In Vitro Determination of Defoaming Inactivation of Silicone Antacid Tablets

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A simple and inexpensive *in vitro* test was utilized to evaluate the defoaming activity of a silicone defoamer in tablet combination with a number of commonly used antacid materials. The results covered the complete range of defoaming action.

THE USE OF silicone defoamers with routine antacid therapy has come into common practice where gas formation has been implicated as a difficulty in effective antacid therapy (1), and where gaseous distention is a factor in patient distress (2–4).

A study conducted in this laboratory indicated that the silicone defoaming action in an antacid-defoamer tablet was not stable, and seemed to reduce with aging. The objectives of this study were to (*a*) compare the defoaming activity of a silicone defoamer in tablet combination with commonly used antacids, (*b*) determine the stability of the above products.

EXPERIMENTAL

Selection of Antacids.—The antacids selected as representative of the antacids in use today were calcium carbonate, sodium bicarbonate, sodium citrate, aluminum hydroxide, magnesium trisilicate, magnesium hydroxide, magnesium carbonate, glycine, magnesium carbonate–aluminum hydroxide coprecipitate, magnesium peroxide, and bismuth subcarbonate. The silicone used is simethicone (Antifoam A, Dow Chemical Co.), an activated silicone.

Composition and Manufacture of the Tablets.—The following ingredients were used (mg./tablet): antacid, 400; cornstarch, 30; mannitol, 100; simethicone, 25; polyoxyl 40 stearate,[1] 3; lactose, 50; PVP, 80; microcrystalline cellulose,[2] 35; and magnesium stearate, 7; totaling 730.

Procedure.—The antacid, starch, and mannitol are blended. The simethicone and polyoxyl 40 stearate are melted together and added to the lactose. All the above materials are blended and granulated with an aqueous solution of the PVP. The granulation is wet and dry milled, blended with the cellulose and stearate, and compressed.

Both granulation and tablet were placed on stability at 45°.

PROCEDURES

Materials to be Tested.—The tablet to be tested was passed through a No. 20 screen. The granulation was tested as a granulation.

Foam.—The foam was generated by dissolving 200 mg. of a commercial laundry detergent in 100 ml. of purified water at 37°. The solution was placed in a 250-ml. graduated cylinder, and shaken vigorously until 150 ml. of foam was produced.

Defoaming Rate.—The material to be tested was placed into the graduated cylinder; the cylinder was then stoppered and inverted quickly 5 times to place the granules in contact with both foam and liquid. The clock was started and at each 15-sec. interval, the volume of remaining foam was noted, and the cylinder inverted once again. The test was considered complete after 2 min. or when all the foam disappeared, leaving the original 100 ml. of water in the cylinder.

Prolonged Defoaming Rate.—A defoaming rate was run as above, extending the time to 5 min. Tablets and pure simethicone were tested to obtain some estimate of free simethicone remaining in the tablets. The simethicone was spread out on micro-

TABLE I.—DEFOAMING TIME OF ANTACID-SILICONE TABLETS

Antacid Material	Days on Stability at 45°			
	0	2	7	14
Calcium carbonate	15 sec.	30 sec.	30 sec.	30 sec.
Sodium bicarbonate	15	15	15	15
Sodium citrate	30	15	15	15
Aluminum hydroxide	<120	<120	<120	<120
Magnesium trisilicate	15	15	90	75
Magnesium hydroxide	15	30	30	30
Magnesium carbonate	<120	<120	<120	<120
Glycine	15	15	15	15
Magnesium carbonate–aluminum hydroxide co-ppt.	90	<120	<120	<120
Magnesium peroxide	40	40	70	90
Bismuth subcarbonate	<120	<120	<120	<120

TABLE II.—DEFOAMING TIME OF TABLETS AFTER PROLONGED STORAGE

Antacid	Storage at 45°, Days	Defoaming Time, sec.
Calcium carbonate	57	30
Sodium bicarbonate	44	<120
Sodium citrate	44	15
Magnesium trisilicate	60	90
Magnesium hydroxide	49	30
Glycine	49	15
Magnesium peroxide	44	105

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[1] Marketed as Myrj 52 by the Atlas Powder Co., Wilmington, Del.

[2] Marketed as Avicel by the American Viscose Co., Marcus Hook, Pa.

