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Formulation and Evaluation of Rapidly Dissolving Oral Films of Cetirizine Hydrochloride Using Pullulan by Solvent Casting Method

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KEYWORDS

Rapidly dissolving films, Cetirizine hydrochloride, Pullulan, Solvent casting, Taste masking, In-vitro dissolution, Oral drug delivery.

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Abstract

Rapidly dissolving dosage forms (RDDF) have gained considerable attention due to their ability to disintegrate quickly in the oral cavity without the need for water, thereby enhancing patient compliance, especially in pediatric and geriatric populations. The present study aimed to formulate and evaluate rapidly dissolving films (RDF) of cetirizine hydrochloride, a selective H1-receptor antagonist indicated for allergic rhinitis and chronic urticaria. RDF were prepared using pullulan as a film-forming polymer by the solvent casting method. Polyethylene glycol 400 was incorporated as a plasticizer to improve flexibility, while sweeteners and flavors were added to mask the bitter taste of cetirizine. Preformulation studies confirmed compatibility between drug and excipients. The prepared films were evaluated for mechanical properties, in-vitro disintegration, and dissolution in distilled water, 0.1 N HCl, and simulated saliva. The optimized batch (PA7) exhibited acceptable tensile strength (12.47 N/mm²) and improved flexibility. In-vitro dissolution studies demonstrated rapid drug release, with approximately 75% release within 2 minutes in distilled water and complete release in 0.1 N HCl within 2 minutes. Stability studies indicated sensitivity to high temperature and humidity but acceptable stability under controlled conditions. Overall, the developed pullulan-based RDF of cetirizine hydrochloride showed rapid disintegration, effective taste masking, and satisfactory mechanical properties, suggesting their potential as a convenient alternative to conventional oral dosage forms.

Introduction

Oral drug delivery is the most widely accepted route of administration due to its convenience, safety, and high patient compliance. However, conventional tablets and capsules may present swallowing difficulties, particularly in pediatric, geriatric, and dysphagic patients. To overcome these limitations, rapidly dissolving dosage forms (RDDF) have been developed, which disintegrate quickly in the oral cavity without the need for water (Pfister and Ghosh, 2005, Borsadia et al., 2003). These systems enhance patient compliance and provide faster onset of therapeutic action.

Among RDDF, rapidly dissolving films (RDF), also known as oral thin films, have emerged as a novel drug delivery system characterized by rapid hydration, quick disintegration, and efficient drug release in saliva (Liang and Chen, 2001). RDF offer

advantages such as improved stability compared to liquid dosage forms, accurate dosing, enhanced bioavailability, and improved patient acceptability (Vollmer and Galfetti, 2006).

The selection of an appropriate film-forming polymer plays a critical role in the development of RDF. Pullulan, a natural polysaccharide produced by *Aureobasidium pullulans*, has gained considerable attention due to its excellent film-forming ability, water solubility, transparency, non-toxic nature, and favorable mechanical properties (Leathers, 2003, Singh et al., 2010). Pullulan-based films exhibit rapid dissolution characteristics and compatibility with a variety of pharmaceutical excipients, making them suitable for oral film formulations.

Cetirizine hydrochloride is a second-generation selective H1-receptor antagonist widely prescribed for the management of seasonal allergic rhinitis, perennial allergic rhinitis, and chronic urticaria (Simons, 2004). Although therapeutically effective, cetirizine possesses a bitter taste that may reduce patient adherence, especially in children (Gupta et al., 2010). Incorporation of cetirizine hydrochloride into a rapidly dissolving film system may enhance palatability, ensure rapid drug release, and improve patient convenience. Therefore, the present study was undertaken to formulate and evaluate rapidly dissolving oral films of cetirizine hydrochloride using pullulan as a film-forming polymer prepared by the solvent casting method, and to assess their mechanical properties, disintegration characteristics, and in-vitro dissolution behavior.

MATERIALS AND METHODS

Chemicals and Reagents

Cetirizine hydrochloride was obtained as a gift sample from Troikaa Pharmaceuticals Ltd., Ahmedabad, India. Pullulan (PI-20 grade) was kindly supplied by Hayashibara Co. Ltd., Japan. Polyethylene glycol 400 (PEG 400), menthol and citric acid anhydrous were procured from S.D. Fine Chem Ltd., Mumbai, India. Aspartame and sucralose were obtained from Hi-Media Laboratories Pvt. Ltd., Mumbai, India. Passion fruit and lemon flavours were procured from Pentagon Trading Company, Ahmedabad, India. All other chemicals and reagents used in the study were of analytical grade. Double distilled water was used throughout the investigation.

Preformulation Studies

Preformulation studies were carried out to evaluate the physicochemical properties of cetirizine hydrochloride and its compatibility with selected excipients. Drug–excipient compatibility was assessed using Fourier Transform Infrared Spectroscopy (FTIR). The spectra of pure drug and physical

mixtures were recorded and compared to detect any possible chemical interactions.

