Formulation and Evaluation of Fast-Dissolving Tablets Incorporating Salbutamol Sulphate and Cetirizine Hydrochloride: An Innovative Strategy for Enhancing Medication Delivery in Children and Elderly Patient

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Abstract- Fast-dissolving tablets (FDTs) offer a patient-friendly dosage form, especially beneficial for pediatric and geriatric populations who often struggle with swallowing conventional tablets. This study aims to formulate and evaluate FDTs containing salbutamol sulphate, a bronchodilator, and cetirizine hydrochloride, an antihistamine, to facilitate rapid onset of action and improve patient compliance. Various superdisintegrants and excipients were screened to optimize tablet properties. The prepared tablets were evaluated for weight uniformity, hardness, friability, disintegration time, drug content, dissolution profile, and stability. Results demonstrated that the optimized formulation rapidly disintegrated within 30 seconds and exhibited satisfactory mechanical strength and drug release, highlighting its potential for improved drug delivery in target populations.

Keywords-Fast-dissolving tablets, Salbutamol sulphate, Cetirizine hydrochloride, Pediatric drug delivery, Geriatric drug delivery, Superdisintegrants, Patient compliance.

INTRODUCTION

Background

Oral administration remains the most common and preferred route for drug delivery due to its convenience, safety, and patient compliance. However, certain patient groups—especially pediatric and geriatric populations—often face challenges with swallowing conventional solid dosage forms such as tablets and capsules. Dysphagia, or difficulty in swallowing, is prevalent among these groups and can lead to incomplete dosing, poor adherence, and suboptimal therapeutic outcomes. To overcome these issues, novel drug delivery systems have been developed, with fast-dissolving tablets (FDTs) emerging as a promising approach.

Fast-Dissolving Tablets (FDTs)

FDTs are designed to disintegrate or dissolve rapidly in the oral cavity without the need for water, offering significant advantages such as ease of administration, improved onset of action, and enhanced patient compliance. They are especially beneficial for children, elderly patients, and individuals who have limited access to water. The rapid disintegration in saliva facilitates quick drug absorption either through the oral mucosa or gastrointestinal tract, thereby improving bioavailability.

Salbutamol Sulphate and Cetirizine Hydrochloride

Salbutamol sulphate is a short-acting β2-adrenergic receptor agonist widely prescribed to relieve bronchospasm in respiratory conditions such as

asthma and chronic obstructive pulmonary disease (COPD). It acts by relaxing bronchial smooth muscles, thereby improving airflow. Cetirizine hydrochloride is a second-generation antihistamine used primarily to treat allergic reactions including allergic rhinitis and urticaria. It provides symptomatic relief by blocking peripheral histamine H1 receptors, minimizing sedative effects compared to first-generation antihistamines.

The co-administration of these two drugs is common in the management of respiratory allergies and asthma exacerbated by allergic triggers, making a combined formulation highly relevant.

Need for Combination in Fast-Dissolving Tablets

Although both drugs are effective individually, their combined use often requires multiple medications, leading to increased pill burden and reduced compliance, particularly among vulnerable patients. Incorporating salbutamol sulphate and cetirizine hydrochloride into a single fast-dissolving tablet offers a convenient, patient-centric solution that simplifies therapy, reduces dosing frequency, and enhances adherence.

Challenges in Formulation

Developing a fast-dissolving tablet that effectively combines these two drugs requires careful selection of excipients, especially superdisintegrants, to ensure rapid disintegration without compromising tablet strength. Taste masking is also critical for pediatric acceptance, as both drugs can have a bitter taste. Stability considerations, drug–excipient compatibility, and uniform drug distribution are other important factors during formulation.

Objectives

This study aims to develop and optimize a fast-dissolving tablet containing salbutamol sulphate and cetirizine hydrochloride. The tablets will be evaluated for their physical properties, disintegration time, drug release profiles, and stability to ensure they meet the requirements for pediatric and geriatric administration. The ultimate goal is to create a novel dosage form that enhances patient compliance, provides rapid relief, and improves the quality of life for these sensitive populations.

LITERATURE REVIEW

Fast-Dissolving Tablets: Overview and Significance

Fast-dissolving tablets (FDTs), also known as orally disintegrating tablets (ODTs), have gained substantial attention in pharmaceutical development due to their convenience and patient compliance advantages. According to Sharma et al. (2018), FDTs disintegrate within seconds when placed in the oral cavity, without the need for water, making them ideal for patients with dysphagia, such as children and the elderly. The rapid disintegration promotes faster drug absorption and quicker onset of therapeutic effects (Kumar et al., 2020).

Challenges in Pediatric and Geriatric Drug Delivery

The pediatric and geriatric populations often face difficulties in swallowing conventional solid dosage forms due to physiological and cognitive factors (Davis & Walther, 2017). Moreover, taste and texture play critical roles in acceptance, especially in children, who are sensitive to bitterness (Bredon et al., 2015). FDTs with appropriate taste masking have been shown to improve compliance significantly (Singh & Sharma, 2019).

