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CHEMICAL EVALUATION OF ANTACID PROPERTIES OF SACCHARATED ALUMINIUM HYDROXIDE

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An vitro antacid properties of polynuclear Al-hydroxide chelate of sucrose (Al-saccharate) have been studied and compared with those of the pharmaceutical preparations available in Pakistan. 15.6225g of Al-saccharate contained 1g of elemental A1. The neutralizing capacity of Al-saccharate revealed that one g of elemental Al can neutralize 129.3meq HC1. In respect of efficacy of the dose, duration of activity and maximum pH, it was observed that 0.032g of elemental A1 can neutralize 50ml of 0.1N HC1 to pH 2 in 15 minutes. On successive addition of another 0.032g of elemental A1 pH was raised to 3.8 and on third successive dose of 0.032g elemental A1 pH was raised to 4.7. The buffering capacity showed that 3.943ml of 1N HC1 was required to lower the pH of 0.064g elemental A1 from 4 to 3.

Key words: Antacid, Aluminium saccharate, Chelate of aluminium.

INTRODUCTION

The antacids are used to relieve heartburn and hyperacidity. These may also be used regularly as a part of ulcer therapy.

Al-hydroxide, the main ingredient of many antacid preparations, is generally made by precipitation of aqueous solution of A1 chloride with alkali, but other methods [1] are also available. The form [2] and the reactivity or efficacy of the Al-hydroxide depend on the method of precipitation, subsequent washing and drying.

Gratzel *et. al.* [3] reported that a paste of Al-hydroxide which is produced simply by precipitation, washing and concentrating; without intermediate drying, reacts with hydrochloric acid upto 90% in less than 15 minutes. On the other hand 30-60 minutes were needed for the reaction in the case of spray-dried Al-hydroxide [4]. Logically it is expected that better reactivity and efficacy will be observed with a water soluble form of Al-hydroxide.

Water soluble polynuclear Al-hydroxide chelate with sugars have been prepared and characterised earlier [5, 6]. The evaluation of antacid activity of this complex is reported in the present communication.

Antacids are available for self medication, but the labels do not contain information in respect of their efficacy, acid neutralizing capacity and buffering capacity etc. In literature, studies on the antacid efficacy of Pakistani preparations is not found. Although in other countries such reports have been published [7-11]. Therefore, studies on the antacid efficacy of the preparations popular in Pakistan have been included in this paper alongwith Al-saccharate.

MATERIALS AND METHODS

Pharmaceutical antacids were purchased from the market. All chemicals used were of analytical grade. Al-saccharate used in this experiment was prepared and characterized by the method reported earlier [5, 6].

Al-hydroxide was prepared by reacting $A1C1_3.6H_2O$ with Sodium hydroxide and was freed from electrolyte using distilled water. The Al-hydroxide gel was mixed with required quantities of sucrose and sodium hydroxide in ratio of A1 2: Sucrose 20: NaOH. This mixture was heated at 170°-180° for 3 hours till a brown cake was formed which gave a clear and stable solution, when dissolved in water. The complex was powdered and extracted with dried ethanol to remove excess alkali. The yield was 23.010g, m.p. 185°-210° (decomp.). 1% aqueous solution has a pH 10.5, density 1.0047g/cc, viscosity 0.01116 poise 35° and Al 64mg/g powder.

Al was estimated in the powder by wet oxidation, colorimetrically [12].

Purification of dried Al-saccharate powder. Dried Al-saccharate powder (2.00g) was dissolved in freshly boiled water (20ml). Alcohol (95%) was added (250ml) slowly with vigrous stirring, a dark brown precipitate was formed which was separated by centrifugation. The precipitate was washed twice with 95% alcohol, then with dried acetone and finally with ether. The precipitates were further dried under vacuum at 30°-40°. 0.7g dried residue was obtained, having m.p. 180°-210° (decomp.), Al content 71mg/g. The pH of its 1% aqueous solution was dropped to 9.15.

Evaluation of products. The composition and the code numbers of the selected commercial antacid preparations are shown in Table 1.

Determination of pH. Antacid (1g) was dispersed in 50ml of distilled water and pH [13] was recorded with the help of a pH meter, Table 2.

Table 1. Composition of the antacids as given on the label.

