IJPSR (2011), Vol. 2, Issue 5 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 26 January, 2011; received in revised form 11 March, 2011; accepted 17 April, 2011

FORMULATION AND EVALUATION OF OLANZAPINE AS "ORODISPERSIBLE DRUG DELIVERY SYSTEM" BY USING BETA CYCLODEXTRIN AND SUPER DISINTEGRANT

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Keywords:

Olanzapine,
Orodispersible,
β- cyclodextrin

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ABSTRACT

As the psychotic, pediatric and geriatric patients are unable to swallow the medicine mouth dissolving drug delivery systems are designed for rapid dissolution and absorption of drug in the mouth within minutes without the need of water or chewing. Olanzapine is water insoluble drug hence to make it solubilize it is formulated as drug- polymer inclusion complex by using. The aim of the present study was to formulate olanzapine orodispersible tablets by using β-cyclodextrin and superdisintegrants to enhance the solubility of the drug. The drug, polymer and inclusion complex were investigated for drug interactions, complex formation and change in crystallinity by using infrared, differential scanning calorimetry, x-ray diffraction and the tablets were developed by using the direct compression and were investigated for *in-vitro* dissolution behavior and drug content. β-cyclodextrin (1:1M) can be used to enhance the solubility and dissolution rate of the drug. AC-DC-SOL (crosscarmellose sodium) as a super disintegrant shows faster release than both control and formulation by other superdisintegrants for quick release of the drug from the tablet.

INTRODUCTION: Fast mouth dissolving/dispersing [1] have become as a new drug delivery system, they are easy to administer and quick onset of drug action is possible Since drug is directly absorbed in the systemic circulation, degradation in the gastro intestinal tract and first pass effect can be avoided. Moreover better patient compliance is expected because this system does not require being swallowed as in the case of conventional tablet therefore beneficial in patient with dysphasia or difficulty in swallowing.

In this method most of water insoluble drug are formulated, and water insoluble drug can also formulated by using solublizing enhancement technique.

Like, complexation with ion exchange resin, inclusion complexes, and formulation of different salts etc, Olanzapine is an antipsychotic agent block serotonin-dopamine receptor, which is used in the treatment of schizophrenia. It is practically insoluble in water, can enhance the solubility by forming inclusion complex by using β-cyclodextrin. Orodispersible tablet of olanzapine is prepared by using direct compression method [1, 2, 3, 4]. The other method for the preparation of mouth dissolving tablet like freezing drying molding, sublimation method [5].

MATERIALS AND METHODS: Olanzapine was obtained as a gift sample from Nulite Pharmaceuticals, Pane. β-cyclodextrin, microcrystalline cellulose, crosspovidone, crosscarmellose sodium, mannitol, were laboratory graded ingredients from Bross chemicals.

Formulation of Olanzapine Inclusion Complex [2, 6]:

Kneading Method: One molar of olanzapine and one molar of β-cyclodextrin were mixed using mortar and pestle. After physical mixture, added 1:1 portion of water and ethanol in physical mixture and continuously kneaded the mixture by using motor and pestle for 10-15 minutes, a paste like consistency formed, and keep in hot Air oven at 40-45^{o}C for one hour. After complete dryness, it passed through sieve number 40.

Preparation of Orodispersible Tablet by Direct Compression Method [2, 6]**:** Direct compression method was employed to develop an orodisdipersible tablet with taste and texture acceptable to patient and with sufficient structural integrity. Tablets were prepared from control formulation, using various concentration of superdisintegrant such as 2-5% of crosspovidone, 2-5% of crosscarmellose sodium, 2-5% of sodium starch glycolate. Mixed blend drug inclusion complex and excipient was compressed on single punch rotary tablet punching machine the total weight of tablet were made to 175mg the formula for the formulation of tablet were shown in **table 1.** Compressed tablet were subjected to evaluate as per monograph.

