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Design and Evaluation of Mouth Dissolving Tablets of Eletriptan Hydrobromide for Rapid Migraine Relief

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ABSTRACT -

Background: Migraine is a prevalent neurological disorder characterized by recurrent headaches, often accompanied by nausea and vomiting, which limits the effectiveness of conventional oral drug delivery. EletriptanHydrobromide, a selective 5-HT1 receptor agonist, is approved for acute migraine management. However, its conventional tablet form delays therapeutic onset. This study aimed to formulate and evaluate mouth dissolving tablets (MDTs) of EletriptanHydrobromideto enhance patient compliance.

Methods: MDTs were developed using a modified dry granulation technique incorporating varying concentrations of croscarmellose sodium (as superdisintegrant) and a wax mixture (Gelucire 39/01 and PEG 6000). A 3^2 factorial design was applied to optimize formulation variables. Prepared tablets were evaluated for physical properties, drug content, disintegration time, and in vitro dissolution. Optimization was guided using statistical models assessing tablet hardness, friability, and disintegration.

Results: All batches exhibited uniform weight, thickness, and diameter. The disintegration time ranged between 15.26 and 36.41 seconds, with batch F3 showing the most rapid disintegration. Drug content was within pharmacopeial limits (85–115%). The optimized batch demonstrated over 85% drug release within 15 minutes, indicating rapid onset. The model showed significant influence of superdisintegrant on hardness and disintegration time, with R^2 values >0.86 confirming model reliability.

Conclusion: The study successfully developed and optimized mouth dissolving tablets of EletriptanHydrobromide, which offered fast disintegration, acceptable mechanical strength, and enhanced drug release. This formulation holds promise for rapid migraine relief, especially in patients with swallowing difficulties or during acute migraine episodes.

Keywords: Eletriptan Hydrobromide, Mouth Dissolving Tablets, Migraine, Rapid Relief, Factorial Design, Super disintegrants, In Vitro Dissolution

I. INTRODUCTION

A condition of the brain that primarily affects the cranium, migraine is probably caused by changes in the regulation and control of afferents. Understanding the morphology and physiology of the cranial pain-producing structures in conjunction with their central nervous system modulation is essential to comprehending the pathophysiology of migraine.[1]The mechanism of migraine is significantly influenced by calcitonin gene-related peptides (CGRP). 5-HT1F receptor agonists have also been shown in research to be therapeutically effective in treating migraine attacks.[2] Migraine prevalence in India is very high, ranging from 14.1% to 25.2%, especially in rural regions. Despite being quite common, migraine is still not well understood or adequately treated in many areas, primarily because of cultural norms and restricted access to healthcare.[3]

To effectively treat migraines, rapid-onset medication delivery systems are crucial. Traditional dosage form often has limitations, such as delayed absorption and gastrointestinal issues. Novel administration methods like nasal sprays, mouth-dissolving tablets, or sublingual formulations can provide quicker relief, increase bioavailability, and improve patient compliance, leading to better therapeutic outcomes.[5] Patients frequently suffer nausea and vomiting during a migraine episode, which makes it challenging to swallow or hold onto oral medications. This results in reduced therapeutic efficacy and delayed drug absorption. Furthermore, conventional formulations could function more slowly, which is a significant disadvantage when quick relief is required. These restrictions draw attention to the necessity of alternate delivery methods that can provide a quicker start and better patient compliance during severe migraine episodes, like mouth-dissolving tablets.[6] The benefits of Oral Disintegrating Tablet (ODT) are numerous; make them preferable in the majority of situations for those who are unable to

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swallow traditional dosage forms, including bedridden, pediatric, psychiatric, and elderly patients who are busy, disabled, unwilling, or who don't always have access to water [7]. Furthermore, improve palatability, increase bioavailability because of absorption starting in the Digestion, enable quick drug action to perform a medical intervention or emergency, permit high drug loading, eliminate the need for chewing, make administration more practical, and provide precise dosing in comparison to liquids, preventing the risk of physical obstructions, requiring no special Due to their unique packaging and push-through blister availability, they are reasonably priced, provide good chemical stability due to their solid dosage form, and open up commercial opportunities like increased product diversity, longer patent life, marketing benefits, and life cycle management .[8]

The US Food and Drug Administration (FDA) approved the relatively new medication eletriptan on December 26, 2002For immediate relief.of adult migraines with or without aura. Eletriptan is a member of the type of heterocyclic compound called indoles. and is a methylpyrrolidinyltryptamine that has been replaced with a benzene sulfonyl derivative.[9] A triptan drug called eletriptanhydrobromide works by focusing on the brain's serotonin receptors to cure migraines. It functions by preventing the release of chemicals that cause pain from nerve endings and by narrowing dilated blood vessels in the brain, which are a major cause of migraine headache.[10]The main objective of this research paper is to formulate and evaluate mouth dissolving tablets of Eletriptan Hydrobromide for the treatment of Alzheimer's disease.This study focuses on designing a fast-acting drug delivery system to improve patient adherence, especially in elderly individuals with swallowing difficulties. By improving the onset of action and bioavailability, the formulation seeks to offer a convenient and effective therapeutic approach suitable for managing Migraine.