Code	A (Tablet)	B (Tablet)	C (Tablet)	D (Tablet)	E (Tablet)	F (Tablet)	G (Suspension) 5ml, minimum dose contains 0.746g solid
Magnesium trisilicate B.P.	500mg	25mg	–	–	–	–	–
Al-hydroxide gel B.P.	250mg	100mg	–	165mg	300mg	215mg	305mg
Sodium bicarbonate Ph. Eur.	–	170mg	–	–	–	–	–
Alginic acid B.P.	–	500mg	–	–	–	–	–
Al-hydroxide and magnesium carbonate codried	–	–	282mg	–	–	–	–
Semithicone (activated methyl polysiloxane)	–	–	25mg	–	–	–	–
Magnesium hydroxide	–	–	85mg	–	150mg	85mg	–
Oxethazaine	–	–	–	5mg	–	–	–
Magnesium carbonate	–	–	–	83.8mg	–	–	–
Simethicone	–	–	–	–	40mg	25mg	–

Table 2. pH, acid neutralizing and buffering capacity of antacid preparations.

Sr.	Product code	Prelim. pH of antacid	Wt. of antacid (g)	Al-hydroxide content/tab. in g (given)	Elem. Al/tab. in g (found)	Elem. Al/g of antacid in g (found)	ANC meq meq HCl/tab.	BC ml 1N HCl/tab.
1.	A	9.95	1.289 tablet	0.250	0.0764	0.0594	11.858	4.769
2.	B	7.30	2.524 tablet	0.100	0.0318	0.0125	4.292	3.180
3.	C	9.15	0.808 tablet	0.282	0.0862	0.1069	12.023	2.036
4.	D	9.80	0.496 tablet	0.165	0.0562	0.1133	6.409	1.944
5.	E	8.30	0.816 tablet	0.300	0.1089	0.133	8.324	5.140
6.	F	8.85	1.003 tablet	0.215	0.0702	0.0700	8.665	1.003
7.	G	7.30	0.746 (suspn) 5 ml	0.305	0.1042	0.1418	8.765	1.347
8.	H	10.5	1.00 powder	–	–	0.0640	8.28 (per g powder)	3.943 (per g powder)
9.	I	7.5	1.00 powder	1.00	–	0.3543	3.30 (per g powder)	2.2 (per g powder)

H = Al-saccharate; I = Al-hydroxide

Acid neutralizing capacity (ANC). The acid neutralizing capacity was determined according to the B.P. [14] Codex (Fig. 1 and 2).

Buffering capacity (BC). A slurry of the compound under test was prepared by adding powdered solid (1.0g) to distilled water (200ml). The contents were maintained at 37° with stirring at a constant speed through out the test. 1N hydrochloric acid (1ml) was added and when the system had equilibrated the pH was recorded after each addition. The buffering capacity is defined as the number of ml of 1N hydrochloric acid required to change the pH from 4 to 3 (Fig. 3 and 4).

Buffering action given by repeated doses. The buffering action given by the repeated doses was determined by the method of Davison [1]. The antacid (0.5g) was added with stirring to 50ml of 0.1N HCl at 37° and pH was recorded. After 15 minutes another 0.5g antacid was added stirred for 15 minutes and the pH was recorded. On the third successive addition of another 0.5g antacid and stirring for 15 minutes the pH was raised to 4.7 (Fig. 5). It was further confirmed by dispersing 0.5g, 1.0g and 1.5g of antacid in separate experiment (Fig. 6).

Rapidity of action. Rapidity of action of Al-saccharate was determined with three doses, 0.5, 1.0 and 1.5g. Each

dose of Al-saccharate was added with stirring to 50ml of 0.1N HC1 at 37° and the pH values were recorded after 5, 10, 15 and 20 minutes (Fig. 6).

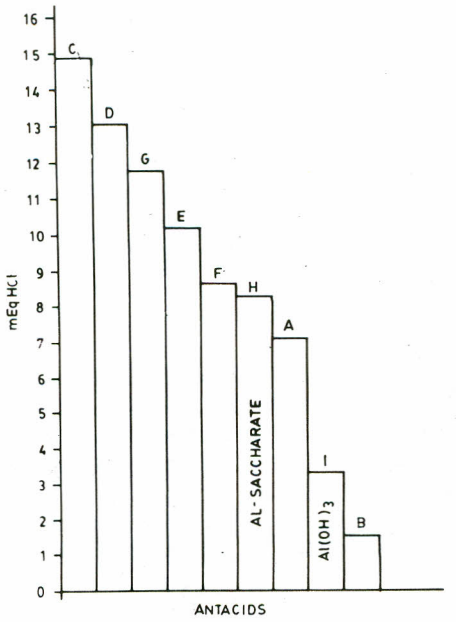


Fig. 1. Acid neutralizing capacity meqHC1/g of antacids. H = Al-saccharate; I = Al $(OH)_3$.

