

Formulation And Evaluation of Fast-Dissolving Oral Films of Rizatriptan Benzoate for Rapid Drug Release in Migraine Management

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Abstract—Background: Migraine is a disabling neurological disorder frequently associated with severe headache, nausea, vomiting, photophobia and phonophobia. These symptoms may interfere with the administration of conventional oral dosage forms, creating a need for convenient formulations capable of releasing the drug rapidly. Rizatriptan benzoate, a selective serotonin 5-HT_{1B/D} receptor agonist, is used for the acute treatment of migraine. Fast-dissolving oral films offer a patient-friendly approach because they hydrate and disintegrate in the oral cavity without requiring water. **Objective:** The present study aimed to formulate and evaluate fast-dissolving oral films of Rizatriptan benzoate using suitable hydrophilic polymers and excipients to achieve rapid disintegration and efficient in-vitro drug release.

Methods: The formulation development involved preformulation assessment, drug–excipient compatibility studies, solvent casting, optimization of polymer and plasticizer concentrations, and evaluation of the prepared films. Hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA) and pullulan were considered as film-forming polymers. Plasticizers, sweetening agents, flavoring agents and citric acid were incorporated as appropriate. The films were evaluated for appearance, thickness, weight variation, folding endurance, surface pH, drug content, mechanical properties, disintegration time, dissolution and stability. **Results:** Preformulation findings indicated that Rizatriptan benzoate was suitable for incorporation into a hydrophilic film matrix. Fourier-transform infrared spectroscopy and differential scanning calorimetry findings were reported to indicate no significant drug–excipient incompatibility. The thesis reported a rapid-release profile of 35%, 55%, 78%, 94% and 99% at 1, 2, 5, 10 and 15 minutes, respectively. The optimized formulation was reported to disintegrate in approximately 18 seconds and exhibited an initial drug content of 99.2%. During the reported six-month

accelerated stability study, drug content decreased to 97.6%, while disintegration time increased to 20 seconds. **Conclusion:** The findings support the feasibility of developing fast-dissolving Rizatriptan benzoate oral films with rapid in-vitro drug release and satisfactory preliminary stability. Further confirmation through complete formulation records, validated analytical testing and comparative pharmacokinetic studies is required before claiming improved bioavailability or clinical therapeutic superiority.

Index Terms—Rizatriptan benzoate; fast-dissolving oral films; migraine; solvent casting; HPMC; disintegration time; in-vitro dissolution; stability studies.

I. INTRODUCTION

Migraine is a recurrent neurological disorder characterized by moderate-to-severe headache, often accompanied by nausea, vomiting, photophobia and phonophobia. The symptoms can substantially interfere with daily activities and quality of life. Effective acute treatment requires appropriate drug selection and a dosage form that patients can administer conveniently during an attack¹.

Rizatriptan benzoate belongs to the triptan class of antimigraine agents and acts primarily through serotonin 5-HT_{1B} and 5-HT_{1D} receptors. Its pharmacological activity helps inhibit trigeminovascular pain transmission and the release of neuropeptides involved in migraine. Although conventional oral dosage forms are effective, nausea, vomiting and delayed gastric emptying during migraine attacks can complicate their administration and absorption.

Fast-dissolving oral films are thin polymeric dosage forms designed to disintegrate or dissolve rapidly

when exposed to saliva. Their principal advantages include administration without water, portability, ease of handling and suitability for patients who have difficulty swallowing tablets. Their thin structure and large surface area promote rapid hydration and dissolution of the incorporated drug².

The performance of oral films depends on the selection and concentration of film-forming polymers, plasticizers and other excipients. Hydrophilic polymers such as HPMC, PVA and pullulan can produce continuous films with suitable mechanical properties. Plasticizers such as polyethylene glycol 400 (PEG 400) and glycerol improve flexibility and reduce brittleness. Citric acid may promote salivation, while suitable sweeteners and flavoring agents can improve palatability³.

The solvent-casting method is frequently used for oral-film development because it permits the preparation of films under relatively mild processing conditions⁴. The polymer is dissolved in a suitable solvent, the drug and excipients are incorporated, and the homogeneous mixture is cast and dried to obtain a thin film⁵. The resulting dosage form must demonstrate adequate mechanical strength, uniform drug content, rapid disintegration, acceptable surface pH and reproducible drug release⁶.

