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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF FEXOFENADINE HYDROCHLORIDE BY DIRECT COMPRESSION METHOD

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Abstract

Formulation and Evaluation of Fast Dissolving Tablets of Fexofenadine HCL by using direct Compression method. Fast dissolving tablet can offer quick onset of action, as compared to conventional tablet, Relief of disease can be found in less time. The major issue in the development of fast dissolving tablet is not enhance the bioavailability or prevention of pre systemic metabolism, but to found the fast disintegration of dosage form and quick onset of action or. In current study, may the conclusion is that the fast disintegrating Fexofenadine Hydrochloride tablets can be prepared by direct compression method using combination of various Superdisintegrants. Crospovidone with magnesium stearate combination was found to be the best as compare to the other concentration of Superdisintegrants. Crospovidone with combination showed the least disintegration time of 10.22 ± 1.35 seconds and the highest release of more than 96% of drug in 15 minutes. For confirmation of result is need to be performed the in-vivo studies and compared with in-vitro studies.

Keywords: Superdisintegrants, Crospovidone, Fexofenadine HCL.

INTRODUCTION

Fast Dissolving Tablet

The theory of fast-dispensing delivery drug delivery systems is designed to provide traditional methods of taking their drugs due to physiologically associated changes, in particular the aging science and pediatrics who are unable to swallow (dysphasia).[1]

This is a common problem in patients of all ages. The oral dose can be diluted, diluted or diluted with saliva, resulting in easy dosage and significant benefits for pediatricians and geriatrics and other patients who prefer the convenience of easily swallowed tablets. When placed in the oral cavity, the tablet decomposes rapidly, releasing a drug that dissolves or dissolves in the oral cavity and saliva.[2,3,4]

The rapidly dissolving tablet decomposes and spreads immediately into the oral cavity and saliva without the need for drinking water.[5] When these tablets are placed in the mouth, saliva immediately enters the pores, causing immediate breakdown of the tablet.[6]

Formulation of fast dissolving tablet (FDT) is the recent advantage in the novel drug delivery system (NDDS), that gives significance benefits like absorption of drug directly into the blood There are some of the new methods to formulation of fast dissolving dosage forms include Zydis, Wow tab, Oraquick, Ziplet, Orasolv, Flashtab.[7]

Allergy is most common issue in both developing and developed countries. Due to uncontrolled elevation of blood pressure can lead to a variety of changes in the coronary vasculature, and conduction system of H1 Histamine. Pediatric patients who allergic conditions may be at risk for the formation of dysphasia due to interventions such as Tran's esophageal echocardiography and intubation. [8,9]

Fast dissolving tablets are an excellent result for hypertensive patients to take formulation of an anti-hypertensive easily [10] faster action and better stability have made these tablets popular as an option in the current market. [11]

MATERIAL & METHODS

Ingredients: All Ingredients used in the formulation and evaluation are mentioned as following.

Table 1:- List of ingredients

S.No.	Ingredients
1	Drug (Fexofenadine Hydrochloride)
2	Magnesium stearate
3	Talc
4	Mannitol
5	Microcrystalline Cellulose
6	Cross Povidone
7	Sodium Starch Glycolate
8	Cross Carmellose Sodium
9	Aerosil

Preformulation studies

Formulation testing is the first step to the rational development of dosage forms of the drug. It can be defined when the physical and chemical properties of a substance are isolated and combined with excipients. The data shown below on substances commonly required for preformulation studies are physical properties Chemical properties: test, dissolution and related substances.

Organoleptic Characteristics: Color, smell and taste of the drug is classified and recorded using descriptive vocabulary.

Melting Point

The melting point of a substance changes from solid to liquid state under atmospheric pressure. The liquid and solid phases are in equilibrium at the melting point. The melting point of the material depends on the pressure and is usually specified at standard pressure. The temperature of the reverse change from liquid to solid.

Solubility Studies

For solubility analysis, drug was added to 5 ml of different dissolution media i.e. water, 0.5 N HCl, 0.1 N NaOH, Ethanol and Chloroform in a test tube at room temperature till saturation occurred. After that samples were filtered, appropriately diluted and analyzed at 374 nm using UV visible double beam spectrophotometer (UV 1601, Shimadzu, Japan).

