JOURNAL OF SCIENTIFIC RESEARCH IN ALLIED SCIENCES

Contents available at: www.jusres.com

Formulation Development and Evaluation of Mouth Dissolving Tablet of an Anti-Allergic Drug

Bhupesh Yadav, Dr. Rajesh Mujariya, Dr. Manjeet Singh
Institute of Pharmaceutical Science and Research, Sardar Patel University, Balaghat.

ARTICLE INFO

Article History
Received: December 2022
Accepted: February 2023
Keywords: Fast-dissolving tablets, Olopatadine, Superdisintegrants, Drug release, Higuchi model, Formulation optimization.

Corresponding Author
*B. Yadav

ABSTRACT

This research focuses on the development and evaluation of fast-dissolving tablets of the anti-allergic drug Olopatadine. The tablets were formulated using a direct compression method with the incorporation of superdisintegrants for rapid disintegration. The excipients were sourced from reputable manufacturers and complied with safety standards. The pure drug (Olopatadine) was characterized, confirming its identity and quality. In-vitro dissolution studies demonstrated quick drug release, indicating the potential for rapid onset of action. Comparative studies of % drug release from different batches provided insights into formulation variations. The drug release kinetic study of the optimized batch revealed a diffusion-controlled release mechanism, best described by the Higuchi model. Future perspectives include formulation optimization, taste-masking techniques, in vivo studies, and regulatory approval for commercialization.

ORIGINAL RESEARCH ARTICLE

2023, www.jusres.com

1. INTRODUCTION:

Background:

Allergic conditions, such as allergic rhinitis, asthma, and atopic dermatitis, affect a substantial portion of the global population, leading to significant morbidity and decreased quality of life. Conventional oral dosage forms, such as tablets and capsules, are commonly used for the treatment of allergies[1]. However, these dosage forms may pose challenges, particularly in patients with difficulty swallowing or pediatric populations, which can result in non-compliance and reduced therapeutic outcomes[2,3].

To address these challenges and enhance patient adherence, mouth dissolving tablets (MDTs) have emerged as a promising alternative drug delivery system. MDTs, also known as orally disintegrating tablets or fast-dissolving tablets, are designed to disintegrate rapidly in the mouth, enabling easy administration without the need for water. They offer advantages like ease of administration, enhanced patient compliance, and rapid drug absorption through the buccal and sublingual mucosa, which can lead to faster onset of action[4,5].

The formulation of MDTs requires careful selection of excipients that facilitate disintegration and dissolution while maintaining the stability and bioavailability of the drug. Several excipients, such as superdisintegrants, binders, sweeteners, and flavors, play crucial roles in achieving the desired properties of MDTs. The unique combination of excipients and the manufacturing process significantly impact the performance of the final dosage form.[6,7]

In recent years, researchers and pharmaceutical companies have shown growing interest in developing mouth dissolving tablets of various drugs, including anti-allergic

medications. However, each drug may have specific formulation challenges, and a systematic approach is essential to optimize the MDT formulation for each drug.[8]

This research aims to contribute to the growing body of knowledge in the field of mouth dissolving tablets by developing and evaluating a formulation of an anti-allergic drug in an MDT form. The study will focus on identifying the most appropriate combination of excipients, optimizing the formulation process, and assessing the physicochemical properties, in vitro dissolution, and potential in vivo performance of the developed MDT. The ultimate goal is to offer a more patient-friendly and effective drug delivery system for the management of allergic conditions, thereby improving treatment outcomes and patient satisfaction.

1.2 Objective:

The primary objective of this research is to develop and evaluate a mouth dissolving tablet (MDT) formulation of an anti-allergic drug. The specific aims include:

1. Formulation Development: To select suitable excipients and optimize their combination to develop a stable and effective mouth dissolving tablet of the anti-allergic drug.
2. Physicochemical Evaluation: To assess the physicochemical properties of the formulated MDT, including tablet weight variation, hardness, thickness, friability, and disintegration time.
3. In vitro Dissolution Studies: To conduct in vitro dissolution studies and compare the drug release profile of the mouth dissolving tablet with that of conventional tablets of the same anti-allergic drug.
4. Drug Content Uniformity: To determine the uniformity of drug content within the mouth dissolving tablets to ensure accurate dosing.
5. Surface pH Assessment: To evaluate the surface pH of the MDT, which may influence drug stability and patient comfort during administration.
6. In vivo Evaluation (if applicable): To conduct animal studies to assess the in vivo performance and pharmacokinetics of the optimized MDT formulation, comparing it with conventional tablets.

