World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

FORMULATION DEVELOPMENT AND INVITRO EVALUATION OF FEXOFENADINE MOUTH DISSOLVING TABLETS

Rayapati Raju, V. Jhansi Priya Marabathuni* and Naidu Narapusetty

Department of Pharmaceutics, Bellamkonda Institute of Technology & Science, Podili. A.P-523240.

***Corresponding Author: V. Jhansi Priya Marabathuni**
Department of Pharmaceutics, Bellamkonda Institute of Technology & Science, Podili. A.P-523240.

Article Received on 17/01/2023 **Article Revised on 07/02/2023** **Article Accepted on 27/02/2023**

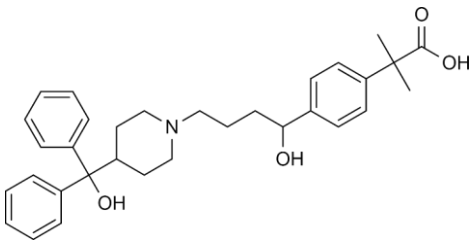
ABSTRACT

In the present study, attempt was made to formulate instant palatable mouth dissolving tablets of Fexofenadine. Formulation F9 revealed promising results which was formulated by Crosspovidone in 5:4 ratio. This formulation exhibited highest water absorption and hydration capacity, showed least disintegrate time and highest percent drug release which provides quick onset of action and immediate relief in suddenly arising allergic reactions. Moreover, they showed pleasant mouth feel. This formulation satisfied all the tablet evaluation parameters for Mouth Dissolving Drug Delivery System. Hence, it was concluded that the F9 Formulation is optimized formulation amongst F1 to F9. Optimized Formulation F9 was tested for Accelerated stability as per ICH guidelines was found to be a stable at 40oC ± 2oC temperature and 75% ± 5% relative humidity for three months. Undoubtedly Fexofenadine MDT will surely give the rapid onset of action, quick relief, low side effects, pleasant mouth feel, good stability, improved patient compliance, and its popularity in the near future.

KEYWORDS: mouth dissolving tablets**,** stability, dissolution rate.

INTRODUCTION

Mouth dissolving tablet disintegrate or dissolve in saliva and are swallowed without the need for water. They offer an advantage over swallowing tablets and capsules. Difficulty to swallow is particularly experienced by pediatric and geriatric patients. Technique that are frequently employed in the preparation of mouth dissolving tablets include, freeze drying, sublimation, spray drying, moulding, mass extrusion and direct compression.[1] Fexofenadine is a H1-receptor antagonist that is widely used in the treatment of motion sickness, vomiting and vertigo. It is chemically called as 2-[4-[1-hydroxy-4-[4- [hydroxy(diphenyl) methyl] piperidin-1-yl]butyl]phenyl]-2-methylpropanoic acid. It is water insoluble and tasteless.[2] Hence it was select as a model drug for the preparation of mouth dissolving tablets. In the present work effervescent, superdisintegrant addition and sublimation technique were tried for formulation of tablets. Superdisintegrant addition method was found as best and further study carried out using three superdisintegrants in different ratios.



EXPERIMENTAL WORK

Materials: Fexofenadine **was** gift sample from M/S. MATRIX Laboratories Ltd, Hyderabad, Sodium starch glycollate, Crospovidone, Croscarmellose sodium, (Ac-di-sol), Aerosil Magnesium stearate, Mannitol, Microcrystalline cellulose, Aspartame, Strawberry (flavor) were purchased form orchid chemicals ltd, All the instruments and equipment used in this work calibrated.

METHODOLOGY

Preformulation study

Identification of drug

By FTIR spectroscopy

The infrared spectrum of Fexofenadine and polymers were recorded by using FT-IR (Schimadzu 8400 SCCE). A small quantity of sample was mixed with equal quantity of potassium bromide and placed in sample cell to record its IR spectra.

By Melting point
Melting point is the one of important parameter for identification of pure drug and it is tested by using melting point apparatus.

Physiochemical parameter
Organoleptic properties
The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Included in are tablet's sizes, shape, color, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking which was observed visually.

Solubility profile
Solubility is a useful parameter mainly for poorly soluble drugs. Bioavailability problems are often present, when the solubility of a drug is less than 10 mg/ml over the pH range 1-8. The solubility of drug was recorded by using various descriptive terminology specified in Indian pharmacopoeia, 2007. In this maximum amount of solvent required to dissolve the solute was determined.

Determination of absorption maximum in Solvents
10 mg of Fexofenadine was weighed and transfer in to 3 individual 100 ml standard flask and made up to the mark with methanol, 0.1N HCL and Phosphate Buffer pH 6.4 separately. From the above solution took each 1 ml from each solution and make up with 10 ml standard flask to get the concentration of 10 µg/ ml of each solution. Each blank was kept separately and scan in the region 200 - 400 nm and determine the absorption maxima of drug in three solvents. 247.5 nm for 0.1N HCl, 275.0 nm for Methanol, 274.0 nm for Phosphate buffer 6.8.

Preparation of standard calibration curve of fexofenadine in solvents
A stock solution of Fexofenadine from the above solution and to get the concentration of 5 to 30 µg/ ml in three solvents and its obey the beer's law.

Determination of percentage purity of drug
Accurately weighed 100 mg of fexofenadine was dissolved in little quantity of 0.1 N HCl and volume was adjusted to 100 ml with the same to prepare standard solution having concentration of 1000 µg/ ml. From the above solution, aliquots of 3 ml were transferred to 10 ml volumetric flasks and final volume was made to 10 ml with 0.1N HCl. Absorbance values of these solutions were measured against blank (0.1N HCl) at 275 nm using Shimadzu-1700 Pharmaspec UV-Visible spectrophotometer. The percentage purity of drug was calculated by using calibration graph method (least square method).

