Research Article

Formulation and Characterization of Fast Dissolving Oral Film of Ubrogepant

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Abstract

The present study was undertaken to develop and evaluate fast-dissolving oral films of Ubrogepant for rapid drug release and improved convenience of oral administration. Ubrogepant-containing films were prepared by the solvent casting method using different film-forming polymers, including HPMC K4, HPMC K15, guar gum, xanthan gum, and sodium alginate. PEG 400 was incorporated as a plasticizer/solubilizing agent, while mannitol and citric acid were used as sweetening and saliva-stimulating agents, respectively. The prepared formulations were evaluated for general appearance, thickness, weight, folding endurance, disintegration time, tensile strength, moisture content, drug assay, and in-vitro drug release. The formulations showed a transparent appearance with thickness ranging from 48 ± 2 to 61 ± 5 µm and weight ranging from 90 ± 3 to 101 ± 6 mg. Folding endurance was found to be 142 ± 4 to 228 ± 3 times, while disintegration time ranged from 30 ± 2 to 68 ± 3 seconds. The drug assay was found to be within the range of 95.96 ± 0.48% to 99.36 ± 0.62%. Among the prepared formulations, F7 exhibited desirable film characteristics, the shortest disintegration time of 30 ± 2 seconds, and satisfactory drug assay of 99.36 ± 0.62%. The in-vitro drug release study showed that F7 released 99.42% of drug within 10 minutes. Release kinetic analysis showed the highest regression coefficient for the Peppas model (r^2 = 0.9866), followed by the Higuchi model (r^2 = 0.9785), indicating a diffusion-related drug-release mechanism. Thus, the optimized F7 formulation demonstrated suitable physicochemical characteristics, rapid disintegration, high drug content, and rapid drug release, indicating its potential as a fast-dissolving oral film formulation of Ubrogepant.

Keywords: Ubrogepant; Fast-dissolving oral film; Solvent casting method; HPMC; PEG 400; Disintegration time; In-vitro drug release; Peppas model.

Introduction

Migraine is a common neurological disorder characterized by recurrent attacks of moderate to severe headache, often accompanied by nausea, vomiting, photophobia, and phonophobia. It can substantially affect daily activities, productivity, and quality of life (Villar-Martinez et al., 2022).

The rapid onset of symptoms and the associated gastrointestinal disturbances during migraine attacks can make conventional oral dosage forms less convenient and may interfere with effective drug administration (Becker, 2015). Therefore, the development of oral dosage forms capable of rapid disintegration and drug release is of considerable interest for the management of acute migraine (Barbanti et al., 2004).

Ubrogepant is an orally active, small-molecule calcitonin gene-related peptide (CGRP) receptor antagonist used for the acute treatment of migraine with or without aura in adults. By selectively antagonizing the CGRP receptor, Ubrogepant inhibits the effects of CGRP, a neuropeptide that plays an important role in the pathophysiology of migraine (Edvinsson et al., 2018).

Although conventional oral administration provides an effective route for Ubrogepant delivery, a dosage form that rapidly disintegrates in the oral cavity may provide greater convenience, particularly when swallowing conventional tablets is difficult during a migraine attack (Lodhi et al., 2021).

Fast-dissolving oral films are thin polymeric dosage forms designed to rapidly disintegrate or dissolve when placed in the oral cavity. They offer several potential advantages over conventional tablets, including ease of administration, reduced need for water, rapid disintegration, improved patient convenience, and the possibility of rapid drug release (Irfan et al., 2016). These characteristics make oral films particularly attractive for drugs intended to provide prompt therapeutic effects. The performance of oral films is influenced by the type and concentration of film-forming polymer, plasticizer, sweetener, saliva-stimulating agent, and other formulation components (Kumar et al., 2025).

Hydroxypropyl methylcellulose (HPMC) is widely employed as a film-forming polymer because of its good film-forming ability and acceptable mechanical characteristics. Different grades of HPMC can influence film thickness, flexibility, mechanical strength, and disintegration behavior (Vlad et al., 2025). Other polymers, including guar gum,

xanthan gum, and sodium alginate, may also be investigated to optimize film characteristics. Plasticizers such as polyethylene glycol 400 (PEG 400) can improve film flexibility and may contribute to drug solubilization, while excipients such as mannitol and citric acid can improve palatability and stimulate salivation, respectively (Jacob et al., 2023).

