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FORMULATION DEVELOPMENT AND EVALUATION OF ORODISPERSIBLE TABLETS OF FEXOFENADINE BY USING COMBINATIONS OF SUPERDISINTEGRANTS

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Abstract:

Fexofenadine is prescribed for the treatment of allergy symptoms in males. The liver plays a crucial role in fexofenadine's metabolism. Orodispersible tablets, which are not metabolised in the stomach, were a good choice of dosage form to counteract these limitations. With the goal of achieving rapid disintegration when held beneath the tongue and facilitating direct absorption of the active ingredient by the oral mucosa, the present study sought to design and develop a Fexofenadine Orodispersible Tablet using Croscarmellose Sodium, Cross povidone, and Sodium starch Glycolate as superdisintegrants. Fexofenadine Orodispersible granules were prepared using a wet granulation process, and evaluation findings indicated that all precompression parameters fulfilled the acceptance criteria, indicating that the granules had outstanding flow qualities. A variety of post-compression characterizations of tablets were performed and the results met the requirements of the pharmacopoeia. Different formulations were tested for in vitro release using a USP II paddle type dissolution equipment. Both a first order kinetic model and a zero-order kinetic model were tested in vitro for release kinetics. Compatibility between the medication and excipients was confirmed by FTIR analysis. following conducting DSC investigations to determine the drug and excipient thermal stabilities, it was determined that both were thermally stable following the aforementioned formulations. The optimized formulation was confirmed to be stable over an adequate time period in accelerated stability testing.

Key Words: *Orodispersible, Fexofenadine, Croscarmellose Sodium, crosspovidone, Sodium starch glycolate*

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INTRODUCTION:

There are a number of ways to administer medicinal and other curative substances that have a systemic effect, but the oral route is thought to be the most efficient and has the highest patient compliance [1]. When compared to conventional dosage forms, orally disintegrating tablets have significantly higher rates of drug absorption, dissolution, clinical effect onset, and bioavailability [2-4]. The fundamental method for creating ODTs is to make the tablet more porous by using the right disintegrating agents and high water-soluble excipients in the formulation [5]. When these dose forms come into immediate contact with saliva, they quickly disintegrate in the mouth and release the medication. Even better for paediatric and geriatric patients, there is no requirement for water during drug administration [6].

Orodispersible tablets are those without coatings that dissolve quickly in the mouth before being swallowed. The terms "melt in the mouth tablets," "mouth dissolving tablets," "Rapimelt tablets," "Porous tablets," and "Quick dissolving tablets" are all used to describe orodispersible tablets. The US Pharmacopoeia, the (CDER) Centre for Drug Evaluation and Research, and the British Pharmacopoeia recently authorised the name ODT [7]. ODT is a solid dose form that, according to the US Food and medication Administration, comprises medication ingredients that, when placed on the tongue, quickly dissolve [8].

ODT is described as "A tablet which is to be placed in the mouth disperses rapidly within three minutes before swallowing"[9] by the European Pharmacopoeia. Due to their regular need for tablets to maintain their healthy lifestyles, elderly patients find it difficult to administer conventional tablets. Children may also have difficulty swallowing tablets due to their underdeveloped nervous and muscular systems, and patients who travel may also experience this issue. These issues can be resolved by using orodispersible patents, which allow chemists to formulate and develop a drug into a new dosage form.

Fexofenadine is a medication that is administered to alleviate allergic symptoms. Fexofenadine works by selectively antagonisting H1 receptors on the cell surfaces of several organ systems. It is an H1 receptor blocker of the second generation. Inflammatory mediators are also affected by fexofenadine. Following oral dosing, fexofenadine is quickly absorbed, with a 33% absolute bioavailability. 60% to 70% of the plasma proteins, predominantly albumin and 1-acid glycoprotein, are bound to fexofenadine hydrochloride. The distribution volume is 5.4-5.8 L/kg on average. 60% to 70% of the plasma proteins, predominantly albumin and 1-acid glycoprotein, are bound to fexofenadine hydrochloride. Although fexofenadine is a substrate of CYP3A4, the liver only processes around 5% of it, suggesting that hepatic metabolism plays a relatively small role in the drug's removal from the body. Due to fexofenadine's slow metabolism, approximately 80% of an ingested dose is removed in the faeces and 11% is eliminated in the urine. The biliary and renal systems are the main elimination mechanisms for fexofenadine. Fexofenadine has a renal clearance of around 4.32 L/h and an oral clearance of about 50.6 L/h. After giving normal volunteers 60 mg twice daily, the mean elimination half-life of fexofenadine was 14.4 hours. The Biopharmaceutics Classification System (BCS) class for fexofenadine is III. It is completely insoluble in hexane, but easily soluble in methanol and ethanol, and only moderately soluble in chloroform and water. Adults and kids 12 years old and older should take 60 milligrammes (mg) twice daily or 180 mg all at once. [10]

The primary objective of the current studies was to create and carry out in vitro evaluation tests of orodispersible Fexofenadine tablets using super disintegrants such as sodium starch glycolate, crosscarmellose, and crosspovidone in order to achieve rapid dispersion when taken through the buccal cavity, allowing a rapid onset of action.

MATERIALS AND METHODS:

Materials

Fexofenadine was received as a gift sample from Dr. Reddy's laboratories Pvt. Ltd. in Hyderabad, India. Also provided from Dr. Reddy's Laboratories Pvt. Ltd. was a gift sample of the superdisintegrant sodium starch glycolate, croscarmellose and crosspovidone. The diluent was purchased from Otto Manufacturers. Lactose, PVP K30, talc, and magnesium stearate were purchased from S.D. Fine Chemicals Pvt. Ltd. in Mumbai, India. Each component was of the highest calibre for a lab. The double distillation method was used in the lab to produce the distilled water that was used in the study.

