Volume 3, Issue4, October 2012
Available Online at www.ijppronline.com
International Journal Of Pharma Professional's Research
Research Article

PREPARATION AND EVALUATION OF OXCARBAZEPINE FAST DISSOLVING TABLETS

ISSN NO:0976-6723

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Abstract

A fast dissolving tablet was prepared by using various super disintegrants like Polyplasdone XL10, Primojel, Ac-Di-Sol was taken in different concentration (10%, 12%, and 14%) and one control batch is prepared without disintegrants designated as four different groups of formulations(A,B,C and D) . 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 on the disintegration behaviour was evaluated, and all the tablets were evaluated for hardness, friability, weight variation, water absorption ratio, dissolution, and assay. Among the four groups, group (B) containing Ac-Di-Sol emerged as the best formulation and showed maximum dissolution rate.

Keywords: - Fast Dissolving Tablets, Super Disintegrants, Oxacarbazapine.

Introduction

The purpose of pharmaceutical research is to develop a new dosage form. Considering so many parameters among them one of the parameter is ease of administration[1]. Recently a new dosage form is developed to ease of administration. Fast dissolving tablet is one of the most popular commercial product[2-4]. Fast dissolving tablet rapidly disintegrate when it contact with water or saliva[5]. So many patients have problem to swallow the tablet like paediatric and geriatric[6,7] and those people who are travelling or little access to water[8,10] 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[11] So many methods are used to prepare fast dissolving or oral dis integrating tablets[12]. Direct compression method involves the incorporation of superdisintegrants in to the formulation. Direct compression does not require water or heat during formulation procedure and it is well suited for moisture and heat sensitive drugs. Fast dissolving tablets have so many advantages over liquid dosage form and conventional tablets. Fast dissolving tablet is suited for tablets which are undergoing first pass effect, and it is increase their bioavailability.

Oxcarbazepine, a keto analogue of carbamazepine has been registered by US FDA in Dec 2001. It is used as an add-on or first line treatment in patients with generalized tonic clonic seizures and partial seizures with or without secondary generalization in adults and as an adjunctive in children. The drug having half life of 2 hr is completely absorbed and extensively metabolized to its pharmacologically active 10-monohydroxy metabolite, which has a half life of 9 hr. Its pharmacological activity is primarily exerted through 10-monohydroxy metabolite. Its insolubility in water and bland taste makes it an ideal candidate for fast disintegrating tablets with regards to palatability[13].

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Materials And Methods

Oxacarbazapine, Avicelp[H] 102, Sodium saccharine, Magnesium stearate, Polyplasdone Xl10, Primogel, Ac-Di-Sol were gifted from cipla limited.

Evaluation Of Blends

Bulk Density

Apparent bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight.

BD = Weight of the powder / initial Volume

Tapped Density

It was determined by placing a graduated cylinder, containing a known mass of drug-excipient blend. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10cm at 2- second intervals.

The tapping was continued until no further change in volume was noted.

TBD = Weight of the powder / final volume

Compressibility Index

The Compressibility Index of the blends was determined by Carr's compressibility index.

Carr's compressibility index (%) = [(initial volume-final volume) ×100] /initial volume

A similar index has been defined by Hausner

Hausner's ratio = Tapped density /Bulk density

Hausner's ratio

< 1.25 – Good flow = 20% Carr

> 1.25 – Poor flow = 33% Carr

1.25 > Hausner's ratio < 1.5 Added glidant normally improve

Angle of repose

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug-excipient blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation

$$\tan \theta = h/r$$

Where h and r are the height and radius of the powder cone.

Drug Content Uniformity

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.

Evaluation Of Tablets

Weight variation test

The U.S.P. weight variation test was run by weighing 10 tablets and then the average weight was determined. All the 10 tablets were weighed individually and compared with the average weight

Drug content uniformity

Five tablets were selected from each batch. The tablets were assayed individually by extracting the drug from the tablets using least amount of methanol and distilled water. The drug samples were analyzed by measuring the absorption at 255nm by using Jasco V 530 UV-visible spectrophotometer.

Friability test

The friability test was performed for all the formulated Oxacarbazapine tablets. Ten tablets were taken and their weight was determined. Then they were placed in the friabilator and allowed to make 100 revolutions. The tablets were then dedusted and reweighed. The percentage weight loss were calculated.

