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FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF OXCARBAZEPINE

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ABSTRACT

The concept of Mouth Dissolving Drug Delivery System emerged from the desire to provide patient with conventional mean of taking their medication. Oxcarbazepine is an anticonvulsant drug, mainly used as an add-on or first line treatment in adults and children. Due to sudden onset of attack, it is necessary to formulate antiepileptics into such a delivery system, which provide immediate relief. Hence, the present investigation was undertaken with a view to develop mouth-dissolving tablets of oxcarbazepine, which offers a new range of product having desired characteristics and intended benefits. In this study, the mouth dissolving tablets were prepared. A mouth dissolving tablet was prepared by using superdisintegrants viz; crospovidone, croscarmellose sodium and sodium starch glycolate All the batches are prepared by direct compression method. Effect of disintegrants concentration on the disintegration behavior was evaluated, and all the tablets were evaluated for hardness, friability, weight variation, water absorption ratio, dissolution, and assay. Among the all preparations F8 emerged as the best formulation and showed maximum dissolution rate.

KEYWORDS: Mouth dissolving tablet, Oxcarbazepine, Direct compression, Superdisintegrant.

INTRODUCTION

The tablet is the most widely used dosage form existing today because of its convenience in terms of self-administration, compactness and ease in manufacturing. However, geriatric, pediatric and mentally ill patients experiences difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome these problems, scientists have developed innovative drug delivery system known as mouth dissolving/disintegrating tablets (MDTs) or fast dissolving tablets. The benefits of MDTs is to improve patients compliance,

rapid onset of action, increased bioavailability and good stability which make these tablets popular as a dosage form of choice in the current market.[1,2,3] MDTs are distinguished from conventional, sublingual tablets, buccal tablets and lozenges, which require more than a minute to dissolve in oral cavity. In the literature, MDTs also are called oral disperse, mouth-dissolving, quick-dissolve, fast-melt and freeze-dried wafers. It is estimated that 50% of the population is affected by dysphasia which results in high incidence of noncompliance and ineffective therapy. To overcome this problem, it is necessary to design a formulation which rapidly disperse / dissolve in the oral cavity without the need of water for swallowing. Such dosage form should disintegrate when placed in the mouth and can be swallowed in the liquid form.[4,5] Oxcarbazepine (10,11-dihydro-10-oxo-5Hdibenz[b,f]azepine-5-carboxamide) is a 10- keto analogue of carbamazepine with anticonvulsant activity.[6] Oxcarbazepine (as both monotherapy and adjunctive therapy) has shown efficacy in the treatment of partial onset seizures in children with epilepsy. The drug having half-life of 2 h is completely absorbed and extensively metabolized to its pharmacologically active 10-monohydroxy metabolite, which has a half-life of 9 h. Its pharmacological activity is primarily exerted through 10-monohydroxy metabolite.[6,7] Its insolubility in water and bland taste makes it an ideal candidate for fast disintegrating tablets with regards to palatability. Since epileptic patients have to strictly follow dosage regimen for preventing sub therapeutic concentration, MDT will avoid missing out of dose even during traveling or other situations where there is no access to water. The present investigation deals with the development of an effective and stable MDT of oxcarbazepine having adequate hardness, low disintegration time and pleasant taste.

MATERIALS AND METHODS

Materials

oxcarbazepine was obtained as a gift sample from Psycho Remedies, Ludhiana. Pvpk 30,Crosscarmellose sodium, Crospovidone, Sodium starch glycolate, MCC, Talc, Magnesium stearate, Aspartame, Lactose, spray dried Polo mannitol were purchased from S. D. fine Chemicals, Mumbai. All other chemicals and reagents used were of analytical grade.

METHODS

All of the formulations contained oxcarbazepine, Aspartame, Magnesium Stearate, Lactose, Mannitol, PVP K30, Talc and different amounts of various superdisintegrants. Superdisintegrants include Crospovidone, Cross Carmellose Sodium, Sodium Starch

Glycolate. PVP K 30 is used as Tablet Binder. Composition of various formulations is listed in Table 1.