Determination of drug-polymer compatibility
By Fourier Transforms Infra-Red (FTIR) Spectroscopy
By Differential Scanning Calorimetry Study (DSC Method
Accurate quantity of drug and all ingredients were weighed according to formula shown in Table 7.1 and powder except aerosil and magnesium sterate was blended homogeneously in mortor and pestel for 15 minutes. Prepared powder blend was passed through sieve No.#60. Finally aerosil and magnesium sterate passed through sieve No. #30 was added and further mixed for10 minutes. The powder blend was evaluated for angle of repose, bulk density, Tapped density, Compressibility Index and Hausner ratio.

Angle of Repose
Angle of repose was determined using cylinder method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (q) was calculated using the formula
$\Theta = \tan^{-1}(r/h)$

Method
Weighted quantity of Fexofenadine was passed through funnel kept at height at 9 cm from base. The powder forms heap and touches the tip of the funnel. The radius was measured and angle of repose was calculated.

Bulk density
Apparent bulk density (ρb) was determined by pouring blend into a graduated cylinder. The bulk volume (Vb) and weight of the powder (M) was determined.The bulk density was calculated using the formula.
ρ b =M/Vb (or)
BD = Weight of the powder/Volume of the powder.

Tapped density
It was determined by placing a graduated cylinder, containing a known mass of drug excipients blend, which was tapped for a fixed time until the powder bed volume has reached a minimum. The minimum volume (Vt) occupied in the cylinder and the weight (m) of the blend was measured. The tapped density (ρt) was calculated using the following formula.
ρt = m /Vt (or)
TBD = Weight of the powder/Tapped volume of the powder

Compressibility Index
The simplest way for measurement of free flow of powder is compressibility, a indication of the case with which a material can be induced to how is given by compressibility index (I) which is calculated as follows
Carr's compressibility index (%) = [(TBD-BD)/ TBD x100

Hausner's ratio
Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula;
Hausner's ratio= ρt/ρb

Where, ρt is tapped density and ρb is bulk density
A hausner's ratio less than 1.25 indicates good flow while greater than 1.5 indicates poor flow.

Formulation of Mouth Dissolving Tablet of Fexofenadine
Table 1: Formulated Composition of different Batches of Mouth Dissolving Fexofenadine Tablets.

S. No.	Ingredients (mg/tab)	Formulation code								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Fexofenadine	10	10	10	10	10	10	10	10	10
2	Croscarmellose sodium (Ac-di-sol)	4	6	8	-	-	-	-	-	-
3	Sodium starch glycollate(Explotab)	-	-	-	4	6	8	-	-	-
4	Crospovidone (Polyplasdone)	-	-	-	-	-	-	4	6	8
5	Microcrystalline cellulose	74	72	70	74	72	70	74	72	70
6	Mannitol	100	100	100	100	100	100	100	100	100
7	Aerosil	4	4	4	4	4	4	4	4	4
8	Aspartame	6	6	6	6	6	6	6	6	6
9	Magnesium stearate	2	2	2	2	2	2	2	2	2
10	Strawberry flavour	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
11	Total	200	200	200	200	200	200	200	200	200

Preparation of mouth dissolving fexofenadine tablets Method
The mouth dissolving tablets were prepared by direct compression method with the use of three different superdisintegrants namely Croscarmellose sodium, Sodium starch glycolate, Crospovidone in the ratio of 5:2, 5:3 and 5:4. Microcrystalline cellulose, Mannitol was used as a diluents as and mixture of Aerosil and Magnesium sterate (2:1) was used as a glidant and lubricant respectively. The composition of mouth dissolving formulation was shown in Table1.

Accurate quantity of drug and all ingredients were weighed according to formula shown in Table 7.3 and powder except Aerosil and Magnesium sterate was blended homogeneously in mortor and pestle for 15 minutes. Prepared powder blend was passed through sieve no. #60. Finally Aerosil and Magnesium sterate passed from sieve no. #30 added and was further mixed for10 minutes.

Accurately weighed 200 mg homogeneously mixed powder blend was fed manually and compressed with constant compression force and hardness on 16 stations Cadmach tablet compression machine with 9 mm, breakthrough, and flat faced punches. Total nine formulations were prepared.

Evaluation of Fexofenadine MDTs
Appearance
The tablets were visually observed for capping, chipping and lamination.

Weight Variation Method
Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviate from the average weight.

Thickness uniformity Method
Three tablets were selected randomly from each batch and thickness was measured by using Vernier Caliper.

Hardness
Hardness or tablet crushing strength (Fo) the force required to break a tablet in a diametric compression was measured using Monsanto Hardness Tester.For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm2. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted in kg/cm2.

Friability
Friability of the tablets was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and roping the tablets ata height of 6 inches in each revolution. Preweighed sample of tablets was placed in the Friabilator and were subjected to 100 revolutions. Tablets were dedusted using a soft muslin cloth and reweighed, the friability.

(F) is given by the formula.
% F = (Initial wt. - Final wt. / Initial wt.) x 100.
7.3.6.Content uniformity
The Fexofenadine content in the tablets was estimated as follows.

Method
20 tablets were finely powdered and weight equivalent to 10 mg of Fexofenadine was dissolved in 100 ml of

methanol and assayed for drug content using UV-Visible spectrophotometer at 275.00 nm.

Disintegration time Method

The Disintegration time of the tablets was determined as per Indian Pharmacopoeia monograph. The test was carried out using USP disintegrate test apparatus, (Veego scientific VTD-DV). It consists of an apparatus in which 6 tablets was introduced into each of six cylindrical tubes, the lower end of which was covered by a 0.025 in wire mesh. The tubes were then raised and lowered through a distance of 5.3 to 5.7 cm in a test fluid phosphate buffer pH 6.8 and 0.1N HCl pH 1.2 as a disintegrating media maintained at 370 ± 20 C. and the time in second taken for complete disintegrate of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

Wetting time of water absorption Ratio

The wetting time characteristic of the loose disintegrant powder allows an evaluation of both the intrinsic swelling and the wettability of the superdisintegrants. Wetting time of the ODT is important parameter, which needs to be assessed to give an in sight into the disintegrate properties of the tablets; a lower wetting time implies a quicker disintegrate of the tablet. Wetting time was performed at room temperature.

