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# FORMULATION AND CHARACTERIZATION FAST DISSOLVING ORAL WAFERS OF AN ANTIMIGRAINE DRUG RIMEGEPANT

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## ABSTRACT

The present study focuses on the formulation and evaluation of fast-dissolving oral wafers of Rimegepant, an anti-migraine drug aimed at providing rapid relief in acute migraine conditions. Rimegepant, a calcitonin gene-related peptide (CGRP) receptor antagonist, suffers from poor water solubility and a slower onset when administered orally in conventional forms. To overcome these limitations, oral wafers were developed using suitable film-forming agents and superdisintegrants to ensure rapid disintegration and drug release in the oral cavity without the need for water. Nine formulations (F1–F9) were prepared and evaluated for physical appearance, weight variation, surface pH, folding endurance, moisture content, drug content, disintegration time, and *in-vitro* drug release. Among all, formulation F7 demonstrated the best characteristics, with a disintegration time of 15 ± 2 seconds**,** drug content of 99.45 ± 0.15%**,** and cumulative drug release of 98.85% within 5 minutes. These results suggest that fast-dissolving oral wafers of Rimegepant could serve as a patient-friendly, effective, and fast-acting alternative for migraine management.

**Keywords:** Rimegepant, Fast-dissolving oral wafers, Migraine, CGRP antagonist, Disintegration time, Rapid drug release, Oral drug delivery.

## INTRODUCTION

Migraine is a common and debilitating neurological condition characterized by recurrent episodes of severe headache, often accompanied by nausea, vomiting, and heightened sensitivity to light and sound. These symptoms can significantly affect daily activities and quality of life. During migraine attacks, conventional oral drug delivery is often compromised due to difficulty in swallowing and delayed gastric emptying caused by nausea and vomiting.

Fast dissolving oral wafers (FDOWs) represent an innovative drug delivery system that offers a convenient alternative to conventional tablets and capsules, particularly for patients who experience difficulty in swallowing or require rapid drug action. These wafers dissolve instantly in the mouth without the need for water, providing faster onset of action and improved patient compliance (Arya *et al.*, 2010; Mahajan *et al.*, 2014).

Rimegepant, a calcitonin gene-related peptide (CGRP) receptor antagonist, is approved for the treatment of acute migraine. It provides targeted relief by blocking CGRP receptors implicated in migraine pathophysiology, with fewer cardiovascular side effects compared to traditional triptans (Croop *et al.*, 2019). Despite its efficacy, the oral bioavailability of Rimegepant may be reduced during migraine

episodes due to impaired gastrointestinal function (Cilurzo *et al.*, 2010).

In this context, the present study focuses on the formulation and characterization of Rimegepant-loaded fast dissolving oral wafers using hydrophilic film-forming polymers and suitable excipients. The goal is to develop a dosage form with rapid disintegration, uniform drug content, and efficient in vitro drug release to ensure effective and patient-friendly migraine management.

## MATERIALS AND METHODS

### Materials

Rimegepant and excipients such as sodium starch glycolate, croscarmellose sodium, guar gum, citric acid, and talc were procured from Loba Chemie, Mumbai. pH adjusters like disodium hydrogen phosphate, di-potassium hydrogen orthophosphate, and hydrochloric acid were sourced from S.D. Fine Chem. Ltd. Solvents (methanol, ethanol, chloroform) came from Qualigens Fine Chemicals, and magnesium stearate was obtained from Jiangsu Huaxi International.

### Methods

### Formulation development of oral wafers of Rimegepant

### Solvent casting technique

Rimegepant containing fast dissolving wafers were fabricated by the solvent casting method. The optimized amount of Polymers was dissolved in 5ml of water and stirrer continuously for 1 hour, optimized amount of drug was dissolved in 95% ethanol and then added to the polymeric solution and kept on sonication for proper dispersion. Polymeric solution was stirred for 30 min using magnetic stirrer and was kept in undisturbed condition till the entrapped air bubbles were removed. The aqueous solution was casted in a glass moulds having 15 x 5$cm^2$ area and was dried at controlled room temperature (25°-30°C, 45 %RH). The wafers took approximately 48 hr to dry at controlled room temperature. The dried wafers were carefully removed from the glass plates and were cut into size 2.5*2.5$cm^2$) required for testing. The wafers were stored in air tight plastic bags till further use (Boateng *et al.*, 2010).

### Evaluation of prepared wafers

### Thickness

Three random wafers were selected from each batch and the thickness was measured at three different places using a vernier caliper (El-Feky *et al.*, 2018).