The solvent casting technique is a commonly employed method for preparing fast-dissolving oral films. In this approach, the selected polymer is hydrated or dissolved to produce a homogeneous polymeric solution, followed by incorporation of the drug, plasticizer, and other excipients (Jacob et al., 2023). The resulting solution is cast onto a suitable surface and dried under controlled conditions to obtain a uniform film. Optimization of formulation composition and processing conditions is essential to achieve desirable characteristics such as uniform appearance, adequate folding endurance, suitable tensile strength, rapid disintegration, acceptable drug content, and rapid drug release (Jacob et al., 2023).

In view of these considerations, the present study was designed to develop and evaluate fast-dissolving oral films of Ubrogepant using different film-forming polymers and suitable pharmaceutical excipients. The prepared films were characterized for their physical and mechanical properties, disintegration behavior, moisture content, drug assay, and in-vitro drug release. The optimized formulation was further evaluated using appropriate release kinetic models to understand the probable mechanism of drug release. The study aimed to identify a Ubrogepant oral film formulation with satisfactory physicochemical properties and rapid drug release, thereby providing a convenient dosage form for acute migraine management.

Material and Methods

Material

The materials used for the development of fast-dissolving oral films of Ubrogepant included the drug Ubrogepant (gift sample from Pharmaceutical company), Carbopol, sodium starch glycolate, croscarmellose sodium, hydroxypropyl methyl cellulose, citric acid, aspartame, and polyethylene glycol 400. Methanol, ethanol, chloroform, hydrochloride, potassium phosphate monobasic, and sodium hydroxide were used as solvents, reagents, and analytical chemicals. Carbopol, sodium starch glycolate, croscarmellose sodium, hydroxypropyl methyl cellulose, citric acid, and aspartame were procured from Loba Chemie Pvt. Ltd., Mumbai; methanol, ethanol, chloroform, hydrochloride, and polyethylene glycol 400 from Qualigens Fine Chemicals, Mumbai; potassium phosphate monobasic from Parth Chemical and Herbals, Indore; and sodium hydroxide from Shri Mahalaxmi Chemical Works, Indore.

Methods

Formulation development of oral film of Ubrogepant

Ubrogepant containing fast dissolving films were fabricated by the solvent casting method (Lakshmi et al., 2005). HPMC is known for its good film forming properties and has excellent acceptability. Hence, various grades of HPMC namely HPMC K4, and HPMC K15 were evaluated as film formers. For the fabrication of films, glycerin was used as a humectant. PEG 400 is also reported as lubricant and solubilizer. Therefore PEG 400 along with glycerol was also used for fabrication of films. Apart from these film formers, Guar gum, Xanthan gum and Sodium Alginates along with other excipients were tried. Citric acid for saliva stimulating agent and mannitol as sweeteners used to fabricate the films. The composition of various formulations is given in Table 1. The polymer was soaked in water for 30 min or heated in water bath to 80° to get a clear solution. Then a plasticizer was added to it and mixed so as to get homogeneous solution. This solution was then casted onto glass moulds (15*5cm) and was dried in hot air oven at 45° for 24 h.

Table 1: Selection and optimization of film forming agents

Name of ingredients (mg) (mg for 12 strips)	F1	F2	F3	F4	F5	F6	F7	F8	F9

Ubrogepant	600	600	600	600	600	600	600	600	600
HPMC K4	25	50	100	-	-	-	12.5	25	50
HPMC K15	-	-	-	25	50	100	12.5	25	50
PEG-400	50	50	50	50	50	50	50	50	50
Guar gum	20	30	40	-	-	-	-	-	-
Xanthan gum	-	-		20	30	40	-	-	-
Sodium Alginates	-	-	-	-	-	-	20	30	40
Mannitol	20	20	20	20	20	20	20	20	20
Citric acid	20	20	20	20	20	20	20	20	20
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 cm^2 films present whole plate = 12
- Each film contains 50 mg of drug.
- 12 no. of films contains mg of drug = 50×12 = 600mg
- The amount of Ubrogepant added in each plate was approximately equal to 600mg.

