Work on Various Methods Used for the Determination of Acid Neutralizing Capacity of Multifarious Antacid Formulations with Their Comparison

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Abstract- ***Acidity is a condition which may be defined as heart burn, formation of gas in stomach due to excess production of stomach acid. Antacids, among other medications, are widely used medicines to reduce the incommodious symptoms of acidity through neutralizing the excess stomach acid. The potency of antacid formulations depends on the Acid Neutralizing Capacity (ANC). However, there is no review work on the methods used for the determination of acid neutralizing capacity of antacid formulations. Therefore, the objectives of the present study are to find out different methods through literature review used for the determination of acid neutralizing capacity of antacid formulations, compare them from different perspectives, and to compile the reported standard specifications for ANC. Besides, another objective is to employ the reported methods to evaluate acid neutralization capacity of an antacid tablet formulation. Reviewed articles include three reported methods viz. pH meter method, back titration method and direct titration method for ANC value determination. The authors of the present review work found from their own experimental study that the pH meter method has some advantages over back titration method such as the pH meter method is cost-effective, easy to carry out, and less time consuming.***

Indexed Terms- ***Acid Neutralizing Capacity, Antacids, Ph Meter Method, Direct Titration Method, Back Titration Method.***

I. INTRODUCTION

Human life is getting more competitive than previously and people are experiencing more stress, having no time to take food on time, and facing so on obstacles in their social life. Moreover, it is a matter of penance that people are depending on unhealthy fast foods day by day. As a result, people are suffering from numerous gastrointestinal disorders such as peptic ulcer, heart burn, indigestion, stomach upset, gastro-esophageal reflux disease, stomach pain, belching, bloating, stomach pressure [1] etc. Gastrointestinal disorders are caused by various factors [2] and treated by decreasing gastric acidity as well as enhancing mucosal defense system [3]. A number of medications like antacids, H_2 blockers, proton pump inhibitors (PPI), sucralfate, bismuth chelate and some others are used to treat these sorts of stomach problems. H_2 blockers (cimetidine, ranitidine, famotidine, etc.) competitively block H_2 receptors on parietal cells and inhibit the gastric acid secretion but they have some common side effects like headache, diarrhea, confusion, restlessness [4] etc. Proton pump inhibitors (PPI) are the prodrugs which are activated in acidic environment and the activated form binds irreversibly to H+K+ATPase in order to inhibit proton pumping. However, the proton pump inhibitors such as esomeprazole, lansoprazole, pantoprazole etc. also possess various side effects including: headache, nausea, dizziness, fatigue, abdominal pain [4] etc. Therefore, antacids are one of the most widely used agents to treat hyper acidity associated problems [5] because of its comparative less side effects and quick onset of action.

