Development and Evaluation of Rimegepant fast Dissolving Tablets

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ABSTRACT :
The present study was aimed at the development and evaluation of fast dissolving tablets of Rimegepant for the rapid treatment of migraine. Fast dissolving tablets were formulated to improve patient compliance and provide rapid onset of therapeutic action. Preformulation studies, including organoleptic evaluation, melting point determination, solubility studies, and Fourier Transform Infrared (FTIR) spectroscopy, were performed to assess the physicochemical properties and compatibility of the drug with excipients. The standard calibration curve of Rimegepant was prepared in phosphate buffer pH 6.8 at 278 nm and was found to obey Beer-Lambert's law with an R^2 value of 0.997.The fast dissolving tablets were prepared by direct compression and evaluated for pre-compression parameters such as bulk density, tapped density, compressibility index, Hausner ratio, and angle of repose. The prepared tablets were further evaluated for weight variation, thickness, hardness, friability, drug content, disintegration time, wetting time, and in vitro drug release. All formulations exhibited satisfactory flow properties and acceptable tablet characteristics. Among the formulations, F4 showed the best performance with a drug content of 85.98%, disintegration time of 26 seconds, friability of 0.25%, and cumulative drug release of 98.49% within 60 minutes.Stability studies of the optimized formulation were carried out for 90 days under different storage conditions, and no significant changes were observed in physical appearance or drug release profile. The results demonstrated that the optimized formulation possessed satisfactory physicochemical properties, rapid disintegration, enhanced dissolution, and good stability. Therefore, the developed Rimegepant fast dissolving tablets may serve as a promising dosage form for the effective management of migraine.
Keywords: Rimegepant, Gastro retentive drug delivery system, Polymers,Sodium Starch Glycolate, In vitro drug release studies.

I.INTRODUCTION

Fast dissolving tablets (FDTs), also referred to as orally disintegrating tablets (ODTs), mouth dissolving tablets, or rapid disintegrating tablets, have emerged as an innovative oral dosage form designed to disintegrate or dissolve rapidly in the oral cavity, typically within seconds, without the need for water. The United States Food and Drug Administration (USFDA) defines orally disintegrating tablets as solid dosage forms containing medicinal substances that disintegrate rapidly, usually within 30 seconds, when placed upon the tongue. The rapid disintegration of FDTs results in improved drug dissolution, faster absorption, and enhanced bioavailability, especially for drugs that undergo extensive first-pass metabolism. Fast dissolving tablets offer several advantages over conventional oral dosage forms. The most notable benefit is improved patient compliance, particularly among populations such as pediatric, geriatric, psychiatric, and bedridden patients, as well as patients suffering from nausea, vomiting, or motion sickness. FDTs are also advantageous in emergency conditions where immediate drug action is required, such as allergic reactions, migraines, epileptic seizures, and pain management. Furthermore, these dosage forms reduce the risk of choking and enhance convenience during travel or in situations where access to water is limited.From a pharmacokinetic perspective, FDTs may enhance the onset of action by allowing partial drug absorption through the oral mucosa, thereby bypassing hepatic first-pass metabolism. This is particularly beneficial for drugs with poor oral bioavailability due to extensive metabolism in the liver. Additionally, rapid tablet disintegration increases the surface area available for dissolution, which can significantly improve the dissolution rate of poorly water-soluble drugs.

II. EXPERIMENTAL WORK

MATERIALS

Rimegepant was procured from Synpharma Research Labs, Hyd, Croscaramellose, Sodium starch glycolate, Magnesium stearate , Talc , Lactose , Aspartame and Micro crystalline cellulose were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY

Fourier Transform Infrared Spectroscopy (FTIR)

Fourier Transform Infrared (FTIR) spectroscopy was performed for pure Rimegepant, individual excipients, and physical mixtures of Rimegepant with excipients. A small quantity of the sample (approximately 1–2 mg) was accurately weighed and triturated with dry, IR-grade potassium bromide (KBr) in a ratio of 1:100 to obtain a uniform mixture. The mixture was then compressed using a hydraulic press to form a thin, transparent KBr pellet. The prepared pellet was placed in the sample holder of the FTIR spectrophotometer, and the spectrum was recorded over a wavelength range of 4000–400 cm^{-1} at room temperature. The same procedure was followed for the pure drug and physical mixtures. The obtained spectra were analyzed for the presence of characteristic functional group peaks of Rimegepant such as C=O, N–H, C–N, and aromatic C–H stretching vibrations. The spectra of the physical mixtures were compared with that of the pure drug to detect any shifts, disappearance, or formation of new peaks, which would indicate possible chemical interactions.

