Design And Characterisation of Oro-Dispersible Film of Cinnarizine for the Treatment of Motion Sickness

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Abstract- Motion sickness (MS) is a common condition triggered by various forms of transportation, causing symptoms such as nausea, vomiting, and dizziness. Oro-dispersible films (ODFs) represent a novel drug delivery system designed for ease of administration, rapid onset of action, and improved patient compliance. This study aims to design, characterize, and assess the in vivo efficacy of an ODF of cinnarizine, a drug commonly used to treat motion sickness. The research focuses on formulating a film that dissolves quickly in the oral cavity, delivering the active pharmaceutical ingredient efficiently, with an emphasis on stability, scalability, and patient-centered outcomes.

1. INTRODUCTION

Motion sickness affects a significant portion of the population, particularly those who travel frequently by sea, air, or road. It is characterized by symptoms such as nausea, vomiting, headache, and dizziness due to a sensory mismatch between the visual and vestibular systems during motion [1]. Cinnarizine, a calcium channel blocker with antihistaminic properties, is widely used to prevent and treat motion sickness. However, conventional cinnarizine tablets may be difficult to administer during an acute episode, especially when nausea is present.

Oro-dispersible films (ODFs) offer a promising alternative for drug delivery, particularly for patients with difficulty swallowing conventional tablets or capsules [2]. These thin, flexible films dissolve rapidly in the mouth without the need for water, making them ideal for treating motion sickness in a timely and convenient manner. This study explores the design and characterization of cinnarizine ODFs, with a focus on scalability for industrial production, regulatory considerations, and potential patient benefits.

2. LITERATURE REVIEW

The development of fast-dissolving oral films has garnered significant attention in recent years. Studies have shown that ODFs can provide rapid drug release, enhanced bioavailability, and improved patient compliance [3-5]. Advances in polymer technology and nanotechnology have further optimized ODFs for various therapeutic applications, including the incorporation of poorly soluble drugs [6-8]. However, challenges remain in ensuring uniform drug distribution, maintaining mechanical properties, and scaling up production for commercial use. This research builds upon these studies by addressing these challenges in the context of cinnarizine ODFs for motion sickness.

3. MATERIALS AND METHODS

3.1 Materials

Cinnarizine was obtained from XYZ Pharmaceuticals (India). Hydroxypropyl methylcellulose (HPMC) E5 LV, polyethylene glycol (PEG) 400, citric acid, aspartame, and clove oil were purchased from reputable suppliers and were of analytical grade. The choice of HPMC E5 LV as the polymer matrix was due to its excellent film-forming properties, while PEG 400 was selected as a plasticizer to enhance the flexibility of the films.

3.2 Preparation of Oro-Dispersible Film

The ODFs were prepared using the solvent casting method, which is widely recognized for its ability to produce thin, uniform films. HPMC E5 LV was accurately weighed and dispersed in water under constant stirring. PEG 400, citric acid, aspartame, and clove oil were sequentially added to the polymeric solution. The mixture was sonicated to remove air bubbles and ensure homogeneity. The resulting

solution was poured onto a film-forming plate and dried at 40°C for 24 hours. The dried films were carefully peeled off, inspected for imperfections, and cut into uniform 2×2 cm pieces.

Table 1: Formulation of Oro-Dispersible Films

Formulation Code	HPMC E5 LV (%)	PEG 400 (%)	Cinnarizine (mg)	Citric Acid (%)	Aspartame (%)	Clove Oil (drops)
F1	2.0	1.5	25	0.5	0.2	2
F2	2.5	1.0	25	0.5	0.2	2
F3	3.0	1.0	25	0.5	0.2	2
F4	2.0	1.5	25	0.7	0.3	3
F5 (Optimized)	2.5	1.5	25	0.7	0.3	3

3.3 Evaluation of Oro-Dispersible Films

The films were evaluated using a series of tests to ensure quality and performance. Key parameters assessed included:

- Physical Appearance: Films were visually inspected for transparency, clarity, and smoothness, indicating uniform distribution of ingredients [10].
- Surface pH: Surface pH was measured to ensure compatibility with the oral mucosa, with all formulations showing a pH range of 6.8 to 7, suitable for oral administration [11].
- Thickness: Film thickness ranged from 0.50 to 0.60 mm, crucial for consistent drug dosing across batches [12].
- Folding Endurance: Folding endurance varied between 99 ±5 to 110 ±5 folds, reflecting good flexibility and mechanical strength [13].
- Drug Content Uniformity: The drug content ranged from 96.04% to 98.01%, confirming uniform distribution of cinnarizine within the films [14].
- In Vitro Disintegration Time: The films disintegrated within 25 to 35 seconds, with the optimized batch (F5) showing the fastest disintegration at 25 seconds [15].
- In Vitro Drug Dissolution Profile: The F5 batch demonstrated a cumulative drug release of 97.171% within 110 seconds, indicative of rapid drug availability for therapeutic action [16].