A piece of tissue paper of 10cm folded twice was placed in small petri dish of diameter 10cm containing 6 ml of water. A tablet was put on the paper and the timerequired for water to reach upper surface of tablet was noted.

For water absorption ratio the same wetted tablet was taken out from petri dish and weighed.Water absorption ratio (R) was determined by using following equation.

$R=100\times Wa- Wb/Wb$

Where,

Wb =Weight of tablet before water absorption Wa = Weight of tablet after water absorption.

In-vitro Dissolution studies Method

Dissolution profiles of Fexofenadine tablets were determined using the USP Type II Dissolution test apparatus (Veego scientific VDA-8DR) set with a paddle speed of 100 rpm. Dissolution was performed in 900 ml of 0.1N HCl maintained at 370± 0.50C. Aliquot of dissolution medium, 5 ml was with drawn at 3, 6, 9, up to 12 min with 5minutes interval, and filtered through Whatmann filter paper. The amount of drug dissolved was determined by UV-Visible spectrophotometer (Shimadzu-1700 Pharmaspec UV-VIS Spectrophotometer) by measuring the absorbance of the sample at 247.5 nm. An equal volume of fresh medium, prewarmed at 37oC was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Three trials for each batch were performed and average percentage drug release was calculated by using PCP disso V3 software.

Stability studies of the tablets

Stability of a formulation can be defined as the time from date on manufacture of the formulation until its chemical or biological activity is not less than a predetermined level of labeled potency and its physical characteristics have not changed appreciably or deleteriously. Formulation and the development of a pharmaceutical product are not complete without proper stability analysis, carried out on it to assess the physical and chemical stability and the safety. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time. Under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf lives.

Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid the undesirable delay, the principles of accelerated stability studies are adopted.

The International Conference on Harmonization (ICH) Guidelines titled “Stability testing of new drug substance and products” (QIA) describes the stability test requirements for drug registration application in the European Union, Japan and United States of America.

ICH specifies the length of study and storage conditions.
Long-term testing 25o C ± 2o C/60 % RH ± 5% for 12 months. Short term testing 30o C ± 2o C/65 % RH ± 5% for 1 month.
Accelerated testing 40o C ± 2o C/75 % RH ± 5% for 6 months.
Stability studies for the present work carried out at 40o C ± 2o C/75% ± 5% RH for the selected formulation for 3 months.

Method

The selected formulations were packed in tightly closed container which were tightly plugged with cotton and capped. They were then stored at 40o C ± 2o C /75 % RH ± 5% for 3 months and evaluated for their physical appearance, hardness, disintegrate time, dissolution testing and drug content at specified intervals of time. The drug solutions were further scanned to observe any possible spectral changes.

RESULTS AND DISCUSSION

In the present study, an attempt was made to formulate nine formulations of the mouth dissolving tablets of Fexofenadine were prepared with different level addition of superdisintegrants; sodium starch glycollate, crosspovidone and Croscarmellose sodium, For each designed formulations, powder mixed blend of drug and excipients was prepared and evaluated for various parameters as follows.

Preformulation parameters
Identification of drug By FTIR spectroscopy

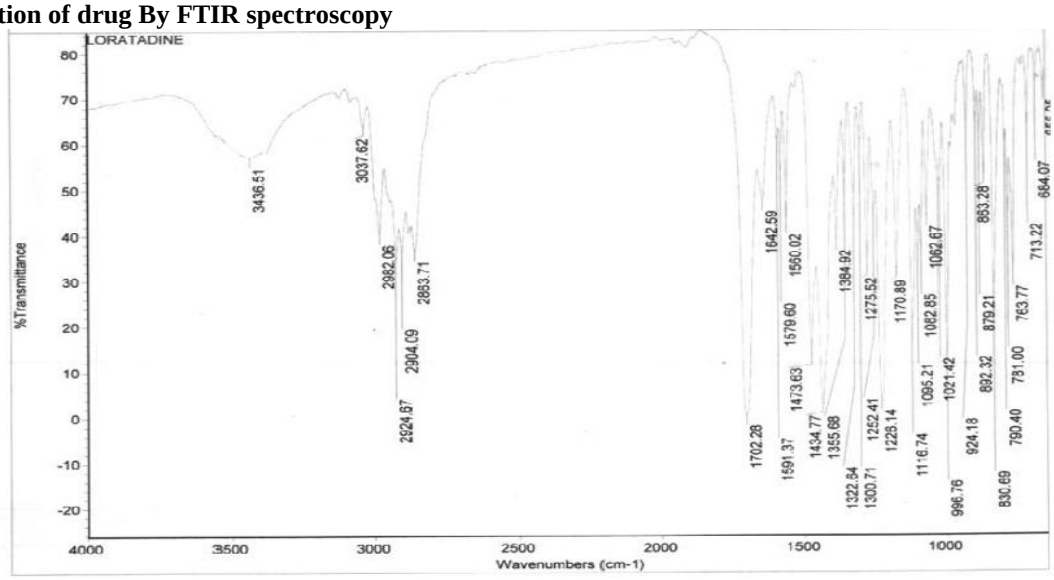


Figure 8.1: FTIR spectra for Fexofenadine.

Physicochemical parameters of drug
1. Organoleptic properties
Colour: White **Nature:** Fine powder **Odour:** Odourless

Solubility study of the drug
Table 2: The solubility of Fexofenadine in different solvents.

S. No.	Solvent	Parts of solvent required per part of solute	Inference
1	Distilled water	1000	Practicallly Insoluble
2	Acetone	2	Freely Soluble
3	Methanol	2	Freely Soluble
4	Chloroform	2	Freely Soluble
5	Toluene	2	Freely Soluble
6	0.1 N HCl	2	Freely Soluble

8.1.4 Loss on drying

The percentage loss on drying after 4 hours was found to be 0.4%. The sample passes test for loss on drying as per the limits specified in I.P.(N.M.T. 0.5%).

Table 3: Percentage loss on drying for Fexofenadine.

