

**FORMULATION AND EVALUATION OF ORO DISPERSIBLE TABLETS OF  
FAMOTIDINE USING SUPERDISINTEGRANTS****V. Jhansi Priya Marabathuni\*<sup>1</sup>, G. Nireesha<sup>1</sup>, I. Adilakshmi<sup>1</sup>, J. Krishnaveni<sup>1</sup>, K. Anjaneya Gupta<sup>1</sup>, K. Venkata Lakshmi<sup>1</sup> and Ch. M. M. Prasada Rao<sup>2</sup>**<sup>1</sup>Department of Pharmaceutics, Bellamkonda Institute of Technology & Science, Podili. A.P-523240.<sup>2</sup>Department of Pharm. Chemistry, QIS College of Pharmacy, Vengamukka Palem A.P-523272.**\*Corresponding Author: V. Jhansi Priya Marabathuni**

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**ABSTRACT**

The objective of the present investigation was to prepare oro dispersible tablets of Famotidine, because of their convenience in administration and suitability for patients having dysphagia. Tablets were prepared by direct compression using sodium starch glycolate and croscarmellose sodium and crospovidone as superdisintegrants. Microcrystalline cellulose pH-102 was used as diluent and mannitol, sodium saccharine to enhance the organoleptic properties of tablets. The tablets were evaluated for weight variation, hardness, friability, assay, *in-vitro* disintegration time, *in-vitro* dissolution study. Hardness and friability data indicated good mechanical strength of tablets. The results of *in-vitro* disintegration time indicated that the tablets dispersed rapidly in mouth within 60 seconds. It was concluded that superdisintegrants addition technique is a useful method for preparing oro dispersible tablets by direct compression method.

**KEYWORDS:** Oro dispersible tablets, Famotidine, Superdisintegrant, Sodium starch glycolate, Croscarmellose sodium, Crospovidone.

**INTRODUCTION**

Most of the oral pharmaceutical dosage forms like conventional tablets and capsules are formulated to be swallowed or chewed. Elderly people and children sometimes have difficulties in swallowing these dosage forms. Such problem is more serious for bedridden patients. This problem is also applicable to active working or travelling people who do not have ready access to water.<sup>[1]</sup> Recent advances in novel drug delivery system aims to provide rational drug therapy by enhanced safety and efficacy of drug molecule by formulating a convenient dosage form for administration and also by ensuring better patient compliance.<sup>[2]</sup> One such approach is Oro Dispersible Tablets (ODTs). An ODT is a solid dosage form that disintegrates and dissolves in the mouth (either on or beneath the tongue or in the buccal cavity) without water within 60 seconds or less. The demand for ODTs has increased enormously during the last decade, particularly for geriatric and pediatric patients who have difficulty in swallowing conventional tablets and capsules.<sup>[3]</sup> Research scientists have formulated ODTs of various categories of drugs like Ondansetron hydrochloride<sup>[4]</sup>, ibuprofen<sup>[5]</sup>, lansoprazole<sup>[6]</sup>, hydrochlorothiazide<sup>[7,8]</sup>, cefixime trihydrate<sup>[9]</sup>, furosemide<sup>[10]</sup> and nimesulide<sup>[11]</sup> which are used for therapy in which rapid peak plasma concentration is required to achieve desired pharmacological response.

The various technologies used to prepare ODTs includes freeze drying, tablet moulding, direct compression, spray drying, and sublimation.<sup>[12]</sup> Direct compression represents a simple and cost effective tablet manufacturing technique. Use of conventional equipment, commonly available excipients and limited number of processing steps are the advantages of this technique. Directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agents. The commonly used superdisintegrants are croscarmellose sodium (cross linked carboxymethylcellulose), crospovidone (cross linked povidone) and sodium starch glycolate. In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration.

Famotidine is a selective H<sub>2</sub> receptor blocker and inhibits basal and nocturnal gastric secretion as well as secretion stimulated by food and pentagastrin. Conventional Famotidine tablets available in market show poor patient compliance particularly by the geriatric and pediatric patients who experience difficulty

in swallowing, and by those who are bed ridden or who are traveling and do not have an easy access of water.

