Pak. j. sci. ind. res., vol. 34, no. 12, December 1991

THE PREPARATION AND *IN VITRO* EVALUATION OF ANTACID PROPERTIES OF SACCHARATED MAGNESIUM HYDROXIDE

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(Received December 31, 1990; revised January 5, 1992)

The preparation and *in vitro* antacid properties of polynuclear Mg-hydroxide chelate of sucrose (Sacch-Mg) have been studied. Its properties have been compared with those of a commercially available preparation containing Mg-hydroxide in suspension. 12.562 gm of Sacch-Mg contained 1 gm of elemental Mg. The neutralizing capacity of Sacch-Mg revealed that 1 gm of elemental Mg can neutralize 75.438 mEq. HCl. In respect of efficacy of the dose, duration of activity and maximum pH, it was observed that 0.0398 gm of elemental Mg can neutralize 50 ml of 0.1 NHCl to pH 1.80 in 15 mins, on successive addition of another 0.0398 gm of elemental Mg pH was raised to 3.7 and on addition of another 0.0398 gm elemental Mg pH was raised to 5.05. Buffering capacity showed that 2.2 ml of mEq. HCl was required to lower the pH of 0.0796 gm elemental Mg from 4 to 3.

Key words: Antacid properties, Saccharated Mg-hydroxide.

Introduction

Antacids constitute one of the most widely used classes of drugs available for self-medication. They are used to relieve heart burn and hyper acidity. They may also regularly be used as part of gastric and doudenal ulcer therapy and in hydrochlorhydria.

Mg-hydroxide mixture has also been used as mouth wash to neutralize acidity and has been given in the treatment of poisoning by mineral acids or arsenic.

Because of a laxative effect, Mg-hydroxide is usually used in conjunction with Al-hydroxide which has a constipating effect. In case of Al-hydroxide it was observed that its efficacy is dependent on the method of its preparation. A suspension produced simply by precipitation of $AlCl_3$ without drying, reacts with hydrochloric acid upto 90% in less than 15 mins [1]. On the other hand 30-60 mins were needed for the reaction in the case of spray dried Al-hydroxide [2]. Water soluble polynuclear Al-hydroxide chelate was found more active than the suspension [3]. Sacch-Mg a water soluble polynuclear chelate complex has been tested to ascertain whether this observation is also valid in this case. Only one commercial preparation is available which contains a single ingredient of Mg-hydroxide in suspension while the other preparations contain Al-hydroxide as well. The ratio of Mg to Al in these preparations is in the range of 1:1.693. The acid neutralizing capacity (ANC) and buffering capacity (BC) of these preparations have also been determined and incorporated in this communication.

Materials and Methods

All the chemicals used were of analar quality. Milk of magnesia was purchased from market. Mg was estimated on Hitachi Polarized Zeeman Atomic Absorption Spectrophotometer, Model Z-8000.

Preparation of saccharated Mg-hydroxide. Mg-hydroxide was prepared [4] by precipitation of an aqueous solution of $MgCl_2.6H_20$ (8.3 gm) with 5% sodium hydroxide (60 ml) and was freed from electrolytes by washing with distilled water. The wet Mg-hydroxide was mixed with sucrose and sodium hydroxide in the ratio of Mg 1: Sucrose 8: NaOH 1.5. The mixture was heated at 180° for 2.5 hrs till a brown cake was formed which gave clear and stable solution when dissolved in water. Mg was estimated in the complex by wet oxidation on atomic absorption spectrophotometer. Its aqueous solution having Mg 9.5 mg per ml has a pH 9.65 density 1.00806 gm/c.c and viscosity 33.3 m poise at 28°.

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

Determination of pH. Antacid (1 gm) was dispersed in 50ml distilled water and pH [5] was recorded with the help of pH meter Table 2.

Acid neutralizing capacity (ANC). The acid neutralizing capacity was determined according to the B- Pharmacoepoea [6] and is given in Fig. 1.

Table 1. Composition of the Antacids Evaluated.

