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# FORMULATION AND CHARACTERIZATION OF FAST DISSOLVING ORAL FILMS OF RIZATRIPTAN FOR EFFECTIVE TREATMENT OF MIGRAINE

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**Abstract:**
*Migraine is a common neurological disorder requiring rapid onset of action for effective management. The present study aimed to formulate and characterize fast dissolving oral films of Rizatriptan to improve patient compliance and provide quick relief. Fast dissolving oral films (F1–F6) were prepared using suitable film-forming polymers and evaluated for physicochemical and mechanical properties. All formulations showed acceptable appearance, thickness, and weight uniformity. Folding endurance, tensile strength, moisture content, disintegration time, and drug content were found to be within acceptable limits. Among all formulations, F5 exhibited superior characteristics, including highest folding endurance (240 ± 4), lowest disintegration time (50 ± 3 seconds), and maximum drug content (99.00 ± 0.26%). The in vitro drug release study of optimized formulation F5 showed rapid release, with 47.12% drug release within 1 minute and 99.12% release within 15 minutes, indicating its suitability for immediate therapeutic action. Stability studies confirmed that the formulation remained stable over a period of three months with minimal variation in drug content. In conclusion, the developed fast dissolving oral film of rizatriptan offers a promising alternative to conventional dosage forms by providing rapid drug release, improved patient compliance, and effective management of migraine.*

***Keywords:*** *Rizatriptan, Fast dissolving oral film, Migraine, Solvent casting method, Rapid drug release, Disintegration time, Oral drug delivery, Film formulation, Patient compliance, Stability study.*

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## INTRODUCTION:

Migraine is a chronic neurological disorder characterized by recurrent episodes of moderate to severe headache, often accompanied by nausea, vomiting, photophobia, and phonophobia (Villar-Martinez and Goadsby; 2022).

It significantly affects the quality of life and productivity of individuals worldwide. The pathophysiology of migraine involves complex neurovascular mechanisms, including the release of inflammatory neuropeptides and activation of trigeminovascular pathways. Effective and rapid relief from migraine symptoms is essential to improve patient compliance and therapeutic outcomes.

Rizatriptan is a selective serotonin (5-$HT_1$B/1D) receptor agonist widely used in the acute treatment of migraine attacks. It works by causing vasoconstriction of cranial blood vessels and inhibiting the release of pro-inflammatory neuropeptides, thereby alleviating migraine symptoms. However, conventional oral dosage forms of rizatriptan face limitations such as first-pass metabolism, delayed onset of action, and difficulty in swallowing, especially during migraine attacks when patients often experience nausea and vomiting (Hargreaves et al., 2000).

To overcome these limitations, fast dissolving oral films (FDOFs) have emerged as an innovative drug delivery system. These films are thin, flexible, and rapidly disintegrate when placed on the tongue, releasing the drug for quick absorption without the need for water. This dosage form offers several advantages, including rapid onset of action, improved bioavailability, ease of administration, and enhanced patient compliance, particularly in pediatric and geriatric populations (Bhattarai and Gupta; 2015).

The formulation of fast dissolving oral films involves the use of suitable film-forming polymers, plasticizers, sweeteners, saliva-stimulating agents, and other excipients to achieve desired mechanical strength, flexibility, and rapid disintegration. Commonly used polymers include hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), and pullulan, which provide the necessary film-forming properties.

Characterization of oral films is an essential step to ensure quality, efficacy, and stability. Various evaluation parameters such as thickness, weight variation, folding endurance, surface pH, disintegration time, drug content uniformity, and in vitro drug release are assessed to optimize the formulation. A well-designed formulation ensures rapid drug release and absorption, leading to faster therapeutic action.

In this context, the present study aims to formulate and characterize fast dissolving oral films of rizatriptan for effective migraine treatment. The developed formulation is expected to provide rapid onset of action, improved patient convenience, and enhanced therapeutic efficacy compared to conventional dosage forms.

## MATERIAL AND METHODS:

### Material

Rizatriptan was used as the active pharmaceutical ingredient. Hydroxypropyl methylcellulose (HPMC), guar gum, and xanthan gum were used as film-forming polymers. Polyethylene glycol-400 (PEG-400) was used as a plasticizer, while aspartame was added as a sweetening agent and citric acid as a saliva-stimulating agent. Distilled water was used as the solvent. All chemicals and reagents used were of analytical grade and procured from standard sources.

### Methods

**Formulation of oral film of Rizatriptan**

**Solvent casting technique**

Rizatriptan-containing fast dissolving oral films were prepared using the solvent casting method with suitable modifications based on the method reported (Lakshmi *et al.*, 2014). Initially, the required quantity of Hydroxypropyl Methylcellulose (HPMC) was accurately weighed as per each formulation (F1–F6) and dissolved in 5 mL of distilled water. This mixture was stirred continuously using a magnetic stirrer for about 1 hour to form a uniform polymeric dispersion. Separately, the drug Rizatriptan (600 mg for all formulations) was dissolved in 2 mL of distilled water and subjected to sonication to ensure proper dispersion. Simultaneously, the required quantity of PEG-400 (100 mg) and the drug were dissolved in 95% ethanol and then slowly added to the HPMC solution under constant stirring.