The objective of the present investigation was to prepare ODTs of Famotidine, because in the above mentioned specific conditions, patient convenience is highly desirable. The tablets were prepared by direct compression method using sodium starch glycolate, croscarmellose sodium and crospovidone as superdisintegrants. Mannitol was selected due to its pleasant mouth feel property, good water dispersibility and binding property. It is also an effective tablet disintegrant and provides good hardness on compaction.

## MATERIALS AND METHODS

### Materials

Famotidine was a gift from Kopran Ltd., Mumbai. Microcrystalline cellulose, sodium saccharine, croscarmellose sodium, crospovidone were obtained as gift sample from Astron Research Center, Ahmedabad. Sodium starch glycolate was obtained as gift sample from Micro Labs, Bangalore.

Mannitol from Hi Media Laboratory Limited, Mumbai, Aerosil from S. D. Fine Chemicals, Mumbai, and magnesium stearate from S. D. Fine Chemicals, Mumbai were obtained.

### Preparation of powder blends for compression

Specified quantity of Famotidine, mannitol, MCC, sodium saccharine, SSG, CCS, crospovidone, aerosil and magnesium stearate were weighed accurately and passed through 60 # screen. All the materials were transferred to mortar and triturated till it mixed uniformly. The resulting powder mixture was compressed into tablets using single punch tablet machine. SSG, CCS and crospovidone were used as super disintegrants for preparation of ODTs of Famotidine by direct compression method. Various batches of tablet formulations prepared are shown in Table 1. Optimum combination was worked out based on powder blend properties and disintegration time of the tablets.

### Evaluation of powder blend Bulk density

Apparent bulk density (g/ml) was determined by placing pre-sieved bulk powder blend into a graduated cylinder via a large cylinder and measuring the volume and its weight.

### Tapped density

It was determined by placing a graduated cylinder, containing a known mass of powder on mechanical tapping apparatus, which was operated for fixed number of taps (around 250) until the powder bed volume reached a minimum. Using the weight of powder in a cylinder and this minimum volume, the tapped density was computed. From the results of bulk density and tapped density, Carr's index and hausner ratio were calculated.

### Angle of repose

For the measurement of angle of repose, a glass funnel was secured with its tip at a given height (H) above a piece of graph paper placed on a horizontal surface. Powder was poured through the funnel until the apex of the conical pile touched the tip of the funnel. The angle of repose was calculated with the formula  $\tan a = H/R$ , where a is the angle of repose and R is the radius of the conical pile.

### Evaluation of tablets

#### Weight Variation

Twenty tablets were selected at a random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight

#### Hardness

The tablet crushing load, which is the force required to break a tablet by compression in the radial direction, was determined using a Monsanto hardness tester.

#### Friability

Friability of tablets was measured by using Roche Friabilator. Friability was evaluated from the percentage weight loss of 20 tablets tumbled in a friabilator at 25 rpm for 4 minutes. The tablets were dedusted, and the loss in weight caused by fracture or abrasion was recorded as the percentage weight loss. Friability below 1% was considered acceptable.

#### In-vitro disintegration time

The in-vitro disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

#### Dissolution study

In vitro dissolution studies for all the prepared tablets was carried out using USP paddle method at 50rpm in 900ml of phosphate buffer pH 6.8 as dissolution media, maintained at  $37 \pm 5^\circ\text{C}$ . five ml aliquots were withdrawn at the specified time intervals, filtered through whatmann filter paper and assayed spectrophotometrically at 265nm. An equal volume of fresh medium, which was pre-warmed at  $37 \pm 5^\circ\text{C}$ , was replaced into the dissolution media after each sampling to maintain the constant volume thought the test. Dissolution rate was studied for all designed formulation and conventional tablet.