II. METHODOLOGY

Materials

The gift sample of Eletriptan Hydrobromide was obtained from Swaprop Agency, Sambhaje Nagar. The excipients and chemicals used in the study were sourced from reputable suppliers, including Sigma-Aldrich (now part of Merck), a leading provider of pharmaceutical ingredients and chemicals. The materials used include EletriptanHydrobromide, Mannitol, Gelucire 39/01, Lemon flavor, Sodium Saccharin, Polyethylene Glycol (PEG) 6000, Aerosil, Indion 234, and Croscarmellose Sodium**.**

Methodology

A modified dry granulation method was used to create the orodispersible tablets of eletriptan hydrobromide. To achieve equal dispersion, the medication was first combined with half as much croscarmellose sodium, saccharin, and a wax mixture (Gelucire: PEG 6000 in a 2:1 ratio). After that, this mixture was gradually heated below 50°C to guarantee uniformity without sacrificing the stability of the medication. To get uniform granules, the heated mixture was sieved through sieve number 18 (850 μm). Before being compressed into tablets, the granules were lastly mixed with the remaining croscarmellose sodium, lemon flavor, and Aerosil to guarantee homogeneity and improve flow characteristics.[11]

Eletriptan Hydrobromide's orodispersible tablet was made with carefully chosen excipients to guarantee quick disintegration and patient acceptance. A total tablet weight of 150 mg was the goal of the formulation. A superdisintegrant, sweetener, flavoring agent, dispersion aid based on wax, and diluent were among the components. The table below displays the amounts of each component used in a single representative batch.[12]

Table No 1 - Formulaeforpreparationoforodispersibletablets

Ingredients	Quantity taken in / mg								
Btaches	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	F9
EletriptanHydrobromide	15	15	15	15	15	15	15	15	**15**
Crosscarmellose Sodium	5	5	5	10	10	10	15	15	**15**

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Wax mixture	4	8	12	4	8	12	4	8	**12**
Lemon flavor	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	**1.5**
Saccharin	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	**1.5**
Aerosil	2	2	2	2	2	2	2	2	**2**
Mannitolq.s	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Evaluation of Mouth Dissolving Tablet
Dimensions

For the selected batch, tablet dimensions were measured using a high-precision digital vernier caliper (Aerospace) to ensure uniformity. Each tablet was placed between the jaws, and accurate readings in millimeters were recorded. This method ensured consistency, minimized error, and supported quality control standards.[13]

Weightvariation

A calibrated analytical balance was used to weigh each of the ten pills that were chosen at random from the batch. To evaluate consistency and guarantee adherence to pharmacopeial restrictions, their weights were compared to the computed average. This procedure verified uniformity in formulation and manufacturing, which aided quality control.[14]

Hardness

Hardness and thickness were evaluated for three randomly selected tablets using a Monsanto Hardness Tester and a digital vernier caliper, respectively. These tests assessed mechanical strength and dimensional uniformity, ensuring the tablets could withstand handling and met quality standards for dosage accuracy and dissolution.[15]

Friability

The tablets' hardness was evaluated using a Monsanto hardness tester, with results expressed in kg/cm. Friability testing was performed using a Roche Friabilator, where tablets were subjected to 25 rpm for 4 minutes. The percentage friability was calculated after dedusting and reweighing the tablets, assessing their resistance to abrasion and breakage. This test ensured the tablets met quality standards for durability during handling and transportation, with a friability value below 1% considered acceptable. The formula used was:

Friability (%) = ((Initial Weight - Final Weight) / Initial Weight) × 100.

