Evaluation of Commercial Antacid Tablets in Iraq

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ABSTRACT

Antacids are commonly used drugs which are considered inert and free of pharmacological effect by many patients and physicians. They are weak bases that neutralize the gastric acid and relief pain. These weak bases dissociate to neutralize gastric acid and form neutral salts. The ultimate goal of antacid therapy is to reduce the concentration and a total load of acid in gastric juice to a pH 4 - 5. This in vitro study was promised to study the acid neutralizing capacity (ANC) of six commonly available antacids tablets in the Iraqi market by using back titration method. The highest ANC values were for Rennie (17.131± 0.083 and 16.926± 0.052 mEq) in two different hydrochloric acid (HCl) concentrations 1N and 0.5 N, respectively. The static analysis revealed that there was a significant difference of ANC in favor of Rennie versus other antacid tablets studied. The current 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.

Keywords: Acid Neutralizing Capacity, Antacids, Back titration.

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INTRODUCTION

Antacid tablets are probably one of the most widely used self-prescribed medications [1]. They are weak bases mostly they consist of magnesium and aluminum salts and sodium/calcium carbonate or their combinations [2-6]. The chief indication for administration of antacids is to perform a neutralization reaction (Eq.1), i.e. they buffer gastric acid, raising the gastric pH above 4-5, and inhibition of the proteolytic enzyme, pepsin [7, 8].

$$\text{Antacid (weak base)} + \text{HCl (stomach acid)} \longrightarrow \text{Salts} + H_2O + CO_2 \text{.......Eq.1}$$
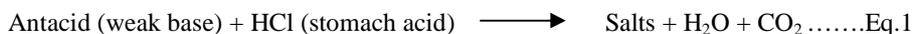
An effective antacid is characterized by the fast onset of action, buffering the pH of the stomach, having a high acid neutralizing capacity (ANC) not less than 5 mEq per minimum single dose, and cause minimal side effects [9]. Moreover, a physician also needs to consider the following factors; the antacid should neutralize the greatest amount of acid per unit cost; should be both palatable and conveniently consumed by the patient [10].

There are several different antacid tablets on the market; the active ingredients are the aluminum, magnesium, and calcium salts. Sodium alginate may be combined with the antacid to encourage the adherence of the antacid to the mucosa and it also acts like a protective to the gastric mucosa. Simethicone and dimethicone are surfactants that may decrease foaming by breaking down bubbles within the gut renders gas available for absorption [11, 12].

Various in vitro tests have been developed to evaluate the performance of antacids which are intended to reflect theirs in vivo efficacy [13]. The measurement of ANC of antacids is one such widely used test which was first

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determined in 1973 by Fordtran and co-workers [14] and they evaluated the ANC values at that time. Since that time, their published results have served as a guide for physicians prescribing antacids.

The objective of this in vitro study was to determine the ANC of six containing antacid tablets (Rennie, Gaviscon Extra strength, Barkalox plus, Ballox plus, Maalox plus, and Moxal plus), table 1, which were the most commonly prescribed brands, commercially available in the Iraqi market in two different acid concentrations.

Table 1: List of the commercial antacids and their composition

Brand Name	Manufacturer	Ingredients
Rennie	Bayer/ France	Calcium Carbonate 680mg Magnesium Carbonate 80mg
Gaviscon Extra strength	Reckitt Benckiser Healthcare / UK	Sodium alginate 500mg Sodium hydrogen carbonate 267mg Calcium Carbonate 160mg
Maalox plus	Sanofi-Aventis/ Italy	Aluminum hydroxide 200mg Magnesium hydroxide 200mg Dimethicone 25mg
Barkalox plus	Barakat pharmaceutical industries/ Syria	Aluminum hydroxide 200mg Magnesium hydroxide 200mg Simethicone 25mg
Ballox plus	Brawn/ India	Aluminum hydroxide 200mg Magnesium hydroxide 200mg Simethicone 25mg
Moxal plus	Julphar/ U.A.E	Aluminum hydroxide 200mg Magnesium hydroxide 200mg Simethicone 25mg

MATERIALS AND METHODS

Materials
Six antacids (Rennie, Gaviscon Extra strength, Barkalox plus, Ballox plus, Maalox plus, and Moxal plus) tablet dosage form were obtained from the market. Sodium hydroxide (NaOH) was obtained from Fluka AG, Switzerland, hydrochloric acid (HCl) was purchased from Avantor, USA, and anhydrous sodium carbonate (Na_2CO_3) of GR grade used for standardization was obtained from Merck.

