A general method for estimating the properties of antacids

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EDITORIAL COMMENT  An ingenious physical method of assessing the effect of antacids based on the continuous measurement of the change in pH as the antacid dissolves.

There are many difficulties in estimating the comparative properties of antacids by titration methods. It is not possible to back-titratate all antacid solutions to pH 7, as many antacids, although soluble in HCl, are insoluble in water. For this reason, the method described by Johnson and Duncan (1945) involves back-titration to pH 3-5, where all antacids are still soluble; the British Pharmacopoeia also recommends back-titration to pH 3-5. Piper and Fenton (1965) suggest using pH 4-5 as the endpoint. These methods, however, have the disadvantage that few indicators satisfactorily pinpoint such pH values; they also assume that all antacids, whatever they consist of, will stop reacting at the same point. This is not so, as will be shown.

A general method is therefore required that can be applied to all antacids, whatever their chemical properties. As it was clear that a physical method would be preferable to a chemical one, the following procedure was developed. This method depends entirely on the change in pH resulting from a known amount of antacid being dissolved in a known volume of excess N/10 HCl. The same method can therefore be applied under strictly comparable conditions to all antacids, whether water-soluble or not, and whether they contain hydroxide, silicate, carbonate, bicarbonate, or any other ion. Being a non-titration method, the errors due to adopting an inappropriate endpoint are eliminated.

Since the readings are obtained without altering the solution in any way, it is possible to make a continuous measurement of the change in pH as an antacid dissolves, thus introducing a time factor. By maintaining the reaction temperature at 37°C., this system can provide a model simulating the action of an antacid in the stomach. This is similar in principle to the system described by Rossett and Rice (1954).

The maximum pH attainable by an antacid in HCl solution can be found by a variation of this method. If the preparation is dissolved in a quantity of N/10 HCl that is insufficient to dissolve it completely, an equilibrium will be set up between the undissolved antacid and the solution. By measuring the pH at which this occurs the working limit of the antacid can be found.

METHODS

THEORY  The strength of the original N/10 HCl solution is known, i.e., 0.1 g./ions, or 100 mEq. H⁺ per litre, and the strength of the final solution is found by measuring the pH and converting this to mEq. H⁺ per litre. Subtracting this from the first figure leaves the number of milliequivalents neutralized during the course of the experiment. However, only a fraction of a litre is used in each case, so to find the actual number of milliequivalents of H⁺ neutralized by the sample taken, it is necessary to multiply this figure by the fraction of a litre used. If a known weight of antacid was used, this final figure can be compared with the theoretical figure.

INSTRUMENTAL  The pH meter used was the model 23A manufactured by Electronic Industries Ltd., which has an expanded scale that can be adjusted to cover any part of the pH range. In the first experiment, the pH range involved was pH 1-0 to 2-0, so N/10 HCl was used to calibrate the scale on the pH meter. The other experiments were in the range pH 3-5 to 9-5, so the scale was calibrated with normal buffer solutions. N/10 HCl was used as solvent throughout.

The pH meter, however, measures the pH of a solution electrometrically. The result therefore is a pH reading based on the activity, rather than the concentration, of H⁺ ions in the solution. The difference between the two is
negligible at pH values greater than about pH 3, but below this figure the difference is significant. Since the first experiment is based on the conversion of pH to concentration of H⁺ ions, it is clearly necessary to be able to convert the pH reading into the theoretical pH as simply as possible. This was done as follows.

From activity coefficient tables, the activities of HCl solutions of concentrations ranging from 0-005 molar to 0-1 molar were calculated (Table I). The pH values calculated from the concentrations were then plotted against the pH values calculated from the appropriate activities, i.e., —log [H⁺] against —log aH⁺. The result, over the range taken, was a straight line.

### TABLE I

<table>
<thead>
<tr>
<th>Concentration (moles)</th>
<th>Activity Coefficient</th>
<th>Activity (moles)</th>
<th>pH (concentration)</th>
<th>pH (activity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0·005</td>
<td>0·928</td>
<td>0·0047</td>
<td>2·30</td>
<td>2·33</td>
</tr>
<tr>
<td>0·010</td>
<td>0·904</td>
<td>0·0090</td>
<td>2·00</td>
<td>2·04</td>
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<tr>
<td>0·020</td>
<td>0·875</td>
<td>0·0175</td>
<td>1·70</td>
<td>1·76</td>
</tr>
<tr>
<td>0·050</td>
<td>0·830</td>
<td>0·0415</td>
<td>1·30</td>
<td>1·38</td>
</tr>
<tr>
<td>0·100</td>
<td>0·796</td>
<td>0·0796</td>
<td>1·00</td>
<td>1·10</td>
</tr>
</tbody>
</table>

The concentrations of H⁺ in the first experiment were calculated from pH values obtained directly from this graph. However, by applying the relationship \( y = mx + c \) to the graph, a conversion factor can be obtained. This turns out to be

\[
y = 1·055x - 0·16 \quad \text{where } y = \text{pH (conc)} \quad \text{and } x = \text{pH (activity)}
\]

Thus in experiment 1, the pH meter is set so that N/10 HCl reads pH 1·10, and all results are converted to pH before proceeding to calculate the concentration of H⁺ ion in the solution.

