PHARMACO-ECONOMIC ANALYSIS OF BRANDS OF ANTACID FORMULATIONS AVAILABLE IN ISHAKA TOWN USING TITRIMETRIC METHOD

BY

KAVUMA ADRIANE

BPH/0041/133/DU

A RESEARCH REPORT SUBMITTED TO THE SCHOOL OF PHARMACY IN PARTIAL FULFILMENT OF THE REQUIREMENTS OF THE AWARD OF BACHELORS OF PHARMACY OF KAMPALA INTERNATIONAL UNIVERSITY

DECEMBER, 2017

DECLARATION

To the best of my knowledge, I hereby declare that this research report has not been submitted in full or in part to any other institution for any purpose. And that the views herein are my own, unless stated, and where such has been the case, acknowledgement or reference has been quoted.

Signed..... Date.....

KAVUMA ADRIANE

BPH/0041/133/DU

APPROVAL

This research report has been submitted for examination with my approval as the candidate's supervisor.

Signed..... **Date**.....

RICHARD L. MASERUKA, BSc. MSc.

SUPERVISOR

DEDICATION

This work is dedicated to my mother Mr's Kasiriivu Teddy of Kitwe Village in Masaka district for her moral and financial in the academic course.

ACKNOWLEDGMENT

I acknowledge the love and care the almighty God has provided to me since birth passing through all hard times to the success of my course. I would like to extend my gratitude to my project supervisor Mr. Maseruka L. Richard for his support and guidance. My appreciation also goes to Dr. Samanya Bulhan for all the assistance he gave me towards making the undertaking of this project possible. Great thanks to my late father Mr. Kasirivu Francis for he started the journey of educating us, my sister Nanvuma Brenda for being on my side, my brother Ssebalijja Francis for standing in the shoes of our late father.

LIST OF ABBREVIATIONS

FDA Food and Drug Authority

NDA National Drug Authority

OTC Over-the-counter

ANC Acid Neutralizing Capacity

UAE United Arab Emirates

HCl Hydrochloric acid

API Active Pharmaceutical Ingredients

NaOH Sodium hydroxide

SG Specific gravity

ABSTRACT

Pharmaco-economics involves comparing the cost and consequences of products and services and Cost-effectiveness is the relationship between cost and effectiveness of a given drug. ANC of an antacid is one of the ways of evaluating effectiveness of antacid brands. ANC (mEq per unit dose) is the ability of the antacid to neutralize gastric acid (Shery et al., 2013), and it should be greater or equal to 5mEq per unit dose(FDA), where a unit dose of 0.5g for tablets and 5ml for suspensions was used. Cost was evaluated using cost per unit dose.

Antacid formulations (tablets/suspensions) act by neutralizing gastric acid which is mainly hydrochloric acid (HCl). Normal concentration of stomach HCl is about 0.082M and a person experiences stomach acid when HCl concentration increases to about 0.1M. Antacids are indicated for peptic ulcer disease (PUD), gastro esophageal reflux disease (GERD), acid indigestion and bloating. Antacids contain one of the following compounds as their active ingredients: Magnesium hydroxide, calcium carbonate, sodium bicarbonate, aluminum hydroxide, magnesium trisilicate or ammonium citrate. Side effects due antacid use include: milk-alkali syndrome, osteomalacia, hypophosphatemia, constipation, diarrhea, aluminum-intoxication and dose dependent rebound hyperacidity (Omotosobayomi et al., 2015).

The study design was experimental and during this study, sixteen marketed brands of various dosage forms were purchased from pharmacies in Ishaka and their details recorded. 0.5g of tablet powder or 5ml of suspension was weighed into a 250ml flask. A known volume of 0.1M HCl (20ml for tablets and 30ml for suspensions) was added to the flask and mixture swirled, then boiled for 15 seconds and cooled to room temperature. 8 drops of bromothymol blue were added and the mixture turned yellow. If it was not yellow, more HCl could be added until it turned yellow. The volume of excess acid added was recorded. The mixture was then titrated against 0.1M NaOH until a blue end point was reached.

The data was entered into Microsoft Excel and analyzed using STATA version 12 in which the ANOVA was used to test for differences amongst the ANC values and the costs per unit dose of the selected antacids. A 5% level of significance was considered and a p value less than that was taken to be significant. In this study, the ANC values and costs per unit dose of different brands were significant ($p<0.0001$).

In this study, ANC was classified into three groups; the high ANC (13.08 - 26.48), the intermediate ANC (5.09 - 5.09) and the low ANC (0.69 - 1.98). All tablets were in the low class plus a few suspensions. Most suspensions were in the intermediate and high ANC. For suspensions Maalox plus had the highest ANC value (26.48), followed by Magnesium trisilicate

mixture (22), and Gaviscon (13.68) whereas Stamachfit had the lowest (1.78), followed by Centacid (1.89) and Magnomint (5.10). Meanwhile, for tablets, Maalox plus had the highest ANC of 1.52mEq and CMT the lowest of 0.85mEq.

Antacids with anti-foaming agents had lower ANC values since all were in the intermediate and low ANC group. Antacids with anti-foaming agents in this study were; Acid, Relcergel, Centacid and Mucogel (all with simethicone as the anti-foaming agent).

The unit price of antacid suspension was between shs 50 - 1333.3 per 5ml dose, while that for the tablet antacids was between shs 35.7 - 666.7, thereby making tablets to be cheaper than suspensions.

For suspensions Maloox plus had the highest cost per unit dose (shs 1333.33/5ml) followed by Gaviscon (shs 875/5ml) and Mucogel (shs 600/5ml) whereas Maaga, Magnant and Magnesium trisilicate mixture (SEV) all with unit price of shs. 50/5ml had the lowest cost per unit dose. All local suspensions except Renegel, had the same cost per 5ml of shs 50, however for imported brands like Relcergel, Centacid, Alcid and Stomachfit from the same country (India) also had different cost per 5ml. Meanwhile for the chewable tablets, Maalox plus had the highest cost per unit dose of shs 666.7/0.5g while CMT and Mint o cool had the lowest of shs 35.7/0.5g.

Maalox plus suspension had the highest ANC (26.48) but was not the most cost-effective antacid brand rather it was Magnesium trisilicate mixture (SEV), followed by Maaga, one of the local brands. No positive correlation was found between cost and effectiveness of antacid since local brands of lower cost were found to be equally effective compared with the costly imported brands. Due to high ANC, few tablet antacids can be substituted for liquid antacids. Antacids therefore, can be consumed judiciously provided ANC details are enclosed on the label of these products.

Acid neutralizing capacity details of antacid brands should be incorporated on to the labels to improve good prescribing practices. Further research should be done on other brands. Other research studies like sodium content, physico-chemical parameters and heavy metal (lead) content of antacids should be carried out.

Table of Contents

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

1.1.1 Historical background

In 1978, Bootman *et al* from the university of Minnesota, introduced the concepts of cost - benefit and cost-effectiveness analysis. The actual term pharmaco-economics did not appear in literature until 1986 when it was first presented by Townsend. Cost-effectiveness analysis is a technique designed to assist a decision maker in identifying a preferred choice among possible alternatives. It has been applied to health matters where the program's inputs can be readily measured in dollars but the program's outputs are more appropriately stated in terms of health improvement created (for example, life-years extended, clinical cures) McGhan *et al.*, 1978.