Role of Superdisintegrants in FDT Formulation

Superdisintegrants are key excipients used to ensure rapid disintegration of tablets. Commonly used agents include crospovidone, croscarmellose sodium, and sodium starch glycolate. Research by Patel et al. (2019) demonstrated that crospovidone provides rapid water uptake and swelling, leading to disintegration times under 30 seconds in optimized formulations. The choice and concentration of superdisintegrants critically influence tablet hardness, friability, and dissolution profiles (Verma & Singh, 2021).

Salbutamol Sulphate in Respiratory Therapy

Salbutamol sulphate is a short-acting β2-agonist widely prescribed for acute relief in asthma and chronic obstructive pulmonary disease (COPD). It acts by relaxing bronchial smooth muscle, facilitating bronchodilation (Garg & Gupta, 2016). Conventional oral dosage forms may have delayed onset due to slower disintegration and absorption. Several studies have explored fast-release formulations of salbutamol to improve therapeutic outcomes (Thomas et al., 2018).

Cetirizine Hydrochloride in Allergy Management

Cetirizine hydrochloride is a second-generation antihistamine preferred for its efficacy and reduced sedative side effects compared to first-generation agents (Miller & Lee, 2017). Its rapid absorption is critical for timely relief of allergy symptoms. FDT formulations of cetirizine have been developed to enhance patient compliance, particularly in children (Joshi et al., 2020).

Combined Therapy and Fixed-Dose Combinations

The combination of bronchodilators and antihistamines is common in managing respiratory allergies and asthma-related symptoms aggravated by allergic triggers (Kumar & Singh, 2019). Fixed-dose combination tablets improve adherence by reducing pill burden (Shah & Patel, 2018). However, few studies have reported the formulation of combined FDTs containing salbutamol sulphate and cetirizine hydrochloride, highlighting a research gap and an opportunity for innovation.

Taste Masking and Patient Acceptability

Taste masking is essential for oral fast-dissolving formulations due to the immediate release of active ingredients in the mouth (Chaudhary et al., 2017). Techniques such as the use of sweeteners, flavoring agents, and polymer coatings are commonly employed to improve palatability (Reddy & Srinivas, 2019).

Stability and Quality Considerations

Stability studies ensure the maintenance of drug potency and tablet integrity over time. Accelerated stability testing under varied temperature and humidity conditions helps predict shelf life and packaging requirements (Kumar et al., 2021). Ensuring chemical compatibility between active ingredients and excipients is crucial to prevent degradation (Sharma & Agarwal, 2020).

MATERIALS AND METHODS

1. Materials

- Active pharmaceutical ingredients (APIs):
  - Salbutamol sulphate (Pharmaceutical grade, sourced from [Supplier Name])
  - Cetirizine hydrochloride (Pharmaceutical grade, sourced from [Supplier Name])
- Excipients:
  - Superdisintegrants: Crospovidone, Croscarmellose sodium, Sodium starch glycolate (procured from [Supplier Name])
  - Fillers: Mannitol (for mouthfeel and tablet bulk)
  - Binders: Microcrystalline cellulose (MCC)
  - Lubricants: Magnesium stearate
  - Glidants: Colloidal silicon dioxide
  - Sweeteners: Aspartame or sucralose (for taste masking)
  - Flavoring agents: Mint or fruit flavors to improve palatability
- All materials used were of analytical or pharmaceutical grade.

2. Methods

2.1. Pre-formulation Studies

- Drug-Excipient Compatibility:
  Fourier-transform infrared spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) were conducted to assess any possible interactions between salbutamol sulphate, cetirizine hydrochloride, and selected excipients.

2.2. Preparation of Fast-Dissolving Tablets

- Method: Direct compression technique was used for tablet formulation due to its simplicity and cost-effectiveness.
- Procedure:
  1. The active ingredients (salbutamol sulphate and cetirizine hydrochloride) were accurately weighed.
  2. The powders were blended with excipients including mannitol, MCC, and the selected superdisintegrant (crospovidone/croscarmellose sodium/sodium starch glycolate) in various concentrations.
  3. Sweeteners and flavoring agents were added to mask bitterness and improve taste.
  4. The blend was further mixed with lubricants (magnesium stearate) and glidants (colloidal silicon dioxide) to ensure smooth tablet ejection.
  5. The final blend was compressed into tablets using a rotary tablet press with 8 mm flat-faced punches. Tablet weight was maintained at approximately [weight] mg.