### EXPERIMENT

#### EXPERIMENT 1: TO ESTABLISH THE VALIDITY OF THE METHOD
Three large conical flasks containing different amounts of N/10 HCl were used, normally simple fractions of a litre. The amounts were calculated so that about one-third of the acid would be left after the antacid had completely dissolved. A known weight of Al(OH)₃ was dissolved in each flask, warming if necessary, cooled to room temperature, and the pH of the solution measured. After converting the pH shown on the scale to the theoretical value as described above, the concentration of H⁺ ions per litre was found; from this the amount of H⁺ neutralized by the antacid was calculated. This was compared with the weight of antacid taken. The experiment was then repeated with first CaCO₃, then KHCO₃, warming in each case to remove the dissolved CO₂. The results are shown in Table II.

Having established the validity of the method, the total acid-neutralizing power of the commercial antacids was measured using the same procedure. The results are shown in Table III.

#### EXPERIMENT 2: TO SIMULATE THE ACTION OF AN ANTACID IN THE STOMACH
Five ml of Al(OH)₃ gel (B.P.) was added to a beaker containing 50 ml of N/10 HCl, maintained at 37°C in a waterbath. More N/10 HCl was then allowed
to drip into the beaker from a burette, at a rate of about 1 mEq. in three minutes. The mixture was stirred regularly and the pH measured every 30 seconds. A graph of pH against time was drawn, then the experiment was repeated using 1·0 g. KHCO₃ (Fig. 1).

EXPERIMENT 3: TO MEASURE THE HIGHEST pH ATTAINABLE BY AN ANTACID One tablet of each preparation was crushed in a mortar and added to 50 ml. of N/10 HCl, maintained at 37°C. in a waterbath. The mixture was stirred regularly, and the pH measured every minute while the tablet dissolved. When the pH reached a steady value, this was noted (Table III), and a graph was drawn of pH against time. No conversion of the readings to theoretical figures was necessary here, as in this pH range (pH 4 to 9), the activities and concentrations of HCl are virtually identical. By this method, not only the working limit of each antacid was found, but also the time taken for each one to reach this limit was measured under identical conditions.

RESULTS

EXPERIMENT 1 The accuracy of the method can be seen from a comparison of the figures in the first and last columns of Table II. The former is the theoretical value calculated from the weight of antacid taken in each case, and the latter is the value found by adopting the above method. The corresponding figures are in close agreement.

The maximum neutralizing power of each commercial antacid is shown in column 1 of Table III.

EXPERIMENT 2 Figure 1 shows the variation of pH with time as N/10 HCl is run steadily into a mixture of Al(OH)₃ and HCl, and KHCO₃ and HCl. There is a large excess of antacid at the beginning of each experiment. The shape of the graphs compares well with those obtained in vivo, using a telemetering capsule in the stomach to measure the pH.

EXPERIMENT 3 The highest pH attainable by each preparation is shown in Table III. The variation of pH with time for each antacid can be seen in Figures 2, 3, and 4.

DISCUSSION

It can be seen from Table III that antacids fall broadly into two classes, those based on aluminium...
as the chief neutralizing agent, and those based on magnesium or calcium. The former reach equilibrium at about pH 4.1, the latter at anything between pH 5 and pH 9.2, according to the constituents of the tablet. It was found that the final pH varied with the amount of HCl present in some cases, notably those preparations that contained a mixture of ions. (Of course, the amount of HCl present was never sufficient to dissolve the sample completely.) Generally the larger amount of HCl present, the lower the final pH.

Antacids can also be divided into fast acting and slow acting. The latter are designed to dissolve in the mouth, thus providing a small steady stream of antacid into the stomach over a long period. The former are required to act immediately.

Since the principal aim of the experiment was to provide a comparison between the actions of antacids under identical conditions, all the preparations were crushed to ensure that each antacid was working at maximum efficiency, and the same volume of solvent was used in each case.

**SUMMARY**

A method has been described for the comparative estimation of the neutralizing abilities of antacids. The method is dependent entirely on the change in pH as an antacid dissolves, so all errors due to titrating to an arbitrary pH value are eliminated. That there are such errors involved was shown by measuring the maximum pH attainable by commercial antacids in HCl solution: the results were found to vary from pH 3.7 to 9.2, according to the chemistry of the preparation. Since results are obtained without altering the solution in any way, continuous measurements of pH change can be made; the results obtained from the model simulating the action of an antacid in the stomach compared well with those obtained in vivo.

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**REFERENCES**