Tablets were prepared by Direct compression- Formulations F1-F9, were prepared by blending each superdisintegrant in three different proportions. The superdisntegrant blends were thoroughly mixed with preset fixed amounts of oxcarbazepine, Aspartame, and magnesium stearate, MCC, Talc, Lactose, in a polybag by a geometric dilution method. The powder mixture, thus prepared, was passed through sieve #40 and then compressed into tablets with a multiple punch tablet machine (Lab press).[8,9]

Table 1: Formulations of oxcarbazepine MDT Tablets (in mg) by Direct compression.

Formulations	F1	F2	F3	F4	F5	F6	F7	F8	F9
Oxcarbazepine	100	100	100	100	100	100	100	100	100
PVP K30	10	10	10	10	10	10	10	10	10
Cross Povidone	10	20	30	-	-	-	-	-	-
Cros Carmellose Sodium	-	-	-	10	20	30	-	-	-
Sodium Starch Glycolate	-	-	-	-	-	-	10	20	30
Polo	10	10	10	10	10	10	10	10	10
Aspartame	3	3	3	3	3	3	3	3	3
Lactose	64	54	44	64	54	44	64	54	44
Mannitol	30	30	30	30	30	30	30	30	30
Microcrystalline cellulose	21	21	21	21	21	21	21	21	21
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mg Stearate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total Weight	250	250	250	250	250	250	250	250	250

Total weight – 250mg/tablet

Evaluation Parameters

1. Tablet weight variation

Twenty tablets were randomly selected and accurately weighed. Results are expressed as mean values ± SD.[10]

2. Tablet thickness

A vernier caliper was used to determine thickness of 10 randomly selected tablets. Results are expressed as mean values.[10,11]

3. Friability Test

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Twenty tablets were initially weighed 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. The % friability was then calculated by the following formula.[12]

Percentage Friability = W – W0 × 100 / W

Where, W0 = initially weight W = weight after friability

Percentages Friability of tablets less than 1 % are considered acceptable.

4. Hardness

The hardness of the tablets was determined using Precision dial type hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets was determined.[13,14]

5. Uniformity of drug content

Accurately weighed amount of drug-excipient blend was dissolved in small amount of methanol and the volume was made up to 100ml with distilled water in 100ml volumetric flask, which was previously cleaned and dried. This solution was filtered and measured for absorption at 255nm in UV-visible spectrophotometer.[4]

% Purity = 10 C (Au / As)

Where, C – Concentration, Au and As – Absorbance of unknown and standard respectively.

6. Wetting time

A piece of tissue paper folded twice containing amaranth powder on the upper surface was placed in a small Petri dish (ID =6.5 cm) containing 6 ml of5.4 pH buffer, a tablet was put on the paper and the time required for formation of pink color was measured as wetting time. The study was performed in triplicate.[5]

Table 2 Specifications for tablets as Per Pharmacopoeia of India.

Sr.No.	Average Weight of Tablet	% Deviation
1	80 mg or less	10
2	More than 80 mg but less that 250 mg	7.5
3	250 or more	5

7. Water absorption ratio

A piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of water. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then weighed. Water absorption ratio R was determined using following equation:[15,16]

$$R = \frac{(Wb - Wa)}{Wa} \times 100$$

Wa = Weight of the tablet after wetting,

Wb= Weight of the tablet before wetting.

8. Disintegration time

Initially the disintegration time for oral dispersible tablets was measured using the conventional test for tablets as described in the Pharmacopoeia. Tablets were placed in the disintegration tubes and time required for complete disintegration, that is without leaving any residues on the screen was recorded as disintegration time. A modified method was also used to check the disintegration time. In about 6-8 ml of 5.4 pH buffer was taken in measuring cylinder. Tablet was placed in the cylinder and complete dispersion of tablet in the cylinder was recorded as the disintegration time.[15,16]

9. Dissolution studie

Sample volume of 10 ml was withdrawn at regular time intervals from a zone midway between the surface of dissolution medium and the top of rotating paddle not less than 1 cm apart from the vessel wall. The volume withdrawn was replaced by fresh volume of dissolution medium to maintain constant volume of medium. The filtered samples were analyzed spectrophotometrically at 255 nm using 5.4 pH buffer as a blank. Drug content in dissolution sample was determined by calibration curve.[15,16]

RESULTS AND DISCUSSION

Table 3 Evaluation Parameters.