Hardness test

Pfizer hardness tester was used for measuring the hardness of the formulated Oxacarbazapine fast dissolving tablets. From each batch five tablets were taken and subjected to test. The mean of the five tablets were calculated

Disintegration test

The U.S.P. device to test disintegration uses six glass tubes that are 3" long, open at the top, and held against 10" screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is positioned in 1 liter beaker of distilled water at 37±2°C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker. The disintegration time was recorded.

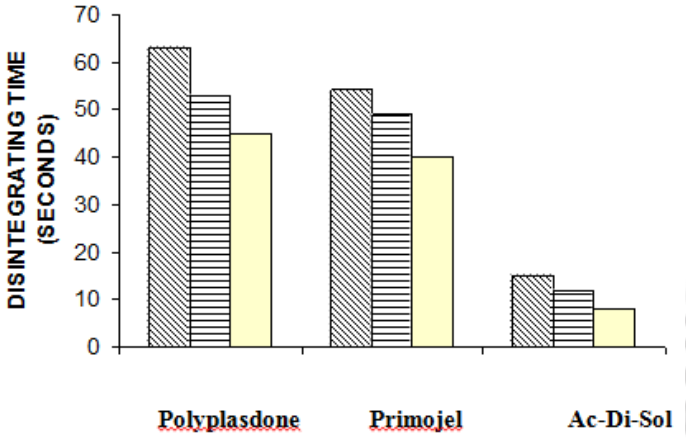

Figure:1 Disintegration Time Of Prepared Oxcarbazepine Fast Dissolving Tablets

Wetting Time

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10cm diameter were placed in a Petri dish containing water (6ml). A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablet was noted as the wetting time.

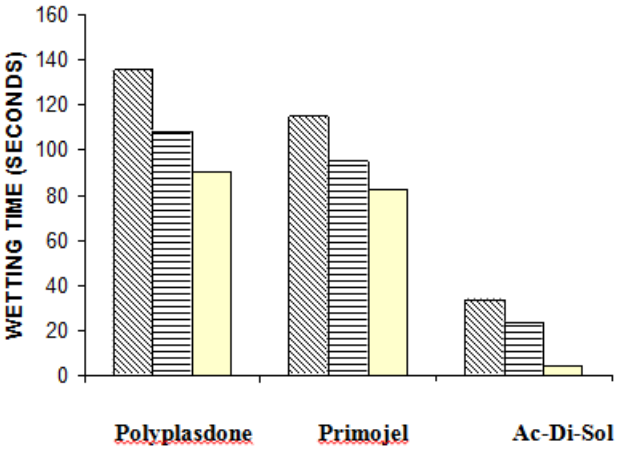

Figure: 2 Wetting Time Of Prepared Oxcarbazepine Fast Dissolving Tablets

Water Absorption Ratio

A small piece of tissue paper folded twice was placed in a small Petri dish containing water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was reweighed. Water absorption ratio, R was determined by using following formula

$$R=10 X (W_a - W_b)$$

W_b is the weight of tablet before water absorption

W_a is the weight of tablet after water absorption.

Dissolution Studies[14-18]

Dissolution was carried out by using Electro lab dissolution apparatus (USP XXI) by paddle method using 900ml of 1%w/v SLS as the medium and rotating the paddle at 50 rpm for 10 minutes. The temperature of dissolution medium was maintained at 37 ± 2^0C. Aliquots were withdrawn at different time intervals of 0, 2, 4, 6, 8 and 10 minutes. And it was replaced by adding equal volumes of fresh dissolution medium. The samples were suitably diluted and absorbance of the solution was determined at 255nm by using Jasco V 530 UV-visible spectrophotometer. The percentage of Oxacarbazapine dissolved from tablet was calculated and the graph was plotted by time vs. % of Oxacarbazapine dissolved.

