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FORMULATION AND *IN VITRO* EVALUATION OF OLANZAPINE IMMEDIATE RELEASE TABLETS

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ABSTRACT

The aim of the present investigation was to formulate Immediate Release Tablets of olanzapine, an anti-psychotic drug. Immediate Release Tablets of Olanzapine were prepared with the addition of different superdisintegrants, namely, crospovidone, croscarmellose sodium, and sodium starch glycolate. Each of these superdisintegrants was used in concentrations of 1% w/w, 2% w/w, 3% w/w. Formulation with 3% w/w crospovidone showed maximum Drug Release (96.44%). The formulation was optimized successfully. The prepared batches were evaluated for organoleptic properties, hardness, friability, weight variation, *in vitro* drug release studies. The drug-excipient interaction was studied by Fourier transform infrared spectroscopy (FTIR) studies. The optimized formulation showed minimum disintegration time and an almost complete release of the drug within 45 minutes. Finally it was concluded that the Immediate Release Tablets of Olanzapine could be successfully formulated by adding superdisintegrants with improved patient compliance.

KEYWORDS

Olanzapine and Immediate Release Tablets.

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INTRODUCTON

Even today these formulations can be considered as primary pharmaceutical product commonly seen in market[1].

Immediate release tablets

Desired criteria for immediate release Drug delivery system

Be portable without fragility concern.

Have a pleasing mouth feel.

It should not leave minimal or no residue in the mouth after oral administration[1,5,6].

Merits of Immediate Release Drug Delivery System[7-9]

Improved compliance/added convenience

Improved stability, bioavailability

Cost- effective

Improved solubility of the pharmaceutical composition.

Decreased disintegration and dissolution times for immediate release oral dosage forms[3].

Disadvantage

Frequent dosing is necessary for drug with short half-life.

Drug release at a time may produce high plasma concentration which may produce toxicity.

MATERIAL AND METHODS

Olanzapine Procured From Sun Pharma Limited, Provided by SURA LABS, Dilsukhnagar, Hyderabad. Croscarmellose sodium, Crospovidone, Sodium starch glycolate, HPMC K4M Procured from Nihar traders Pvt Ltd. Talc Procured from Himedia Laboratories. Magnesium stearate, Microcrystalline cellulose Procured from Nice chemicals Ltd.

Methods

Formulation Development

Drug and different concentrations for super Disintegrates and required ingredients were accurately weighed and passed through a 40-mesh screen to get uniform size particles and mixed in a glass mortar for 15 minutes.

The obtained blend was lubricated with Magnesium stearate and glidant (Talc) was added and mixing was continued for further 5 minutes.

The resultant mixture was directly compressed into tablets by using punch of rotary tablet compression machine. Compression force was kept constant for all formulations.

Evaluation parameters

Pre compression parameters

Measurement of Micromeritics Properties of Powders

Angle of repose

The angle of repose of API powder is determined by the funnel method. The powder blend is allowed to flow through the funnel freely on the surface. The diameter of the powder cone is measured and angle of repose is calculated using the following equation[55].

$\tan \theta = h/r$ …….. (1)

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

Bulk density

The bulk density is calculated in g/cm^3 by the formula[56]

$\text{Bulk density} = M/V_0$ …… (2)

M= Powder mass

V_0= apparent unstirred volume

Tapped density

The tapped density is calculated in g/cm^3 by the formula[57].

$\text{Tapped density} = M/V_f$ …….. (3)

M= weight of sample power taken

V_f= tapped volume

Compressibility Index

The formula for Carr's Index is an below:

Carr's Index (%) = [(TD-BD)/TD] x 100 …….. (4)

Hauser's ratio

The ratio of tapped density to bulk density of the powders is called the Hauser's ratio[58].

$H = \rho T / \rho B$ ……. (5)

Where ρT = tapped density, ρB = bulk density

Post compression parameters

Thickness

The thickness of tablets was determined by using Digital micrometer.

Weight variation

Twenty tablets randomly selected from each batch and individually. Weighed the average weight and standard deviation three batches were calculated. It was calculated on an electronic weighing balance.

Friability

Accurately weighed six tablets were placed in Roche friabilitor and rotated at 25 rpm for 4 min.

Percentage friability was calculated using the following equation.

$\text{Friability} = ([w_0 - w] / w_0) \times 100$

Assay

The five tablets were grinded in mortar to get powder, this powder was dissolved in pH 6.8 phosphate buffer by sonication for 30 min and filtered through filter paper. The drug content was

analyzed spectrophotometrically at 220 nm using UV spectrophotometer.

Disintegration test

Six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets.