Drug Content in Drug Polymer Inclusion Complex: Drug polymer inclusion complex prepared by kneading method it was evaluated for the drug content. Drug polymer complex equivalent to 10 mg of the drug was stirred with 100ml of ethanol (100 mcg/ml) for 60 mints, till the entire drug leached out, then it was filtered further dilution were made with phosphate buffer 6.6 pH and the drug content was noted by using UV- spectrophotometrically at 253.5nm using phosphate buffer 6.6 pH as blank.

Evaluation of Tablet [3, 7]: The compressed tablets were subjected to Weight variation, hardness, friability, disintegration time and contented uniformity (**table 2**).

In Vitro **Dissolution Studies** [4, 8]: Dissolution rate was studied by using USP type I apparatus with 900ml of phosphate buffer pH- 6.6 as dissolution medium maintained at 37±0.5˚C medium was stirred at 50 rpm. Samples were withdrawn at specific time interval, replacing the same amount with the fresh medium. Drug releases were determined by using UV spectrophotometerically at 253.5nm.

TABLE 1: COMPOSITION OF ORODISPERSIBLE TABLET

Ingredients	Control 0%	Cross Povidone				Crosscarmellose Sodium				Sodium Starch Glycolate			
		A1	A2	A3	A4	B1	B2	B3	B4	C1	C2	C3	C4
		2%	3%	4%	5%	2%	3%	4%	5%	2%	3%	4%	5%
Drug inclusion complex	46.31	46.31	46.31	46.31	46.31	46.31	46.31	46.31	46.31	46.31	46.31	46.31	46.31
Cross povidone	-	3.50	5.25	7.00	8.75	-	-	-	-	-	-	-	-
Crosscarmellose sodium	-	-	-	-	-	3.50	5.25	7.00	8.75	--	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	-	-	-	3.50	5.25	7.00	8.75
MCC	83.94	86.44	78.69	76.64	75.14	86.44	78.69	76.64	75.1	86.44	78.69	76.64	75.14
Mannitol	41	41	41	41	41	41	41	41	41	41	41	41	41
Aspartamine	1	1		1		1		1		1		1	
Magnesium stearate	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875
Aerosil	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875	0.875
Vanillin dry flavor	1	1	1	1	1	1	1	1	1	1	1	1	1
Total weight of tablet in mg	175	175	175	175	175	175	175	175	175	175	175	175	175

TABLE 2: PHYSICAL CHARACTERIZATION OF COMPRESSED TABLET

Formulation Properties	Control	Crosspovidone				Crosscarmellose Sodium				Sodium starch Glycolate			
		A1	A2	A3	A4	B1	B2	B3	B4	C1	C2	C3	C4
Weight variation in %	1.32	1.63	1.62	2.67	2.39	1.79	122	1.52	1.27	1.90	1.45	1.52	1.68
Hardness kg/cm^2	4.5	4.2	4.0	4.0	4.0	5.2	5.1	4.5	4.5	4.5	4.5	4	5
Friability in%	0.67	0.75	0.89	0.88	0.89	0.67	0.67	0.99	0.99	0.068	0.067	0.086	0.68
Disintegration time in sec	59.66	33.33	28	25.66	21.33	13.33	12	11.33	8.33	59.66	30.33	71	86
Drug content in %	98.65	98.07	98.14	99.87	98.04	99.02	98.44	98.68	99.09	99.87	99.29	99.38	96.38

RESULT AND DISCUSSION: Olanzapine orodispersible tablet were designed with the objective of immediate release of the drug for improved patient compliance and better bioavailability. Therefore the rapid release of the drug is enhanced by using superdisintegrant like crosspovidone, crosscarmellose sodium, and sodium starch glycolate. Olanzapine is water insoluble in nature, the solubility were enhanced by making drug polymer inclusion complex using beta cyclodextrin and the solubility enhancement by the effect of beta cyclodextrin were studied and compared with the pure drug result were shown in **table 3 & figure 1.** All compressed tablet were observed that the result of weight variation, hardness, friability, disintegration time and drug content were shown in table 2**.**