Where:

- W1W1 = Initial weight of the tablets before testing
- W2W2 = Final weight of the tablets after testing (after dedusting)[17]

Assay of tablet

The tablets were tested for assay and content uniformity to ensure accurate dosing. A sample equivalent to 10 mg of EletriptanHydrobromide was dissolved in methanol, sonicated, filtered, and diluted. The absorbance was measured at 221 nm using a UV spectrophotometer. The drug content was calculated using a calibration curve, and the results were verified to meet pharmacopeial standards (85-115%) for batch consistency.[18]

Dissolution Testing

The coated tablets underwent a dissolution study to evaluate the drug release profile. The study used a USP Dissolution Apparatus Type II with 900 ml of dissolution medium (0.1N HCl and pH 6.8 buffer) at 37°C and 50 rpm. Samples were withdrawn every 10 minutes for 1 hour and analyzed using UV spectrophotometry at 221 nm to determine the dissolution kinetics of Eletriptan Hydrobromide.[20]

Optimization Studies and Selection of suitable experimental design

A 3^2 Factorial design was chosen for the optimization study. The concentration of crosscarmellose sodium and concentration of wax mixture were selected as formulation factors whereas drug release hardness, friability and disintegration time were measured as response. Based on preliminarytrials, levels of independent variables were selected and suitably coded, as shown in table 6.7 nine formulations were prepared

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as per factorial design.[21]This was given in table number 2

Table 2 - Experimental design for Or dispersible tablets of Eletriptan Hydrobromide

Coded Factor	Level	Factor A Crosscarmellose Sodium	Factor Wax Mixture
-1	Low	5	4
0	Intermediate	10	8
1	High	15	12

Preparation of formulations as per factorial design

Formulationswerepreparedasper factorialdesign by formulating core tablets as per Table 3[22]

Table 3 – Formulae for preparation of Mouth dissolving of Eletriptan Hydrobromide for optimization studies

Ingredients	Quantity Taken in mg								
Batches	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
EletriptanHydrobromide	15	15	15	15	15	15	15	**15**	15
Crosscarmellose sodium	5	5	5	10	10	10	15	**15**	15
Wax Mixture	4	8	12	4	8	12	4	**8**	12
Lemon Flavor	1.5	1.5	1.5	1.5	1.5	1.5	1.5	**1.5**	1.5
Saccharin	1.5	1.5	1.5	1.5	1.5	1.5	1.5	**1.5**	1.5
Aerosil	2	2	2	2	2	2	2	**2**	2
Mannitolq.s	150	150	150	150	150	150	150	**150**	150

[#]Totalweight ofthetabletswas kept150mg
[#]Allquantities arein mg

Optimization Data Analysis

The powder blend was evaluated for key flow properties, including angle of repose (to assess flowability**),** bulk density**,** tapped density**,** Carr's index (compressibility), and Hausner ratio (powder flow efficiency)[23]. These tests ensured optimal powder characteristics for uniform tablet compression, with results indicating good flow behavior and minimal segregation risks.[24]

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III. RESULT AND DISCUSSION

Evaluation of Tablet

Table 4– Evaluation OF Batches F1 To F9

Batches	Wright variation	Thickness(mm)	Diameter (mm)	DT(sec)	Hardness(kg/cm)	Friability
F1	148.73	3.022	7.992	17.72	2	**0.62**
F2	150.42	3.108	7.233	22.54	2	**0.63**
F3	149.80	3.236	8.005	30.17	2.05	**0.64**
F4	165.15	3.032	8.04	25.58	2.02	**0.68**
F5	148.88	3.247	8.071	25.16	2.03	**0.64**
F6	149.29	3.197	8.089	25.37	2.06	**0.65**
F7	149.29	2.958	8.078	36.41	2.04	**0.54**
F8	148.21	3.123	8.052	32.24	2.05	**0.52**
F9	**177.22**	**3.571**	**8.157**	**30.17**	**2.8**	**0.48**

Discussion

The evaluation of tablet formulations (F1-F9) demonstrated satisfactory physical properties that comply with standard pharmaceutical requirements. Weight variation analysis showed consistent results across most batches (148.21-165.15 mg), with only F9 exhibiting a slightly higher weight (177.22 mg), suggesting the need for minor process optimization. Tablet dimensions remained uniform, with thickness ranging from 2.958-3.571 mm and diameter between 7.233-8.157 mm, confirming proper tooling setup and compression consistency. Disintegration times (17.72-36.41 seconds) for all formulations were well within pharmacopeial limits (<3 minutes), with F1 showing the fastest disintegration (17.72 seconds), indicating potential for rapid drug release. Tablet hardness values (2.0-2.8 kg/cm²) demonstrated adequate mechanical strength for handling while maintaining acceptable disintegration properties. Friability tests revealed excellent results (0.48-0.68%), significantly below the 1% USP limit, with F7-F9 showing particularly low values (0.48-0.54%), indicating superior tablet durability.[25]These results collectively confirm that the formulation and manufacturing process produced tablets with consistent physical characteristics suitable for oral administration. The optimal combination of fast disintegration and low friability observed in F1 and F7 makes these formulations particularly promising candidates for further development. The study successfully established that all batches meet the essential quality parameters for uncoated tablets, providing a solid foundation for subsequent dissolution and stability studies.[26]

