RESEARCH PAPER

FORMULATION OPTIMIZATION AND EVALUATION OF CHLORPHENIRAMINE MALEATE ORODISPERSIBLE FILMS PREPARED BY SOLVENT CASTING FOR RAPID DRUG RELEASE

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ABSTRACT

Background: Orodispersible films (ODFs) have gained considerable attention as patient-centric drug delivery systems owing to their rapid disintegration, ease of administration, and improved compliance, particularly among pediatric, geriatric, and dysphagic patients. The selection of an appropriate film-forming polymer is a critical determinant of the mechanical strength, disintegration, and drug release characteristics of ODFs.

Objective: This study aimed to develop and optimize chlorpheniramine maleate-loaded ODFs using different viscosity grades of hydroxypropyl methylcellulose (HPMC E3, HPMC E6, and HPMC E15) prepared by the solvent casting method and to evaluate their physicochemical, mechanical, and in vitro performance.

Methods: Eighteen formulations were prepared using varying concentrations of HPMC with polyethylene glycol 400 and propylene glycol as plasticizers. The films were evaluated for appearance, thickness, weight variation, folding endurance, tensile strength, percentage elongation, drug content, disintegration time, and dissolution profile. Drug–excipient compatibility was investigated using Fourier transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC), while surface morphology was characterized by scanning electron microscopy (SEM). Accelerated stability studies were performed in accordance with ICH guidelines.

Results: All formulations exhibited acceptable physicochemical and mechanical properties. Polymer viscosity significantly influenced film performance, with formulation F2 demonstrating rapid disintegration, excellent mechanical characteristics, and 99.53 ± 1.80% drug release within 10 min. FTIR, DSC, and SEM analyses confirmed drug compatibility and uniform drug distribution. The optimized formulation remained stable under accelerated storage conditions.

Conclusion: The optimized HPMC-based chlorpheniramine maleate ODF represents a promising patient-friendly alternative to conventional tablets, with polymer viscosity playing a key role in determining film quality and drug release behavior.

Keywords: Chlorpheniramine maleate; Orodispersible film; Hydroxypropyl methylcellulose; Solvent casting; Drug release; HPMC; Patient-centric drug delivery.

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1. INTRODUCTION

Oral drug delivery remains the most preferred route of drug administration because of its convenience, cost-effectiveness, ease of administration, and high patient acceptance. However, conventional oral dosage forms such as tablets and capsules present significant challenges for pediatric, geriatric, and dysphagic patients who experience difficulty in swallowing. Dysphagia frequently results in poor medication adherence, inaccurate dosing, and reduced therapeutic efficacy, thereby necessitating the development of patient-friendly dosage forms that improve compliance without compromising therapeutic effectiveness [1,2,5].

Orodispersible films (ODFs) have emerged as an innovative solid oral dosage form capable of rapidly disintegrating or dissolving in the oral cavity without the need for water. These thin, flexible polymeric films

rapidly release the incorporated drug upon contact with saliva, thereby providing rapid drug dissolution and, in certain cases, improved bioavailability through pregastric absorption. ODFs combine the stability of conventional solid dosage forms with the convenience of liquid formulations and are particularly beneficial for pediatric, geriatric, bedridden, psychiatric, and dysphagic patients. Their portability, ease of administration, accurate dosing, and enhanced patient compliance have led to increasing research and commercial interest [2–6,11].

The successful development of ODFs depends on the appropriate selection of film-forming polymers, plasticizers, sweeteners, saliva-stimulating agents, and other pharmaceutical excipients to achieve optimum mechanical strength, flexibility, rapid disintegration, acceptable taste, and uniform drug distribution. Among the various film-forming polymers investigated, hydroxypropyl methylcellulose (HPMC) has gained considerable attention because of its excellent film-forming ability, biocompatibility, non-toxicity, and rapid hydration characteristics. Plasticizers such as polyethylene glycol (PEG) and propylene glycol are commonly incorporated to improve film flexibility and reduce brittleness, while sweeteners and flavouring agents enhance patient acceptability by masking the unpleasant taste of drugs [6–15,17,18].

Chlorpheniramine maleate is a first-generation H_1-antihistamine widely prescribed for the symptomatic treatment of allergic rhinitis, urticaria, conjunctivitis, and other allergic disorders. Although it possesses good oral absorption and proven therapeutic efficacy, the conventional tablet and syrup formulations may not be ideal for pediatric, geriatric, and dysphagic patients requiring rapid administration without water. Therefore, incorporation of chlorpheniramine maleate into an orodispersible film offers the potential advantages of rapid onset of action, improved patient compliance, ease of administration, and enhanced convenience [16,19,20].

Recent advances in oral thin-film technology have demonstrated considerable potential for the delivery of antihistamines and several other therapeutic agents requiring rapid onset of action. Nevertheless, optimization of formulation variables including polymer type, polymer concentration, plasticizer concentration, and excipient composition remains essential for obtaining films possessing adequate mechanical properties, satisfactory drug content uniformity, rapid disintegration, and efficient drug release. Consequently, systematic optimization is necessary to develop an ODF with desirable pharmaceutical performance and patient acceptability [9,10,12–15,17,18].

The present study was undertaken to formulate and optimize chlorpheniramine maleate orodispersible films by the solvent casting technique using different grades of hydroxypropyl methylcellulose as film-forming polymers. The prepared formulations were evaluated for their physicochemical properties, mechanical characteristics, drug content uniformity, disintegration time, in vitro drug release, drug–excipient compatibility, and stability. The objective of the study was to identify an optimized formulation capable of providing rapid drug release with satisfactory mechanical strength and stability, thereby offering a promising patient-friendly alternative to conventional oral dosage forms for the management of allergic disorders [16–18].

2. MATERIALS AND METHODS

2.1 Materials

Chlorpheniramine maleate was obtained as a gift sample from a pharmaceutical manufacturer. Hydroxypropyl methylcellulose (HPMC E3, HPMC E6, and HPMC E15) was employed as the film-forming polymer. Polyethylene glycol 400 (PEG 400) and propylene glycol (PG) were used as plasticizers. Aspartame and citric acid served as the sweetening agent and saliva-stimulating agent, respectively. Methanol was used as the casting solvent. All chemicals and reagents used in the study were of analytical reagent grade.

2.2 Preparation of Orodispersible Films

Chlorpheniramine maleate orodispersible films were prepared by the solvent casting technique using different grades of hydroxypropyl methylcellulose (HPMC E3, HPMC E6, and HPMC E15) as film-forming polymers. The required quantity of polymer was dispersed in the casting solvent under continuous magnetic stirring until a clear, homogeneous viscous solution was obtained. Chlorpheniramine maleate, plasticizer, citric acid, and aspartame were subsequently incorporated with continuous stirring until complete mixing was achieved. The resulting solution was sonicated to remove entrapped air bubbles and poured uniformly into glass Petri dishes (7 cm diameter). The films were dried under controlled conditions, carefully peeled from the casting surface, and cut into 2.5 × 2.5 cm strips, each containing 4 mg of chlorpheniramine maleate. Different polymer grades and plasticizer concentrations were investigated to optimize the physicochemical and drug release characteristics of the prepared films [2,6,7,11,17,18,33,36,37].

