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Research Article

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Formulation and *in-vitro* evaluation of orodispersible tablets of olanzapine for the improvement of dissolution rate

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ABSTRACT

The objective of this study was to formulate the orodispersible tablets (ODTs) of Olanzapine (OLZ) by direct compression method for the enhancement of dissolution rate. OLZ ODTs were prepared by direct compression method using co-processed superdisintegrants like sodium starch glycolate (SSG) and Croscarmellose sodium (CCS). It was observed from the evaluation studies that the results were complied with the official limits. In-vitro dissolution studies were carried out by USP dissolution apparatus, paddle method using pH 6.8 phosphate buffer and the formulations F8, F9 showed maximum drug release of 101.16% and 99.45% respectively within 2 min. It was evident from the drug release studies that the formulation F8 and F9 consists of CP-3 showed optimum drug release of 101.80% and 100.33% respectively.

Key words: Olanzapine, Co-processed technique, Orodispersible tablets, Dissolution rate enhancement, superdisintegrants.

INTRODUCTION

The oral route of administration is the most preferred route due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliance [1-2]. Tablets and capsules are the most popular dosage forms. But one important drawback of such dosage forms is Dysphasia or difficulty in swallowing. This is seen to afflict nearly 35% of the general population. To solve the above-mentioned problems, pharmaceutical technologists have put in their best efforts to develop a Fast dissolving drug delivery, i.e. Mouth Dissolving Tablets (MDTs) that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing [3-8].

The optimum concentration of the superdisintegrant can be selected according to critical concentration of disintegrants. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if the concentration of superdisintegrant is above critical concentration, the disintegration time remains almost constant or even increases [9]. Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individuals. Co-processing excipients lead to the formulation of excipient granules with superior properties, compared with physical mixtures of

components or individual components [10-11]. Hence, the present study was concentrated on the enhancement of dissolution rate of OLZ ODTs by using the co-processed superdisintegrants.

EXPERIMENTAL SECTION

Materials

The drug OLZ was purchased from Bright labs, India and superdisintegrants like Microcrystalline cellulose (MCC), Sodium starch glycolate (SSG), Croscarmellose sodium (CCS), lubricant like Magnesium stearate (MS) and glidant talk were obtained from Merck Specialities Pvt. Ltd., Mumbai, India.

Methods

FTIR studies

The compatibility between the pure drug and excipients was detected by FTIR (Model-IR Affinity-1, Shimadzu, Japan). The potassium bromide pellets were prepared on KBr press by grounding the solid powder sample with 100 times the quantity of KBr in a mortar. The finely grounded powder was then introduced into a stainless steel die and was compressed between polished steel anvils at a pressure of about 8 t/in^2. The spectra were recorded over the wave number of 4000 to 400 cm^{-1} and the spectra of pure drug were compared with its spectra of physical mixture.

Formulation of ODTs of OLZ

Preparation of co-processed super disintegrants

Co-processed super disintegrates were prepared by using SSG and CCS. The super disintegrates were mixed in different concentrations and labeled as CP1, CP2, CP3. The blend of super disintegrates was mixed thoroughly for a period of 15 min, collected and used for preparing the OLZ ODTs (Table 1).

Table 1. Composition of co processed super disintegrates

Ingredients (mg)	CP1	CP2	CP3
SSG	100	100	100
CCS	100	200	300

CP = Co-processed super disintegrants

Preparation of tablets

Composition of OLZ ODTs was shown in table 2. All the ingredients were weighed and required quantity of drug and excipients were mixed thoroughly in a polybag. The blend was compressed by direct compression method using rotary tablet machine-8 station with 8 mm flat punch (RIMEK rotary Tablet Punching machine, India). Each tablet contains 3 mg of OLZ and the final tablet weight was fixed to 100 mg.

Table 2. Composition of various tablet formulations

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
OLZ	3	3	3	3	3	3	3	3	3
CP 1	10	20	30	-	-	-	-	-	-
CP 2	-	-	-	10	20	30	-	-	-
CP 3	-	-	-	-	-	-	10	20	30
MS	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
MCC	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs
Total weight	100	100	100	100	100	100	100	100	100

Flow properties

The precompression parameters like Loose bulk Density (LBD) and Tapped bulk density (TBD), angle of repose**,** Hausner's ratio and Carr's index were performed for powder blend according to the standard procedures [12].