Assay of drug

The UV-Visible absorbance spectrum (main plot) shows a sharp and intense peak **at** 221 nm**,** confirming the maximum absorbance (λmax) of the analyte, which corresponds to the π→π* electronic transition in the aromatic ring structure of EletriptanHydrobromide. The absorbance intensity increases steeply around this region, indicating a strong chromophore within the molecular structure .[27]

The inset graph represents the calibration curve obtained by plotting absorbance (AU) against varying concentrations of the drug (2.5 to 10 µg/mL). The linearity of the plot confirms that Beer-Lambert's law is obeyed in this concentration range. The correlation coefficient (R^2), although not shown, appears close to 1, indicating excellent

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linearity and reliability of the developed UV spectrophotometric method for quantitative analysis.[28]

This spectral data and calibration curve validate the method's suitability for further formulation analysis, particularly for the development of orodispersible tablets, as the consistent and reproducible peak at 221 nm enables accurate quantification of Eletriptan Hydrobromide.[29]

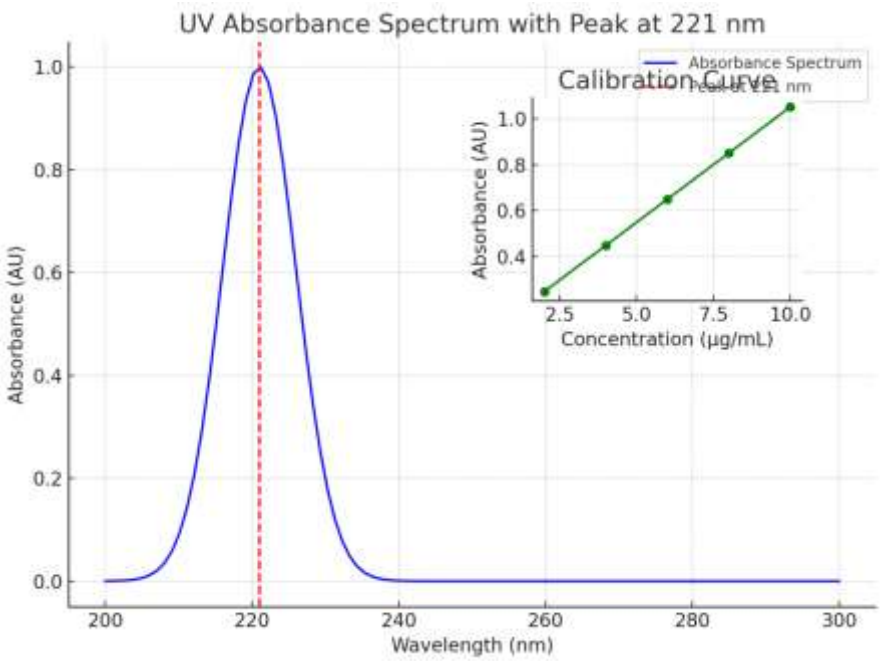

Figure 1 - Assay of Eletripitan Hydrobromide

Invitrodissolution study

Thetablets wereevaluated forin-vitrodissolution profile.

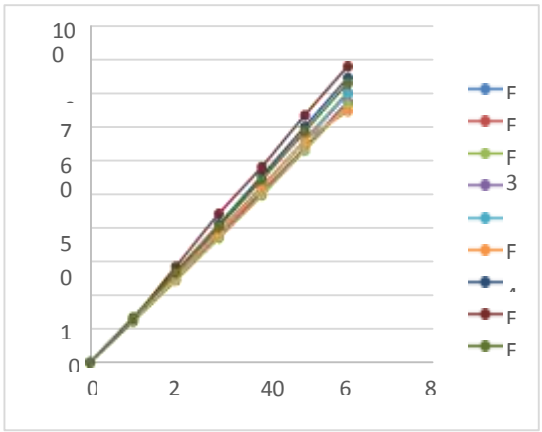

Figure 2 - Dissolution for dispersible tablet of Eletriptan Hydrobromide

Discussion

The in vitro dissolution of eletriptan hydrobromide or dispersible tablets is a critical quality control parameter to ensure drug release and bioavailability. Since orodispersible tablets disintegrate rapidly in the oral cavity, dissolution testing should mimic physiological conditions, typically using USP Apparatus II (paddle) at 50 rpm with a pH 6.8 phosphate buffer (simulating salivary pH). Sampling at short intervals (e.g., 5, 10, 15 mins) helps assess the fast-release profile. High solubility and permeability of eletriptan