Formulation code	Evaluation parameter				
	Thickness ± S.D. (mm) (n = 5)	Hardness ± S.D. (kg/cm2) (n = 5)	Friability (%)	Average weight variation (n=10)	Drug content (%)
F1	4.51±0.04	3.81±0.06	0.41±0.02	247.3±1.6	98.75±0.60
F2	4.46±0.02	3.91±0.02	0.34±0.01	249.5±1.8	99.2±0.67
F3	4.74±0.03	3.69±0.03	0.27±0.03	249.2±1.9	99.4±0.98
F4	4.66±0.06	3.79±0.04	0.52±0.01	245.4±0.9	98.85±0.47
F5	4.46±0.09	3.82±0.02	0.36±0.04	246.6±1.5	99.1±0.65
F6	4.68±0.06	4.08±0.03	0.46±0.03	248.0±2.0	98.6±0.98
F7	4.56±0.08	4.12±0.02	0.52±0.01	246.2± 0.5	98.2±0.90
F8	4.72±0.03	3.71±0.03	0.37±0.03	247.6±1.2	98.2±0.93
F9	4.62±0.07	3.61±0.01	0.28±0.02	248.4±1.3	98.7±0.96

Table 4: Results of, wetting time, water absorption ratio and disintegration time of mouth dissolving tablet formulation of Oxcarbazepine.

Formulation code	Wetting time (Sec) mean ± SD	Water absoption ratio mean ± SD	Disintegration time (Sec) mean ±SD
F1	30±1.2	80.12±0.12	36±1.2
F2	28±2.1	84.45±0.32	34±2.1
F3	25±1.0	90.45±0.74	28±1.0
F4	27±2.0	81.10±0.47	33±2.0
F5	28±7.1	82.42±0.41	34±7.1
F6	26.±7.4	83.12±0.01	31.±7.4
F7	26±1.2	80.47±0.14	32±1.2
F8	25±7.8	85.23±0.02	31±1.8
F9	26±3.6	88.98±0.074	31±3.6

Table 5 In vitro drug release of Nizatidine from formulations.

Time (min)	Percent drug release at time (min)								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
05	47.20±0.9	49.2±0.6	50.31±0.3	46.21±0.9	44.21±0.6	48.13±0.3	43.12±0.2	42.11±0.3	44.56±0.3
10	65.10±0.3	64.21±0.2	69.20±0.9	64.41±0.4	61.23±0.5	60.21±0.5	61.32±0.2	62.23±0.3	59.78±0.6
15	80.01±0.34	79.01±0.1	84.23±0.3	78.14±0.3	79.32±0.4	77.25±0.5	78.23±0.1	75.25±0.3	78.78±0.6
20	84.87±0.32	83.02±0.69	88.35±0.2	83.54±0.1	84.24±0.2	81.36±0.5	83.32±0.2	81.32±0.4	82.36±0.3
25	90.58±0.7	92.58±0.6	97.21±0.7	92.30±0.5	93.25±0.2	94.87±0.6	92.23±0.2	93.24±0.5	96.63±0.1
30	96.58±0.7	97.71±0.1	99.73±0.9	95.21±0.2	96.58±.0.5	97.21±0.4	96.14±0.6	97.36±0.4	98.36±0.3

Among all the formulations, F3 (containing crospovidone 30 mg) showed 99.73% drug release within 30 minutes and it showed least disintegration time. Thus, F3 was considered best among the other formulations.

CONCLUSION

A mouth dissolving tablet was prepared by using superdisintegrants crospovidone, croscarmellose sodium and sodium starch glycolate that could dissolve with in 30 minutes. The post-compression parameters of all formulations were determined and the values were found to be satisfactory. From the drug content and *in-vitro* dissolution studies of the formulations, it was concluded that the formulation F3 i.e. the formulation containing crospovidone 30 mg is the best formulation.

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