



Formulation And Evaluation Of Lafutidine Loaded Fast Dissolving Tablet Using Trigonella Foenum

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ABSTRACT

Tablet and capsules are the most accepted solid dosage form but the drawback of these dosage form is difficult in swallowing for some patients specially children's and old aged patients specially children's and old aged people. Hence, due to this reason tablets that can rapidly dissolve or disintegration in the oral cavity have gained attention. Fast dissolving tablets are those tablets which disintegrates rapidly when put on the tongue and releases the drug which dissolves/disperses in saliva. The main aim of this review is to explore the disintegrating property of the fenugreek mucilage and to find out the activity of drug(lafutidine) in fast dissolving form.

Keywords:

Fast dissolving tablet,
Disintegrating,
Super disintegrate

Graphical Abstract:



Lafutidine API(After mixing with fenugreek Mucilage and other excipients and compressing)

Tablet

(Disintegrates rapidly)



1. Introduction

Tablets and capsules are most preferred solid dosage form because of high patient compliance, easy production marketing, better physical and chemical stability and accurate dose adjustment (1).

The most widely used and accepted delivery system is oral drug delivery system. Since past many years oral route got so much popularity because of its easy administration and also because of a traditional belief that by oral route the drug is well absorbed as the food stuff are daily ingested orally. For successful development of an oral drug delivery system basic understanding of these aspects is required.

- a) Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug.
- b) The anatomic and physiological characteristic of GIT and
- c) Physicochemical chemical characteristic and the drug form to be designed (2).

Orally disintegrating tablets are also called as oral dispersible, fast dissolving, mouth dissolving system. There are two different types of dispersible tablets: -

- a) Which disintegrates rapidly in mouth without drinking water.
- b) Which can be dispersed in water to form dispersion.

As we know that the onset of action increases with rate of absorption. Certain drug absorbs from mouth, pharynx and oesophagus as saliva passes down the mouth to stomach. In this case the bioavailability of drug increases when compared to the conventional tablets.

2. Advantage of Fast Dissolving Tablets

- a) Risk of suffocating due to obstruction in swallowing is reduced.
- b) No need of water to swallow so it is convenient for patients who are travelling.
- c) Easy administration for patients who refuse to swallow conventional tablet specially geriatrics and pediatrics.



- d) Quick onset of action
- e) High bioavailability
- f) Improved patient compliance (3)

Some factors which makes FDT a better option are :

3. Disadvantage of Fast Dissolving Tablet

- a) low mechanical strength.
- b) Very fragile.
- c) Chances of degradation by temperature and humidity. (4)

- a) Patient in compliance due to risk of choking and suffocating while swallowing
- b) Some patient getting radiating therapy cannot swallow because of nauseous feeling due to H2-blocker.

4. Ideal Properties:

- a) Should easy disintegrated
- b) Should have high drug loading
- c) Should have pleasant taste
- d) Should leave no residue in oral cavity after administrating.
- e) Short half-life and frequent dosing drugs are unsuitable for FDT (5)

5.2- Effectiveness Factors: - FDT disperses in oral cavity and pregastric absorption occurs which avoid first pass metabolism and increases the bioavailability(6).

5. Reasons for Development of FDT

5.1- Patient Related Reasons: - FDT is a better choice for the patient who feels difficulty or refuses to swallow the tablet and capsules.

6. Challenges in Development of FDT

6.1 Improvement of Palatability: - Some drugs have relatively no taste and simply adding a suitable flavor can hide any slight unpleasant sensation. Most of the drug require taste masking. When they are incorporated in fast dissolving tablet. Taste masking is also done by using ion exchange resins. Cyclodextrins have better property to improve the bitter taste masking of drug by trapping the drug within the cyclic structure (7).



There are also several taste masking method using electrochemical, hot melt and super critical fluids and encapsulation using coacervation

6.2 Hygroscopy: Several fast dissolving tablets are hygroscopic and are not able to maintain physical integrity under normal condition of temperature and humidity which is done by specialized packaging (8).

6.3 Friability: – To allow fast dissolving tablet to disintegrate rapidly in the mouth are made either very porous or soft moulded matrices or compression force(9).

7. Techniques used for Preparation of FDT:

There are several techniques used the preparation of fast dissolving tablets like:

7.1. Freeze drying or Lyophilization: freeze drying is the process in which water is sublimated from the product after freezing. This freeze-dried form offers more rapid dissolution than conventional products. The lyophilization process provides glossy amorphous structure to the bulky agent and to the drug and enhance the dissolution

characteristics of the formulations (10).