Table 1: Formulation chart of chlorpheniramine maleate oral dissolving film

Code	Drug	HPMC E3	HPMC E6	HPMC E15	PEG	PG	Citric Acid	Aspartame	Methanol
F1	31	92	-	-	9	-	4	6	Q.S
F2	31	154	-	-	15	-	6	8	Q.S
F3	31	215	-	-	22	-	8	10	Q.S
F4	31	92	-	-	-	9	4	6	Q.S

F5	31	154	-	-	-	15	6	8	Q.S
F6	31	215	-	-	-	22	8	10	Q.S
F7	31	-	92	-	9	-	4	6	Q.S
F8	31	-	154	-	15	-	6	8	Q.S
F9	31	-	215	-	22	-	8	10	Q.S
F10	31	-	92	-	-	9	4	6	Q.S
F11	31	-	154	-	-	15	6	8	Q.S
F12	31	–	–	92	–	9	4	6	Q.S.
F13	31	–	–	154	15	–	6	8	Q.S.
F14	31	–	–	215	22	–	8	10	Q.S.
F15	31	–	–	92	–	9	4	6	Q.S.
F16	31	–	–	154	–	15	6	8	Q.S.
F17	31	–	–	215	–	22	8	10	Q.S.
F18	31	–	–	154	18	–	6	8	Q.S.

2.3 Evaluation of Orodispersible Films

2.3.1 Visual Inspection

All prepared films were visually examined for colour, transparency, smoothness, flexibility, homogeneity, and the presence of air bubbles or cracks. Films possessing uniform appearance without visible defects were considered suitable for further evaluation [6,17,19].

2.3.2 Thickness

Film thickness was determined at three different locations using a calibrated digital micrometer. The average value and standard deviation were calculated to ensure uniformity of film thickness, which is essential for dose uniformity and reproducibility [17,29,33].

2.3.3 Dryness (Tack) Test

The tackiness of the prepared films was assessed by gently pressing the film between two surfaces. Films exhibiting no adhesion were considered tack-free, indicating adequate drying and suitability for handling, packaging, and storage [17,33].

2.3.4 Tensile Strength

Mechanical strength of the films was evaluated using a tensile testing apparatus. Tensile strength was calculated as the maximum force required to break the film divided by its cross-sectional area and expressed as kg/mm² [17,29,35].

2.3.5 Percentage Elongation

Percentage elongation was determined from the increase in film length at the point of breakage relative to its original length using the tensile testing apparatus. This parameter reflects the flexibility and elasticity of the prepared films [17,29,35].

2.3.6 Folding Endurance

Folding endurance was determined by repeatedly folding each film at the same position until it broke. The number of folds required to break the film was recorded. Higher folding endurance values indicate superior flexibility and mechanical strength [17,18,33].

2.3.7 Disintegration Time

Disintegration time was determined by placing each film in distilled water at room temperature and recording the time required for complete disintegration. Three determinations were performed for each formulation, and the average value was reported [6,17,23].

2.3.8 Drug Content Uniformity

Individual film samples were dissolved in phosphate buffer (pH 6.8), and the drug content was determined using a UV–Visible spectrophotometer at 265 nm. Drug concentration was calculated from the standard calibration curve, and the results were expressed as mean ± standard deviation [16,17].

2.3.9 Weight Variation

Film samples cut from different regions of the cast film were individually weighed using a calibrated analytical balance. The average weight and standard deviation were calculated to evaluate weight uniformity [17,33].

2.3.10 In Vitro Disintegration Test

The in vitro disintegration behaviour of each film was evaluated using phosphate buffer (pH 6.8) under gentle agitation. The time required for complete disintegration was recorded and expressed in seconds [6,23].

2.3.11 In Vitro Dissolution Study

Drug release studies were carried out using the USP Type II (Paddle) dissolution apparatus containing 900 mL phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C with a paddle speed of 50 rpm. Aliquots were withdrawn at predetermined time intervals and replaced with an equal volume of fresh dissolution medium. Samples were analyzed spectrophotometrically at 265 nm, and cumulative percentage drug release was calculated [16–18,29,30].

2.3.12 Drug–Excipient Compatibility Studies

Drug–excipient compatibility was investigated using Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) by comparing the spectra and thermograms of the pure drug and optimized formulation. These techniques were employed to detect any possible physicochemical interactions

between chlorpheniramine maleate and the selected excipients [16,17].

2.3.13 Scanning Electron Microscopy (SEM)

Surface morphology of the optimized formulation was examined using scanning electron microscopy to evaluate film surface characteristics and uniformity of drug distribution within the polymeric matrix [17,18].

2.3.14 Accelerated Stability Studies

Accelerated stability studies were performed according to ICH guidelines by storing the optimized formulations at 40 ± 2°C/75 ± 5% RH for three months. Samples were periodically evaluated for physical appearance, drug content, disintegration time, and in vitro drug release to assess formulation stability [17,18].

3. RESULTS AND DISCUSSION

3.1 Evaluation of Chlorpheniramine Maleate Orodispersible Films

Eighteen formulations (F1–F18) of chlorpheniramine maleate orodispersible films were successfully prepared by the solvent casting method using different grades and concentrations of hydroxypropyl methylcellulose (HPMC E3, HPMC E6, and HPMC E15) with PEG 400 and propylene glycol as plasticizers. All formulations were evaluated for physicochemical characteristics, mechanical properties, drug content, disintegration behaviour, and in vitro drug release.

3.1.1 Visual Inspection

Visual examination revealed that all prepared films were smooth, transparent, flexible, and free from air bubbles or visible imperfections. Films prepared using PEG 400 showed superior flexibility and surface smoothness compared with formulations containing propylene glycol. Similar observations have been reported for HPMC-based oral films, where PEG acts as an effective plasticizer by improving polymer flexibility and reducing brittleness [17,18,33,36].

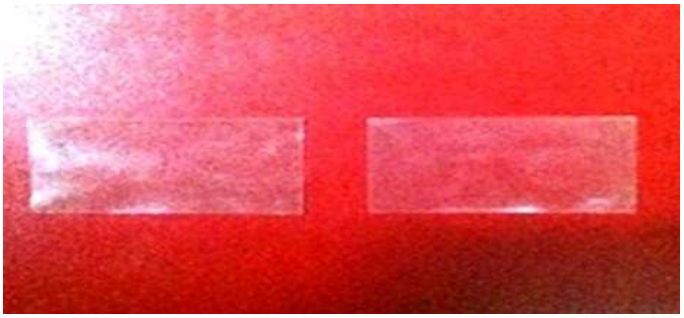

Fig. 1: Appearance of the film

3.1.2 Weight Variation and Thickness

The prepared films exhibited a weight range of 18.21 ± 0.86 to 36.92 ± 0.21 mg, while film thickness varied between 0.210 ± 0.012 and 0.467 ± 0.010 mm. The increase in polymer concentration resulted in proportional increases in both weight and thickness due to greater solid content within the casting solution. Uniform thickness and weight indicate homogeneous casting and uniform drug distribution throughout the films. Comparable findings have been reported for HPMC-based oral films prepared by solvent casting [17,29,33,35].