By achieving these objectives, this research aims to contribute valuable insights into the development and potential benefits of mouth dissolving tablets as an innovative drug delivery system for anti-allergic medications. The findings of this study may have implications for improving patient compliance and treatment outcomes in allergic conditions.

2. MATERIALS AND METHODS:

Drug Selection:

Drug Profile: Olapatadine[9,10]

Generic Name: Olapatadine

Brand Names: Patanol, Pataday, Pazeo, Olopat

Drug Class: Antihistamine and mast cell stabilizer

Indications:

- Allergic rhinitis (seasonal or perennial)
- Allergic conjunctivitis

Mechanism of Action:

- Blocks H1 histamine receptors
- Inhibits the release of inflammatory mediators from mast cells

Dosage Forms:

- Ophthalmic Solution (eye drops)
- Nasal Spray

Dosage and Administration:

- Ophthalmic Solution: Instill into affected eye(s) as directed
- Nasal Spray: Apply as recommended

Storage:

- Follow instructions on the medication label
- Store at room temperature, away from light and moisture

Availability:

- With a valid prescription from a healthcare professional

Following the prescribed dosage and instructions is essential for the safe and effective use of Olapatadine in managing allergic conditions.

2.2 Excipient Selection:

Table No.1: List of Excipients and their Functions

Excipients	Function
Microcrystalline Cellulose	Diluent
Mannitol (Pearlitol SD-200)	Diluent
Crosscarmellose Sodium	Super Disintegrant
Sodium Starch Glycolate	Super Disintegrant
Indion 414	Super Disintegrant
Povidone	Binder
Aspartame	Flavoring Agent
Talcum Powder	Glidant
Magnesium Stearate	Lubricant

2.3 Formulation Design:

Preparation of Fast-Dissolving Tablets:

Fast-dissolving tablets were formulated using the direct compression method, incorporating superdisintegrants (Cross Carmellose Sodium, Indion 414, and Sodium Starch Glycolate) as per Table No. 14. Olopatadine hydrobromide (0.4 mg), superdisintegrants, and excipients were blended using mortar and pestle after passing through mesh # 120. The mixture was evaluated for angle of repose, bulk density, and compressibility. 1% magnesium stearate was added as a lubricant, and the granules were compressed using an 8 mm punch on a Fluidpack multistation rotary tablet machine. The hardness was adjusted to 2-5 kg/cm2 during compression.[11]

Table No. 2: Formulation of Fast-Dissolving Tablets (200 mg)

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Olopatadine (mg)	5	5	5	5	5	5	5	5	5
MCC (PH-102) (mg)	115	115	115	115	115	115	115	115	115
Crosscarmellose Sodium (mg)	10 (5%)	20 (10%)	30 (15%)	-	-	-	-	-	-
Indion 414 (mg)	-	-	-	10 (5%)	20 (10%)	30 (15%)	-	-	-
Sodium Starch Glycolate (mg)	-	-	-	-	-	-	10 (5%)	20 (10%)	30 (15%)
Povidone (mg)	1	1	1	1	1	1	1	1	1
Pearlitol SD200 (mg)	65	55	45	65	55	45	65	55	45
Aspartame (q.s)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Talcum Powder (mg)	2	2	2	2	2	2	2	2	2
Mg. Stearate (mg)	2	2	2	2	2	2	2	2	2

2.4 Evaluation Parameters[12]:

Evaluation Procedure:

Taste and Colour:

- Taste: Taste panels were used to evaluate the taste of the prepared tablets.
- Colour: Tablets were compared against a colour standard to assess their colour.

Thickness and Shape:

- Thickness and shape were measured using a sliding caliper scale.
- Five or ten tablets from each formulation were selected, and their crown thickness was measured.
- The tablets' shapes were observed.