METHODS

Analytical method for the *in vitro* estimation of Fexofenadine in the formulations

A primary stock solution of fexofenadine with a concentration of 1000 g/ml was made using a phosphate buffer with a pH of 6.8. Following the proper dilution, a secondary stock solution with a concentration of 10 g/ml was made from the initial stock solution using the same phosphate buffer pH

6.8. The created secondary stock solution's greatest absorbance was found to be at 225 nm, which was selected and used for further investigation. This was identified after scanning the solution with a UV spectrophotometer (Analytical Technologies Ltd. Spectro 2080) at wavelengths ranging from 400 nm to 200 nm. Using the same phosphate buffer pH 6.8, the secondary stock solution was first diluted to produce a series of concentrations of 2, 4, 6, 8, and 10 g/ml. Then, the corresponding absorbance was determined at 225 nm, the maximum wavelength. Measured absorbencies were plotted against matching concentrations to create the pure Fexofenadine calibration curve. [11]

Drug and excipients compatibility studies

Through FTIR, the drug and excipients used to create various batches of Fexofenadine orodispersible tablets were examined for any potential physical and chemical interactions.

Fourier Transform Infrared (FTIR) spectroscopy

Fourier transforms infrared (FTIR) spectroscopy tests were performed to identify the peaks in the pure medicine and the excipients used that indicate the existence of a specific functional group. If the functional groups present in the pure drug are replicated in the formulations, the drug and excipients are deemed to be compatible. Both the pure drug and a physical mixture of the drug and all excipients (optimised formulation) were examined using FTIR for fexofenadine. Potassium bromide (KBr) pellets were utilised in the technique. After the components had been triturated with KBr, a pellet was made by exerting pressure of 100 kg/cm2 for two minutes. The obtained pellet was investigated in the FTIR 8400S by Shimadzu, Japan. The analysis of the test samples came first, followed by the acquisition of the KBr backdrop. The same steps were performed for the analysis of the drug, each excipient, and the physical mixing of the excipients and the drug. [12]

Differential scanning calorimetry (DSC) research

The physical interaction between a drug and the polymers used in the formulation of different dosage forms can also be determined through thermal analysis utilising DSC or TGA techniques. DSC analysis of Fexofenadine and the physical mixture of drug and excipients (optimised formulation) used in the formulation of Fexofenadine orodispersible tablets was performed in the current studies using a Shimadzu DSC 60 from Japan to evaluate the possibility of polymer drug thermal interaction. The purpose of this was to ascertain the existence of a thermal interaction between the polymer and the medication. Hermetically sealed in an aluminium crucible after meticulous weighing, the samples (varying from 5.6 mg to 5.6 mg) were heated between 40 and 300 degrees Celsius at a continuous rate of 10 degrees Celsius per minute. Flushing the area with nitrogen gas at a rate of 50 ml/min ensured an inert atmosphere was maintained.

Formulation of Fexofenadine Orodispersible tablets ($FORF_1$- $FORF_{10}$)

Wet granulation was used in the production of fexofenadine orodispersible tablets. All ingredients were carefully measured and filtered through a No. 80 mesh screen before being used in the final products. Powders such as Fexofenadine, croscarmellose sodium, crospovidone, sodium starch glycolate, lactose, and PVP K30 and were uniformly mixed and sieved through #20, and PVP K30 and is used as a binder. Aggregates formed following binder addition were dried for 5-10 minutes to reduce moisture content and prevent adhering to the sieve. The aggregates were processed via filter #20 to produce granules. The granules are dried at 40 degrees Celsius for 20 minutes, which reduces the moisture content by around 2-5%. As lubricants, talc and magnesium stearate were mixed with dry granules for two to three minutes. Before compression, the formulations' angles of repose, bulk densities, tapped densities, compressibility indices, and Hausner's ratios were measured. Using a 10-station rotary punching machine (Saimach Pharmaceutical Pvt. Ltd.), and 8mm concave punches, we compressed the sample grains into tablets for testing. Fexofenadine is available in 60 mg doses. The many different formulations are listed in Table 1, and they were all made using the same method. After compression, the orodispersible tablet formulations were studied for their drug content, hardness, friability, and *in vitro* dissolving, among other post-compression properties. [13]

Table 1: Compositions of different formulations of Fexofenadine Orodispersible tablets

F. No.	$FORF_1$	$FORF_2$	$FORF_3$	$FORF_4$	$FORF_5$	$FORF_6$	$FORF_7$	$FORF_8$	$FORF_9$	$FORF_{10}$
Fexofenadine (mg)	60	60	60	60	60	60	60	60	60	60
Sodium starch Glycolate (mg)	---	---	---	---	6	8	---	4	4	2
Crospovidone (mg)	---	---	6	8	---	---	4	4	---	2
Croscarmellose Sodium (mg)	6	8	---	---	---	---	4	---	4	4
Lactose (mg)	107	105	107	105	107	105	105	105	105	105
Starch (Insoluble) (mg)	20	20	20	20	20	20	20	20	20	20
Mg. Stearate (mg)	4	4	4	4	4	4	4	4	4	4
Talc (mg)	2	2	2	2	2	2	2	2	2	2
Aspartame (Mg)	1	1	1	1	1	1	1	1	1	1
Total Wt. (mg)	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Evaluation of precompression parameters of dry granules of Fexofenadine Orodispersible tablet formulations

Angle of Repose (θ)

The dry granules were 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 granules formed.

$$\theta = \tan^{-1}\left(\frac{h}{r}\right)$$

Where θ was called as angle of repose, h and r were height and radius of the granule heap respectably. According to the specifications the angle of repose value less than 25^0 indicates excellent flow whereas angle greater than 40^0 indicates poor flow. [14]