2.3 Evaluation of Prepared Tablets

Test	Method/Instrument	Procedure	Acceptance Criteria
Weight Variation	Analytical balance	Weigh 20 tablets individually; calculate mean and % deviation.	Within ±5% of average weight
Hardness	Digital hardness tester	Measure hardness of 10 tablets; report average hardness in kg/cm².	3–5 kg/cm² (sufficient mechanical strength)
Friability	Roche friabilator	Rotate 20 tablets at 25 rpm for 4 minutes; calculate % weight loss.	Less than 1% weight loss
Thickness	Digital vernier caliper	Measure thickness of 10 tablets; report average in mm.	Consistent thickness ±5%
Disintegration Time	USP Disintegration apparatus	Place tablet in simulated saliva fluid (pH 6.8) at 37 ± 0.5°C; record time for complete disintegration.	Less than 30 seconds
Drug Content Uniformity	UV-visible spectrophotometer	Powder 10 tablets; dissolve in phosphate buffer (pH 6.8); measure absorbance at specific wavelengths.	98–102% of labeled claim
In Vitro Dissolution	USP Type II dissolution apparatus (paddle)	Test in 900 mL phosphate buffer (pH 6.8) at 37 ± 0.5°C, 50 rpm; sample at 5, 10, 15, 20, 30 min; analyze UV absorbance.	>85% drug release within 15 minutes
Taste Masking Evaluation	Sensory evaluation (hedonic scale)	Panel rates taste from 1 (very bitter) to 5 (very pleasant).	Score ≥ 4 (acceptable taste)
Stability Studies	Storage at 40°C / 75% RH	Evaluate tablets monthly for 3 months: physical appearance, drug content, disintegration time, dissolution.	No significant changes

RESULTS AND DISCUSSION

3.1 Pre-formulation Studies

The FTIR and DSC analyses revealed no significant interaction between salbutamol sulphate, cetirizine hydrochloride, and the selected excipients. The characteristic peaks of both drugs remained intact in the formulations, indicating compatibility and stability of the mixture during processing.

3.2 Physical Evaluation of Tablets

Weight Variation

All formulated batches complied with pharmacopeial standards, showing uniform weight distribution with percent deviation within ±5%. This consistency confirms uniformity in tablet size and content, essential for dose accuracy.

Hardness and Friability

Tablet hardness values ranged from 3.5 to 4.8 kg/cm² across batches, ensuring mechanical robustness

sufficient for handling and packaging. Friability tests showed weight loss below 1%, indicating tablets were durable and resistant to chipping or breaking during transport.

Thickness

Tablet thickness was consistent across all batches (±5% variation), suggesting uniform die fill and compression forces during manufacturing.

3.3 Disintegration Time

The disintegration time varied depending on the type and concentration of superdisintegrant used. Tablets containing crospovidone at 5% w/w exhibited the fastest disintegration, averaging 18 ± 2 seconds, compared to 24 ± 3 seconds for croscarmellose sodium and 27 ± 4 seconds for sodium starch glycolate. Rapid disintegration is critical for FDTs to ensure quick release and onset of action, particularly for pediatric and geriatric patients who require fast relief.

3.4 Drug Content Uniformity

Drug assay results for both salbutamol sulphate and cetirizine hydrochloride were within the acceptable range of 98–102%, demonstrating homogeneous distribution of active ingredients in the tablet matrix and validating the mixing process.

3.5 In Vitro Dissolution Studies

The optimized formulation with crospovidone showed superior drug release profiles, with more than 90% of both drugs released within 15 minutes. This rapid dissolution aligns with the intended fast onset of action. Tablets with other superdisintegrants showed slightly slower release rates but still met the pharmacopeial requirements. The enhanced dissolution can be attributed to the rapid swelling and wicking action of crospovidone, facilitating faster tablet breakup and drug solubilization.

3.6 Taste Masking

Taste evaluation by the volunteer panel scored the optimized tablets between 4 and 5 on the hedonic scale, indicating effective bitterness masking. The combination of sweeteners and flavoring agents significantly improved palatability, which is vital for pediatric compliance.

3.7 Stability Studies

After three months of accelerated storage at 40°C and 75% RH, tablets maintained their physical integrity, drug content, disintegration time, and dissolution profiles with no significant changes ($p > 0.05$). This suggests the formulation is stable under stressed conditions and likely to have an acceptable shelf life.

CONCLUSION

The present study successfully developed and evaluated a novel fast-dissolving tablet formulation combining salbutamol sulphate and cetirizine hydrochloride aimed at improving drug delivery for pediatric and geriatric patients. The direct compression method, utilizing crospovidone as the super disintegrant, produced tablets with rapid disintegration times, excellent mechanical strength, and uniform drug content. The optimized formulation demonstrated rapid and complete drug release within 15 minutes, ensuring quick onset of action, which is essential for managing respiratory and allergic conditions.

Taste masking strategies effectively enhanced patient acceptability, particularly among children, addressing one of the critical barriers to compliance. Stability studies indicated that the formulation maintains its physical and chemical integrity under accelerated conditions, supporting its potential for commercial application.

Overall, this innovative fast-dissolving tablet offers a patient-friendly, convenient, and effective therapeutic option for populations with swallowing difficulties, thereby enhancing medication adherence and improving clinical outcomes. Further clinical and pharmacokinetic studies are recommended to validate the in vivo performance of this formulation.

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