Table-1: Formulation table of fast dissolving tablets

S.No	Ingredient	F-1	F-2	F-3	F-4
1	Rimegepant	75	75	75	75
2	Croscaramellose	10	20	-	-
3	Sodiumstarch glycolate	-	-	10	20
4	Lactose	95	85	95	85
5	Aspartame	5	5	5	5
6	Magnesium stearate	3	3	3	3
7	Talc	2	2	2	2
8	MCC	10	10	10	10
9	Total	200	200	200	200

Preparation technique

Direct compression method:

Preparation of Rimegepant Fast Dissolving Tablets

Accurately weighed quantities of Rimegepant and excipients were passed through sieve no. 60 to ensure uniform particle size. The drug was mixed with diluents and superdisintegrants using geometric dilution. Lubricants such as magnesium stearate and talc were added and blended gently. The final blend was compressed into tablets using a rotary tablet compression machine with suitable punches.

EVALUATION STUDIES

1. Angle of Repose

The angle of repose was determined by the funnel method. The powder blend was allowed to flow through a funnel onto a flat surface, forming a conical heap. The height (h) and radius (r) of the heap were measured, and the angle of repose (θ) was calculated using the formula:

$\tan\theta = h/r$

Lower values of angle of repose indicate better flow properties of the powder blend.

2. Bulk Density

Bulk density was determined by gently pouring a known weight of the powder blend into a graduated measuring cylinder without tapping. The initial volume was recorded, and bulk density was calculated as:

Bulk density= Mass of powder /Bulk volume

3. Tapped Density

Tapped density was measured by tapping the cylinder containing the powder blend using a tapped density apparatus until a constant volume was obtained. The tapped density was calculated using the formula:

Tapped density = Mass of powder/ Tapped volume

4. Carr's Compressibility Index

Carr's index indicates the compressibility of the powder blend and was calculated using the equation:

Carr's Index (%) = Tapped density – Bulk density /Tapped density × 100

5. Hausner's Ratio

Hausner's ratio was calculated to assess inter-particle friction using the formula:

Hausner's ratio= Tapped density/ Bulk density

Evaluation of tablet

Weight variation

The weight variation test is performed to ensure uniformity of tablet weight. Twenty tablets are randomly selected from the batch and weighed individually using an analytical balance. The average weight is calculated, and the deviation of each tablet from the mean is determined. Tablets should comply with pharmacopoeial limits, which vary according to tablet size.

Thickness

The thickness of tablets is measured using a vernier caliper or screw gauge. Ten tablets are selected at random, and the thickness of each tablet is measured at the center. The average thickness is calculated to ensure uniformity, as significant variation can affect packaging and appearance.

Hardness

The hardness test evaluates the mechanical strength of tablets. Ten tablets are randomly selected and tested using a tablet hardness tester, such as Monsanto or Pfizer type. The force required to break each tablet is recorded, and the average hardness is calculated. Adequate hardness ensures that tablets can withstand handling while still allowing proper disintegration.

Friability

The friability test measures the ability of tablets to resist abrasion during handling and transportation. Ten tablets are weighed and placed in a Roche friabilator, which is rotated at 25 rpm for four minutes. After dedusting, the tablets are reweighed, and friability is calculated as the percentage weight loss. Tablets with weight loss less than 1% are considered acceptable, indicating good mechanical resistance.

The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100$$

Where,

% F = friability in percentage

Wo = Initial weight of tablet

W = weight of tablets after revolution

Drug Content

The drug content (assay) test is performed to determine the amount of active pharmaceutical ingredient (API) present in a tablet and to ensure uniformity of dosage. Ten tablets are randomly selected from the batch and accurately weighed. The tablets are then powdered and a quantity equivalent to the label claim of the drug is taken. The powder is dissolved in a suitable solvent or buffer, depending on the solubility of the drug, and the solution is filtered to remove insoluble excipients. The filtrate is diluted to a known volume, and the drug concentration is determined using a validated analytical method such as UV-visible spectrophotometry or HPLC. The measured drug content of each tablet is compared with the label claim, and the percentage content is calculated. According to pharmacopoeial standards, the drug content should be within ±5% of the labeled amount for conventional tablets, ensuring dose uniformity and quality of the batch.

