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Formulation and Evaluation of Fast Disintegrating Tablet of Eletriptan Hydrobromide.

Vishal B Ambekar¹, Mr. Babasaheb L Chopade², Dr. Megha T Salve³.

Department of B. Pharmacy, Shivajirao Pawar College of Pharmacy, Pachegaon, Newasa-413725.

E-mail: ambekarvishal9890@gmail.com.

ABSTRACT:

The present study focuses on the formulation and evaluation of fast disintegrating tablets (FDTs) of Eletriptan hydrobromide, an antimigraine agent with poor oral bioavailability due to extensive first-pass metabolism. The aim was to develop a formulation that ensures rapid onset of action by enhancing disintegration time and drug release. Different amounts of superdisintegrants, such as croscarmellose sodium (CCS) and sodium starch glycolate (SSG), were employed. Among the formulations developed, formulation F5, containing SSG and CCS, demonstrated optimal results with a disintegration time of less than 15 seconds, meeting all required physicochemical parameters. In vitro drug release studies showed up to 99.7% release, indicating excellent dissolution characteristics. These findings support the potential of FDTs of Eletriptan hydrobromide as a fast-acting, patient-friendly alternative for the effective management of acute migraine attacks.

KEYWORDS: Eletriptan Hbr, Fast Disintegrating Tablets (FDTs), talc, Sodium Starch Glycolate.

INTRODUCTION:

Structurally, it falls under the indole category and is a modified form of methylpyrrolidinyltryptamine, featuring a benzene sulfonyl substitution (refer to Figure 1). Its molecular weight is 382.52 daltons, and its IUPAC name is (R)-3-(1-methyl-2-pyrrolidinylmethyl)-5-(2-phenylsulfonyl)ethyl-1H-indole. Eletriptan exhibits excellent oral bioavailability, ensuring quick and consistent absorption, along with strong agonist activity at 5-hydroxytryptamine receptor subtypes 1B and 1D (5-HT_{1B/1D}). Although there have been remarkable developments in drug delivery technologies, the oral route still remains the most preferred method for administering medications. This is largely due to its ability to deliver accurate doses, its affordability, convenience for self-administration, non-invasive approach, and ease of intake, which collectively promote better patient adherence to treatment. Traditional dosage forms such as tablets and hard gelatin capsules are widely used; however, a significant disadvantage is the issue of dysphagia, or difficulty in swallowing, which impacts nearly half of the population. This challenge often leads to patients avoiding their medications, contributing to poor compliance and ultimately diminishing the effectiveness of the treatment. In specific conditions like motion sickness, sudden allergic reactions, coughing fits, or when water is not readily available, taking traditional tablets can be problematic. This challenge is more pronounced in children and elderly individuals. To resolve such swallowing difficulties and enhance patient compliance, Fast Disintegrating Tablets (FDTs) have been introduced as a convenient and effective alternative dosage form.

In scenarios like motion sickness, sudden allergic attacks, coughing episodes, or lack of access to water, using conventional tablets can be inconvenient. This problem is especially prevalent in children and the elderly. To address these swallowing difficulties and improve medication adherence, Fast Disintegrating Tablets (FDTs) have been formulated as a user-friendly and efficient alternative dosage form. Fast Disintegrating Tablets (FDTs) are solid forms that dissolve or break apart almost instantly when placed on the tongue, releasing the medication within seconds, without the need for water. The saliva in the mouth helps to quickly disintegrate the tablet, allowing for rapid drug release. The speed at which a drug dissolves directly influences how quickly it is absorbed and begins to produce a therapeutic effect. To achieve faster onset of action, pharmaceutical researchers have focused extensively on creating fast dissolving or rapidly disintegrating drug delivery systems (FDDTs).

Fast Disintegrating Tablets (FDTs) are also referred to by various other names, including "fast dissolving," "mouth dissolving," "rapid-dissolve," "quick disintegrating," "orally disintegrating," "rapimelt," "fast melts," "orodispersible," "melt-in-the-mouth," "quick dissolving," "Porous tablets, and EFVDA or bubble absorption systems". The U.S. FDA's Center for Drug Evaluation and Research (CDER) describes Fast-Dissolving/Disintegrating Tablets (FDDTs) as solid dosage forms that contain medicinal ingredients and rapidly disintegrate, usually within seconds, when placed on the tongue. In a similar context, the European Pharmacopoeia has introduced the term "Orodispersible Tablet," which refers to an uncoated tablet designed for use in the buccal cavity, where it breaks down before being swallowed.