Antacids contain weak bases which neutralize the excess stomach acid [6] and inhibit the formation of pepsin as well. They are categorized into two classes namely: systemic antacid and non-systemic antacid [7]. Sodium bicarbonate is the most commonly used as systemic antacid which is water soluble and completely absorbable. It reacts with gastric acid to form sodium chloride and carbon dioxide, while carbon dioxide is responsible for the sense of abdominal discomfort. The common demerits are systemic alkalosis [8], distension, sodium overload etc. As a result, systemic antacids are not as popular as non-systemic antacids. Most of the non-systemic antacid formulations contain magnesium hydroxide or aluminum hydroxide or combination of both as active ingredients and simethicone in small quantity for an additional purpose. Magaldrate is also used in some non-systemic antacid formulation, which is a hydroxymagnesium aluminate. Magnesium hydroxide is available as milk of magnesia which contains 7-8.5% of magnesium hydroxide. Milk of magnesia is more palatable than other formulations of magnesium. The key side effect of magnesium hydroxide is diarrhea. On the other hand, aluminum hydroxide has astringent property and it forms a protective layer on ulcer crater and may absorb toxins, bacteria, gases. But, aluminum containing antacids cause constipation, that is why the combination of magnesium hydroxide and aluminum hydroxide is used to overcome the problem. Furthermore, simethicone and dimethicone are used as antifoaming agent which helps to break up the gas bubbles in the gut to give up flatulence [7]. Antacid works only on existing stomach acid but not to prevent acid production. However, antacids are evaluated for their efficacy based on acid neutralization capacity (ANC) [9]. Some authors [10, 11, 12] determined acid neutralization capacity using pH meter method. Abdu and Abbagana [14] used back titration method for the same purpose while some others [1] evaluated acid neutralizing capacity value by direct titration method. pH meter method is a pharmacopoeia adopted method in which, 1 N HCl was added to the antacid solution until pH 3.5 was reached to evaluate the ANC value. On the other hand, in case of back titration, excess 1N HCl was back calculated with 0.5 N NaOH for the purpose of ANC value determination. Regarding direct titration method, 0.1 N HCl was added to the antacid solution until pH 7 was attained to determine ANC value of antacid formulations. Therefore, the authors of the present work took interest to compile and compare the methods used in literatures for the determination of ANC of antacid formulations. In addition, the authors determined the ANC values of an antacid formulation employing the reported acid neutralizing capacity evaluation methods. Findings of the present work have been reported and discussed in the present article to facilitate other researchers working in this field.

II. METHODOLOGY

The present review work was done browsing the Google Scholar website. Keywords like acid neutralizing capacity, antacids and their efficacy measurement, methods for evaluating acid neutralizing capacity of antacids etc. were used for finding the relevant articles on the methods that are employed for acid neutralizing capacity measurement of antacids. Out of the articles appeared after browsing, it was found that about 80 papers were somehow relevant with the objectives of the authors of the present work, which were published in the time period 1939 to 2023. The articles were downloaded and carefully checked and finally fifty (50) articles were found to be related to the acid neutralization capacity evaluation of antacid formulations and those were then reviewed systematically. The various ANC evaluation methods found from the literature review were identified and those have been detailed in the results and discussion section in the present paper. Next, to see the prevalence of the cited ANC evaluation methods, references of the respective method were counted and the prevalence was expressed in percent (%) and the results has been presented as a table (Table1) in the results and discussion part in the present article. Next, authors assembled the reported ANC values measured by different methods for the same antacid formulations to see the consistency of the results found by the different methods in different laboratories. The accumulated data have been shown in the Table 2 of this article. Finally, authors employed the three different methods [1, 10, 13] found from literatures for evaluating the ANC of an antacid tablet formulation having the same batch number. Details of the methods used are available in the results and discussion portion of the present manuscript. The ANC evaluation experiment was doneto give an idea to the readers about the

accuracy and precision of the reported three methods. The obtained results have been produced in the Table 3 of the present article. Standard specification for ANC is important to comment on potency status of any assessed antacid formulation. So, various standard specifications of ANC that were set by different organizations as well as the same was cited by other workers to rationalize their data on ANC values were searched out through meticulously reviewing the relevant downloaded articles on ANC measurement methods and the findings were compiled in the Table 4 in the results and discussion segment of the present manuscript.

III. RESULTS AND DISCUSSIONS

Potency of the respective antacid formulation is the key factor in alleviating acidity problem which is usually determined by its acid neutralizing capacity (ANC). Acid neutralizing capacity is the amount of acid that can be neutralized by antacid preparation and it is thus important to know the various methods that are used for this purpose. Therefore, one of the objectives of the present study was to find out different methods reported in the literature for the determination of acid neutralizing capacity of antacids. Literature review resulted in three methods viz. pH-meter method, back titration method, and direct titration method for the evaluation of ANC of antacid formulations. Each of the methods has been comprehensively described below so that one working in the same field can follow the method if he/she would like to employ it.