Angle of Repose (θ)

The angle of rest was determined by the funnel method. The exact weight of the powder was taken in a funnel. The height of a funnel is adjusted so that its tip touches the top of the dry pile. Allowed to flow freely through the funnel across the dry surface. The diameter of the dry pile is measured and the resting angle is calculated using the following equation,

$$\tan(\theta) = h/r$$

$$\theta = \tan^{-1}(h / r)$$

Where, θ is the angle of repose is the height in cms r is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particals slip and roll over each other through the sides of the funnel.

Table 3:- Relationship between angle of repose and powder flow property.

S. No	Angle of repose (θ)	Type of flow
1	<20	Excellent
2	20 – 30	Good
3	30 – 34	Passable
4	>34	Very poor

Density Measurement

Performed a variety of density calculations. The method of calculating the above two densities is determined by the following API and the following to characterize its flow characteristic. There are generally two types of APIs and its streaming property.

Bulk Density

bulk density is calculated by the following formula:

Bulk density = Weight of powder / Bulk volume

Tapped Density

The tape density is calculated by:

Tapped density = Weight of powder / Tapped volume

Carr's (Compressibility)Index

This is one of the most important parameters to describe the nature of powders and granules. It can be calculated by the following formula:

Carr's Index= Tapped density-Bulk density / Tapped densityX100

Table 4:- Comparison b/w compressibility and flow ability

Compressibility (%)	Flow ability
5-15	Excellent
12-16	Good
18-21	Fair possible
23-35	Poor
33-38	Very poor
More than 40	Very very poor

Hausner's Ratio

This is an important parameter to determine the flow property of powders and granules. Volume less than 1.26. Indicates good flow. Suggest more than 1.50. Poor flow between 1.25 and 1.5 indicates that the addition of glades improves the flow. When the force is equal to the bulk density of the dye it is necessary to fill evenly on the pellet machines and to consolidate to reach the tapped density before compression.

Hausner's ratio – Tapped density / Bulk density

Formulation of fast dissolving tablets:

Formulation & Batch codes

The mixed blend of drug and ingredients was compressed using tablet punching machine, weighing approx. 100 mg each with a diameter of 8 mm. there are nine formulations with varying percentage of Superdisintegrants.

- Formulations coded as F1, F2, and F3 for crospovidone 6, 8, and 10mg w/w with microcrystalline cellulose 57, 55, 53mg w/w and mannitol 1mg w/w.

- Formulations coded as F4, F5 and F6 for sodium starch glycolate 6, 8, and 10mg w/w with microcrystalline cellulose 57, 55, 53mg w/w and mannitol 2mg w/w.

- Formulations coded as F7, F8 and F9 for croscarmellose sodium 6, 8, and 10mg w/w with microcrystalline cellulose 57, 55, 53mg w/w and mannitol 3mg w/w.

- All batches were formulated with Magnesium Stearte 2mg w//w, Talc 2mg w/w and Aerosil 2mg w/w.

Table 5:- Composition of fast dissolving tablet prepared by direct compression method

S. No.	Batch Code	Fexofinadine HCL (mg)	CP (mg)	SSG (mg)	CCS (mg)	MS (mg)	Aerosil (mg)	MCC (mg)	Talc (mg)	Mannitol (mg)
1.	**F1**	30	6	-	-	02	02	57	02	01
2.	**F2**	30	8	-	-	02	02	55	02	01
3.	**F3**	30	10	-	-	02	02	53	02	01
4.	**F4**	30	-	6	-	02	02	57	02	02
5.	**F5**	30	-	8	-	02	02	55	02	02
6.	**F6**	30	-	10	-	02	02	53	02	02
7.	**F7**	30	-	-	6	02	02	57	02	03
8.	**F8**	30	-	-	8	02	02	55	02	03
9.	**F9**	30	-	-	10	02	02	53	02	03

- CP: Crospovidone , SSG: Sodium Starch Glycolate, CCS: Croscrmellose Sodium, MS Magnesium Stearate, MCC : Micro Crystalline Cellulose.

EVALUATION OF TABLETS

Post Compression Parameters-
Size and Shape - formulated tablets were round in shape and diameter.

Uniformity & Thickness - The thickness of the tablets was measured using digital venire calliper scale. Six tablets were analyzed to determine the mean thickness. It is expressed in micrometres and was found to be within ± 0.5mm.

Organoleptic property - The colored tablets were found to be uniformly yellow in colour. All tablets formulated were tested for taste and odor. All yogas have been found to give a sweet taste and a pleasant aroma.