S. No.	Percentage LOD	Avg. percentage LOD
1	0.3	0.3±0.1
2	0.2	
3	0.4	

8.1.5 Analytical Methods

Determination of λmax. and Preparation of Calibration Curve of Fexofenadine by using 0.1 N HCl.

UV absorption spectrum of Fexofenadine in 0.1 N HCl shows λmax at 247.5 nm. Absorbance obtained for various concentrations of Fexofenadine in 0.1 N HCl are given in table 8.4.The graph of absorbance vs. concentration for Fexofenadine was found to be linear in the concentration range of 10µg /ml. The drug obeys Beer- Lambert's law in the range of 10µg/ml.

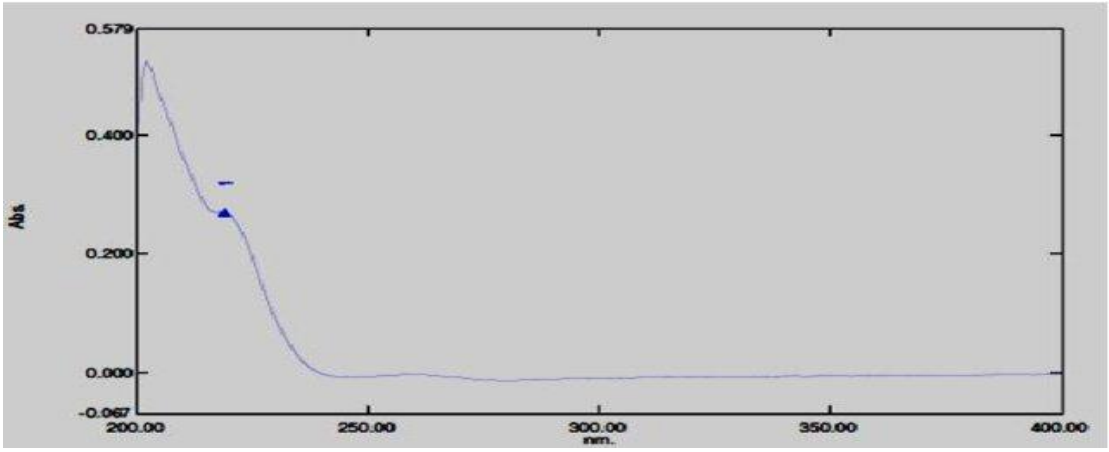


Figure 2: UV Spectra of Fexofenadine in 0.1 N HCl.

Table 4: Data of Concentration and Absorbance.

S. No.	Concentration (µg/ml)	Absorbance at 247.5 nm
1	5	0.186
2	10	0.339
3	15	0.527
4	20	0.663
5	25	0.879
6	30	1.050

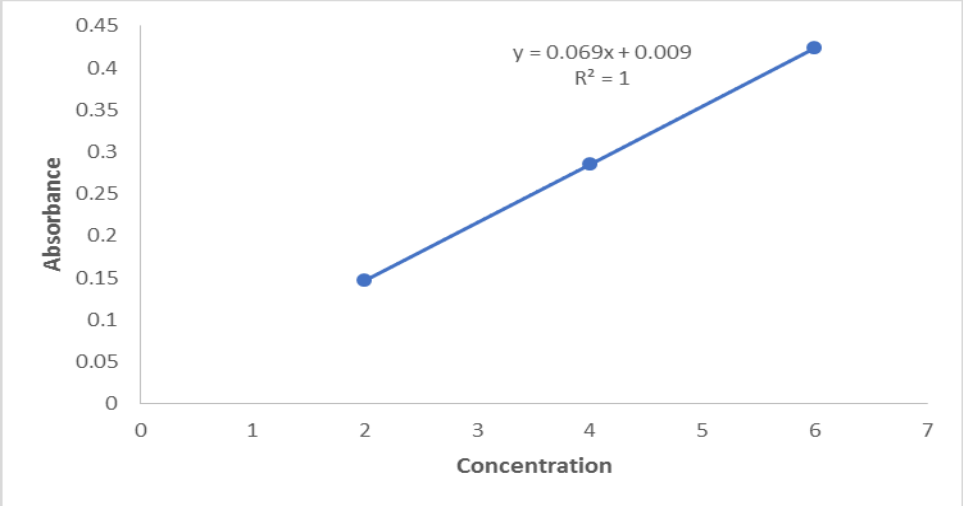


Figure 3: Calibration curve for Fexofenadine in 0.1 N HCl.

Percentage purity of pure drug

The percentage purity of drug was calculated by using calibration graph method (least square method).

Table 5: Percentage purity of pure drug.

S. No.	Percentage purity (%)	Avg. percentage purity (%)
1	100.98	100.10 ± 0.64
2	99.64	
3	99.58	

All values are expressed as mean± SE, n=3.

The reported percentage purity for Fexofenadine is 99 to 101% (I.P. 2007).

Fourier Transform Infra-Red Spectroscopy (FT-IR) differential scanning calorimetry According to, DSC thermogram showed that there was no major difference

in onset temperature, end set temperature and peak temperature when compared with pure drug thermogram. Therefore it could indicate that there was no incompatibility between drug and different polymers.

Table 6: DSC thermogram parameters of Fexofenadine with various polymers.

S. No.	DSC thermogram	Onset temperature (°C)	Peak temperature (°C)	End set temperature(°C)
1	Fexofenadine	134.13	139.56	148.00
2	Fexofenadine + CCS	134.17	140.32	154.55
3	Fexofenadine+ SSG	135.66	141.26	149.67
4	Fexofenadine + CP	135.75	140.55	149.16

Evaluation Of Powder Blends Of Fexofenadine

Table 7: Evaluation of Powder Blends of Fexofenadine.

