GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

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Analysis of gastrointestinal acid-neutralizing potency of some commercial antacid tablet formulations

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GSC Biological and Pharmaceutical Sciences, 2022, 19(02), 008–013

Publication history: Received on 19 March 2022; revised on 29 April 2022; accepted on 01 May 2022

Article DOI: https://doi.org/10.30574/gscbps.2022.19.2.0159

Abstract

In dyspepsia, formulations known as antacids are regularly used to alleviate symptoms as quickly as possible. Gastric contents are acidic; therefore, antacids are usually weak bases with the potential to neutralize excess acid and raise gastric pH accordingly. Acid-neutralizing capacity is what determines the effectiveness of an antacid. Some antacid tablets formulation from different manufacturers were tested for their acid-neutralizing capacity and effectiveness for patients in this study. The South-East region of Nigeria had pharmacies vending antacids of different brands. To remove potential bias from the study, the brands were coded A-F. Labels on all samples indicated that they would expire more than one year from now. To determine each antacid tablet's acid-neutralizing capacity, the titrimetric method was used. In terms of acid-neutralizing capacity, brands D, A, B, C, F, and E showed the greatest acid-neutralizing capacity (8.2mEq/g), and brand E showed the lowest capacity (5.7 mEq/g). An analysis of the ANC of all the tablets found that they exceeded the FDA standard of >5mEq for antacids. An inexpensive, simple, and easy-to-use titrimetric method could be used routinely to monitor antacid tablet quality.

Keywords: Antacid; Acid- neutralizing; Ulcer; Titrimetry; Gastric acid; Tablet

1. Introduction

Antacids are substances, generally, salts or basic bases that neutralize stomach acidity. Typically, they are basic medicines with a characteristic ability to neutralize the acid in gastric contents (stomach) and thus lower the acidity of the gastric contents[1]. There are several ways antacids reduce stomach acidity, including directly neutralizing acidity, increasing pH, or blocking the secretion of acid by the gastric mucosa cells[2]. Antacids also prevent irritation of stomach ulcers and relieve associated pain, and help relieve stomach ulcer pain by preventing irritation of the ulcer. Antacids are also known to act as pepsins, thus reducing peptic activity. An antacid contains bases usually pH above 7.0, and a buffer, which minimizes variations in hydrogen (H^+) and hydroxyl (OH^-) concentrations, as pepsin is inactive at this pH 4.0 and above. Nevertheless, they do not influence the rate of peptic ulcer healing, but relieve ulcer pain and promotes ulcer healing process[3]. It is also documented that antacids promote the recovery of duodenal ulcers[4]. Commercial antacids come in two forms, either as liquids or solid tablets. The principal constituents of antacids are magnesium and aluminum as hydroxides alone or in combination[4]. Some contain salt of calcium, sodium, carbon, or bismuth. Various antacids differ in their ability to neutralize acids and their transit time through the stomach. In comparison to tablets, an antacid suspension is more effective. An effervescent antacid can contain baking soda, a traditional home remedy for tummy aches. The combination of antacids with alginate to guard the esophagus from acid aggression is called an alginate-

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antacid derivative[6]. In general, two major types of antacids are systemic and non-systemic. Following oral administration of an antacid, it is absorbed completely by the body. Oral administration of non-systemic antacids does not cause them to be fully absorbed into the body. Aluminium hydroxide, aluminum phosphate, magnesium trisilicate, calcium carbonate, magnesium hydroxide, and magnesium carbonate are the most commonly used non-systemic antacids[7,8]. Antacids have a wide range of mechanisms of action. Preventing the back-diffusion of hydrogen ions across the GI mucosa is one of the mechanisms involved. By raising stomach pH to about 1.6, 50% of acid in gastric juice with a pH of 1.3 can be neutralized. This can be reached by raising the pH to 2.3, with 90% of the success, and 100% when it is 3.3. It is generally accepted that raising the stomach's pH to around 4 will protect against stress ulcers. Acid back diffusion is thought to treat this problem[9]. In addition to preventing pepsinogen from being converted into pepsin, antacids also work by inhibiting a process called gastric acidification. At pH5, pepsinogens become irreversibly inactive. For the greatest benefit from antacids, the pH needs to be raised to 5. Antacids are thought to be effective by inactivating bile salts located in the duodenum, which are thought to reflux into the stomach and contribute to acid peptic disease[10]. Some major antacids types include sodium bicarbonate ($NaHCO_3$), magnesium oxide (MgO), and magnesium hydroxide gel (Al_2O_3), calcium carbonate ($CaCO_3$), and peppermint flavor antiflatulents: Simethicone, Alginate: This seaweed extract acts as an acid barrier and prevent acid reflux in the peptic region of the gastrointestinal tract[11].