Weight variation - I.P. Limit for tablets according to Twenty tablets were randomly selected, weight and average weight calculated. Not more than two per cent of the individual weight should not deviate more than 5% from the average weight.

Table 6:- Limit of Weight Variation

Average weight of tablet (mg)	Maximum% difference allowed
80 mg or less	10 %
More than 80 but less than 250 mg	7.5 %
250 or more	5 %

Hardness: The monsanto hardness tester is the most widely used device for measuring the hardness or compressive strength of a tablet. The results were calculated from the mean results of

six tablets. The hardness across the tablet is determined to determine the need for pressure adjustment in the tablet compression machine.

Friability: % Loss was calculated using the weight and formula of the resulting tablets: -

% Friability = Initial wt-Final Wt/Initial Wt×100

Wetting Time: The wetting time of the tablet is the ability of the fluid to maintain contact with a solid surface, resulting in inter-molecular interactions when the two are combined. Wetting (wetting) is determined by the energy balance between the coadhesive and the adhesive forces.

Swelling index : The study was performed using a 100 ml Stopford graduate cylinder. The initial bulk volume of 1 gram of starch was noted. Adequate amount of water is added to disperse 25 ml uniformly and stir vigorously for 1 hour every 10 minutes and then allowed to stand for 24 hours. The dispersion was stored at room temperature and the swelling mass was measured after 24 hours of total precipitation.

Swelling index=100 X (V2-V1/V1)

Where,

V1=Initial volume of material before hydration
V2=Volume of hydrated material

Disintegration: In order to release the component drug component from the tablet, it has to decompose. So the breakdown time is determined after adding six tablets to each cylinder (basket rack assembly) of the DT appliance containing the dissolved water. Sensing and reducing device at a constant frequency frequency of 28 to 32 cycles / min over a distance of 50 to 60 mm. This device is set at a temperature of 370C. The resulting bullets last 6 to 8 seconds.

Dissolution test: The vessels of the melting method are usually partially immersed in a water bath solution or heated by a jacket. A device is used on a solution for a predetermined time depending on the method of the specific for drug. The soluble medium in the vessels is heated to 37 ° C with an acceptable difference of 0.5 C. Of drug concentration is calculated from the standard graph and is dissolved or released as % of the drug. Release studies were performed in replication and were inverted.

RESULT AND DISCUSSION

Preformulation Studies

Melting point Determination

The melting point of a substance changes from solid to liquid state under atmospheric pressure. At the melting point, the liquid and solid phases are in equilibrium. The melting point were found to be 148°C to 150°C

Solubility Studies

For solubility analysis, drug was added to 5 ml of different dissolution media i.e. water, 0.5 N HCl, 0.1 N NaOH, Ethanol and Chloroform in a test tube at room temperature till saturation occurred. After that samples were filtered, appropriately diluted and analyzed at 374 nm using UV visible double beam spectrophotometer (UV 1601, Shimadzu, Japan).

Table 7:- Solubility Studies

S. No.	Solubility Medium	Solubility (mg/ml)
1	Water	0.00266 mg/ml
2	Chloroform	3.0 mg/ml
3	Ethanol	12 mg/ml

Some preformulation parameters are described into the table as following like Bulk Density, Tapped Density, Angle of Repose, Hausner's Ratio, Carr's Index.

Table 8:- Preformulation Studies

S.No.	Batch Code	Bulk Density gm/ml	Tapped Density gm/ml	Angle of Repose (Θ)	Hausner's Ratio	Carr's Index (%)
1.	F1	0.64	0.72	21.44	1.11	10.22
2.	F2	0.68	1.78	20.55	1.14	12.22
3.	F3	0.68	0.80	21.45	1.17	14.81
4.	F4	0.70	0.82	20.67	1.18	14.81
5.	F5	0.63	0.72	20.81	1.17	14.82
6.	F6	0.63	0.74	20.82	1.12	11.11
7.	F7	0.64	0.82	22.29	1.13	12.32
8.	F8	0.70	0.83	22.32	1.16	14.45
9.	F9	0.71	0.70	21.27	1.14	12.50

Physical Evaluation Thickness

Table 9:- Thickness of Tablets

Batch Code	Thickness (um)
F1	2.39 ± 0.04
F2	2.46 ± 0.02
F3	2.50 ± 0.02
F4	2.45 ± 0.03
F5	2.39 ± 0.11
F6	2.51 ± 0.03
F7	2.32 ± 0.15
F8	2.51 ± 0.02
F9	2.40 ± 0.03

