Comparative Evaluation of Antacid Suspensions in the Kenyan Market

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Acid-neutralizing antacid products are widely used to alleviate the symptoms of excess gastric acidity, gastro-esophageal reflux disease and related disorders. Several commonly used antacid suspensions in the Kenyan market were evaluated for their sedimentation characteristics, redispersibility, pH values, flow properties and acid neutralization capacity values. There was considerable variation in the properties of the antacid suspensions. All products, however, had acid neutralization capacity values greater than 5 mEq/ 5 ml.

Keywords: Antacids, suspensions, acid neutralization capacity

INTRODUCTION

Medicines which control gastric acid are used to treat the symptoms of heartburn, gastro-esophageal reflux disease (GERD), peptic ulcers and other disorders which are aggravated by low pH from gastric acid secretion. These products may be classified into antacids which directly neutralize excess acidity or medicines which decrease gastric acid secretion such as H_2 (histamine receptor) antagonists and proton pump inhibitors. The advantages of acid neutralizing products include rapid action for mild and infrequent therapy as well comparatively low cost compared to other antacid therapeutic products. They are typically available over the counter and self-prescribed which frequently makes them the first choice for many patients who require rapid symptomatic relief of heartburn or regurgitation due to GERD. While local epidemiological estimates are not available, a review by El-Serag et al. reported GERD prevalence estimates of 18.1% – 27.8% in North America, 8.8% – 25.9% in Europe, 2.5% – 7.8% in East Asia, 8.7% – 33.1% in the Middle East, 11.6% in Australia and 23.0% in South America [1]. This high prevalence creates a large demand for antacid products.

The active ingredients in acid neutralizing antacids are salts of aluminum, calcium or magnesium either alone or in combination. These antacids act by partial neutralization of gastric hydrochloric acid and inhibition of the proteolytic enzyme, pepsin [2]. Acid neutralizing antacids are available in a number of dosage forms including suspensions, chewable tablets and powders filled into sachets. Of these suspensions are the most popular as the active components are pre-dispersed in a liquid which provides for a large surface area upon administration and potentially more rapid acid neutralization. Despite the widespread availability and use of antacid suspensions in Kenya, there are limited studies characterizing the products that are currently available on the market. In a 1995 study, Kibwage et al. studied the acid neutralizing capacities and the sodium content of various antacid products in the local market and found a high degree of variation in both these characteristics of the products investigated [3]. In the present study, in addition to acid neutralizing capacity we sought to characterize antacid suspensions currently available in the Kenyan market by physical characteristics, specifically their product sedimentation, redispersibility and liquid flow properties.

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MATERIALS AND METHODS

Materials

Seven antacid suspension products were procured from local pharmacies. The selected antacids are shown in Table 1. Reagents were provided by the Pharmaceutics and Pharmaceutical Chemistry Laboratories of the School of Pharmacy at the University of Nairobi.

Table 1. Composition of the antacid suspensions by active ingredients

Code	Active Ingredients	Recommended dose
A	Each 5 ml contains aluminum hydroxide 120 mg and magnesium trisilicate 250mg	10 ml
B	Each 5 ml contains aluminum hydroxide 225 mg and magnesium hydroxide 200 mg	10 ml
C	Each 10 ml contains sodium alginate 500 mg, sodium bicarbonate 267 mg and calcium carbonate 160 mg	10 ml
D	Each 5 ml contains aluminum hydroxide 200 mg, magnesium trisilicate 200 mg, magnesium hydroxide 100 mg, sodium alginate 100 mg and simethicone 25 mg	10 ml
E	Each 15 ml contains alginic acid 200 mg, magnesium hydroxide 250 mg, aluminum hydroxide 250 mg, magnesium trisilicate 250 mg, simethicone 125 mg	15 ml
F	Each 5 ml contains aluminum hydroxide 365 mg, magnesium hydroxide 80 mg, simethicone 100 mg	10-20 ml
G	Each 5 ml contains aluminum hydroxide 400 mg, magnesium hydroxide 100 mg, simethicone 25 mg	10 ml

Acid Neutralization Capacity Test

The acid neutralization capacity (ANC) was analyzed in triplicate determinations as per the USP method [4]. An accurately weighed quantity of the uniform mixture of antacid suspension equivalent to the minimum labeled dosage, was transferred to a 250 ml beaker. Water was added to the beaker to make a total volume of about 70 ml. The contents of the beaker were then mixed for 1 minute using a magnetic stirrer. 30 ml of 1.0 N hydrochloric acid VS was pipetted into the test preparation and stirring continued for 15 minutes. The excess hydrochloric acid was then titrated with 0.5 N sodium hydroxide to attain a stable pH of 3.5. The milliequivalents (mEq) of acid consumed were then calculated using equation 1:

$$\text{Total mEq} = (N_{NaOH} \times V_{NaOH}) - (N_{HCl} \times 30) \quad \text{(Equation 1)}$$

where N and V refer to normality and volume, respectively.

Physical Tests

The pH of the antacid suspensions was determined using a Jenway 3510 pH meter (Cole-Parmer, Staffordshire, United Kingdom).