Table 2: Evaluation Parameters of All Formulations of Orodispersible Films

Code	Mean weight (mg) ± S.D	Mean Thickness (mm) ± S.D	Mean Tensile strength (Kg/mm²) ± S.D	Mean Percent elongation ± S.D	Mean Folding endurance ± S.D	Mean Drug Content (%) ± S.D	Mean disintegration time (sec) ± S.D
F1	18.21±0.86	0.210±0.012	0.798± 0.521	1.62 ±0.82	99.33 ± 7.67	99.27 ± 0.15	32 ± 0.85
F2	27.23±0.54	0.243±0.037	0.690± 0.532	1.82 ±0.78	95.66 ± 6.22	99.94 ± 0.32	34 ± 1.46
F3	34.86±0.59	0.250±0.022	0.633± 0.420	2.24 ±0.69	103.33±9.87	99.95 ± 0.41	37 ± 0.42
F4	19.01±0.02	0.224±0.024	0.739± 0.620	1.73 ±0.67	98.33 ± 3.88	98.95 ± 0.39	33 ± 1.51
F5	27.58±0.32	0.246±0.021	0.660± 0.612	1.96 ±0.37	93.66 ± 8.12	97.62 ± 0.47	35 ± 0.35
F6	35.38±0.91	0.293±0.014	0.612±0.580	2.43 ±0.59	103.23±4.56	97.85 ± 0.58	38 ± 1.78
F7	18.51±0.44	0.240±0.019	2.12 ± 0.210	2.67 ±0.62	122.35±6.45	99.41 ± 0.15	37 ± 2.52
F8	27.77±0.53	0.269±0.019	1.45 ± 0.20	4.21 ±0.93	128.66±5.87	99.05 ± 0.32	39 ± 0.89
F9	35.10±0.61	0.268±0.026	0.971 ± 0.63	3.56 ±0.53	113.02±8.55	99.54 ± 0.23	47 ± 1.45
F10	19.10±0.09	0.257±0.014	1.84± 0.182	2.34 ±0.81	120.66±5.39	100.1 ± 0.23	34 ± 0.78
F11	28.02±0.51	0.272±0.023	1.23 ± 0.38	4.78 ±0.87	125.66±7.55	99.75 ± 0.23	41 ± 1.57
F12	36.67±0.66	0.270±0.018	0.912±0.32	3.94±0.98	110.2 ± 9.45	101.10±0.39	48 ± 1.62
F13	19.01±0.48	0.269±0.022	2.59 ± 0.42	4.35 ±0.66	114.33±8.33	98.63 ± 0.63	78 ± 0.85
F14	27.82±0.49	0.374±0.019	1.97 ± 0.15	3.9 ± 0.91	117.33±8.23	97.26 ± 0.39	109 ± 1.45
F15	36.52±0.49	0.450±0.025	0.95 ± 0.25	2.89 ±0.45	105.12±8.10	99.98 ± 0.26	210 ± 0.52

F16	19.52±0.89	0.268±0.016	2.35 ± 0.56	4.29 ±0.67	112.33±5.88	97.85 ± 0.23	79 ± 0.64
F17	28.23±0.21	0.397±0.020	1.49 ± 0.33	3.21±0.21	101.22±6.21	99.10 ± 0.21	110 ± 0.18
F18	36.92±0.21	0.467±0.010	0.70 ± 0.35	2.21±0.54	103.40±5.12	100.52±0.50	230 ± 0.68

3.1.3 Dryness Test (Tack Test)

All prepared formulations were found to be non-tacky after drying, indicating complete solvent evaporation and adequate drying conditions. Tack-free films possess improved handling characteristics and are suitable for packaging and storage. Similar observations have been reported in previous investigations on oral thin films prepared using HPMC polymers [17,33].

3.1.4 Mechanical Properties

The tensile strength of the prepared formulations ranged from 0.612 ± 0.580 to 2.59 ± 0.42 kg/mm², whereas percentage elongation varied between 1.62 ± 0.82 and 5.94 ± 0.88%. Formulations prepared with HPMC E6 demonstrated comparatively higher tensile strength and mechanical integrity than formulations prepared with HPMC E3 and HPMC E15. Increasing polymer concentration improved tensile strength because of enhanced intermolecular hydrogen bonding within the polymeric matrix. However, excessive polymer concentration reduced elasticity and prolonged disintegration time. Similar relationships between polymer concentration and mechanical strength have been reported previously [17,18,33,35–37].

3.1.5 Folding Endurance

The folding endurance values ranged from 93.66 ± 8.12 to 128.66 ± 5.87, indicating excellent flexibility of the prepared films. Formulations containing PEG 400 demonstrated higher folding endurance than those containing propylene glycol, confirming the superior plasticizing effect of PEG 400. Among all formulations, HPMC E6-based films exhibited the highest flexibility, suggesting better polymer chain mobility and film integrity. These observations agree with earlier reports describing PEG 400 as an efficient plasticizer for HPMC oral films [17,18,33].

3.1.6 Drug Content Uniformity

Drug content ranged from 97.02 ± 0.47 to 101.10 ± 0.39%, indicating excellent content uniformity among all formulations. Uniform drug distribution confirms adequate mixing during formulation and efficient solvent casting. Similar levels of drug content uniformity have been reported for chlorpheniramine maleate oral films and other HPMC-based orodispersible films [16–18].

3.1.7 In Vitro Disintegration Time

The in vitro disintegration time varied from 32 ± 0.85 to 230 ± 0.68 seconds. Films prepared with lower-viscosity HPMC grades at lower polymer concentrations exhibited significantly faster disintegration than formulations prepared with higher polymer concentrations. Increased polymer concentration resulted in formation of a thicker gel layer upon hydration, thereby delaying film disintegration. These findings are consistent with previously published reports on HPMC-based orodispersible films [6,17,23,33].