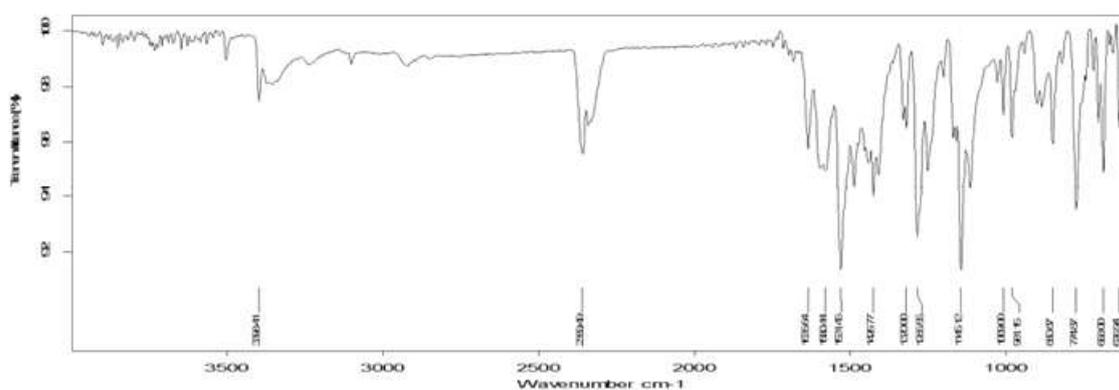
#### Assay

20 tablets were randomly selected and weighed. Average weight was calculated. Tablets were powdered in a glass mortar. Powder equivalent to 20mg was dissolved in 20ml of methanol in volumetric flasks to obtain a stock solution of 1000 $\mu\text{g/ml}$ . 1ml was pipetted out and diluted with methanol to 10 ml, so as to get 100 $\mu\text{g/ml}$  solutions. The absorbance was noted down after filtering off the

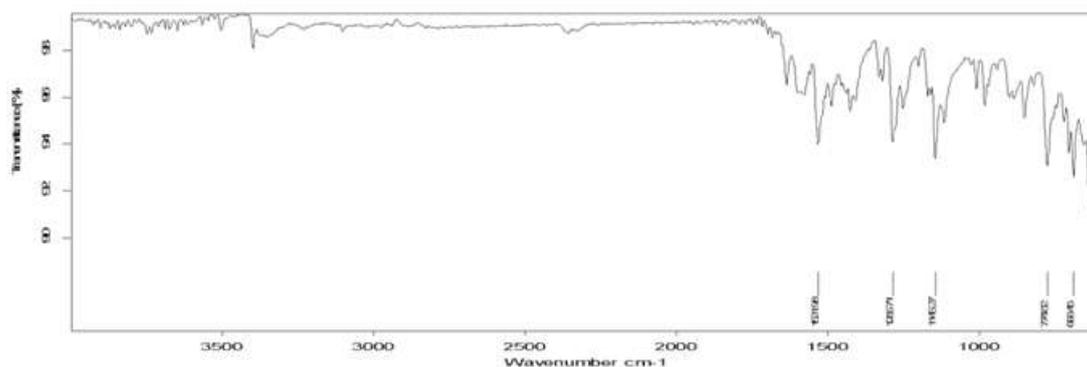
solution at 265nm and content of Famotidine was calculated.

**Table 1: Composition of Oro dispersible Tablet of Famotidine.**

Formulations	F1	F2	F3	F4	F5	F6	F7	F8	F9
Famotidine	20	20	20	20	20	20	20	20	20
Sodium starch	10	-	-	5	7.5	5	7.5	-	-
croscarmellose	-	10	-	7.5	5	-	-	5	7.5
crospovidone	-	-	10	-	-	7.5	5	7.5	5
Mannitol	25	25	25	25	25	26	25	25	25
Microcrystalline	135	135	135	132.5	132.5	132.5	132.5	132.5	132.5
sodium saccharine	5	5	5	5	5	5	5	5	5
Aerosil	3	3	3	3	3	3	3	3	3
magnesium	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200



