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Formulation and evaluation of oral disintegrating tablet of oxcarbazepine

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Abstract

A fast dissolving tablet was prepared by using various Ingredients like Crosepovidone , Mannitol Sodium lauryl sulphate (SLS) , Magnesium stearate was taken in different concentration (5-10% 50%, 2-6%, 1%,).Chemical incompatibility studies confirmed that there is no interaction between drug and excipients used in the formulations. 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.

Key-Words: Oral Disintegrating Tablets, Super Disintegrants, and Oxacarbazapine

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 (ODTs) or fast dissolving tablets. The benefits of ODTs 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]. ODTs are distinguished from conventional, sublingual tablets, buccal tablets and lozenges, which require more than a minute to dissolve in oral cavity. In the literature, ODTs also are called orodisperse, 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 non-compliance 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]

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These tablets are designed to dissolve or disintegrate rapidly in the saliva generally within <60 seconds (range of 5-50 seconds). Due to the constraints of the current FDDT technologies as highlighted above, there is an unmet need for improved manufacturing processes for fast dissolving tablets that are mechanically strong, allowing ease of handling and packaging and with production costs similar to that of conventional tablets.

Material and Methods

Materials

Oxacarbazapine, Magnesium stearate, Crosepovidone, Manitol and Sodium lauryl sulphate (SLS).

Fourier transforms infrared (FT-IR) spectroscopy

Compatibility studies were carried out to know the possible interactions between Oxcarbazapine and excipients used in the formulation. Physical mixtures of drug and excipients were prepared to study the compatibility. Drug polymer compatibility studies were carried out using FT-IR spectroscopy. IR spectrum of pure drug and polymers was seen in between 600- 4000 cm^{-1}.

Preparation of oral disintegrating tablets

Preparation of Oxcarbazepine Fast Dissolving Tablets by Direct Compression Method Direct compression method involves following steps:-

1. Blending
2. Compression

Blending Procedure for Preparation of Mixed Blend of Drug and Excipients All ingredients were mixed as per the formula.

Oxcarbazepine, SLS, manitol were triturated thoroughly in a glass mortar using a pestle. Super disintegrates were incorporated in the powder mix. And finally magnesium stearate was added as lubricant. Control tablet was prepared without any super disintegrants.

Compression

Mixed Blends were compressed by direct compression method.

Evaluation of Tablets

Thickness[4]

The thickness of the tablets was determined using a Micrometer screw gauge. Five tablets from each type of formulation were used and average values were calculated. It is expressed in mm.

Hardness[5, 6]

The resistance of tablets to shipping, breakage, under conditions of storage, transportation and handling before usage depends on its hardness. For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm^2. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted.

Friability[6, 7]

Friability is the measure of tablet strength. Roche Friabilator was used for testing the friability using the following procedure. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of preweighed 6 tablets was placed in Roche friabilator which was then operated for 100 revolutions i.e. 4 minutes. The tablets were then dusted and reweighed. A loss of less than 1 % in weight in generally considered acceptable. Percent friability (% F) was calculated as follows:

$$\% F = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \times 100$$

Weight variation test[5, 6]

To find out weight variation, 20 tablets of each type of formulation were weighed individually using an electronic balance, average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight.

Wetting time[4, 5]

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.[12]

Table 1: Specifications for tablets as Per Pharmacopoeia of India

S/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

Water absorption ratio[5]

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.[13]

Water absorption ratio R was determined using following equation:

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

Wa = Weight of the tablet after wetting, Wb= Weight of the tablet before wetting

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 a Jasco V 530 UV-visible spectrophotometer.

$$\% \text{ Purity} = 10\ C\ (Au / As)$$

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

Disintegration time[5]

Initially the disintegration time for orodispersible 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.

Dissolution studies[8-12]

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

Stability studies

The optimized formulation was tested for stability of period of 3 Month accelerated study at 40°C ± 75% RH, for their drug content and other parameters.

Results and Discussion

Drug polymer compatibility studies using FTIR

All the characteristic IR peaks related to pure drug, Oxacarbazapine were also appear in the IR spectrum of mixture of Drug-excipients so there was no any chemical incompatibility between drug, polymer and excipients (Fig 1).

