Comparative assessment of price and quality of liquid antacids in Nigeria: a beacon of informed choice for Gastroenterologists and Obstetricians

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ABSTRACT
Introduction: Liquid antacids prices in Nigeria differ widely. Previous study using acid neutralizing capacity reported that price differences had no relationship with therapeutic efficacy. Present study evaluated the technical quality of most popular liquid antacids in Nigeria and sought link between product price and quality. Method: Sixteen brands were randomly purchased from pharmacies in different zones of Nigeria and evaluated for organoleptic, sedimentation, ease of redispersion, pH, flow rate and rheological characteristics using standard protocols. Results: All products possessed attractive colours, tastes, smells; with smooth viscous feel on the tongue and mouth. Products prices ranged from $1–$9, amounts which are not related to products’ listed drug contents. The pH values of products were range: 8–10. Product D pH was significantly higher (p<0.05) than any other’s. Sedimentation volumes after seven days ranged from 0.54–1.00 Sedimentation rate was highest in I and insignificant in four products. Products D and L were the easiest to redisperse, while B, A, and E were significantly the most difficult (p<0.05). Flow rates of products C and L were similar and significantly higher (p<0.05) than those of other products. G and P displayed the highest viscosity profiles and I’s was significantly lowest (p<0.05). Conclusion: Expensive antacids possess no better quality than cheap ones. There is no technical justification for the high cost of some liquid antacids since cheap ones have been shown to be as good and in some cases better both physiologically and technically. Key words: Antacids, Quality, Price, Informed choice, Gastroenterologist and Obstetrician.

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INTRODUCTION
Antacids are medicines taken to effect reduction of acidity of the stomach, treat oesophageal reflux disease and peptic ulcer. Most Nigerians, especially pregnant women usually consume antacids to relieve heartburn (commonest symptom of hyperacidity, acid reflux and peptic ulcer). Clinically, antacids are also indicated for acid indigestion, excessive stomach gas and bloating, prophylaxis for aspiration pneumonia during child birth.1,2 Some studies reported increased incidence of peptic ulcer and other hyperacid secretory related diseases in Nigeria.3,4 This observation may be unconnected with multi-factorial causes including, increased emotional, physical and mental stress, poor feeding culture, poor hygiene status with attendant increase in Helicobacter pylori infections and consumption of alcoholic beverages and spirits, consumption of over the counter (OTC) non steroidal anti-inflammatory analgesics. Gastroesophageal reflux disease (GERD) is experienced by about 80% of pregnant women.5 Reduction in lower oesophageal sphincter pressure due to increased maternal oestrogen and progesterone secretion during pregnancy has been linked to this condition. These hormonal changes during pregnancy also decrease gastric motility, giving rise to prolonged gastric emptying time and increased risk for GERD.5 Antacids containing aluminum, calcium, and magnesium are recommended as first-line treatment of heartburn and acid reflux during pregnancy; however high dose and prolonged use of magnesium trisilicate, or use of bicarbonate antacids often lead to adverse effects in maternal and foetal systems.6 Furthermore, antacids are the first choice of medications for the treatment of GERD in non-obstetric patients, peptic ulcer and related diseases, the presence of H1 antagonists and proton pump inhibitors in the therapeutic armoury of these ailments notwithstanding. This may be informed by the OTC class of antacids in that patients do not need prescriptions to procure them, coupled with their fast pain relieving nature.7,8 In addition, advertisement of antacids unlike prescription medications has popularized many brands even beyond their clinical effectiveness. Among antacids, other factors that may influence choice include palatability (taste, texture, smell and aftertaste),9 portability, availability and cost. Active ingredients content of antacids include calcium carbonate, magnesium hydroxide, aluminium hydroxide, sodium bicarbonate, simethicone, etc, and they act by neutralizing the acidic pH of the gastric juice, with simethicone countering build up of gas thereby preventing bloating. In Nigeria, many brands of antacid suspensions are available, some registered by the national agency for food and drug administration and control (NAFDAC), while many are not. Some are locally produced whereas many are imported; hence diverse prices of the products.10 Why are there still wide differences in prices if ANC are similar? This study therefore was aimed to empirically assess the physicotechnical properties of most popular liquid antacids in Nigeria and relate the finding to their market prices in major cities in Nigeria.