**Figure 1: FT- IR Spectra of Famotidine.**



**Figure 2: FT- IR Spectra of Famotidine + Crospovidone.**

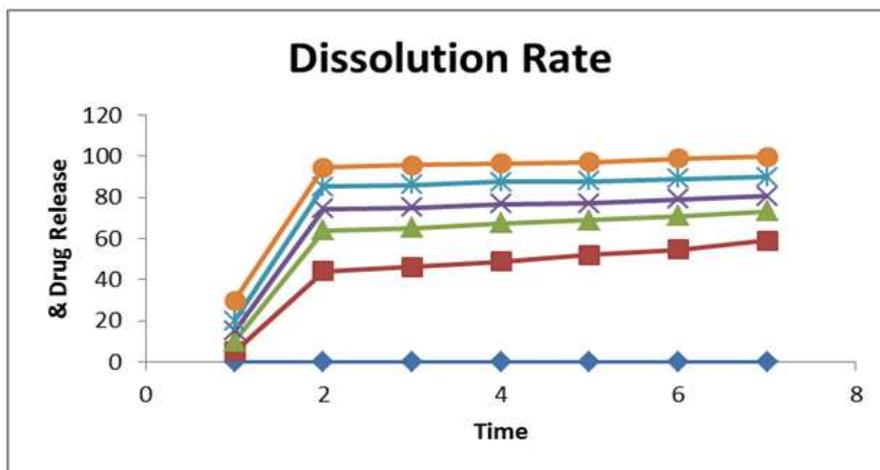


Figure 3: Dissolution profile for prepared ODTs of Famotidine batches and marketed conventional tablet formulation.

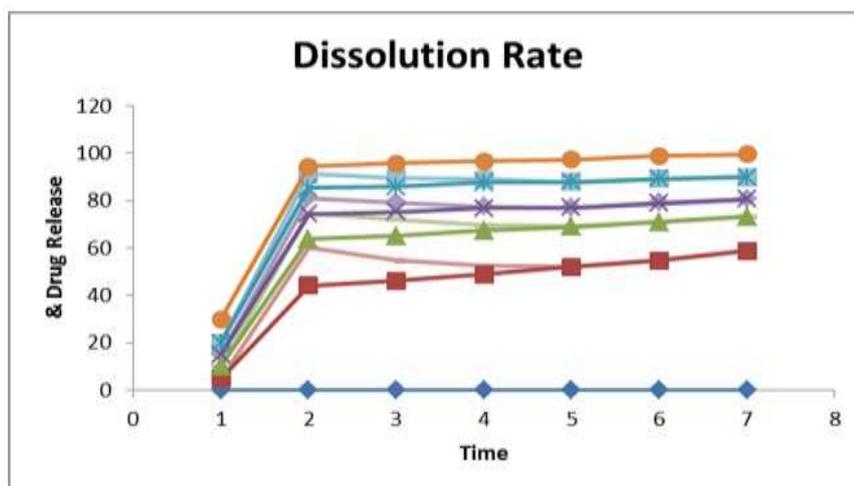


Figure 4: Stability study of in-vitro dissolution for formulation F5 stored at temperature  $40^{\circ}\text{C}\pm 2^{\circ}\text{C}$  /  $75\% \text{RH}\pm 5\% \text{RH}$ .

## RESULTS AND DISCUSSION

The present investigation was undertaken to formulate and evaluate orally dispersible tablets of Famotidine by direct compression method using sodium starch glycolate, croscarmellose sodium and crospovidone as superdisintegrants. Superdisintegrants are generally used by formulation scientists for developing ODTs or for improvement of solubility for active pharmaceutical ingredients. The primary requirement for both dosage forms is quicker disintegration. Major functional groups present in Famotidine show characteristic peaks in IR spectrum. Figure 1 to 4 shows peaks observed at different wave numbers and the functional group associated with these peaks for drug and drug with different polymer. The major peaks are identical to functional group of Famotidine. Hence, it was confirmed that there was no incompatibility between drug and various polymers. The results obtained by evaluating the powder blends of drug and excipients is shown in Table 2. The two most important attributes for the direct compression formula are good flow and good compressibility.