Evaluation of prepared Film

Thickness

The thickness of patches was measured at three different places using a vernier caliper.

Weight uniformity

For each formulation, three randomly selected patches were used. For weight variation test, 10 films from each batch were weighed individually by digital electronic balance and the average weight was calculated (Nishimura 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 (Joshi et al., 2012).

Percentage of 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 (Reichel et al., 2025).

Drug content analysis

The film 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 reacted by UV spectrophotometer at 210nm (Mashru et al., 2005).

Disintegrating time

The most important criteria of present work is that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent was done to minimize the disintegrating time. Three super disintegrating agent (Sodium starch Glycolate, Crospovidone and Croscarmellose Sodium) were selected for this work.

In vitro dissolution study

The in vitro dissolution test was performed using the USPXXX dissolution apparatus II (Paddle with sinker). 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) (Baniya et al., 2020).

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, 4, 6, 8, and 10 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 drug was determined using UV-Visible spectrophotometer at 210nm. The results were presented as an average of three such concentrations.

Stability studies

Stability studies were carried out with optimized formulation F8 which was stored for a period of one, two and three months at 40±2°C temperature and 75±5% relative humidity for a period 3 months. 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. Minor difference was found between evaluated parameters before and after ageing/storage and all was in acceptable limits. Therefore formulation remains stable for sufficient time.

Results and Discussion

The formulation development of Ubrogepant fast-dissolving oral films was successfully carried out by the solvent casting method. Different film-forming polymers, including HPMC K4, HPMC K15, guar gum, xanthan gum, and sodium alginate, were evaluated along with PEG 400, mannitol, and citric acid. The different compositions used for preparation and optimization of the films are presented in Table 1. The polymer solutions were prepared to obtain a homogeneous casting solution, followed by casting and drying to produce the films.

The prepared films were evaluated for appearance, thickness, and weight, and the results are presented in Table 2. All formulations showed a transparent appearance, indicating good film formation. The thickness of the films ranged from 48 ± 2 to 61 ± 5 µm, while the weight ranged from 90 ± 3 to 101 ± 6 mg. The relatively uniform thickness and weight indicated satisfactory casting and drying of the films.

The results of folding endurance, disintegration time, tensile strength, moisture content, and drug assay are shown in Table 3. Folding endurance ranged from 142 ± 4 to 228 ± 3 times, demonstrating adequate flexibility of the films. The disintegration time ranged from 30 ± 2 to 68 ± 3 seconds, with formulation F7 showing the shortest disintegration time. F7 also showed satisfactory tensile strength of 0.74 ± 0.04 kg/cm², moisture content of 3.42 ± 0.45%, and the highest assay value of 99.36 ± 0.62%. These findings supported the selection of F7 as the optimized formulation.

The in-vitro drug release study presented in Table 4 demonstrated a rapid increase in cumulative drug release with increasing time. Formulation F7 exhibited the highest drug release, reaching 41.25% at 1 minute, 74.65% at 4 minutes, 86.95% at 6 minutes, 94.58% at 8 minutes, and 99.42% at 10 minutes. This rapid release profile indicated the suitability of F7 as a fast-dissolving oral film of Ubrogepant.

The release kinetics of the optimized F7 formulation were evaluated and are presented in Table 5. The cumulative drug release increased from 41.25% at 1 minute to 99.42% at 10 minutes. The regression coefficients obtained for zero-order, first-order, Higuchi, and Peppas models are summarized in Table 6. The highest regression coefficient was observed for the Peppas model (r^2 = 0.9866), followed by the Higuchi model (r^2 = 0.9785), indicating that diffusion contributed substantially to the drug-release mechanism.