MATERIALS AND METHODS
Sixteen brands of antacid suspensions were randomly purchased from pharmacies in different zones of Nigeria. The same batch was procured for each brand and their identities are shown in Table 1.
**Organoleptic tests**

Each brand was inspected for characteristics like colour, feel, smell, and taste. The evaluation was conducted by a team of eight people (four males and four females). Each team was asked to state the colour and smell of four products. Thereafter they do same for another four until all products have been evaluated at 2 h intervals. The feel and taste evaluations were conducted by giving them 10 ml of the product under test and allowing them to swirl it in their mouths for 20 s and then spit out. Each volunteer was allowed to rinse off the product with plenty of distilled water several times and wait for 2 h before tasting another product.

**Evaluation of pH of samples**

From each brand of antacid suspension, 5 ml was withdrawn after sufficient agitation and transferred into a 25 ml beaker. Each suspension’s pH was then determined using a digital pH meter (Corning, model 10 England) at room temperature (35 ± 2°C). Triplicate determinations were conducted on each sample.

**Evaluation of suspension sedimentation volume and rate**

After adequate agitation, 100 ml of suspension was carefully transferred from each brand into 100 ml measuring cylinder and left undisturbed for seven days. Observations were made on daily basis for the seven days. Sedimentation volume (F) was calculated using the equation:

\[ F = \frac{V_u}{V_0} \]  

where \( V_u \) = ultimate volume of sediment on the day of measurement and \( V_0 \) = initial volume of suspension at zero time. Triplicate determinations were carried out for each brand.

Sedimentation rate (SR) of each brand of antacid suspension was evaluated as the slope of the regression analysis curve of sediment volume as a function of time.

**Determination of ease of redispersibility of samples sediment**

The 100 ml suspension samples which were allowed to settle in measuring cylinders for seven days were utilized for this study. The opening of each cylinder was closed firmly before inverting through 180°. The number of inversions required for the sediment to completely remix with the dispersion medium was taken as the redispersibility number. Triplicate determinations were conducted on each sample.

**Evaluation of sample flow rate**

The time required for 25 ml of each suspension brand sample to flow through a 25 ml pipette was determined and the flow rate (ml/s) was evaluated using the equation:

\[ \text{Flow rate} = \frac{\text{Volume of suspension}}{\text{Time of flow}} \]  

Triplicate determinations were carried out on each brand.

**Rheological characterization of samples**

From 180 ml of each brand of antacid suspension, 50 ml was withdrawn after adequate agitation to ensure uniform dispersion of product and then its viscosity measured with a digital viscometer (Shangi and Nirun intelligent, China) at room temperature (35 ± 1°C) using spindle numbers: one, two and three at 6, 12, 30 and 60 rpm for each spindle (Figure 1).

**STATISTICAL ANALYSIS**

Graphing and regression analyses were performed with Graph pad Prism 7 (Graph Pad Prism software Inc., 2016 San Diego, California, USA) while analysis of the results of various parameters tested was performed using one-way analysis of variance in Excel statistical package 2007. Significant differences were defined by \( P<0.05 \).

**RESULTS**

**Organoleptic properties, listed contents and price of products**

The result of organoleptic evaluation of the products is shown in Table 2. Four colours were identified: two products were cream in colour, six were pink, seven were white and one was yellow (Table 2). With the exception of products C,D and E, others possessed peppermint taste and aroma. Product C was lemon to taste, D was cherry and E was slightly sweet (Table 2). Most of the products were viscous, smooth/fine particled to feel. Only one product (J) gave a fluffy coarse sensation to the mouth and tongue when tasted. Products C and D were not viscous to mouth feel in comparison to others, yet they were smooth/fine particles (Table 2).

**Product listed contents and market price**

The active pharmaceutical ingredients (APIs) listed as contents of the products studied are shown in Table 3. The contents included sodium alginate, sodium bicarbonate, calcium carbonate, aluminium hydroxide, magnesium hydroxide, simethicone, magnesium carbonate, magnesium trisilicate, dimethylpolysiloxane and activated methylpolysiloxane. Activated methylpolysiloxane and dimethylpolysiloxane are synonymous to simethicone, the well known antifoaming or antigas agent in antacids.

