

FAMOTIDINE SOLID DISPERSION AND ADMINISTRATION BY ORAL ROUTE

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ABSTRACT

Background: famotidine is a H₂ Blockers drugs having a component of low aqueous solubility and less oral bioavailability. Its need to develop of solubility and dissolution rate obtained for good therapeutic effect. Materials and Methods: The objectives of famotidine current work to formulation of solid dispersion (SDs) by kneading method for aqueous solubility enhancement. The low solubility problems were eliminated by preparing the solid dispersion using the poloxamer 188 as hydrophilic carrier. Result and Conclusion: The Famotidine tablets of solid dispersion characterized by employing solubility, FTIR, friability test, disintegration test, wetting time in-vitro drug release. The high value of solubility of Famotidine (FAM) solid dispersion were prepared Successfully, enhance dissolution rate and bioavailability.

KEYWORDS: Famotidine (FAM), Solid dispersion (SDs), Solubility, Bioavailability, Dissolution rate.

INTRODUCTION

Famotidine (C₈H₁₅N₇O₂S₃, MW 337.45) is a histamine H₂ receptor antagonist medication that decrease stomach acid production. Famotidine is used as medicine and used to treat peptic ulcer disease. Dosage forms that retained in the stomach are called gastro retentive drug delivery system (GRDDS). GRDDS can improve the controlled drug delivery gastroesophageal reflux disease and Zollinger-Ellison syndrome. Famotidine is taken from oral and by injection into vein. It prepared by various dosage forms such as tablet, microspheres, pellets, suspensions, nanoparticles.

MATERIALS AND METHODS

Materials

Famotidine & Poloxamer 407 was purchased by akums and drug Pvt. Ltd, Haridwar. Lactose magnesium stearate and sodium starch glycolate, polyvinylpyrrolidone (PVP), APS biotech, Bhagwanpur, Roorkee. All other chemicals and reagents were of analytical grade and used as provided.

Methods

Preparation of solid dispersion (SDs)

Preparation of solid dispersion with different polymers and different techniques used. Solid state characterization of prepared by solid dispersion. The dissolution properties of solid dispersion-Wood and flow through cell dissolution. Prediction of flow through cell dissolution according to the specific release rate based on Wood's dissolution. The Kneading method was used for the preparation of solid dispersion. Four different batches containing different drugs. Famotidine and Poloxamer

407 aeration solid dispersion. The drugs are weight and triturates with small volume of Isopropyl alcohol to give a thick paste. Take 20-30 min and dried at 45°C in oven. The dried powder was passed through mesh no.20 and stored for 48 hrs. in a Desiccator (vacuum) packing in airtight container.

Saturation solubility studies

The pure Famotidine of 5mg equivalent of Famotidine containing SDs prepared by Kneading method were added separately in conical flask containing 25 ml of distilled water. The sonication for 10min for all mixtures at room temperature and shaken after sonication for 24 hrs. at 37 °C after shaken 5 ml sample are collected and filtered through Whatman paper. The filtrate was analyzed by UV VISIBLE Spectrophotometer (HP-8452A, USA) at 249nm.

Evaluation of Granules

Bulk density

Bulk density was determined, weighed number of granules taken 20 gm of capacity measuring cylinder (50 ml). The volumes of granules occupied the measuring cylinder without compaction was measured and noted bulk density. Bulk density was calculated as below –

Bulk density (g/ml) = Mass of powder/volume of apparent unstirred

Where M= mass of powder

V₀ = apparent unstirred volume

Tapped density

Tapped density was determined, weighed number of granules taken 20 gm of capacity measuring cylinder (50 ml). the cylinder containing granules was tapped until a

constant volume obtained. Tapped density was calculated as below –

Tapped Bulk Density(g/ml) = Mass of Powder/Tapped Volume of Packing

Where, M= mass of powder

V_t = tapped volume

Compressibility

The compressibility index of the granules was determined by Carr's index. It is useful empirical guide is given by Carr's index.

Carr's index (%) = $(TBD - LBD)/TBD \times 100$

Where, TBD= Tapped Density

LBD = Bulk Density

Wetting time

The wetting time was determined by petri plate (6.5cm diameter) having a piece of tissue paper double folded 8ml of water. Then noted the time required in seconds for complete wetting.

Angle of repose (θ)

The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

The angle of repose was calculated by the following-

$\tan \theta = h/r$

Where, θ is the angle of repose,

h is the height,

r is the radius.

In-vitro drug release studies

Rate of dissolution studies for Famotidine SDs and pure Famotidine were carried out separately using the USP paddle method at 37°C by dissolution test apparatus (Electro lab autoTDT-08L) at 55 rpm with 900ml. of phosphate buffer Ph -7.4 as dissolution liquid. The weight of SDs equivalent to 20mg of Famotidine 20mg pure Famotidine were filled in to the SDs and then exposed the dissolution liquid for 1.5 hrs. the sample were collected at various time (i.e., 10,20,30,50,60, and 120 min) and then filtered using a Whatman filter paper. The samples of 5ml collected and filtered was analyzed by UV spectrophotometer at 265nm.