Bulk density and tapped density

Both the bulk density (BD) and tapped density (TD) of prepared Fexofenadine Orodispersible dry granules of all the formulations were determined using the following formulas. [15]

$$BD = \frac{weight\ of\ the\ dry\ powder}{volume\ of\ the\ packing}$$

$$TD = \frac{weight\ of\ the\ dry\ powder}{tapped\ volume\ of\ the\ packing}$$

Compressibility Index (Carr's index):

The flow ability of powder and granule can be evaluated by comparing the bulk density (BD) and tapped density (TD) of granules and the rate at which it packed down. Compressibility index (Carr's index) of prepared Fexofenadine Orodispersible dry granules were calculated by following formula

$$Carr's\ index\ (\%) = \frac{TD-BD}{TD} \times 100$$

According to the specification the Carr's index values "between" 5-15 indicates excellent flow where as between 12-16 indicates good flow. Values "between" 18-21 indicate fare-passable where as between 23-25 indicates poor. "Between" 33-38 indicates very poor and greater than 40 indicates extremely poor. [16]

Hausner's ratio:

The Hausner's ratios of prepared Fexofenadine Orodispersible dry granules were determined by following formula.

$$Hausner's\ ratio = \frac{TD}{BD}$$

According to specifications values less than 1.25 indicate good flow (=20% of Carr's index), where as greater than 1.25 indicates poor flow (=33% of Carr's index). Between 1.25 and 1.5, glidant need to be added to improves flow. [17]

Evaluation of post compression parameters of Fexofenadine Orodispersible tablets formulations

Each new orodispersible tablet formulation was evaluated based on the following criteria.

Shape of Tablets

The tablets' shapes were determined by using a magnifying glass to study them closely.

Average thickness

To compare the thickness of different Fexofenadine orodispersible tablet formulations, we randomly sampled 10 tablets from each formulation. Each

tablet's thickness was measured using a digital Vernier calliper (a Mitutoyo dial thickness gauge, made in Japan), and the results were reported as the average of 10 measurements plus the standard deviation. [18]
The specification calls for a maximum variation in tablet thickness of 5%.

Tablet Hardness
Using a Monsanto hardness tester (Cad Mach), the hardness of all Fexofenadine Orodispersible tablet formulations was assessed. Ten orodispersible tablets with known weights from each formulation were tested for crushing strength, which was measured in kg/cm2, averaged, and then shown with standard deviation. For orodispersible tablets, hardness values between 3 and 4 kg are regarded as an acceptable upper limit by USP requirements. [19]

Friability
Ten tablets from each batch that had previously been weighed were placed in the Roche friabilator (Roche friabilator, Secor India, Delhi, India). Tablets were found after a hundred friabilator revolutions. The tablets were then cleaned of dust, and the total weight that remained was noted. This formula was used to determine friability.

$$\%F = \frac{(Wi - Wf)}{Wi} \times 100$$

Where W_i and W_f were the initial and final weight of the tablets before and after friability test. For compress tablet that lose less than 0.1 to 0.5 % and maximum upto 1% of the tablet weigh are consider acceptable. [20]

Weight variation test
The USP standard states that the weight variation tolerance limit for uncoated tablets with an average weight of 130 mg or less is 10%, 7.5% for tablets with an average weight between 130 and 324 mg, and 5% for tablets with an average weight of more than 324 mg. The weight of the tablet must not differ from the average weight by more than two tablets' weight, and no tablet may deviate by more than 15%. Weight variation was assessed for all Fexofenadine orodispersible tablet formulations in accordance with the USP standard. Using an electronic balance, 20 pills from each batch were weighed both collectively and individually. Calculations were made on the average weight and % variance of each tablet. [21]

Content uniformity
Twenty tablets were taken and ground into a powder to test the consistency of all formulations' content. One tablet's worth of powder was taken, diluted in 100 cc of phosphate buffer with a pH of 6.8, and heated at 37 0C for 15 to 20 minutes while stirring continuously. The Fexofenadine content was determined using a UV Spectrophotometer (Analytical Technologies Ltd. Spectro 2080) at 225 nm after the solution had been cooled, filtered, and appropriately diluted. The average medication content of each formulation was computed after each measurement was made in triplicate. [22]

Wetting time and water absorption ratio
The disintegrating process of the tablet formulation is reflected in the wetting time. The disintegration rate increases as wetting time decreases. Twice-folded tissue paper was placed in a petri dish with an internal diameter of 6.5 cm, 10 ml of phosphate buffer pH 6.8, and 0.1% w/v of methylene blue for the purpose of determining the wetting time. The surface of the tissue paper in the petri dish was carefully covered with a tablet from each type of Fexofenadine orodispersible tablet. Wetting time was measured as the length of time it took for the dye to reach the tablet's top surface. The standard deviations were also calculated, and measurements were done in triplicate.

By weighing the tablet (Wb) before placing it on the Petri dish and then after recording the wetting duration, it is possible to estimate the water absorption ratio (R). The moist tablet was taken out and weighed again (Wa). The following equation was used to calculate the water absorption ratio. [23]

$$R = \frac{(Wa - Wb)}{Wb} \times 100$$

***In vitro* disintegration time (D_t)**
The USP specifies 2 minutes as the acceptable time limit for tablet disintegration meeting official criteria, whereas 2 minutes for orodispersible dosage form when using the disintegration apparatus for oral tablets without the covering plastic discs. Tablet disintegration equipment (type EI D-16, Electrolab, Mumbai, India) was used for the test. A modified disintegration method was used to conduct an in vitro disintegration test on a disintegration tester that was kept at 37°C 0.5°C in phosphate buffer pH 6.8 (n = 6). The time it took for each pill to totally break down into smaller particles was observed while the tablets were stored in the basket. [24]

***In vitro* drug release (dissolution) study**
Using an eight station USP dissolving rate test apparatus type-II (LABINDIA DS 8000, Mumbai, India), the in vitro dissolution research for all of the formulations was carried out. The dissolution medium, a total volume of 900 ml of phosphate

buffer pH 6.8, was kept at 37°C 0.5°C at 50 rpm. At regular intervals, 5ml of aliquots were removed and replaced with an equivalent volume of new dissolving medium. Samples were taken every 5 minutes and then filtered using Whatmann filter paper. Fexofenadine emitted from orodispersible tablets was identified in samples using spectrophotometric analysis at 225 nm. [25]

Characterization of the *in vitro* drug release profile

The rate and mechanism of release of Fexofenadine from prepared orodispersible tablets were analyzed by fitting the dissolution data into following exponential equations.