Ingredients	Product code A mg/tablet	B mg/tablet	C mg/tablet	D mg/5ml suspension
Al-hydroxide and magnesium carbonate co-dried	—	—	282	—
Dried Al-hydroxide gel B.P.	300	250	—	—
Magnesium hydroxide	150	—	85	464
Magnesium trisilicate	—	500	—	—
Semithicone (activated methyl polysiloxane)	—	—	25	—
Semithicone N.F.	40	—	—	—

TABLE 2. ELEMENTAL MAGNESIUM, pH, ACID NEUTRALIZING AND BUFFERING CAPACITY OF ANTACIDS.

Product code	pH of antacid	Wt. in gm	Elem-Mg/tablet in gm (found)	Elem-Mg/gm of antacid in gm (found)	ANC mEq. HCl/tablet	BC ml 1N HCl/tablet
A	8.30	0.8160/tablet	0.0793	0.0971	8.324	5.140
B	9.95	1.2890/ "	0.0537	0.0416	11.858	4.760
C	9.15	0.8080/ "	0.0509	0.0631	12.023	2.036
D	9.95	0.4641/ (5 ml suspension)	0.1670	0.3599	25.257 (1 gm of powder)	1.20 (1 gm of powder)

Buffering capacity (BC). A slurry of the compound under test was prepared by adding powdered solid 1 gm (equivalent to 0.0796 gm elem. Mg) to distilled water (200 ml). The contents were stirred at a constant speed and the temperature was maintained at 37°, through out the test, 1 ml of mEq. HCl was added and the system allowed to equilibrate. The pH was recorded after each addition. The buffering capacity is defined as the number of ml of mEq. HCl required to change the pH from 4 to 3, (Fig. 2).

Rapidity of action. Rapidity of action of saccharated Mg (Code E) was determined by the method of Davison [7] with three doses of 0.0398, 0.0796 and 0.1194 gm elem. Mg. Each dose of saccharated Mg was added with stirring to 50 ml of 0.1 N HCl at 37° and pH values were recorded after 5, 10 and 20 mins (Fig. 3). The rapidity of action of milk of magnesia (Code D), Mg-hydroxide powder prepared in Lab. (Cod E) was also observed. Each of the product containing 0.04, 0.06 and 0.07gm of elem. Mg were added with stirring to 50 ml of 0.1N HCl at 37° and pH values were recorded after 20 mins. The values of these two products were compared with that of sacch-Mg (Fig. 4).

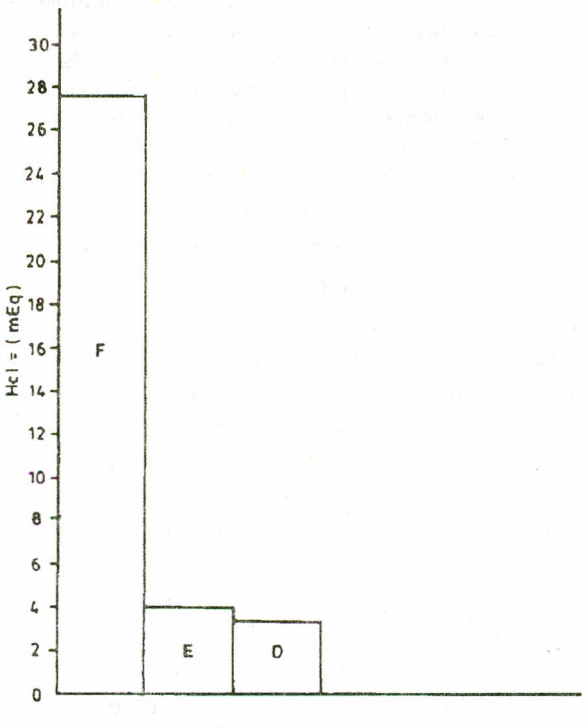

Fig. 2. Buffering capacity in m Eq. HCl/gm of elemental Mg D=milk of magnesia, E=Mg $(OH)_2$, F=Sacch.Mg-hydroxide.