Requirements for tablet disintegration:

1. The tablet should break down or dissolve in the mouth within seconds, eliminating the need for water during administration.
2. The wording should support the inclusion of a substantial amount of active drugs.
3. It should work well with taste-masking agents and other necessary formulation ingredients.
4. The tablet should provide a comfortable and agreeable feel in the mouth.
5. After disintegration, the tablet should leave little to no leftover material in the oral cavity.
6. The formulation should be stable and maintain its integrity under varying temperature and humidity conditions.
7. The product should be easily produced using standard manufacturing and packaging equipment without requiring major adjustments.

Advantages of fast disintegrating tablet's:

1. **Accurate and Convenient Dosing:** These solid dosage forms ensure precise drug delivery, are easy to carry, simple to manufacture, and offer excellent physical and chemical stability.
2. **Increased Drug Absorption:** Absorption through the oral cavity, including the mouth, throat, and esophagus, enhances the drug's bioavailability by partially bypassing the digestive system.
3. **Fast Therapeutic Effect:** Ideal for conditions requiring quick relief, such as nausea, sudden allergic reactions, or severe coughing, due to their rapid onset of action.
4. **Improved Patient Convenience:** Can be taken without water, making them perfect for patients who are traveling or lack immediate access to drinking water.
5. **Ease of Use:** Especially helpful for those who have trouble swallowing, such as the elderly, young children, mentally challenged individuals, or bedridden patients.
6. **Reduced Risk of Choking:** As the tablet disintegrates in the mouth, there is minimal risk of airway blockage, thus improving safety.
7. **Better Taste Experience:** Designed to have a pleasant taste and texture, often using taste-masking agents to hide any bitterness, which is particularly useful for pediatric use.
8. **Simplified Packaging:** These tablets don't require specialized packaging and can be conveniently stored in standard blister packs.
9. **Market Expansion Opportunities:** Offers potential for product innovation, brand distinction, extended product lines, and longer market life.
10. **Low Production Costs:** Compatible with conventional manufacturing and packaging systems, allowing cost-effective production.

MATERIALS AND METHODS:***MATERIALS:***

Eletriptan Hydrobromide was received as a gift sample from Micro Lab Pharmaceuticals Mumbai, India. Crospovidone, Croscarmellose Sodium, Sodium Starch Glycolate, Mannitol, Microcrystalline cellulose, aspartame, Talc, Magnesium Stearate all excipients obtained from Shivajirao Pawar College of Pharmacy, Pachgaon, Newasa are used without Purification.

Table no:1 Formulation table:

Ingredients(mg/tablet)	F1	F2	F3	F4	F5
Eletriptan Hydrobromide	20	20	20	20	20
Crospovidone(CP)	15	-	-	7.5	7.5
Croscarmellose Sodium(CCS)	-	15	-	7.5	-
Sodium Starch Glycolate(SSG)	-	-	15	-	7.5
Mannitol	60	60	60	60	60
Microcrystalline Cellulose	200	200	200	200	200
Aspartame(sweetener)	3	3	3	3	3
Talc	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2
Total	300	300	300	300	300

Preformulation Study :

The flow characteristics of the powder blend were evaluated using parameters such as angle of repose, Carr's index, and Hausner's ratio.

1. Bulk density (BD):

The apparent bulk density was assessed by gently filling a graduated cylinder with the pre-sieved drug and excipient blend, followed by measuring its weight and volume without applying any external pressure. It is represented in g/ml and determined using the formula below.

$$\text{Bulk Density (BD)} = \text{Weight of the powder (g)} / \text{Bulk Volume (ml)}$$

2. Angle of repose:

The stationary angle of the powder mixture was determined by the funnel method. Accurately measured powder blends were collected in a funnel. The height of the funnel was set when the tip of the funnel touched the tip of the powder mixture. The powder mix was able to flow freely to the surface through the funnel. The diameter of the powder control was measured and the gentle angle was calculated using the following equation:

$$\tan^{-1} = h/r$$

where, h = height, r = radius

3. Tapped density (TD):

The powder was subjected to tapping until no further volume change was observed. The tapped density, expressed in g/ml, was then calculated using the appropriate formula.