Post-compression parameters

Post-compression parameters like friability, hardness, thickness, weight variation, content uniformity, disintegration tests were evaluated for the tablets according to the standard procedures [13].

Drug Content

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among the tablets within a batch. Four tablets were weighed and crushed in the mortar. The powder

equivalent to 1.25 mg of the drug were weighed and dissolved in 100 ml pH 6.8 phosphate buffer, suitably diluted and estimated by using UV Visible spectrophotometer (Lab India, UV-3200) at 278nm.

***In-vitro* dissolution studies**

In-vitro release studies were carried out by using USP dissolution apparatus type-II (Lab India, DS-800). It was performed by using 900 ml dissolution fluid (pH 6.8 phosphate buffer) at a speed of 50 rpm and temperature of 37^0C. Samples of dissolution medium (5ml) were withdrawn for specified time intervals (2, 4, 6, 8, 10, 15, 20, 30, 45 & 60 min) and assayed for OLZ by measuring absorbance at 278 nm and replaced with the same volume of pH 6.8 phosphate buffer.

Application of release rate kinetics to dissolution data

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release and rate kinetics of the dosage form, the obtained *in-vitro* drug release data was subjected to zero order, first order, Higuchi and Korsmeyer-Peppas release models.

RESULTS AND DISCUSSION

FTIR studies

From the FTIR data it was evident that the drug and super disintegrants, other excipients do not have any interactions**.** Hence they were compatible (Figure 1 & 2).