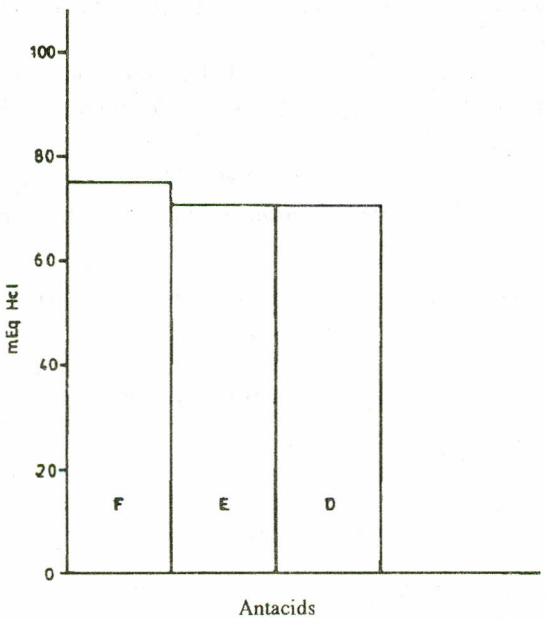

Fig. 1. Acid neutralizing capacity of antacids in mEq. HCl/gm of elemental Mg, D=milk of magnesia, E=Mg $(OH)_2$, F=Sacch. Mg.-hydroxide.

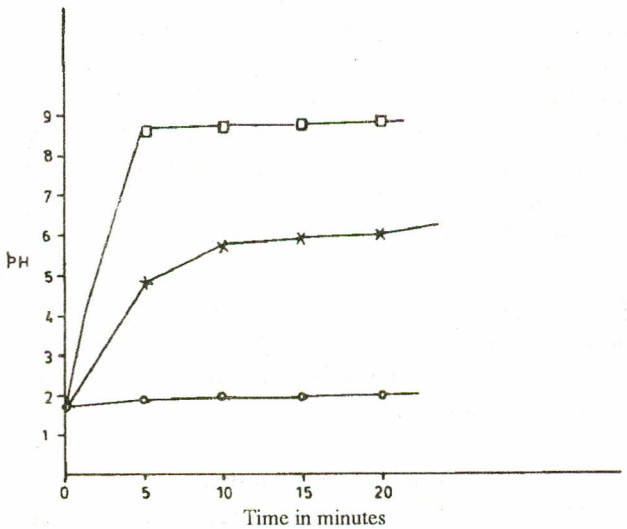

Fig. 3. Rapidity of action of sacch-Mg-hydroxide.

O=0.0398 gm Mg (0.5gm Sacch, Mg-hydroxide); x=0.0796gm Mg (1 gm Sacch. Mg-hydroxide); □=0.1194gm Mg (1.5gm Sacch. Mg-hydroxide).

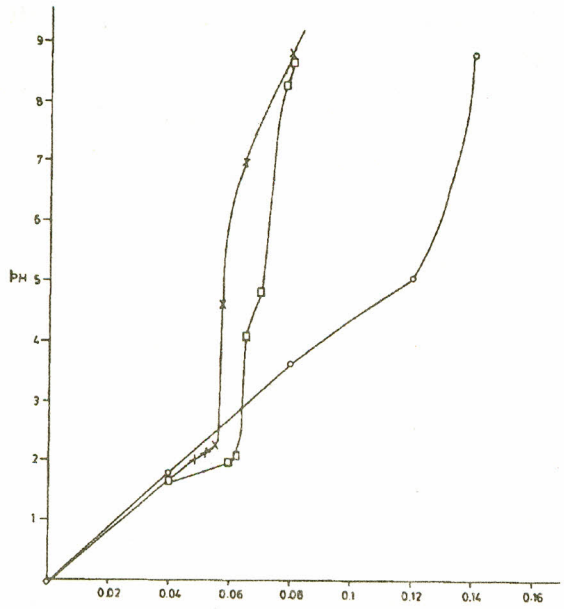

Fig. 4. Rapidity of action of antacids,
o=Sacch. Mg-hydroxide; x=milk of magnesia; □ =Mg $(OH)_2$.

