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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF FEXOFENADINE HYDROCHLORIDE: A REVIEW

Sarang V. Dalvi*[1] and Dr. Vikrant P. Wankhade[2]

[1]Department of Pharmaceutics, Vidyabharti College of Pharmacy, Amravati, MH, India.
[2] Associate Professor, Vidyabharti College of Pharmacy, Amravati, MH, India.

***Corresponding Author: Sarang V. Dalvi**
Department of Pharmaceutics, Vidyabharti College of Pharmacy, Amravati, MH, India.

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ABSTRACT
Recent developments in fast disintegrating tablets have brought convenience in dosing to pediatric and elderly patients who have trouble in swallowing tablets. The objective of the present study was to prepare the fast-disintegrating tablet of Fexofenadine Hydrochloride for allergic and respiratory disorders. As precision of dosing and patient's compliance become important prerequisite for a long-term treatment, there is a need to develop a formulation for this drug which overcomes problems such as difficulty in swallowing, inconvenience in administration while travelling, and patient's acceptability. Hence, the present investigation was undertaken with a view to develop a fast-disintegrating tablet of Antihistamine Drug which offers a new range of products having desired characteristics and intended benefits. Super disintegrants such as Sodium Starch Glycolate were optimized. Different binders were optimized along with optimized super disintegrant concentration. The tablets were prepared by direct compression technique. The tablets were evaluated for hardness, friability, weight variation, wetting time, disintegration time and uniformity of content. Optimized formulation was evaluated by in vitro dissolution test, drug excipient compatibility and accelerated stability study. It was concluded that fast disintegrating tablets of Antihistamine Drug were formulated successfully with desired characteristics which disintegrated rapidly, provide rapid onset of action, and enhance the patient convenience and compliance.

KEYWORDS: Fast dissolving tablets, Fexofenadine Hydrochloride, Antihistamine Drug, Super disintegrants, Cross Povidone.

INTRODUCTION
In spite of the increased focus and interest generated in the area of controlled release and targeted drug delivery system in recent years, tablet dosage forms that are intended to be swallowed whole, disintegrate, and release their medicaments rapidly in the gastrointestinal tract still remain the formulation of choice from both a manufacturing as well as a patient acceptability point of view. Thus, a drug given in the form of a tablet must undergo dissolution before being absorbed and eventually transported into systemic circulation.

Disintegrants are important excipient of the tablet formulation, are always added to tablet to induce breakup of tablet when it comes in contact with aqueous fluid and this process of desegregation of constituent particles before the drug dissolution occurs, is known as disintegration process and excipients which induce this process are known as Disintegrants.[1,2]

The objectives behind addition of disintegrants are to increase surface area of the tablet fragments and to overcome cohesive forces that keep particles together in a tablet. The demand for faster disintegrating formulation is increased as per time. So, pharmaceutical manufacturers need to formulate fast disintegrating dosage forms by employing disintegrants which are effective at low concentrations and have greater disintegrating efficiency.[3]

Disintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction which causes the tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.[4] Despite several theories proposed, still there is a lack of understanding the complete mechanism of disintegration. Proposed mechanisms for the action of disintegrants include water uptake through wicking, swelling, deformation (shape) recovery, particle repulsion, and heat of wetting, though the latter two are not well supported by researchers.[5]

The swelling of disintegrant particles is the most widely accepted mechanism for tablet disintegration. Primarily, this is because almost all disintegrants swell to some extent. Also, the concentration of the disintegrants and the effect of other ingredients like diluents used in the formulation of the tablets in promoting disintegration are very important in case of immediate release tablets.[6]

Most immediate release tablets are intended to disintegrate in the stomach, where the pH is acidic. The purpose of this study is to accelerate the release and action of the drug, Fexofenadine HCL.

Fexofenadine is a second-generation antihistamine approved for the treatment of allergic rhinitis (AR) and chronic urticaria (CU). Fexofenadine, with its efficacy and safety profile epitomizes the evolution of research on antihistamines Fexofenadine works by blocking histamine receptors.

