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Note

A novel raft-forming antacid suspension using a natural dietary fibre

Sandhya V. Mandlekar, Suneeta S. Marathe, Padma V. Devarajan *

Pharmaceutical Division, University Department of Chemical Technology (Autonomous), Matunga, Mumbai-400019, India

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Abstract

The formulation and in vitro evaluation of a raft-forming antacid suspension using a natural dietary fibre, isapgol (*Plantago ovata*) husk, along with sodium bicarbonate and aluminium hydroxide, is described. The effect of various formulation variables on the neutralisation profile was determined by a static neutralisation test and simulated in vivo neutralisation was determined using the modified Rossett-Rice test. Raft strength was measured using the Steven's LFRA texture analyser. Rheological determinations were also carried out. A comparative in vitro evaluation with a marketed alginate/antacid formulation 'Acigon' indicated that isapgol can be successfully used in the formulation of a 'raft-forming antacid suspension. © 1997 Elsevier Science B.V.

Keywords: Raft-forming antacid; Isapgol; Aluminium hydroxide; Sodium bicarbonate; *Plantago ovata*; In vitro evaluation

Antacid formulations containing sodium bicarbonate along with alginic acid and/or sodium alginate are advocated for the treatment of gastrooesophageal reflux (GOR). Various mechanisms of action have been postulated to explain the symptomatic benefits associated with these preparations (Malmud et al., 1979; Washington et al., 1986. Alginate seems to play an important role by virtue of its corking action, thereby acting as a physical barrier at the cardia.

Isapgol (*Plantago ovata*), an indigenously available natural dietary fibre is official in the Indian Pharmacopoeia. Made up of polysaccharides it is popularly used as a bulk laxative (CSIR, 1969). Biological experiments have confirmed its cytoprotective action (Nadkarni, 1976). A viscous dispersion of isapgol husk in water forms a swollen gel-like mass in acidic medium. The present study

* Corresponding author.

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Table 1
Composition of antacid formulations

Code	Ingredients (w/v%)			
	Aluminium hydroxide gel paste (8% w/w)	Sodium bicarbonate	Isapgol husk (60 #)	Purified water
1	12	0.70	2.00	q.s.
2	24	0.70	2.00	q.s.
3	12	1.40	2.00	q.s.
4	24	1.40	2.00	q.s.
5	12	0.70	4.00	q.s.
6	12	1.40	4.00	q.s.
7	24	0.70	4.00	q.s.
8	24	1.40	4.00	q.s.
9	12	0.70	1.50	q.s.
10	24	1.40	1.50	q.s.
11	12	0.70	1.50	q.s.
12	24	1.40	1.50	q.s.
13	12	0.35	1.50	q.s.
14	30	0.70	1.50	q.s.
15	12	0.70	1.30	q.s.

Each formulation in addition contained methyl paraben 0.25% w/v, propyl paraben 0.15% w/v, and disodium edetate 0.1% w/v.

was designed to evaluate the possibility of developing a raft-forming antacid suspension utilizing the gelling behaviour of isapgol husk.

Isapgol husk I.P. grade was procured from the local market. Aluminium hydroxide gel was obtained as a gift from Nicholas Piramal (India). All the other ingredients were of pharmacopoeial grade. The various formulations prepared are listed in Table 1.

The neutralisation behaviour of the formulations was assessed by a static neutralisation test. In the static test 15 ml of the antacid suspension was added to 50 ml of 0.2 N HCl (pH 0.85 0.05) contained in a 100-ml pyrex beaker. This was kept stirred on a magnetic stirrer, the speed optimised to prevent both, vortex mixing of the raft and settling of aluminium hydroxide. The pH was monitored for 3.5 h in the bulk phase and within the raft at intervals of 15 min.

Increasing the concentration of aluminium hydroxide caused a considerable increase in neutralisation (Fig. 1) which appears to be due to either increased potency of a dose or increased density of the raft, which resulted in mixing of the raft with the medium. Increase in isapgol concentration to 2% and above, caused a decrease in neutralisation (Fig. 2). Increased isapgol concentration resulted in increased viscosity, and a more compact three dimensional network structure within the raft which inhibited release of active ingredients. Increasing the concentration of sodium bicarbonate, however, caused only a marginal increase in neutralisation probably due to its entrapment in the raft.