Formulation Code	Bulk density(g/ml)	Tapped density(g/ml)	Angle of repose(Ɵ)	Carr's index(%)	Hausner's ratio
F1	0.45±0.0125	0.50±0.0231	31.78±1.8815	11.19±0.00	0.8880±0.00
F2	0.43±0.0165	0.49±0.0099	30.67±0.9514	11.45±0.00	0.8854±0.00
F3	0.45±0.0042	0.50±0.0063	34.53±1.7870	9.56±0.00	0.9043±0.00
F4	0.41±0.0105	0.47±0.0124	28.42±1.2725	12.26±0.00	0.8773±0.00
F5	0.45±0.0090	0.52±0.0213	33.78±1.4577	13.79±0.00	0.8620±0.00
F6	0.47±0.0120	0.54±0.0217	29.04±1.1461	12.69±0.00	0.8730±0.00
F7	0.46±0.0103	0.50±0.0107	33.65±0.5445	9.65±0.00	0.9034±0.00
F8	0.48±0.0134	0.56±0.0216	28.66±1.673	14.18±0.00	0.8581±0.00
F9	0.43±0.0171	0.48±0.0263	26.59±0.4705	10.31±0.00	0.8968±0.00

All values are expressed as mean± SE, n=3.

Angle of Repose

The Angle of repose of various powder mixed blends, prepared with different superdisintegrants, was measured by funnel method.Angle of repose was found in the range**26.59 ± 0.4705 - 34.53^0 ± 1.7870.** The good flow ability of powder blend was also evidence with angle of repose.

Bulk density

The bulk density of various powder mixed blends prepared with different superdisintegrants was measured by graduated cylinder. The bulk density was found in the range **0.41 ± 0.0105 - 0.48 ± 0.0134 g/ml**

Tapped Density

The Tapped density of various powder mixed blends prepared with different superdisintegrants was measured by using measuring cylinder.The tapped density was found in the range **0.47 ± 0.0124 - 0.56 ± 0.0216 g/ml.**These values indicate good packing characteristics and the powder was not bulky.

Compressibility Index

The Compressibility index of various powder mixed blends, prepared with different superdisintegrants, using bulk density and tappeddensity data, compressibility index was calculated. It was found in the range **9.56 ± 0.00 - 14.18± 0.00 %.** This indicates good flow properties.

Hausner's ratio

The Hausner's ratio of various powder mixed blends, prepared with different superdisintegrants, it is calculated by using bulk density and tapped density data. It was found in the range of **0.8581 ± 0.00 – 0.9043 ± 0.00**, reveals good flow properties (<1.25).

Evaluation of Fexofenadine Tablets

Table 8: Evaluation of Fexofenadine tablets.

Formulation Code	Dimension		Hardness (kg/cm2)	Friability (%)	Drug content (%w/w)	Weight variation
F1	2.90±0.10	7.86±0.20	3.26± 0.05	0.8±0.05	98.50±0.11	204.6± 1.18
F2	2.9±0.17	7.73±0.32	3.36± 0.11	0.8±0.15	98.75±0.01	205.15 ± 1.59
F3	2.76±0.25	7.83±0.24	3.26± 0.15	0.9±0.1	98.25±0.15	206.15 ± 1.63
F4	2.80±0.10	7.96±0.20	3.36± 0.15	0.9±0.13	95.25±0.13	207.15 ± 1,53
F5	2.70±0.17	7.76±0.32	3.33± 0.25	0.8±0.07	98.50±0.06	207.10 ± 1.61
F6	3.0±0.10	7.80±0.45	3.4± 0.10	0.8±0.09	97.70±0.23	205.10 ± 1.48
F7	2.86±0.11	7.93±0.35	3.4± 0.10	0.8±0.06	97.75±0.14	206.40 ± 1.66
F8	2.96±0.05	7.76±0.30	3.4± 0.10	0.9±0.10	98.75±0.17	207.15 ± 1.53
F9	2.8±0.10	7.83±0.20	3.0± 0.10	0.9±0.11	98.75±0.01	201.55 ± 1.63

All values are expressed as mean± SE, n=3.

Dimension (Thickness and Diameter)
Tablets were evaluated by using Vernier caliper. Excessive variation in the tablet thickness and diameter can result in problems with packaging as well as consumer acceptance. There were no marked variations in the thickness and diameter of tablets within each formulation indicating uniform die fill throughout the compression process.

The size (diameter) of the tablets of all formulations was found to be 7.73 ± 0.3214 – 7.96 ± 0.2081 mm and thickness ofthe tablets was found in the range of 2.70 ± 0.17 mm – 3.0 ± 0.10 mm.

Weight variation
Tablets were prepared using direct compression technique. Since the material was free flowing, tablets were obtained of uniform weight due to uniform die fill. Tablets were obtained in the range with acceptable weight variations as per Pharmacopoeia specifications, less than 7.5.

Hardness
Tablets were evaluated by using Monsanto Hardness tester. Hardness of the tablets was in the range **3.0 ± 0.1 - 3.4 ± 0.1 kg/cm^2**. Uniform hardness was obtained due to equal compression force. The obtained hardness range showed good mechanical strength with an ability to withstand physical and mechanical stress conditions.

Friability
Tablets were evaluated by using Roche Friabilator and friability of tablets was observed in acceptable range. **0.8 ± 0.090 - 0.9 ± 0.117** (less than 1%) This indicated a good mechanical resistance of the prepared mouth dissolving tablets.

Drug content of Fexofenadine
Tablets were evaluated by using assay method. The drug content was obtained in the acceptable limit. The drug content was found in therange **95.25 ± 0.13 - 98.75 ± 0.01 %w/w.** (i.e. 99-101% w/w). The found range was within the specified limit as per Indian Pharmacopoeia 2007.

Disintegration time
Tablets were subjected for the in-vitro disintegrate time in the USP Disintegrate test apparatus.(Veego scientific VTD-DV) The in-vitro disintegrate time for all nine formulations varied from 12 ± 1.8973 to 30 ± 1.8973 seconds. The rapid disintegrate was seen in the formulations containing Crospovidone and Croscarmellose sodium. This is due to rapid intake of the water from the medium, swelling and burst effect. It also noticed that the concentration of Croscarmellose sodium followed by Crospovidone and Sodium starch glycollate increased, the time taken for the disintegrate was reduced.Figure 16. Reveals that the formulations with highest concentration of Croscarmellose sodium with Crospovidone shown significant rapid disintegrate. Disintegrate time was to be found very less for F9 formulation which contains highest concentration and efficiency of Crosspovidone.