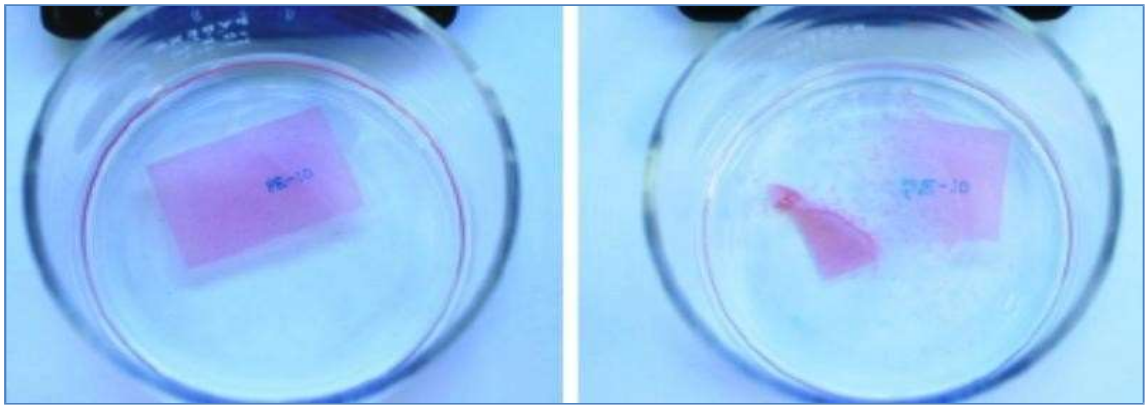

Fig. 2: Disintegration of the film

3.2 In Vitro Drug Release Studies

The dissolution profiles demonstrated that polymer grade and concentration significantly influenced drug release behaviour. Drug release decreased with increasing polymer concentration because thicker polymer matrices required longer hydration and erosion times before complete drug diffusion could occur. Similar observations have been reported for HPMC oral films containing antihistamines and other water-soluble drugs [16–18,29,31,33].

Formulations F1–F6

Among formulations F1–F6, cumulative drug release after 10 minutes ranged from 85.45 ± 1.31% to 99.53 ± 1.80%. Formulation F2 exhibited the highest drug release (99.53 ± 1.80%) and the shortest disintegration time, demonstrating an optimum balance between rapid hydration and adequate mechanical strength. Therefore, formulation F2 was selected as the optimized formulation.

Table: 3 In-vitro drug releases for F1 to F6 formulation

Time (min)	Cumulative percent drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
2	47.69±1.85	50.05±1.22	42.89±1.17	46.75±1.11	48.99±1.53	40.42±1.43
4	58.02±1.96	65.21±1.56	52.78±1.09	55.49±1.19	60.62±1.34	51.22±1.22
6	69.58±1.65	78.56±1.72	60.54±1.22	64.65±1.72	75.23±1.75	58.32±1.72
8	77.82±1.47	82.46±1.98	71.27±1.45	74.65±1.65	79.25±1.36	68.44±1.64
10	95.63±1.33	99.53±1.80	90.83±2.27	94.76±2.43	98.05±1.74	85.45±1.31

Data represents Mean ± Standard deviation, n =3

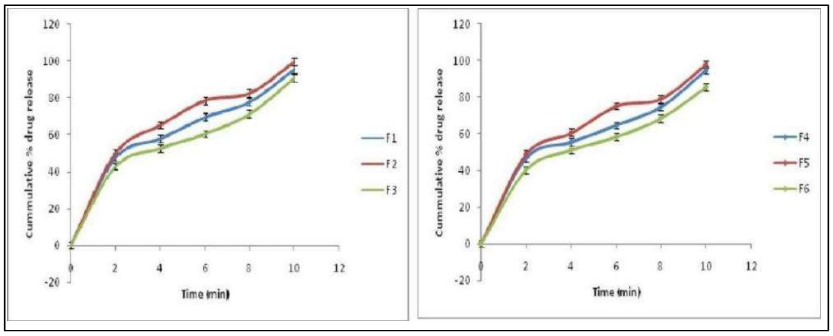

Fig. 3: Plot for in vitro drug release for F1 to F6 formulations

Formulations F7–F12

Drug release from formulations F7–F12 varied between 85.73 ± 1.82% and 99.48 ± 1.37% after 16 minutes. Formulation F8 showed the highest drug release among this group, whereas F12 exhibited the slowest release due to higher polymer concentration and increased matrix viscosity.

Table: 4 In-vitro drug releases for F7 to F12 formulation

Time (min)	Cumulative percent drug release					
	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
2	30.72±1.15	32.16±1.36	24.16±1.11	28.35±1.44	30.45±1.12	23.27±1.33
4	36.18±1.44	41.42±1.45	32.54±1.54	35.48±1.72	42.52±1.18	30.51±1.72
6	48.11±1.27	52.18±1.11	46.8±1.19	46.74±1.35	50.74±1.21	45.7±1.46
8	65.9±1.54	68.8±1.41	56.06±1.33	59.80±1.22	65.38±1.10	55.24±1.15
10	82.1±1.31	84.2±1.42	78.2±1.24	80.52±1.10	83.78±1.47	75.4±1.12
12	89.63±1.33	92.53±1.80	85.83±1.27	85.76±1.43	89.05±1.74	80.45±1.31
14	96.42±1.74	98.47±1.52	92.46±1.54	94.85±1.57	95.25±1.58	90.52±1.45
16	95.19±1.39	99.48±1.37	90.70±1.78	93.41±1.42	98.95±1.64	85.73±1.82

Data represents Mean ± Standard deviation, n =3

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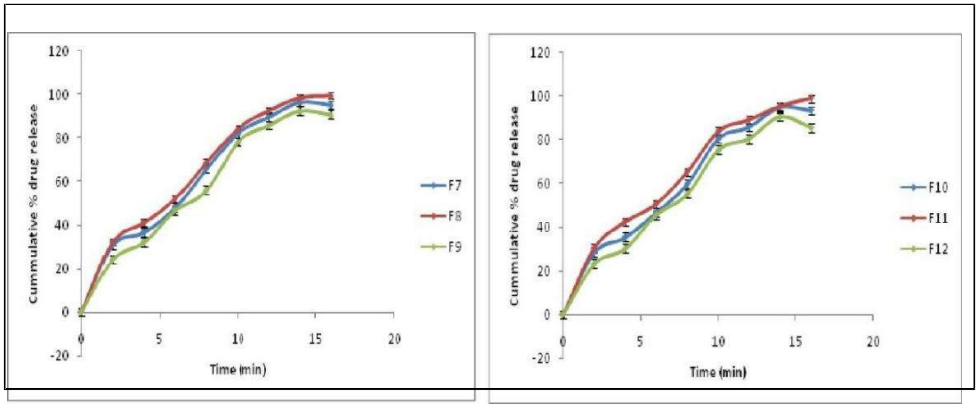

Fig. 4: Plot for in vitro drug release for F7 to F12 formulation

Formulations F13–F18

Drug release among formulations F13–F18 ranged from 90.45 ± 1.73% to 102.23 ± 1.48% after 22 minutes. Although formulation F14 exhibited the highest cumulative release, it required a considerably longer time than formulation F2 to achieve maximum release. This confirms that increasing polymer viscosity prolongs drug release despite achieving complete dissolution.