Results and Discussion

Evaluation of the antacid properties of saccharated polynuclear Mg-hydroxide Sacch-Mg have been carried out. The popular antacid preparations which contain Mg in significant proportions have also been evaluated. In addition to Mg the popular antacid preparations usually contain Al, oxethazain, methyl polysiloxane etc. The composition, properties and code nos. of these preparations are given in Tables 1 and 2.

Mg-hydroxide is prepared from $MgCl_2$.6HO by precipitation with sodium hydroxide. The wet hydroxide is mixed with sugar and alkali and heated at 180° for 2.5 hrs to form a brown spongy product. It is dissolved in water filtered and estimated for Mg.

Aqueous solution of Sacch-Mg Code F containing 1% elemental Mg has a pH 9.65, density 1.0806 gm/cc and viscosity 33.3 m poise at 28°. Its solid content is 12.6% and the structure is shown in Fig 5.

The ANC of Sacch-Mg (F), Mg-hydroxide prepared in the Lab (E) and milk of magnesia (D), containing a single ingredient of Mg-hydroxide in suspension has been compared on the basis of their elemental Mg content (Fig. 1). One gram of elemental Mg is contained in 12.562 gm of Sacch-Mg, 2.5 gm of Mg-hydroxide preparation in the Lab and 2.778 gm in milk of magnesia, respectively. The value, 75.438 and 71 of the last two compounds are nearly the same. It is evident from these findings that in case of Mg-hydroxide the ANC is not dependent on its surface area. In contrast to this fact we observed that Sacch-Al [3] had the highest value, because it had the highest surface area.

The BC of these preparations have also been compared on the basis of elemental Mg (Fig. 2), Sacch-Mg F, Mg-hydroxide E, milk of magnesia D had the BC 2.2 ml, 1.55 and 1.2 ml of mEq. HCl respectively. BC of Sacch-Mg is much higher than the other two preparations.

The rapidity of action of Sacch-Mg, F, milk of magnesia, D, and Mg-hydroxide prepared in Lab, E was determined in 50 ml of 0.1N HCl and is shown in Fig. 4. All the three products gave nearly same pH of 1.7, 1.75 and 1.78 on addition of 0.04gm elem.Mg. On addition of 0.06 gm of elem-Mg contained in milk of magnesia and Mg-hydroxide pH was raised upto 2.1 but on addition of 0.07 gm of either of these products, pH shoots up abruptly to 8.3. Sacch-Mg on the other hand, raised the pH linearly: 0.06 gm elem-Mg raised the pH to 2.7, 0.08 gm to pH 3.65, 0.12gm Mg pH 5, and 0.14 gm Mg pH 8.75.

It is known that the pH level of gastric juice in stomach is 1.2-1.7 and an elevated level of pH favourable to ulcer healing is 3-3.5. Above pH 3.5 pepsin activity is inhibited, a further rise, in pH upto 5 or more, can induce the secretion of

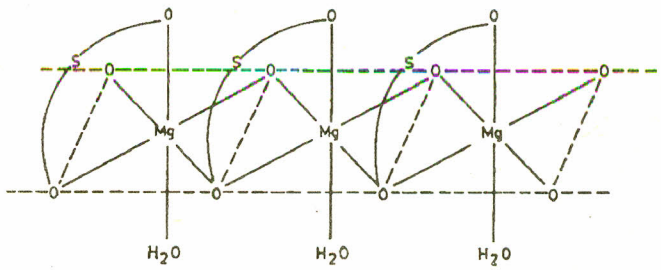

Fig. 5. Polynuclear Mg-hydroxide chelate of sucrose, S=Sugar.

extra acid, a phenomenon known as acid rebound. This may also cause alkalosis because of excessive alkalanity.

Thus Sacch-Mg can efficiently maintain the pH of gastric juice at an elevated level favourable to ulcer healing. It will not cause alkalosis as well. It raises pH 8 or more only when much larger quantities, double that of milk of magnesia and Mg-hydroxide are added (Fig. 4).

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