The present investigation focused on developing fast-dissolving oral films of Rizatriptan benzoate using solvent casting. The study evaluated the suitability of the selected excipients, the physical and mechanical characteristics of the prepared films, their in-vitro dissolution performance and preliminary stability⁷. The intended outcome was a convenient immediate-release formulation for further pharmaceutical development⁸.

II. MATERIALS AND METHODS

2.1 Materials

Rizatriptan benzoate was used as the active pharmaceutical ingredient. HPMC, PVA and pullulan were considered as film-forming polymers. PEG 400 and glycerol were considered as plasticizers. Aspartame or another suitable sweetener, a compatible flavoring agent and citric acid were used as formulation aids where applicable. Distilled water and phosphate buffer (pH 6.8) were used for relevant preparation and evaluation procedures.

The thesis identifies Sun Pharmaceutical Industries Ltd., India, as the source of Rizatriptan benzoate and Colorcon Asia Pvt. Ltd. as the supplier of HPMC. The supplier details of other materials should be confirmed from the original laboratory records.

2.2 Preformulation studies

Preformulation studies were undertaken to assess the physical appearance, solubility characteristics and suitability of Rizatriptan benzoate for incorporation into an oral-film matrix. The drug was described as a white to off-white crystalline powder without a characteristic odour. Its solubility was evaluated in aqueous media, including distilled water and phosphate buffer at pH 6.8.

Drug-excipient compatibility was investigated using Fourier-transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC). FTIR spectra were examined for changes in characteristic functional-group bands, while DSC thermograms were assessed for significant changes in thermal transitions. These techniques provide preliminary evidence of compatibility; definitive conclusions require examination of the actual spectra and thermograms.

2.3 Preparation of fast-dissolving oral films

The films were prepared using the solvent-casting technique. The selected hydrophilic polymer was dispersed or dissolved in a suitable solvent under continuous stirring until a homogeneous polymer solution was obtained. The solution was allowed to hydrate adequately, avoiding excessive air entrapment.

Rizatriptan benzoate was incorporated into the polymeric solution with suitable mixing to promote uniform distribution. The selected plasticizer was then added to improve flexibility. Appropriate quantities of sweetening agent, flavoring agent and citric acid were incorporated where specified in the formulation design.

The resulting mixture was mixed until uniform and, where necessary, allowed to stand to remove entrapped air. It was poured onto a clean, level casting surface and spread uniformly. The cast solution was dried under controlled conditions until a peelable film was obtained. The dried film was carefully removed and cut into uniform units.

The concentrations of the drug, polymer, plasticizer and other excipients must correspond to the actual

formulation batch records. These quantities should not be inferred from the general excipient list.

2.4 Formulation optimization

Formulation optimization was intended to balance rapid disintegration, efficient drug release and adequate mechanical integrity. Polymer concentration was considered an important variable because increasing polymer content may improve film strength but can also increase thickness and prolong hydration. Plasticizer concentration influences flexibility, folding endurance and tensile behaviour, while citric acid may affect wetting and disintegration.

The thesis describes the use of response-surface methodology and experimental optimization. However, the experimental-design description should be reconciled with the actual batch matrix before submission, because the methodological discussion refers to a central composite design. The independent variables, factor levels, experimental runs, regression equations and model-validation statistics should be reported only from the original design output.

2.5 Evaluation of oral films

Physical appearance: The films were visually inspected for uniformity, smoothness, transparency, cracks, air bubbles and other visible defects.

Thickness: Film thickness was measured at multiple locations using a calibrated Vernier caliper. The mean and standard deviation were calculated to assess thickness uniformity.

Weight variation: Individual film units were weighed using an analytical balance. The mean weight and variation among units were assessed as indicators of casting consistency.

Folding endurance: Each film was repeatedly folded at the same location until it fractured. The number of folds tolerated was recorded as an indicator of flexibility and resistance to handling stress.

Surface pH: The film was brought into contact with a small quantity of distilled water, and the pH of the wetted surface was measured using a calibrated pH meter. A surface pH close to that of the oral environment is desirable to reduce the risk of irritation.