The products prices ranged two hundred naira-₦200 (about $1) to one thousand eight hundred and fifty naira-₦1850 (about $9) (Table 3). It is obvious from Table 3 that the products prices do not have any relationship with contents of APIs. Product D for example which is the most expensive contains only one API, in contrast to product J which is the cheapest, but yet contains three APIs. Furthermore, product C contains...
the same APIs as product B, yet its price is more than three times that of B. Sodium alginate, a polysaccharide gum is present only in one product (A), not as a suspending agent but as an API for the treatment of gastric hyperacidity and GERD. Product G contains liquorice, another polysaccharide that can replace sodium alginate effectively both technically and therapeutically, yet it is about two and half times cheaper than product A.

**pH of liquid antacids studied**

pH is an important parameter in the assessment of the quality of all liquid pharmaceutical products. For antacids, its evaluation is key in predicting the ability of a product to neutralize or reduce gastric hyperacidity and bring relief to patients. The pH values of all the products were in the alkaline range (8-10) (Figure 2 Y and Z). Product D was the most alkaline with a pH of approximately 10.7, while product E was the least with pH of about 8.1. The pH of D is significantly higher (p<0.05) than any other product’s pH. The other products can be grouped according to similar pH values since no significant difference existed between their pH values. Three groups were distinguished as follows: products B,E,G,I and N; products A,C and J; products F,H,K,L,M,O and P. Product D was a standalone with respect to pH. This may be connected to its content which is solely magnesium hydroxide.

**Sedimentation volume and sedimentation rate**

Sedimentation volume is a standard quality assessment tool for pharmaceutical suspensions and provides insight to their physical stability. Its scale is 0 to 1 (i.e. high sedimentation to no sedimentation respectively). For flocculated suspensions in which the floccules are fluffy however, sedimentation volume may be greater than 1, because the floccules formed on standing may increase the products volume above the initial volume filled into the container. The relationship between sedimentation
Figure 4: Redispersibility number of products (mean ± SD, n = 3).

Figure 5: Flow rate of products (mean ± SD, n = 3).

Figure 6: Viscosity profile of products (mean ± SD, n = 3).
volumes of products studied and time is shown in Figure 3. Their sedimentation volumes after seven days ranged from approximately 0.54 to 1. Products G, H, N and P did not sediment at all after seven days hence gave sedimentation volume of 1. Products A, B, C, F and M sedimented slightly and gave values in the range of 0.95 to 0.98. Products E and L displayed similar values of 0.85 and 0.82 respectively. The most sedimented products with clear supernatants are in order J > I > O > K (Figure 3Q).

Sedimentation rates on the other hand are of the order I > P > D > E > K > L > J > C > F > B = A > M > G = H = N = P (Figure 3R). Fast sedimentation rate may not be technically unacceptable as long as the suspension can easily be redispersed, although the clear supernatant may be unsightly to patients. On the other hand, slow sedimentation rate may eventually lead to the formation of sediment that will be difficult to redisperse.

**Ease of redispersion of samples**

Redispersibility number is the number of times a sedimented suspension in a cylindrical container is inverted through 180° in order to get the sedimented particles completely mixed in the dispersion medium. Products D and L possessed the highest ease of redispersion (ease of redispersion being the inverse of redispersibility number) as shown in Figure 4. The redispersibility number is highest in products B, A and E. Their redispersion numbers were significantly higher (p<0.05) than those of other products. Products F,G,I,K,N, and O displayed similar ease.
of redispersion characteristics, which were significantly lower (p<0.05) than those of D,J,L and P (Figure 4).

**Flow rate of samples**

The flow rates of 25 ml of products through the orifice of 25 ml pipette are shown in Figure 5. Slurry flow rate may be influenced by the viscosity of the product, its density and composition. Figure 5 shows that the flow rates of products C and L were similar and significantly higher (p<0.05) than those of other products. Suspension flow rate is influenced by viscosity, which is dependent on type of suspending agent, particle size and shape, presence of floccules and concentration of solid components of the suspension. In pharmaceutical suspension dosage forms, flow rate is important in characterizing a products pourability, syringeability and injectability. For oral suspensions, pourability of product may be predicted from flow rate studies, although currently there is no standard/Pharmacopoeial test for suspension pourability. Just as a very fast flowing suspension has the tendency to flow off a dispensing measure, a sluggish flowing one may be difficult to pour into a measure. It is therefore pertinent that an intermediate flow characteristic be achieved using good suspending and viscosity enhancing agents.