Table: 5 In vitro drug releases for F13 to F18 formulation

Time (min)	Cumulative percent drug release					
	F13	F14	F15	F16	F17	F18
0	0	0	0	0	0	0
2	13.79±1.21	15.11±2.1	10.53±2.1	9.89±0.9	13.21±1.2	8.77±1.28
4	21.54±1.3	25.98±2.3	19.09±1.5	11.64±1.8	14.21±1.5	10.03±1.6
6	35.79±1.4	40.33±1.1	32.29±1.4	28.21±1.5	33.1±3.1	22.53±1.98
8	59.9±1.6	62.12±1.4	55.03±1.8	45.98±1.4	50.74±1.9	44.59±1.9
10	72.4±1.32	74.85±1.6	70.03±1.2	69.48±1.7	73.84±1.8	67.44±1.7
12	77.82±1.45	82.46±1.98	71.27±1.45	74.65±1.65	79.25±1.36	68.44±1.64
14	83.1±1.38	85.2±1.45	79.2±1.58	81.52±1.10	84.78±1.46	76.4±1.12
16	88.63±1.33	92.53±1.80	83.83±1.27	84.76±1.43	90.05±1.74	79.45±1.31
18	96.92±1.74	98.75±1.52	92.77±1.54	94.43±1.57	95.55±1.58	90.73±1.45
20	93.76±1.39	98.48±1.37	89.11±1.78	92.40±1.42	97.82±1.64	84.72±1.82
22	96.29±1.47	102.23±1.48	92.52±1.84	95.46±1.78	100.76±1.56	90.45±1.73

Data represents Mean ± Standard deviation, n =3

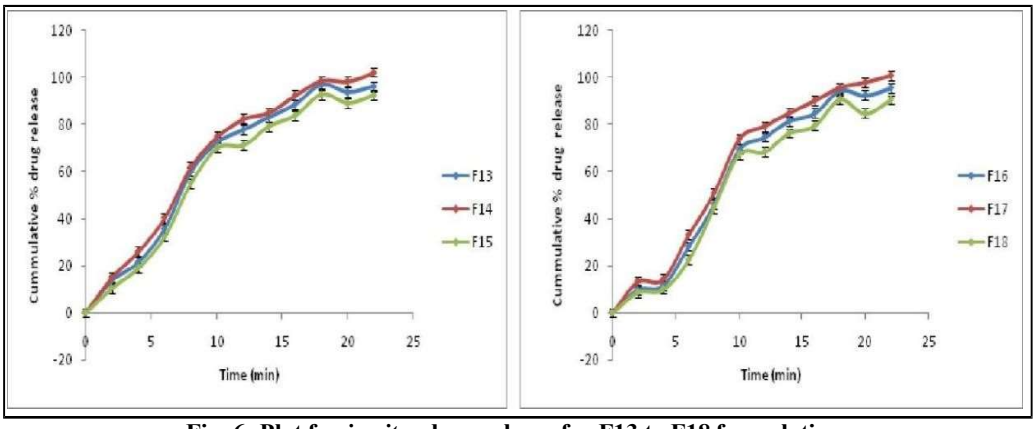

Fig. 6: Plot for *in vitro* drug release for F13 to F18 formulations

Comparison with Marketed Tablet

The optimized formulation (F2) demonstrated substantially faster dissolution than the marketed chlorpheniramine maleate tablet (Trofil 4 mg). Within 10 minutes, formulation F2 released 99.53 ± 1.80% of drug compared with 68.81 ± 2.10% released from the marketed tablet. The enhanced dissolution performance can be attributed to rapid hydration of the thin polymeric film, large surface area, and immediate drug availability following film disintegration. Similar improvements in

dissolution have been reported for oral thin-film formulations prepared using HPMC polymers [2,3,16–18,33].

Table 6: In vitro drug releases for F2, F8, F14 and marketed tablet formulations

Time (min)	Cumulative percentage drug release			
	F2	F8	F14	Marketed tablet
0	0	0	0	0
2	50.05±1.22	32.16±1.36	15.11±2.1	11.54±2.2
4	65.21±1.56	41.16±1.45	25.98±2.3	20.41±2.5
6	78.56±1.52	52.18±1.11	40.33±1.1	40.20±1.9
8	82.46±1.98	68.8±1.41	62.12±1.4	52.52±2.4
10	99.53±1.80	84.2±1.42	74.85±1.1	68.81±2.1

Data represents Mean ± Standard deviation, n =3

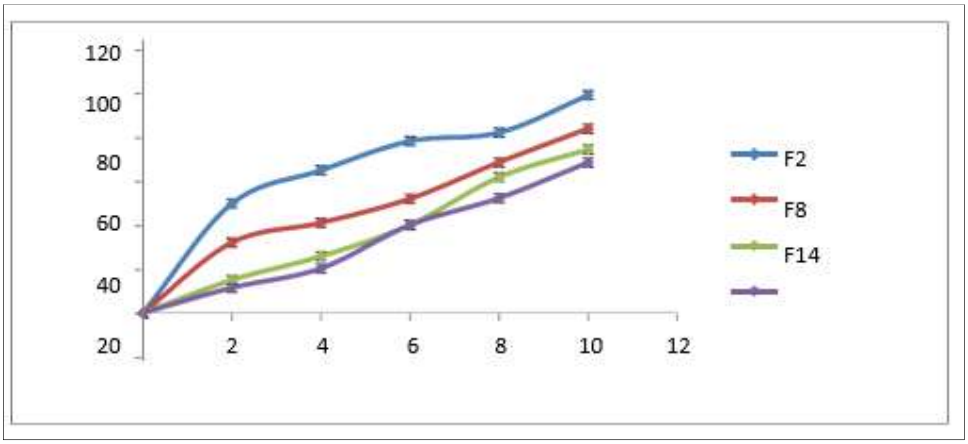

Fig. 7: Plot for in vitro drug release for F2, F8, F14 and marketed 4mg tablet

3.3 Drug–Excipient Compatibility Studies

3.3.1 Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopy was performed to investigate the compatibility between chlorpheniramine maleate and the selected excipients used in the optimized formulation. The FTIR spectrum of pure chlorpheniramine maleate exhibited characteristic absorption bands at 3545 cm^{-1} corresponding to N–H stretching, 2985 cm^{-1} for C–H stretching, 1683 cm^{-1} representing aromatic C=C stretching, 1417 cm^{-1} due to C–H deformation, and 1149 cm^{-1} corresponding to C–N stretching. These characteristic peaks were retained in the spectra of the physical mixture and optimized formulation without any significant shift, disappearance, or formation of additional peaks.

The preservation of all characteristic functional group vibrations indicates that chlorpheniramine maleate remained chemically stable during formulation and that no significant interaction occurred between the drug and the selected excipients. These observations confirm the compatibility of HPMC polymers, PEG 400, and other excipients with chlorpheniramine maleate and are consistent with previously reported FTIR studies on HPMC-based oral films [16–18,33,36].