The values obtained for bulk density and tapped density does not affect the compression of tablets. The angle of repose gives important information about the flow characteristics of the powder mixture. The powder flow depends on three general areas: the physical properties of the particle (e.g., shape, size, compressibility), the bulk powder properties (e.g., size distribution, compaction); and the processing environment (e.g., storage, humidity). The angle of repose  $< 30^{\circ}$  indicates free flowing material and  $> 40^{\circ}$  with poor flow properties. Values for angle of repose were found in the range of  $25$  to  $28^{\circ}$  showing that the blend of powder was free flowing and can be used for direct compression. The value for Carr's index was in between  $10$ - $13$  ( $< 10$ ), indicating that all the batches of powder blends were having good compressibility.

The results for evaluation of different batches of Famotidine ODTs prepared by direct compression method are shown in Table 3. Weight variation was observed within the acceptable limit for uncoated tablets as per United States Pharmacopoeia. One of the primary requirements of immediate release preparation is faster

disintegration. It is well known to formulation scientists that the tablets with higher crushing strength show longer disintegration time. Since mechanical integrity is of paramount importance in successful formulation of ODTs, hence the hardness of tablets was determined and was found to be in the range of 3.0 to 3.5 Kg/cm<sup>2</sup>. Friability was observed between 0.5 to 0.7%, which were below 1% indicating sufficient mechanical integrity and strength of the prepared tablets. Thus, hardness and friability data indicates good mechanical resistance of tablets. *In-vitro* disintegration time for different batches of ODTs was 25 to 45 seconds. The tablet formulations containing SSG, CCS and crospovidone alone showed higher values of 45 to 32 seconds for *in-vitro* disintegration time. The *in-vitro* disintegration time for formulations containing super disintegrants in combination was observed to be 25 to 32 seconds. The formulations containing 8mg of SSG and 6mg CCS in combination per tablet showed 25 seconds value for *in-vitro* disintegration time. This result of *in-vitro* disintegration time indicates that the batch F5 containing 8mg/tab of SSG and 6mg/tab of CCS showed minimum time of 25 seconds to disintegrate *in-vitro*.

*In-vitro* dissolution studies were carried out for all 9 formulations by using 0.1N HCl. *In-vitro* dissolution data shows that formulation F5 shows improved dissolution as compared to other formulations. F5 shows 99.82% drug release in 10 min. *In vitro* dissolution study was carried out for conventional marketed Famotidine tablet and was also compared with best formulation F5 containing 8mg/tab of SSG and 6mg/tab of CCS. F5 shows 99.82% drug release in 10 min. while conventional tablet shows 69.78% drug release in 10 min. Stability study was carried out for the optimized formulation according to ICH guide lines at 40°C±2°C / 75%RH±5%RH for 2 month. The results showed that there was no significant change in physical and chemical parameter of the tablet, hence the formulation was found to be stable.

From the above result and discussion it is concluded that formulation of oro dispersible tablets of Famotidine containing Sodium Starch Glycolate (4%) and croscarmellose sodium (3%) i.e. F5 can be taken as an optimized formulation of oro dispersible tablets for 99.82% release within 10 min. The study shows that the dissolution rate of Famotidine can be enhanced through the great extent by addition of superdisintegrant methods. The rapid drug dissolution might be due to easy breakdown of the particles due to porous structure formation after super disintegration addition method and rapid absorption of drugs into the dissolution medium.

## CONCLUSION

Oro dispersible tablets of Famotidine were prepared by direct compression method using sodium starch glycolate, croscarmellose sodium and crospovidone as superdisintegrants. The tablets disintegrated rapidly in oral cavity and had acceptable hardness and friability. *In-*

*vitro* drug release from the tablets shows significantly improved drug dissolution. Hence it could be concluded that the superdisintegrant based oro dispersible tablets of Famotidine would be quite effective in providing quick onset of action without need for water for swallowing or administration.

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