A. pH meter method for solid dosage [10,11,12]

- Take weight of one tablet, record it and then triturate it in a mortar with a pestle to make fine powder.
- Transfer the whole powder of the tablet to a 250 mL beaker. Measure 70 mL of distilled water (DW) in an another 100 mL beaker and rinse the mortar vessel taking aliquots from the measured 70mL of DW and transfer that water into the beaker containing powder of the tablet. Repeat the rinsing process two more times and finally, add the rest portion of the 70 mL DW into the beaker where you had added the first rinsed portion.
- Stir the content of the 250 mL beaker with a magnetic stirrer for one minute to turn it into a suspension.
- After completing the above three steps, add 30 mL of 1N HCl to the 70mL of the antacid suspension with constant stirring for 15 min. Titrate the excess HCl using 0.5N sodium hydroxide solution until a stable pH of 3.5 is attained.
- Repeat the experiment two more times taking tablets from the same batch.

B. pH meter method for liquid dosage [10]

- In case of liquid antacids, shake the bottle well for one minute and pour 5mL of the preparation into a 250mL glass beaker. Add seventy (70) milliliters of distilled water into the beaker containing the liquid antacid and mix it well with a magnetic stirrer for 1 minute.
- Add 30 mL of 1N HCl to the content in the beaker with constant stirring for 15 min. Titrate the excess HCl using 0.5N sodium hydroxide solution until a stable pH of 3.5 is attained.
- Repeat the experiment two more times taking liquid antacids from the same batch.

It is important to mention here that the pH meter method was mostly referred in the reviewed journals as it is the method that one is identical to the method stated in the United State Pharmacopoeia (USP) for ANC determination of antacid formulations.

- Calculation of ANC from pH meter method [13]

Total mEq of acid consumed
= (Volume of HCl x Normality of HCl) - (Volume of NaOH x Normality of NaOH) …… (1)

- Drawbacks and limitations of pH meter method:
- It needs a good quality pH meter.
- Acid has to be added drop wise very carefully so that pH does not change abruptly.

- Standardization procedures in pH meter method:
- Standardization of 1N HCl solution:

Sodium carbonate (5.3 g) was taken in a 100 mL volumetric flask. Then, distilled water was added up to 100 mL mark of the flaskto make 1 N Na_2CO_3solution. Ten milliliters (10 mL) solution of Na_2CO_3. was taken in a beaker. Few drops of methyl

orange indicator were added.to the beaker. Then, Na_2CO_3solution was titrated with HCl solution until color was changed from yellow to orange-pink. This process was repeated for three times. The average volume of HCl required for titrating $Na_2CO_3$was 9.98mL. Then, the concentration of HCl solution was calculated using $V_1S_1 = V_2S_2$ formula and the obtained result was 1 N.

- Standardization of 0.5 N NaOHsolution:

Oxalic acid (6.3 g) was taken in a 100 mL volumetric flask. Then, distilled water was added up to 100 mL mark of the flaskto make 1 N oxalic acid solution. Ten milliliters (10 mL) oxalic acid solution was taken in a beaker. Few drops of phenolphthalein indicator were added.to the beaker. Then,oxalic acid solution was titrated withNaOH solution until pink color was appeared. This process was repeated for three times. The average volume of NaOH required for titrating oxalic acid was 10mL.Finally, concentration of HCl solutionwas calculated by using $V_1S_1 = V_2S_2$ formula and the obtained result was 0.5 N.

C. Back titration method for solid dosage [10]

- Take weight of one tablet record it and then triturate it in a mortar with a pestle to make fine powder.
- Transfer the whole powder of the tablet to a beaker. Measure 70 mL of DW and rinse the mortar vessel taking aliquots from the measured 70mL of DW and transfer that water into the beaker containing powder of the tablet. Repeat the rinsing process two more times and finally, add the rest portion of the 70 mL DW into the beaker.
- Stir the content of the beaker with a magnetic stirrer for one minute to turn it into a suspension.
- After completing the above three steps, add 30 mL of 1N HCl into the 70mL of the antacid suspension with constant stirring for 15 min.
- Add 2-3 drops of methyl orange indicator to the preparation and then titrate the excess HCl with 0.5N Sodium hydroxide. At the end point, the test solution changes from red to yellow color. In some papers, other indicators were used instead of methyl orange viz. phenolphthalein [14] and bromophenol [15].
- Repeat the experiment two more times with two different tablets of the same batch.