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suggest that >85% drug release within 15-30 mins is desirable for BCS Class I compliance.[30] Variability in disintegration time or dissolution may indicate formulation issues, necessitating optimization of superdisintegrants or solubilizing agents. Comparative dissolution studies with reference products ensure bioequivalence, supporting regulatory approval.[31]

Experimental design:

Variables at various levels were investigated using the three level two factor approach. Nine batches' hardness, friability, and disintegration time vary greatly, ranging from 2 to 2.8 kg/cm2. 0.48to 0.68 (%)and 15.26 to 28.32 (sec.).

Table 5: formulation and measured response

Run	Factor 1 A Crosscarmellose Sodium (mg)	Factor 1Bees Wax mixture (mg)	Response-1 Hardness (kg/cm_2)	Response 2-Friability(%)	Response 3-Disintegration time(sec)
1	5	4	2	0.62	28.32
2	10	4	2.02	0.68	20.52
3	15	4	2.4	0.54	15.26
4	5	8	2	0.63	22.54
5	10	8	2.03	0.64	21.16
6	15	8	2.5	0.52	16.2
7	5	12	2.05	0.64	24.48
8	10	12	2.06	0.65	22.37
9	15	12	2.8	0.48	18.24

Mathematical model**:**

R1=+2.01+0.28 *A+0.082 *B+0.087 *AB+0.25 *A2+0.045 * is the hardness equation.The friability equation is B2=+0.65+0.58 *A+0.012 *B+0.020 *AB+0.085 *A2+5.000E-003 *.B2. R3=+20.31-4.27 *A+0.17 *B+1.70 *AB-0.51 *A2+1.56 *B2 is the dissolution time equation.

Hardness, friability, and disintegration time were found to have respective r2 values of 0.9425, 0.9671, and 0.8600. Hardness, friability, and disintegration time were determined to have F values of 27.23, 48, and 10.83, respectively. Hardness, friability, and disintegration time were determined to have P values of 0.0105, 0.0046, and 0.0389, respectively. We can therefore conclude that the model is significant based on the data presented.

Discussion

The experimental study employed a three-level, two-factor design to investigate the effects of crosscarmellose sodium (CCS) and wax mixture on tablet hardness, friability, and disintegration time. The results demonstrated significant variations in tablet properties, with hardness ranging from 2 to 2.8 kg/cm², friability between 0.48% and 0.68%, and disintegration time spanning 15.26 to 28.32 seconds. A quadratic model best described the relationship between the independent variables and responses, as supported by high R^2 values (0.9425 for hardness, 0.9671 for friability, and 0.8600 for disintegration time) and statistically significant ANOVA results ($p < 0.05$).[32] The analysis revealed that increasing CCS concentration significantly enhanced tablet hardness and reduced disintegration time, owing to its superdisintegrant properties, while the wax mixture contributed to hardness but prolonged disintegration at higher levels due to its hydrophobic nature. Interaction effects between the two factors further indicated that their combined influence was non-linear, emphasizing the need for careful optimization. These findings underscore the importance of balancing CCS and wax mixture levels to achieve optimal tablet performance, ensuring adequate

mechanical strength without compromising disintegration. The study provides valuable insights for formulators in designing robust tablet formulations with tailored dissolution and mechanical properties. Further optimization using techniques like desirability function analysis could refine the formulation for specific therapeutic requirements.[33]

Approach in formulation optimization, where response surface methodology aids in identifying the ideal balance between excipients to achieve optimal tablet performance. The successful development of this formulation highlights its potential for industrial scalability and therapeutic efficacy, ensuring rapid drug release while maintaining sufficient mechanical strength for handling and packaging.[34]Further studies, including stability testing and in vivo bioavailability assessments, would be essential to validate the clinical applicability of this optimized formulation.[35]

IV. CONCLUSION

The present study successfully formulated and evaluated mouth dissolving tablets of Eletriptan Hydrobromide to provide rapid onset of action for effective migraine relief. The optimized formulation showed excellent disintegration time, satisfactory drug release, and good mechanical strength, making it a promising alternative to conventional dosage forms for enhancing patient compliance and therapeutic efficacy in acute migraine management.

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