Preparation of Rapidly Dissolving Films

Rapidly dissolving films (RDF) of cetirizine hydrochloride were prepared by the solvent casting method. Pullulan was dissolved in distilled water under continuous stirring to obtain a clear viscous polymeric solution. Cetirizine hydrochloride was added to the polymer solution with constant stirring to ensure uniform distribution. Menthol was dissolved separately in 95% ethanol and incorporated into the mixture. PEG 400 was added as a plasticizer to improve film flexibility and reduce brittleness.

Sweeteners such as aspartame and sucralose, along with citric acid and flavouring agents, were added to mask the bitter taste of the drug. The resulting homogeneous solution was subjected to mild vacuum to remove entrapped air bubbles. The solution was cast onto Teflon-coated petridishes and dried at room temperature for 24 h. After drying, the films were carefully removed and cut into strips of 2 × 2 cm^2, each containing 10 mg of cetirizine hydrochloride. The prepared films were stored in a desiccator maintained at 30–35% relative humidity until further evaluation.

Evaluation of Rapidly Dissolving Films

Thickness Measurement

Film thickness was measured using a digital micrometer screw gauge at three different locations on each film strip and the mean value was calculated.

Mechanical Properties

Mechanical properties including tensile strength, percentage elongation and elastic modulus were determined using a Lloyd Universal Testing Machine (Model LR 100K, UK). Film strips of dimensions 10 × 2.5 cm^2 were clamped between two grips separated by a distance of 5 cm and pulled at a speed of 50 mm/min until rupture. Tensile strength was calculated as the ratio of force at break to the initial cross-sectional area. Percentage elongation was calculated from the increase in length relative to the original length. Elastic modulus was determined from the slope of the stress–strain curve in the elastic deformation region.

***In-vitro* Disintegration Study**

The *in-vitro* disintegration time was determined by placing a film strip in a petridish containing simulated saliva maintained at 37 ± 0.5°C. The time required for complete disintegration of the film was recorded visually.

***In-vitro* Dissolution Study**

In-vitro dissolution studies were performed using USP Dissolution Apparatus XXIV (Electrolab, Mumbai, India). Dissolution media employed were distilled water, 0.1 N HCl and simulated saliva maintained at 37 ± 0.5°C. Samples were

withdrawn at predetermined intervals, filtered, and analyzed spectrophotometrically at 231 nm using a UV-Visible spectrophotometer. The cumulative percentage drug release was calculated.

Environmental Scanning Electron Microscopy

Surface morphology of the optimized film was examined using Environmental Scanning Electron Microscopy (Philips XL-30, Netherlands). Samples were mounted on aluminium stubs and observed under appropriate magnifications.

Stability Studies

Stability studies of the optimized formulation were carried out in accordance with ICH guidelines. Films were packed in high-density polyethylene (HDPE) containers and stored at 25°C/60% RH and 40°C/75% RH. Samples were periodically evaluated for physical appearance, mechanical properties, disintegration time and in-vitro drug release.

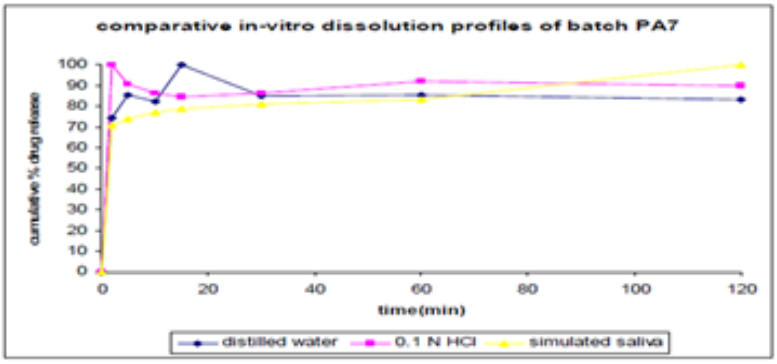
RESULTS AND DISCUSSION

Characterization of Rapidly Dissolving Films Using Pullulan

Preliminary trails- In-vitro dissolution studies

Table 1: *In-vitro* dissolution study of optimized batch PA7 in different dissolution medium

Time (min)	Cumulative % drug release		
	Dissolution medium		
	Distilled Water	0.1N HCl	Simulated saliva
2	74.46	100	70.93
5	85.51	-	73.76
10	82.23	-	77
15	100	-	78.65
30	-	-	80.78
60	-	-	83.4
120	-	-	100



Comparative in-vitro dissolution profile of batch PA7

Environment scanning electron microscopy (ESEM) References

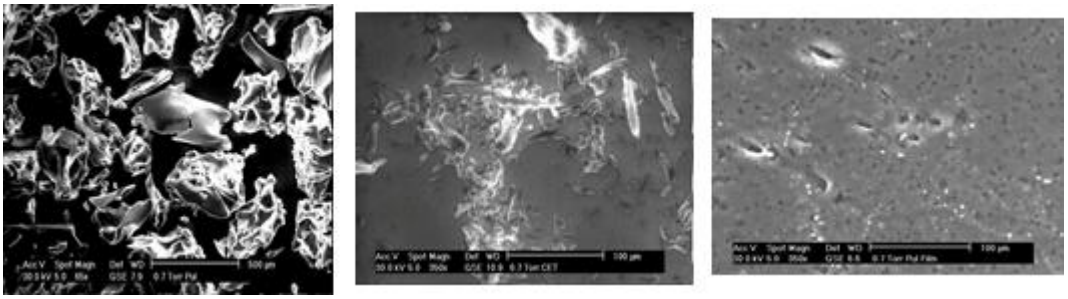


Fig.2: ESEM of pullulan powder at a) pullulan powder 65x magnification b) Cetirizine hydrochloride 350x magnification c) PA7 film at 350x magnification