**Rheological profiles of products**

Rheological study of suspension dosage forms gives information on how the products may flow under applied stress in order to reduce the strain. The measure of a flowing liquid or slurry to resist applied stress is known as viscosity, or liquid internal friction. Viscosity may be defined simply as force per unit area required to maintain a certain rate of fluid flow. Viscosity of the liquid phase in suspensions plays an important role on the flow properties of such products. Suspensions are structured fluids and typically exhibit non-Newtonian flow characteristics, and this property is revealed in Figure 6. The apparent viscosity values for all products studied decreased with increasing spindle speed, a characteristic known as pseudo-plastic behaviour (shear thinning effect). It can also be seen from Figure 6 IX that viscosity values increased as spindle size decreased from spindle 1 to 3. This makes the definition of viscosity as force per unit area easily appreciated because spindles' cross sectional areas are of the order: 1 > 2 > 3; so at constant shearing rate, viscosity has an inverse relationship with cross sectional area. Products G and P displayed the highest viscosities (Figure 6 IV and VIII), followed by products C and E (Figure 6 II and III), while product I displayed values (Figure 6 V) that were significantly lower (p<0.05) than those of G,P,C and E. Viscosity of suspension dosage forms affects dispersed particles sedimentation profiles, ease of redispersion, product flowability, pourability, syringeability and injectability.

**DISCUSSIONS**

Sedimentation volume as a quality assessment tool for suspension dosage forms gives information about their physical stability. Sedimentation volume of products may affect their appeal to healthcare practitioners, patients or their caregivers. It is common expectation that these groups of users may prefer products with sedimentation volume of approximately 1.0 to those of ≤ 0.5 because the high volume of clear supernatant may be interpreted as a sign of poor product quality. On the other hand however, health professionals based on their experience with some products may prefer them irrespective of their sedimentation volumes especially if they possess excellent redispersibility profiles. Suspension stability depends on sedimentation rate of dispersed particles, and this according to Stokes law, depends on particle size, density difference between dispersed particles and dispersion medium, and the viscosity of the system. The rate of particle sedimentation in suspension dosage forms affects the accurate/uniform dosing of the drug product because the lag time between agitation of container and withdrawal of dose may decrease the amount of drug in the withdrawn volume. It is desirable that suspension dosage forms, especially multidose ones be viscous enough or flocculated in order to prevent rapid sedimentation of drug particles. Sedimentation rate is inversely related to the viscosity of a suspension dosage form, and in products where suspending agent largely accounts for viscosity profile, sedimentation rate will be slow, thereby affecting uniformity of withdrawn dose positively. Other factors like particle size, particle size distribution, particle shape and density, density of dispersion medium, flocculation and aggregation of particles might have influenced the differences in the sedimentation rates as well as the sedimentation volumes of the products studied. The best sedimentation volumes and rates were not displayed by expensive products; rather relatively cheap ones did (Figure 3 and Table 3), suggesting the lack of relationship between technical quality and product price.