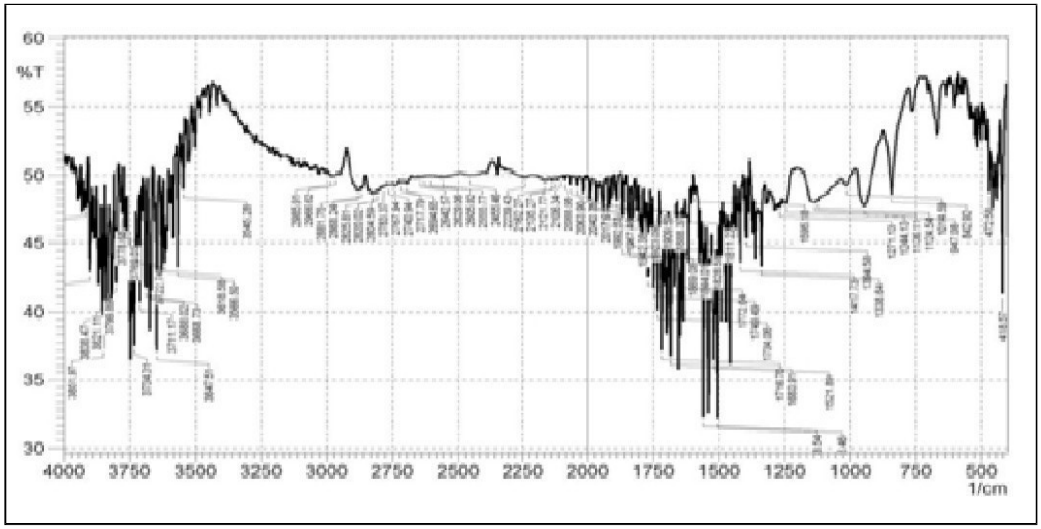

Fig. 8: FTIR spectrum of CPM

Table: 7 Vibrations and frequency for spectrum of CPM

S. No.	Type of vibrations	Frequency(cm^{-1})
1	N-H Stretching in (amines)	3545.28
2	N-H Stretching	3545.28
3	C-H Stretching in methyl or aromatic	2985.91
4	C-H Stretching	2966.62
5	C=C Stretching in aromatic nuclei	1683.91
6	C=C Stretching	1595.18
7	C-H deformation in methyl	1417.73
8	C-H deformation in –CH3	1394.58
9	C-N Stretching	1124.54
10	C-N Stretching	1014.59

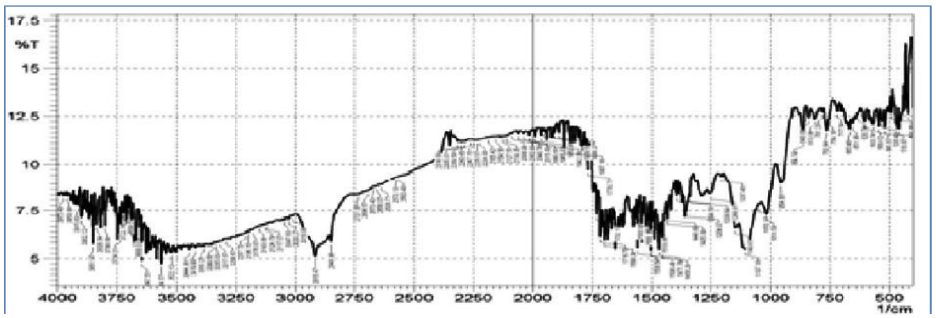

Fig. 9: FTIR spectra of CPM WITH HPMC E3

Table 8: Vibrations and frequency for spectrum of CPM AND HPMC E3

S. No.	Type of vibrations	Frequency(cm^{-1})
1	N-H Stretching in (amines)	3522.13
2	N-H Stretching	3444.98
3	C-H Stretching in methyl or aromatic	2916.47
4	C-H Stretching	3010.96
5	C=C Stretching in aromatic nuclei	1699.34
6	C=C Stretching	1583.6
7	C-H deformation in methyl	1435.09
8	C-H deformation in –CH3	1394.58
9	C-N Stretching	1149.61
10	C-N Stretching	1014.59

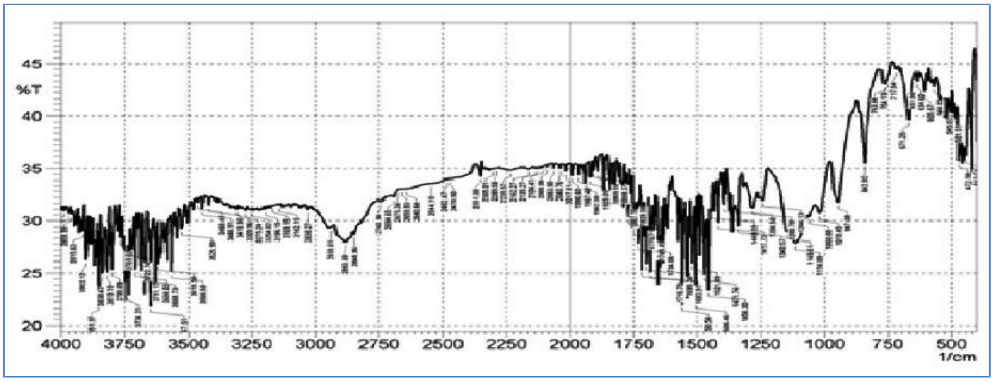

Fig. 10: FTIR spectra of physical mixture (formulation 2)

Table 9: Vibrations and frequency for spectrum of physical mixture (formulation 2)

S. No.	Type of vibrations	Frequency(c m^{-1})
1	N-H Stretching in (amines)	3525.99
2	N-H Stretching	3460.41
3	I Stretching in methyl or aromatic	2939.61
4	C-H Stretching	3030.27
5	C Stretching in aromatic nuclei	1683.91
6	C=C Stretching	1521.89
7	C-H deformation in methyl	1417.73
8	C-H deformation in –CH3	1394.58
9	C-N Stretching	1149.61
10	C-N Stretching	1018.45

3.3.2 Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry was employed to evaluate the thermal behaviour of chlorpheniramine maleate and to further confirm drug–excipient compatibility. The DSC thermogram of pure chlorpheniramine maleate exhibited a sharp endothermic peak at approximately 136°C, corresponding to its melting point. The optimized formulation also showed a similar endothermic peak with only negligible variation in peak intensity and position.

The absence of additional thermal events or significant peak shifts suggests that the drug remained stable throughout the formulation process and that no incompatibility existed between chlorpheniramine maleate and the selected excipients. These findings corroborate the FTIR results and agree with previously published compatibility studies of oral thin films [16–18].