Zero order release equation is calculated by following equation.

$$Q = K_0 t$$

Where Q is the amount of drug released at time t and K_0 is the zero order release rate constant.

The first order equation is calculated by following equation.

$$\log(100 - Q) = log100 - K_1 t$$

Where, K_1 is the first order release rate constant. [26]

Stability studies of best formulation

According to ICH recommendations, research on the optimal formulation of Fexofenadine orodispersible tablets' short-term stability were conducted. The best formulation was put under accelerated stress conditions for 90 days at 40 oC ± 2 oC/ 75% ± 5% relative humidity. Following that, the product's friability, hardness, weight variation, thickness, drug content, and in vitro drug release research were assessed. [27]

RESULTS AND DISCUSSION:

Drug-Excipient Compatibility studies by FTIR:

The FTIR spectra of Fexofenadine in its pure form and in a physical mixture with the excipients used in its manufacturing are shown in Figures. Fexofenadine's large peak at 3664 cm-1 is attributable to N-H stretching, and the sharp peaks seen in spectra of Fexofenadine's formulation with excipients are also seen. CH stretching (Alkene) causes the wide peak at 3283 cm-1 to shift to 3293 cm-1 when Fexofenadine is physically mixed with formulation excipients. Typical IR absorption peaks of Fexofenadine were present in the physical mixture of Fexofenadine with excipients used in formulation, with no shift in the major peaks and no additional peaks observed at 1703 cm-1 (C=O stretching (Amide)), 3664 cm-1 (N-H stretching), 2928 cm-1 (CH stretching (aromatic), and 832 cm-1 (CH bending (aromatic)). Thus it is evident that all the characteristic peaks that were present in the spectra of pure drugs replicated almost in the same region in the spectra of best formulations of Fexofenadine orodispersible tablet indicating that there is no significant interaction between the drugs and the excipients. The FTIR spectra of pure drug Fexofenadine and best formulations were shown in **figures 1 and 2**.