$$\text{Tapped density (TD): weight of powder(g)} / \text{tapped volume(ml)}$$

4. Compressibility Index:

The compressibility index of the powder blend was determined using Carr's compressibility index. This straightforward test helps to assess the bulk density (BD), tapped density (TD), and the extent to which the powder compresses. The formula for calculating Carr's index is as follows:

$$\text{Carr's index (\%)} = [(TD-BD) \times 100] / TD.$$

5. Hausner's Ratio:

Hausner's Ratio is a parameter that correlates with the flowability of a powder.

$$\text{Hausner's Ratio} = TD / BD.$$

METHODS:

The fast disintegrating tablets (FDT) of Eletriptan Hydrobromide were formulated using the direct compression technique. This process involves blending the drug with various excipients in specific proportions. The concentration of Croscarmellose Sodium, which serves as a super disintegrant, is adjusted across different formulations (F1 to F5) to identify the optimal batch. Each batch consists of 50 tablets, with each tablet weighing 300 mg. The goal is to determine the ideal level of Croscarmellose Sodium that ensures rapid disintegration and efficient drug release.

Evaluation of Test:

1.Thickness:

The crown size of a tablet can be measured using a micrometer for precise measurements. To measure the size of several tablets at once (usually 5 to 10), a sliding caliper scale is employed. In laboratory settings, a Vernier caliper is typically used for measuring tablet size. It is essential to control the tablet thickness, ensuring it remains within a $\pm 5\%$ variation of the standard value to maintain uniformity and quality

2.Hardness:

The hardness of six tablets from each wording was determined using a Monsanto cure tester. The mean value and standard deviation were subsequently calculated to assess the uniformity and quality of the tablets.

3.Weight variation:

An electronic digital balance was used to weigh 20 tablets from each formulation for the weight variation research. To assess consistency, the average weight of the tablets was determined, and the weight deviation as a percentage was computed.

4.Friability:

Tablets were subjected to rotation in a Roche Friabilator (Electrolab) at 25 rpm for 4 minutes. Following the rotation, the tablets were weighed again, and the weight loss due to fracture or abrasion was calculated as the percentage weight loss (% friability).

$$\% \text{ Friability} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100$$

5. Disintegration Time:

The disintegration time of the FDTs was evaluated using the USP disintegration apparatus, employing phosphate buffer with a pH of 6.8 as the medium. The medium volume was set to 900 ml, and the temperature was maintained at $37 \pm 0.2^\circ\text{C}$.

6. Water absorption Ratio:

A tablet was positioned on the paper, and the time taken for the tablet to become fully wetted was recorded. After the tablet was completely wetted, its weight was measured. The water absorption ratio, R, was then calculated using the following formula .