D. Back titration method for liquid dosage [10]

- In case of liquid antacids, shake the bottle well for one minute and pour 5mL of the antacid suspension into a 250 mL glass beaker. Add seventy (70) milliliters of distilled water into the beaker containing the liquid antacid and mix it well with a magnetic stirrer for 1 minute.
- Add 30 mL of 1N HCl to the content in the beaker with constant stirring for 15 min.
- Finally, add 2-3 drops of methyl orange indicator into the titrating mixture (titrand) and titrate the excess HCl with 0.5N sodium hydroxide.
- At the end point, color of the test solution changes from red to yellow.

- Calculation of ANC from back titration method [10]

ANC value is calculated using the formula as given below.

Acid neutralizing capacity (ANC) in mEq = Moles of HCl added – Moles of NaOH required

= (Volume of HCl x Normality of HCl) – (Volume of NaOH x Normality ofNaOH) …….(2)

- Standardization procedures in back titration method:
- Standardization of 1N HCl solution:

Sodium carbonate (5.3 g) was taken in a 100 mL volumetric flask. Then, distilled water was added up to 100 mL mark of the flask to make 1 N Na_2CO_3solution. Ten milliliters (10 mL) solution of Na_2CO_3 was taken in a beaker. Few drops of methyl orange indicator were added.to the beaker. Then, Na_2CO_3solution was titrated with HCl solution until color was changed from yellow to orange-pink. This process was repeated for three times. The average volume of HCl required for titrating $Na_2CO_3$was 9.98mL. Then, the concentration of HCl solution was calculated using $V_1S_1 = V_2S_2$ formula and the obtained result was 1 N.

- Standardization of 0.5 N NaOHsolution:

Oxalic acid (6.3 g) was taken in a 100 mL volumetric flask. Then, distilled water was added up to 100 mL mark of the flaskto make 1 N oxalic acid solution. Ten milliliters (10 mL) oxalic acid solution was taken in a beaker. Few drops of phenolphthalein indicator were added.to the beaker. Then,oxalic acid solution was

titrated with NaOH solution until pink color was appeared. This process was repeated for three times. The average volume of NaOH required for titrating oxalic acid was 10mL.Finally, concentration of HCl solution was calculated by using $V_1S_1 = V_2S_2$ formula and the obtained result was 0.5 N.

Direct titration method for solid dosage [1]

- Firstly, triturate one antacid tablet in a mortar with pestle to powder.
- Take the whole powder of the tablet in a separate beaker containing 200 mL of distilled water. Mix the content of the beaker properly with a magnetic stirrer.
- After the above steps, pour 0.1N HCl from a burette into the beaker containing the antacid powder mixture until the pH 7 is attained.
- The required amount of acid to reach pH 7 is the acid neutralizing capacity (ANC) of the antacid used.

- Direct titration method for liquid dosage [16, 17]
- Add 1 mL of antacid to 100 mL of distilled water in a 250 mL beaker and stir with a magnetic stirrer at 60 rpm with a 2.5 cm magnet.
- Attach a pH meter and record the pH constantly.
- Thereafter titrate the prepared mixture with 0.1 M HCl to attain pH 3 and record the required volume of HCl.

No specific equation for calculating the ANC value under direct titration method was included in any of the reported literature.