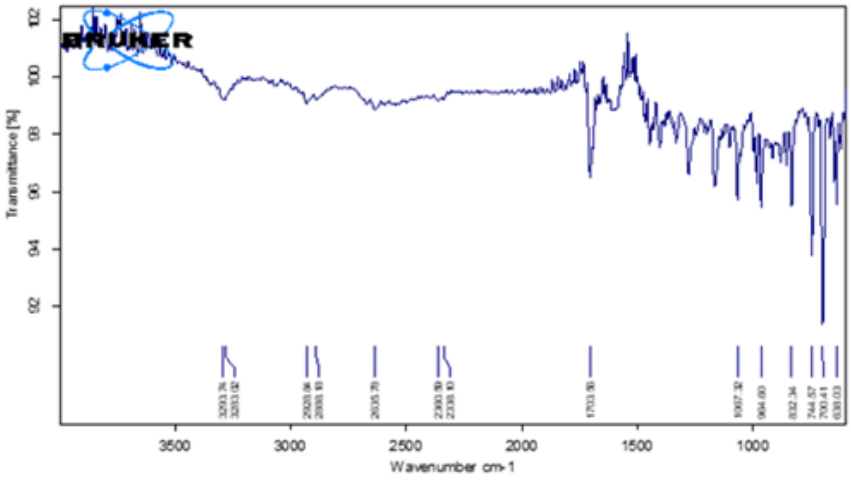

Fig. 1: FT-IR spectra of Fexofenadine pure drug

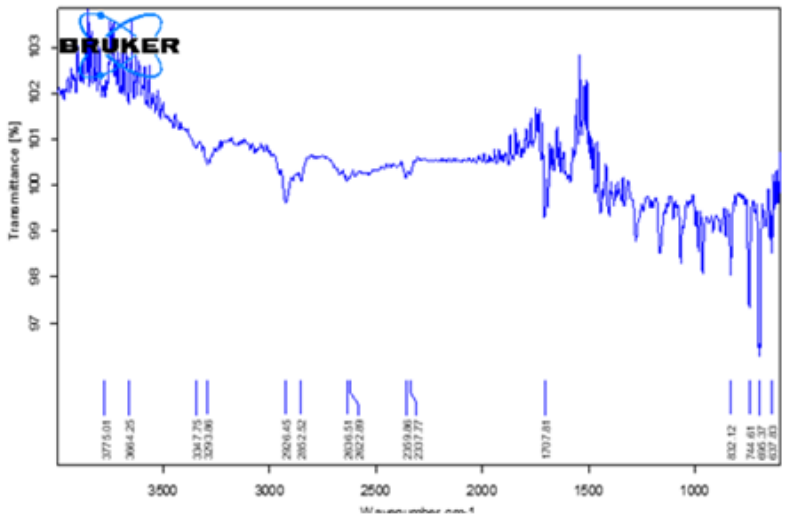

Fig. 2: FT-IR spectra of physical mixture of Fexofenadine with excipients

Drug-Excipient thermal Compatibility studies by DSC Research

By obtaining both a DSC thermogram of Fexofenadine and a physical combination of Fexofenadine with excipients, we were able to rule out the possibility of a thermal interaction between the drug and polymer. In this study, we compared the appearance of endothermic peaks in the physical mixture of the drug and excipients used to make the orodispersible tablet formulation to those seen in the pure drug. Both pure medication and the physical mixture showed an endothermic peak for Fexofenadine at 142.5ºC. The excipients crospovidone, croscarmellose sodium, and sodium starch glycolate caused an extra endothermic peak at 262ºC to appear in the DSC thermogram of the physical mixture. Since the DSC studies showed that the formulation required roughly the same amount of heat as the pure medication, and that the addition of other excipients to the drug did not result in thermal changes, the formulation is thermodynamically stable. Furthermore, there was no evidence of a transition from an endothermic to an exothermic peak. The DSC thermograms for Fexofenadine and the physical mixture of Fexofenadine and excipients used in the production of orodispersible tablets are shown in figures 3 and 4, respectively.

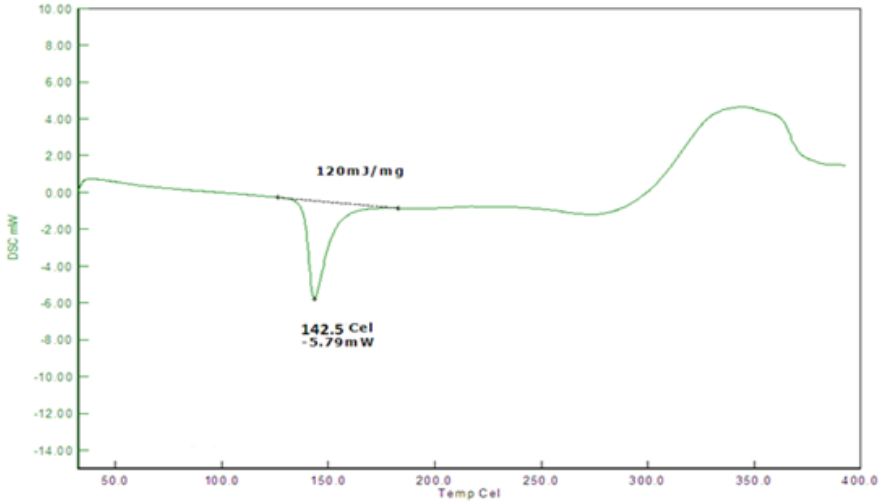

Fig. 3: DSC Thermogram of Fexofenadine pure drug

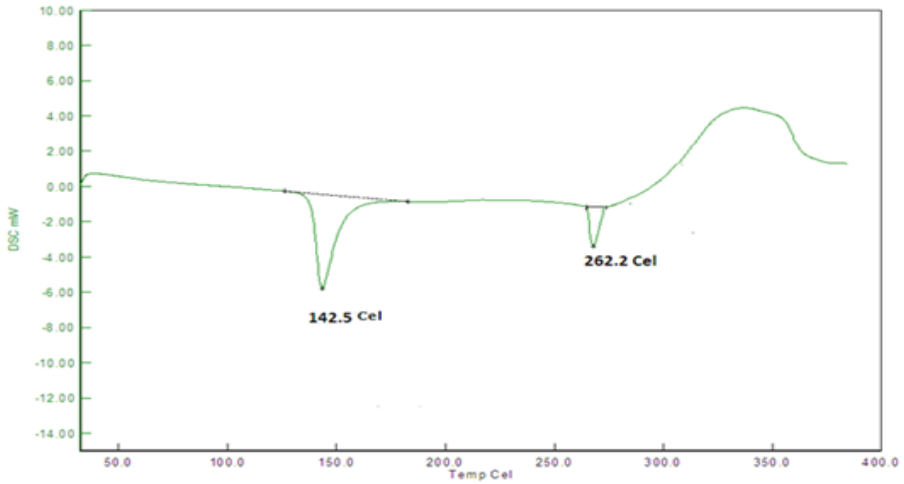

Fig. 4: DSC Thermogram of physical mixture of Fexofenadine with excipients

When it comes to making tablet granules, wet granulation is by far the most popular and beneficial method. A granule is a cluster of discrete particles held together by links of limited strength. The rate of drug dissolution and, hence, their total bioavailability in a heterogeneous formulation can be significantly affected by the granules' surface area, shape, hardness, and size. The granules' angle of repose after being combined with magnesium stearate and talc was less than 25 degrees, showing high granule flow characteristics across all formulations. The compressibility index (also called the Carr's index) is less than 16% across the board for all of the formulations, with the greatest values found in FORF1 and FORF6. The granules' flow properties are greatly improved with a low Carr's index value. A greater number of particles must be included in certain formulations because their bulk densities are higher than those of others. Based on the measured porosity percentage, the granules' packing could be anything from dense to loose.

Table 2: Evaluation of pre-compression parameters of formulated Fexofenadine Orodispersible granules

F. No.	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose (θ)	Carr's Index (%)	Hausner's ratio
$FORF_1$	0.312±0.02	0.363±0.04	21.50±0.18	14.04	1.16
$FORF_2$	0.344±0.01	0.386±0.03	19.60±0.20	10.88	1.12
$FORF_3$	0.351±0.02	0.388±0.03	18.85±0.17	09.53	1.10
$FORF_4$	0.319±0.02	0.356±0.03	19.65±0.18	10.39	1.12
$FORF_5$	0.326±0.03	0.355±0.04	18.80±0.10	08.17	1.08
$FORF_6$	0.329±0.02	0.377±0.03	20.52±0.14	12.73	1.15
$FORF_7$	0.332±0.02	0.369±0.03	20.42±0.17	10.02	1.11
$FORF_8$	0.343±0.02	0.378±0.01	20.60±0.13	09.26	1.10
$FORF_9$	0.329±0.02	0.361±0.02	18.92±0.11	08.86	1.10
$FORF_{10}$	0.343±0.03	0.371±0.04	18.15±0.13	07.54	1.08

All values are expressed as average± SD; (n=3)

All versions of Fexofenadine orodispersible tablets were found to have commendable average values for hardness, weight variation, friability, and thickness. (n=3) All data are presented as mean + standard

deviation. The common tablet defects of capping, chipping, and picking were not present.