Weight variation and thickness The maximum average weight of the tablets was found to be 316±8.60 mg. As none of the formulation shows a deviation (I.P. limit, ± 7.5%) for any of the tablets tested, the prepared formulations comply with the weight variation test (Table 3). The average thickness from all the formulations was found to be 2.95±0.02 mm. (Table No.3)

Hardness and Friability: - Hardness of tablets ranged from 3.4±0.10 kg/cm^2. Friability of tablets was found to be within the limits of conventional oral tablets stated in the Indian Pharmacopoeia. (Table No. 3)

Disintegration time, wetting time, water absorption ratio and uniformity of content: - The disintegration time was found 24.47 to 38.23 sec. The wetting time was found 12 to 32 sec. Drug contents of tablets from each batch showed uniformity of content as the concentration of drug in tablet was found in between 98.06% to 99.87%.

***In vitro* dissolution studies: -** From the data it was found that F8 formulation showed optimum drug release of 98.055%. The release of F6, F7, and F4 was 95.986%, 97.484%, 89.867% respectively and for marketed preparation 80.497%. It was revealed that the increase in disintegrants concentration increases percentage friability and less hardness and drug release was found.

The powder mixtures for all eight formulations were evaluated for bulk density which ranged from 0.73 to 0.76 (g/ml), tapped density ranged from 0.81to 0.79 (g/ml), angle of repose ranged from 25.63 to 27.59° was found. All these results indicated that, the powder mixture had satisfactory flow of powder blend into the die cavity and compressibility properties.

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The hardness of tablets was found to be 3.2 to 3.9 kg/cm^2. The formulations containing low concentration of disintegrants have shown maximum hardness so they shows less % friability and it was found that hardness was increased with decrease in the proportion of concentration of disintegrants. The lowest hardness was obtained in formulations containing high disintegrants concentration and shows % friability just near to the limit. All the tablets shows % friability in the range of 0.05-0.09 % which is within the limit. All the formulations pass the weight variation test as all tablets within the range limit for weight variation.

Conclusion

In the present study total eight formulations were prepared using direct compression technique, each containing 100 mg of Oxcarbazepine. All formulations (F1-F9) were prepared by using 5% ,10%, 15% of crospovidone, 2%,4%,6% of SLS, to the total weight of pharmaceutical ingredients. The total weight of tablet was taken as 300 mg. Magnesium stearate was added as 1% and Mannitol was added as q.s.

Physical mixers of Oxcarbazepine and exipients were examined for drug polymer interaction by FT-IR. The IR spectrum did not show presence of any additional peaks for new functional groups indicating no chemical interaction between Oxcarbazepine & the used disintegrants. Formulations were evaluated for their physicochemical properties. Powder blend were evaluated for various parameters like angle of repose, bulk density, tapped density. Directly compressed tablets were analyzed for the uniformity of drug content, thickness, hardness, weight variation, friability and *in-vitro* dissolution testing.

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The stability studies of the optimized formulation F8 of tablets revealed that there was no significant change in the physical parameters when stored at temperature and humidity conditions of 45 ± 2°C/ 75 ± 5 % RH and at room temperature.

The optimum formulation did not show any significant change in % cumulative release and drug content when kept at different condition and periods.

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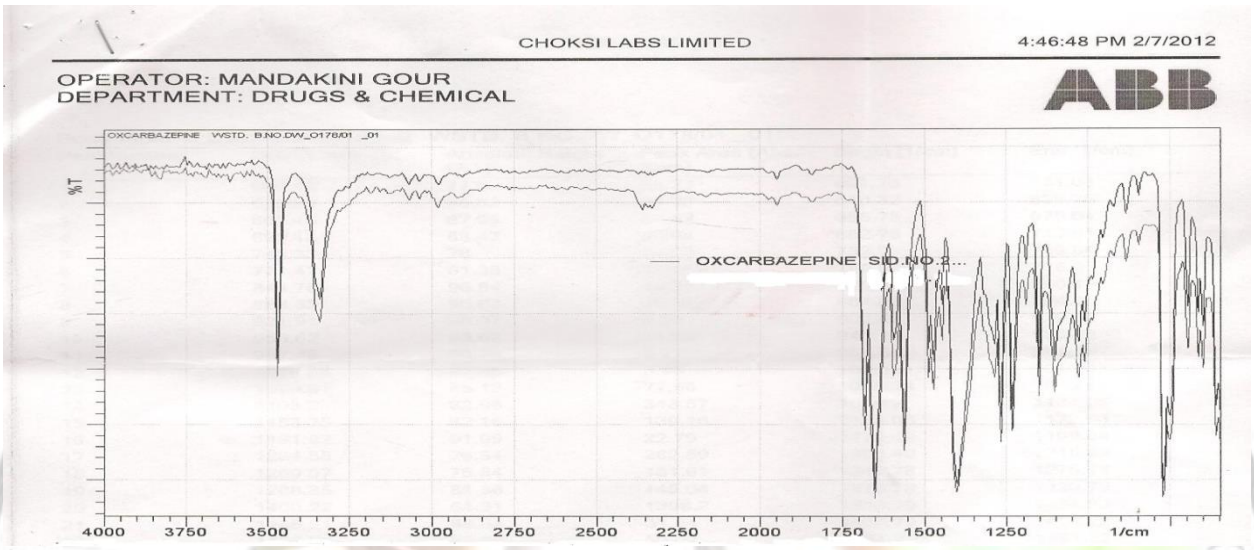