Various in-vitro tests have been developed to evaluate the performance of antacids which are intended to reflect their in vivo efficacy. The measurement of Acid neutralizing capacity of antacids is one of the widely used test which was first determined in 1973 by Fordtran and co-workers and they evaluated the ANC values at that time. Since that time, their published results have served as a guide for physicians prescribing antacids. He suggested that dosage should be determined by milliequivalents of ANC rather than arbitrary volume or number of tablets (May *et al.*, 2016).

In, India Vedavathi *et al.*, 2013, carried out this cost-effectiveness study and from their results they were able to conclude that: the cost effectiveness and efficacy studies are very essential in improving the prescription pattern. They are informative both from patient and doctor point of view. A patient will benefit from the availability of the best quality drug at a cheaper cost. A doctor will get information regarding the choice of the drug for a particular patient.

In United Arab Emirates, the study results revealed that monthly cost of high dose therapy per day for high ANC tablet antacids is much cheaper than low ANC tablet antacids and

recommended that ANC of should be included on the product label for accurate dosages (May *et al.*, 2016).

In Southern Nigeria, this study was able to show that the effectiveness of an antacid is not a function of the price but rather it's ANC (Omotosobayomi *et al.*, 2015).

1.1.2 Conceptual background

Bootman *et al* defined pharmaco-economics as the description and analysis of the costs of drug therapy to health care systems and society. Pharmaco-economic research identifies, measures and compares the costs (i.e. resources consumed) and consequences (i.e. clinical, economic and humanistic) of pharmaceutical products and services. Within this framework are included the research methods related to cost-minimization, cost-effectiveness, cost-benefit, cost-consequences, cost-of-illness, cost-utility and decision analysis; as well as quality-of-life and other humanistic assessments. In essence pharmaco-economic analysis is used as a tool for examining the impact (desirable or undesirable) of alternative drug therapies and other medical interventions. The analysis of antacid formulations is important for obtaining optimum therapeutic concentrations for the different constituents of antacids and also to determine the most cost-effective brand. Antacids are medicines taken to effect reduction of acidity of the stomach, treat gastro-esophageal reflux disease (GERD) and peptic ulcer disease. Clinically, antacids are also indicated for acid indigestion, excessive stomach gas and bloating.

Peptic ulcer and other hyper acid secretory related diseases may be caused by increased emotional, physical and mental stress, poor feeding culture, alcohol consumption, smoking, H. pylori and use of OTC non-steroidal anti-inflammatory analgesics (Omotinuolaw *et al.*, 2017).

Antacids are available in two dosage forms (tablets and suspensions) commonly prescribed world over as Over-the-Counter (OTC) or prescription medications, administered orally. They mainly contain calcium carbonate, magnesium hydroxide, sodium bicarbonate and aluminum hydroxide as the principle active ingredients, and act by neutralizing the acidic pH of gastric juice. They

may cause milk-alkali syndrome, osteomalacia, hypophosphatemia, constipation, diarrhea, aluminum-intoxication and dose dependent rebound hyperacidity (Omotosobayomi *et al.*, 2015).

All antacids contain at least one of the primary active 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 systemic absorption. It is documented that the buffering capacity of magnesium salts is greater than that of aluminum salts but less than that of sodium bicarbonate and calcium carbonate (Lutchman *et al.*, 2016).

This study is driven by two concepts namely: local and imported antacid brands as the independent variables and their effectiveness and cost as the dependent variables. Acid neutralizing capacity (ANC) will be used to evaluate the effectiveness of the brands while cost per unit dose of the antacid brand will be used to evaluate the cost.Shery *et al* (2013) defined ANC of an antacid tablet or liquid formulation the ability of an antacid tablet or liquid formulation to buffer against stomach acid expressed in mEq. And milliequivalent (mEq) as gram equivalent expressed in one thousandth of a chemical element, an ion, a radical or a compound. The ANC of an antacid should be greater than or equal to 5mEq per dose (FD

1.2 Problem statement

In Uganda, many brands of antacids, both suspensions and tablets are available; some registered by NDA, while others are not. Some are locally produced whereas many are imported, hence their prices differ without reliable relationship between brand's price and its effectiveness. Generally imported antacids are more expensive than locally produced ones, with no even proven therapeutic advantage in terms of effectiveness. Therefore there is a need to determine the effectiveness of local and imported antacids using ANC and their relative prices in order to determine the most cost-effective antacid available in Ishaka pharmacies. Due to the fact that the effectiveness of the antacid brand cannot be determined by its name or its manufacturing company but rather its API content that is responsible for producing the neutralizing effect of the antacid, it is necessary to determine ANC of these brands.

PUD, GERD (heartburn), bloating, flatulence and indigestion are common conditions in Ishaka and Uganda in general. These conditions often present with painful burning sensation in the stomach, abdominal discomfort and pain but can be treated with antacids and therefore, there is a need for the most effective antacid that will relieve pain within a short time period and available at the most affordable price to the patient.

OBJECTIVES

1.3 General objective

To determine the most cost-effective antacid brand by using ANC and cost per unit dose of different brands of antacids in Ishaka town

1.4 Specific objectives

1. To determine the ANC levels of both imported and local antacid brands in Ishaka town.
2. To determine the cost per unit dose of both imported and local antacid brands in Ishaka town.

1.5 Research Questions

1. What are the ANC levels of both imported and local antacid brands in Ishaka?
2. What is the cost per dose of both imported and local antacid brands in Ishaka town?

1.6 Scope of the study

1.6.1 Content scope

In this study, the independent variable is the antacid formulations in Ishaka town and the dependent variable is the cost-effectiveness of antacid formulations. The content in this study is about medicine, health, economics, chemistry, pharmacological and pharmacy.