The tablets ranged in thickness from 4.24±0.12 mm to 4.73±0.32 mm. The thickness was constant throughout all batches. Different formulas showed weight discrepancies between 3.660.31 and 4.220.52%. Due to falling within the allowable average percentage variation for tablet formulations with weights of 200mg, all formulations pass the official standard's test for weight uniformity.

The average hardness of the various Fexofenadine orodispersible tablet formulations was between 3.34 and 4.23 kg/cm^2. In the case of formulations FORF2, FORF4, FORF6, and FORF7, the hardness reduced as the superdisintegrant concentration increased.

Percent friability ranged from 0.50±0.02% to 0.65±0.01% across all formulations, with higher values observed at higher superdisintegrant concentrations. The percentage of friability in this investigation was well within the range considered acceptable. The drug content percentages for FORF1–FORF10 in the Fexofenadine orodispersible tablets ranged from 98.30±1.2% to 102.33±1.2%, which is well within the permitted range.

The disintegration times of each formulation were measured, and it was found that increasing the concentration of the superdisintegrant shortened the disintegration times. However, the hardness value was outside of the allowable limit at concentrations higher than 6%.

The wetting times for all the different formulations were between 60.42 and 87.51 seconds. Wetting times decrease with increasing superdisintegrant content, as seen in FORF2, FORF4, FORF6, FORF9, and FORF10 formulations. When compared to cross carmellose, cross povidone has a lower wetting time at high concentrations.

Water absorption ratios were measured, and they varied from 12.25±0.35 to 26.48±0.48 across all ten formulations (FORF1–FORF10). An increase in the superdisintegrant concentration, which may lead to a more porous formulation, raises the water absorption ratio. The physical and chemical characteristics of several lots of Fexofenadine orodispersible tablets are summarised in Table 3.

Table 3: Evaluation of Post-compression parameters of Fexofenadine Orodispersible tablets

F. code	Hardness (kg/cm^2)	Weight Variation (%)	Friability (% w/w)	Thickness (mm)	Drug content uniformity (%)	D_t (Sec)	Wetting time (Sec)	Water absorption ratio
$FORF_1$	4.23±0.4	3.74±0.41	0.52±0.02	4.73±0.32	99.64±1.1	135±0.35	87±0.51	12.25±0.35
$FORF_2$	3.52±0.3	3.82±0.25	0.65±0.01	4.60±0.20	98.30±1.2	112±0.44	74±0.33	14.62±0.28
$FORF_3$	3.98±0.3	3.96±0.22	0.50±0.02	4.53±0.11	98.72±1.3	125±0.52	87±0.22	12.40±0.67
$FORF_4$	3.34±0.4	3.73±0.21	0.65±0.02	4.64±0.12	99.21±1.1	95±0.36	74±0.32	20.47±0.42
$FORF_5$	4.19±0.6	4.05±0.40	0.50±0.04	4.72±0.12	101.79±1.3	146±0.55	85±0.44	14.65±0.38
$FORF_6$	3.45±0.3	4.22±0.52	0.64±0.02	4.46±0.10	101.12±1.2	130±0.66	74±0.20	21.28±0.45
$FORF_7$	3.36±0.4	3.66±0.31	0.62±0.03	4.24±0.12	102.33±1.2	98±0.28	76±0.42	20.48±0.27
$FORF_8$	3.42±0.2	4.15±0.20	0.63±0.02	4.36±0.14	98.52±1.4	85±0.54	62±0.24	25.36±0.42
$FORF_9$	3.38±0.4	4.21±0.32	0.62±0.02	4.28±0.12	99.21±1.2	94±0.47	61±0.33	25.16±0.56
$FORF_{10}$	3.76±0.5	3.96±0.21	0.61±0.03	4.39±0.15	99.62±1.2	81±0.60	60±0.42	26.48±0.48

All values are expressed as average± SD; (n=3)

Fexofenadine orodispersible tablets' *in vitro* drug release properties were studied for 45 minutes in phophate buffer pH 6.8 dissolution media using a USP type-II paddle type dissolution device. The dissolving rate might be maximised by increasing the concentration of the superdisintegrant to around 4 percent. The cumulative drug release from the 3% Crosscarmellose Sodium ($FORF_1$) formulation took 40 minutes, while the 4% Crosscarmellose Sodium ($FORF_2$) formulation took just 35 minutes. Comparison of drug release times between $FORF_3$ (containing 3% Cross povidone) and $FORF_4$ (containing 4% Cross povidone) reveals that the latter formulation (99.58% drug release in 35 minutes) is preferable. Formulation $FORF_5$, with only 3% sodium starch glycolate, released 99.63% of the medicine in 40 minutes, whereas formulation $FORF_6$, with 4% sodium starch glycolate, released 99.75% of the drug.

The dissolving profile is enhanced and drug release is nearly complete within 30 minutes when two superdisintegrants are used simultaneously at a total concentration of 4%. The medication in Formulation $FORF_{10}$ is released at a rate of greater than 99% within 30 minutes, which is the best initial release rate of all formulations. Formulation $FORF_{10}$ contains all three superdisintegrants at a concentration of 4% (2% Crosscarmellose, 1% Cross povidone, and 1% Sodium starch Glycolate). The dissolution characteristics of all formulations ($FORF_1$ to ($FORF_{10}$) are shown in Figure 4.6 and 4.7, as well as Table 4.7. In vitro studies of drug release kinetics:

Multiple kinetic release studies, including those using zero-order and first-order kinetic models, were conducted to validate the improved in vitro dissolving findings of the optimised formulation ($FORF_{10}$). Regression coefficients in the final tally were analysed. The results of the kinetic investigation of drug release performed *in vitro* are shown in Figures **figure 5 &6**.