The standard solutions were prepared and standardized as per the procedures of United States Pharmacopoeia (USP) [15].

Experimental
The reaction between the weak base of the antacid which is slightly soluble in water and an acidic standard solution is problematic. So, a back titration procedure is applied. Firstly the antacid tablet of different commercial sources was weighed and then triturated in mortar and pestle to a fine powder .The powder was transferred to flask then dissolved in an excess exactly measured volume of a known concentration of the HCl solution, the mixture was heated to ensure a complete and timely reaction. There will always be some excess left after neutralizing the antacid. The amount of unreacted HCl that remained in the solution was determined by back- titration of the solution with a standardized solution of NaOH.

Two different HCl concentrations in vitro have been developed to evaluate the performance of antacids which are intended to reflect theirs in vivo efficacy.

The first acid concentration was 1N
Procedure: 30 ml of 1N HCl was pipetted into the flask containing the crushed antacid tablet. Stir the mixture well, heat to boiling for 15 seconds to ensure complete tablet dissolving, cool, and 3 drops of phenolphthalein indicator was added to the mixture and the excess HCl was titrated with 0.5N Sodium hydroxide. At the end point, the test solution changes from colorless to pink.

The second acid concentration was 0.5N
Procedure: 50 ml of 0.5N HCl was pipetted into the flask containing the crushed antacid tablet. Stir the mixture well, heat to boiling for 15 seconds to ensure complete tablet dissolving, cool, and 3 drops of phenolphthalein indicator

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was added to the mixture and the excess HCl was titrated with 0.5N Sodium hydroxide. At the end point, the test solution changes from colorless to pink.

Calculations

The amount of acid reacted with NaOH would, therefore, give the neutralizing capacity for the antacid which represents the ANC of assigned antacid tablet, the ANC were expressed in terms of milliequivalents (mEq) of acid consumed per one tablet by the following formula [3, 16]:

mEq of acid consumed per one tablet $= (V_{HCl} \times N_{HCl}) - (V_{NaOH} \times N_{NaOH})$………. Eq.2

Where:
V_{HCl} =Volume of HCl used in ml
N_{HCl} =Normality of HCl
V_{NaOH} =Volume of NaOH used in ml
N_{NaOH} =Normality of NaOH

The protocol of this work; for each antacid brand, three different strips were selected and seven tablets were chosen from each strip, seven readings of ANC were obtained and the mean (per strip) was calculated. The weighted mean was calculated by considering all 21 readings (3 strips) for each brand using two different HCl concentrations (1 and 0.5 N).

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 18 was used for data coding and analysis. Continuous variables were presented as the mean ± Standard deviation (SD), Coefficient of variation and weighted mean were calculated for each brand. Analysis of variance (ANOVA) was used to test the significant differences between means of different brands followed by Posthoc analysis using Tukey's test. The P value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The mean of ANC values in mEq. for each strip were tabulated in table 2 and the weighted mean of all the three strips was calculated per brand. The highest ANC value was obtained from Rennie followed by Gaviscon whereas all the other brands with anti-foaming agents were observed to have the lowest ANC values in both acid concentrations (Table 2, Figures 1and 2).