Figure 4: Disintegration of tablet.

Table 9: Disintegration time in seconds.

Formulations	Disintegrate time (sec) (Mean ± S.D. n = 3)
F1	25±3.2863
F2	19±1.4142
F3	15±1.4142
F4	30±1.8973
F5	22±1.4142
F6	18±1.4142
F7	20±2.000
F8	15±1.4142
F9	12±1.8973

All values are expressed as mean± SE, n=3.

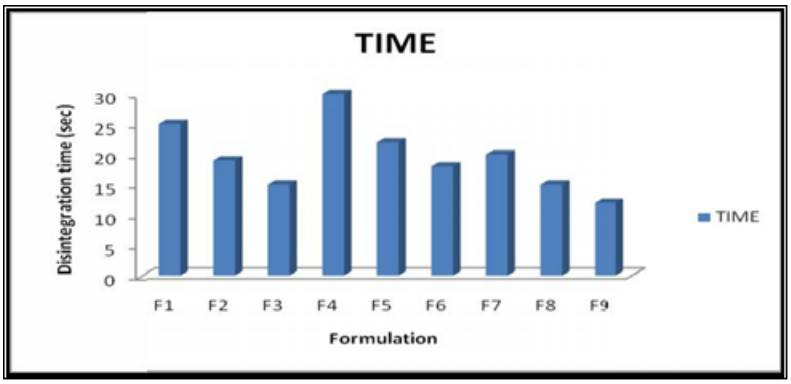


Figure 5: Disintegrate profile of mouth dissolving Fexofenadine tablets (F1 - F9).

Wetting time and water absorption ratio

The wetting time for all nine formulations was performed in duplicate. The values lie between 11 ± 1.4142 to 42 ± 1.8973 seconds. The wetting time was rapid in Crosscarmellose sodium followed by Crosspovidone and Sodium starch glycollate. Here also it was observed that as the concentration of disintegrant increased the time taken for wetting was reduced.

Water absorption ratio which is important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water was calculated. It was found in the range of 78.45 ± 5.92 to 125.80 ± 5.10 %. (table 8.16) Water absorption ratio (R) increases with the increased concentration of Croscarmellose sodium followed by crosspovidone and sodium starch glycollate. Hence Crospovidone had shown highest water absorption 125.80 % of F9 and in turn rapid bursting of the same formulations.

Table 10: Wetting time and Water absorption ratio.

Formulation	Wetting time(sec)	Water absorption ratio (%)
F1	25±3.2863	81.26±0.9832
F2	20±2.0000	90.28±3.982
F3	17±1.4142	117.40±1.88
F4	42±1.8973	78.45±5.92
F5	31±1.4142	84.44±2.96
F6	23±2.2803	96.66±1.41
F7	26±2.0000	84.24±6.02
F8	17±1.4142	96.66±5.40
F9	11±1.4142	125.80±5.10

*All values are expressed as mean± SE, n=3.

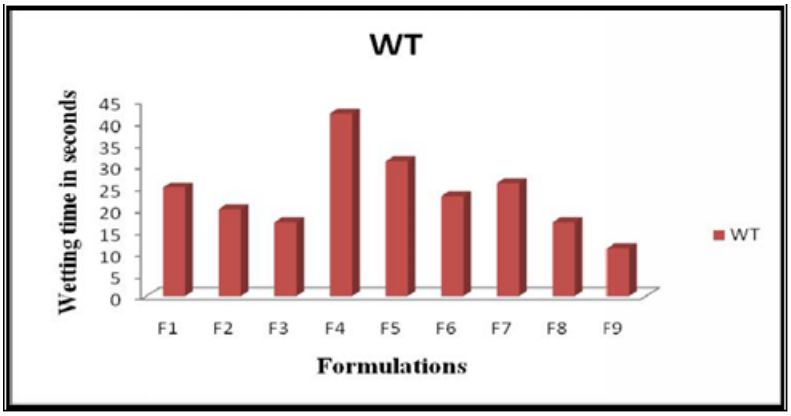


Figure 6: Wetting profile of mouth dissolving Fexofenadine tablets (F1 - F9).

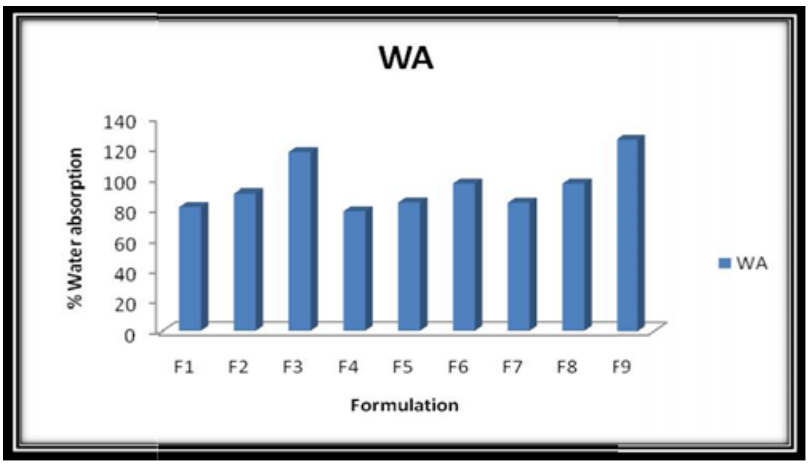


Figure 7: Water absorption ratio of mouth dissolving Fexofenadine tablets (F1 - F9).

***In –Vitro* Dissolution Studies**

Table 11: *In-vitro* dissolution data of formulation F9.

