instruments Inc., Lisbon, Portugal) was used for all experiments. Temperature was maintained at 22 - 23°C.

Methods

As stated, buffering capacities were determined for the individual products and for the combinations (Fig. 1).

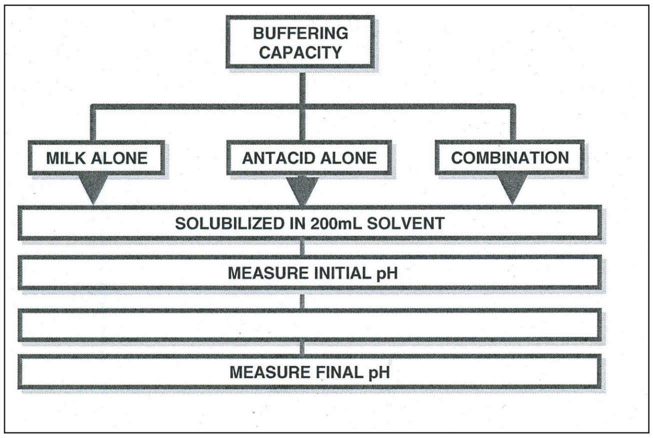

Fig. 1. Flow diagram depicting the method used to determine buffering capacity.

To maintain standardisation, calculated quantities of powdered milk, in accordance with label specifications, were solubilised in 200 ml distilled water to produce individual standardised solutions. Each antacid tablet was triturated and adequately solubilised in 200 ml distilled water. Thereafter each individual antacid tablet was triturated and solubilised in 200 ml powdered milk solution. Twenty-five millilitre aliquots of each of these solutions were used as representative samples in the *in vitro* testing. This incorporated measurement of the initial pH of the solutions without treatment with hydrochloric acid. One-millilitre increments of 0.5M hydrochloric acid were then added to the standardised solutions of the milk, antacid or the combination solution, reaching a maximum volume of 5 ml. It was found that any further addition of acid did not result in a fluctuation in pH, i.e. the pH remained constant. In this step the final pH was measured after the treatment with the 0.5M hydrochloric acid. A minimum of 3 runs per tablet were performed to obtain an average measure of pH change. Using van Slyke's[8] proposed mathematical equation, the buffering capacities of each individual product and combination were determined as follows:

$$\frac{dBC}{dpH} = \frac{\text{(volume of acid added)} \times \text{(molarity of acid)}}{\text{(volume of milk/antacid/combination solution)} \times \text{(pH change)}}$$

Statistical analysis

The data generated were analysed by applying the appropriate statistical package to establish whether there was significance within products and within combinations. The techniques employed were analysis of variance (ANOVA) and the general linear model which incorporated Duncan's multiple range test. The level of significance was set at $p < 0.05$.

Results and discussion

Comparative analysis of buffering capacities revealed the following:

Drug alone

Fig. 2 shows that brand A provided a significantly higher buffering capacity than brands B or C ($p < 0.05$).

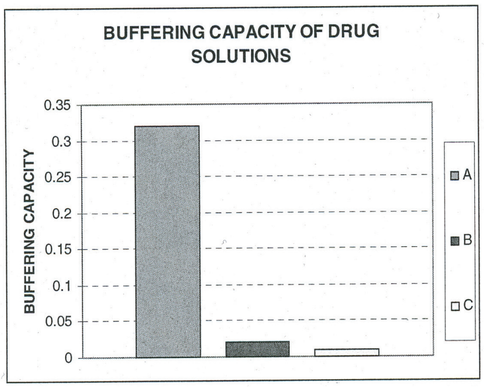

Fig. 2. Buffering capacity of individual drugs.

It has been stated that calcium carbonate and sodium bicarbonate have the best buffering capacity followed by magnesium salt and then aluminium hydroxide.[3] Therefore the difference in buffering capacity can be attributed to the different constituents in each formulation.

Although brands A and B contained equally superior buffering capacity constituents, i.e. calcium carbonate and sodium bicarbonate respectively, brand A's superior buffering capacity could be attributed primarily to its higher quantity of calcium carbonate (680 mg) compared with 170 mg of sodium bicarbonate in brand B.

Calcium carbonate dissolves more slowly in the stomach than sodium bicarbonate, but it produces a potent and prolonged neutralisation of gastric acid. It reacts with gastric acid to produce calcium chloride, carbon dioxide and water. The chemical reaction is as follows:

$$CaCO_2 + 2HCl \rightarrow CaCl_2 + H_2O + CO_2$$

Sodium bicarbonate is a potent, highly soluble compound that reacts almost instantaneously with acid in the stomach to produce sodium chloride, carbon dioxide and water. The chemical reaction is as follows:

$$NaHCO_3 + HCl \rightarrow NaCl + H_2O + CO_2$$

The loss of carbon dioxide as a gas makes the reaction irreversible.