Dissolution test of Olanzapine HCL tablets

Drug release from Olanzapine HCL tablets was determined by using dissolution test United States Pharmacopoeia (USP) 24 type II (paddle). The parameters used for performing the dissolution were pH 6.8 phosphate buffer as the dissolution medium of quantity 500ml. The whole study is being carried out at a temperature of 37^{o}C and at speed of 50 rpm. 5ml aliquots of dissolution media were withdrawn each time at suitable time intervals (5, 10, 15, 20, 25 and 30 minutes) and replaced with fresh medium.

Drug-Excipients compatibility studies

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany (Alpha T). The solid powder sample directly place on yellow crystal which was made up of ZnSe. The spectra were recorded over the wave number of 4000 cm^{-1} to 400cm^{-1}.

RESULTS AND DISCUSSION

Evaluation

Characterization of pre-compression blend

The pre-compression blend of Olanzapine were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio. Angle of repose was less than 28^{o}, Carr's index values were less than 11 for the pre-compression blend of all the batches indicating good to fair foldability and compressibility. Hausner's ratio was less than 1.25 foe all batches indicating good flow properties

Physical evaluation of Olanzapine immediate release tablets

The results of the weight variation, hardness, thickness, friability and drug content of tablets are given in table. All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limit. The hardness of the tablets ranged from 4.6-5 kg/cm^2 and the friability values were < than 0.561% indicating that the tablets were compact and hard. The thickness of the tablets ranged from 4.71- 4.91 cm. All the formulations satisfied the content of the drug as they contained 98-100% of Olanzapine HCL and good uniformity in drug content was observed. Thus all physical attributes of the prepared tablets were found to be practically within control limits.

***In vitro* release studies**

The drug release rate from tablets was studied using the USP type II dissolution test apparatus. The dissolution medium was 500 ml of pH 6.8 phosphate buffer at 50 rpm at a temperature of 37±0.5^{o}C. Samples of 5 ml were collected at different time intervals up to 1 hr and has analyzed after appropriate dilution by using UV spectrophotometer at 258 nm.

Finally, the tablets were evaluated for *in vitro* dissolution studies in simulated gastric fluid and the results were shown in the Table. Final optimized formulation F6 showed 96.44% drug release. Formulation F6 which contain Crospovidone, the drug release at 45 mins was found to be 96.44% respectively. The formulation with Crospovidone shows more release than the tablets with Sodium starch glycolate, Cross carmellose sodium. The experiment proves that the drug release is a release rate-limiting step. The disintegrant Crospovidone shows the faster disintegration than other. So release of drug and release rate was higher from these tablets.

Table No.1: Formulation of Immediate Release tablets

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Olanzapine	15	15	15	15	15	15	15	15	15
2	Croscarmellose sodium	15	30	45	-	-	-	-	-	-
3	Crospovidone	-	-	-	15	30	45	-	-	-
4	Sodium starch glycolate	-	-	-	-	-	-	15	30	45
5	HPMC K4M	6	6	6	6	6	6	6	6	6
6	Talc	3	3	3	3	3	3	3	3	3
7	Magnesium stearate	3	3	3	3	3	3	3	3	3
8	Microcrystalline cellulose	78	63	48	78	63	48	78	63	48
9	Total weight	120	120	120	120	120	120	120	120	120

Table No.2: Physical properties of pre-compression blend

Formulation code	Angle of repose (Ɵ)	Bulk density (gm/cm^3	Tapped density(gm/cm^3)	Carr's index (%)	Hausner's ratio
F1	21.11	0.51	0.57	8.43	1.12
F2	25.43	0.54	0.50	9.10	1.04
F3	24.31	0.53	0.47	10.01	1.07
F4	25.20	0.55	0.62	10.14	1.12
F5	27.12	0.52	0.53	10.28	1.03
F6	26.41	0.45	0.61	9.12	1.09
F7	27.21	0.55	0.64	10.13	1.14
F8	28.14	0.51	0.56	10.21	1.07
F9	27.12	0.56	0.68	10.27	1.12

All the values represent n=3

Table No.3: Physical evaluation of Olanzapine

Formulation code	Average Weight (mg)	Thickness (cm)	Hardness (Kg/cm^2)	Friability (%)	Content uniformity (%)
F1	120.4	4.76	2.1	0.478	99.10
F2	119.9	4.73	2.0	0.356	99.02
F3	120.5	4.72	2.2	0.361	100.02
F4	117.7	4.81	2.3	0.562	100.21
F5	120.8	4.80	2.0	0.472	99.33
F6	120.1	4.76	2.1	0.514	99.21
F7	120.5	4.78	2.3	0.452	97.84
F8	120.3	4.73	2.2	0.423	96.56
F9	118.7	4.72	2.5	0.510	100.11

Table No.4: *In vitro* data for formulation F1-F3

S.No	TIME (MIN)	% DRUG RELEASE		
		F1	F2	F3
1	0	0	0	0
2	5	16.28	21.35	12.26
3	10	39.42	37.52	25.38
4	15	43.15	49.43	39.99
5	20	57.75	55.67	47.62
6	25	64.74	71.42	69.75
7	30	72.28	93.27	75.31
8	45	85.52	85.38	81.36