TABLE 3: DISSOLUTION PROFILE OF PURE DRUG AND DRUG INCLUSION COMPLEX

Time interval	Drug release in %	
	Pure drug	Drug inclusion Complex
2	18.57	51.42
4	25.43	65.23
6	39.12	71.31
8	43.09	81.61
10	52.77	100
12	59.68	
14	65.21	
16	73.15	
18	81.32	
20	84.20	

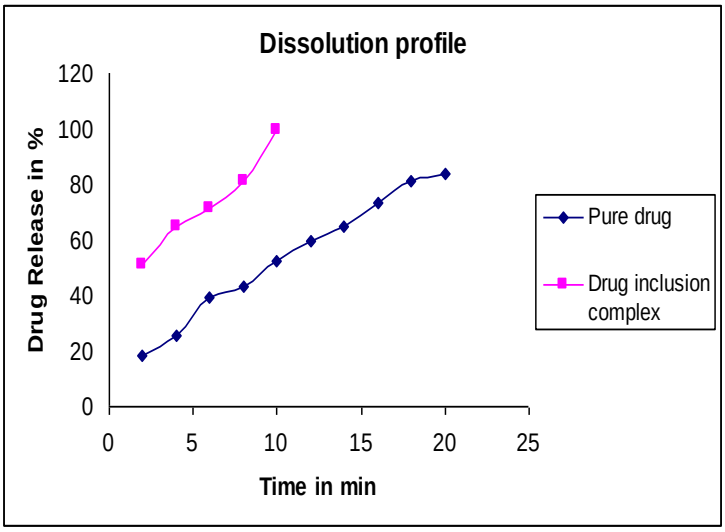

FIG. 1: EFFECT OF BETA CYCLODEXTRIN ON THE SOLUBILITY OF OLANZAPINE

The dissolution study was carried out to determine the profile of drug release from the formulation. The dissolution study for the control tablet was observed that 100 percent drug release in 8 minutes. Dissolution profiles for the tablets prepared by A1, A2, and A3 & A4 formulation containing 2, 3, 4 and 5% of crosspovidone as super disintegrant respectively. It was observed that 100 % drug release at 5 minutes in the formulation of A1 & A2 while for A3 and A4 formulation at 4 minutes were as for B1, B2, B3 & B4 formulation containing crosscarmellose sodium as super disintegrant respectively. It was found that the 100 percent drug released at 3 & 2 in the formulation B1, B2 & B3 respectively were as B4 released the drug within a minutes. For the tablet made with sodium starch glycolate (C1, C2, and C3) were release at 10 to 13 minutes. These are shown in **table 4 & figure 2.**

TABLE 4: *IN VITRO* DRUG RELEASE OF COMPRESSED TABLET

Time Interval In Min	Control 0%	Percentage of Drug Release										
		Cross Povidone				Crosscarmellose Sodium				Sodium Starch Glycolate		
		A1	A2	A3	A4	B1	B2	B3	B4	C1	C2	C3
		2%	3%	4%	5%	2%	3%	4%	5%	2%	3%	4%
1	62.43	71.50	82.89	75.03	75.06	81.44	84.44	87.20	100	28.0	16.10	18.47
2	69.72	83.99	88.20	88.20	88.89	94.38	96.80	100		52.23	40.35	35.54
3	75.49	90.27	93.27	95.00	97.48	100	100			64.45	46.26	45.76
4	82.12	95.84	99.88	100	100					89.57	55.47	53.24
5	90.00	100	100	-	-					98.68	70.41	70.08
6	92.55	-	-	-	-					100	73.60	73.29
7	95.91	-	-	-	-						85.27	82.50
8	100	-	-	-	-						89.66	87.15
9	-	-	-	-	-						97.09	90.28
10	-	-	-	-	-						100	92.03
11	-	-	-	-	-							98.93
12	-	-		-	-							100