Drug content uniformity: An individual film was dissolved in a measured volume of phosphate buffer (pH 6.8), appropriately diluted and analysed using a UV spectrophotometer at the validated analytical wavelength. Drug content was calculated from a suitable calibration curve. The wavelength, calibration equation, dilution factor and replicate results should be supplied from the laboratory records.

Mechanical properties: Tensile strength and percentage elongation were evaluated, where applicable, to assess the film's ability to withstand handling and stretching. These parameters are influenced by the polymer-plasticizer ratio and residual moisture.

Disintegration time: The film was placed in a suitable aqueous medium maintained at approximately 37°C, and the time required for complete disintegration was recorded. The endpoint and replicate measurements should be defined consistently.

In-vitro dissolution: Drug release was evaluated in an appropriate dissolution medium. Samples were collected at predetermined time intervals and analysed using the validated analytical method. Percentage drug release was calculated relative to the intended drug content, accounting for sample withdrawal and replacement where applicable.

Stability studies: The thesis reports accelerated storage at $40 \pm 2^\circ\text{C}$ and 75% relative humidity for six months. Appearance, drug content, disintegration time and in-vitro release were monitored at the specified intervals.

2.6 Statistical analysis

The thesis describes expression of experimental data as mean $\pm$ standard deviation and use of analysis of variance (ANOVA), with $p < 0.05$ considered statistically significant. For publication, the number of replicates, the specific statistical test applied to each dataset and the associated test statistics should be provided. Statistical significance should not be claimed unless supported by the underlying data.

III. RESULTS AND DISCUSSION

3.1 Preformulation and compatibility assessment

The drug was described as a white to off-white crystalline powder without a characteristic odour. The

reported solubility observations indicated moderate aqueous solubility, with relatively higher solubility in phosphate buffer at pH 6.8. These characteristics supported further investigation of a hydrophilic oral-film matrix.

The thesis reports that FTIR spectra showed retention of the characteristic drug peaks in the presence of selected excipients and that DSC thermograms showed no major shift in the drug's melting endotherm. These observations were interpreted as evidence of no significant incompatibility under the conditions studied. Nevertheless, such findings should be interpreted alongside the actual spectral data, thermal profiles and, where appropriate, stability-indicating analytical results.

3.2 Film formation and formulation characteristics

The solvent-casting approach provided a practical route for producing thin polymeric films. Uniform distribution of the drug, consistent casting thickness and adequate drying are important for obtaining reproducible individual doses.

HPMC, PVA and pullulan were considered for their film-forming properties. Plasticizers such as PEG 400 and glycerol were intended to improve flexibility and reduce brittleness. Citric acid was included as a potential saliva-stimulating agent, while sweeteners and flavoring agents were intended to improve acceptability. The formulation requires an appropriate balance between mechanical strength and rapid disintegration. Excessive polymer concentration may increase film thickness and hydration time, whereas insufficient polymer or plasticizer may lead to fragile films. Consequently, optimization should be based on the measured properties of individual batches rather than on polymer selection alone.

3.3 In-vitro drug-release profile

The thesis reports rapid release of Rizatriptan benzoate from the developed oral-film formulation. The reported values are summarized in Table 1.

Table 1: Reported in-vitro drug-release profile of Rizatriptan benzoate oral films

Time (min)	Drug released (%)
1	35
2	55
5	78
10	94
15	99

The reported profile demonstrates an increase in cumulative drug release from 35% at 1 minute to 78% at 5 minutes. Release reached 94% at 10 minutes and 99% at 15 minutes. The rapid release may be associated with hydration of the hydrophilic polymeric matrix, disintegration of the thin film and diffusion of dissolved drug into the surrounding medium.

The increase in drug release during the initial minutes is relevant to the design objective of immediate-release delivery. Nevertheless, dissolution data alone do not establish a faster clinical onset of action or improved systemic bioavailability. A direct comparison with a marketed Rizatriptan dosage form under appropriately matched dissolution conditions, followed by suitable pharmacokinetic evaluation, would be necessary to establish those advantages.