Depending on the formulation, additional film-forming agents were incorporated. For F1 to F3, sodium alginate was added in increasing concentrations (100, 150, and 200 mg respectively), while in F4 to F6, guar gum was used in the same graded amounts. Xanthan gum was included in all formulations in increasing concentrations from 150 to 250 mg. Sweetening agent aspartame (25 mg) and salivating agent citric acid (50 mg) were also added to all batches. The entire solution was then stirred for an additional 30 minutes to ensure homogeneity. The solution was allowed to stand undisturbed to remove any entrapped air bubbles.

The prepared bubble-free solution was cast into clean, flat glass molds with dimensions of 2.5 × 2.5 cm² to form 12 films per formulation. The films were then subjected to drying at controlled room temperature (25–30°C, 45% relative humidity) for approximately 48 hours. In some trials, microwave oven drying was also explored as an alternative to reduce the drying time. Once dried, the films were carefully removed from the glass molds and cut into the desired size. The final films were stored in airtight plastic bags to prevent moisture absorption and were kept at room temperature until further evaluation.

**Table 1: Selection and optimization of film forming agents**

| Name of ingredients (mg for 12 strips) | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| **API** | 60 | 60 | 60 | 60 | 60 | 60 |
| **HPMC (mg)** | 400 | 600 | 800 | 400 | 600 | 800 |
| **PEG-400 (mg)** | 100 | 100 | 100 | 100 | 100 | 100 |
| **Sodium alginate (mg)** | 100 | 150 | 200 | - | - | - |
| **Guar Gum (mg)** | - | - | - | 100 | 150 | 200 |
| **Xanthan gum (mg)** | 150 | 200 | 250 | 150 | 200 | 250 |
| **Aspartame** | 25 | 25 | 25 | 25 | 25 | 25 |
| **Citric acid** | 50 | 50 | 50 | 50 | 50 | 50 |
| **DM water qs to (ml)** | 30 | 30 | 30 | 30 | 30 | 30 |

HPMC=Hydroxypropyl methylcellulose, PEG 400= Polyethylene glycol 400,

**Evaluation of prepared film**

**Thickness**

The thickness of films was measured at three different places using a vernier caliper (Devi *et al.*, 2016).

**Weight uniformity**

For each formulation, three randomly selected films were used. For weight variation test, 10 films from each batch were weighed individually by digital electronic balance and the average weight was calculated (Shimoda *et al.*, 2009).

**Folding endurance**

This was determined by repeatedly folding one film at the same place until it broke. The number of times the film could be folded at the same place without breaking cracking gave the value of folding endurance (Rama Krishna, 2014).

**Percentage moisture content**

The films were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs. Individual films 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 (Bala and Sharma, 2018).

**Drug content analysis**

The films (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 228nm (Raza *et al.*, 2019).

**Disintegrating time**

The objective of present work is that films should be dissolved within few seconds. Three super disintegrating agent were selected for minimizing the disintegration time (Dasari *et al.*, 2016).

***In vitro* dissolution study**

The *in vitro* dissolution test was performed using the USP dissolution apparatus II (Paddle with sinker) (Maheswari *et al.*, 2014). 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). Film 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 Rizatriptan was determined using UV-Visible spectrophotometer at 228nm. The results were presented as an average of three such concentrations.

**Stability studies**

Stability studies were carried out for optimized formulation F5 which was stored for a period of one, two and three months at 40±2ºC temperature and 75±5% relative humidity for a period 3 months (Dinge and Nagarsenker, 2008; Chaudhary *et al.*, 2013). The % Assay of formulation was determined by U.V. spectrophotometer using calibration curve method. The % assay of film was found to slightly decrease at higher temperature.

## RESULTS AND DISCUSSION:

The present study focused on the formulation and characterization of fast dissolving oral films of Rizatriptan for rapid and effective treatment of migraine. The prepared formulations (F1–F6) were evaluated for various physicochemical and mechanical properties to identify the optimized formulation.

The evaluation of prepared films indicated that all formulations were translucent in appearance, suggesting uniform dispersion of drug and excipients within the polymeric matrix. The thickness of films ranged from 53 ± 5 µm to 60 ± 6 µm, and weight variation was within acceptable limits, indicating uniformity in casting and formulation process. Such uniformity is essential for ensuring consistent drug dosing.

Mechanical properties such as folding endurance and tensile strength are critical for handling and packaging of oral films. The folding endurance values ranged from 160 ± 7 to 240 ± 4, with formulation F5 showing the highest value, indicating excellent flexibility and mechanical strength. Tensile strength values were found to be within the acceptable range for all formulations, suggesting adequate film integrity.