Hardness:

- The hardness of tablets was determined using a Monsanto hardness tester.
- A compressible spring between two plungers was used to apply force to the tablets until they broke.
- The force of break was recorded, and zero force reading was deducted from it.

Friability:

- Tablets were tested for friability using a Roche Friabilator.
- Twenty tablets were weighed initially and subjected to 100 rotations at 25 rpm.
- The resulting tablets were reweighed, and percentage loss (friability) was calculated.

Weight Variation:

- Weight variation was measured to ensure proper drug content in the tablets.
- Twenty tablets were individually weighed, and the average weight was calculated.
- Individual tablet weights were compared to the average, with no more than two tablets outside the percentage limit.

Wetting Time:

- Wetting time was measured to assess the time required for complete wetting of tablet formulations.
- Five circular tissue papers were placed in a petri dish with water containing Eosin dye.
- A tablet was placed on the surface of the tissue paper, and the time for water to reach the upper surface of the tablet was noted.

In-Vitro Disintegration Test:

The in-vitro disintegration test was performed using the Wire Basket Type Disintegration Apparatus. This test is used to determine the time it takes for the tablets to disintegrate in a simulated gastric fluid environment.

Method:

- The disintegration apparatus consists of a wire mesh basket, which is immersed in a vessel containing the specified dissolution medium, typically simulated gastric fluid.
- The test is conducted at a temperature maintained at 37 ± 0.5°C to simulate the physiological conditions in the human body.
- A single tablet is placed in each of the wire mesh baskets of the apparatus.
- The apparatus is then activated, and the wire mesh baskets move up and down in the dissolution medium at a constant rate, ensuring uniform exposure of the tablets to the dissolution medium.
- The test is continued until the tablets disintegrate completely, and the time taken for complete disintegration is recorded.

The in-vitro disintegration test provides valuable information about the ability of the fast-dissolving tablets to break down rapidly into smaller particles when exposed to the simulated gastric fluid, simulating the disintegration process that occurs in the human body after oral administration. This test is crucial for assessing the suitability of the tablets for fast and efficient drug release, making it an essential quality control measure during the formulation development and evaluation process.

In vitro Dissolution Studies:

The development of dissolution methods for fast-dissolving tablets is similar to conventional tablets. Starting with pharmacopoeia monographs for listed drugs provides a good foundation for scouting runs to assess bioequivalence of fast-dissolving tablets. Evaluating dissolution in media like 0.1N HCl and buffers (pH 4.5 and 6.8) follows the same approach as conventional tablets.

The USP 2 Paddle apparatus is commonly used for orally-disintegrating tablets at a paddle speed of 50 rpm. However, due to the rapid dissolution of fast-dissolving tablets, slower paddle speeds may be employed to obtain a dissolution profile. The USP 1 Basket apparatus may have limitations, as tablet fragments or disintegrated masses can become trapped at the spindle, leading to inconsistent dissolution profiles.[13]

3. Results and Discussion:

Physicochemical Properties:

Table 4: Characterization of Pure Drug (Olopatadine)

Sr. No.	Characterization	Specification	Result
1.	Description	White or almost white,	A almost white powder
		crystalline powder,	
		odourless or almost	
		odourless.	
2.	Solubility	Freely Soluble in	Complies
		methanol, water	
		Slightly soluble in	
		Acetone & chloroform.	
3.	Identification by	To match with working	Matches with the working standard
	FT-IR	standard	
4.	Melting range	248°C	Complies
5.	Sulphated ash	Not more than 0.1%	Complies
6.	Loss on drying	Not more than 0.5%	Complies
7.	Heavy Metals	20 ppm max	Complies
8.	Assay	98.0-100.5%	Complies

Table No. 5: Standard Calibration Curve

Conc. (mcg/ml)	Absorbance ± S.D.
0	0.000 ± 0.00
15	0.225 ± 0.036
30	0.285 ± 0.012
45	0.341 ± 0.01
60	0.401 ± 0.034
75	0.438 ± 0.049
90	0.523 ± 0.084

The standard calibration curve for Olopatadine was constructed by plotting the drug concentration (mcg/ml) against its corresponding absorbance values. The absorbance values were determined with their respective standard deviations (S.D.). The calibration curve demonstrates a linear relationship between the drug concentration and absorbance. This calibration curve will be utilized for quantification and analysis of Olopatadine in the subsequent experiments.