In pharmaceutical suspension dosage forms, flow rate is important in characterizing products pourability, syringeability and injectability. For oral suspensions however, pourability of product may be predicted from flow rate studies, although currently there is no Pharmacopoeial test for suspension pourability. Just as a very fast flowing suspension has the tendency to flow off a dispensing measure, a sluggish flowing one may be difficult to pour into a measure. It is pertinent that intermediate flow characteristics be built into products, as was observed in all products except C and L, again suggesting price and quality none relationship. Redispersibility number is the number of times a sedimted suspension in a cylindrical container is inverted through 180° in order to get the sedimented particles completely mixed in the dispersion medium. It gives subjective information on how easy such a product may be remixed before withdrawal of a dose which must contain adequate amount of drug. The implication of the results of redispersibility is that among the sixteen brands studied, products B, A and E which displayed the highest redispersibility numbers may need long agitation before complete remixing of sedimented particles may be achieved in order to ensure that each withdrawn dose contains adequate amount of drug and this amount is uniformly withdrawn each time after agitation. Rheological study of suspension dosage forms gives information on how the products may flow under applied stress in order to reduce the strain. Viscosity of the liquid phase in suspensions plays an important role on the flow properties of such products. Suspensions are structured fluids and typically exhibit non-Newtonian flow characteristics. The products studied displayed pseudo-plastic flow characteristics, a property that has been shown to enhance good suspendability, pourability and uniformity of doses withdrawn after agitation. Antacid suspensions containing moderate to high viscosity imparting polymers may be beneficial in coating ulcer surfaces thereby improving healing and reduction of pain for longer duration. The most expensive product (D) displayed low viscosity profile (Figure 6II); and although it has the highest pH (Figure 2), its best functionality may be fast reduction of gastric pH for short duration and concurrent incidence of acid rebound. This may account for the observed frequent intake of the product by ulcer patients. The differences in prices of the various products do not have any direct or indirect relationship with the type of active ingredients contained or their technical qualities. From the results, products that contained more active ingredients sell at lower prices than some with fewer active ingredients, even where taste and palatability were similar. In addition, the technical qualities of products selling at approximately five to ten times higher prices were in many cases lower than those of cheaper products. Previous studies in Nigeria showed that using acid neutralizing capacity (ANC) of antacids as a tool to estimate clinical and cost effectiveness, some otherwise cheap antacids were found to better or similar to expensive ones. Results from this study have shown that expensive antacids
imported into Nigeria do not possess better technical quality than locally manufactured ones; hence there is no justification for the wide price differences. Price discrimination on similar goods in commerce may be justified by functional differences in technical or other qualities (therapeutic effectiveness for medicines); otherwise, it can only be attributed to ostentatious life style. In pharmaceuticals, marketing strategies by various manufacturers or importers may also contribute to price discriminations. Among the antacids studied, none was an innovator’s product, so there is no case for such product’s usual higher prices tied to issues of specialty/uniqueness of API. It is worthwhile while that practitioners, especially gastroenterologists and obstetricians be aware of the current and previous findings in order to advise their patients creditably especially now that the exchange rate of Naira to other hard currencies is greatly unfavourable for Nigerian consumers.

CONCLUSION

The physicochemical qualities of liquid antacids studied revealed that most expensive antacids are not of better quality than relatively cheap ones. There is therefore no justification for the high cost of most imported liquid antacids since cheap ones have been shown to be as good as the expensive ones and in some cases even better both physiologically and technically. The organoleptic properties of the products are similar so expensive ones and in some cases even better both physiologically and technically. There is therefore no justification for the high cost of most imported antacids. Most expensive antacids are not of better quality than relatively cheap ones. There is therefore no justification for the high cost of most imported antacids. Most expensive antacids are not of better quality than relatively cheap ones. There is therefore no justification for the high cost of most imported antacids.

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CONFLICTS OF INTEREST

No conflicts of interest exists for this study.

REFERENCES

PICTORIAL ABSTRACT

This study evaluated the technical quality of most popular liquid antacids in Nigeria and sought link between product price and quality. Sixteen brands were assessed and all possessed attractive colours, tastes, smells and smooth viscous feel on the tongue and mouth. Products prices ranged from $1–$9, amounts which are not related to products’ technical qualities. The findings of this study indicate that expensive antacids possess no better quality than cheap ones. There is therefore no technical justification for the high cost of some liquid antacids since cheap ones have been shown to be as good and in some cases better both physiologically and technically.

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SUMMARY

- This study evaluated the technical quality of most popular liquid antacids in Nigeria and sought link between product price and quality. Sixteen brands were assessed and all possessed attractive colours, tastes, smells and smooth viscous feel on the tongue and mouth. Products prices ranged from $1–$9, amounts which are not related to products’ technical qualities. The findings of this study indicate that expensive antacids possess no better quality than cheap ones. There is therefore no technical justification for the high cost of some liquid antacids since cheap ones have been shown to be as good and in some cases better both physiologically and technically.