Histamine and Allergy

Several mediators are involved in the pathophysiology; however, histamine plays a vital role in the allergic immediate reaction.[7] Once an allergen is introduced to Ig E-sensitized mast cells, a degranulation is triggered which causes histamine to be released. The effects of histamines are mediated through several receptors including H1, H2, H3, and H4 receptors that belong to the superfamily of G-protein-coupled receptors.[8] The biological effects of histamine in the allergic reaction are mediated through H1 receptors that coexist in active and inactive forms of g-protein-coupled receptors which balance each other. Histamine works as an agonist that pushes the balance to the active side leading to effects such as muscular contraction, bronchospasms, upregulation of endothelial permeability, and stimulation of sensory nerves and cough receptors.[9] H1 antihistamines work as inverse agonists that drive the balance toward the inactive side and suppress the effects of histamine. Since these effects are not genuine antagonistic but rather represent a balance displacement between active and inactive forms of H1 receptors, now, the term H1 antihistamine rather than the former "antihistamine antagonist" is used.[10]

Duration of treatment

For allergic rhinitis the treatment should be limited to the period of exposure to allergens. For seasonal allergic rhinitis treatment could be discontinued after the symptoms have resolved and reinitiated upon their reappearance. In perennial allergic rhinitis continued treatment may be proposed to the patients during the allergen exposure periods. For urticaria the duration of treatment depends on the type, duration and course of the complaints.

Method of administration

Oral use. The tablet is to be placed in mouth and it will dissolve within sec. It is recommended to take the daily dose in one single intake or twice.

LITERATURE REVIEW

- **Panigrahi et al (2012)** have formulated fast dissolving tablet of gliclazide for rapid action by direct compression method and evaluated for post compression parameter like hardness, disintegration time, weight variation, friability, wetting time, water absorption ratio and mouth feel. The mouth feel was done by taking human volunteers in a panel scale method. Different formulation was prepared using the superdisintegrants in three individual concentrations i.e. (3%, 5%, and 10%). The result obtained showed that at 10% concentration superdisintegrants showed less disintegration time and good hardness. It was concluded that formulation containing crosspovidone at10% was selected to be the bestformulation.[14]

- **Mehul Dekivadia et al (2012)** have formulated fast Dissolving tablet of levocetirizine HCL using sodium starch glycolate, Croscarmellose sodium and Crosspovidone as superdisintegrants by direct compression method. The tablets prepared were evaluated for various parameters like weight variations, hardness, friability, in vitro dispersion time, drug content, wetting time, in vitro drug release, FTIR and XRD. The tablets prepared by direct compression method possess a weight variation below ±7.5%, hardness of 3 to 4.0 Kg/cm², percentage friability of 0.51 to 0.85, in vitro dispersion time of 17 to 58 seconds, wetting time of 13 to 48 seconds, and in vitro drug release showed 94% to 99.00% within 20 min. The formulation (MD6) contains Crosspovidone and Sodium Starch Glycolate shows better Disintegration time and 99% drug release within 20 min.[15]

- **Rajnikant M. Suthar, et al (2013)** have formulated fast dissolving tablets (FDTs) with an objective to improve solubility and enhance dissolution of drug. Solid Dispersion of drug using superdisintegrants like croscarmellose sodium (CCS), crospovidone (CP), sodium starch glycolate (SSG), and low substituted hydroxy propyl cellulose (L-HPC) respectively as carriers was prepared by solvent evaporation method. Various batches of FDTs (F1-F10) were prepared using selected SD formulation of drug and carrier (1:3 ratio) and evaluated for various physical parameters and drug release study. The batch containing SD formulation in Cross Povidone (F3) showed fastest disintegration (3.22s), least wetting time (10.5s) and higher dissolution (97.98% drug release in 30 min).[16]

- **Deepak Sharma et al (2014)** have formulated fast dissolving tablets of Cetirizine Hydrochloride for allergic and respiratory disorders. Different binders were optimized along with optimized

superdisintegrant concentration. The tablets were prepared by direct compression technique. The tablets were evaluated for hardness, friability, weight variation, wetting time, disintegration time and uniformity of content. From study, it was concluded that, by employing commonly available pharmaceutical excipients, such as superdisintegrants, hydrophilic and swellable excipients and proper filler, a fast-disintegrating tablet of Cetirizine Hydrochloride can be developed which can be commercialized.[17]

OBJECTIVE

1. To enhance patient compliance and adherence to therapy.
2. To formulate fast dissolving tablet of Bilastine using disintegrants in different concentration by direct compression method.
3. To perform pre-formulation study.
4. Screening of the various natural and synthetic disintegrants.
5. To carry out in-vitro evaluation of the optimized formulation.

Preformulation characteristics of Drug

Preformulation testing is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It is the first step in the rational development of dosage forms.

- **Objective**

The overall objective of preformulation testing is to generate information useful to the formulation in developing stable and bioavailable dosage forms.