Table 2: The mean and the weighted mean of calculated ANC of antacid brands in different HCl concentrations

| Antacid brands	Calculated ANC in mEq using 1N HCl				Calculated ANC in mEq using 0.5 N HCl			
	Mean per strip			Weighted mean	Mean per strip			Weighted mean
Rennie	17.121	17.129	17.143	17.131	16.928	16.935	16.914	16.926
Gaviscon Extra strength	8.086	8.114	8.078	8.093	7.919	7.922	7.957	7.933
Maalox plus	5.521	5.486	5.571	5.526	5.343	5.336	5.35	5.343
Barkalox plus	6.035	6.029	6.157	6.074	5.938	5.941	5.957	5.945
Ballox plus	5.857	6.064	5.914	5.945	5.929	5.95	5.928	5.936
Moxal plus	6.314	6.293	6.314	6.307	6.107	6.114	6.136	6.119

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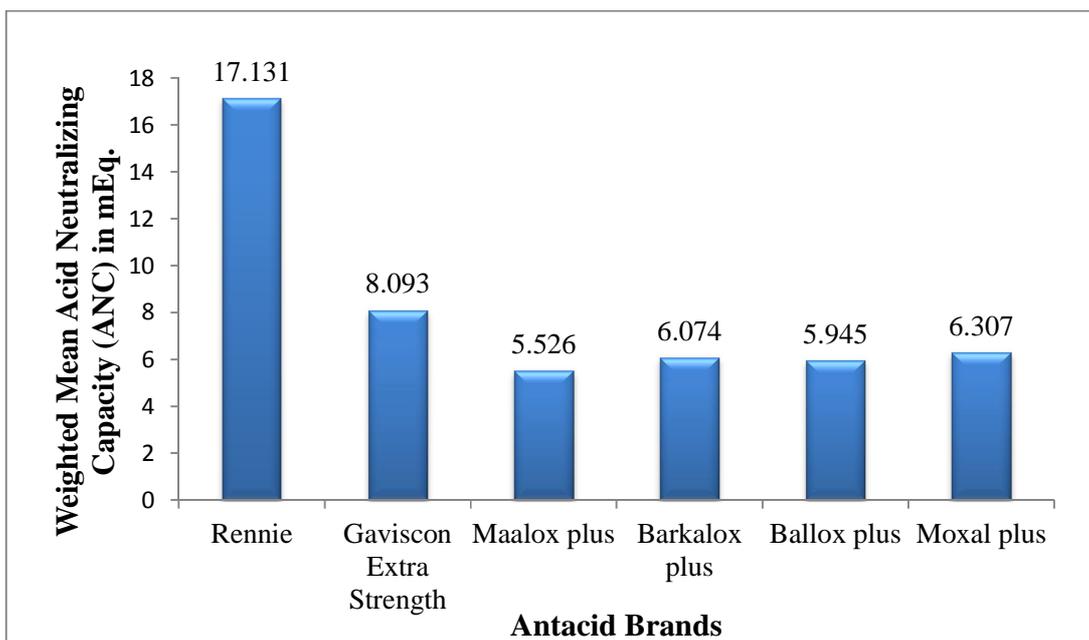
Figure 1: Weighted Mean Acid Neutralizing Capacity (ANC) (in mEq) of antacid brands using 1N HCl standard solution
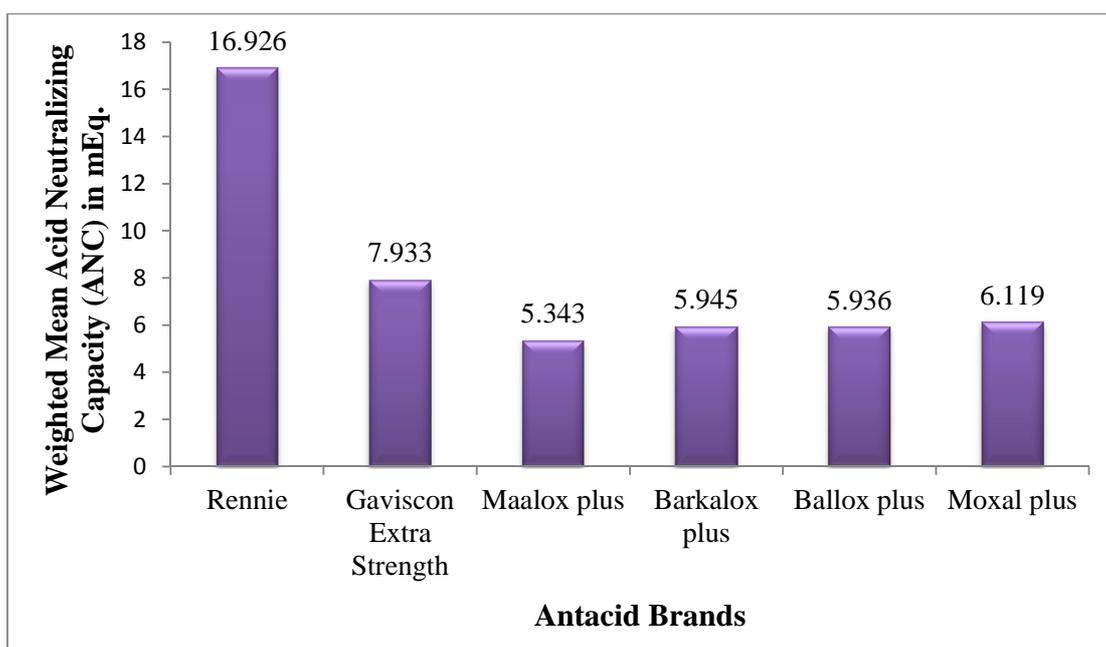