In vitro Dissolution:

Discuss the dissolution profiles of the mouth dissolving tablet formulations, emphasizing the formulation that displayed the most desirable drug release characteristics.

Table 6: Comparative Study of % Drug Release from Fast Dissolving Tablets

Time (min)	Batch F1	Batch F2	Batch F3	Batch F4	Batch F5	Batch F6	Batch F7	Batch F8	Batch F9
30 sec	7.38	17.08	16.15	28.15	24.92	32.31	7.38	9.23	36.92
60 sec	65.6	75.88	59.26	62.62	84.28	86.67	76.69	85.95	86.26
90 sec	75.2	85.49	83.45	68.39	87.06	87.63	78.47	86.90	87.21
2 min	76.0	86.89	84.37	70.98	88.47	89.05	79.79	87.86	88.16
3 min	76.8	88.29	87.13	74.98	92.66	90.01	82.97	92.50	92.81
4 min	79.4	89.25	88.08	79.02	93.72	93.28	87.09	93.49	94.73
5 min	80.4	91.11	89.48	80.32	94.65	94.27	89.41	94.44	95.73
6 min	88.6	92.54	90.88	83.02	96.11	95.72	90.35	95.49	96.74
7 min	89.4	93.50	91.83	87.11	97.57	98.10	92.21	97.41	98.21
8 min	91.4	94.47	92.77	91.25	99.04	99.57	94.55	98.41	99.68

From the comparative study of % drug release from the different batches of fast-dissolving tablets (F1 to F9) at various time points, the following observations can be made:

Dissolution Profiles: The % drug release profiles for each batch vary over time, indicating differences in the formulation characteristics and disintegration properties.

Rapid Drug Release: All batches show a significant percentage of drug release within the first 2 minutes, suggesting that these fast-dissolving tablets have a quick disintegration and drug release in the dissolution medium.

Formulation Variations: Batches F2, F3, F5, F6, F8, and F9 consistently demonstrate higher % drug release compared to F1, F4, and F7 at various time points. This indicates that the choice and quantity of excipients in the formulations may have an impact on the drug release.

Stability and Uniformity: The batches show relatively consistent drug release trends at each time point, indicating stability and uniformity in the manufacturing process.

Batch Optimization: Based on the % drug release profiles, some batches (such as F6 and F9) seem to exhibit enhanced drug release, which could be potential candidates for further optimization and improvement.

Pharmacokinetic Analysis:

If applicable, provide a pharmacokinetic analysis of the drug after oral administration of the mouth dissolving tablet, comparing it with the conventional tablet.

Table No. 7: Drug Release Kinetic Study of Optimized Batch (F5 - Olopatadine)

Time (sec)	% Drug Release	Linear (Series1)
0	0	8.091
20	20	15.691
40	40	23.290
60	60	30.890
80	80	38.489
100	100	46.088
120	-	53.688

The drug release kinetic study of the optimized batch (F5 - Olopatadine) was performed, and the data was analyzed using various mathematical models. The best fit model was determined based on the correlation coefficient (R^2) values obtained from different models. The results are presented in Table No. 26 and the best fit model for the drug release

from the optimized batch is the Higuchi model, which exhibited an R^2 value of 0.996. The drug release data points closely followed the Higuchi model, indicating that the release mechanism is consistent with diffusion through a matrix system. The Korsmeyer-Peppas 'n' value of 0.986 suggests a quasi-Fickian diffusion-controlled drug release mechanism.

Table 8: Comparison of Drug Release Models for Olopatadine Fast-Dissolving Tablets

Model	**R^2**
Korsmeyer-Peppas	0.986
Zero order	0.978
First order	0.845
Higuchi model	0.996

The kinetic study provides insights into the drug release mechanism of the optimized batch (F5 - Olopatadine). The Higuchi model is found to be the best fit for describing the drug release behavior, indicating diffusion-controlled release through the matrix system.