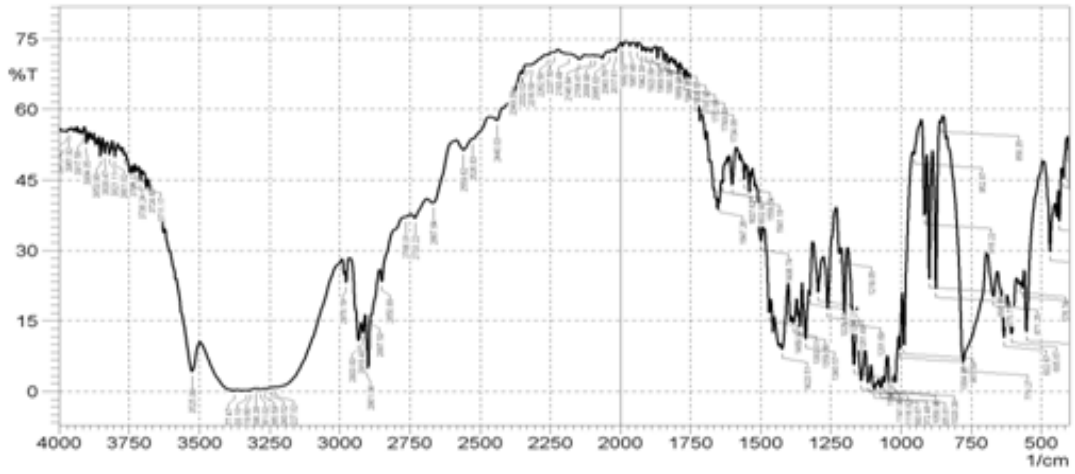

Figure 1. FTTR Spectrum of OLZ pure drug

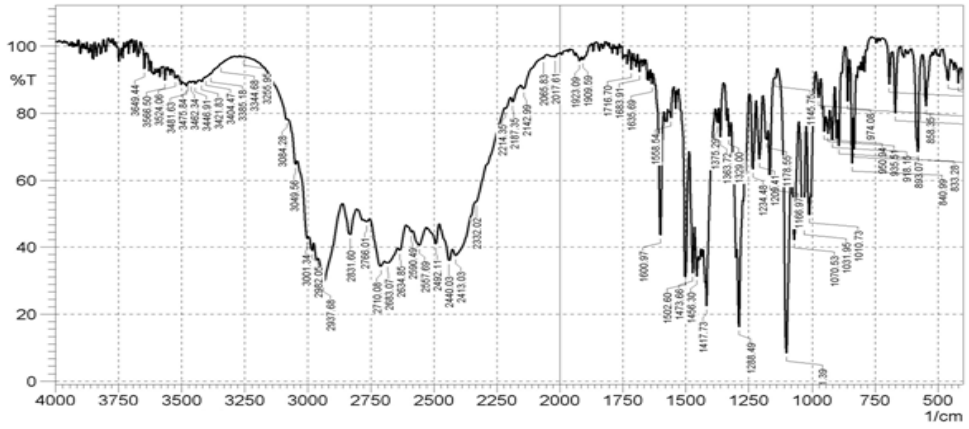

Figure 2. FTIR Spectrum of Optimized Formulation

Precompression parameters

The values for angle of repose were found in the range of 25.78°-29.34°. Carr's index of the prepared blends was fall in the range of 13.06% to 18.18% and Hausner's ration fall in range of 1.14 to 1.22. From the results, it was concluded that the powder blends had good flow properties and these can be used for tablet manufacture (Table 3).

Table 3. Precompression parameters

Formulations	Bulk Density (gm/cm^2)	Tapped Density (gm/cm^2)	Carr's Index (%)	Hausner's ratio	Angle of Repose (Θ)
F1	0.45	0.55	18.18	1.22	27.91
F2	0.47	0.55	14.54	1.17	28.23
F3	0.50	0.58	13.79	1.16	29.34
F4	0.46	0.55	16.36	1.19	26.71
F5	0.50	0.58	13.79	1.16	29.34
F6	0.47	0.55	14.54	1.17	28.23
F7	0.50	0.58	13.79	1.16	29.34
F8	0.41	0.50	18	1.21	26.78
F9	0.41	0.50	18	1.21	26.78

Post compression Parameters

Tablets of each batch were subjected to weight variation test. The average weight of the tablet was approximately in the range of 98.5 to 107 and the permissible limit is ±10% (90-110 mg). The results of the test showed that the tablet weights were within the pharmacopoeia limit. Hardness of the three tablets of each batch was checked by using Monsanto hardness tester and it was in the range of 2.5 to 3.00 kg/cm^2, which was within the IP limits. Thickness of three tablets of each batch was checked by using Vernier Caliper and the thickness of the tablet was raging from 3.56 to 3.64 mm. The average friability of all the formulations lies in the range of 0.30 to 0.51% which was less than 1%, as per official requirement of IP indicating a good mechanical resistance of tablets. The results showed that the disintegration time of prepared tablets were in the range of 12.66 to 30.33 sec. Assay studies were performed for the prepared formulations. From the content uniformity studies, it was observed that all the formulations were showing the % drug content values within 97.23 to 99.25 % (Table 4).

Table 4. Post compression studies of OLZ ODT

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Content uniformity (%)
F1	105	2.5	3.59	20.33	0.43	97.23
F2	104	2.6	3.64	22.66	0.34	98.55
F3	110	2.5	3.59	30.33	0.49	98.16
F4	109	2.6	3.58	19.00	0.47	99.34
F5	99.4	2.3	3.59	30.33	0.49	98.16
F6	102	2.7	3.64	22.66	0.34	98.55
F7	101	2.5	3.59	30.33	0.49	98.16
F8	107	2.6	3.56	17.00	0.34	99.25
F9	102	2.5	3.56	17.00	0.34	99.25

Table 5. *In-vitro* drug release of all the formulations

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
2	25.4	31.7	30.8	24.3	39.5	14.9	48.3	101.16	99.45
4	39.6	34.5	36.72	31.6	76.3	28.4	82.9	101.80	100.33
6	48.6	41.9	56.16	49.3	96.2	33.1	98.7		
8	64.3	62.4	87.4	58.3	99.7	59.7			
10	76.4	89.1	98.5	74.3		79.3			
15	97.1	99.5		88.1		88.9			
20	97.6			94.6		93.5			
25				98.1		98.1			

***In-vitro* Dissolution studies**

In-vitro dissolution studies were carried out by USP dissolution apparatus, paddle method using pH 6.8 phosphate buffer. The dissolution studies were carried out for about 30 min. From the results, it was evident that the formulations prepared with CP3 showed maximum % drug release in 2 min i.e.101.80% and 100.33% (F8 and F9

respectively). F8 formulation was considered as an optimized formulation as it contains less concentration of super disintegrates (Table 5 and Figure 3).

