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FORMULATION OPTIMIZATION AND EVALUATION OF ELEPTRIPTAN BROMIDE ORAL DISINTEGRANT TABLET USING DIFFERENT SUPERDISINTEGRANTS

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Keywords:

Eleptriptan bromide, Crospovidone, cross carmellose sodium, Sodium Starch Glycollate and Pregelatinized starch

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ABSTRACT

The aim of the present investigation is to formulate Eleptriptan bromide oral disintegrating tablet by using superdisintegrents.. ODTs may also be used to deliver drugs to the oral cavity, for local action or, in some cases, absorption across the oral mucosa, thereby avoiding first-pass hepatic metabolism and potentially increasing the rate and extent of uptake, and reducing undesirable metabolites. The objectives of the research work is to formulate oral disintegrating tablets of Eleptriptan bromide by using super disintegrants and tablets were evaluated for precompressional such as angle of repose, bulk density, tapped density, compressibility index and postcompressional Parameters like Weight variation, Hardness, Friability, Wetting Time, Disintegration and Dissolution Studies. Drug and excipients compatability studies cinducted by using FTIR studies and showed that there was no marked changes between them. From all the formulations F3 formulation showed better drug release when compared to remaining Formulations.

INTRODUCTION

Oral disintegration tablets are the novel technology for administration of the drug through the oral route. ODT's are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. Many patients find it difficult to swallow like pediatric and geriatric and those people who are travelling or little access to water and some patients who are mentally ill like schizophrenia they are also did not take medicine, oral disintegrating tablets solve these problems. An Oral disintegration tablets is a solid dosage form that disintegrates and dissolves in the mouth without water within 60 seconds or less. orally disintegrating tablets provide an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. Additionally, pediatric patients may suffer from ingestion problems as a result of underdeveloped muscular and nervous control[1,2].

Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Orally disintegrating tablets offer an advantage for populations who have difficulty in swallowing. It has been reported that Dysphagia[3] (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. ODTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population. "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue[4]." ODT products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia).

MATERIALS AND METHODS:

Eleptriptan bromide was obtained from the Nectar lifes ciences Ltd. And all excipients were purchased from the S. D. Fine Chemicals, Mumbai. All excipients and solvents used were in analytical grade.

Compression of Eleptriptan bromide oral Disintegrating Tablets:

The drug Eleptriptan bromide was thoroughly mixed with the superdisintegrants and then other exipients are added to the mixer and passed through the sieve (sieve no. 40). Collected the powder mixer, blended with magnesium stearate (pre sieved through sieve no. 60), the powder blend is subjected to drying for removal of moisture content and then subjected the

blend for tablet compression by using Round and flat faced punches in CADMACH 16 punches tablet punching machine. Punches of 8.7 mm diameter were used for compression. Tablet of 100 mg was prepared by adjusting hardness and volume screw of compression machine properly.

Evaluation of Powder Blend

Bulk Density (D_b):

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below

$$D_b = M / V_b$$

Where, M is the mass of powder

V_b is the bulk volume of the powder.

Tapped Density (D_t):

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by

$$D_t = M / V_t$$

Where, M is the mass of powder

V_t is the tapped volume of the powder.

Angle of Repose (θ):

The friction forces in a loose powder can be measured by the angle of repose (θ). It is an indicative of the flow properties of the powder.

It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\tan(\theta) = h / r, \quad \theta = \tan^{-1}(h / r)$$

Where, θ is the angle of repose , h is the height in cms r is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of

the heap of powder formed. Care was taken to see that the powder partials slip and roll over each other through the sides of the funnel.

Carr's index (or) % compressibility: It indicates powder flow properties. It is expressed in percentage and is given by

$$I = \frac{D_t - D_b}{D_t} \times 100$$

Where, D_t is the tapped density of the powder and

D_b is the bulk density of the powder.

Hausner ratio:

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

$$\text{Hausner ratio} = \frac{D_t}{D_b}$$

Where, Dt is the tapped density.

D_b is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25)

EVALUATION OF ELEPTIPTAN HBR HCL TABLETS

1. Organoleptic properties of tablets

Organoleptic properties such as taste, color, odour, were evaluated. Ten tablets from each batch were randomly selected and tested for taste, color, odour and physical appearance**.**

2. Thickness

The thickness of individual tablets of 6 numbers were measured with vernier calipers, it permits accurate measurements and provides information of the variation between tablets. Tablet thickness should be controlled within ± 5% variation of standard value.

3. Weight Variation Test

Twenty tablets from each batch were weighed with electronic digital balance and average weight was determined. Then individual tablets were weighted and individual weight was compared with the average weight. The percentage deviation was calculated and checked for weight variation. Standard deviation was calculated. Using this procedure weight variation range of all the batches were determined and recorded.