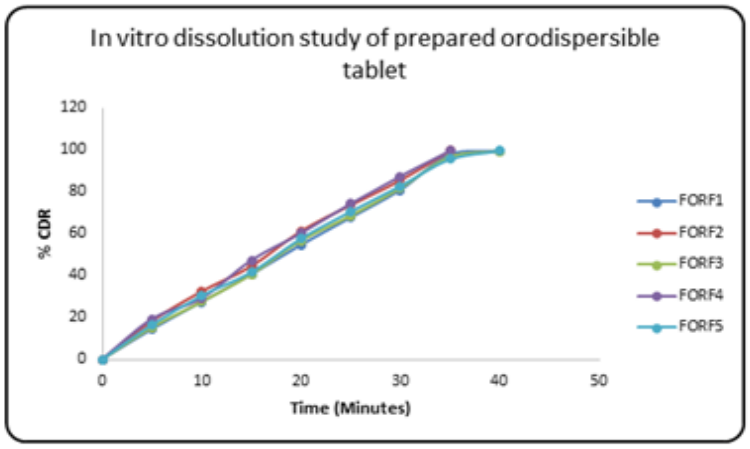

Fig. 5: *In vitro* drug release study of Fexofenadine Orodispersible tablet formulations ($FORF_1$ to $FORF_5$)

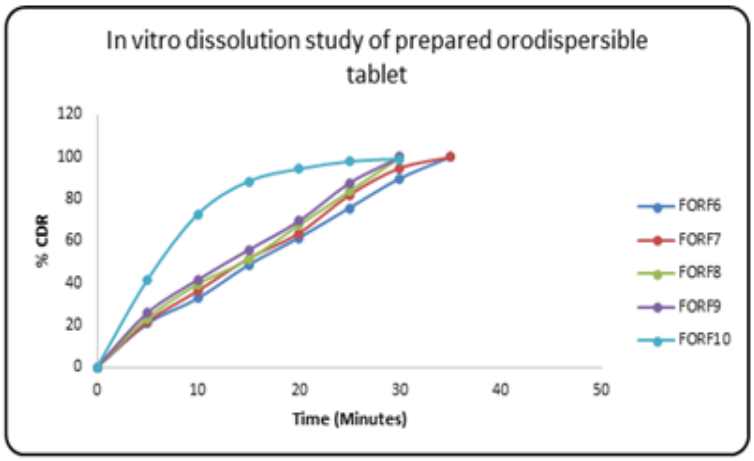

Fig. 6: *In vitro* drug release study of Fexofenadine Orodispersible tablet formulations ($FORF_6$ to $FORF_{10}$)

The formulation $FORF_{10}$ was selected for drug release kinetic and mechanism of drug release tests because it had the best dissolving profile. Using *in vitro* dissolving data for Fexofenadine orodispersible tablets ($FORF_{10}$), figures 7 and 8 were generated by fitting the data to several kinetic models, including zero order and first order equations. Since the first-order kinetic curve showed the highest regression value in this study, it was concluded that the rate of drug release from the Fexofenadine orodispersible pill followed first-order kinetics.

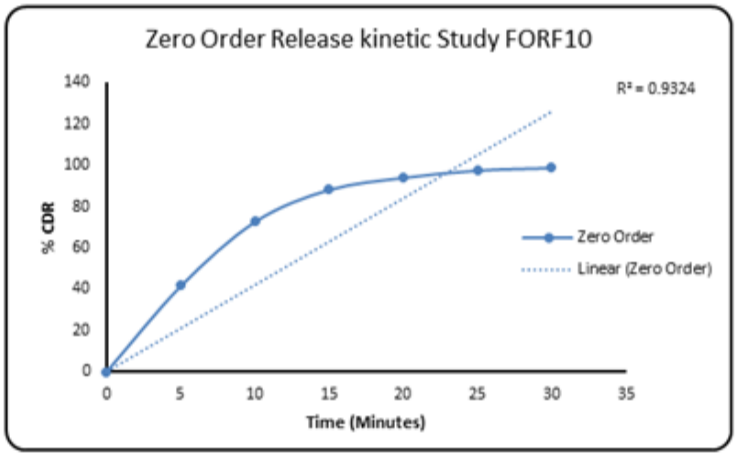

Fig. 7: Zero order release kinetic study of best formulation $FORF_{10}$

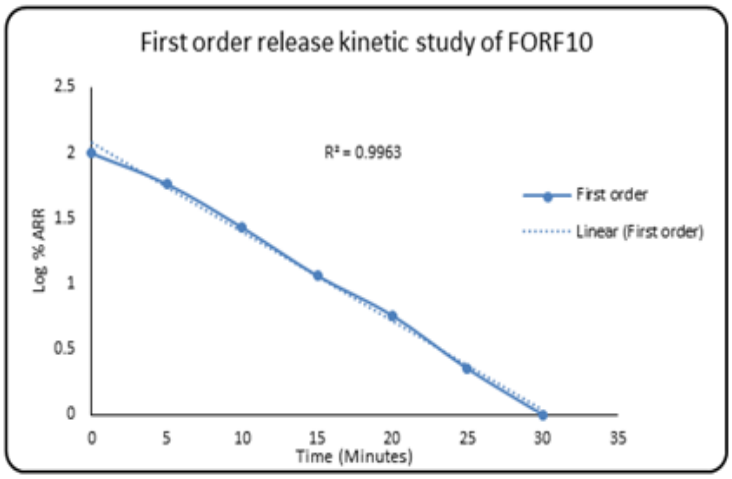

Fig. 8: First order release kinetic study of best formulation $FORF_{10}$

Table 4: Regression values of *in vitro* release kinetic study best formulation ($FORF_{10}$)