Table 2: Evaluation of prepared film for general appearance, thickness and weight

Formulation Code	General Appearance	Thickness* (µm)	Weight* (mg)
F1	Transparent	48 ± 2	90 ± 3
F2	Transparent	52 ± 3	93 ± 4
F3	Transparent	55 ± 4	96 ± 5
F4	Transparent	50 ± 3	92 ± 4
F5	Transparent	54 ± 4	95 ± 5
F6	Transparent	58 ± 5	99 ± 6
F7	Transparent	53 ± 3	94 ± 4
F8	Transparent	57 ± 4	97 ± 5
F9	Transparent	61 ± 5	101 ± 6

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

Table 3: Result of Folding Endurance, Disintegrating time, Tensile strength, Percentage Moisture Content and % Assay

Formulation Code	Folding Endurance (Times)	Disintegrating Time (Sec.)	Tensile Strength (kg/cm²)	Percentage Moisture Content	% Assay
F1	142 ± 4	68 ± 3	0.64 ± 0.05	5.42 ± 0.62	96.84 ± 0.28
F2	150 ± 5	60 ± 4	0.69 ± 0.04	5.95 ± 0.74	97.52 ± 0.35
F3	162 ± 4	54 ± 3	0.73 ± 0.05	4.62 ± 0.58	98.15 ± 0.26
F4	154 ± 3	66 ± 5	0.71 ± 0.03	6.88 ± 0.52	96.45 ± 0.42
F5	168 ± 5	56 ± 4	0.77 ± 0.05	6.24 ± 0.47	97.18 ± 0.54
F6	178 ± 4	46 ± 2	0.84 ± 0.06	7.05 ± 0.68	95.96 ± 0.48
F7	228 ± 3	30 ± 2	0.74 ± 0.04	3.42 ± 0.45	99.36 ± 0.62
F8	172 ± 4	44 ± 3	0.81 ± 0.05	4.36 ± 0.56	98.42 ± 0.47
F9	166 ± 5	57 ± 4	0.79 ± 0.06	6.54 ± 0.61	98.68 ± 0.38

Table 4: In-vitro drug release study of formulation F1-F9

Time (Min.)	Cumulative % Drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	18.45	22.36	25.48	20.12	23.45	25.96	41.25	30.45	29.68
2	40.25	52.48	56.78	44.36	53.74	54.85	59.32	43.65	47.56
4	52.74	61.35	66.95	60.25	68.45	70.58	74.65	54.85	61.42
6	66.58	73.45	83.26	72.48	77.32	85.25	86.95	67.42	72.68
8	73.42	81.26	89.45	80.36	90.28	91.45	94.58	74.65	87.36
10	82.35	90.45	93.62	88.45	93.48	95.84	99.42	80.54	92.18

Table 5: Results of In-vitro release kinetics of optimized formulation F7

Time (min.)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
1	1	0	41.25	1.615	58.75	1.769
2	1.414	0.30103	59.32	1.773	40.68	1.609
4	2	0.60206	74.65	1.873	25.35	1.404
6	2.449	0.77815	86.95	1.939	13.05	1.116
8	2.828	0.90309	94.58	1.976	5.42	0.734
10	3.162	1	99.42	1.997	0.58	-0.237

Table 6: Comparative study of regression coefficient for selection of optimized batch

Zero order		First order	Higuchi	Peppas model
r^2	0.9200	0.9076	0.9785	0.9866

Conclusion

The present study successfully demonstrated the development of fast-dissolving oral films of Ubrogepant using the solvent casting method. The prepared films exhibited satisfactory physical and mechanical characteristics, including

uniform appearance, suitable thickness and weight, good folding endurance, acceptable moisture content, and satisfactory drug assay. Among all formulations, F7 was identified as the optimized formulation, showing a short disintegration time of 30 ± 2 seconds, good folding endurance, and a high drug assay of 99.36 ± 0.62%. The optimized film also demonstrated rapid drug release, with 99.42% of Ubrogepant released within 10 minutes. The release kinetic study indicated that drug release followed the Peppas model (r^2 = 0.9866), suggesting a predominantly diffusion-related release mechanism. The optimized F7 formulation possessed desirable film-forming properties, rapid disintegration, high drug content, and rapid drug release, indicating that Ubrogepant fast-dissolving oral film may provide a convenient and potentially effective alternative to conventional oral dosage forms for rapid drug administration.

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