### Weight uniformity

For each formulation, three randomly selected patches were used. For weight variation test, 10 wafers from each batch were weighed individually by digital electronic balance and the average weight and relative standard deviation was calculated (Matthews *et al.*, 2006).

### Surface pH Determination

The surface pH of fast dissolving wafers was determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may cause irritation to the oral mucosa, it is important to keep the surface pH as close to neutral as possible (Boateng *et al.*, 2012). The wafer to be tested was placed in a petridish and was moistened with 0.2 ml of distilled water. The electrode of pH meter (Electronic India) was placed on the surface of wafer to determine the surface pH.

### Folding Endurance

This was determined by repeatedly folding one wafers at the same place until it broke. The number of times the wafers could be

folded at the same place without breaking cracking gave the value of folding endurance.

**Percentage of Moisture Content**

The wafers were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs. Individual wafers were weighed repeatedly until they showed a constant weight. The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight.

$$\% \text{ Moisture Content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \text{x } 100$$

**Drug Content Analysis**

The patches (n=3) of specified area were taken into a 10 ml volumetric flask and dissolved in methanol and volume was made up with 10 ml methanol. Subsequent dilutions were made and analyzed by UV spectrophotometer at 264nm.

**Disintegrating time**

The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of polymers to minimizes the disintegrating time. *In vitro* disintegration time was determined by placing the wafer in a petridish containing 10ml distilled water with swirling every 10 sec. The time at which the wafer disintegrated was noted (Boateng *et al.,* 2012).

***In vitro* dissolution study**

The *in vitro* dissolution test was performed using the USPXXX dissolution apparatus II (Paddle type) (Boateng *et al.,* 2012). The dissolution studies were carried out at 37±0.5°C; with stirring speed of 50 rpm in 900 ml phosphate buffer (pH 6.8). Wafers size required for dose delivery (2.5×2.5 $cm^2$) was used. Five ml aliquot of dissolution media was collected at time intervals of 1, 2, 5, 10 and 15 minutes and replaced with equal volumes of phosphate buffer (pH 6.8). The collected samples were filtered through 0.45 µm membrane filter and the concentration of the dissolved Rimegepant was determined using UV-Visible spectrophotometer at 264nm. The results were presented as an average of three such concentrations.

**RESULTS AND DISCUSSION**

The present study was focused on the formulation and evaluation of fast-dissolving oral wafers of Rimegepant, an antimigraine drug, to enhance patient compliance and provide a rapid therapeutic effect through buccal absorption. The prepared wafers (F1–F9) were all observed to be translucent, thin, and uniform in appearance, indicating successful casting and drying of film formulations without visual defects (Table 2). The physical evaluation parameters, such as thickness and weight, remained within a narrow range (78–93 µm and 105–117 mg respectively), confirming the reproducibility and consistency of the formulations.

The surface pH values of all wafers ranged from 6.65 to 6.85, which are close to the physiological pH of the buccal cavity and suggest a lower likelihood of causing irritation upon administration (Table 3). The folding endurance values (165–185 folds) further indicated that the films possessed good mechanical strength and flexibility, essential characteristics for handling and patient acceptability. Moisture content in all formulations was found to be low (1.85% to 2.86%), which is beneficial for the long-term stability of the product.

Drug content analysis showed values ranging from 95.45% to 99.45%, which is within acceptable limits, demonstrating uniform drug distribution in the films (Table 4). Among all formulations, F7 exhibited the shortest disintegration time of 15 ± 2 seconds, a key requirement for fast-dissolving oral dosage forms, indicating its potential for rapid onset of action.

The *in-vitro* drug release study of the optimized formulation F7 demonstrated that 66.85% of Rimegepant was released within 60 seconds, and 98.85% within 300 seconds, confirming that the wafer quickly dissolves and delivers the drug efficiently (Table 5). This rapid release behavior is desirable in the management of acute migraine attacks, where swift relief from symptoms is critical.

In summary, formulation F7 showed the best overall performance based on mechanical properties, disintegration time, and drug release profile. The results suggest that fast-dissolving oral wafers of Rimegepant could serve as a promising alternative to conventional oral dosage forms, offering a faster therapeutic effect and improved patient convenience.