- Standardization procedures in direct titration method
- Standardization of 1N HCl solution:

Sodium carbonate (5.3 g) was taken in a 100 mL volumetric flask. Then, distilled water was added up to 100 mL mark of the flask to make 1 N Na_2CO_3 solution. Ten milliliters (10 mL) solution of Na_2CO_3. was taken in a beaker. Few drops of methyl red indicator were added.to the beaker. Then, Na_2CO_3solution was titrated with HCl solution until color was changed from yellow to orange-pink. This process was repeated for three times. The average volume of HCl required for titrating Na_2CO_3 was 10.07mL. Then, the concentration of HCl solution was calculated using $V_1S_1 = V_2S_2$ formula and the obtained result was 0.99 N.

Based on the sorted out of the reviewed methods for ANC evaluation of antacid formulations, the percentage of usage of the different methods was figured out in the Table I. Among the obtained reported methods, most researchers (77%) used the pH-meter method (Table I) i.e. it was favored by the most investigators, but why? It has been answered later.

TABLE I: Numbers and prevalence of various ANC evaluation methods in literatures

Name of Method	References	Number of times the method was usedor followed in literatures	Prevalence (%) of use of the methods in literatures
pH Meter Method	[7-10, 18, 23-50].	33	77
Direct Titration Method	[1,16-17,19]	4	9
Back Titration Method	[10, 14,15,20-22]	6	14

Next, the authors of the present review work wanted to compare the ANC results obtained by different investigators when they employed different methods for the same antacid formulation. Some representative results were presented in the Table II. It is clear from the Table 2 that the reported three different methods were not used in common to analyze the ANC for the same antacid formulation but at most two of the methods were found to be used todo so. Interestingly, the ANC results reported by the pH meter method as well as by the back titration method were almost identical (Table II). This finding indicated that both the methods have similar accuracy and precision as well as equally acceptable for ANC determination of antacid formulations. However, the reason behind the

finding of almost identical results by the mentioned two methods could not be explained until an experiment was done by the author for ANC evaluation of an antacid formulation using the mentioned methods.

TABLE II: Reported ANC, by different method, for the same antacid formulation

Brand Name	Dosage form	Active ingredients	Excipients	ANC by pH Meter method, [Ref.]	ANC by back titration method,[Ref.]	ANC by direct titration method, [Ref.]
Gelusil	Tablet	Aluminum hydroxide (250 mg), Magnesium hydroxide (300 mg)	Dimethicone, Mg and Al silicate	23.19 ± 0.06 mEq/g, [10]	23.21 ± 0.27 mEq/g, [10]	NA*
Ulgel	Tablet	Aluminum hydroxide (200 mg), Magnesium hydroxide (200 mg)	Simethicone	23.96 ± 0.09 mEq/g, [10]	23.91 ± 0.11 mEq/g, [10]	NA*
Digene	Suspension	Aluminum hydroxide (830 mg), Magnesium hydroxide (185 mg)	Simethicone	20.96 ± 0.09 mEq/5mL, [10]	20.79 ± 0.06 mEq/5mL,[10]	NA*
Diovol	Suspension	Aluminum hydroxide (300 mg), Magnesium hydroxide (250 mg)	Dimethicone	26.28 ± 0.05 mEq/5mL, [10]	26.17 ± 0.18 mEq/5mL, [10]	NA*
Entacyd plus	Tablet	Dried aluminum hydroxide(425 mg), Magnesium hydroxide(400 mg)	Simethicone 30 mg	NA*	NA*	2ml 0.1N HCl/ tablet, [1]
Maganta plus	Tablet	Magaldrate 480 mg	Simethicone 20 mg	NA*	NA*	1 ml 0.1N HCl/ tablet, [1]