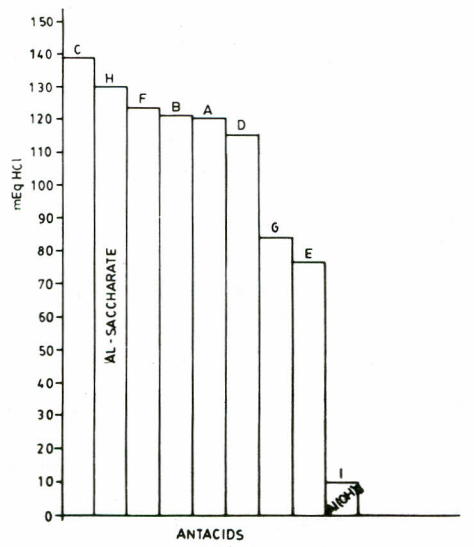


Fig. 2. Acid neutralizing capacity of antacids meq HC1/g of elemental Al. H = Al-saccharate; I = Al $(OH)_3$.

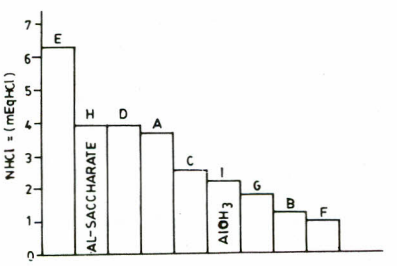


Fig. 3. Buffering capacity meq HCl/g of antacid.

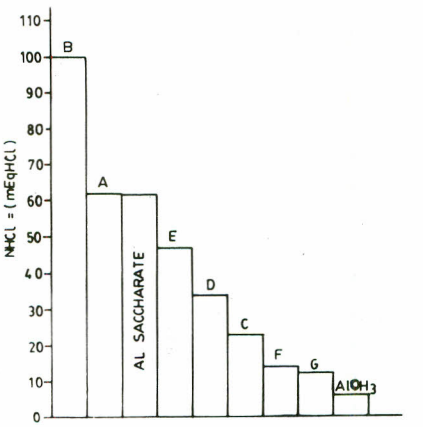


Fig. 4. Buffering capacity meqHC1/g of elemental Al. H = Al-saccharate; I = Al $(OH)_3$.

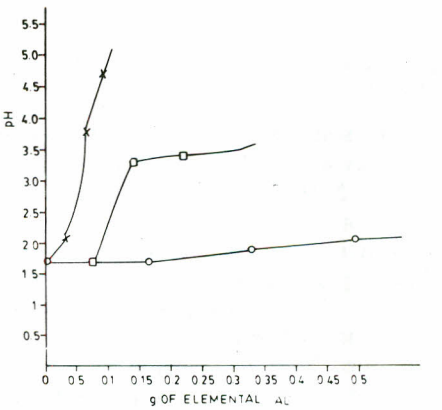


Fig. 5. Buffering action given by repeated doses/g of elemental Al. X = Al-saccharate; O = Al $(OH)_3$. □ = G.

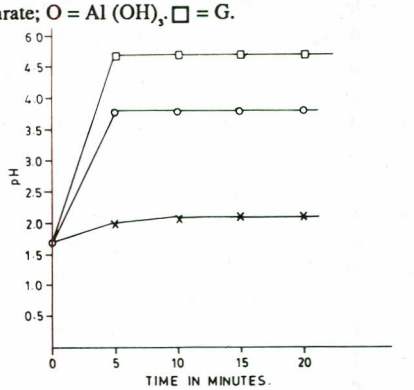


Fig. 6. Rapidity of action of Al-saccharate. X-0.032g Al (0.5g Al-sacch), 0-0.064g Al (1g Al-sacch); □ = 0.096g Al (1.5g Al-sacch).

RESULTS AND DISCUSSION

This study is mainly concerned with the evaluation of the antacid activity of the polynuclear Al-hydroxide chelate of sucrose (Al-saccharate). The antacid preparations popular in Pakistan have also been evaluated. Their composition, and code numbers are given in table 1 and 2. It is evident from the tables that there is only one preparation, code G, which contains a single ingredient, Al-hydroxide in suspension.