$$R = 100(W1/W2)$$

RESULTS AND DISCUSSION:**Table no:2 preformulation study**

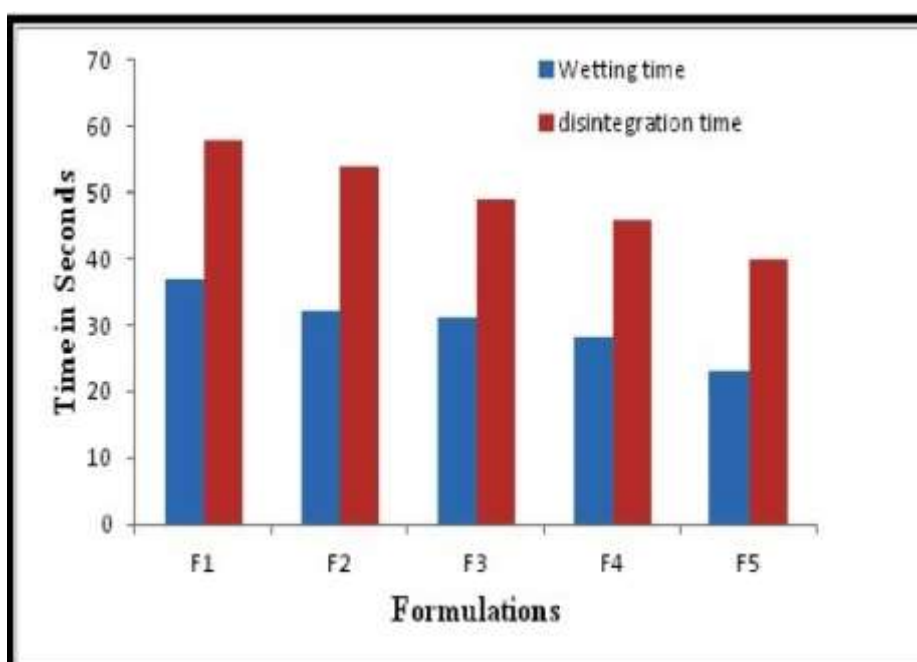
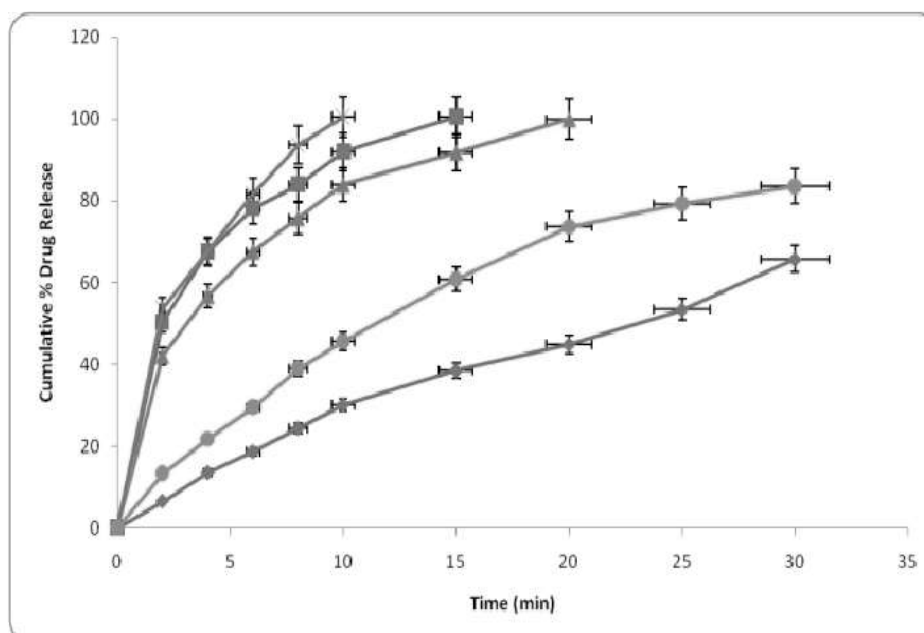
Batch	Bulk density (gm/ml)	Angle of repose (θ)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	0.430	22.57	0.522	19.23	1.23
F2	0.536	28.44	0.611	12.50	1.13
F3	0.525	23.1	0.62	10.45	1.10
F4	0.424	16.22	0.511	18.4	1.23
F5	0.514	29.81	0.632	12.41	1.13

Table no:3 evaluation test

Batch	Thickness (mm)	Hardness (kg/cm^2)	Weight variation	% Friability (%)	Water absorption ratio
F1	3.51	3.2	Pass	0.64	86.23
F2	3.35	3.2	Pass	0.46	92.66
F3	3.22	2.8	Pass	0.85	96.66
F4	3.51	3.1	Pass	0.93	92.43
F5	3.38	3.1	Pass	0.641	88.14

Table 4:Percentage drug release of Fast Disintegrating Tablet

Time in min	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	70.9±0.76	60.3±0.77	82.2±1.21	61.15±1.32	71.6±1.52
2	77.25±1.23	72.4±1.6	85±0.86	70.7±1.4	82.25±1.50
3	79.6±1.88	84.55±0.65	91.6±1.2	80.7±1.1	88±1.36

**Fig.1. Wetting time and Disintegration Time graph.****Fig. 2. Percentage drug release of Fast Disintegrating Tablet.**

CONCLUSION:

The development of fast disintegrating tablets (FDTs) of Eletriptan hydrobromide offers a promising approach to overcome the limitations of poor oral bioavailability by bypassing the first-pass metabolism and ensuring a rapid onset of action. Among the formulations studied, formulation F5—containing 5.06% sodium starch glycolate (SSG) and 3.33% croscarmellose sodium (CCS)—emerged as the optimized version, meeting all required physicochemical criteria and disintegrating within 15 seconds. This rapid disintegration is crucial for quickly addressing migraine symptoms and minimizing risks during an attack. Furthermore, the formulation demonstrated an impressive in vitro drug release of up to 99.7%, highlighting its potential effectiveness. Therefore, the development of FDTs of Eletriptan hydrobromide is highly justified.

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