NA= Not Applicable, Ref.= Reference

Finally, authors of the present review work performed a comparative study with the same antacid tablets of same batch using the three different reported methods

in order to see the relative accuracy and precision of the results obtains by the mentioned three reported methods. The Hanna pH meter (pH 300, Portugal) was used to evaluate the ANC value in pH meter method. In the experiments, the antacyd plus tablet of Square pharma having MA No of 012-258-007 was used. The obtained results were tabulated in the Table III. In case of pH meter method, 11.26 mL/g, 10.94mL/g, and 10.62 mL/g of 0.5 N NaOH wererequired to reach pH 3.5 in titrating the three test solutions of antacid formulation. The ANC values were calculated using the eq-1for the respective above mentioned three solutions and the results were 24.37 mEq/g, 24.53 mEq/g, and 24.69 mEq/g, respectively.It was found that the average ANC of the antacyd plus tablets in pH meter method was 24,53 mEq/g.In the back titration method,13.42 mL/g, 13.28 mL/g, 13.56 mL/gof 0.5 N NaOH were required for titrating the three solutions of antacid formulation and to change the colour of indicator.The ANC values of the three respective antacid solutions were calculated as 23.29 mEq/g, 23.36 mEq/g, 23.56 mEq/g. The average ANC value for back titration method was 23.29 mEq/g. And the findings (average ANC values 24.53 mEq/g in pH meter method, and 23.29 mEq/g in back titration method) resonated the similarity of ANC results observed by the other authors in pH meter method, and back titration method, respectively (Table-2).It was so because pH meter method and the back titration methods were essentially same except in the back titration method, an external indicator was used while in the pH meter method the electrode response was used to end the titration. On the other hand, only 1.7 mL 0.1 N HCl was neutralized per antacyd plus tablet in direct titration method (Table II). Similar results were also reported by Jakaria*et al*.[1] in 2015 (Table 3). Now, if one converts the direct titration method results for example 1.7 mL 0.1 N HCl to mEq/g for the sake of comparison then it appears as (1.7×10^{-3} L x 0.1 mEq x1000/L=) or 0.14 mEq/g, which is too low compared to the other methods (Table-III) and also out of compliance with the FDA and USP specifications. It is not acceptable as well as not explainable to the authors of the present work. Anyway, out of the three methods employed for ANC determination

TABLE III: Results of ANC values obtained by different method for the sameantacid tablets of the same batch

Methods of Analysis	Brand Name, Manufacturer of the tablet	Contents of the Tablet	ANC Results
pH meter method	Antacyd plus tablet, Square Pharma, Bangladesh	Dried aluminum hydroxide gel(400 mg), Magnesium hydroxide(400 mg), Simethicone 30 mg	[a]24.53 mEq/g [b]24.62 mEq/g
Back titration method	Do	Do	23.29 mEq/g
Direct titration method	Do	Do	1.7 ml 0.1N HCl /tablet [1] Equivalent to 0.14mEq/g (converted by the authors of this work)

a = ANC values as per calculation by the reported formula (eq. 1); b = ANC values as per calculation by the formula used in the local pharmaceutical company (eq. 3)

The formula reported by the literature was supposed to results in different ANC values for tablet to tablet as the weight of one tablet (1.212 g) differed from the weight of the other tablet (1.166 g) of the same batch. Therefore, the authors wanted to know what formula is used in the QC of the local pharmaceutical companies. Upon personal communication, it was found that one of the leading company uses the

following formula for the calculation of ANC value (mEq) in case of pH meter method:

$$\frac{(V1*1*F1)-(V2*0.5*F2)}{Wu}*Rw \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

Here,
V1 = Volume of 1 N HCl
F1 = Factor of 1 N HCl
V2 = Volume of 0.5 N NaOH
F2 = Factor of 0.5 N NaOH
Wu = Weight of the sample in mg
Rw = Average weight of a tablet in mg.

It seemed to the authors of the present work that afore mentioned formula (eq. 3) is more acceptable as it considered the weightage of the tablet weight in the formula. However, the obtained result (24.62 mEq/g) was not differed much (Table-3) with the results calculated using the reported formula (eq.1).Note that, the local pharmaceutical company that was mentioned earlier by the authors of this work does not use the back titration method. As a result, the authors could not report ANC values (two results) for back titration method as like that of the pH meter method in the Table-3.