Disintegration time is a key parameter for fast dissolving films. Among all formulations, F5 exhibited the shortest disintegration time (50 ± 3 seconds), indicating rapid breakdown of the film in the oral cavity. This can be attributed to the optimized combination of polymers such as HPMC, guar gum, and xanthan gum, which facilitated faster hydration and disintegration.

Moisture content of the films ranged between 1.80% and 2.70%, which is within acceptable limits and ensures stability of the formulation by preventing brittleness or microbial growth. Drug content uniformity was also found to be satisfactory (95.80%–99.00%), indicating uniform distribution of rizatriptan within the films.

Based on overall evaluation parameters, formulation F5 was selected as the optimized formulation. The composition of F5 demonstrated an appropriate balance of polymer, plasticizer, and other excipients, resulting in superior mechanical and disintegration properties.

The in vitro drug release study of optimized formulation F5 showed rapid drug release, with 47.12% release within 1 minute and 99.12% release within 15 minutes. This rapid release profile confirms the suitability of the formulation for immediate therapeutic action, which is crucial in the management of acute migraine attacks.

Stability studies conducted over a period of three months indicated that the optimized formulation remained stable, with only slight variations in drug content (99.00% to 97.30%), demonstrating good stability under storage conditions. The study confirms that fast dissolving oral films of rizatriptan can be successfully formulated with desirable physicochemical properties, rapid disintegration, and efficient drug release. The optimized formulation F5 offers a promising alternative to conventional dosage forms, providing rapid onset of action and improved patient compliance in migraine therapy.

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

| Formulation code | General Appearance | Thickness (µm) | Weight (mg) |
|---|---|---|---|
| F1 | Translucent | 60±6 | 187±8 |
| F2 | Translucent | 57±3 | 189±6 |
| F3 | Translucent | 56±5 | 191±4 |
| F4 | Translucent | 59±9 | 185±7 |
| F5 | Translucent | 55±8 | 180±9 |
| F6 | Translucent | 53±5 | 183±2 |

**Table 3: Result of folding endurance, disintegration time, tensile strength moisture content and assay**

| Formulation code | Folding endurance | Disintegration time (min) | Tensile strength (kg/cm²) | Moisture Content (%) | % Drug Content |
|---|---|---|---|---|---|
| F1 | 160 ± 7 | 90 ± 5 | 0.74 ± 0.04 | 2.20 ± 0.12 | 96.70 ± 0.15 |
| F2 | 180 ± 6 | 83 ± 4 | 0.77 ± 0.06 | 2.40 ± 0.28 | 98.80 ± 0.32 |
| F3 | 205 ± 5 | 78 ± 6 | 0.75 ± 0.05 | 2.60 ± 0.25 | 97.70 ± 0.14 |
| F4 | 185 ± 6 | 76 ± 5 | 0.74 ± 0.07 | 2.70 ± 0.34 | 96.10 ± 0.36 |
| F5 | 240 ± 4 | 50 ± 3 | 0.72 ± 0.06 | 1.80 ± 0.14 | 99.00 ± 0.26 |
| F6 | 190 ± 6 | 67 ± 2 | 0.70 ± 0.07 | 2.10 ± 0.52 | 95.80 ± 0.36 |

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

**Table 4: Results of optimized formulation F5**

| Name of Ingredients | Composition (mg) Per Strip |
|---|---|
| **API** | 60 |
| **HPMC (mg)** | 600 |
| **PEG-400 (mg)** | 100 |
| **Sodium alginate (mg)** | - |
| **Guar Gum (mg)** | 150 |
| **Xanthan gum (mg)** | 200 |
| **Aspartame** | 25 |
| **Citric acid** | 50 |
| **DM water qs to (ml)** | 30 |

**Table 5: Results of *in-vitro* release study of optimized formulation of fast dissolving oral film F5**

| S. No. | Time (Min.) | Cumulative % Drug Release |
|---|---|---|
| 1 | 1 | 47.12 ± 1.80 |
| 2 | 2 | 75.05 ± 1.50 |
| 3 | 5 | 90.32 ± 1.90 |
| 4 | 10 | 92.75 ± 1.82 |
| 5 | 15 | 99.12 ± 1.70 |

**Table 6: Characterization of stability study of optimized Film (F5)**

| Characteristic | Time (Month) | | | |
|---|---|---|---|---|
| | **Initial** | **1 Month** | **2 Month** | **3 Month** |
| **% Drug content*** | 99.00 ± 0.26 | 98.45±0.35 | 97.45±1.20 | 97.30±0.25 |

***Average of three determination (n=3)**

## CONCLUSION:

The present study successfully developed fast dissolving oral films of Rizatriptan with desirable physicochemical and mechanical properties. All formulations showed good uniformity, flexibility, and drug content. Among them, formulation F5 was found to be optimized due to its highest folding endurance, fastest disintegration time, and maximum drug release. The optimized film demonstrated rapid drug release within a short time, ensuring quick onset of therapeutic action. Stability studies confirmed that the formulation remained stable over time. The developed oral film is a promising alternative to conventional dosage forms for effective and patient-friendly migraine management.

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