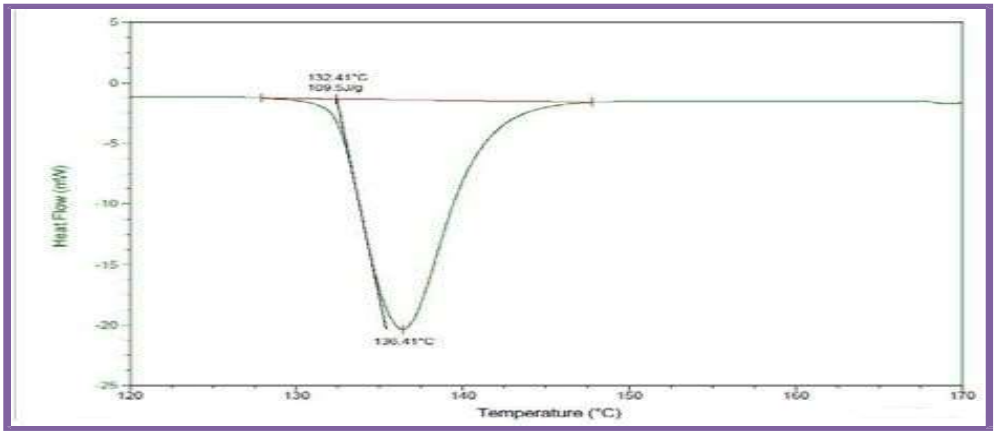

Fig. 11: DSC spectrum of chlorpheniramine maleate

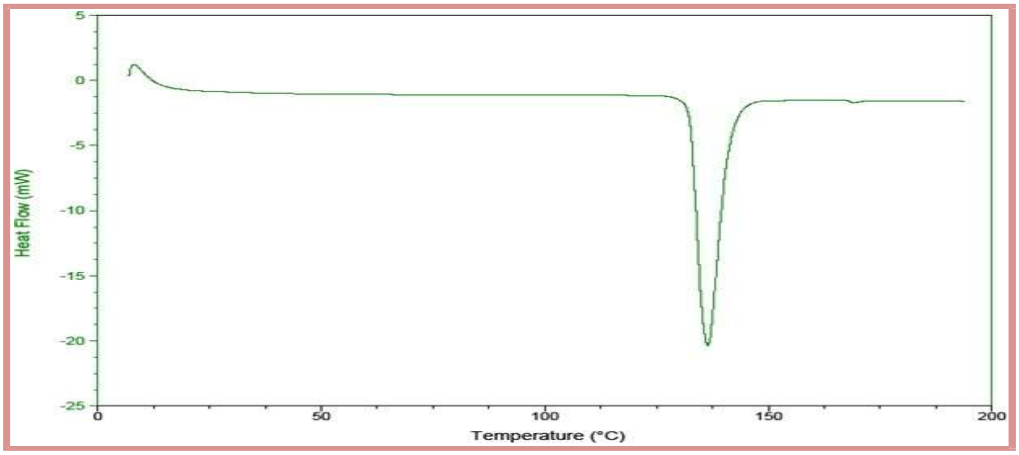

Fig. 12: DSC spectra of physical mixture

3.3.3 Scanning Electron Microscopy (SEM)

Scanning electron microscopy was performed to examine the surface morphology of the optimized formulation (F2). The SEM micrographs revealed a smooth, uniform, and continuous film surface without visible cracks, pores, or drug crystals. The absence of crystalline drug particles indicated homogeneous dispersion of chlorpheniramine maleate throughout the polymeric matrix.

Uniform distribution of the drug within the HPMC matrix contributes to content uniformity, rapid hydration, and reproducible drug release characteristics. Similar SEM observations have been reported for HPMC-based orodispersible films prepared by solvent casting [17,18,33].

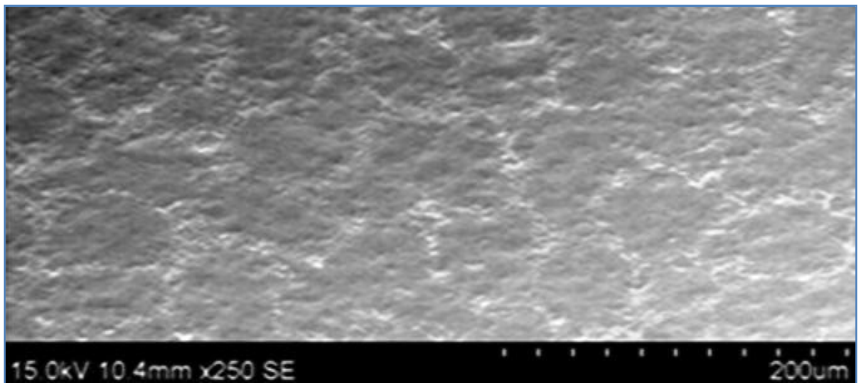

Fig. 13: Scanning electron microscopy image of formulation F2

3.4 Accelerated Stability Studies

Accelerated stability studies were carried out according to ICH guidelines by storing the optimized formulation under accelerated conditions (40 ± 2°C / 75 ± 5% RH) for three months. Throughout the study period, no significant changes were observed in physical appearance, thickness, weight variation, folding endurance, drug content, disintegration time, or cumulative drug release.

The optimized formulation retained excellent physicochemical properties and drug release characteristics after storage, demonstrating adequate formulation stability. These findings indicate that the selected polymeric system possesses sufficient stability for pharmaceutical application and are in agreement with previously reported stability studies of HPMC-based oral films [17,18,33].

Table 10: Characteristics of the films during stability studies

Evaluation	Storage condition $40^0C \pm 2^0C$ / 75±5 % RH			
Parameters	**Initial**	**1st month**	**2nd month**	**3rd month**
Disintegration time (sec)	34 ± 1.46	34±0.52	34±0.14	34±0.48
Thickness (mm) ± S.D	0.243±0.017	0.242±0.058	0.242±0.058	0.242±0.058
Mean weight(mg) ± S.D	27.23 ± 0.54	27.23 ± 0.52	27.23 ± 0.52	27.23 ± 0.52
Mean Tensile strength (Kg/mm^2) ± SD	0.690±0.532	0.690±0.535	0.690±0.535	0.690±0.535

Percent Elongation	1.82 ± 0.78	1.82 ± 0.80	1.82 ± 0.80	1.82 ± 0.80
Folding endurance	95.66 ± 6.23	95.66 ± 6.20	95.66± .20	95.66 ± 6.20
Drug content uniformity (%)	99.94 ± 0.32	99.94 ± 0.30	99.95 ±0.10	99.94 ± 0.20
% Cumulative drug release (10min)	99.53±1.80	99.53±1.80	99.53±1.80	99.53±1.80

CONCLUSION

The present investigation successfully developed chlorpheniramine maleate orodispersible films using the solvent casting technique with different grades of hydroxypropyl methylcellulose as film-forming polymers. All prepared formulations exhibited satisfactory physicochemical properties, acceptable mechanical strength, good flexibility, uniform drug content, and rapid disintegration characteristics.

Among the eighteen formulations investigated, F2 demonstrated the most desirable overall performance, exhibiting optimum mechanical properties, rapid disintegration, excellent content uniformity, and 99.53 ± 1.80% cumulative drug release within 10 minutes, which was superior to the marketed chlorpheniramine maleate tablet. The improved dissolution behaviour can be attributed to the optimized polymer concentration and rapid hydration characteristics of the HPMC-based film matrix.

FTIR and DSC studies confirmed the absence of significant drug–excipient interactions, while SEM analysis demonstrated uniform drug distribution throughout the polymeric matrix. Accelerated stability studies further established the physicochemical stability of the optimized formulation under ICH storage conditions.

Overall, the developed chlorpheniramine maleate orodispersible film represents a promising patient-friendly dosage form capable of improving patient compliance, particularly in pediatric, geriatric, and dysphagic patients. The optimized formulation has the potential to serve as an effective alternative to conventional oral dosage forms by providing rapid drug release, ease of administration, and enhanced therapeutic performance [2–6,16–18].