Table No.5: *In vitro* dissolution data for formulations F4-F6

S.No	TIME(MIN)	% DRUG RELEASE		
		F4	F5	F6
1	0	0	0	0
2	5	10.25	18.12	18.15
3	10	28.85	27.38	34.93
4	15	36.79	39.27	47.69
5	20	42.67	52.85	62.26
6	25	58.53	66.85	74.88
7	30	63.26	78.43	85.57
8	45	72.38	89.73	96.44

Table No.6: *In vitro* dissolution data for formulations F7-F9

S.No	TIME (MIN)	% DRUG RELEASE		
		F7	F8	F9
1	0	0	0	0
2	5	13.37	15.33	22.28
3	10	24.39	27.57	34.58
4	15	36.47	45.36	45.35
5	20	45.69	59.75	64.88
6	25	52.66	68.33	72.74
7	30	79.54	79.18	87.63
8	45	93.58	89.65	95.04

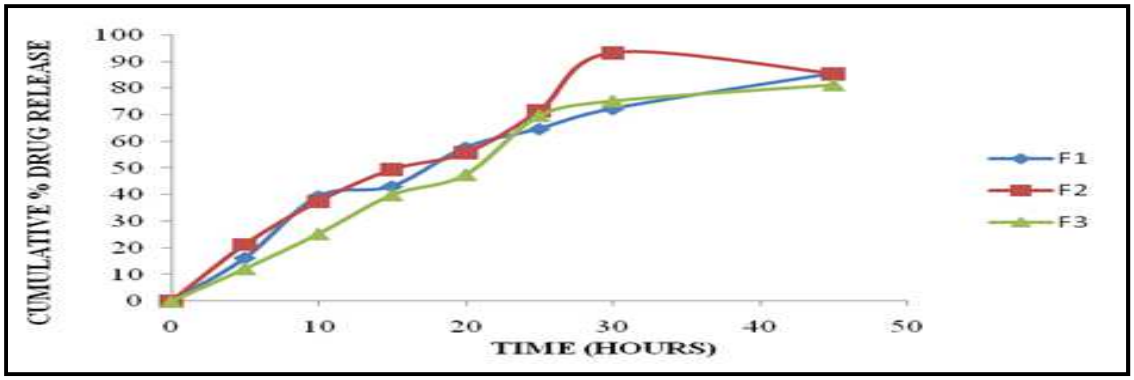

Figure No.1: *In vitro* dissolution data for formulation F1-F3

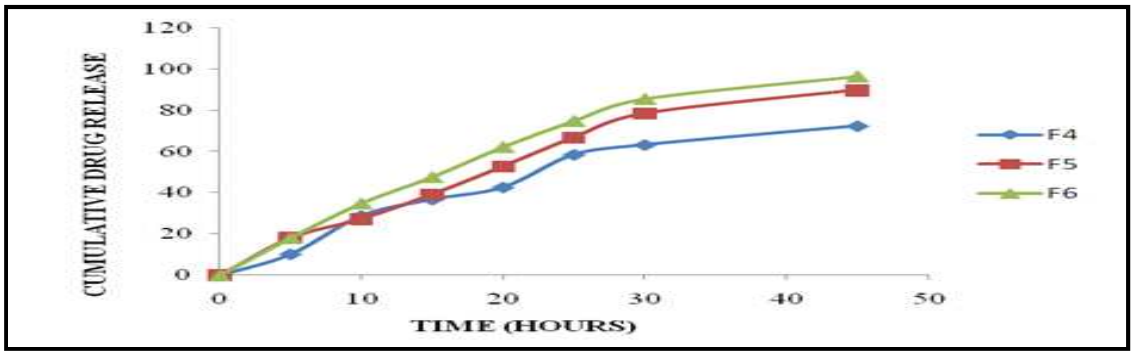

Figure No.2: *In* vitro dissolution data for formulations F4-F6

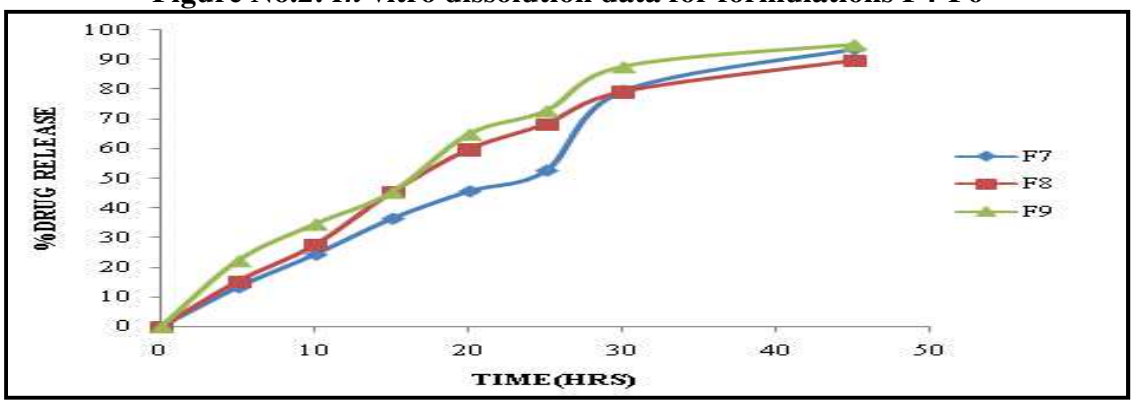

Figure No.3: *In vitro* dissolution data for formulations F7-F9

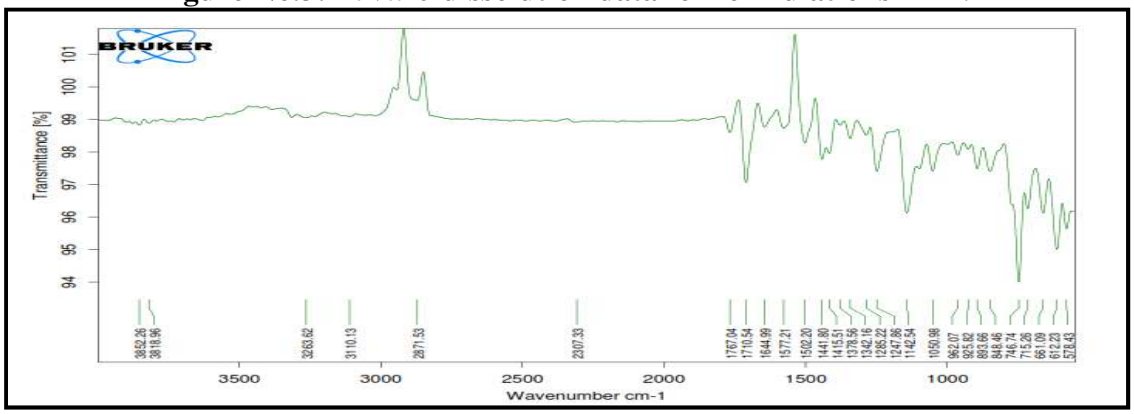

Figure No.4: FTIR spectra of pure drug

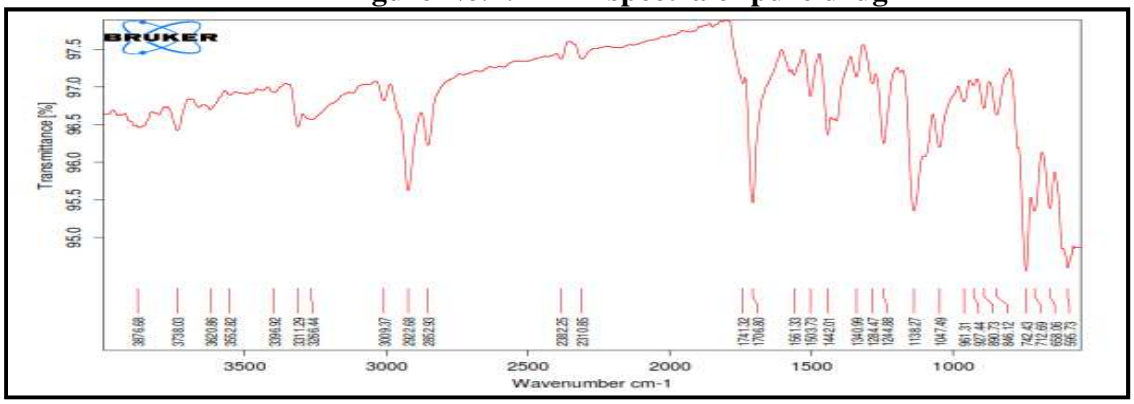

Figure No.5: FTIR spectra of optimized formulation

CONCLUSION

The immediate release tablets of Olanzapine were prepared by direct compression method. From the results of evaluation, it was concluded that by F6 Formulation is optimized Formulation 96.44%. Bioavailability could be increased for a drug e.g. Olanzapine, by preparing immediate release formulations with enhanced absorption in simulated gastric fluid. Conclusively the % drug release was best found in the batch containing 45mg (w/w) crospovidone. All the data satisfactorily complied with the characteristic requirements of the formulation as immediate release tablets. Thus the objective of the research work of formulating an immediate release tablet of Olanzapine with optimization could have been achieved with success. The present worker tended to provide impetus for the future researchers to design immediate release pharmaceutical formulations of such other drugs superseding conventional dosage forms with significant pharmacokinetic and pharmacodynamic properties.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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