RESULT AND DISCUSSIONS

The solubility of Famotidine in distilled water and phosphate buffer pH 7.4 were 0.0068 mg/L. and 0.0078 mg/L. respectively. The prepared granules are subjected for characterization and result are given table no.3. The drug contented of Famotidine formulation were in range from 64.015 to 92.36% for all experimental values. The uniformity of weight all SDs formulation range is 186 mg to 202 mg.

Table 1: Pre-compressed granules parameters.

Sr.no.	Parameters	Result
1	Angle of repose (θ)	26.65
2	Bulk density (g/ml)	0.465
3	Tapped density (g/ml)	0.561
4	% compressibility	1.175

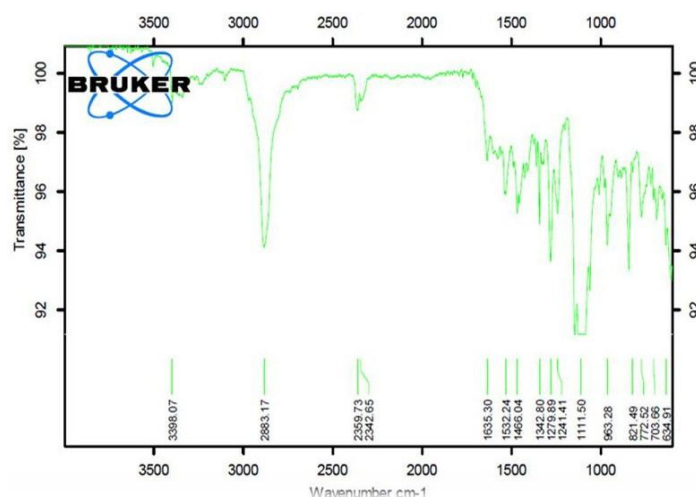


Figure 1(a): FTIR spectra of famotidine.

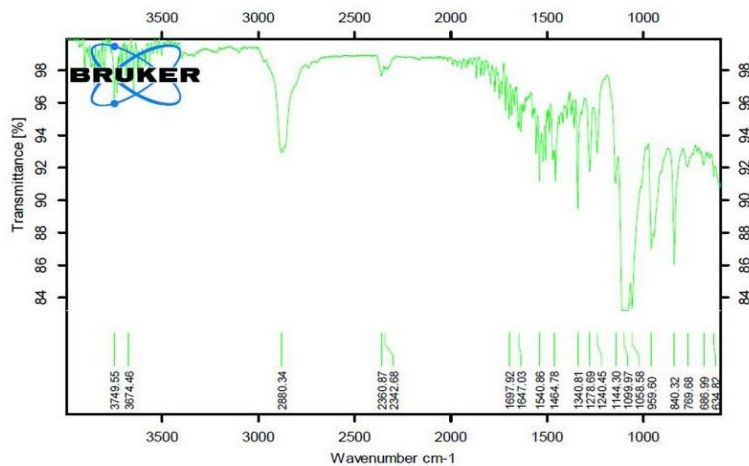


Figure 1(b): FTIR spectra of Famotidine + poloxamer 407.

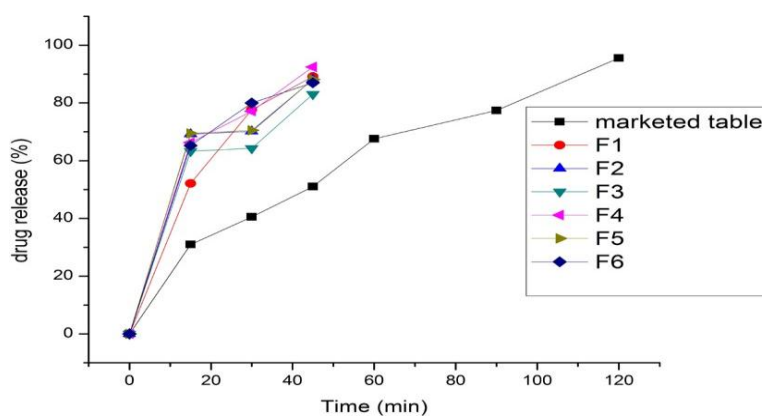


Figure 2: Dissolution profile of all six prepared Famotidine formulation and pre formulated Famotidine.

CONCLUSION

Solubility plays a key role in effective therapeutic action of drugs. Lesser the solubility and dissolution rate of poorly aqueous-soluble drugs leads to lesser efficiency as well as oral bioavailability. For the enhancement of solubility of BCS class II drugs i.e., famotidine, we prepared solid dispersion of famotidine using a kneading method and poloxamer 188 as hydrophilic carrier. The prepared novel formulation was evaluated using different techniques like solubility analysis, FTIR, disintegration test, friability, wetting time and in-vitro drug release. The optimum values of solubility and in-vitro drug release of prepared novel formulation were found maximum than conventional dosage form. From the study, we conclude that, the prepared formulation is improved solubility, dissolution rate and oral bioavailability of famotidine.

ABBREVIATIONS

FAM: Famotidine. **SDs:** Solid dispersions. **FTIR:** Fourier transform infrared spectroscopy **GRDDS:** Gastro retentive drug delivery system.

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