Potential sources of error or precision for pH meter method are:

- Selection of pH meter (it needs a pH meter of high precision).
- The addition process of acid to the antacid solution to make pH 3.5. From the present experimental study, it is recommended to add minute amount of acid slowly each time.
- Error may be introduced during the solution preparation procedures of 1 N HCl and 0.5 NaOH. They need to be standardized properly.

Potential sources of error or precision for back titration method are:

- Selection of indicator and the amount of it added to the antacid solution.
- Observation of color change of the indicator at the end point of titration.

Potential sources of error or precision for direct titration method:
Selection of pH meter (it needs a pH meter of high precision).
Addition technique of acid (acid has to be added drop wise very carefully so that pH does not change abruptly).

Authors of the present work compiled the standard specifications for ANC (Table-IV) established by the different organizations contributing to the pharmacy fields. It appeared from the Table-IV that the standard specification values varied slightly and tolerably between FDA and USP for the solid dosage form andthere was no specification for liquid dosage form in FDA and BP. Next, the authors of the present work compared ANC result for an antacid formulation assessed by the authors to the reported standard specifications (Table-IV). The findings (Table-III) of the authors of the present work as well as the reported ANC values (Table-II) of the other authors complied with the specifications of ANC (Table-IV) only because the standard specifications were set to one ended value like greater than or not less than a certain value (Table-IV). The authors felt that ANC values should have a range otherwise for example: the specification ≥ 5 mEq/dose may comply with ANC 50 mEq/dose or even with ANC 500 mEq/dose and so on. Likewise, not less than 7 or 9 mEq/dose specification may comply with for example ANC 40 mEq/dose or even ANC 800 mEq/dose and so on, which is not logical and scientific.

TABLE IV – The standard ANC specifications set by the different relevant organizations

Organization	ANC value mentioned
FDA	≥ 5 mEq/dose
USP	Not less than 7 mEq per dose of tablet preparation Not less than 9 mEq per dose of liquid preparation
BP	No specification for solid as well as liquid dosage forms

The authors of the present review work found from their experimental study that the pH meter method has some advantages over back titration method such as the pH meter method is more precise, cost-effective, easy to carry out, and less time consuming. Similarly,

pH meter method is more precise than direct titration method. In addition, pH meter method is the authorized method by USP while remaining two other methods are not any pharmacopoeia or organization like FDA, ICH etc. adopted method. All these factors might have led the pH meter method to be the favored method to the most of the investigators and it to appear as the topmost used method (Table-I) for ANC evaluation of antacid formulations.

CONCLUSION

As per the present literature review, three methods viz. pH-meter method, back titration method and direct titration method were found to use for the ANC evaluation of antacid formulations. Prevalence of use of the methods in the literatures was 77 %for pH meter method, 14 % for back titration method, and 9 % for direct titration method. Among the reported methods, pH meter method was used by most of the investigators (77 %) working in this field even though the pH meter method and the back titration method resulted in almost identical ANC values for the same antacid formulation. The authors of the present review work found from their experimental study that the pH meter method has some advantages over back titration method such as it is a pharmacopoeia adopted method, more precise, does not use extra chemicals like indicator (so cost effective), less time consuming and easy to carry out with fewer steps in the titration process. Similarly, the pH meter method is found to be superior than the direct titration method because pH meter method is a pharmacopoeia adopted, and more precise method. It is important to investigate why the direct titration method results in too low ANC value compared to the other methods. Pharmacopoeia methods are usually validated. So, back titration and direct titration methods are recommended for validation.

It appeared that the standard specification for ANC values was mentioned in the literatures but as greater than or less than of certain values which are very vague and confusing. And hence it (specification of ANC value) needs to be established as a range.

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