Interaction of digoxin with activated dimethicone and other antacid constituents

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Summary. A study was made of the effect of activated dimethicone on the absorption of digoxin in relation to other commonly used antacid constituents using an in vitro experimental model. Dimethicone was found not to affect the absorption of digoxin in relation to aluminium hydroxide, bismuth carbonate, light magnesium carbonate and magnesium trisilicate whose effects on the absorption of digoxin were in agreement with values reported in the literature.

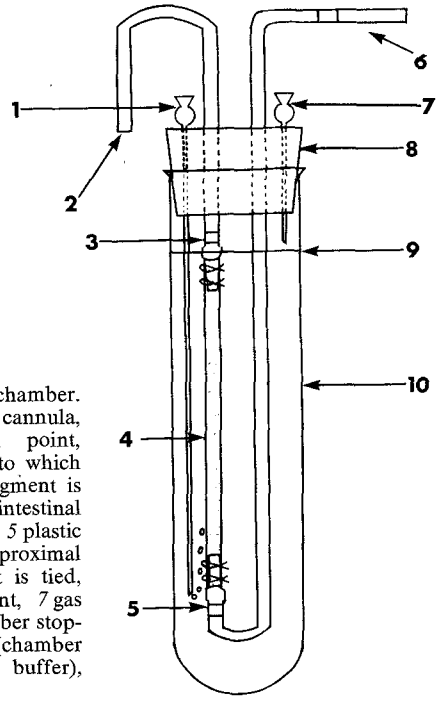
Activated dimethicone is being increasingly used as an antifoaming agent in proprietary antacid preparations. A previous report in the literature[1] suggested that dimethicone affected the absorption of anticoagulant drugs. It therefore seemed important to investigate the effect of dimethicone, in relation to other antacid constituents, on the absorption of digoxin, another drug with a narrow therapeutic range (0.8–2.0 ng ml^{-1})[2]. This was particularly relevant as other antacid constituents cause adsorption[3] and effect absorption of digoxin[4,5].

Materials and methods. The absorption of digoxin, while alone and while in combination with antacid constituents, was measured using an in vitro model of drug interaction in the gut[6]. This model has been shown to correlate well with the in vivo situation[6]. The method consisted of separately collecting drug absorbed across 2 similar everted rat intestinal segments by the infusion of 10 ml buffer samples at 10-min intervals through the segments. The perfusion apparatus is shown in the figure. The control perfusion chamber contained digoxin (0.25 mg) alone in buffer (120 ml, pH 7.4) while the test chamber contained digoxin plus a unit dose of antacid constituent. The level of dosage of the antacids used in this study was within the normal clinical range. The constituents tested were activated dimethicone, aluminium hydroxide gel, bismuth carbonate, light magnesium carbonate and magnesium trisilicate. The cumulative digoxin transferred across 2 consecutive intestinal segments during a 100-min time period was followed simultaneously. The results from 3 experimental runs were then averaged; any changes in absorption recorded in the presence of the antacid constituents are shown in the table. Digoxin was assayed using radio-immunoassay.

Results. The percentage decreased absorption of digoxin by dimethicone was negligible as compared with the other constituents tested (table). Aluminium hydroxide gel, bismuth carbonate and light magnesium carbonate gave slight reductions in the amount of digoxin absorbed (11.4–15.3%) while magnesium trisilicate gave very marked reduction (99.5%) in digoxin absorption as compared with controls over the 100-min time period.

Decreased digoxin absorption in the presence of antacid constituents. The absorption of digoxin (0.25 mg) was compared while alone and while in combination with the given quantities of antacid constituents using an in vitro model. The results are expressed as percentage decreased absorption of digoxin in the presence of antacid constituent with respect to digoxin alone

Antacid constituent	Amount of constituent used	Percentage decreased absorption
35% aqueous emulsion of activated dimethicone	1 ml	3.4
Aluminium hydroxide gel B.P.	7.5 ml	11.4
Bismuth carbonate	500 mg	15.2
Light magnesium carbonate	250 mg	15.3
Magnesium trisilicate	500 mg	99.5



Intestinal perfusion chamber. Key: *1* Aerator inlet cannula, *2* sample collection point, *3* plastic cannula unto which distal end of gut segment is tied, *4* everted rat intestinal segment (7.5 cm), *5* plastic cannula unto which proximal end of gut segment is tied, *6* infusion inlet point, *7* gas outlet cannula, *8* rubber stopper, *9* buffer level (chamber contains 120 ml buffer), *10* glass boiling tube.

Comment. The results indicate that activated dimethicone will not give rise to absorption problems with digoxin. An in vivo study in this department on healthy volunteers has since confirmed this finding, i.e., no change was seen in pharmacokinetic parameters when digoxin was taken alone and while in combination with dimethicone. The other constituents tested, however, gave rise to varying decreases in digoxin absorption. Magnesium trisilicate gave the greatest absorption reduction.

These findings suggest that if a patient stabilized on digoxin requires antacid therapy, then the doses of the 2 medicaments should be separated by as long a period as possible, and that concomitant use of digoxin and magnesium trisilicate should be avoided.

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