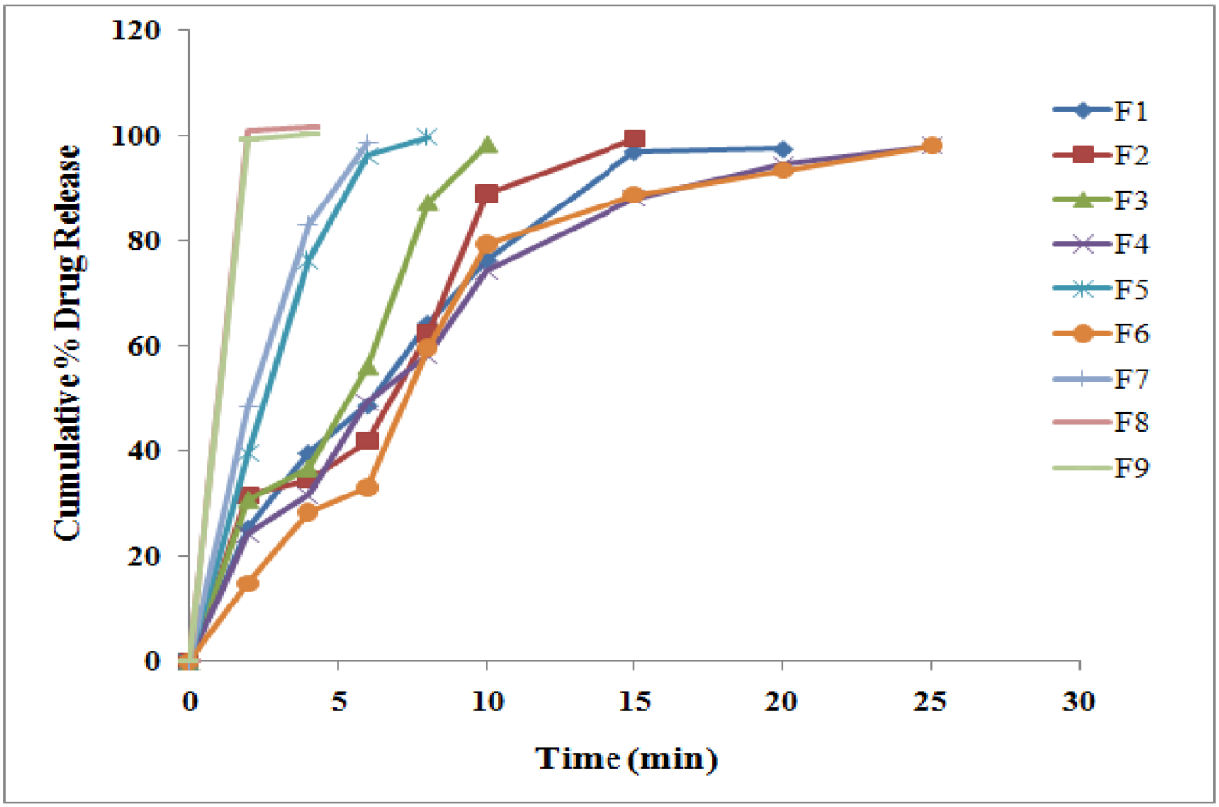

Figure 3. Dissolution profiles of all the formulations

CONCLUSION

OLZ ODTs were successfully prepared by co-processed super disintegrants and evaluated. From the results, it could be concluded that the formulation F8 and F9 showed maximum drug release within short period of time i.e. 2 min, hence there is a lot of scope for *in-vivo* studies.

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