Although brand B was a multi-ingredient product, it proved to have a lower buffering capacity than brand A. Its buffering capacity was mainly provided by the sodium bicarbonate and the aluminium hydroxide. Alginic acid, on the other hand, reacts with the sodium bicarbonate and aluminium hydroxide to provide a cytoprotective role. In addition the magnesium trisilicate is metabolised to the magnesium carbonate buffer and the trisilicic acid which also has a cytoprotective role.

Another reason for its weaker buffering capacity is as stated above in terms of quantity of buffering capacity constituents.

Aluminium hydroxide is slowly dissolved in the stomach, where it reacts with gastric acid to form aluminium chloride and water. The chemical reaction is as follows:

$$Al(OH)_3 + 3\,HCl \rightarrow AlCl_3 + 3\,H_2O$$

Alginic acid works by reacting with sodium bicarbonate and saliva to form a viscous solution of sodium alginate. This viscous solution floats on the surface of the gastric contents so that when reflux occurs, sodium alginate rather than acid is refluxed and irritation is minimised.

Use of alginic acid-containing products is not indicated for acid-peptic diseases other than gastro-oesophageal disease because the amount of antacid ingredients included does not provide sufficient acid-neutralising capacity to be useful.

Brand B had a significantly higher buffering capacity than brand C ($p < 0.05$). Although both products contained magnesium trisilicate and aluminium hydroxide, the reason for the higher buffering capacity of brand B was the sodium bicarbonate content.

Magnesium trisilicate is decomposed by hydrochloric acid into a magnesium salt and trisilicic acid:

$$2\,MgO.\,3SiO_3 + 4\,HCl \rightarrow MgCl_2 + \underset{\text{Trisilicic acid}}{H_4Si_3O_8} \downarrow$$

In the stomach, the gelatinous trisilicic acid is formed with gastric hydrochloric acid.[3]

Milk alone

Fig. 3 shows that powdered cow's milk provided a better buffering capacity than either powdered goat's or soy milk ($p < 0.05$).

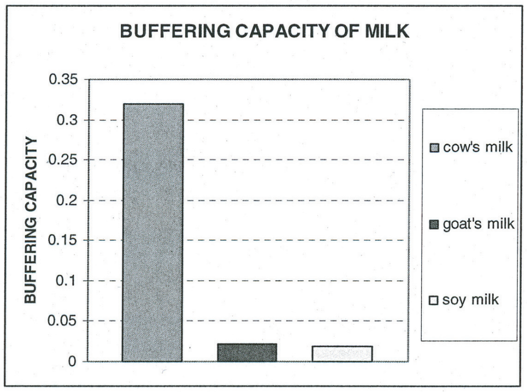

Fig. 3. Buffering capacity of powdered milks.

The composition of milk has a direct influence on the buffering capacity. The concentrations of proteins, phosphates and calcium in milk generally provide potent buffering mechanisms.[5]

Proteins contain amino acids that undergo the following equilibria:

$$NH_2 + H^+ \longleftrightarrow NH_3$$

$$COOH + OH^- \longleftrightarrow COO^- + H_2O$$

Addition of acid drives both equilibria in the direction that absorbs the added H^+, thereby minimising the decrease in pH. Similarly, addition of a buffer removes H^+ from the solution, driving both equilibria in the direction that increases H^+, again minimising the increase in pH.[9]

Phosphates undergo the following equilibria:

$$PO_4^{-3}{}_{(aq)} + H^+{}_{(aq)} \longleftrightarrow HPO_4^{-2}(aq)$$

$$HPO_4^{-2}{}_{(aq)} + H^+{}_{(aq)} \longleftrightarrow H_2PO_4^-(aq)$$

$$H_2PO_4^-{}_{(aq)} + H^+{}_{(aq)} \longleftrightarrow H_4PO_4(aq).$$

Addition of acid will drive the equilibria to the right, removing much of the added acid and maintaining a constant pH. Addition of base will drive all equilibria to the left (by removing H^+ ions in the equilibrium $H^+ + OH^- \longleftrightarrow H_2O$) and in the same way counteract the effect of the addition of the base. In both cases, the overall effect is to minimise the change in pH.[9]

Calcium. At the normal pH of milk more than 90% of the calcium is bound in colloidal form to the casein micelles and less than 10% exists in ionised form. As the pH is lowered, the colloidal calcium is displaced from the micelles as the binding sites become protonated. In milk, calcium is bound to phosphates, which in turn are bound to the protein micelles. On addition of acid, phosphate ions are displaced from the calcium. Further addition of acid increases the solubility of the phosphate ions.[7]

According to package specifications the cow's milk contained not only all three buffering constituents, but all three in a greater quantity than in goat's milk or soy milk powder.