Ease of Redispersion

Suspension samples of 100 ml were allowed to settle in measuring cylinders for 7 days. After the 7 days, the opening of the measuring cylinder was sealed and inverted through 180°. The redispersibility number (the number of inversions required to uniformly disperse any sedimented material completely) was recorded.

Sedimentation Volume

Suspension samples of 100 ml were transferred into 100 ml measuring cylinder and left undisturbed for 7 days at room temperature. The final height of the sediment was recorded at the end of each day. The sedimentation volume (F) was calculated by dividing the final height of sediment (H_U) by the initial height of the suspension (H_O).

Flow Rate

The flow rate was determined by assessing the time required for a 10 ml sample of suspension to flow through a 10 ml pipette. The flow rate was determined by dividing the volume of suspension by the time of flow.

Statistical Analysis

Where applicable, test results were subjected to statistical analysis using analysis of variance (ANOVA) or the Kruskal-Wallis test (non-parametric data) with a p-value of 0.05. Excel (Microsoft Corporation, USA) data analysis and spreadsheets were used to conduct both tests. The null (H_0) and alternative (H_a) hypotheses were:

H_0: $\mu_1 = \mu_2 = \ldots\ldots = \mu_k$

(where μ refers to the mean values and k refers to the number of products)

H_a: at least two of the mean values differed

RESULTS AND DISCUSSION

The acid neutralizing active ingredients in the antacids that were evaluated are shown in Figure 1. All the suspensions were combination products with at least two active ingredients. Aluminum hydroxide, the most common acid neutralizing ingredient, was present in 38% of the suspensions, followed by magnesium hydroxide (31%), magnesium trisilicate (19%), sodium bicarbonate (6%) and calcium carbonate (6%). Alginic acid/sodium alginate (raft formation) and simethicone (antiflatulent) were present in some of the suspensions as well.

The results of the tests are shown in Table 2. The acid neutralization capacity (ANC) values ranged from 6.4 to 14.6 mEq per 5 milliliters. There was a statistically significant difference between the ANC values for the different products (between groups ANOVA $F(6, 14) = 53.01$, $p < 0.05$). The pH values ranged from 8.1 to 8.9. There was a statistically significant difference between the pH values for the different products (between groups ANOVA $F(6, 14) = 3635.79$, $p < 0.05$). Linear regression showed no correlation between the product pH and the acid neutralization capacity values ($R^2 = 0.12$).

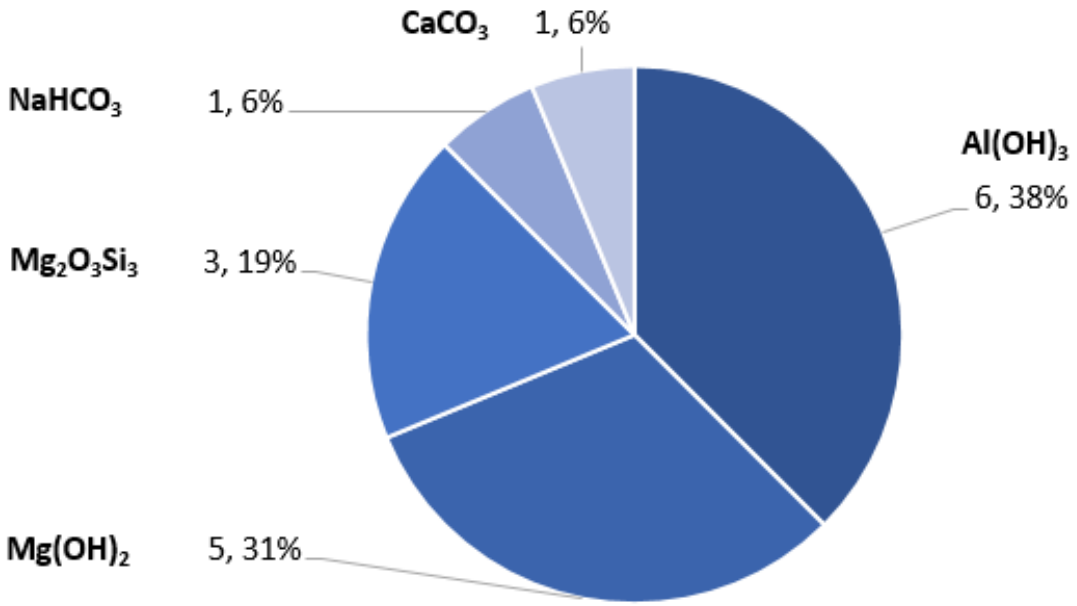

Figure 1. Active ingredients in the study products.
Values indicate the number of products with the active and the equivalent value on a percent basis.