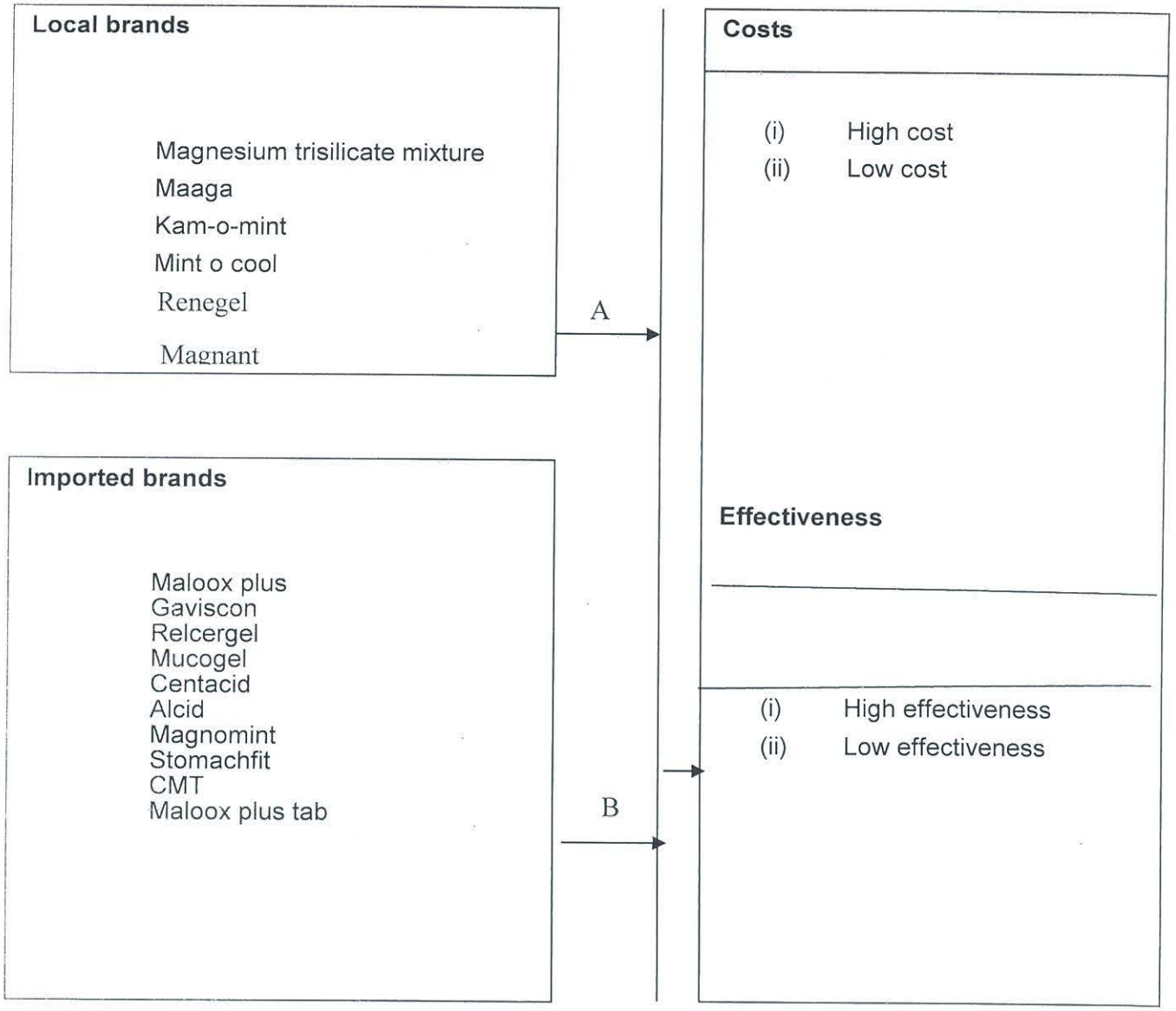
1.6.2 Geographical scope

The study was carried out in Ishaka town and it covers five pharmacies. The people to give information about the available antacid brands, their formulation and cost and were pharmacists or pharmacy technicians certified by the council and they were running these five pharmacies.

1.7 CONCEPTUAL FRAMEWORK

Independent variable

Dependent variable



Source: Developed by the researcher.

Arrow A finds the objective 1

Arrow B finds objective 2

1.8 Significance of the study

Including ANC on the antacid label can help policy makers to decide for people what to buy putting the cost in consideration thus improving the quality of life of patients and also improve accurate dosing by physicians. This has also enabled me acquire my academic qualification of bachelor of pharmacy, changing my status in the society. Also my literature can be used by other people for referencing.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1. Effectiveness of antacid brands using ANC

In the study to evaluate efficacy of some antacid brands as it relates to their cost effectiveness, brands analyzed were; milk of magnesia, Gaviscon, Ulgicid, Gestid, Grenocid, Relcer gel, Gascol, Jawasil, Juhel-mistmag, Maloox, Gastosil, Antasil, Krisacid, Danacid, Polygel, Sodamint, Julsil and Rulox . Similar trends in terms of specific gravity, pH and ANC were followed by different brands with similar active ingredients but Physcio-chemical properties are different, and this may be as a result of formulation factors employed in the manufacturing of the products. Milk of magnesia which contains only a single antacid as the active ingredient (Mg (OH)2) had the highest ANC when compared to other antacid suspension. This may be as a result of this brand having the lowest SG, which translates to higher surface area for the suspended Mg (OH)2 particles in the suspension, better flow ability and thus better contact with the stomach acid. On closer look at Gascol, a brand without any chemically classified antacid component but purely antacid foaming agents, also exhibit a relatively high ANC value. Formulations with both anti-foaming agents and antacids as their components were observed to have low ANC value. The possible reasons may be because antacids in the combined formulation, in acidic environment may have reacted with only the excess stomach acid that cannot be sequestered by the gel formed by anti-foaming agents thus explaining the reason why they had low ANC values when compared with preparation containing only anti-foaming agent which sequester with acid better.

The ANC of the most potent antacid (milk of magnesia) was found to be thirteen times that of the least potent (polygel). The ANC of milk of magnesia per 5ml of suspension was found to be the highest while Relcer gel had the lowest. Meanwhile for the antacid tablets, Antasil was found to have the highest ANC value and Polygel with the lowest. This literally means that 5ml of Milk of magnesia will neutralize an equal amount of acid as eight tablets of polygel. From the results, liquid antacids are better compared to chewable tablets. The nineteen antacid formulations were

classified into three groups according to their ANCs, those with the highest ANC (13.55-9.51mEq), those with an intermediate ANC (5.48- 3.17 mEq) and those with a lowest (2.98-1.10mEq). According to this categorization, it was observed that antacid suspensions mostly fall under the high and intermediate class while the tablet formulation belong mostly to low class antacid in terms of ANC.

The SG of an antacid suspension is not a major determining factor for the effectiveness of an antacid suspension because the brand with the lowest SG value does not have the lowest ANC value. The brand Jawasil with the highest SG value had a higher ANC value than Maloox with the lowest SG value.

From the average pH values of the antacids assayed, none of the product's pH is significantly different from the average value (pH=7.12) obtained for different brands. There is no correlation between the obtained pH values, cost-effectiveness and their ANCs. The antacid suspension with the highest product pH neither had the highest nor lowest values of cost-effectiveness or ANC (Omotosobayomi *et* al., 2015).

In the study of the ANC of ten solid and five liquid antacids, purchased from community pharmacies in the Ajman area of UAE, ANC was analyzed in triplicate. The tablet and liquid antacids fall into four statistically different ANC groups. All groups indicated no correlation of ANC to the total amount of antacid ingredients.

The ANC of most effective liquid antacid analyzed was twice that of least effective. This variation in neutralization was not observed in any one product label of antacid brands. Undoubtedly, the actual ANC was not shown on the labels of all product manufacturers. Most companies advocate a regular dose of 1-2 teaspoonful (5-10ml) of antacid, disregarding of the product's ANC. High /intermediate high ANC (liquid or tablet) contributed maximum acid neutralization with the lowest dose volume /weight. The consumption of these antacids also allows minimum sodium and calorie intake and cost to the pharmacist. Liquid antacids compared

to tablet antacids have been endorsed in the treatment of gastric ulcer condition due to greater surface area, which is responsible for their excellent neutralization capacity. Nevertheless, three tablet antacids analyzed found to have ANCs that are comparable to those of higher ANC liquid antacids and higher than the lower ANC group. High group (35.83-31.27), intermediate (20.12-30.26) and low ANC group (18.22-19.42) (Shery *et al.*, 2013).