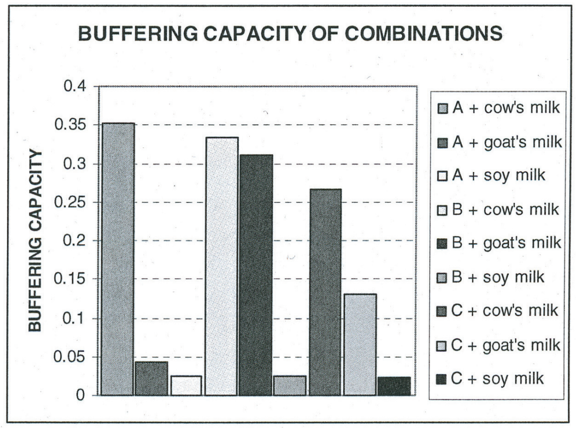

Fig. 4. Buffering capacities of combinations.

In addition, cow's milk contains the protein, casein, which provides the most potent buffering capacity when used in combination with phosphates. On the other hand, goat's milk and soy milk powder contain no or very little casein.

Hence in strongly buffered milk the pH will decline only slightly, and in weakly buffered milk the pH will drop rapidly.[5]

When cow's milk and antacids were examined together, brands A and B had similar buffering capacities, significantly higher than that of brand C ($p < 0.05$) (Fig. 4). This was attributed to the casein, phosphates and calcium in cow's milk and the greater quantities of calcium carbonate in brand A.

When goat's milk and antacids were examined together brand B had the greatest buffering capacity, greater than those of both brands A and C.

When soy milk and antacids were examined together brand A had a slightly higher buffering capacity than those of either brands B or C in soy milk.

Brand A once again provided greater buffering owing to the greater quantity of calcium carbonate in the formulation.

Table III shows the mean buffering capacity and standard deviation of the samples tested in this study.

Conclusion

In conclusion, brand A alone and cow's milk alone provided equally superior buffering capacity compared with the other products, and as a combination they provided the most potent buffering capacity, although not significantly greater ($p > 0.05$) than when used alone. Therefore, when using cost-effectiveness as a factor, cow's milk powder alone (R1.20/200 ml), or brand A alone (R 0.41/tablet), would have to be recommended as treatment options in NUD.

Recommendations

The study focused on three commonly used antacids, and future studies should therefore include analysis of a wider spectrum of OTC antacids with varied buffering constituents.

Table III. Mean buffering capacity and the standard deviation of the samples tested

	Mean	Standard deviation
Brand A alone	0.3245	0.0079
Brand B alone	0.0215	0.0014
Brand C alone	0.0112	0.0002
Cow's milk	0.3196	0.0154
Goat's milk	0.0221	0.0004
Soy milk	0.0192	0.0001
Brand A + cow's milk	0.3515	0.0162
Brand A + goat's milk	0.0423	0.0137
Brand A + soy milk	0.0250	0.0004
Brand B + cow's milk	0.3346	0.0154
Brand B + goat's milk	0.3105	0.0537
Brand B + soy milk	0.0246	0.0002
Brand C + cow's milk	0.2656	0.0281
Brand C + goat's milk	0.1301	0.0433
Brand C + soy milk	0.0225	0.0001

It has been documented that buffering capacities of formulas were lower than those of natural products;[7] since powdered milk was used in this study, analysis of natural (liquid) preparations of each of the milk products is therefore recommended. Development of a product containing the principal buffering components of both cow's milk and brand A would be beneficial in the treatment of NUD. Future studies should also include a comparative analysis of acid-neutralising capacity and buffering capacity.

References

1. Berkow R. *The Merck Manual of Medical Information*. Home ed. New York: Pocket Books Publishers, 1997: 65-66, 559-560.
2. Vishnar A, Ghulam R, Mittal RA. Non-ulcer dyspepsia and its correlation with life stress, anxiety and depression. *Indian Journal of Psychiatry* 1999; **41:** 88-93.
3. Covington TR, Berardi RR, Young LL, *et al*., eds. *Handbook of Nonprescription Drugs*. 11th ed. Washington, DC: American Pharmaceutical Association, 1996.
4. **http://www.inform.umd.edu/EdRes** (last accessed 10 May 2004).
5. **http://sci.agr.ca/crda/pubs/goat 2000_chevre_e.htm** (last accessed 12 May 2004).
6. **http://soyfoods.com/soyfoodsdescription/soymilk.html** (last accessed 12 May 2004).
7. Park YW. Relative buffering capacity of goat milk, cow milk, soy-based infant formulas, and commercial nonprescription antacid drugs. *J Dairy Sci* 1999; **74:** 3326-3333.
8. Van Slyke DD. On the measurement of buffer values and on the relationship of buffer and the concentration and reaction of the buffer solution. *J Biol Chem* 1992; **52:** 525.
9. **http://beerandwine.hobart.tased.edu.au/Generalchem/Chemicals/Proteins.doc** (last accessed 5 July 2004).