Wetting time

The wetting time test is used to evaluate the water absorption rate of a tablet, which is particularly important for fast-dissolving and orally disintegrating tablets, as it affects the disintegration and dissolution rate. In this test, a small piece of tissue paper is placed in a Petri dish containing 6–10 mL of water. A tablet is carefully placed on the tissue paper, and the time taken for the tablet to become completely wet and for the water to reach

the upper surface of the tablet is recorded using a stopwatch. The wetting time is indicative of the tablet's ability to absorb moisture and start disintegration in the oral cavity. A shorter wetting time generally correlates with faster disintegration and improved patient compliance for fast-dissolving tablets.

In Vitro Disintegration Test

The in vitro disintegration test is performed to determine the time required for a tablet to break down into smaller particles in a specified liquid medium under standardized conditions. The test is carried out using a disintegration test apparatus, which consists of a basket-rack assembly that moves up and down in a beaker containing the disintegration medium, usually distilled water, simulated gastric fluid (pH 1.2), or phosphate buffer (pH 6.8) at 37 ± 2 °C to mimic body conditions. A tablet is placed in each of the six tubes of the apparatus, and the time taken for the tablet to completely disintegrate into particles that pass through the mesh of the basket is recorded. This time, known as the disintegration time, is an important quality parameter, especially for immediate-release and fast-dissolving tablets, as it predicts the onset of drug release and bioavailability. Tablets should meet pharmacopoeial limits, and shorter disintegration times generally indicate faster drug availability in the gastrointestinal tract.

In- Vitro Release study

The in vitro drug release study is performed to evaluate the rate and extent of drug release from a tablet in a controlled environment, which helps predict its bioavailability. The test is carried out using a dissolution apparatus such as USP Apparatus I (basket) or II (paddle), with a suitable dissolution medium like distilled water, simulated gastric fluid (pH 1.2), or phosphate buffer (pH 6.8) maintained at 37 ± 0.5 °C. The tablet is placed in the dissolution vessel containing the medium, and the apparatus is operated at a specified rotation speed (usually 50–100 rpm). At predetermined time intervals, samples of the dissolution medium are withdrawn, filtered, and analyzed for drug content using a UV-visible spectrophotometer, HPLC, or other validated analytical method. Fresh medium of equal volume is replaced after each sampling to maintain sink conditions. The percentage of drug released at each time point is calculated, and a drug release profile is plotted. This study provides essential information on the dissolution kinetics and release behavior of the tablet, ensuring consistent therapeutic efficacy and batch-to-batch uniformity.

Stability studies

Stability studies are conducted to evaluate the effect of environmental factors such as temperature, humidity, and light on the quality, efficacy, and shelf life of a pharmaceutical formulation. Tablets are stored under controlled conditions, typically at room temperature (25 °C/60% RH), accelerated conditions (40 °C/75% RH), or refrigerated conditions (2–8 °C), as per ICH (International Council for Harmonisation) guidelines. Samples are withdrawn at predetermined time intervals, such as 0, 1, 3, and 6 months, and evaluated for physical appearance, hardness, friability, disintegration time, drug content, and in vitro drug release. Any significant changes in these parameters indicate instability of the formulation. Stability studies are crucial for determining the shelf life, packaging requirements, and storage conditions of the product, ensuring that it remains safe, effective, and of high quality throughout its intended period of use.

III. RESULTS AND DISCUSSION

Fourier Transformation Infra-red (FTIR) analysis:

Table-2: Characteristic Peaks and frequency of drug

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3500	3783.48
2	OH Bending	1500-1000	1204.65
3	C-H stretching	3000-2500	2839.31
4	C=O stretching	2000-1500	1599.93

Table-3: Characteristic Peaks of drug and excipients

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3500	3907.91
2	OH Bending	1500-1000	1481.39
3	C-H stretching	3000-2500	2838.91

4	C=O stretching	2000-1500	1635.73

The FTIR analysis confirms that the drug maintains its structural integrity in the formulation and that the excipients are physically compatible with the drug, suggesting that they are suitable for use in tablet or other solid dosage forms.

Evaluation studies

Pre compression parameters
Characterization of Formulation

Table-4: Pre compression parameters of Rimegepant Fast dissolving tablets

S.No	Bulk density	Tappeddensity	Compressibility index	Hausner ratio	Angle of repose(0)
F1	0.506	0.603	16.08	1.19	27^0c
F2	0.511	0.615	16.91	1.2	28^0c
F3	0.502	0.61	17.7	1.21	30^0c
F4	0.516	0.618	16.5	1.19	29^0c

Overall, the pre-compression evaluation indicates that the powder blends of all Rimegepant formulations have satisfactory flow and compressibility, which is essential for producing tablets with uniform weight, content, and mechanical strength. Formulations F4 and F1, with slightly better compressibility and flow properties, were expected to perform optimally during tableting.