In the in-vitro study of ANC of six commonly available antacid tablets in Iraqi market using back titration method, the tablet brands used were; Rennie, Gaviscon, Barkalox plus, Ballox plus, Maloox and Moxal plus. The highest ANC value was obtained from Rennie followed by Gaviscon whereas all the other brands with anti-foaming agents were observed to have a lowest ANC value in both acid concentrations. This in vitro study showed that ANC value is the most important factor in determining the potency of the antacid which may help in designing and manufacturing new antacid formulation. An effective antacid is characterized by the fast onset of action, buffering of the pH of the stomach, having ANC of not less than 5mEq per minimum single dose and cause minimal side effects. Moreover, a physician also needs to consider the following factors; the antacid should neutralize the greatest amount of acid per unit cost, should be both palatable and conveniently consumed by the patient (May *et al.*, 2016).

In the analysis study of seven different brands of antacid gel preparations commonly available and prescribed in the local area of Shimoga for the various properties, the study was divided under two heads, cost effectiveness and efficacy studies. The cost effectiveness study included the palatability test and the cost per ml of antacid preparation. There was no much variation in the palatability score of different antacids because in the present competitive market, majority of the manufacturing companies take out most care to improve the palatability. There was a wide variation in the costs of antacids but no much difference in ANC values.

In this study there wasn't much difference in the ANC of antacid preparations (Vedavathi *et al.*, 2013).

2.2 Cost per dose of antacids

In the study carried out to evaluate efficacy of some antacid brands as it relates to their cost effectiveness in Nigeria, the unit price of antacid suspension was found to be between ₦5-₦50 per 5ml dose, while that for the tablet antacids was found to be between ₦1-15 per tablet, thereby making the tablet to be cheaper than the suspension. The most expensive antacid suspension was Maalox with unit price of ₦10/ml while the cheapest brand is Juhel -Mist Mag ₦1/ml. For chewable tablets, Gastosil was the most expensive brand at ₦15/tablet while the cheapest brand, Julisil chewable antacid tablet goes for ₦1/tablet. This study revealed no correlation between the unit price and the ANC of the antacids. These prices vary from one pharmacy to another and the price is determined by different factors such as how and where the products were sourced and also the product make up which varies from one pharmaceutical premise to another. Thus there is need for both health care provider and the patient come to an agreement and select the appropriate antacid considering both the effectiveness as well as the price (Omotosobayomi *et al.*, 2015).

In the pharmaco-economic analysis study of ten solid and five liquid antacids, purchased from community pharmacies in the Ajman area of UAE, the tablet antacids were than liquid antacids. Monthly cost of large dose therapy for high ANC tablet antacid is much cheaper than low ANC tablet antacid. Liquid antacids monthly dose therapy is one by third of cheapest tablet antacid therapy. Sodium content and calorific value of all antacids are negligible due to availability of non-calorific and non -sodium containing excipients (May *et al.*, 2016).

In the study aimed to empirically assess the physicotechnical qualities of most popular liquid antacids in Nigeria and relate the finding to their market prices in major cities. The results showed that the products prices ranged between two hundred naira to one thousand eight hundred and fifty naira. The products prices do not have any relationship with contents of API (Omotinuolaw *et al.*, 2017).

CHAPTER THREE

3.0 methods and materials

3.1 MATERIALS

3.1.1 Samples and Reagents

1. Antacid tablet /suspension
2. 0.1M hydrochloric acid
3. 0.1M sodium hydroxide
4. Bromothymol blue indicator solution
5. Distilled water
6. 0.1M Potassium Hydrogen Phthalate

3.1.2 Instruments

1. Two 250ml Erlenmeyer flasks and at least two 100ml breakers
2. Mortar and pestle
3. Two burets, 50ml
4. Analytical balance
5. Pestle and mortar
6. Measuring cylinder
7. Pipettes
8. Water bath

3.2 METHODS

3.2.1 Study design

The study design was experimental

3.2.2 Area of study

The study was conducted at the Pharmacy Laboratory of KIU.

3.2.3 Sample size

Sixteen antacid brands were used

3.3 Procedure

3.3.1 Preparation of samples and reagents

3.3.1.1 0.1 M Hydrochloric Acid Solution

0.1 M HCl was prepared by diluting 8.6 cm3 of 12 M HCl with deionized water in 1litre volumetric flask. After the addition of the acid, the volume of the flask was made to the mark using deionized water.

3.3.1.2 0.1M Sodium Hydroxide solution.

0.1 M NaOH was prepared by dissolving 4.0 g of NaOH in deionized water in 1litre volumetric flask. After the dissolution process, the volume was made to the mark.

3.3.1.3 0.1 M Potassium Hydrogen Phthalate (KHP) Solution

2.04 g of KHP was weighed and properly dissolved with deionized water in 100 cm3 volumetric flask. After the dissolution process, the volume was made to the mark with the deionized water.

3.3.1.4 Standardization of Sodium Hydroxide Solution

20 cm3 of 0.1 M KHP was measured into a 250 cm3 Erlenmeyer flask followed by the addition of 3 drops of phenolphthalein indicator. The solution was titrated with 0.1 M sodium hydroxide solution until it turns pink which persisted for at least 30 seconds. The volume of 0.1 M NaOH

solution used was recorded. The titration procedure was repeated 3 more times, and the average titre value was recorded.

3.3.1.5 Standardization of Hydrochloric Acid Solution

20 cm3 of the 0.1 M HCl solution was measured into a 250 cm3 Erlenmeyer flask followed by the addition of 3 drops of phenolphthalein indicator. The solution was then titrated with 0.1 M NaOH until the solution turns pink which persisted for 30 seconds without fading. The titration procedure was repeated 3 times, and the average titre value was recorded.

3.3.2 Evaluation of the Neutralizing Capacity of Antacids

For each antacid brand, two different strips (for tablets) and bottles (for suspensions) were selected and each was tested and the mean titre value calculated. Sixteen marketed formulations of various dosage forms were purchased from pharmacies in Ishaka. Details are summarized in Table 1.

3.3.2.1 Tablets

The antacid tablet was crushed using a mortar and pestle. 0.5 g of the crushed tablet was weight and transferred into a 250 cm3 Erlenmeyer flask. This was followed by addition of 20 cm3 of the 0.1M HCl and the mixture swirled. The solution was boiled for 2mins and cooled to room temperature. 8 drops of bromothymol blue indicator were added to the mixture, which turned yellow (if the mixture was still blue, more HCl was added until the solution was yellow). The mixture was titrated with 0.1M NaOH until when the blue color could persist for at least 30 seconds. The titration procedure was repeated 3 times, and the titre values was recorded. The same procedure was repeated on all the other brands (Santa Monica College, Chemistry 11).