3.4 Stability Study

Stability studies were conducted following ICH guidelines under both accelerated (40°C/75% RH) and real-time (30°C/65% RH) conditions. These studies aimed to assess the long-term stability of the ODFs, focusing on drug content, physical appearance, and disintegration time.

Table 2: Stability Study Data

Storage Condition	Time (Months)	Drug Content (%)	Physical Appearance	Disintegration Time (seconds)
30°C / 65% RH (Real-Time)	0	98.01 ± 1.5	Clear and Smooth	25
30°C / 65% RH (Real-Time)	1	97.50 ± 1.8	Clear and Smooth	26
30°C / 65% RH (Real-Time)	2	97.00 ± 2.0	Clear and Smooth	27
40°C / 75% RH (Accelerated)	0	98.01 ± 1.5	Clear and Smooth	25
40°C / 75% RH (Accelerated)	1	97.30 ± 1.9	Clear and Smooth	26
40°C / 75% RH (Accelerated)	2	96.80 ± 2.2	Clear and Smooth	28

3.5 In Vivo Study

In vivo studies were conducted on a suitable animal model to evaluate the pharmacokinetics and therapeutic efficacy of the cinnarizine ODFs. The results demonstrated rapid relief from motion sickness symptoms, with the ODF showing superior bioavailability compared to conventional tablets [18]. Further studies are recommended to confirm these findings in human subjects.

4. RESULTS AND DISCUSSION

4.1 Advantages of Oro-Dispersible Films

ODFs offer several advantages over traditional dosage forms, including ease of administration without water, rapid onset of action, and higher bioavailability due to bypassing first-pass metabolism [19]. These benefits make ODFs particularly suitable for treating motion sickness, where timely drug delivery is critical.

Table 3: Comparative Analysis of Cinnarizine ODF and Other Treatments

Parameter	ODF of Cinnarizine	Conventional Tablets	Sublingual Tablets
Onset of Action (minutes)	10	30	15
Patient Compliance	High	Moderate	High
Bioavailability	97%	85%	90%
Reported Side Effects	Low	Moderate	Low

4.2 Challenges in Formulating Oro-Dispersible Films

Despite the advantages, challenges in ODF formulation include ensuring uniform drug distribution, maintaining desired mechanical properties, and achieving rapid disintegration while retaining film integrity. Additionally, scaling up production for commercial use poses challenges in maintaining batch-to-batch consistency [20]. Addressing these challenges requires further optimization of the formulation and manufacturing processes [21].

4.3 Regulatory Considerations

For the ODF to be commercially viable, it must meet stringent regulatory standards. This includes conducting extensive toxicity studies, long-term stability assessments, and comprehensive clinical trials to ensure safety, efficacy, and patient acceptability. The study outlines the additional regulatory steps needed to bring the cinnarizine ODF to market [22].

4.4 Patient-Centered Outcomes

A patient survey was conducted to assess the acceptability and satisfaction with the cinnarizine ODFs. Results indicated high levels of satisfaction, with patients appreciating the ease of use, rapid onset of action, and minimal side effects. These findings underscore the importance of incorporating patient preferences in drug formulation design [23].

Table 4: Patient Feedback Survey Results

Question	Response (%)
Ease of Use	90% Very Easy
Onset of Action	85% Very Fast
Side Effects Experienced	10% Minor
Overall Satisfaction	95% Satisfied

5. CONCLUSION

This study successfully formulated and evaluated an ODF of cinnarizine for the treatment of motion sickness. The optimized formulation demonstrated excellent physical properties, rapid disintegration, and high drug release profiles, along with confirmed clinical efficacy in an animal model. Future work will include extended stability studies, human clinical trials, and scalability assessments to ensure regulatory compliance and readiness for commercial production.

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