***In-vitro* dissolution profile of batch F3 and F4 in distilled water**

Table 2: *In-vitro* dissolution profile of batch F3 and F4 in distilled water

Time(min)	**Cumulative % drug release**	
	Batch	
	F3	F4
0	0	0
2	59.01	60.72
5	75.51	70.66
8	92.62	89.98
10	100	85.64
15	-	96.77
30	-	100
60	-	-

In-vitro disintegration time of blank preliminary batches

Table 3: In-vitro disintegration time of blank preliminary batches

	In-vitro disintegration time(sec)			
Grade/Concentration	1%	2%	3%	4%
HPMC E3 LV	7.5**(1E)**very thin, brittle	12.5**(2E)**	12.5**(3E)**	22.5**(4E)**
HPMC E5 LV	7.5**(1F)** very thin, brittle	12.5**(2F)**	25**(3F)**	25**(4F)**
HPMC E15 LV	12.5**(1G)** very thin, brittle	17.5**(2G)**	25**(3G)**	30**(4G)**

Stability studies of optimized batch

Table 4: Stability studies of optimized batch

Time	**% of drug dissolved in 2min (distilled water)**	**In-vitro disintegration time (sec)**	**In-vivo disintegration time(sec)**	**Appearance**
Initial	100	50	20	Transparent, white, acceptable
1Month	100	50	21	Transparent, white, acceptable

3 Months	100	45	20	Transparent, white, acceptable
6 Months	79	45	22	Transparent, white, acceptable
12 Months	79	55	22	Transparent, white, acceptable

DISCUSSION

The present investigation was undertaken to formulate and evaluate rapidly dissolving oral films (RDF) of cetirizine hydrochloride using pullulan as a film-forming polymer. The solvent casting method was selected due to its simplicity, reproducibility and suitability for uniform film formation. Initial trials indicated that films prepared without plasticizer were brittle and difficult to separate from the casting surface. Incorporation of polyethylene glycol 400 significantly improved flexibility and facilitated proper film formation, confirming the essential role of plasticizer in reducing internal polymer–polymer interactions and enhancing film elasticity.

Drug–excipient compatibility studies performed using FTIR revealed no significant shift or disappearance of characteristic peaks of cetirizine hydrochloride, indicating absence of chemical interaction between the drug and selected excipients. This confirms the stability of the drug within the polymeric matrix.

Mechanical property evaluation demonstrated that films containing only pullulan exhibited high tensile strength but low flexibility. Addition of plasticizer reduced tensile strength while increasing percentage elongation, which is consistent with the plasticization effect. The optimized batch (PA7) showed acceptable tensile strength with improved flexibility, indicating a balanced mechanical profile suitable for handling and packaging. The elastic modulus values suggested adequate toughness of the film matrix while maintaining sufficient pliability.

In-vitro disintegration studies showed rapid film disintegration in simulated saliva, confirming the hydrophilic nature and fast hydration capacity of pullulan. Dissolution studies demonstrated rapid drug release, with nearly complete release observed within a short duration in 0.1N HCl and significant release in distilled water and simulated saliva. The rapid dissolution behavior may be attributed to the thin film structure, large surface area, and immediate wetting of the hydrophilic polymer matrix.

Environmental scanning electron microscopy revealed a uniform and smooth film surface with minimal drug aggregation, indicating homogeneous drug distribution within the polymer matrix. Stability studies indicated sensitivity of pullulan films to high

temperature and humidity, which may be due to the hygroscopic nature of the polymer. However, the optimized formulation remained stable under controlled storage conditions.

Overall, the results demonstrate that pullulan is a suitable film-forming polymer for the development of rapidly dissolving films of cetirizine hydrochloride with desirable mechanical strength, rapid disintegration and efficient drug release characteristics.

CONCLUSION

The present study successfully developed rapidly dissolving oral films of cetirizine hydrochloride using pullulan by the solvent casting method. The optimized formulation exhibited satisfactory mechanical properties, rapid disintegration in simulated saliva, effective taste masking and prompt in-vitro drug release. Compatibility studies confirmed stability of the drug within the polymeric matrix.

The developed RDF system offers a promising alternative to conventional oral dosage forms, particularly for pediatric and geriatric patients who experience difficulty in swallowing tablets. However, appropriate moisture-protective packaging is essential due to the humidity sensitivity of pullulan-based films. The formulation strategy adopted in this study may be further explored for other antihistaminic or centrally acting drugs requiring rapid onset of action and improved patient compliance.

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CONFLICT OF INTERESTS

The authors declare no conflict-of-interest

ETHICS APPROVAL

Not applicable

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AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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