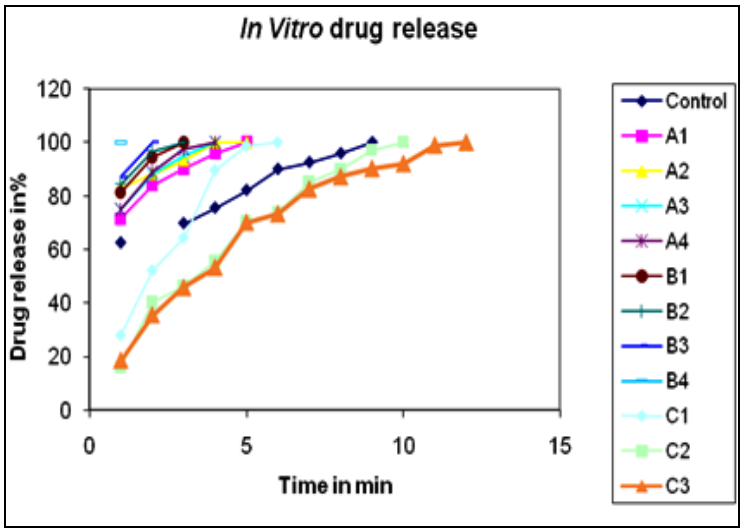

FIG. 2: *IN VITRO* DRUG RELEASE PROFILE FOR THE COMPRESSED TABLET

CONCLUSION: β- cyclodextrin (1:1M) can be used to enhance the solubility of the drug also it increased the dissolution rate of the drug with increase in concentration of superdisintegrant, disintegration time is decreased. The orodispersible tablet were prepared by using crosscarmellose sodium (Ac-Di-Sol) as a super disintegrant shows faster release of the drug than both control formulation and formulation prepared by other superdisintegrant.

REFERENCE:

1. Kuchekar, B.S and Badhan, A.C (2003). "Mouth Dissolving Drug Delivery System" Pharmatimes, 6(35), 7-11.
2. Kei-Ichi, K and Yoshiteru, W (1997). .Preparation Of Rapidly Soluble Com pressed Tablets of Meclizine Using Mannitol with Camphor Subliming Material by Direct Compression Method".Internationl Journal of Pharmaceutics 152, 193-198.
3. M. Vamshi Krishna, Theja Pavan Kumar, (2010). "Formulation and Evaluation of Baclofen Orally Disintegrating Tablets". International Journal of Pharmaceutical Science and Nanotechnology. 2(4), 733-738.
4. Tarun Patel, Rathan Kumar, (2010). "Development of Fast Dissolving Carbamazepine Tablets; Effect of Functionality of Super Disintegrating". International Journal of Pharmaceutical Sciences and Nanotechnology, 3(1), 824-833
5. Yoshiteru. W and Noki Utoguchi (1999). "Preparation and Evaluation of Tablets Rapidly Disintegrating In Saliva Containing Bitter Taste Masked Granules by Direct Compression Method". Chem.Pharm.Bull, 47(10), 1451-1454.
6. Jayachandra, B and Pandit, J.K (1999). "Study of Dissolution Characterization of Glibenclamide with β- cyclodextrin Prepared by Kneading Method". Ind.Pharm, 25(11), Pp.1215-1219.
7. Koland, M and Sandeep, V.P (2010) "Fast dissolving sublingual films of onansetron hydrochloride: Effect of additives on in vitro drug release and mucosal permeation" journal of young pharmacists 2(3), 216-221.
8. S. Jacob, Ashirwarkar, (2009). "Preparation and Evaluation of Microencapsulated Fast Melt Tablets of Ambroxol Hydrochloride". Indian Journal of Pharmaceutical Sciences 71(3), 276-284.

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