Weight Variation

Table 10:- Weight Variation of Tablets

Batch Code	Weight Variation (mg)
F1	199.20 ± 0.92
F2	198.65 ± 0.83
F3	199.90 ± 0.47
F4	200.10 ± 0.94
F5	200.15 ± 0.48
F6	199.45 ± 0.96
F7	199.20 ± 0.95
F8	199.30 ± 0.93
F9	199.35 ± 0.92

Hardness

Table 11:- Hardness of Tablets

Batch Code	Hardness
F1	3.03 ± 0.32
F2	3.06 ± 0.39
F3	3.36 ±0.51
F4	3.55 ± 0.45
F5	3.61 ± 0.29
F6	3.53 ± 0.24
F7	3.66 ± 0.35
F8	3.66 ± 0.65
F9	3.63 ± 0.34

Friability

Table.12 Friability of Tablets

Batch Code	Friability (%)
F1	0.86
F2	0.27
F3	0.60
F4	0.24
F5	0.27
F6	0.42
F7	0.60
F8	0.75
F9	0.72

Wetting time

Table 13:- Wetting time of Tablets.

Batch Code	Wetting Time
F1	22.10± 1.53
F2	16.04± 1.23
F3	26.04± 1.90
F4	27.44 ± 2.21
F5	22.06 ± 1.85
F6	22.05± 1.02
F7	20.25± 1.50
F8	16.25± 1.36
F9	16.45± 2.01

Disintegration time

Table 14:- Disintegration Time of Tablets

Batch Code	Disintegration time
F1	22.85± 1.54
F2	18.05± 1.65
F3	10.22 ± 1.95
F4	38.21 ± 1.56
F5	26.55 ± 2.01
F6	19.80 ± 1.35
F7	60.05 ±1.54
F8	55.55 ± 1.85
F9	30.75 ± 1.65

Swelling index

Table 15:- Swelling Index of Tablets

Batch Code	Swelling index (%)
F1	57.44 ± 1.06
F2	58.44 ± 0.84
F3	56.56 ± 1.35
F4	34.54 ± 1.16
F5	45.16 ± 1.08
F6	34.54 ± 0.82
F7	56.43 ± 1.65
F8	34.01 ± 1.48
F9	45.43 ± 2.07

In Vitro Dissolution Study

Table 16:- Dissolution of Tablets

Time (Min)	% of Drug Release in 900ml 0.1N Hydrochloric Acid									
	F1	**F2**	**F3**	**F4**	**F5**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0	0
5	32	37	45	23	42	48	43	39	36	34
10	65	68	69	42	65	69	67	69	71	73
15	79	72	96	68	78	80	83	81	78	76

Graphical represantation of values:

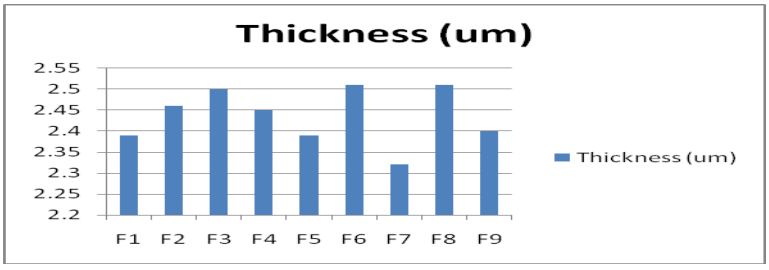

Fig.1 Plot of thickness of tablets

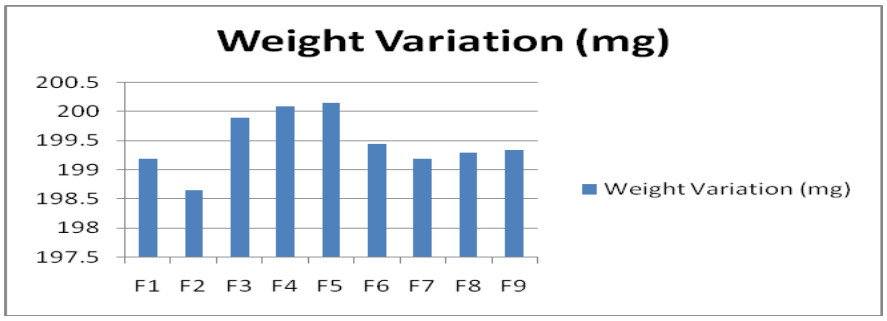

Fig.2 Plot of weight variation of tablets

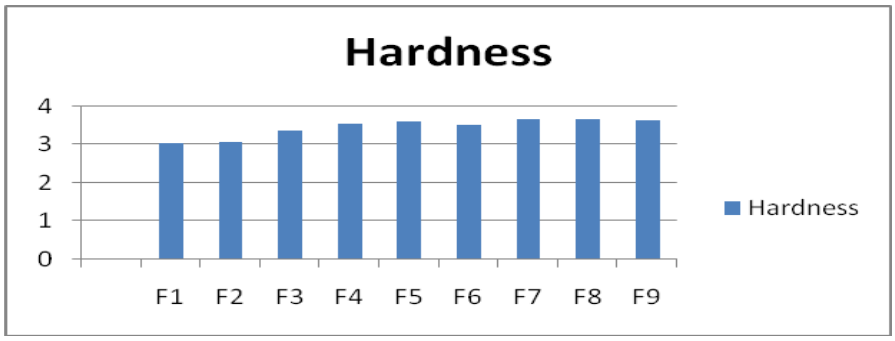

Fig.3 Plot of Hardness of tablets

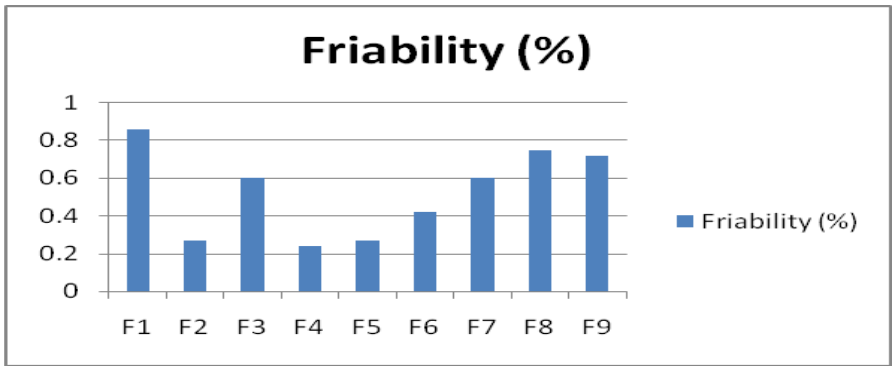

Fig.4 Plot of friability of tablets

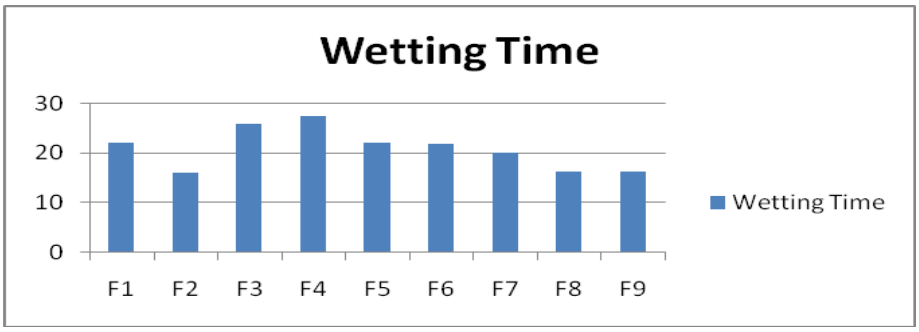

Fig.5 Plot of wetting time of tablets

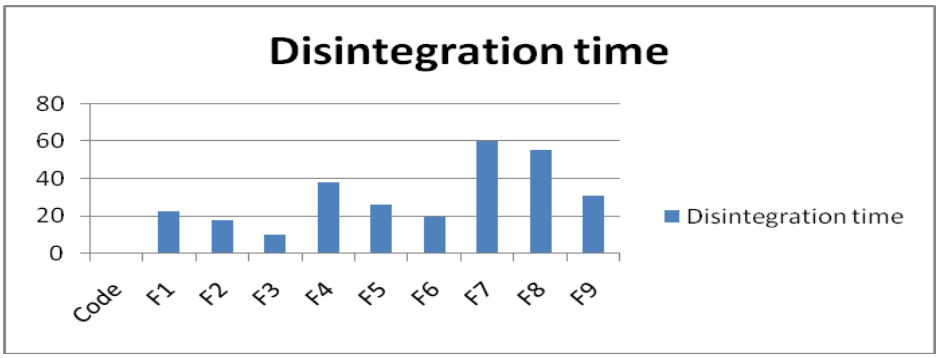

Fig.6 Plot of disintegration time of tablets

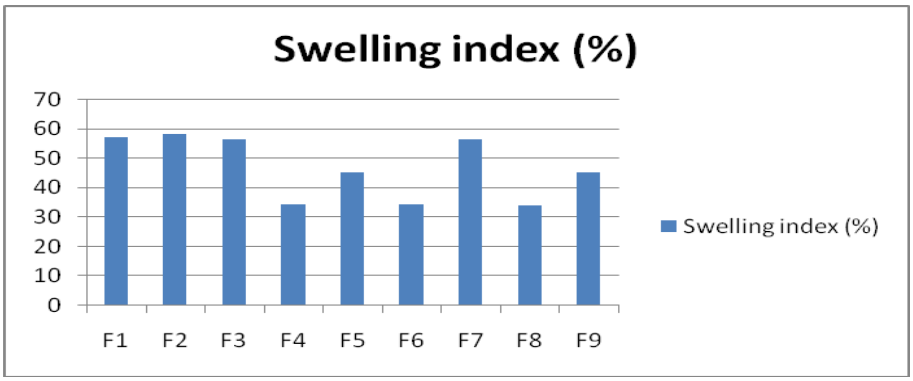

Fig.7 Plot of Swelling Index of tablets

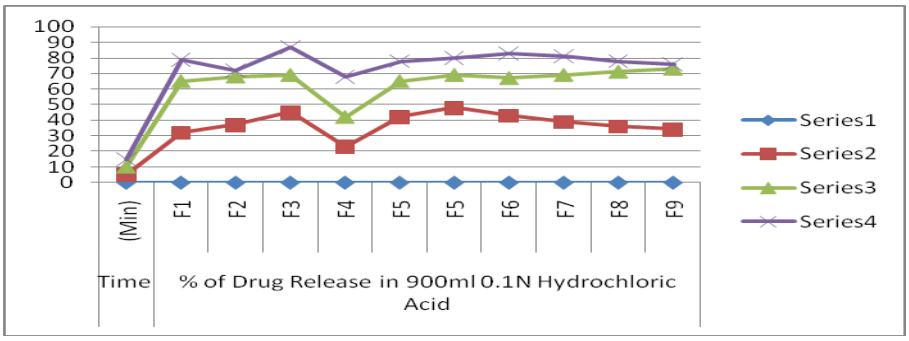

Fig.8 Plot of dissolution time of tablets

- The best combination of superdisintegrants are mentioned in batch code name F3. The composition of batch F3 is shown below.

Table 17:- Best Batch Composition

Batch Code	Fexofinadine HCL (mg)	CP (mg)	SSG (mg)	CCS (mg)	MS (mg)	Aerosil (mg)	MCC (mg)	Talc (mg)	Mannitol (mg)
F3	30	10	-	-	02	02	53	02	01

- The batch code name F3 is gives the best result as per desired. The result of batch code F3 is shown below.

Table.18 Result of Best Batch

Batch Code	Thickness (um)	Weight Variation	Hardness	Friability	Wetting Time	Disintegration time	Swelling Index
F3	2.50 ± 0.02	199.90 ± 0.47	3.36 ±0.51	0.60 %	26.04± 1.90	10.22 ± 1.95	56.56 ± 1.35

Conclusion

Fast dissolving tablet can offer quick onset of action, as compared to conventional tablet, Relief of disease can be found in less time. The major issue in the development of fast dissolving tablet is not enhance the bioavailability or prevention of pre systemic metabolism, but to found the fast disintegration of dosage form and quick onset of action or. In current study, may the conclusion is that the fast disintegrating Fexofenadine Hydrochloride tablets can be prepared by direct compression method using combination of various superdisintegrants. crospovidone with magnesium stearate combination was found to be the best as compare to the other concentration of superdisinte-grants. crospovidone with combination showed the least disintegration time of 10.22 ± 1.35 seconds and the highest release of more than 96% of drug in 15 minutes.

For confirmation of result is need to be performed the in-vivo studies and compared with in-vitro studies.

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