Figure 2: Weighted Mean Acid Neutralizing Capacity (ANC) (in mEq) of antacid brands using 0.5 N HCl standard solution

As the highest mean of ANC value was obtained with Rennie in comparison to the five other brands the relative effectiveness of the other antacids was then calculated considering Rennie as 100. Table 3 showed the relative effectiveness using 1 N HCl, and table 4 using 0.5 N HCl.

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Table 3: Weighted mean, Standard Deviation, Coefficient of Variance and Relative Effectiveness of antacid tablets with respect to Rennie (1N HCl)

Antacid Brands	Weighted mean of ANC (mEq)	Standard Deviation	Coefficient of Variance	Relative Effectiveness
Rennie	17.131	0.083	0.484	100
Gaviscon Extra strength	8.093	0.137	1.695	47.24
Maalox plus	5.526	0.312	5.640	32.26
Barkalox plus	6.074	0.379	6.246	35.46
Ballox plus	5.945	0.651	10.952	34.70
Moxal plus	6.307	0.138	2.190	36.82

Table 4: Weighted mean, Standard Deviation, Coefficient of Variance and Relative Effectiveness of antacid tablets with respect to Rennie (0.5 N HCl)

Antacid Brands	Weighted mean of ANC (mEq)	Standard Deviation	Coefficient of Variance	Relative Effectiveness
Rennie	16.926	0.052	0.304	100
Gaviscon Extra strength	7.933	0.080	1.003	46.87
Maalox plus	5.343	0.121	2.259	31.57
Barkalox plus	5.945	0.197	3.310	35.12
Ballox plus	5.936	0.153	2.571	35.07
Moxal plus	6.119	0.176	2.883	36.15

To study the differences between mean ANC of the six brands ANOVA was used to test the significant differences in mean ANC using HCl, 1 N, and 0.5 N concentrations. Table 5 and 6 showed the differences in mean ANC using posthoc Tukey's test. The differences were statistically significant (P< 0.05) between all brands except between Barkalox plus and Ballox plus using 1N HCl concentration and between Barkalox plus and Ballox plus and Moxal plus using 0.5 N HCl concentration.

Table 5: Differences in mean ANC (in mEq) between the six tested antacid brands (1N HCl)

Antacid Brands	Rennie	Gaviscon Extra strength	Maalox plus	Barkalox plus	Ballox plus	Moxal plus
Rennie	X	0.000	0.000	0.000	0.000	0.000
Gaviscon Extra strength	0.000	X	0.000	0.000	0.000	0.000
Maalox plus	0.000	0.000	X	0.000	0.000	0.000
Barkalox plus	0.000	0.000	0.000	X	1.000*	0.001
Ballox plus	0.000	0.000	0.000	1.000*	X	0.000
Moxal plus	0.000	0.000	0.000	0.001	0.000	X

The differences in mean ANC was statistically not significant (P>0.05) using ANOVA-Tukey's test.