Isapgol husk is prone to microbial contamination because of its natural source, method of collection and storage. The utility of the husk in the formulation of a raft forming antacid prompted further investigations using gamma-irradiated isapgol husk. A gamma-radiation dose of 15 kGy was found to cause total decontamination. Table 2 gives the composition of antacid suspensions prepared using irradiated isapgol husk.

The effect of formulation variables on the neutralisation profile as obtained in the static test for these formulations was similar to that obtained for formulations containing non-irradiated isapgol. As sodium bicarbonate did not markedly influence neutralisation properties, its concentration was kept constant at a level required for optimum raft formation.

Increasing aluminium hydroxide caused an increase in neutralisation and at 6% w/v aluminium

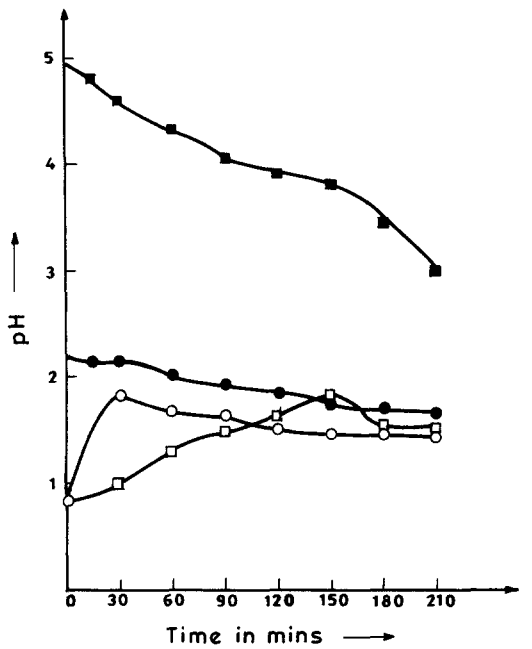

Fig. 1. Effect of aluminium hydroxide concentration on acid neutralisation. (Isapgol 0.75%, $NaHCO_3$ 1.4%) $Al(OH)_3$: (△) 2%, (•) 1%, (○) 0.5%.

hydroxide, maximum elevation in pH was obtained in the static test. The pH within the medium was raised from the initial 0.8 to 3.8 and that within the raft was maintained between 4–5. Increasing the isapgol concentration caused a decrease in neutralisation.

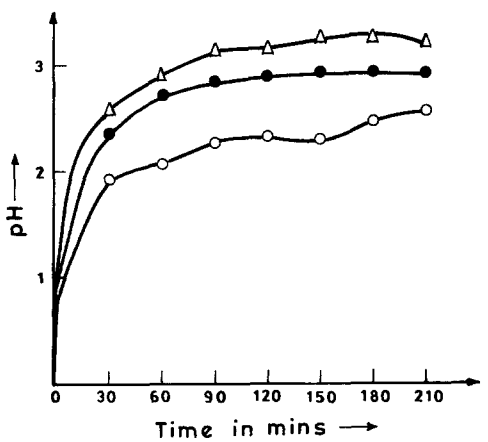

Fig. 2. Effect of isapgol concentration on acid neutralisation. ($Al(OH)_3$ 1%, $NaHCO_3$ 1.4%) Isapgol: (○) 1.3%, (△) 1.5%, (•) 2%, (▲) 4%

The strength of the raft obtained in vitro was monitored using a Stevens LFRA texture analyser. A raft was allowed to form by adding 15 ml of the antacid to 50 ml of 0.2 N HCl contained in a 100-ml pyrex glass beaker and allowing to stand for 5 min. The load in g required for penetration of a cylindrical probe at a speed of 1 mm/s through the raft was recorded. The raft strength which ranged from 2–7 g increased with increase in the isapgol concentration and could be related to the viscosity of the formulations. The effect of aluminium hydroxide and sodium bicarbonate on raft strength was not marked.

The rheological behaviour of the formulations was studied using a Brookefield synchrolectric viscometer, Model RVT. All the formulations exhibited pseudoplastic, thixotropic behaviour unlike the marketed formulation Acigon which exhibited near Newtonian behaviour. No raft formation occured for an isapgol formulation having a low viscosity (~ 135 cps at 5 rpm) equivalent to that of Acigon. This suggested that viscosity was a major factor determining raft formation.

