

Research Article

Development and characterization of orodispersible tablets of famotidine containing a subliming agent

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Abstract

Purpose: The purpose of the present research was to the effect of camphor as a subliming agent on the mouth dissolving property of famotidine tablets.

Method: Orodispersible tablets of famotidine were prepared using camphor as subliming agent and sodium starch glycollate together with crosscarmellose sodium as superdisintegrants. The formulations were evaluated for weight variation, hardness, friability, drug content, wetting time, in vitro and in-vivo dispersion, mouth feel and in vitro dissolution.

Result: All the formulations showed low weight variation with dispersion time less than 30 seconds and rapid in vitro dissolution. The results revealed that the tablets containing subliming agent had a good dissolution profile. The drug content of all the formulations was within the acceptable limits of the United States Pharmacopoeia XXVII. The optimized formulation showed good release profile with maximum drug being released at all time intervals.

Conclusion: This work helped in understanding the effect of formulation processing variables especially the subliming agent on the drug release profile. The present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.

Keywords : Mouth dissolving tablet, Famotidine, Subliming agent, Super disintegrant, Camphor.

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INTRODUCTION

Tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness and ease in manufacturing. Patients often experience difficulty in swallowing conventional tablets when water is not available nearby. Furthermore, paediatric and geriatric patients may also encounter inconvenience in swallowing it¹. 'Mouth dissolving' (MD) or 'melt in mouth' tablets are a perfect fit for these patients as they immediately release the active drug, when placed on the tongue, by rapid disintegration, followed by dissolution of the drug^{2,3,4}. Mouth dissolving tablets combine the advantage of both liquid and conventional tablet formulations allowing the ease of swallowing the drug in the form of liquid dosage form. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, the bioavailability of the drug is significantly increased over those observed in the conventional tablet dosage form.

The basic approach to the development of mouth dissolving tablets is the use of superdisintegrants such as crosscarmellose sodium and sodium starch glycolate. Another approach used in developing MD tablets is maximizing the pore structure of the tablet matrix. Freeze drying and vacuum drying techniques have been tried by researchers to maximize the pore structure of the tablet matrix. However, freeze drying is cumbersome and yields a fragile and hygroscopic product. Vacuum drying along with the sublimation of volatilizable ingredient has been employed to increase tablet porosity. While designing dispersible tablets, it is possible to achieve effective taste masking as well as a pleasant feel in the mouth. The main criterion for MD tablets is the ability to disintegrate or dissolve rapidly in saliva of the oral cavity in 15 to 60 seconds and have a pleasant mouth feel⁵.

Famotidine is a highly selective H₂ receptor antagonist with properties of inhibiting gastric acid secretion and healing gastric & duodenal ulcers⁶. Since the aqueous solubility of the drug is 0.1%w/v at 20°C⁷, it gives rise to

difficulties in the formulation of dosage forms leading to variable dissolution rates^{8,9}. In the present study, an attempt was made to develop mouth dissolving tablets of famotidine and to investigate the effect of subliming agent on the release profile of the drug in the tablets.

MATERIALS AND METHODS

Materials

Famotidine was obtained as a gift from Tonira Pharmaceuticals, Ankhleshwar. sodium starch glycollate (SSG) and crosscarmellose sodium were also gifts from Recon Health Care Ltd, Bangalore. Camphor, sodium saccharin, mannitol, polyvinyl pyrrolidone(PVP), talc and magnesium stearate were purchased from S.D. Fine Chemicals, Mumbai, India.

Method

Formulation of mouth dissolving tablets

The orodispersible tablets of famotidine were prepared using the subliming agent, camphor, SSG and crosscarmellose sodium as superdisintegrants, mannitol as a diluent, sodium saccharin as sweetening agent, alcoholic solution of PVP (10%w/v) as binder and magnesium stearate with talc as a flow promoter (see Table 1). The drug and other ingredients were mixed together, and a sufficient quantity of alcoholic solution of PVP (10%w/v) was added and mixed to form a coherent mass. The wet mass was granulated using sieve no. 12 and regranulated after drying through sieve no. 16. Granules of the formulations containing either of the superdisintegrants but without camphor (F₁ or F₂) were dried in a tray dryer (Tempo instruments and equipments, Mumbai) at 60°C for 30 min. resulting in localized drying. Since the melting point of famotidine is 163-164 °C⁷, drying the granules at 60 °C does not affect the stability of famotidine. Other granular formulations (F₃ to F₆) contained a subliming agent and were dried at room temperature, 20-22 °C for 8hrs. The final moisture content of the granules was found to be between 4-5%^{10, 11}, which was determined using an IR moisture balance. The dried granules were then blended with talc,

Table 1: Composition of different batches of mouth-dissolving tablets of famotidine

Ingredient	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Famotidine	20	20	20	20	20	20
Sodium starch glycollate	25	--	25	--	25	--
Crosscarmellose sodium	--	25	--	25	--	25
Camphor	--	--	25	25	50	50
Sodium saccharin	2.5	2.5	2.5	2.5	2.5	2.5
Mannitol	195	195	170	170	145	145
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5
Talc	5	5	5	5	5	5