Table 2. Test results for the study products

Code	Acid Neutralization Capacity (mEq/5 ml)	pH	Average Sedimentation Volume*	Redispersibility Number	Liquid Flow Rate (ml/s)
A	8.8 (0.3)	8.9 (0.0)	1.00	2.3 (0.6)	0.14 (0.0)
B	12.7 (0.8)	8.3 (0.0)	0.95	13 (0.7)	0.59 (0.0)
C	6.4 (1.4)	8.4 (0.0)	0.99	10.3 (0.6)	0.03 (0.0)
D	9.7 (0.3)	8.5 (0.0)	0.99	9.3 (1.2)	0.03 (0.0)
E	8.8 (0.2)	8.1 (0.0)	0.99	3.0 (0.0)	0.17 (0.0)
F	14.6 (0.5)	8.1 (0.0)	1.00	6.0 (0.0)	0.07 (0.0)
G	11.3 (0.3)	8.6 (0.0)	0.98	6.0 (1.0)	0.08 (0.0)

Mean and standard deviation (parentheses) values (n = 3). * mean values of daily sedimentation volume over a period of one week (7 days)

The suspension flow rates ranged from 0.03 to 0.59 milliliters per second. There was a statistically significant difference between the flow rates for the different products (between groups ANOVA $F(6, 14) = 649.79$, $p < 0.05$). Simple linear regression did not show any clear correlations between the suspension flow rate, sedimentation volumes and redispersibility. Multiple linear regression did not show any significant effect of either flow rates or sedimentation volumes on the redispersibility values. Theoretically flow rates outside a certain range may influence pourability as they are a function of the cohesive forces in the liquid suspension (viscosity). Sedimentation and redispersibility relate more so to ensuring dose to dose content uniformity. While a large degree of sedimentation may be tolerable, redispersion should occur readily and rapidly upon shaking as not all patients will be expected to agitate the suspension container to the same degree. Since the redispersibility was measured in this study by the number of times the suspension

was inverted to disperse sedimented material, the values for each individual measurement were whole numbers and a non-parametric test was considered more appropriate. Therefore, statistical comparison of the products was conducted by the Kruskal-Wallis test. The Kruskal-Wallis test of the seven products indicated statistically significant differences in redispersibility ($H = 18.85$ (6, $N = 21$), $p < 0.05$).

Figure 2 shows the sedimentation volume ratio measured as a function of time. The ratio of the sediment after seven days compared to the initial value ranged from 0.93 to 1.0 indicating that there was minimal settling of the dispersed phase. Visually, high sedimentation volumes are preferable due to greater aesthetic appeal and dose uniformity (in cases where redispersion is insufficient).

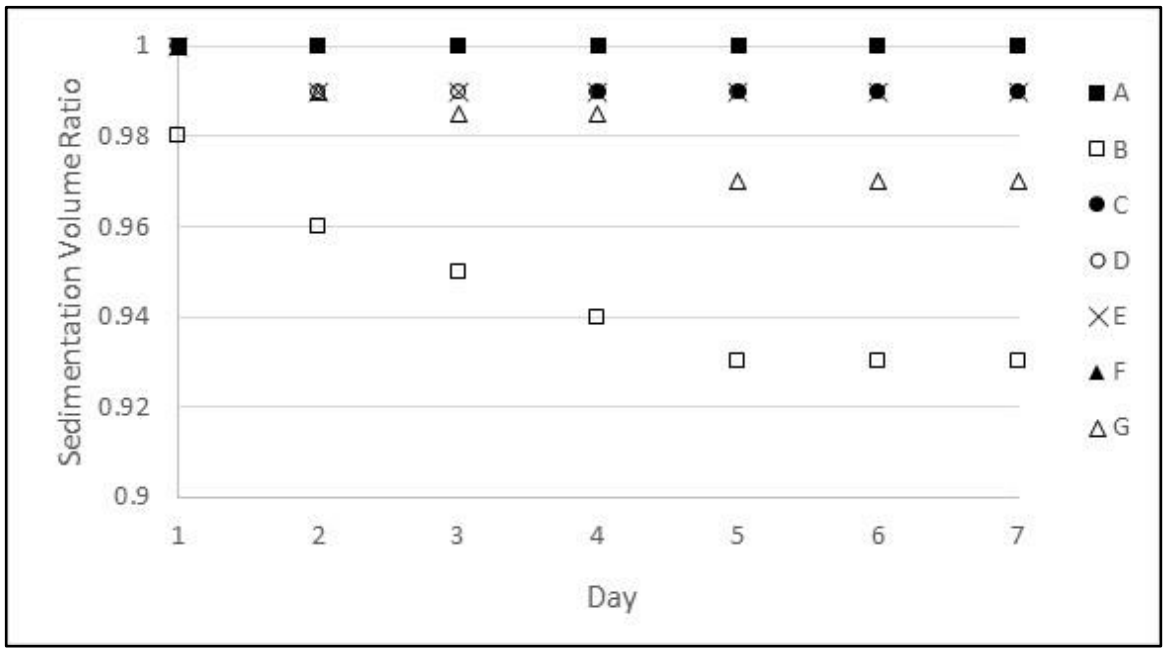

Figure 2. Sedimentation volumes recorded over the course of one week
Values for products A and F are equivalent and therefore superimposed.
Values for products C, D and E are equivalent and superimposed from day 4 onwards.

CONCLUSION

The acid neutralization capacity and physical characteristics of several locally available antacid suspensions were evaluated. There was wide variation between products in the experimental values measured. All products tested, however exceeded the 5 mEq limit in the US CFR Title 21 Part 331 [5].

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