- **Physical Properties**

For a drug substance to formulate into a dosage form, it is necessary to study the physicochemical properties of the bulk drug.

- **Determination of Bulk density and Tapped density**

Bulk density is the ratio of the weight of a powder to the volume it occupies. It is expressed as gm/ml. Volume occupied by powder includes volume of the solid portion of the particle and voids between the particles. Bulk density is important in determining the size of the containers needed for handling and processing.

- **Flow Properties**

Irregular flow of powders from the hopper produces tablets with non-uniform weights. As respects content uniformity and dose precision cannot be achieved in a production of tablets & capsules. Flow properties depend on particle size shape porosity and density of bulk powder. The flow characteristics are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by angle of repose. Angle of repose is defined as the maximum angle possible between the height of a pile of the powder and the horizontal plane.

$$\tan Q = \frac{H}{R}$$

Where, H = Height of pile.
R = Radius of the base of pile.
Q = Angle of repose.

Lower the angle of repose better the flow property through and irregular surface of the particles give higher angle of repose. It can be decreased by addition of lubricants, of low concentration decreases the angle of repose at high concentration; enhances angle of repose.

Relationship belongings angle of repose (a) & powder flow

Sr. No.	Angle of Repose	Flowability
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	40 & Above	Very Poor

- **Compressibility Index**

Compressibility is indirectly related to the relative flow rate, cohesiveness and particle size of a powder. The compressibility of a material can be estimated from the tap and bulk density measurements.
Compressibility index were calculated using the formula:

$$\text{Compressibility index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100$$

Sr. No.	% Compressibility Index	Flowability
1	5 – 12	Excellent
2	13 – 17	Good
3	18 – 22	Fair
4	23 – 32	Poor
5	33 – 38	Very Poor

- **Hausner ratio**

It indicates the flow property of the powder and Measured by the ratio of tapped density to bulk density.

Hausner ratio	Properties
0 – 1.2	Free Flowing
1.2 – 1.6	Cohesive Powder

Formulation Process

Material Required

Sr.No.	Ingredients	Category
1	Fexofenadine HCL	API
2	Microcrystalline Cellulose	Diluent/ Binder
3	Croscarmellose Sodium	Disintegrants
4	Sodium Starch Glycolate	
5	Cross Povidone	
6	Mannitol	Sweetener
7	Talc	Glidant
8	Magnesium Stearate	Lubricant

Instrument Required

Sr. No.	Equipment
1	Electronic balance
2	Double cone blender
3	Friability test apparatus
4	Tablet hardness tester
5	Rotary Tablet punching machine
6	Disintegration test apparatus
7	Tablet dissolution apparatus

Direct compression

Weigh accurately Drug, Microcrystalline Cellulose, Mannitol DC grade and Disintegrants, pass through 40 mesh and mix and collect in poly bags. Blend the above ingredients in a double cone blender for 15 minutes. Accurately weigh Talc and magnesium stearate are passed through 60 mesh and add to the above blend and compress the tablets with 8mm punches.

EVALUATION

Physical parameters

A. Weight Variation test

Twenty tablets are collected and individually weighed. The average weight and standard deviation of 20 tablets is calculated. The weight variation limits are given in below table.

Average weight of Tablet	Percent Deviation
Less than 80 mg	10
80 mg to 250 mg	7.5
More than 250 mg	5

B. Thickness

Twenty tablets are collected, and each tablet thickness is measured by using Vernier calliper. The allowable limit is ± 0.3%.

C. Hardness

The resistance of the table t to chipping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness. If the table t is too hard, it may not disintegrate in the required period of time and if it is too soft, it will not withstand the handling during coating, packaging and shipping operations. Hardness was measured using hardness tester. For each batch three tablets were tested, and mean was calculated.

Disintegration Study

The hardness of the dry granulated and compressed tablets is adjusted depending on the settings of the device used for compression. The disintegration time of tablets is determined according to the US Pharmacopeia (USP) test for uncoated tablets in 37°C deionized water.

Dissolution Study

The dissolution test is carried out according to the following dissolution test methods and conditions.

Dissolution conditions and methods:

The test is carried out using tablets at a paddle speed of 50 revolutions per minute (RPM) according to method 2 (Paddle) of dissolution test of the USP, using 900 mL of acetate buffer at pH 4.5. The temperature of the medium is maintained at 37°C ± 0.5°C using a water bath. Sample solutions is obtained at 5, 10, 15, 20, 30, 45 and 60 minutes after starting the test.

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