S. No.	Time (Minute)	Amount of drug released (mg)	%DE	MDT (Minute)	Cumulative % drug Release
1	0	0.00	0.00	0.00	0.00 ± 0.00
2	3	9.49	42.92	1.50	85.42 ± 1.6733
3	6	9.17	65.79	1.68	91.78 ± 0.9055
4	9	9.69	75.33	2.04	96.40 ± 1.5832
5	12	9.90	81.12	2.23	99.10 ± 0.9422

All the values are expressed as a mean ± SD., n = 3

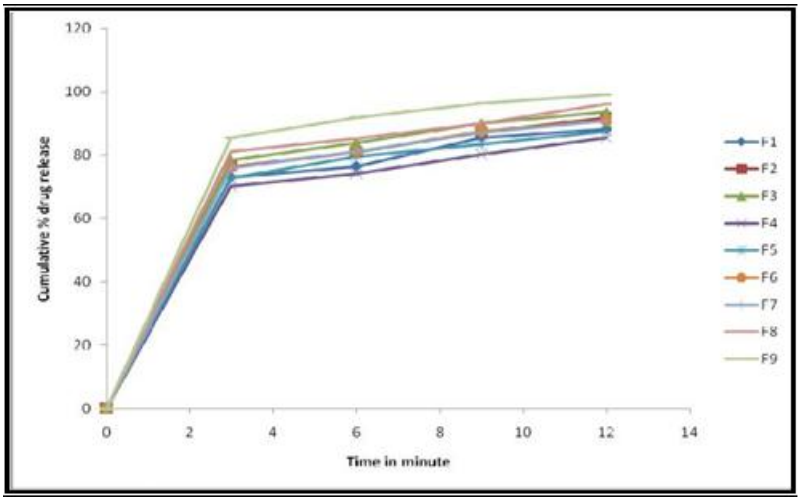


Figure 8: Cumulative % drug release profile of formulation F1 – F9.

Stability Studies

Ageing studies for optimized formulation F9 of mouth dissolving Fexofenadine tablet at accelerated condition of 40°C ± 2°C/75% RH ± 5% (Initial)

Comparative Stability *In–Vitro* Release Study of optimized F9 formulation

Table 12: Comparative In-vitro dissolution data of formulation F9.

Time in minute	Cumulative % Release of Fexofenadine (Mean ± S.D., n = 3)			
	Initial	First month	Second month	Third month
05	85.42 ± 1.673	85.10 ± 0.1	84.22 ± 0.230	83.99 ± 0.09
10	91.78 ± 0.905	90.68 ± 0.13	88.78 ± 0.1501	86.56 ± 0.103
15	96.40 ± 1.583	96.10 ± 0.1	94.56 ± 0.103	92.78 ± 0.04
30	99.10 ± 0.942	99.02 ± 0.011	98.52 ± 0.041	98.70 ± 0.264

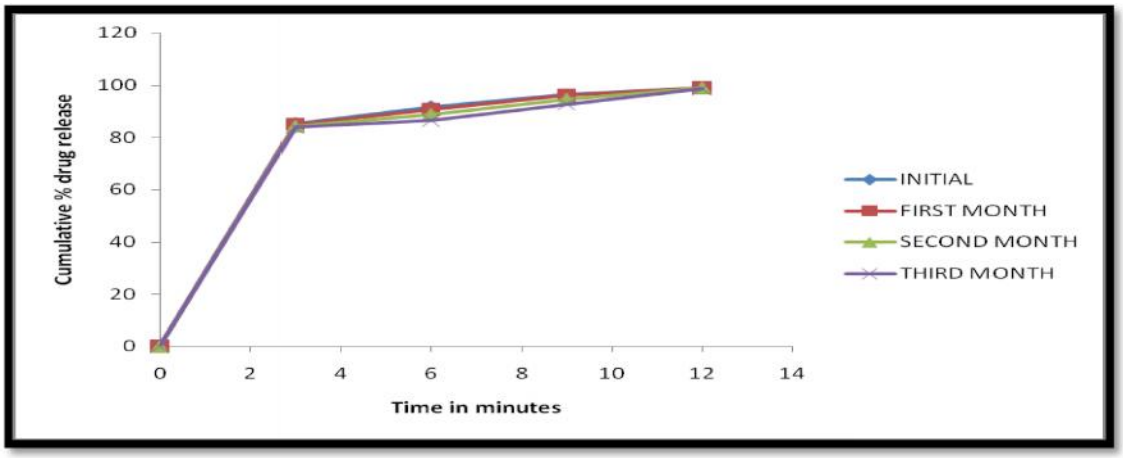


Figure 9: Comparative % Drug release of all three months with initial of optimized formulation F9.

Comparative Ageing studies for optimized formulation F9 with initial results

Table 13: Stability results (Initial to 3rd Month).

S. No.	Evaluation Parameter	Formulation- F9 observations			
		Initial	First month	Second month	Third month
1	Physical Appearance	White, round, Break - through, flat tablet.	No change	No change	No change
2	Hardness (kg/cm2)	3.0±0.1	2.93±0.12	2.93±0.23	2.90 ± 0.1
3	Disintegrate test(seconds)	12±1.897	11.80±1.673	11.65±1.522	11.55±1.79
4	Dissolution test (%)	99.1± 0.9422	99.02±0.01	98.52±0.041	98.70±0.264
5	Drug content (% w/w)	98.75±0.01	98.73±1.123	98.70±0.114	98.64±0.136

Stability studies of formulation F9 were carried out by placing the samples at temperature 40o C and different relative humidity conditions 75% RH. From the above observations it was found that there were no significant changes in disintegrate time, release characteristics and physicochemical properties of the tablets used in the release study. Based on the results it can be concluded that the formulated mouth dissolving tablets were stable at accelerated stability conditions (40oC ± 2oC and 75% ± 5% RH) over a period of 3 months. Even though its stability is assured for three months, further studies as per the ICH guidelines are to be needed to establish it shelf-life.

SUMMARY AND CONCLUSION

The present investigation was undertaken to fabricate and evaluate instant release mouth dissolving tablet of Fexofenadine with the main objective of quick onset of action followed by pleasant mouth feel and improved patient compliance.