GERD symptoms can be relieved quickly and temporarily with over-the-counter (OTC) antacids. Antacids were commonly used in a previous study of 1,009 patients with GERD who failed to respond to standard PPI medication. The effectiveness of antacids in treating erosive esophagitis has been questioned[12]. GERD is the reflux of stomach content back to the esophagus, causing distressing symptoms and sometimes complications[13]. GERD is associated with heartburn; a symptom experienced by 7% of US citizens every day[14]. Another common GERD symptom is regurgitation. Clinical investigation of GERD can also be subdivided into non-erosive esophageal reflux disease (NERD) and the additional pathologies that may result from GERD, including esophageal ulcers, esophageal strictures, Barrett's esophagus, and Barrett's cancer[13]. The most common diagnosis for gastrointestinal complaints in the U.S. is GERD, which accounts for about 4% hospital visits[15]. Proton pump inhibitors, the first-line therapy for people with GERD, are indirectly responsible for the prevalence of GERD symptoms as well[16]. The United States spends over 10 billion dollars a year on PPIs, with two PPIs ranking among the top five selling pharmaceuticals[17]. Although PPIs have been recommended to treat erosive esophagitis, the rate of esophageal adenocarcinoma has increased significantly during the past 20 years[18].

To measure the actual amount of an analyte, titration, or titrimetry, is part of quantitative chemical analysis. Titrants and titrators, two biochemical reagents, are prepared as standard solutions[19, 20]. Analytes are titrated against titrants to determine their concentration. Titration volume refers to how much titrant reacts with the analyte[21]. Different methods are available for determining the most effective product out of all the competitors. With the right information, patients could decide the particular brand(s) of antacid to be used. Patients must be able to experience high levels of relief from their symptoms and also reduce their costs by using an antacid. The study aimed to determine which antacids tablet formulations are more effective for neutralizing gastrointestinal acids based on their acid-neutralizing capacities, through titrimetric analysis.

2. Methods

2.1. Sample Collection

The Pharmaceutical products used in this study were purchased from Pharmacies in Enugu State and Onitsha, South-East, Nigeria. The details of the drugs samples profiles are shown in Table 1.

2.2. Preparation of Reagents

2.2.1. Hydrochloric Acid Solution (0.1M)

Hydrochloric acid - HCl (0.15 M) was prepared by diluting 12.5 ml of 12 M HCl with deionized water in a 1-liter volumetric flask. After the addition of the acid, the volume of the flask was made to the mark using deionized water.

2.2.2. Sodium Hydroxide Solution (0.1M)

NaOH (0.1M) was prepared by dissolving 4.0 g of NaOH with deionized water in a 1-liter volumetric flask. After the dissolution process, the volume was then be made to the mark.

2.2.3. Preparation of 0.1M Potassium Hydrogen Phthalate (KHP) Solution

2.04 g of KHP was weighed and properly dissolved with deionized water in a 100 ml volumetric flask. After the dissolution process, the volume was made to the mark with the deionized water.

Table 1 Brands of Antacids

Brand In Tablet	NAFDAC No	Maf Date	Expiry Date	Batch No	Label claim (Constituent)
Brand A	A4-6606	12/19	12/22	5410X	Magnesium trisilicate 50 mg
					Aluminum hydroxide 300 mg
					Magnesium hydroxide 25 mg
Brand B	B4-4506	20-Feb	23-Feb	320	Aluminum hydroxide 300 mg
					Magnesium hydroxide 25 mg
					simethicone 10mg
Brand C	Apr-85	20-Apr	23-Mar	AB39834	Dried aluminum hydroxide 300 mg
					Magnesium trisilicate 50 mg
					Magnesium hydroxide 25 mg
					Simethicone 10 mg
Brand D	04-1068	20-Jul	23-Jun	MT4097	Magnesium trisilicate 250 mg Aluminium hydroxide 120 mg Peppermint flavor
Brand E	B4-4704	20-Aug	23-Aug	2006	Dried aluminum hydroxide 300 mg
					Magnesium hydroxide 25 mg
					simethicone 10 mg
Brand F	A4-1902	Jan-19	011/2022	J9002	Dried Aluminium hydroxide 300 mg
					Magnesium aluminum silicate 50 mg
					Magnesium hydroxide 25 mg
					simethicone 25 mg