3.3.2.2 Suspensions

5ml of the suspension were measured and transferred into a 250ml Erlenmeyer flask. 30ml of 0.1M HCl was added to the flask and swirled. The amount of excess acid added was recorded. The solution was boiled for 2mins and cooled to room temperature. 8drops of bromothymol blue

indicator was added and mixture turned yellow. If it was not yellow, more HCl was added until it turned yellow. The amount of excess acid added was recorded. The mixture was titrated against 0.1M NaOH until a blue end point was reached. The above was repeated three times and titre values recorded (Omotosobayomi *et al*., 2015).

The ANC expressed in terms of milliequivalent (mEq) of acid consumed per unit dose was calculated using:

mEq of acid consumed per unit dose = (V HCl × N HCl) - (V NaOH × N NaOH)

Where: V HCl =Volume of HCl used

N HCl =Normality of HCl

V NaOH =Volume of NaOH used

N NaOH =Normality of NaOH

3.4 Data analysis

The data was entered into MS Excel and analyzed using statistical package STATA version 12 in which analysis of variance was used to test for the differences amongst the ANC values and the costs per dose of the selected antacids. A 5% level of significance was considered and a p value less than that was taken to be significant.

CHAPTER FOUR

RESULTS

This chapter presents the pertinent study results with due consideration of the specific research objectives and research questions as in chapter one of this study.

Table 1; showing active ingredients of different antacid brands

Imported brands	**Active ingredient(s)**
Suspensions	
Maalox plus	Magnesium trisilicate, Aluminum hydroxide
Gaviscon	Sodium bicarbonate, Calcium carbonate, Sodium alginate
Relcergel	Aluminum hydroxide, Magnesium hydroxide, Simethicone
Mucogel	Aluminum hydroxide, Magnesium hydroxide, Simethicone and oxethazine
Centacid	Aluminum hydroxide, Magnesium hydroxide, Simethicone
Alcid	Magnesium hydroxide, Aluminum hydroxide, Simethicone
Magnomint	Magnesium trisilicate, Aluminum hydroxide
Stomach fit	Ammonium citrate, Bismuth, Belladonna
Tablets	
CMT	Magnesium trisilicate and Aluminum hydroxide
Maalox plus	Magnesium hydroxide, Aluminum hydroxide, Simethicone
Local brands	
Suspensions	
Maaga	Magnesium trisilicate, Magnesium carbonate, Sodium bicarbonate
Rene gel	Magnesium trisilicate, Aluminum hydroxide
Magnesium trisilicate mixture (SEV)	Magnesium trisilicate, Magnesium carbonate and Sodium bicarbonate
Magnant	Magnesium trisilicate, Magnesium carbonate and Sodium bicarbonate
Tablets	
Mint o cool	Magnesium trisilicate and Aluminum hydroxide
Kam o mint	Magnesium trisilicate and Aluminum hydroxide

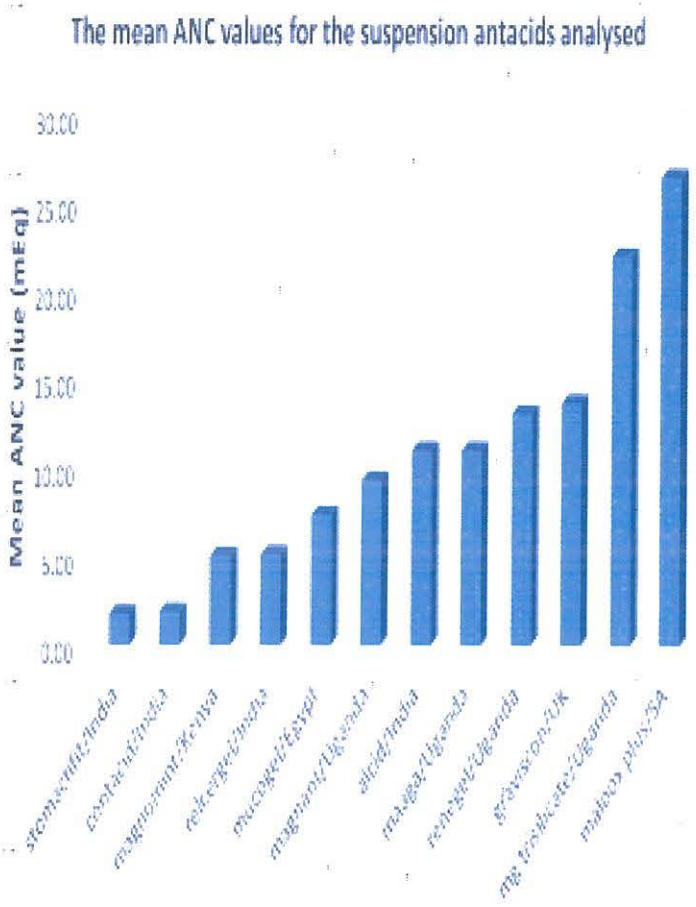
Most brands contained Aluminum hydroxide and Magnesium trisilicate or Magnesium hydroxide. Simethicone is an antifoaming agent whereas sodium alginate prevents heartburn. Oxethazine is a local anesthetic for pain relief and belladonna is an anti-diarrheal.

Table 2; showing variation in ANC values of different antacid brands (imported and local)

Drug name	ANC Mean ± SD (mEq; n=3)	Effectiveness	Origin	P value
Both susp and tabs	8.25±7.57			<0.0001
Suspension				<0.0001
Maloox plus	26.48±0.01	High	South Africa	
Gaviscon	13.68±0.01	High		
Relcergel	5.17±0.04	Intermediate	United Kingdom	
Mucogel	7.37±0.02	Intermediate	India	
Centacid	1.98±0.06	Low	Egypt	
Alcid	10.98±0.00	Intermediate	India	
Magnomint	5.09±0.03	Intermediate	India	
Stomachfit	1.76±0.00	Low	Kenya	
Mg trisilicate	22.0±0.00	High	Uganda	
Maaga	10.99±0.01	Intermediate	India	
Renegel	13.08±0.00	High	Uganda	
Magnant	9.29±0.02	Intermediate	Uganda	
Tablet			Uganda	<0.0001
Maloox plus	1.52±0.00	Low		
CMT	0.69±0.01	Low	South Africa	
Kam o mint	1.22±0.00	Low		
Mint o cool	0.88±0.00	Low	India	
			Uganda	
			Uganda	

The p value (<0.0001) is less than 0.05 indicating that the ANC values for the selected antacid suspensions and tablets are statistically different. Mean ANC for all the antacid samples was found to be 8.25 with a standard deviation of 7.57, 0.69 and 26.48 being the minimum and maximum values obtained.