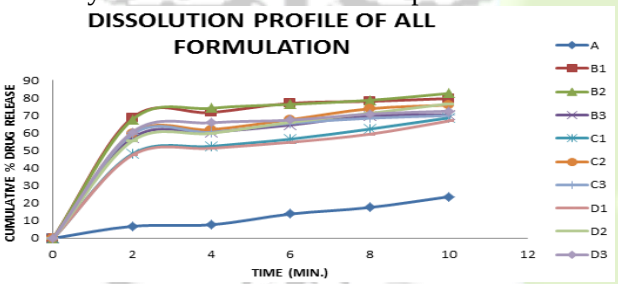

FIGURE: 1 DRUG RELEASE PROFILE OF ALL FORMULATIONS

Moisture Uptake Studies

Oxacarbazapine fast dissolving tablets of B_2, C_2, and D2 were exposed to 79.3% relative humidity condition at room temperature. Controlled humidity chamber (79.3% [RH]) was constructed using ammonium chloride saturated salt solution in dessicator. Tablets were subjected to 79.3% humidity for approximately 90 days. The effect of moisture on the hardness and disintegration were calculated after three months.

Preparation Of Oxcarbazepine Fast Dissolving Tablets By Direct Compression Method

Direct compression method involves following steps

- Blending
- Compression

Blending Procedure For Preparation Of Mixed Blend Of Drug And Excipients

All ingredients were mixed as per the formula given in table No.1. Oxacarbazapine, Sodium saccharine and Avicel P^H 102 were triturated thoroughly in a glass mortar using a pestle. Super disintegrates were incorporated in the powder mix. And finally magnesium stearate and talc were added as lubricant. Control tablet was prepared without any super disintegrant.

Compression

Mixed Blends were compressed by direct compression method using Rimek Minipress I

Result And Discussion

Compatibility studies

The IR Spectrum of pure Oxacarbazapine drug was compared with the IR spectrum of formulated Oxacarbazapine fast dissolving tablets (B_1, C_1 and D_1). There was no significant change in peaks. Hence it concludes that the drug was compatible with the polymer and the results were shown in Figure no.4

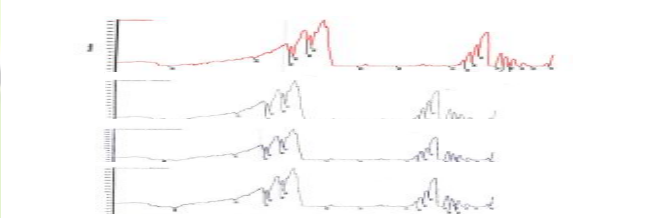

Figure: 4 Ftir Spectra's Of Oxacarbazapine, Oxacarbazapine+ Primojel, Oxacarbazapine+Polyplasdone,And Oxacarbazapine+Ac-Di-Sol

TABLE 1: GENERAL COMPOSITION OF ALL FORMULATION

S.NO	Ingredients	A	B			C			D		
		C (mg)	B1 (mg)	B2 (mg)	B3 (mg)	C1 (mg)	C2 (mg)	C3 (mg)	D1 (mg)	D2 (mg)	D3 (mg)
1	OXA	150	150	150	150	150	150	150	150	150	150
2	AV	60	60	60	60	60	60	60	60	60	60
3	PP	-	-	-	-	-	-	-	30	36	42
4	PJ	-	-	-	-	30	36	42	-	-	-
5	AC	-	30	36	42	-	-	-	-	-	-
6	SS	40	40	34	28	40	34	28	40	34	28
7	MG	10	10	10	10	10	10	10	10	10	10
8	Talc	10	10	10	10	10	10	10	10	10	10

OXA- Oxacarbazapine, AV- AvicelpH 102, PP- Polyplasdone XL10, PJ- PRIMOJEL, AC- AC-DI- SOL, SS- Sod Saccharine, MG- Magnesium stearate.

Evaluation Of Blend

Powder blend of drug and excipients were evaluated for angle of repose, bulk density, tapped density and percentage compressibility and the results were shown in Table no. 2. The angle of repose was found to be in the

TABLE 2: Evaluation Of Final Blend Ofoxcarbazepine Fast Dissolving Tablets And Control Tablet (C)

Formulation		Angle of repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Compressibility index (%)	Hausnr ratio
A	C	28±0.04	0.59	0.69	14.49	1.16
B	B1	29.2±0.0	0.58	0.69	14.7	1.18
	B2	29.6±0.04	0.60	0.68	13.6	0.88
	B3	28±0.02	0.57	0.67	14.9	1.3
C	C1	28.85±0.02	0.57	0.66	13.63	1.15
	C2	30.5±0.01	0.58	0.68	14.7	1.17
	C3	27±0.07	0.56	0.65	13.9	1.16
D	D1	25.8±0.03	0.55	0.64	14.5	1.16
	D2	26±0.02	0.57	0.66	13.6	1.16
	D3	27.0±.04	0.56	0.65	13.8	1.32

range of 26^0-31^0, it revealed that the flow properties of prepared powdered blend were good and all the evaluated parameters were complied with the official specifications.