Table 2: Reported stability results for the optimized formulation

Storage period (months)	Drug content (%)	Disintegration time (s)	Drug release (%)
0	99.2	18	99.0
1	98.7	18	98.6
3	98.3	19	98.2
6	97.6	20	97.9

Storage condition reported in the thesis: 40 ± 2°C and 75% relative humidity for six months.

3.4 Stability assessment

The reported accelerated stability results indicate a gradual decrease in drug content from 99.2% at the initial assessment to 97.6% after six months. Disintegration time increased from 18 to 20 seconds, while drug release decreased from 99.0% to 97.9%.

These changes were relatively small in the reported dataset and suggest that the formulation retained rapid disintegration and a high drug-release percentage during the stated storage period.

The findings are encouraging for further development; however, they should not be interpreted as definitive proof of the commercial shelf life of the formulation. Confirmation requires documented replicate measurements, analytical-method performance, specified packaging, moisture assessment and longer-term stability data under the applicable stability protocol.

3.5 Interpretation of formulation performance

The findings indicate that the developed films achieved the principal pharmaceutical objective of rapid in-vitro drug release. The reported disintegration time of 18 seconds for the optimized formulation is consistent with the intended rapid-disintegrating characteristics. The high initial drug content also suggests that the casting process produced a film with a satisfactory measured drug content, although content uniformity across individual units must be confirmed using replicate measurements.

The performance of a fast-dissolving film is determined by the combined effects of polymer hydration, film thickness, drug distribution, plasticizer concentration and the properties of the dissolution medium. Hydrophilic polymers facilitate liquid penetration into the film matrix, which promotes swelling, disintegration and drug diffusion. Plasticizers improve flexibility but may also influence moisture uptake and polymer-chain mobility. These factors should therefore be considered together during formulation optimization.

The observed release profile supports further investigation of rizatriptan benzoate films as an immediate-release dosage form. However, the term *enhanced therapeutic efficacy* requires clinical evidence. Rapid dissolution may improve the availability of dissolved drug, but it does not necessarily demonstrate faster absorption, greater bioavailability or superior clinical outcomes. These outcomes depend on the drug's absorption characteristics and must be established through comparative studies.

3.6 Study limitations and future scope

The present study provides preliminary pharmaceutical evidence supporting the development of rizatriptan benzoate oral films. Several aspects require further investigation before the formulation can be considered for clinical or commercial application.

First, the complete composition of each formulation batch, including the precise quantities of the active ingredient, polymers and excipients, should be reported. Second, all physical and mechanical evaluation parameters should be supported by numerical data, replicate measurements and

appropriate statistical analysis. Third, the dissolution method should be described in sufficient detail to permit reproducibility, including the apparatus, medium volume, agitation conditions, analytical wavelength and sampling procedure.

Further studies should evaluate moisture content, residual solvent where applicable, microbial quality, packaging compatibility and stability-indicating assay performance. Optimization should be supported by the complete experimental-design matrix and statistical model, including regression coefficients and model-validation results.

Finally, comparative dissolution and pharmacokinetic studies are required to establish whether the developed film provides any measurable advantage over marketed rizatriptan formulations. Patient acceptability and taste-masking studies would also be valuable because palatability is an important determinant of adherence to oral-film therapy.

IV. CONCLUSION

Fast-dissolving oral films of rizatriptan benzoate were investigated using the solvent-casting technique with hydrophilic film-forming polymers and suitable formulation excipients. The thesis reports no significant drug–excipient incompatibility in the FTIR and DSC assessments. The reported in-vitro drug-release profile reached 99% at 15 minutes, while the optimized formulation exhibited a disintegration time of approximately 18 seconds and an initial drug content of 99.2%.

During the reported six-month accelerated stability study, drug content decreased to 97.6%, disintegration time increased to 20 seconds and drug release remained at 97.9%. These findings support the feasibility of preparing rapidly disintegrating rizatriptan benzoate films with promising in-vitro performance.

Further work is necessary to establish reproducibility, complete the statistical validation of formulation optimization, confirm stability under appropriate storage conditions and assess clinical performance. In particular, the potential for faster onset of action and improved bioavailability should be evaluated through direct comparison with an established rizatriptan dosage form and appropriate pharmacokinetic studies.

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