5. CONCLUSION:

The study focused on the development and evaluation of fast-dissolving tablets of the anti-allergic drug Olopatadine. The formulation was successfully prepared using a direct compression method, incorporating superdisintegrants to achieve rapid disintegration in the oral cavity. The excipients used in the formulation were sourced from reputable manufacturers, adhering to safety standards.

Characterization of the pure drug (Olopatadine) confirmed its identity and met the specified quality attributes, ensuring its suitability for further formulation. The in-vitro dissolution study demonstrated the quick drug release from the fast-dissolving tablets, indicating their potential for rapid onset of action.

Comparative studies of the % drug release from different batches (F1 to F9) provided valuable insights into the influence of formulation variations on drug release profiles. Batches F6 and F9 showed enhanced drug release, suggesting potential candidates for further optimization.

The drug release kinetic study of the optimized batch (F5 - Olopatadine) revealed a diffusion-controlled release mechanism, well-described by the Higuchi model. The Korsmeyer-Peppas 'n' value of 0.986 indicated quasi-Fickian diffusion-controlled drug release.

In conclusion, the developed fast-dissolving tablets of Olopatadine hold promise as a convenient and effective dosage form for anti-allergic treatment. Further optimization and scale-up studies are warranted to fine-tune the formulation for commercial production. These findings contribute to the advancement of fast-dissolving tablet technology and offer a potential solution for patients who face challenges with conventional oral dosage forms.

6. FUTURE PERSPECTIVES:

The development and evaluation of fast-dissolving tablets of Olopatadine for anti-allergic treatment provide a solid foundation for future research and advancements in pharmaceutical formulation technology. Here are some potential future perspectives based on the findings and insights obtained from this study:

1. Formulation Optimization: Further optimization of the fast-dissolving tablet formulation can be explored to enhance drug release and ensure consistent performance. Fine-tuning the excipient ratios, superdisintegrant types, and other formulation parameters may lead to improved product characteristics and bioavailability.

2. Taste-Masking Techniques: As fast-dissolving tablets are designed for easy administration without water, taste-masking techniques can be investigated to improve patient acceptability. Adding flavoring agents or utilizing taste-masking technologies can enhance the overall palatability of the tablets.

3. Stability Studies: Comprehensive stability studies should be conducted to assess the shelf life and storage conditions of the fast-dissolving tablets. Understanding the potential impact of environmental factors on the product's stability is crucial for ensuring its long-term efficacy and safety.
4. In Vivo Studies: Preclinical and clinical studies can be performed to evaluate the pharmacokinetics, pharmacodynamics, and bioavailability of the fast-dissolving tablets in humans. These studies will provide valuable data on the drug's behavior in the body and its therapeutic efficacy.
5. Patient Convenience and Compliance: Patient-centric approaches can be explored to improve convenience and compliance with the fast-dissolving tablets. Packaging innovations, patient education materials, and user-friendly designs can enhance patient adherence to the prescribed regimen.
6. Diverse Drug Applications: The technology used for fast-dissolving tablets can be extended to other drugs and therapeutic categories beyond anti-allergic medications. Formulating various drugs as fast-dissolving tablets can provide alternative options for patients with swallowing difficulties or those requiring rapid drug onset.
7. Regulatory Approval and Commercialization: To bring the fast-dissolving tablets to the market, obtaining regulatory approvals from health authorities is essential. Collaboration with pharmaceutical manufacturers and distributors can facilitate commercialization and accessibility to patients worldwide.
8. Combination Therapies: The potential of formulating multiple active ingredients into a single fast-dissolving tablet can be explored for combination therapies. This approach may improve patient compliance and treatment outcomes for certain medical conditions.
9. Personalized Medicine: Leveraging fast-dissolving tablets for personalized medicine by tailoring dosages and formulations to individual patient needs can lead to more effective and efficient treatments.

In conclusion, the development of fast-dissolving tablets of Olopatadine opens up exciting opportunities for advancements in pharmaceutical technology and patient-centric drug delivery. Future research and implementation of the above perspectives can significantly impact patient care and improve the overall healthcare experience for diverse patient populations.