Al-hydroxide is prepared from $AlCl_3$ $6H_2O$ by pre-

cipitation with sodium hydroxide. The insoluble wet hydroxide is mixed with sugar and alkali and heated at 170°-180° for 3 hours to form a soluble Al-saccharate.

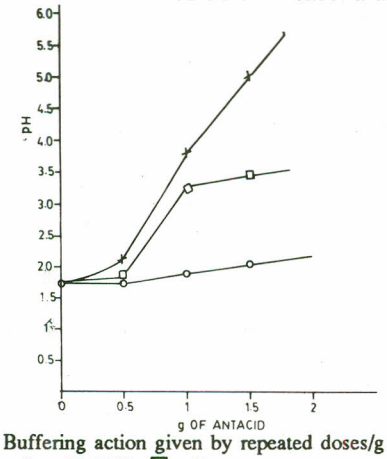


Fig. 7. Buffering action given by repeated doses/g of antacid. X = Al-saccharate; O = Al $(OH)_3$. □ = G.

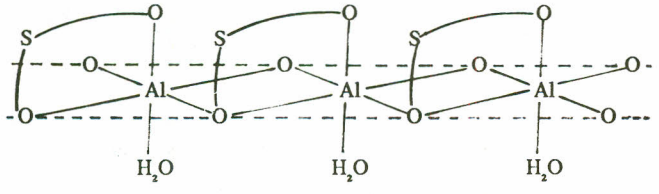
Aqueous solution of Al-saccharate containing elemental Al 1% has a pH of 10.5. On purification its pH was dropped to 9.15. However the ANC and BC of the purified product did not show deterioration in the antacid activity.

The antacid activity of Al-hydroxide depends on the method of its preparation and processing. Furthermore the suspension of Al-hydroxide is more active than that of its dried state. The Al-hydroxide from which sugar chelate is formed, in dried form, had an ANC of 3.2meq. HC1 per g of the antacid, while Al-saccharate made from the same quantity of wet Al-hydroxide had 8.3meq HC1 (Fig. 1). On the basis of elemental Al the values of ANC are 130meq HC1 per g of Al-saccharate, code H, and 10meq HC1 per g of A1 $(OH)_3$, code I (Fig. 2). This is in agreement with the earlier observations.

The BC of Al-saccharate is 4meq HC1 per g antacid and 60meq HC1 per g of elemental Al. As expected in a similar pattern $Al(OH)_3$ has lower BC 2.2meq HC1 per g antacid and 6meq HC1 per g elemental Al (Fig. 3 and 4).

The pharmaceutical preparation, code G, which contains a single ingredient A1 $(OH)_3$ in suspension, shows ANC of 11.8meq HC1 per g antacid and 80.4meq HC1 per g elemental Al. Its BC is 1.8meq HC1 per g antacid and 10.2meq HC1 per g elemental Al. Logically Al-saccharate can only be compared, to some degree, with this preparation, since it contains a single ingredient Al-hydroxide, in suspension form. Evidently ANC and BC of Al-saccharate are much higher than those of G.

Polynuclear Al-hydroxide chelate of sugar has the following structure similar to that of iron-saccharate.



S = Sucrose

Dried $Al(OH)_3$ powder code I has lower values than that of both the pharmaceutical preparation, code G, containing $Al(OH)_3$ in suspension form and Al-saccharate.

The dose of Al-saccharate which could raise the pH in the range, acceptable to many workers [15-17] of 3.5 to 5.5 was determined by the method of Davison [1]. It was found that 64mg of elemental Al which is equivalent to 1g of Al-saccharate can raise the pH of 0.1N HC1 to 3.8 (Fig. 7). Dried $Al(OH)_3$ on the other hand did not raise the pH above 2 even when 1.5g was used. Similarly 1g of the preparation coded G, could raise the pH to 3.25 but it is equivalent to 141mg of elemental Al i.e. double the quantity of that of Al-saccharate. The rapidity of action of Al-saccharate reveals that 1g can raise the pH of 50ml. O.1N HC1 to 3.8 in 5 minutes (Fig. 6).

The variation in ANC and BC of selected Pakistani commercial preparations (Fig. 1-4) are due to their composition combination of different ingredients. The ANC ranged between 12.023 to 4.292meq HC1 and BC between 5.140 to 1.347meq HC1.

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