Table 2: Evaluation of mouth-dissolving tablets of famotidine

Formulation	Weight Variation (mg)	Assay (%)	Hardness* (Kg/cm ²)	Friability (%)	In vitro Dispersion Time (sec)	Wetting time* (sec)
F1	254 ± 3	97.4	4.3±1.2	0.457	48	65±2.1
F2	255 ± 6	99.0	4.8±1.6	0.524	41	45±1.8
F3	248 ± 7	94.5	4.3±2.1	0.635	20	28±1.4
F4	249 ± 4	99.1	4.6±1.6	0.608	22	26±1.3
F5	252 ± 2	96.3	3.8±1.4	0.968	17	24±1.7
F6	253 ± 3	98.4	3.6±1.1	0.912	14	21±1.2

* Average of three determinations

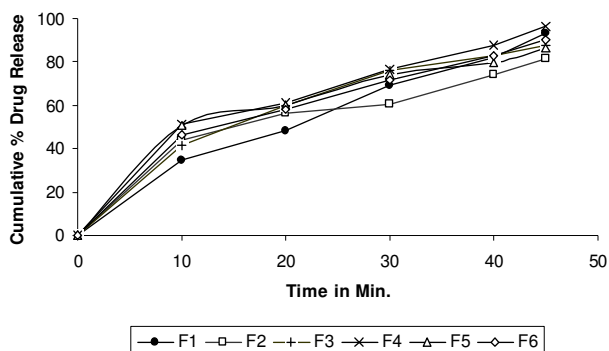


Fig. 1: *In vitro* release profile of Famotidine formulations

magnesium stearate and compressed into tablets using a 8mm punch rotary tablet

machine (Rimek, RSB-4 mini press Cadmach, Ahmedabad, India). Tablets from formulations

F₃ to F₆ were further vacuum-dried at 60°C until they reached constant weight. During drying, the camphor sublimed with the formation of a porous structure on the surface of the tablet.

Evaluation of the tablets

Hardness

The crushing strength of the tablets was measured using a Monsanto hardness tester. Three tablets from each formulation batch were tested randomly and the average reading noted.

Friability¹²

Ten tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted and reweighed. The percentage friability of the tablets was measured as per the following formula,

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight Variation

Randomly, twenty tablets were selected after compression but before vacuum-drying (in the case of F3 to F6) and the mean weight was determined. . None of the tablets deviated from the average weight by more than $\pm 7.5\%$ (USP XX).

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 20mg of famotidine was dissolved in 100ml of pH 6.8 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 265nm using UV-Visible spectrophotometer (UV 160-Shimadzu, Japan).

Wetting time¹³

A piece of tissue paper (12cmx10.75cm) folded twice was placed in a Petri dish (Internal Diameter=9cm) containing 9ml of buffer solution simulating saliva pH 6.8, which had the following composition, NaCl (0.126g), KCl (0.964g), KSCN (0.189g), KH₂PO₄ (0.655g) and urea (0.200g) in 1Litre of distilled water¹⁴. A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average

wetting time was noted. The results are tabulated in Table 2.

In vitro dispersion time¹⁵

In vitro dispersion time was measured by dropping a tablet in a 10ml measuring cylinder containing 6ml of buffer solution simulating saliva fluid (pH 6.8).

Dissolution studies

In vitro drug release studies of all the formulations were carried out using tablet dissolution test apparatus (USP TDT 06 PL, Electrolab, Mumbai) at 50rpm. Phosphate buffer pH6.8 was used as the dissolution media with temperature maintained at $37 \pm 1^\circ\text{C}$. Samples were withdrawn at different intervals, diluted suitably and analyzed at 265nm for cumulative drug release using Shimadzu UV-Visible spectrophotometer.

RESULTS

Table 2 shows that all the formulated tablets exhibited low weight variation. Addition of a subliming agent had no pronounced effect on hardness and increased friability of the tablets. The wetting time, *in vitro* dispersion time of the tablets were also considerably reduced in tablets containing camphor (Table 2). The drug content of all the formulations was found to be between 94.5 - 99.1% which was within the acceptable limits as per USP XXVII. The *in vitro* dissolution profile (Fig.1) indicated faster and maximum drug release from formulation F4.

DISCUSSION

Tablets were prepared using superdisintegrants alone (F1 & F2) and in combination of a superdisintegrant and a subliming agent, camphor (F3 to F6). Addition of camphor in the formulation improved the tablet properties with respect to wetting time and *in vitro* dispersion time. Comparatively increased concentration of camphor in formulation F5 and F6 showed relatively decreased wetting time and *in vitro* dispersion time which may be attributed to faster uptake of water due to the porous structure formed thus facilitating the disintergrant to bring about faster disintegration.

CONCLUSION

Overall, the results suggest that suitably formulated mouth-dissolving tablets of famotidine containing camphor as a subliming agent along with a super disintegrant (crosscarmellose sodium or sodium starch glycollate) can be achieved. The tablets exhibited good *in vitro* dispersion and wetting properties in presence of subliming agent. Thus the present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.

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