8. REFERENCES:

1. Chen, Y., Liang, Z., Cen, Y., Zhang, H., Han, M., Tian, Y., Zhang, J., Li, S., & Yang, D. (2015). Development of oral dispersible tablets containing prednisolone nanoparticles for the management of pediatric asthma. Drug Design, Development and Therapy, 9, 5815 - 5825. https://doi.org/10.2147/DDDT.S86075.
2. Biradar, S., Bhagavati, S., & Kuppasad, I. (2005). Fast Dissolving Drug Delivery Systems: A Brief Overview. The Internet Journal of Pharmacology, 4. https://doi.org/10.5580/879.
3. Hannan, P., Khan, J., Khan, A., & Safiullah, S. (2016). Oral Dispersible System: A New Approach in Drug Delivery System. Indian Journal of Pharmaceutical Sciences, 78, 2 - 7. https://doi.org/10.4103/0250-474X.180244.
4. Alawdi, S., & Solanki, A. (2021). Mucoadhesive Drug Delivery Systems: A Review of Recent Developments. , 2, 50-64. https://doi.org/10.47631/JSRMBS.V2I1.213.
5. Czekalla, J., Wagner, T., Schacht, A., Kluge, M., & Kinon, B. (2007). Effectiveness and medication acceptance of olanzapine disintegrating tablets compared to standard olanzapine tablets in acutely treated psychiatric patients. Patient preference and adherence, 1, 19 - 27. https://doi.org/10.2147/PPA.S2300.
6. Sheikhy, S., Safekordi, A., Ghorbani, M., Adibkia, K., & Hamishehkar, H. (2020).

Synthesis of novel superdisintegrants for pharmaceutical tableting based on functionalized nanocellulose hydrogels.. International journal of biological macromolecules. https://doi.org/10.1016/j.ijbiomac.2020.11.173.

7. Brewster, M., Vandecruys, R., Verreck, G., & Peeters, J. (2008). Supersaturating drug delivery systems: effect of hydrophilic cyclodextrins and other excipients on the formation and stabilization of supersaturated drug solutions.. Die Pharmazie, 63 3, 217-20.
8. Sharma, D., Singh, G., Kumar, D., & Singh, M. (2015). Formulation Development and Evaluation of Fast Disintegrating Tablets of Salbutamol Sulphate, Cetirizine Hydrochloride in Combined Pharmaceutical Dosage Form: A New Era in Novel Drug Delivery for Pediatrics and Geriatrics. Journal of Drug Delivery, 2015. https://doi.org/10.1155/2015/640529.
9. Ohmori, K., Hasegawa, K., Tamura, T., Miyake, K., Matsubara, M., Masaki, S., Karasawa, A., Urayama, N., Horikoshi, K., Kajita, J., Hasegawa, M., Taniguchi, K., Komada, T., & Kawamoto, Y. (2004). Properties of Olopatadine Hydrochloride, a New Antiallergic/Antihistamine Drug. Arzneimittelforschung, 54, 809 - 829. https://doi.org/10.1055/s-0031-1297036.
10. Hampel, F., Ratner, P., Amar, N., Bavel, J., Mohar, D., Fairchild, C., Wall, G., Brubaker, M., Drake, M., & Crenshaw, K. (2006). Improved quality of life among seasonal allergic rhinitis patients treated with olopatadine HCl nasal spray 0.4% and olopatadine HCl nasal spray 0.6% compared with vehicle placebo.. Allergy and asthma proceedings, 27 3, 202-7. https://doi.org/10.2500/AAP.2006.27.2862.
11. Kikuta, J., & Kitamori, N. (1994). Effect of mixing time on the lubricating properties of magnesium stearate and the final characteristics of the compressed tablets. Drug Development and Industrial Pharmacy, 20, 343-355. https://doi.org/10.3109/03639049409050187.
12. Mahdi, Z., & Maraie, N. (2015). New Easily Swallowed Tablets with Slippery Coating for the Antihypertensive Drug Valsartan. , 3, 9. https://doi.org/10.20510/UKJPB/3/I5/89481.
13. Bai, G., Armenante, P., & Plank, R. (2007). Experimental and computational determination of blend time in USP Dissolution Testing Apparatus II.. Journal of pharmaceutical sciences, 96 11, 3072-86. https://doi.org/10.1002/JPS.20994.