Formulation	Zero order (R^2 value)	1st order (R^2 value)	Remarks
$FORF_{10}$	0.9324	0.9963	A first order release kinetic model was Followed

Fexofenadine Orodispersible Tablets, Optimised Formulation ($FORF_{10}$), were selected for Accelerated Stability Testing. The improved formulation ($FORF_{10}$) of Fexofenadine orodispersible tablets did not significantly alter the drug release characteristics and physicochemical properties when tested *in vitro*. According to *in vitro* dissolution trials, more than 90% of the medicine was still present in the body after 90 days of exposure to an accelerated stress environment. After placing the orodispersible Fexofenadine ($FORF_{10}$) tablets in accelerated short-term storage settings, it was discovered that they maintained their stability for at least 3 months. The comparative physicochemical properties at different interval of time are presented in **table 5** and comparative release profile has been represented in **figure 9.**

Table 5: Comparative physicochemical properties of $FORF_{10}$ at accelerated conditions (40 °C ± 2 °C/ 75% ± 5% RH)

Tablet Properties	Initial	30 days after	Within 60 days	Within 90 days
Physical Surfacing	A smooth, concave surface that is light white and free of fractures	No Change	No Change	No Change
Weight variation	3.96±0.21	4.07±0.32	4.22±0.41	4.30±0.53
Hardness	3.76±0.5	3.58±0.30	3.46±0.21	3.35±0.42
Friability	0.61±0.03	0.69±0.02	0.71±0.02	0.74±0.03
Disintegration time {D_t (Sec)}	81±0.60	85±0.26	90±0.51	95±0.42
Wetting time (Sec)	60±0.42	63±0.18	67±0.42	72±0.30
Drug content	99.62±1.2	98.54±1.13	96.68±1.29	93.77±1.21

All values are expressed as mean± SD; (n=3)

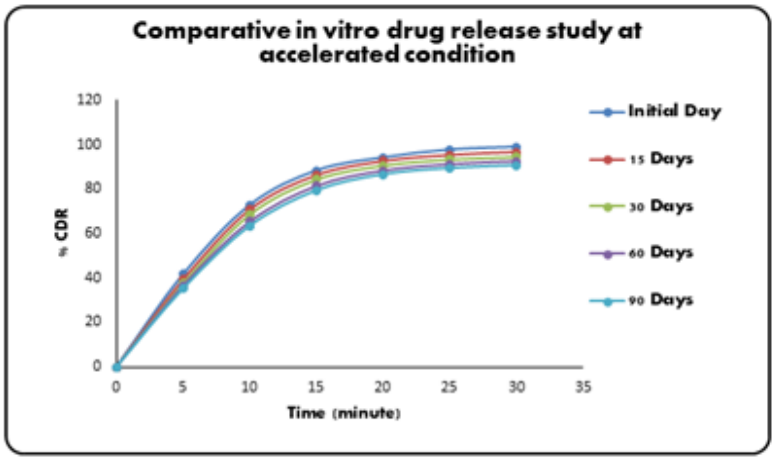

Fig. 9: *In vitro* release study of best formulation ($FORF_{10}$) at stressed condition

CONCLUSION:

In this study, an efficient method for making fexofenadine orodispersible pills was developed. The most challenging aspect of this project was analysing the effect of the superdisintegrants Crosscarmellose Sodium, Cross povidone and Sodium starch Glycolate on the *in vitro* release rate of an orodispersible Fexofenadine tablet. The orodispersible drug delivery device showed promise as a means of treating severe conditions in males with allergy symptoms. By avoiding rapid metabolism, rapid drug release was accomplished. FTIR and DSC analyses show that the medication and excipients are stable in the formulation and are compatible with one another. Wet granulation methods were employed to create Fexofenadine Orodispersible granules, and their examination showed that all precompression parameters satisfied acceptance norms, attesting to their superior flow properties. Measurements taken after compression reveal no unacceptable trends in any quality attribute, including thickness, hardness, friability, weight variation, or crumbling. All formulations used lactose, a hydrophilic diluent, to enhance the drug release profile. The drug is released at a rate of more than 99% within 30 minutes with the best initial release rate in Formulation $FORF_{10}$, which contains all three superdisintegrants at a concentration of 4% (2% Crosscarmellose, 1% Cross povidone, and 1% Sodium starch Glycolate). A more favourable drug release profile was also achieved by combining all three superdisintegrants. Faster drug release could be achieved by increasing the superdisintegrant concentration, however this came at the expense of the formulation's hardness and friability. The formulation FORF10 was selected for drug release kinetic and mechanism of drug release tests because it had the best dissolving profile. Anomalous diffusion associated with erosion was identified as the drug release mechanism for Fexofenadine orodispersible tablet because it provided the highest regression value. Stability experiments were carried out according to ICH recommendations, and it was determined that a selected $FORF_{10}$ formulation could be stored at 40°C/75% RH for up to 3 months with only a slight alteration in the formulation's physicochemical and drug release characteristics. Friability, hardness, weight variation, thickness, and medication content were some of the tablet physical qualities compared. Both before and after an expedited stability investigation, the improved fresh formulation ($FORF_{10}$) was tested in vitro. The criteria for stability have been met by the test. Fexofenadine orodispersible tablets are a promising new drug delivery system because they release the medication rapidly through fast pass metabolism and are useful for treating acute diseases in men with symptoms of an enlarged prostate gland. More clinical research is required to see if this method is effective for patients with allergy conditions.

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