Fexofenadine is act as an anti-histaminic and used as potential drug to get the quick relief in suddenly arising allergic reactions like urticaria, angeoedema, in treatment of perennial and seasonal allergic rhinitis, considering this parameter there is a need formulate the Fexofenadine as fast disintegrating mouth dissolving tablet. Present Mouth dissolving tablet by passes the hepatic metabolism unlikely of the other conventional oral dosage forms which are relatively less bioavailable. This MDT gives absorption of drug from oral cavity, pharynx and oesophagus; results in quick onset of action, improved bioavailability and patient compliance.

The present study is an attempt to select best possible combination of superdisintegrants to formulate MDDDS of Fexofenadine which disintegrates within seconds in

mouth, thereby reducing the time of onset of action, with maximum bioavailability of Fexofenadine.

Sodium starch glycollate, Crospovidone and Croscarmellose sodium were selected as super disintegrants. Microcrystalline cellulose is selected as diluents and it also act as a disintegrant in the lesser extent. Likewise the Mannitol used as diluents and it have the property to produce cooling sensation in the mouth. Aerosil added as a glident in all formulations in same concentrations. Magnesium sterate as a lubricant. Aspartame wasincorporated as sweetening and taste inhibiting agent. Whereas, strawberry used as flavoring agent, for to get the cool and pleasant mouth feel.

Drug-excipients interaction study was carried out using FT-IR i.e. by KBr pellet method (1:1). The FT-IR spectra revealed that there was no compatibility related problems between the drug and excipients used in the formulation.

Direct Compression method was used to formulate the tablets, because of its cost effectiveness, reduced number of manufacturing steps.

Pre-compression parameters; bulk density, tapped density,Compressibility index and Hausner's ratio for all formulations were found to be in good agreement of the prescribed limits. Showed good powder flow properties.

Post-compression parameters; hardness, friability, weight variation, drug content was evaluated and found to be acceptable with the prescribed limits.

Wetting time and swelling capacity of disintegrants are the important parameters for comparing efficiency of disintegrate process. The use ofhighest concentration of Crospovidone in F9 formulation showed highest hydration and swelling capacity of 11 seconds and 125.80 % respectively. Crospovidone has 5 to 10 folds more swelling capacity in just 10 seconds. Crospovidone showed faster disintegrate followed by Croscarmellose sodium and Sodium starch glycollate formulations.

Disintegrate time for all formulations was found in between 12 ± 1.67 to 30 ± 1.89 seconds. Disintegrate time was found to be very less for F9 formulation which contains highest concentration of Crospovidone.

Percent cumulative drug release for all nine formulations was found in the range of 88.94 ± 0.2214 to 99.10 ± 0.9422 %. Drug release was increased with the increased concentration of with crosspovidone. F9 formulation showed highest drug release i.e. 99.10% w/w in almost first 12 minutes.

CONCLUSION

In the present study, attempt was made to formulate instant palatable mouth dissolving tablets of Fexofenadine. From the studies carried out and above obtained results following conclusions are drawn;Formulation F9 revealed promising results which was formulated by Crosspovidone in 5:4 ratio. This formulation exhibited highest water absorption and hydration capacity, showed least disintegrate time and highest percent drug release which provides quick onset of action and immediate relief in suddenly arising allergic reactions. Moreover, they showed pleasant mouth feel. This formulation satisfied all the tablet evaluation parameters for Mouth Dissolving Drug Delivery System. Hence, it was concluded that the F9 Formulation is optimized formulationamongst F1 to F9. Optimized Formulation F9 was tested for Accelerated stability as per ICH guidelines was found to be a stable at 40oC ± 2oC temperature and 75% ± 5% relative humidity for three months.Undoubtedly Fexofenadine MDT will surely give the rapid onset of action, quick relief, low side effects, pleasant mouth feel, good stability, improved patient compliance, and its popularity in the near future.

BIBLIOGRAPHY

1. Amin P.D, Gupta S.S., Prabhu N.B., Wadhwani A.R., Fast disintegrating dosage form of Ofloxacin and Metronidazole benzoate, Indian Drugs, 2005; 42(9): 614 – 617.
2. Amit ananda., Kandarapu R., Garg S., An update on taste masking technologies for oral Pharmaceuticals, Indian Journal of Pharmaceutics science, 2002; 10 – 17.
3. Anil Kumar., Beenta., Prescription writing trends of anti-histamines at the University Health Centre, Indian Journal of Pharmaceutical sciences, 2009; 25 – 33.
4. Anne Waugh and Allison Grant., Ross and Wilson Anatomy and Physiology in Health and illness,10 th edn., Churchill livingstone, London, 2006; 301-304.
5. CIMS, CPM Medica India Pvt. Ltd.banglore, 2011; 470.
6. http//www.drugbank.ca/drugs/DB00186 accessed on 10 Dec., 2009.
7. http//www.pharmainfo.net/reviews/new-generation-tablet-fast dissolving-tablet, Accessed on, 2009.
8. http//www.pharmpedia.com/Fexofenadine/spectroscopy/word #ixzz0quf.
9. Indian Pharmacopoeia, Published by the Controller of Publication, Govt. of India, Ministry of Health and Family Welfare, New Delhi, 2007; 1,2,3: 1045.
10. The British Pharmacopoeia, London, Controller of her majesty's stationary office, 2002.
11. The United States Pharmacopoeia, XXVII, NF XXII., The United States Pharmacopoeial convention Inc, 2009; 2: 2175.
12. www.drugs.com, detail drug profile information.
13. www.ich.org/cache/compo.com, International Conference on Harmonisation (ICH) guidelines.
14. Ansel H.C., Popvich N. G. Introduction to Pharmaceutical Dosage form, 2nd edn., 1989, 265.
15. Marabathuni VJ, Dinesh P, Ravikumar R, Yamini P, Kiran PS, Hussain SP, Rao CM. Chitosan based sustained release mucoadhesive buccal patches

containing amlodipine besylate (AMB). Asian J Res Pharm Sci., 2017; 7: 97-104.
16. Marabathuni VJ, Bhavani M, Lavanya M, Padmaja K, Madhavi N, Babu P, Rao CM. Formulation and evaluation of mouth dissolving Tablets of carbamazepine. Asian Journal of Pharmacy and Technology, 2017; 7(3): 137-43.