Table-5: Evaluation parameters of Rimegepant Fast dissolving tablets

F. No.	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug Content (%)	Disintegration time(sec)	Wetting time (sec)
F1	201	2.1	3.71	0.35	76.98	43	125
F2	199	1.9	3.69	0.37	79.88	56	130
F3	200	2.5	3.55	0.29	80.12	41	129
F4	200	2.3	3.50	0.25	85.98	26	116

The pre- and post-compression evaluation of all four formulations (F1–F4) revealed satisfactory weight, thickness, hardness, friability, drug content, disintegration time, and wetting time, indicating consistent formulation quality. The weight variation of all tablets ranged from 199–201 mg, which is within acceptable pharmacopoeial limits, suggesting uniformity in die filling and content uniformity. The thickness varied from 1.9–2.5 mm, reflecting minor differences in compression force and excipient composition, but all were acceptable for proper handling and packaging.The hardness values ranged from 3.50–3.71 kg/cm², indicating that the tablets possessed adequate mechanical strength to withstand handling, while still allowing rapid disintegration. Correspondingly, the friability values were low (0.25–0.37%), well below the acceptable limit of 1%, confirming the tablets' resistance to abrasion and mechanical stress.The drug content ranged from 76.98–85.98%, with F4 showing the highest content, likely due to optimal blending and compression, indicating good uniformity of the active ingredient across formulations. The disintegration times varied from 26–56 seconds, with F4 demonstrating the fastest disintegration (26 sec), suggesting the effectiveness of superdisintegrants and excipient selection in promoting rapid breakdown in the oral cavity. Similarly, the wetting times ranged from 116–130 seconds, reflecting the tablet's ability to absorb moisture, with shorter times correlating with faster disintegration.Overall, F4 emerged as the optimized formulation, showing high drug content, fastest disintegration, acceptable hardness, and low friability, making it most suitable for achieving rapid onset of action as required for fast-dissolving Rimegepant tablets. Minor variations among other formulations can be attributed to differences in excipient composition, compression force, and superdisintegrant concentration.

Drug release studies
Table-6: Drug release studies of all formulations

Time (min)	F1	F 2	F 3	F 4
0	0	0	0	0
5	25.39	27.43	26.46	29.81
10	35.71	36.59	34.97	41.25
15	48.32	47.81	46.35	59.86
30	69.83	70.25	65.34	69.81
45	81.50	82.35	79.58	82.33
60	94.55	95.68	93.15	98.49

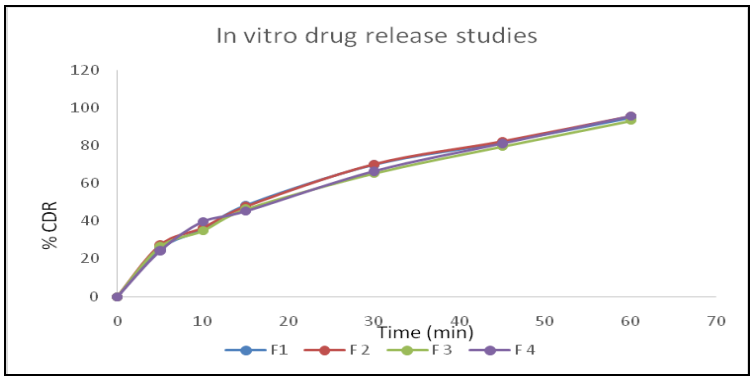

Fig-1: Dissolution Profile of F1 to F4 formulations

Among the formulations, F4 exhibited the highest cumulative release (98.49% at 60 minutes), suggesting that the optimization of its excipient composition resulted in superior disintegration and dissolution characteristics.The overall release profiles indicate that all formulations are suitable for immediate release, with differences in the early phase release likely due to variations in superdisintegrant concentration, binder type, and tablet hardness. This rapid and consistent drug release ensures that Rimegepant can achieve therapeutically effective plasma levels quickly, which is critical for the acute treatment of migraine attacks.

Stability studies

Table-7: Stability Studies of Optimized Formulation

S.No	Time in days	Physical changes	Mean % drug release		
			Fast dissolving tablet		
			25^0C/60%	30^0C/75%	40^0C/75%
1	01	No Change	98.49	98.49	98.49
2	30	No Change	97.86	97.53	97.60
3	60	No Change	96.35	96.72	96.37
4	90	No Change	95.68	95.69	95.33

The stability study of the optimized Rimegepant fast-dissolving tablet formulation was carried out at different temperature and humidity conditions (25 °C/60% RH, 30 °C/75% RH, and 40 °C/75% RH) over a period of 90 days, and both physical appearance and in vitro drug release were monitored. As shown in the table, the tablets exhibited no noticeable physical changes throughout the study period, indicating that the formulation retained its integrity, shape, and color under the tested conditions.