Graph showing the ANC values values of different antacids analyzed



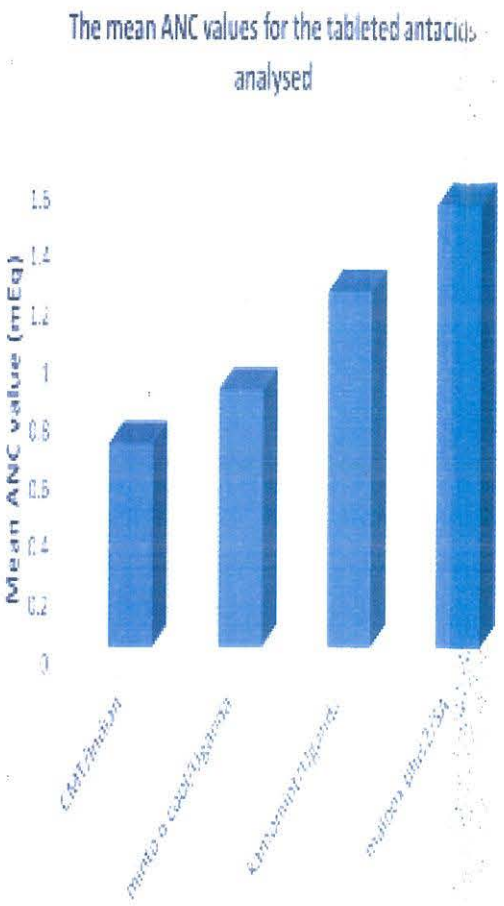
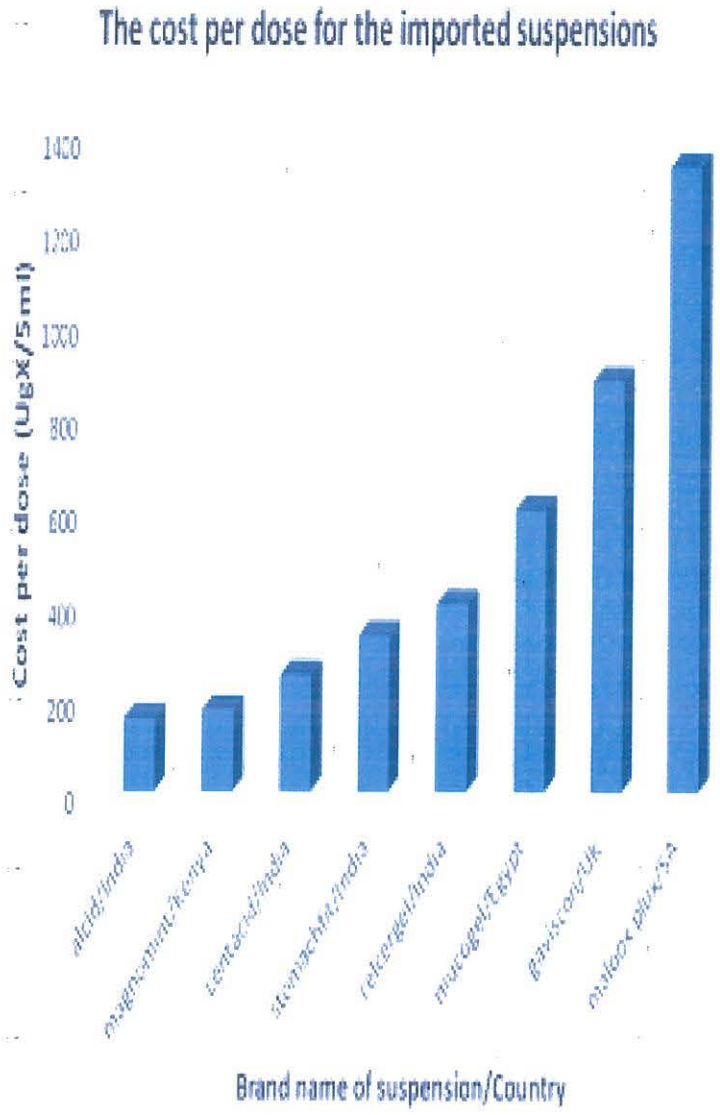


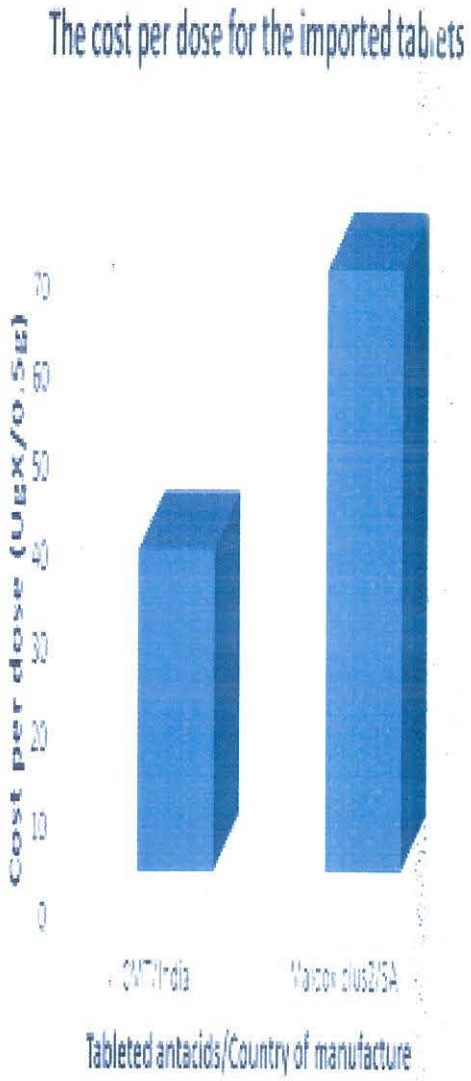
Table 3; showing cost per bottle, cost per dose and cost-effectiveness of different antacid brands analyzed.

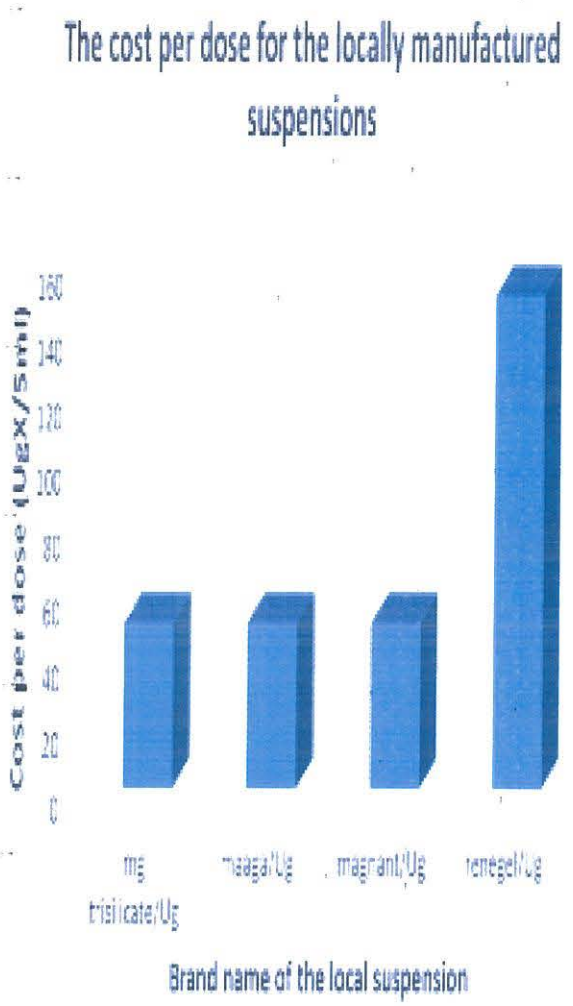
Brand name	Dosage form	Cost per bottle/strip Mean± SD ($x10^3$UgX, n=5)	Cost per dose (UgX/dose)	Cost-effectiveness (%)	P value
Local and imported	Susp/tabs	7.6±11.3			<0.0001
Imported					<0.0001
Maloox plus	Susp	39.0±4.2	1333.3	2.0	
Graviscon	Susp	35.0±0.0	875	1.6	
Relcergel	Susp	8.0±0.8	400	1.3	
Mucogel	Susp	15.0±0.0	600	1.2	
Centacid	Susp	5.0±0.0	250	0.8	
Alcid	Susp	5.0±0.0	156.3	7.0	
Magnomint	Susp	3.5±0.0	175	2.9	
Stomachfit	Susp	15.0	333.3	0.5	
CMT	Susp	0.5±0.0	35.7	4.3	
Maloox plus2	Tab	2.0±0.0	666.7	1.0	
Local	Tab				<0.0001
Mg trisilicate	Susp	2.0±0.0	50	44.0	
Maaga	Susp	2.0±0.0	50	22.0	
Magnant	Susp	2.0±0.0	50	6.2	
Renegel	Susp	3.0±0.0	150	6.2	
Mint o cool	Tab	0.5±0.0	35.7	3.4	
Kam o mint	Tab	0.5±0.0	38.5	2.3	