4.**Friability**

The friability of tablets was determined by using Roche Friabilator. It is expressed in percentage (%). Thirty three tablets (6.600gms.) were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The percentage friability was then calculated by,

$$\% \textbf{ Friability} = \frac{\textbf{Loss in weight}}{\textbf{Initial weight}} \times \textbf{100}$$

5. Hardness

The tablet hardness of different formulations was measured using the Monsanto hardness tester for 6 tablets. The tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger was placed in contact with the tablet, and a zero was taken. The upper plunger was then forced against the spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge on the barrel to indicate the force. The force of fracture is recorded and the zero force reading is deducted from it. Generally, a minimum hardness of 5 - 7 kg/cm^2 is considered acceptable for uncoated tablets. The hardness for ODTs should be preferably 2-4 kg/cm^2.

6. Wetting time

The wetting time of the tablets can be measured by using the simple procedure. Five circular tissue papers of 10cm diameter are placed in a petridish. Ten millilitres of water containing a water soluble dye eosin is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as the wetting time.

7. Drug Content Uniformity

Twenty tablets were selected randomly and powdered. A quantity of this powder corresponding to one tablet was dissolved in 100 ml of 6.8 pH phosphate buffer, stirred for 15 min and filtered. 1 ml of the filtrate was diluted to 100 ml with 6.8 pH phosphate buffer. Absorbance of this solution was measured at 226nm using 6.8 pH phosphate buffer as blank and content of drug was estimated.

8. In vitro Disintegration time

Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 phosphate buffer maintained at 37±2C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained

at 37±2c. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

9. In vitro Dissolution studies:

Dissolution of the tablet of each batch was carried out using USP type II apparatus (ELECTRO LAB) using paddles at 50 rpm. As per the official recommendation of IP 900ml of 6.8 pH of phosphate buffer used as dissolution medium and the temperature of the medium was set at 37 ± 0.5 ^{0}C. 5 ml of sample was withdrawn at predetermined time interval of 2min., 4min., 6min., 8min and 10min. And same volume of fresh medium was replaced. The withdrawn samples were analyzed by an UV-visible spectrophotometer at 310 nm using buffer solution as blank solution.

DISCUSSION

SUMMARY AND CONCLUSION

Clinically Eleptriptan bromide is a Serotonin Type 3 receptor antagonist. It is effective in the treatment of nausea and vomiting during Chemotherapy. Conventionally Eleptriptan bromide tablets are not suitable where quick onset of action is required. Conventional Eleptriptan HBR tablets available in market are not suitable where quick onset of action is required. To overcome these problems, there is a need to develop a rapidly disintegrating dosage form, particularly one that would rapidly disintegrate in saliva and could be administrated without water anywhere at any time.In the present work oral disintegrating tablets were prepared by superdisintegrant addition, and evaluated for disintegration time, hardness and friability. From all these techniques, Super disintegrant addition technique was selected based on less disintegration time.The mouth dissolving tablets of Eleptriptan HBR were prepared by super disintegrants addition method using crospovidone, croscarmellose sodium and Microcrystalline cellulose There are total six formulations were prepared and evaluated for Weight variation, thickness, friability, hardness, disintegration time, Wetting time, assay and in-vitro dissolution study.

The results of all formulations for weight variation, friability, hardness and assay were found to be within the IP limit and no significant variation. The Disintegration time for all formulations was found to be 25 to 60 seconds and wetting time was between 20 to 60 seconds. Based on the In-vitro dissolution studies, it was found that the drug release for all the formulations were less than 10 minutes.Formulation F3 containing crospovidone and MCC in concentration of 10% and 8% showed minimum disintegration time, wetting time as compared to other formulations. Dissolution studies conclude that the total drug was released

within 30 minutes. Disintegration profile was increased in the following manner such as as crosprovidone greater compared to Croscarmellose sodium. It is showed and concluded that F3 is the best formulation which is done by use of super disintegration addition technique which is known to be cost effective

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Table No: 1 Formulation composition of Eleptiptan HBR mouth dissolving tablets

Ingredients*	F1	F2	F3	F4	F5	F6
Eleptiptan HBR	40	40	40	40	40	40
Anhydrous lactose	40	40	40	40	40	40
Preglelatinise starch	-	-	-	8	8	8
Magnesium stearate	2	2	2	2	2	2
Ccs	10	-	-	10	-	-
Ssg	-	10	-	-	10	-
Crosprovidone	-	-	10	-	-	10
Mcc	8	8	8	-	-	-