Table 6: Differences in mean ANC (in mEq) between the six tested antacid brands (0.5N HCl)

Antacid Brands	Rennie	Gaviscon Extra strength	Maalox plus	Barkalox plus	Ballox plus	Moxal plus
Rennie	X	0.000	0.000	0.000	0.000	0.000
Gaviscon Extra strength	0.000	X	0.000	0.000	0.000	0.000
Maalox plus	0.000	0.000	X	0.000	0.002	0.000
Barkalox plus	0.000	0.000	0.000	X	0.831*	0.246*
Ballox plus	0.000	0.000	0.000	0.831*	X	0.01
Moxal plus	0.000	0.000	0.000	0.246*	0.01	X

The differences in mean ANC was statistically not significant (P>0.05) using ANOVA-Tukey's test.

DISCUSSION

This study clearly shows that there is considerable variation in the in vitro ANC of different antacid brands in the Iraqi market. The order of ANC values from highest to lowest potency of the tested brands are Rennie, Gaviscon Extra Strength, Moxal plus, Barkalox plus, Ballox plus and Maalox plus in different HCl concentrations.

The relative effectiveness gives indication that the ANC value of Rennie is almost three times more comparing to the ANC values of the antacid brands containing an anti-foaming agent (Barkalox plus, Ballox plus, Maalox plus, and Moxal plus) and more than two times concerning to the ANC value of Gaviscon Extra strength probably this is due to the presence of Magnesium carbonate and Calcium carbonate combination in Rennie tablets formulation when compared with other brands. Mostly, carbonate salts considered as very potent antacids with prolonged time of action [12, 17]. Drake et al [18], demonstrated a tenfold difference in the ANC between the lowest and the highest effective antacid formulations. Another study established by Kibwage et al [19] showed that the ANC per tablet of

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antacids varied three times among seventeen commercial products. Later on Ebenezer et al [20] found that the ANC of the most potent antacid formulation was thirteen times potent than the least one. Because of this wide variation in the neutralizing capacity, the product as well as its ANC must be known, when antacid therapy is being recommended.

Moreover, the statistical observation showed that most antacids ANC variation with statistically significant difference. The potency in term of ANC varied from 17.131± 0.083 mEq (Rennie) to 5.526± 0.312 mEq (Maalox plus) and 16.926± 0.052 mEq (Rennie) to 5.343± 0.121 mEq (Maalox plus) using 0.5N HCl. While, differences in mean ANC was observed statistically not significant (P>0.05) between Barkalox plus and Ballox plus using 1N HCl concentration and between Barkalox plus and Ballox plus and Moxal plus using 0.5 N HCl concentration, and also a variation in the ANC values in the same formulation but with different acid concentration may be related to various reasons, such as manufacturing, formulation, tablet weight and the amount of the active ingredient in brand itself.

CONCLUSION

In this in vitro study the antacid tablets were evaluated, various potencies were measured in terms of their ANC values. According to this fact, the treating physician should use the antacids with the higher ANC to obtain faster symptomatic relief from dyspepsia. It is recommended that the ANC values be included in the leaflets of the antacid products and also in hospital formulation to enhance proper prescribing practices.

This work may help further research works such as designing and manufacturing new antacid formulation.

Abbreviations: *N: Normality; V: Volume; HCl: Hydrochloric Acid; NaOH: Sodium Hydroxide; H_2O: Water; CO_2: Carbon dioxide; Na_2CO_3: Sodium Carbonate; Eq: Equation; mEq: milliequivalents; ml: milliliters; ANC: Acid neutralizing capacity; SPSS: Statistical Package for Social Sciences; USP: United States Pharmacopeia; ANOVA: Analysis of variance.*

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