Evaluation Of Tablets

All the prepared formulations were found to contain the medicament within 150±14% of labelled claim. Hardness of the tablets in all the batches was found to be in the range of 3.0-3.6 kg/cm^2 and was satisfactory. The percentage weight loss in the friability test was found to be less than 1% in all the batches and results were shown in Table No.3. Thus all the formulated Oxacarbazapine fast dissolving tablets employing superdisintegrants were coincide with official specifications. All the formulated Oxacarbazapine fast dissolving tablets employing, Ac-Di-Sol, Primojel, Polyplasdone XL10 disintegrated within 60 seconds fulfilling official requirements for compressed tablets, and results were shown in Table No. 3.

Formulation		Weight variation (mg)	Hardness	Friability (% w/w)	*In-vitro* dis integration time (sec)	Water absorption ratio	Assay (%)
A	C	303	3.4±1	0.5	1200±15	19	97.7
B	B1	301	3.5±1	0.78±.002	21±3	40.3	98.9
	B2	302	3.2±2	0.6±0.04	9±2	43	98.7
	B3	300	3.4±2	1.05±0.002	15±4	52.2	101.2
C	C1	305	3.6±1	0.98±0.03	24±3	46.5	99.2
	C2	303	3.2±3	0.78±0.02	19±5	53.1	100.4
	C3	301	3.3±2	0.65±0.02	17±3	55.7	98.4
D	D1	304	3.1±2	0.5±0.03	25±3	64.3	102.1
	D2	299	3.0±3	0.4±0.02	30±2	66	100
	D3	304	3.3±1	0.6±0.03	28±3	69.7	98.5

TABLE 3: PHYSICAL EVALUATION PARAMETER OF OXACARBAZAPINE FAST DISSOLVING TABLETS AND CONTROL TABLET (C)

This can be attributed to the extent of water uptake and consequently the strong swelling power of this superdisintegrant causing sufficient hydrodynamic pressure to induce complete disintegration. It can be correlated to tablet matrix pore size distribution created by the use of superdisintegrant. Higher levels of disintegrant probably made large pores with continuous network or skeleton providing enough pressure within a matrix for fast disintegration. *In vitro* dissolution study conducted for all batches (Figure: 1). among the batches formulated, B_2 released the 82.4% of the medicaments at the end of 10minutes. All the other formulated tablets released 70-80% at the end of 10minutes. The moisture uptake studies carried out for the three batches (B_2, C_2 and D_2) of the formulated tablets the average equilibrium moisture uptake by the Oxacarbazapine fast dissolving tablets at 79.3% RH was 1.4, 1.0 and 1.2 respectively. Hence, the formulated batches need the protection from humidity, which calls for specialized product packaging and results were shown in Table No.4.

TABLE 4: MOISTURE UPTAKE STUDIES

Formulation	Hardness(Kg/cm^2)	Disintegration Time (Seconds)	% of Moisture up take	Effect on Hardness (Kg/cm^2)	Effect on Disintegration (Seconds)
B_2	3.4±2	8±1	1.4	2.8±1	6±2
C_2	3.3±1	40±2	1.0	3.0±1	38±1
D_2	3.3±2	45±2	1.2	2.7±1	36±2

Conclusion

In the present study it can be concluded from the characterization of fast dissolving tablets of oxacarbazapine that formulation containing ac-di-sol is most acceptable, "patient-friendly dosage form" of bitter drugs, especially for pediatric, geriatric, bedridden, and non cooperative patients, can be successfully formulated using this technology.

Acknowledgements

Authors are thankful to principal of Lalitha College of pharmacy for providing laboratory facilities for present research work.

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