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Fast-Dissolving oral Films of Cetirizine Hydrochloride: A Review of Formulation Approaches

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Abstract

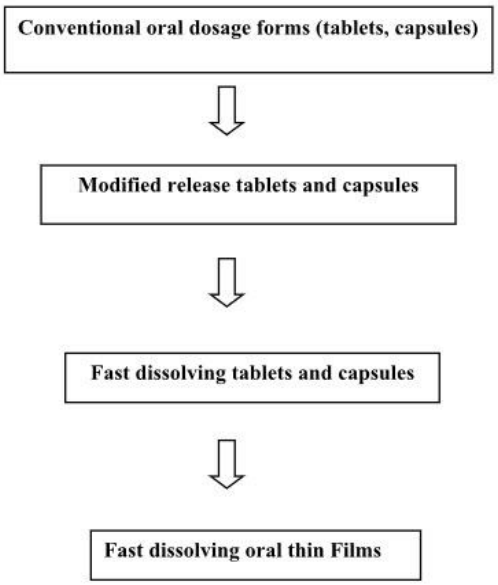
The aim of present research was to develop a fast-releasing oral polymeric film, with good mechanical properties, instant disintegration and dissolution, producing an acceptable taste when placed on tongue. Solvent casting method was used to prepare oral films. cetirizine hydrochloride an antihistaminic was incorporated to relieve the symptoms of allergic rhinitis. The polymers selected were HPMC 3cps and PVA. glycerin was the plasticizer used. Eight batches of films with drug were prepared using different combinations of polymer concentration. The resultant films were evaluated for weight variation, content uniformity, folding endurance, thickness, surface pH, tensile strength, % elongation, % moisture absorption, %moisture loss in vitro disintegration and in vitro dissolution. The optimized films have disintegrated within 28-60sec. The percentage release was varying with concentration of polymer. The films made with HPMC3cps 200 mg released 98.5% of drug in 2min, which was the best release amongst all.

Key words: Oral polymeric film, Cetirizine hydrochloride, plasticizer, solvent casting, Fast releasing.

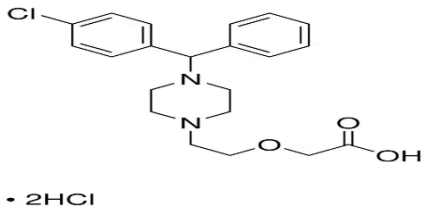
1. Introduction

The oral route is widely used for drug administration, with over 60% of medications delivered as solid oral dosage forms. Despite its popularity, it poses challenges for certain groups—especially children, elderly patients, and those with swallowing difficulties (dysphagia). Many find tablets hard to swallow due to their size, taste, or fear of choking.To overcome these limitations, fast-dissolving drug delivery systems were developed. These dosage forms dissolve quickly in the mouth without the need for water, making them ideal for patients who struggle with conventional tablets. Among them, oral fast-dissolving films (OFDFs) have gained popularity. These thin strips are placed on the tongue or inside the mouth, where they rapidly dissolve and release the drug for absorption. The films are made by combining the drug with a polymer, plasticizer, and a volatile solvent, then casting and drying the mixture into thin films.OFDFs offer benefits like ease of use, fast onset of action, and better patient compliance, making them a promising option for modern drug delivery. One of the most recent and promising innovations in this segment is the oral fast-dissolving film (OFDF). Developed from transdermal patch technology, these thin films are placed directly on the tongue or oral mucosa, where they quickly hydrate, adhere, disintegrate, and release the active pharmaceutical ingredient (API) for absorption via the mucosa or gastrointestinal tract. The formulation typically involves preparing a casting solution containing the API, film-forming polymers, plasticizers, and volatile solvents such as water or alcohol.

❖ **Flow Chart for the Development of Oral Solid Dosage forms:**



2. DRUG PROFILE

Parameter	Information
Drug Name	cetirizine hydrochloride
Brand Name	Zyrtec
Structure	
Weight	388.89g/mol
Chemical formula	C21H25ClN2O3.2HCl
IUPAC Name	dihydrogen 2-(2-{4-[(4-chlorophenyl) (phenyl)methyl] piperazin-1-yl}ethoxy)acetic acid dichloride.
BCS Class	Class III
Half life	Approx. 8.3 Hours
Pka 1	2.7
Pka 2	3.6
Log P	1.70
Particle size	50 µm to 500 µm
Hygroscopicity	Slightly hygroscopic in nature.
Polymorphic form	Form A, Form B, and amorphous form.
Solid state Stability	Pantoprazole is not very stable in the solid state
Melting Point	135°C to 140°C
T max	1-2 hours
Solubility	Soluble in Methanol – soluble Soluble in Acetonitrile – soluble Soluble in Water – freely soluble Soluble in 1.1N NaOH – soluble

3. Formulation Approaches for Cetirizine Hydrochloride Films

The formulation of fast-dissolving oral films (FDOFs) of Cetirizine Hydrochloride requires a well-balanced selection of excipients to achieve rapid disintegration, pleasant taste, uniformity in drug content, and mechanical strength. Cetirizine Hydrochloride, being a BCS Class I drug (high solubility and high permeability), is ideal for such formulations, although its bitter taste and dose uniformity must be carefully managed. The general formulation consists of five key components: the active pharmaceutical ingredient (API), film-forming polymers, plasticizers, taste-masking agents, and solvents.