TABLE III.—DEFOAMING TIME OF TABLET GRANULATIONS

Aluminum hydroxide	<120 sec.
Magnesium carbonate	<120
Magnesium carbonate–aluminum hydroxide co-ppt.	90
Bismuth subcarbonate	<120

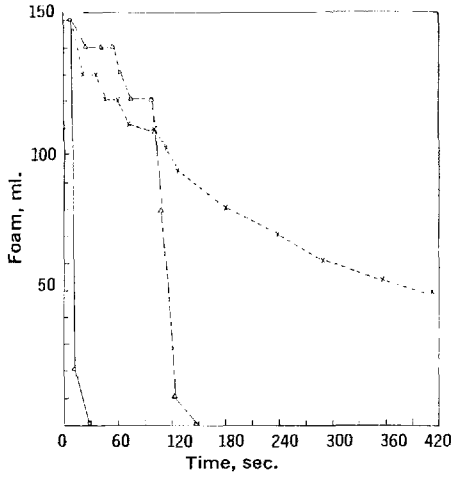

Fig. 1.—Foam depression of antacid-silicone tablets. Key: O, calcium carbonate tablet; ×, aluminum hydroxide; Δ, magnesium carbonate–aluminum hydroxide coprecipitate.

crystalline cellulose at a concentration of 25 mg./Gm. to facilitate testing.

RESULTS AND DISCUSSION

The speed of action of a gastrointestinal defoaming agent may be an indication of its efficiency in dispersing gas *in vivo* (5). This can be demonstrated by its defoaming action. The results listed in Table I indicate that there is a wide variation of defoaming action depending upon the antacid used in a silicone defoamer-antacid tablet.

There is also an apparent aging effect on these tablets, as some of the tablets exhibited a decrease in defoaming activity with storage at 45°. These test results can be seen in Table II.

It is significant that those antacids which most inactivate the simethicone (Antifoam A) did so independently of whether or not the material was compressed. In Table III it is evident that the simethicone inactivation is just as pronounced in these granulations as in the compressed tablets.

An attempt was made to correlate the defoaming activity of the tablets with the defoaming activity of the pure simethicone. In Figs. 1 and 2, the foam reduction as a function of time is shown.

The complete defoaming range of the tablets is shown in Fig. 1. The calcium carbonate tablet releases the simethicone almost immediately, so that

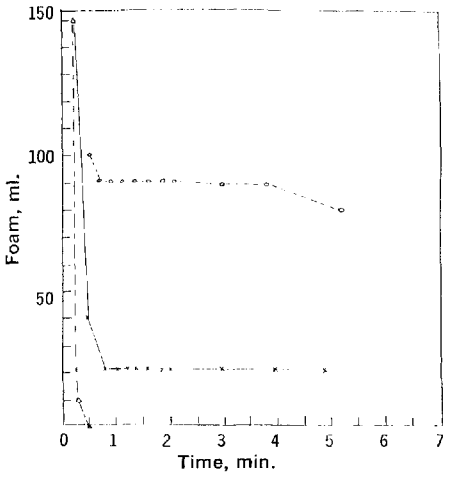

Fig. 2.—Foam depression of simethicone. Key: O, 5 mg.; ×, 10 mg.; Δ, 15 mg.

the foam disappears in 30 sec. The magnesium carbonate–aluminum hydroxide coprecipitate retards the simethicone, so that the foam drops after a 90-sec. delay. The aluminum hydroxide adsorbs the simethicone to a significant degree, so that a very slow reduction in foam height takes place.

In Fig. 2, a 15-mg. dose of plain simethicone approximates the calcium carbonate tablet curve in Fig. 1. The calcium carbonate tablet is at least equivalent to 15 mg. of free simethicone. Smaller doses of the simethicone quickly reduce smaller amounts of the foam, and do not approximate the simethicone-antacid tablet curves of Fig. 1.

There appears to be a gross correlation of the amount of foam reduction with the amount of free simethicone. In Fig. 2, we can see that 5 mg. of simethicone will reduce 60 ml. of foam, 10 mg. of simethicone will reduce 130 ml. of foam, and 15 mg. of simethicone will reduce at least 150 ml. of foam. Therefore, after 5 min., the aluminum hydroxide tablet had released the equivalent of approximately 7.5 mg. of free simethicone.

SUMMARY

An *in vitro* evaluation of the defoaming ability of antacid-silicone tablets was conducted. It was demonstrated that there are marked differences among the antacids tested with regard to their effect of the activity of the silicone defoamer.

The role of the amount of silicone defoamer was studied and correlated with foam depression. Stability studies indicate that some antacids will adsorb the silicone over a period of time.

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