7.2. Moulding – Tablet produced by molding are made of water-soluble ingredients to achieve fast disintegration. The powder is first blended with hydro-alcoholic solution, and then the wet mass is molded into a tablet with pressure lower than that used in making conventional tablets. Removal of solvent result in porous structure. One of the disadvantages of this technique is the poor mechanical strength of molded tablets (11).

7.3. Sublimation: In this technology, the high porosity necessary for fast disintegration is achieved by using volatile material (12). Inert solid ingredients, such as urea, ammonium carbonate, camphor etc, can volatilize readily. When these volatile materials are compressed into tablet, they can be removed via sublimation, which generates porous structure (13).

7.4. Spray Drying: This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous composition containing support matrix and other components to form highly porous and fine powder. This is then mixed into Active ingredients and compressed into tablet.



7.5. Dry Granulation: - In this technique the powder mixture is compressed with the use of heat and solvent. Two methods are used for granulation.

a) Slugging

b) Pre-compressing the powder using chilonator.

7.6. Direct Compression: In this method, tablets are compressed directly from the mixture of the drug and excipients without any preliminary treatment.

8. Basic GIT Physiology:

The gastrointestinal tract is a tube about 9m long which run from mouth to anus also includes pharynx, oesophagus, stomach and intestine (large and small).

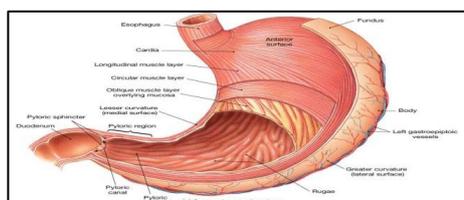


Fig.8.1: - Anatomy of stomach

The shape of the stomach is J-Shaped. The stomach of fundus, above opening of the oesophagus into stomach, body, antrum and central part. Pylorus is an anatomical sphincter located between the terminal antrum and the duodenum.

Fasting gastric Ph is 2, food and buffers neutralizes gastric acids and may increase the Ph upto 6.5 after injection of meal, the Ph falls below 5 and then slowly declines. The ph of small intestine is 6to7 and transit time is 3 ± 1 hour, which is comparatively constant and not affected by food.

The present work deals with design and development of lafutidine fast dissolving tablets to increase the bio-availability. Lafutidine is a new H₂ receptor antagonist, after absorption it reaches to gastric cell, then directly and quickly binds to gastric cell H₂ receptor and results in inhibition of gastric acid secretion. The drug is predominantly metabolised in liver by microsomal enzyme CYP3A4 and CYP2D6. It has a biological half of 1.92 hrs. lafutidine has a receptor binding affinity which is 2 to 80 times higher than other H₂ receptor antagonists like Renetidine, Fomitidine and Cimetidine.



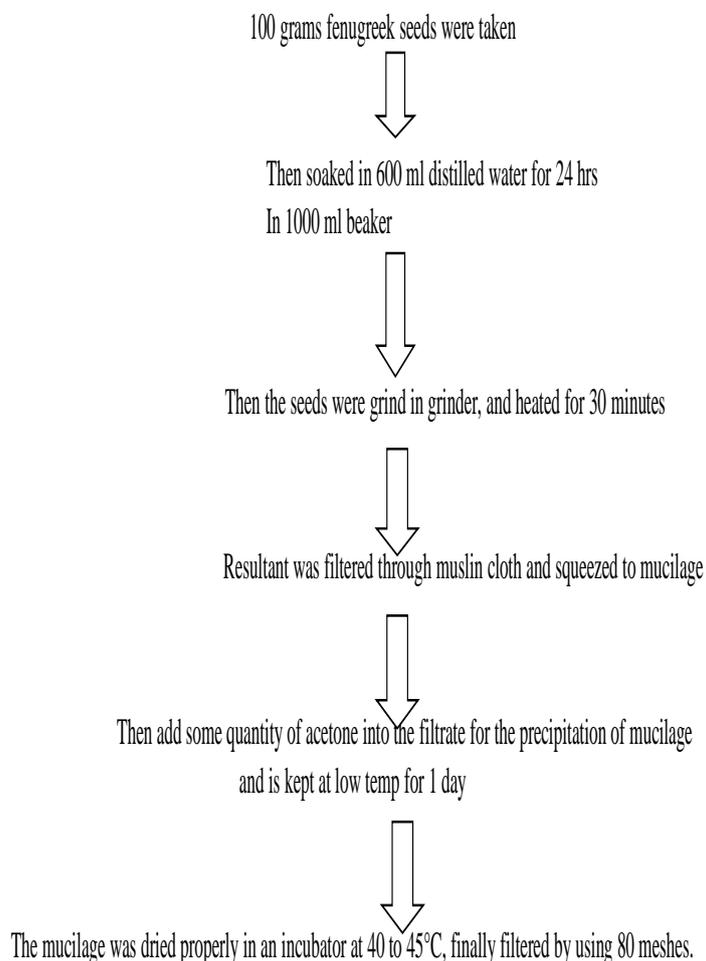
9. Mechanism of Disintegration.