CONCLUSION

The present study successfully developed and evaluated fast dissolving tablets of Rimegepant for the rapid management of migraine. Preformulation studies, including organoleptic evaluation, melting point determination,

solubility analysis, FTIR compatibility studies, and standard calibration curve preparation, confirmed the purity, identity, and suitability of the drug for formulation development.The prepared powder blends exhibited satisfactory flow properties and compressibility characteristics, indicating their suitability for tablet compression. All formulations (F1–F4) showed acceptable physical characteristics, including weight variation, thickness, hardness, friability, drug content, disintegration time, and wetting time. Among the formulations, F4 demonstrated the best overall performance, exhibiting the highest drug content (85.98%), the shortest disintegration time (26 seconds), acceptable hardness (3.50 kg/cm²), and the lowest friability (0.25%).In vitro dissolution studies revealed that formulation F4 achieved the highest cumulative drug release of 98.49% within 60 minutes, indicating efficient drug release and rapid availability of the drug. Stability studies conducted under different storage conditions for 90 days showed no significant changes in physical appearance or drug release profile, confirming the stability of the optimized formulation.Therefore, it can be concluded that formulation F4 is the optimized fast dissolving tablet formulation of Rimegepant and has the potential to provide rapid drug release, improved patient compliance, and effective therapeutic action for the acute treatment of migraine. Further in vivo studies may be carried out to establish its clinical performance and bioavailability.

REFERENCES

1. Litchenckert, S.; Lurdgren, C. and Ferno, O.; "Chewable smoking substitute composition", US Patent, 1975, 3901248.
2. Lowenthal, W.; "Journal of Pharmaceutical Sciences", 61, 1972, pp 1695
3. Siegel, S.; "Journal of Pharmaceutical Science", 51, 1962, pp 1069. Allen, L.V., Wang, B. and Davis, J.D.," Rapidly Dissolving Tablet", **US patent No.,** US5807576, 1998. , Bhaskaran, S. and Narmada, G.V., Fast Dissolving drug delivery systems: A brief overview, **Indian Pharmacist**, 2002, 1 (2), 9-12.
4. Devrajan, P.V, Gore, S.P., Fast Dissolving Tablets: The Future Compaction, Express Pharma Pulse, 2000: 23, 7(1), 16.
5. Kuchekar, B.S., Badhan, A.C., Mahajan, H.S., Fast Dissolving drug delivery systems: A brief overview, Pharma Times, 2003, 35, 7-9.
6. Reddy, L. H., Ghose, B. and Rajneesh, Fast Dissolving drug delivery systems: A brief overview, Indian J. Pharm. Sci.**, 2002**, 64(4): 331- 336.
7. Parakh, S.R. and Gothoskar, A.V., Fast Dissolving drug delivery systems: A brief overview, **Pharma. Tech.**, 2003, 92- 100.
8. Indian Pharmacopoeia, Ministry of Health and Family Welfare, Govt. of India, Vol 1, 342.
9. LachmmanL,LibermanHA,KonigJl.The theory & practice of industrial pharmacy,3rdEdn,Vargheese publishing house, Bombay,1991:297-300.
10. G.r Chatwal textbook of pharmaceutical inorganic chemistry.
11. Subrahmanyamcvs and thimmasettyj.Laboratory manual of physical pharmaceutics,1 stEdn, vallabhprakasham ,Delhi;2002:24-25
12. Siji Rose raj formulation and evaluation of mouth dissolving famotidine tablet, International Journal of PharmTechResearch;Oct-Dec2009, Vol. 1 Issue 4, p1251.
13. SeemaFarheen "formulation and evaluation of fast dissolving tablets of lansoprazole" world journal of pharmacy and pharmaceutical sciences, Volume 6, Issue 7, 979-1002.
14. MangeshMachhindranathSatpute, Formulation and in vitro evaluation of fast dissolving tablets of metoprolol tartrate, Brazilian Journal of Pharmaceutical Sciences vol. 49, n. 4, oct./dec., 2013.
15. DivyaVishwakarma., Formulation and Evaluation of Metoprolol Tartrate Fast Dissolving Tablet, Am. J. PharmTech Res. 2012; 2(4) ISSN: 2249-3387.
16. B P Patel Formulation and Evaluation of Mouth Dissolving Tablets of Cinnarizine, Indian J Pharm Sci. 2010 Jul-Aug; 72(4): 522–525.