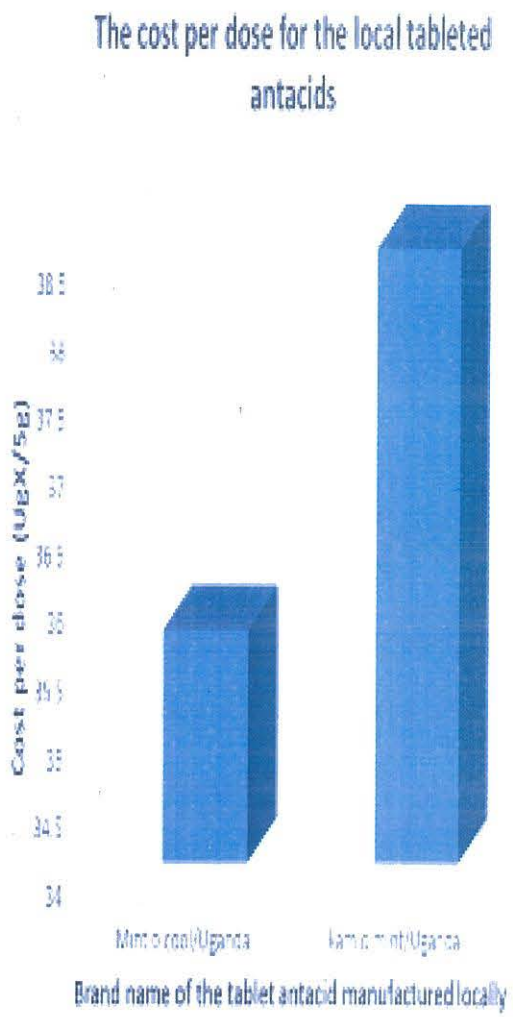
The cost per dose the antacids ranged from UgX.35.7 to 1333.3 The costs per dose for the selected drugs were found to be statistically significant even with the two origins of the drugs compared with p values of <0.0001. The cost-effectiveness ranged from 0.5 to 44%.

Graphs showing cost per unit dose of the different formulations of antacid analyzed (imported and local).

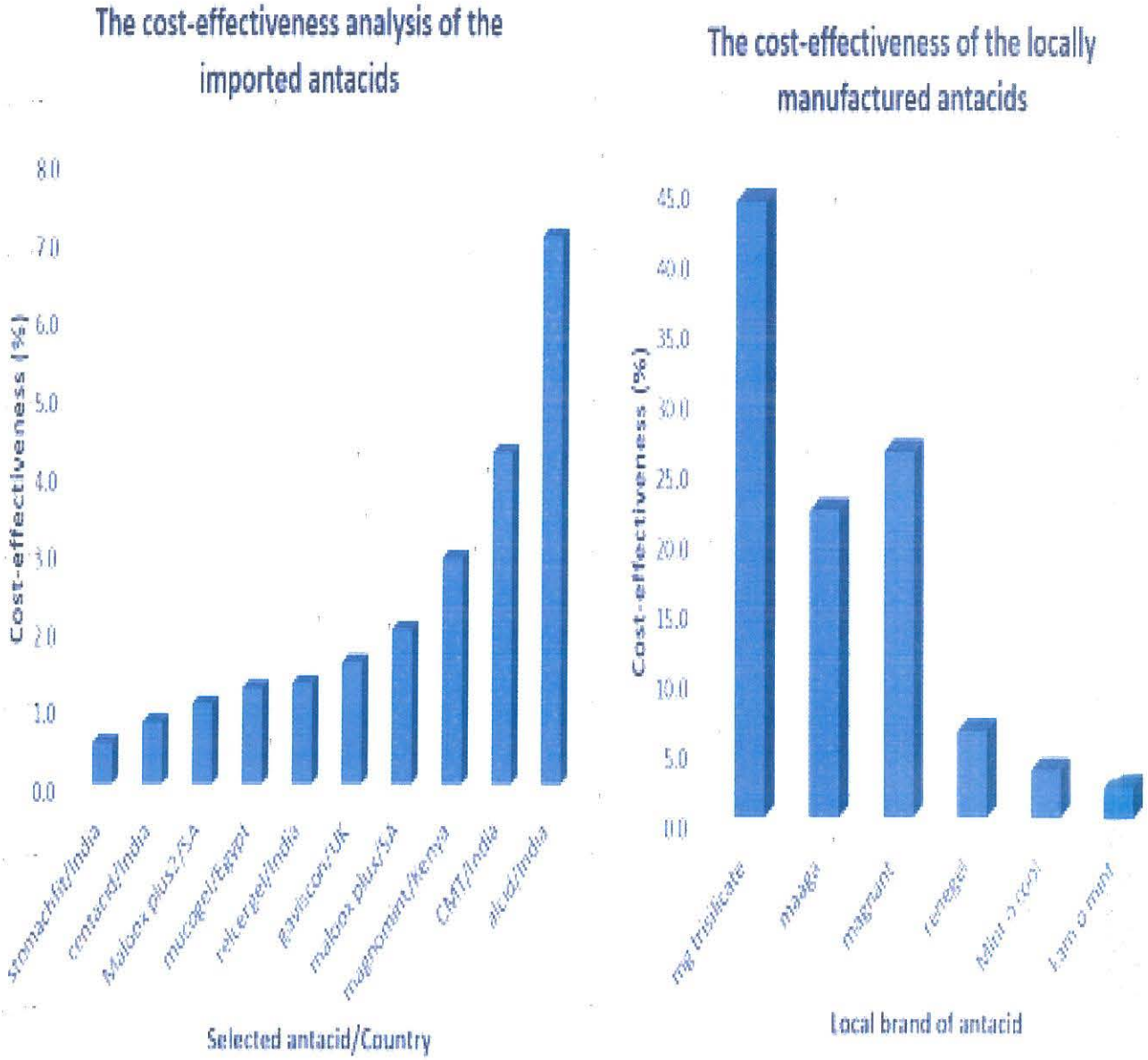





The cost per dose for the locally manufactured suspensions
Cost per dose (Ugx/5ml)
160
140
120
100
80
60
40
20
0
mg trisilicate/Ug
maalox/Ug
magrant/Ug
renegel/Ug
Brand name of the local suspension


The cost per dose for the local tableted antacids
Cost per dose (Ugx/5s)
38.5
38
37.5
37
36.5
36
35.5
35
34.5
34
Brand name of the tablet antacid manufactured locally

Graph showing cost-effectiveness of different antacid brands analyzed



CHAPTER FIVE

5.1 DISCUSSION

This chapter presents the pertinent study results with due consideration of the specific research objectives and research questions as in chapter one of this study.