Fig. 1: FTIR of Oxcarbazepine with excipients

Table 2: Composition of fast disintegrating tablet

Formulation Code	Drug (mg)	Crospovidone (mg)	SLS (mg)	Manitol (mg)	Mg. stearate (mg)
F1	100	15	6	150	3
F2	100	30	6	150	3
F3	100	45	6	150	3
F4	100	15	12	150	3
F5	100	30	12	150	3
F6	100	45	12	150	3
F7	100	15	18	150	3
F8	100	30	18	150	3
F9	100	45	18	150	3

Table 3: Physical parameters of powder blend

Parameters / Formulations	Bulk Density (g/ml) ±SD	Tapped Density (g/ml) ±SD	Angle of Repose (^{0}) ±SD
F1	0.73±0.04	0.79±0.03	25.93±0.39
F2	0.74±0.01	0.8±0.02	26.71±0.36
F3	0.74±0.03	0.8±0.04	26.71±0.39
F4	0.74±0.03	0.8±0.03	25.74±0.61
F5	0.74±0.02	0.81±0.02	26.31±0.85
F6	0.75±0.03	0.81±0.01	27.59±0.38
F7	0.75±0.02	0.81±0.03	25.85±0.23
F8	0.76±0.03	0.82±0.03	25.63±0.86
F9	0.76±0.03	0.81±0.01	26.71±0.39

Table 4: Results of disintegration time, wetting time, water absorption ratio and uniformity of content of fast disintegrating tablet formulation of Oxcarbazepine

Formulations	Disintegration time (Sec) mean ± SD	Wetting time (Sec) mean ± SD	Water absoption ratio mean ± SD	Uniformity of content mean ± SD
F1	38.32 ± 1.33	30.02±.1.14	84.32±0.044	98.72±0.60
F2	35.56 ± 0.5	29.50±1.673	88.92±0.046	98.23±0.48
F3	31.12 ± 0.5	28.83 ± 2.00	94.52±0.058	99.34±0.62
F4	37.87 ± 0.2	24.30±1.483	97.98±0.029	98.99±0.60
F5	34.14 ± 0.60	23.98±1.580	99.66 ±0.031	98.72±0.83
F6	30.11 ± 0.60	23.02±1.571	100.58±0.023	98.59±0.52
F7	36.66 ± 0.07	19.82±2.236	77.50 ±0.019	99.21±0.52
F8	32.47 ± 0.05	19.28±3.050	80.80 ±0.047	99.90±0.70
F9	28.11 ± 0.65	18.58±3.050	94.02±0.013	98.50± 0.02

Table 5: Physical parameters of tablets

Parameters / Formulations	Hardness (kg/cm^2) (± SD)	Thickness (mm) (± SD)	% Friability (± SD)	Weight Variation (mg) (± SD)
F1	3.9±0.10	2.94±0.05	0.05±0.05	274±3.70
F2	3.3±0.15	2.95±0.05	0.07±0.03	289±7.40
F3	3.5±0.06	2.96±0.06	0.06±0.06	304±6.80
F4	3.8±0.10	2.94±0.03	0.05±0.04	280±5.30
F5	3.4±0.10	2.96±0.01	0.07±0.03	295±5.90
F6	3.5±0.21	2.97±0.05	0.06±0.04	310±8.2
F7	3.8±0.14	2.95±0.02	0.05±0.06	286±5.40
F8	3.3±0.10	2.96±0.05	0.07±0.05	301±6.70
F9	3.2±0.18	2.98±0.09	0.08±0.06	316±8.60

n=3