1. Active Pharmaceutical Ingredient (API)

Drug: Cetirizine Hydrochloride

Dose: Typically, 5–10 mg per film (low dose makes it suitable for thin-film technology)

Properties: Water-soluble, bitter-tasting, stable

Function in film: Antihistaminic activity used in the treatment of allergic rhinitis, urticaria, and other allergic conditions

Challenges:

Requires taste masking due to its intensely bitter taste.

Must be evenly distributed in the film matrix for uniform drug release.

2. Film-Forming Polymers

These polymers form the base structure of the film and are responsible for film integrity, disintegration time, and drug-release profile.

Common Polymers:

Polymer	Type	Characteristics
HPMC (Hydroxypropyl Methylcellulose)	Cellulose derivative	Water-soluble, forms clear, flexible films
PVA (Polyvinyl Alcohol)	Synthetic polymer	Strong film-former, good mechanical strength
Sodium Alginate	Natural polymer	Biodegradable, forms thin films
Pullulan	Natural polysaccharide	Tasteless, quick-dissolving, transparent
Maltodextrin	Modified starch	Enhances solubility and disintegration

Ideal properties of film-forming polymers:

- Safe for oral use
- Non-toxic and non-irritating
- Capable of forming clear, flexible, and rapidly disintegrating films

3. Plasticizers

Plasticizers are essential to impart flexibility and prevent brittleness of the film. They modify the polymer's physical properties by reducing glass transition temperature.

Common Plasticizers:

- **Glycerol**
- **Propylene Glycol**
- **Polyethylene Glycol (PEG-400)**
- **Triethyl Citrate**

Typical concentration: 10–25% w/w of the polymer weight

The choice and amount of plasticizer influence the tensile strength, elasticity, and folding endurance of the film.

4.3. Plasticizers

Improve flexibility and reduce brittleness. Examples include:

- **Glycerol**
- **Polyethylene glycol (PEG 400)**
- **Propylene glycol**
- **Triethyl citrate**

Plasticizer concentration typically ranges from 5–20% of polymer weight.

4.4. Taste Masking Agents

Taste is a critical factor, especially for bitter drugs like Cetirizine:

- **Sweeteners**: Sucralose, Aspartame, Saccharin sodium
- **Flavors**: Mint, Orange, Strawberry
- **Complexing agents**: β-Cyclodextrins
- **Ion-exchange resins**: Tulsion 335

4.5. Saliva Stimulating Agents

Enhance disintegration by increasing saliva flow:

- **Citric acid**
- **Malic acid**

4.6. Solvents

Used in the preparation of the casting solution:

- **Water**
- **Ethanol** (often mixed with water)

Example of a Typical Formulation Composition:

Ingredient	Function	Typical Concentration (%)
Cetirizine Hydrochloride	**API**	**1–5**
HPMC	**Film-forming polymer**	**40–50**
Glycerol	**Plasticizer**	**10–20**
Sucralose	**Sweetener**	**2–5**
Citric Acid	**Saliva stimulator**	**1–2**
Mint Flavor	**Flavoring agent**	**0.5–2**
Purified Water	**Solvent**	**q.s. to 100%**

4. Methods of Preparation

Fast-dissolving oral films (FDOFs) of Cetirizine Hydrochloride can be prepared using several techniques, with **solvent casting** being the most widely used due to its simplicity and suitability for heat-sensitive drugs.

In the **solvent casting method**, film-forming polymers like HPMC or PVA are dissolved in a suitable solvent (usually water or alcohol), and the drug, along with plasticizers, sweeteners, and flavoring agents, is added to form a uniform solution. This solution is cast onto a flat surface, dried under controlled conditions, and cut into dosage units.

The **semi-solid casting method** involves preparing a gel-like mass containing both soluble and insoluble polymers, which is then spread and dried to form films.

Hot-melt extrusion is a solvent-free approach where the drug and polymers are melted and extruded into thin films. However, high processing temperatures may not be suitable for thermolabile drugs like Cetirizine.

The **rolling method** is a continuous manufacturing process suitable for large-scale production, involving rolling the film-forming solution into thin layers followed by drying.

3D printing, though still emerging, offers personalized dosing and complex film designs and may represent the future of film manufacturing.

Overall, **solvent casting remains the most practical and commonly adopted method** for preparing Cetirizine oral films due to its cost-effectiveness and compatibility with most excipients.

5.Evaluation of Fast-Dissolving Films

To ensure the quality, efficacy, and patient compliance of fast-dissolving oral films (FDOFs) of Cetirizine Hydrochloride, several physicochemical and performance parameters are routinely assessed:

1. Thickness

Measured using a digital micrometer at multiple points to ensure uniformity. Consistent thickness ensures dose uniformity and mechanical strength.