The comparative neutralisation profiles of the isapgol formulation II7 and Acigon as obtained in the dynamic neutralisation test are shown in (Fig. 3).

The dynamic neutralisation test was a modified version of the modified Rossett-Rice test. A mixture of 15 ml of 0.2 N HCl and 35 ml distilled water was kept stirred on a magnetic stirrer, and 15 ml of the antacid suspension added. HCl (0.2 N) was continuously added at a rate of 2 ml/min and the reaction mixture removed at the same rate. pH was monitored as described for the static test. This test was carried out at 37°C.

The results suggest that a majority of the antacid component remains associated with the raft material and does not neutralise the acid layer below. The isapgol formulation gave a below raft pH profile similar to that obtained by Washington et al. (1985) in the modified Rossett-Rice test carried out on an alginate antacid product—'Liquid Gaviscon'. A good correlation between the in vitro pH profiles and below raft pH in human volunteers has been demonstrated by the same workers. Moreover, the results of various clinical

Table 2
Antacid suspensions prepared using irradiated isapgol husk

Code	Ingredients (w/v%)				
	Dried aluminium hydroxide	Sodium bicarbonate	Isapgol husk irradiate	CMC sodium	Purified water
II1	2	1.5	1	—	q.s.
II2	4	1.5	1	—	q.s.
II3	2	1.5	2	—	q.s.
II4	4	1.5	2	—	q.s.
II5	4	1.5	1.5	—	q.s.
II6	6	1.5	1.75	—	q.s.
II7	6	1.5	1.25	0.25	q.s.

Each formulation in addition contained methyl parabon 0.25% w/v, propyl paraben 0.15% w/v, and disodium edetate 0.1% w/v.

trials (Beelay and Warner, 1972; Stanciu and Benner, 1974; Hasan, 1980) have shown that Gaviscon is very effective in the treatment of GOR despite the low below-raft pH. This effect could be attributed to the barrier and demulcent properties of the alginate raft (pH within Gaviscon raft 3–6). Thus, it appears that measurement of pH below the raft is not the only criterion on which to base the efficacy of such products, pH within the raft plays an equally important role. Hence, isapgol rafts, which showed an in-raft pH above 5.5 for more than 2 h, unlike the Acigon rafts which showed a maximum pH of 2, may also be expected to be effective in the treatment of GOR and to be better mucoprotective than Acigon rafts.

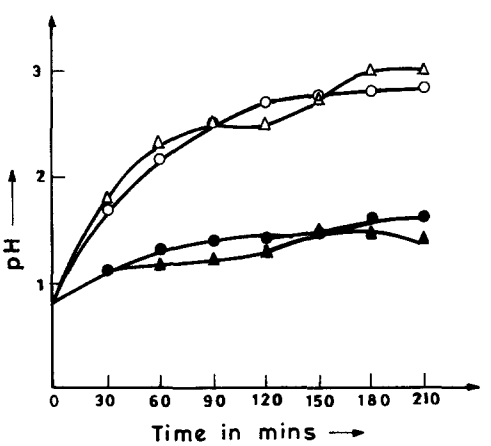

Fig. 3. Comparative neutralisation profiles of Acigon and II7, an irradiated isapgol formulation. (○) Acigon (marketed formulation), (□) II7. (•), (■) Corresponding in-raft pH.

Accelerated stability studies (3 months) on isapgol formulation indicated no marked changes in neutralising capacity at and below 37°C. The maximum variation in pH did not exceed 0.5 units. The raft integrity was also maintained at these temperatures. Moreover, the formulations were found to be physicochemically and microbiologically stable at these temperature conditions.

Isapgol (*Plantago ovata*), a natural dietary fibre can be successfully used in the formulation of raft forming antacid suspensions. Successful raft formation is seen to depend on the viscosity of the formulation suggesting that a whole new range of natural semi-synthetic gums and suspending agents could be used as raft-forming agents in the formulation of antacid suspensions and gels. The in vivo efficacy of this product in the treatment of GOR, however, needs to be established after extensive clinical trials.

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