*All quantities are in mg

Table.No.2: Pre-Compressional Evaluation of the Tablet Blend

Formulation Code	Bulk Density	Tapped Density	Powder Flow properties	Hausner ratio
F1	0.46	0.55	16.36	1.01
F2	0.45	0.54	16.66	1.2
F3	0.46	0.55	16.52	1.19
F4	0.32	0.38	14.73	1.18
F5	0.45	0.52	18.75	1.15
F6	0.48	0.57	15.32	1.18

Table.No.3: Evaluation of the physical parameters of MDTs of Eleptiptan HBR

Formulation Code	Weight Variation	Hardness Kg/cm^2	Friability (%)	Wetting Time (sec)	Disintegration Time (sec)	Assay (%)
F-1	passes	3.7	0.41	45	35	94.81
F-2	passes	3.6	0.46	40	30	88.09
F-3	passes	3.6	0.46	35	24	99.78
F-4	passes	3.5	0.3	55	48	59.26
F-5	passes	3.8	0.3	50	40	73.01
F-6	passes	3.6	0.42	47	38	86.52

Table No.4: In vitro dissolution studies 6.8 Ph phosphate buffer pH 6.8 of F1-F6

Time(min)	F-1	F-2	F-3	F-4	F-5	F-6	MF
0	0	0	0	0	0	0	0
5	65.7	26.8	48.6	25.5	27.88	30.67	25.9
10	70.1	38.3	57.5	33.5	48.34	51.50	41.4
15	71.1	47.4	65.9	45.2	60.34	62.53	68.32
20	74.6	68.5	78.9	57.8	65.9	63.10	89.32
25	77.2	78.2	91.4	60.7	71.19	84.81	97.12
30	77.2	91.4	98.8	60.56	71.71	85.31	97.12

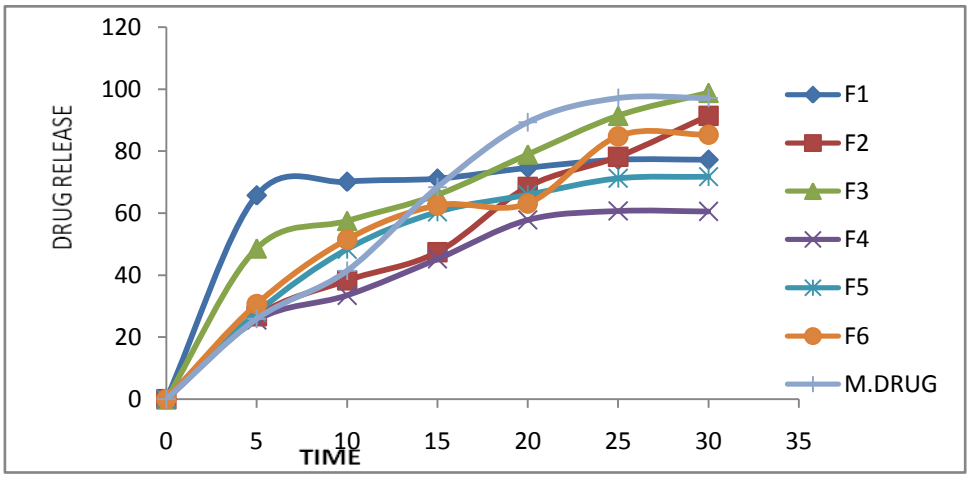

Fig No.1: Comparative dissolution profile of all formulations along with the marketed drug

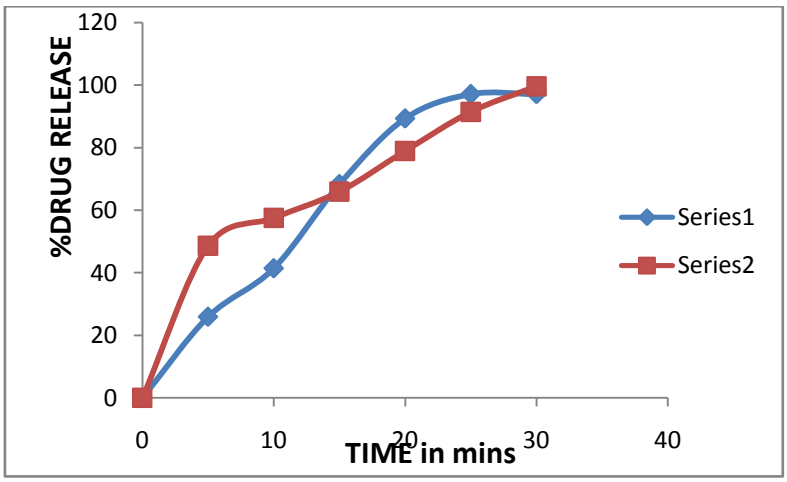

Figure No.2 : compression of Formulation F3 and Marketed drug dissolution Profile