2.3. Standardization of Reagents

2.3.1. Sodium Hydroxide Solution

20 ml of 0.1 M KHP was measured into a 250 ml Erlenmeyer flask followed by 3 drops of phenolphthalein, as indicator. The solution was titrated with 0.1 M sodium hydroxide solution until it turned pink which persisted for at least 30 seconds. The volume of 0.1 M NaOH solution used was then recorded. The titration procedure was repeated 3 more times, and the average titer value was recorded.

2.3.2. Hydrochloric Acid Solution

30 ml of the 0.15 M HCl solution was measured into a 250 ml Erlenmeyer flask followed by 3 drops of phenolphthalein. The solution will then be titrated with 0.1 M NaOH until the solution turns pink which persisted for 30 seconds without fading. The titration procedure should be repeated 3 times, and the average titer value recorded.

2.4. Evaluation of the Neutralizing Capacity of Antacid Tablets

The sample of each antacids tablet was separately weighed and crushed using a mortar and pestle. 0.5 g of the crushed tablet was weighed and transferred into a 250 ml Erlenmeyer flask. This was followed by the addition of 30 ml of the standardized HCl solution and swirled gently to dissolve the crushed tablet as completely as possible. 3 drops of bromophenol blue indicator were added to the solution which then turned yellow. The solution was then titrated with the standardized NaOH until a blue color was formed[22]. The titration procedure was repeated thrice, and average titer

value was obtained. The same procedure was repeated with all other brands of antacid tablets and the average titer value of the NaOH solution required to neutralize the excess acid (HCl) for each brand of the antacid was recorded and the ANC per dose of antacid was calculated.

3. Results and discussion

In this study, we explored the effects of acid-neutralizing property on antacid dosage forms, a widely admired and necessary pharmacological factor. In this study, we used the titrimetric method to analyze six commercially available brands of antacid tablets (Table 1). These antacid tablets were assessed for their organoleptic properties. Table 2 shows all the antacids had peppermint flavor (all antacids had peppermint flavor). It can therefore be concluded that most marketed antacid formulations contain mint as a flavoring agent. To make chewable tablets more acceptable, all the tablets had a sweet taste. The colors of the tablets differed from one another.

Table 2 Organoleptic Properties of Antacid Tablets

Parameter	Brand A	Brand B	Brand C	Brand D	Brand E	Brand F
Taste	Sweet	Sweet	Sweet	Sweet	Sweet	Sweet
Color	Green	Peach	Off-white	White	Light Cream	Pink
Flavor	Peppermint	Peppermint	Peppermint	Peppermint	Peppermint	Peppermint

From the titration analysis performed on the different brands of the antacid tablet formulation, a relationship was depicted between the average titer value and the ANC per gram of antacid. The lower the average titer value the higher the ANC per gram of antacid. The ANC of an antacid is the amount of acid it can neutralize. Miliequivalent is the gram equivalent expressed in one-thousandth of a chemical element. Per FDA requirements, an antacid should possess gastric acid neutralizing capacity of ≥5 mEq per dose (Table 3).

Table 3 Parameters Evaluated For the Antacids

Parameters	Brand A	Brand B	Brand C	Brand D	Brand E	Brand F
Average titer value (cm^3)	5.5	6.5	10.0	4.2	16.5	15.5
The total amount of HCl used (mol)×10^{-3}	4.5	4.5	4.5	4.5	4.5	4.5
Amount of HCl neutralized by NaOH {mol)×10^{-3}	0.55	0.65	1.0	0.42	1.65	1.55
Excess HCl neutralized by antacid(mol)×10^{-3}	3.95	3.85	3.5	4.08	2.85	2.95
Mass of antacid used (g)	0.5	0.5	0.5	0.5	0.5	0.5
ANC per g of antacid (mEq/g)	7.9	7.7	7.0	8.2	5.7	5.9