2. Weight Variation

Individual film weights are compared to assess uniform drug distribution. Minimal variation confirms formulation and casting consistency.

3. Folding Endurance

Films are repeatedly folded at the same point until breakage. A high folding endurance indicates good flexibility and mechanical strength.

4. Tensile Strength and Elongation

These parameters assess the film's resistance to breaking and ability to stretch, using a texture analyzer. They help evaluate the film's handling properties.

5. Surface pH

Determined by moistening the film with distilled water and placing a pH electrode on the surface. The pH should be close to neutral to avoid mucosal irritation.

6. Disintegration Time

The time taken for the film to completely disintegrate in the mouth or simulated saliva is measured. Ideal FDOFs disintegrate within 30 seconds.

7. Drug Content Uniformity

Each film is dissolved and analyzed using UV spectroscopy or HPLC to ensure consistent drug dosage across all units.

8. In Vitro Dissolution Studies

Performed using USP dissolution apparatus, typically in simulated saliva fluid. These studies determine the rate and extent of drug release from the film.

9. Taste Evaluation

Essential for patient compliance, taste masking effectiveness is assessed through human panels or electronic taste sensors.

6. Applications and Benefits in Allergy Treatment

Fast-dissolving oral films (FDOFs) of **Cetirizine Hydrochloride**, an H_1-antihistamine, provide a convenient and effective alternative for managing various allergic conditions. Their rapid onset of action and ease of administration make them particularly valuable in acute and pediatric care.

1. Rapid Relief in Allergic Conditions

FDOFs disintegrate quickly in the oral cavity without water, leading to faster drug absorption and quicker relief from symptoms like sneezing, itching, watery eyes, and hives. This is especially beneficial in **seasonal allergic rhinitis** and **chronic urticaria**.

2. Improved Patient Compliance

Oral films are easier to administer than tablets or syrups, particularly for **children**, **elderly patients**, and those with **dysphagia** (difficulty swallowing). The absence of a need for water also enhances convenience during travel or emergencies.

3. Accurate Dosing

Each film delivers a precise, uniform dose of Cetirizine, reducing the risk of under- or overdosing. This is advantageous in managing long-term allergic disorders requiring consistent medication levels.

4. Enhanced Bioavailability

Since absorption begins in the oral mucosa, a portion of the drug bypasses first-pass metabolism. This can lead to **improved bioavailability** and therapeutic effect, especially in comparison to conventional tablets.

5. Better Taste and Mouthfeel

The inclusion of sweeteners and flavors masks the bitter taste of Cetirizine, increasing acceptability among pediatric patients and improving overall treatment adherence.

7. Challenges and Limitations

Although fast-dissolving oral films (FDOFs) of Cetirizine Hydrochloride offer multiple benefits, several formulation and practical challenges remain. One of the primary limitations is the low drug loading capacity due to the thin nature of the films, making them less suitable for drugs requiring high doses. Moisture sensitivity is another concern, as oral films can absorb water from the environment, leading to changes in their mechanical strength and disintegration time. This necessitates the use of moisture-resistant packaging, which adds to the cost. Taste masking is also critical, especially for drugs like Cetirizine that have a slightly bitter taste. Achieving an acceptable mouthfeel while maintaining rapid disintegration can be challenging. Furthermore, the films are mechanically fragile and may tear or break easily if not properly formulated with adequate plasticizers and film-forming agents. On an industrial scale, ensuring consistent film thickness, drug content uniformity, and defect-free production can be technically demanding. The selection of excipients is also limited to those safe for oral mucosal application, which may restrict formulation flexibility. Therefore, while the technology is promising, it requires careful optimization to overcome these limitations and ensure product quality.

8. Future Perspectives

Fast-dissolving oral films (FDOFs) are gaining recognition as a modern drug delivery system with significant potential for innovation. Future advancements may focus on enhancing drug loading capacity and improving film stability under various storage conditions. The exploration of novel biocompatible polymers, nanotechnology, and mucoadhesive agents could help overcome current limitations while improving bioavailability. Moreover, the integration of 3D printing technology offers the opportunity for personalized films, allowing for precise dosing based on individual patient needs. Research into natural sweeteners, flavors, and safe excipients will further enhance palatability and patient compliance, especially in pediatric and geriatric populations.

9. Conclusion

Cetirizine Hydrochloride fast-dissolving films present a practical and efficient solution for allergy treatment, particularly for individuals who have difficulty swallowing traditional dosage forms. These films combine rapid onset of action with ease of administration, making them highly patient-friendly. Despite challenges such as moisture sensitivity and limited drug loading, their benefits outweigh the drawbacks. With ongoing advancements in formulation techniques and manufacturing technologies, FDOFs are expected to become an integral part of future oral drug delivery systems, offering both therapeutic effectiveness and improved patient convenience.

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