REFERENCES

1. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. J Control Release. 2009;139(2):94–107.
2. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: An innovative drug delivery system and dosage form. Int J ChemTech Res. 2010;2(1):576–583.
3. Cilurzo F, Cupone IE, Minghetti P, Selmin F, Montanari L. Fast dissolving films made of maltodextrins. Eur J Pharm Biopharm. 2008;70(3):895–900.
4. Hoffmann EM, Breitenbach A, Breitkreutz J. Advances in orodispersible films for drug delivery. Expert Opin Drug Deliv. 2011;8(3):299–316.
5. Borges AF, Silva C, Coelho JFJ, Simões S. Oral films: Current status and future perspectives—I. J Control Release. 2015;206:1–19.
6. Borges AF, Silva C, Coelho JFJ, Simões S. Oral films: Current status and future perspectives—II. Intellectual property, technologies and market needs. J Control Release. 2015;206:108–121.
7. Preis M. Oromucosal film preparations: Classification and characterization methods. Expert Opin Drug Deliv. 2015;12(8):1303–1317.
8. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. Int J Pharm Investig. 2013;3(2):67–76.
9. Mahajan A, Chhabra N, Aggarwal G. Formulation and characterization of fast dissolving oral films: A review. Der Pharm Lett. 2011;3(1):152–165.
10. Karki S, Kim H, Na SJ, Shin D, Jo K, Lee J. Thin films as an emerging platform for drug delivery. Asian J Pharm Sci. 2016;11(5):559–574.
11. Visser JC, Woerdenbag HJ, Hanff LM, Frijlink HW. Personalized medicine in pediatric patients: Orodispersible films as flexible dosage forms. Int J Pharm. 2017;523(1):327–335.
12. Preis M, Woertz C, Schneider K, Kukawka J, Broscheit J, Roewer N, Breitkreutz J. Design and evaluation of bilayered oral films for buccal drug delivery. Eur J Pharm Biopharm. 2014;86(3):552–561.
13. Peh KK, Wong CF. Polymeric films as vehicle for buccal drug delivery: Swelling, mechanical and bioadhesive properties. J Pharm Pharm Sci. 1999;2(2):53–61.
14. Boateng JS, Stevens HNE, Eccleston GM, Auffret AD, Humphrey MJ, Matthews KH. Development and mechanical characterization of solvent-cast polymeric films. Drug Dev Ind Pharm. 2009;35(8):986–996.
15. Rowe RC, Sheskey PJ, Quinn ME, editors. Handbook of Pharmaceutical Excipients. 8th ed. London: Pharmaceutical Press; 2017.
16. Indian Pharmacopoeia Commission. Indian Pharmacopoeia 2022. Ghaziabad: IPC; 2022.
17. United States Pharmacopeia Convention. United States Pharmacopeia 47–National Formulary 42. Rockville (MD): USP Convention; 2024.
18. International Council for Harmonisation (ICH). ICH Guideline Q1A(R2): Stability Testing of New Drug Substances and Products. Geneva: ICH; 2003.
19. International Council for Harmonisation (ICH). ICH Guideline Q2(R2): Validation of Analytical Procedures. Geneva: ICH; 2023.
20. European Medicines Agency. Reflection paper on the pharmaceutical development of medicines for use in the older population. London: EMA; 2020.

21. Salawi A. An insight into preparatory methods and characterization of orodispersible films: A review. Pharmaceutics. 2022;14:844.
22. Ferlak J, Guzenda W, Osmałek T. Orodispersible films—Current state of the art, limitations, advances and future perspectives. Pharmaceutics. 2023;15(2):361. (MDPI)
23. Jacob S, Boddu SHS, Bhandare R, Ahmad SS, Nair AB. Orodispersible films: Current innovations and emerging trends. Pharmaceutics. 2023;15(12):2753. (MDPI)
24. Chacko IA, Ramachandran G, Sudheesh MS. Unmet technological demands in orodispersible films for age-appropriate paediatric drug delivery. Drug Deliv Transl Res. 2024;14(4):841–857. (PubMed)
25. Karki S, Kim H, Na SJ, Shin D, Jo K, Lee J. Thin films as an emerging platform for drug delivery. Asian J Pharm Sci. 2016;11(5):559–574.
26. Visser JC, Woerdenbag HJ, Hanff LM, Frijlink HW. Personalized medicine in pediatric patients: Orodispersible films as flexible dosage forms. Int J Pharm. 2017;523(1):327–335.
27. Repka MA, McGinity JW, Zhang F, et al. Development and evaluation of an oral fast-disintegrating anti-allergic film using hot-melt extrusion technology. AAPS PharmSciTech. 2017;18:186–197. (PMC)
28. Naz A, Kulsum S, Ali A, Zama MAH, Akhter M, Akhter S. Oral dissolving films of chlorpheniramine maleate: Formulation and evaluation. Int J Pharm Investig. 2025;15(1):277–286. (jpionline.org)
29. Kotian S, Masuldar S, Rane R, Revankar A, Sarje H, Joshi B. Formulation development and evaluation of orodispersible films of chlorpheniramine maleate. Int J Pharm Res Appl. 2025;10(3):1879–1891. (ijprajournal.com)
30. Suknuntha K, Khumpirapang N, Tantishaiyakul V, Okonogi S. Solubility and physical stability enhancement of loratadine by preparation of co-amorphous solid dispersion with chlorpheniramine and polyvinylpyrrolidone. Pharmaceutics. 2023;15(11):2558. (PubMed)
31. Osmałek T, Froelich A, Jadach B. Recent advances in oral film drug delivery systems for immediate drug release. Eur J Pharm Biopharm. 2023.
32. Jadach B, Misek M, Ferlak J. Comparison of hydroxypropyl methylcellulose and alginate gel films with meloxicam as fast orodispersible drug delivery systems. Gels. 2023;9:687. (PMC)
33. Preis M. Design and quality evaluation of modern orodispersible film formulations. Drug Dev Ind Pharm. 2022.
34. Bala R, Sharma S, Pawar P. Advances in polymer selection for oral thin films. J Drug Deliv Sci Technol. 2022.
35. Borges AF, Silva C, Coelho JFJ, Simões S. Advances in polymeric oral films for drug delivery applications. J Control Release. 2022.
36. Repka MA, Langley N, McGinity JW. Hot-melt extrusion technology in pharmaceutical film formulations: Recent advances. Drug Dev Ind Pharm. 2022.
37. Boateng JS. Characterization of solvent-cast polymeric films for pharmaceutical applications. Drug Dev Ind Pharm. 2021.
38. Preis M, Woertz C, Breitkreutz J. Mechanical characterization and quality evaluation of oral films. Eur J Pharm Biopharm. 2021.
39. European Medicines Agency. Reflection paper on pharmaceutical development of medicines for use in the older population. European Medicines Agency; 2020.
40. International Council for Harmonisation. ICH Q8(R2): Pharmaceutical Development. Geneva: ICH; 2009.