The most effective antacid ought to have a high gastric acid neutralizing capacity and rapid acid neutralization potentials. From the result above Brand D have the highest ANC of 8.2mEq/g while Brand E has the lowest ANC of 5.7 mEq/g though all the brands of antacids analyzed met the USA-FDA requirement of an antacid which states that ANC for an antacid should not be less than 5 mEq per dose[23]. The acid-neutralizing capacity of every brand was calculated by the equation: Total mEq= $(30\times N_{HCl}) - (V_{NaOH} \times N_{NaOH})$, ANC per gram= Total mEq/mass of the antacid; Where N_{HCl} and N_{NaOH} are the normalities of HCl and NaOH respectively and V_{NaOH} is the volume of NaOH consumed for the titration. The result obtained from this study is relative to a precious survey that compared the gastric acid neutralizing potentials of dimethicone and alginate in the therapeutic management of reflux oesophagitis[24]. The effectiveness of the Antacid Brands on the chemical composition was found to be interesting. Brand D which showed the highest ANC contains Magnesium trisilicate and Aluminium hydroxide as its most active constituent. Brand A with the second to highest ANC per dose of 7.9 mEq/g has Magnesium trisilicate, magnesium hydroxide, and aluminum hydroxide as its most active constituent (Figure 1). Magnesium hydroxide, aluminum hydroxide, and magnesium trisilicate had better neutralizing abilities, compared to others. An antacid preparation that contains aluminum hydroxide and magnesium hydroxide will assist in lowering stomach acidity without producing undesirable side effects such as diarrhea or constipation.

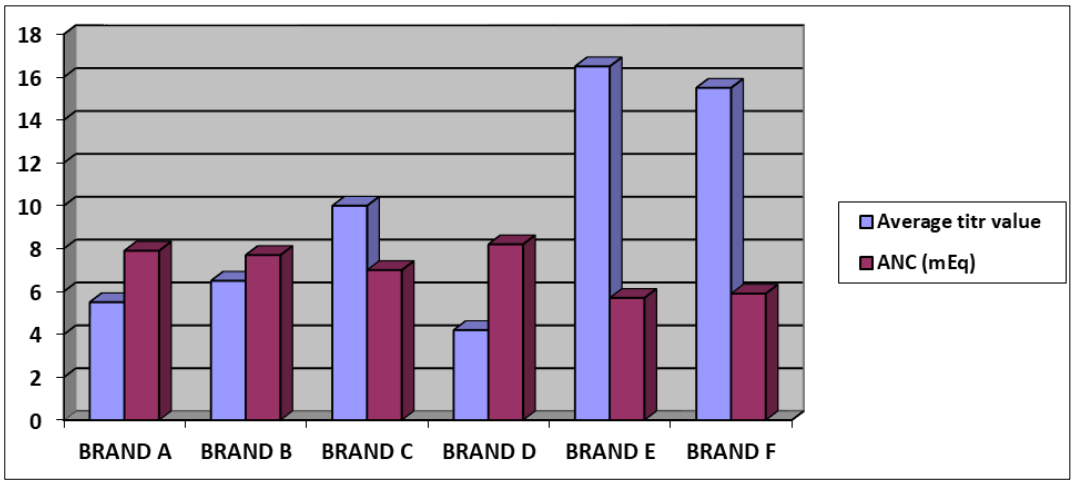

Figure 1 Bar chart of brands of antacid against the ATV and ANC

4. Conclusion

The importance of antacid preparation cannot be over-emphasized in the health of ulcer patients, as well as those with heartburn related symptoms. This study has revealed that different antacid preparations have different acid-neutralizing capacities. The high acid-neutralizing capacity of Brand D makes it the antacid of choice in treating various acid-mediated gastrointestinal problems. Also, Brand D shows the highest acid-neutralizing capacities which contain magnesium trisilicate, dried aluminum hydroxide. However, the difference in the ability to neutralize acid is not reflected on the labels of antacid products. The titrimetric procedure could therefore be employed to analyze the ANC of the antacid formulations. This procedure is cost-effective, simple, and easy to use, thus could be explored in routine monitoring and quality control of antacid tablets, especially in absence of high-quality equipment.

Compliance with ethical standards

Acknowledgments

The authors greatly acknowledge Dr. Edebi N. Vaikosen, Dr. Adesegun Kashimawo, and other staff of the Pharmaceutical and Medicinal Chemistry of Niger Delta University, Wilberforce Island, for their immense support and valuable contributions.

Disclosure of conflict of interest

The authors hereby declare that, there is no conflict of interest in this article.

Statement of ethical approval

All the laboratory experiments and procurement of drug samples for this research work followed laid down ethical standards. Body samples and patient data was not used in the study, hence no formal ethical approval was required.

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