**Table 1: Selection and Optimization of Wafers Forming Agents**

| Name of ingredients (mg) (mg for 12 strips) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| **Rimegepant** | 900 | 900 | 900 | 900 | 900 | 900 | 900 | 900 | 900 |
| **HPMC K4** | 100 | 200 | 300 | - | - | - | 50 | 100 | 150 |
| **Carbopol** | - | - | - | 100 | 200 | 300 | 50 | 100 | 150 |
| **PEG-400** | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| **SSG** | 25 | 50 | 100 | - | - | - | - | - | - |
| **CCS** | - | - | | 25 | 50 | 100 | - | - | - |
| **CP** | - | - | - | - | - | - | 25 | 50 | 100 |
| **Mannitol** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Citric acid** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **DM water qs to (ml)** | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |

**Dose calculations**

- Width of the plate = 5cm
- Length of the plate = 12cm
- No. of 2.5 x 2.5 cm2 wafers present whole plate = 12
- Each wafer contains 75 mg of drug.
- 12 no. of wafers contains mg of drug? = 75×12 = 900mg
- The amount of drug added in each plate was approximately equal to 900mg.

**Table 2: Results of Evaluation of prepared Wafers**

| Formulation code | General Appearance | Thickness* in µm | Weight* mg |
|---|---|---|---|
| **F1** | Translucent | 78±3 | 110±5 |
| **F2** | Translucent | 90±5 | 115±3 |
| **F3** | Translucent | 93±4 | 113±2 |
| **F4** | Translucent | 82±3 | 114±4 |
| **F5** | Translucent | 86±2 | 105±5 |
| **F6** | Translucent | 92±2 | 116±7 |
| **F7** | Translucent | 85±1 | 117±8 |
| **F8** | Translucent | 87±3 | 113±5 |
| **F9** | Translucent | 89±2 | 117±6 |

***Average of three determinations (N=3)**

**Table 3: Result of surface pH determination, folding endurance, percentage of moisture content**

| Formulation code | Folding endurance* (Times) | Surface pH Determination | Percentage of Moisture Content* |
|---|---|---|---|
| **F1** | 168±5 | 6.75±0.15 | 2.86±0.32 |
| **F2** | 173±6 | 6.82±0.25 | 2.72±0.15 |
| **F3** | 182±3 | 6.75±0.25 | 2.63±0.33 |
| **F4** | 170±4 | 6.65±0.15 | 2.75±0.32 |
| **F5** | 169±3 | 6.85±0.32 | 2.83±0.45 |
| **F6** | 175±2 | 6.75±0.45 | 2.64±0.65 |
| **F7** | 185±5 | 6.85±0.25 | 1.85±0.32 |
| **F8** | 165±6 | 6.72±0.15 | 2.15±0.15 |
| **F9** | 170±3 | 6.85±0.20 | 2.36±0.22 |

**Table 4: Drug content analysis and disintegrating time**

| Formulation code | Drug content analysis (%) | Disintegrating time (Sec.) |
|---|---|---|
| **F1** | 96.65±0.15 | 30±6 |
| **F2** | 98.12±0.32 | 35±4 |
| **F3** | 98.65±0.45 | 36±5 |
| **F4** | 97.65±0.32 | 26±3 |
| **F5** | 96.36±0.48 | 25±5 |
| **F6** | 95.45±0.32 | 27±8 |
| **F7** | 99.45±0.15 | 15±2 |
| **F8** | 98.12±0.36 | 20±3 |
| **F9** | 97.54±0.15 | 26±4 |

**Table 5: Results of *in-vitro* release study of optimized formulation F7**

| S. No. | Time (Sec.) | Percentage cumulative drug release |
|---|---|---|
| 1. | 60 | 66.85 |
| 2. | 120 | 76.65 |
| 3. | 180 | 85.45 |
| 4. | 240 | 92.25 |
| 5. | 300 | 98.85 |

## CONCLUSION

The present study successfully formulated and evaluated fast-dissolving oral wafers of Rimegepant for the effective management of migraine. Among the nine formulations developed, formulation F7 emerged as the most promising based on its excellent mechanical strength, rapid disintegration time (15 ± 2 seconds), optimal surface pH (6.85), and high drug content (99.45 ± 0.15%). Additionally, the in-vitro drug release profile of F7 demonstrated a rapid and nearly complete release of the drug (98.85% within 5 minutes), making it ideal for providing fast relief during migraine episodes. The use of suitable film-forming agents and superdisintegrants contributed to the enhanced dissolution and performance of the wafers. These findings indicate that fast-dissolving wafers of Rimegepant offer a patient-friendly, non-invasive drug delivery system that may enhance compliance, especially in individuals with nausea or difficulty swallowing conventional tablets during migraine attacks.

## DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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