9.1. Swelling: although not all effective disintegrants swells in contact with water, swelling is believed to be a mechanism in which certain disintegrating agents (Such as Starch) impart the disintegrating effect. By swelling in contact with water the adhesiveness of other ingredients in a tablet is overcome causing the tablet to break.

9.2. Wicking: Effective disintegrates that do not swell are believe to impart their disintegrating action through porosity and capillary action (wicking). Tablet porosity provides pathway for the penetration of fluid into tablets liquid is drawn up or wicked into these pathways through capillary action and rupture the interparticulate bonds leading breakdown of tablets (14).

10. Isolation of Fenugreek Seed Mucilage.

Fenugreek mucilage acts as a natural super disintegrating agent and is isolated by:



11. Preparation of Tablet (lafutidine FDT):

- Fast dissolving tablets of lafutidine was formulated by direct compression method.
- All the ingredients were passed through 60 mesh sieve separately.
- All the ingredients are mixed with the drug in geometrical order.
- Then the tablets were compressed using punching machine.



12. Medical use of Lafutidine:

- Gastric and duodenal ulcer (10mg bid)
- Stomach ulcer (10mg bid)
- Gastric mucosal lesions (10mg once daily)
- Pre-anesthetic medications (10mg before sleeping on the day before operation).

- FTIR spectroscopy
- Pre-compression parameter
 - Angle of repose
 - Bulk density
 - Tapped density
 - Hausner's ratio
 - Carr's index

13. Preformulation Studies:

It is the investigation of physical and chemical nature of drug. The API have various physiochemical properties which must be considered before development of pharmaceutical formulations. These properties a framework for drugs rational combination with pharmaceutical excipients to develop a suitable formulation. The main aim of pre formulation studies is to develop stable, safe and effective dosage form by determining the physiochemical parameter, compatibility with excipient and establishing kinetic rate profile.

Different Pre formulation Parameter Are:

- Physical identification
- Solubility studies
- Melting Point
- UV spectroscopy

14. Evaluation of Tablet

14.1. Hardness Test- to withstand mechanical shocks of handling in manufacturing, packing and shipping tablets requires a certain amount of strength. Pfizer hardness tester was used to determine hardness of tablet. It is expressed in kg/cm²

14.2. Friability Test – It is the phenomenon where by tablet surfaces are damaged and/or show evidence of breakage when subjected to mechanical check. The test was done by using veego friablator and expressed in (%). The percentage friability was then calculated by:

$$F = \frac{w(\text{initial}) - w(\text{final})}{w(\text{initial})} \times 100$$

% friability of tablets less than 1% is considered acceptable.



14.3. Weight Variation Test: - Weight variation was calculated by picking the tablet from each formulation randomly. The following percentage derivation in weight variation is allowed.

Average wt of tablet	% Derivation
130 mg or less	10
More than 130 and less then 324 mg	7.5
324 mg or more	5

14.4. Content Uniformity: Total five tablets were accurately weight and is powdered. The powder equivalent to 20mg of lafutidine was weighed and extracted in water and the concentration of drug was determined by measuring absorbance at λ_{max} 222nm by spectrophotometer.

14.5. Disintegration: The process of breakdown of a tablet into smaller particles is called as disintegration. The disintegration time of the tablet was determined using disintegration apparatus as per IP specification.

14.6. In-Vitro Dissolution Studies: - It was carried out using USP-II dissolution apparatus.

15. Conclusion:

In this experiment fast dissolving tablet of lafutidine was formulated by direct compression method and using fenugreek mucilage as super disintegrates.

The prepared formulation was then evaluated for several parameters: weight variation, hardness, thickness, disintegration time and dissolution time etc.

And from the study, it was concluded that natural super disintegrates (fenugreek) seed mucilage.

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