The antacid formulations analyzed by Omotosobayomi *et* al., 2015, were classified into three groups according to their ANCs, those with the highest ANC (13.55-9.51mEq), those with an intermediate ANC (5.48 - 3.17 mEq) and those with a lowest (2.98- 1.10mEq) whereas in India as stated by Shery *et al.*, 2013, the high ANC class had (35.83 - 31.27), the intermediate class had (20.12 - 30.26) and the low class had (18.22 - 19.42). In this current study, based on the same classification above, the high class had ANC (13.08 - 26.48), the intermediate class had ANC (5.09 - 5.09) while the low class had ANC (0.69 - 1.98) and all tablets were in the low class plus a few suspensions. ANC for suspensions significantly vary from brand to brand ($p < 0.0001$) where; Maalox plus had the highest ANC value (26.48), followed by Magnesium trisilicate mixture (22), and Gaviscon (13.68) whereas Stamachfit had the lowest (1.78), followed by Centacid (1.89) and Magnomint (5.10), but there was no variation in ANC between the imported and local brands since most of them belonged to high and intermediate ANC group. Meanwhile, for the antacid tablets, Maalox plus had the highest ANC of 1.52mEq and CMT with lowest ANC value of 0.85mEq. The ANCs for other tablets were; Kam o mint (1.22) and Mint o cool (0.88).

Vedavathi *et al.*, 2013 reported that formulations with anti-foaming agents had lower ANC values than those without anti-foaming agent and my results have also proven the same since all were in the intermediate and low ANC group. Antacids with anti-foaming agents in this study were; Acid, Relcergel, Centacid and Mucogel (all with simethicone as the anti-foaming agent).

In the study by Omotosobayomi *et* al., 2015, in Nigeria, the unit price of antacid suspension was between ₦5-₦50 per 5ml dose, while that for tablets between ₦1-15 per tablet, thereby making

the tablet to be cheaper than the suspension. The most expensive suspension was Maalox with unit price of ₦10/ml while the cheapest brand was Juhel -Mist Mag (₦1/ml). In Ishaka, the unit price of antacid suspension was found to be between Shs 50 - 1333.3 per 5ml dose, while that for the tablet antacids was between shs 35.7 - 666.7, thereby making tablets to be cheaper than suspensions.

For suspensions Maloox plus had the highest cost per unit dose (shs 1333.33/5ml) followed by Gaviscon (shs 875/5ml) and Mucogel (shs 600/5ml) whereas Maaga, Magnant and Magnesium trisilicate mixture (SEV) all with unit price of shs. 50/5ml had the lowest cost per unit dose. All the three brands with the highest cost per 5ml were imported ones whereas the three brands with the lowest cost per 5ml were all local brands thereby making imported brands more expensive than local ones. All local brands except Renegel, had the same cost per 5ml of shs 50, however for imported brands like Relcergel, Centacid, Alcid and Stomachfit from the same country (India) also had different cost per 5ml. Meanwhile for the chewable tablets, Maalox plus had the highest cost per unit dose of shs 666.7/0.5g while CMT and Mint o cool had the lowest of shs 35.7/0.5g.

This study revealed no correlation between the unit price and the ANC of the antacids. For suspensions, Maalox plus had the highest ANC (26.48) but also with the highest cost per 5ml (1333.3) making it not the most cost-effective antacid suspension. Meanwhile, Magnesium trisilicate mixture (SEV) had a high ANC value (22), though less than that of Maalox plus, but also had a lower cost per 5ml, making more cost-effective. Both Maaga and Magnant had the same cost per 5ml (50) as Magnesium trisilicate mixture (SEV), but with ANC values (10.98 and 9.29 respectively) lower than that of Magnesium trisilicate mixture (22), making Magnesium trisilicate mixture more cost-effective.

For tablets, Mint o cool and CMT had the lowest unit cost of shs 35.7 though with lower ANC values than Maalox plus (1.52) and Kam o mint (1.22). Kam o mint had a lower unit cost of shs 38.5 than Maalox plus making Kam o mint brand the more cost-effective.

5.2 CONCLUSION

In this study, it was observed that Maalox plus suspension had highest ANC (26.48). Despite this obvious high ANC value obtained, Maalox plus was not the most cost-effective antacid brand rather it was Magnesium trisilicate mixture (SEV), followed by Maaga, one of the local brands. No positive correlation was found between cost and effectiveness of antacid since local brands of lower cost were found to be equally effective compared with the costly imported brands. Due to high ANC, few tablet antacids can be substituted for liquid antacids. Antacids therefore, can be consumed judiciously provided ANC details are enclosed on the label of these products.

5.3 RECOMMENDATIONS

Acid neutralizing capacity details of antacid brands should be incorporated on to the labels to improve good prescribing practices.

Further research should be done on other brands.

Other research studies like sodium content, physico-chemical parameters and heavy metal (lead) content of antacids should be carried out.

REFERENCES

Benibo, I., S., Ezealisiji, K., Omotosobayomi, E., (2015) .*Canadian Open Pharmacy Journal.* Vol. 1.

Annie, J., Mariyam, T., Reham, A., Shery, J., Shijna, A., Mariyam, T. (2013). *Gulf medical journal*, Ajman.

Shreenivas, P., R., Tejasvi, T., S., Vedavathi, H., (2013).*International Journal of Basic and Clinical Pharmacology,* Karnataka. Vol 2 (6).

Ebere, I., O., Omotinuolaw, R., L., (2017). Elele. 8(1).

Senta Monica College, Chemistry 11.

Virginia C. Bitter. (2002).*California State Science Fair Project,* California.

Bootman, J., L., McGhan, W., Rowland, C., (1978).*Cost -benefit and cost-effectiveness: Methodologies for evaluating innovative pharmaceutical services,* Am J hospital Pharm, USA.

Townsend, R., J., (1986). *Post marketing drug research and development: an industry clinical pharmacist's perspective.* Am J Pharm Educ, USA.

Boatman, J., L., Rowland, C., Weitheimer, A., (1979). *Cost -benefit analysis: a research tool for evaluating innovative health programs*, Eval Health Prof, USA.

Lutchman, D., Naidoo, R., Nayala, R., Pillay, S., Rughoobeer, A., (2006). *School of pharm and pharmacology*, University of Kwatulu-Natal, Durban. Vol.96.

Boatman, J., L., Rowland, C., Weitheimer, A., Zaske, D., (1979). *Individualization of aminoglycosides dosage regimens: a cost analysis*, Am J Hosp Pharm, USA.

APPENDIX