Volume 2 (2), 2014, Page-145-156
e-ISSN: 2348-6465

Pharma Health Sciences

International Journal of Pharma Research and Health Sciences

Available online at www.pharmahealthsciences.net

Original Article

Formulation and *In-vitro* evaluation of immediate release Olanzapine tablets

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ARTICLE INFO

Received: 14 Mar 2014
Accepted: 19 Apr 2014

ABSTRACT

The main objective of the present study was to formulate stable immediate release Olanzapine tablets matching in invitro dissolution with the marketed formulation. Olanzapine is hygroscopic and sensitive to heat and moisture. The present work had two objectives-To develop stable Olanzapine tablets and matching in dissolution with the marketed formulation. Tablets were manufactured by direct compression process. Superdisintegrants were chosen to reduce the disintegration time and match the dissolution profile that of marketed formulation. It was found that the dissolution profile of trial T7 which was formulated with 2% Crospovione intragranular and 2% Crospovidone extragranular was similar to marketed formulation. The 10mg and 15mg strengths were formulated by common blend approach, with formula similar to optimized formula of 20mg tablets. The dissolution profiles of 10 mg and 15mg strengths were compared with 20mg strength and the results were found to be satisfactory.

Key words: Formulation**,** Optimization, Immediate Release Tablet, Olanzapine.

1. INTRODUCTION

Tablets are the most widely used dosage forms because of their convenience in terms of self-administration, compactness, and ease in manufacturing. [1] The tablet dosage form is preferred to other oral dosage forms since one accurate dose of the drug can be easily administered. [2]

Olanzapine is a benzodiazepine belonging to Antipsychotics agents which was approved by the Food and Drug Administration (FDA). It is used in the treatment of schizophrenia, depressive episodes

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associated with bipolar disorder, acute manic episodes, and maintenance treatment in bipolar disorder. It is a relatively new drug in the market. [3] The pharmacokinetics of Olanzapine is linear and dose proportional within the approved dosage range from 1 mg up to 20 mg. Olanzapine is well absorbed following oral administration in both fed and fasted states. Food does not affect the rate or the extent of Olanzapine absorption. [4] The absolute bioavailability is only approximately 31.5% due to extensive hepatic metabolism. [5]

Olanzapine chemically is 2-methyl-4-(4-methylpiperazin-1-yl)-5H-thieno[3,2-c][1,5] benzodiazepine. [6] The structure of Olanzapine is shown in fig 1:

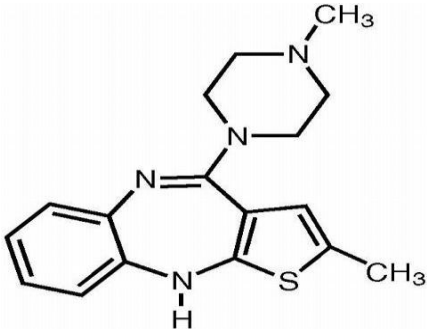

Fig 1: Structure of Olanzapine

Its empirical formula is $C_{17}H_{20}N_4S$. Olanzapine is a yellow solid drug, soluble in water, with higher solubility observed in 0.1N HCl.

The objective of the present study was to develop stable oral immediate release Olanzapine tablets with dissolution profile similar to that of marketed formulation. Immediate release tablets are those intended to be swallowed whole and to disintegrate and release their medicaments rapidly in the gastrointestinal tract (GIT). Superdisintegrants are more effective at lower concentrations typically 1- 10 % by weight relative to the total weight of the dosage unit with greater disintegrating efficiency and mechanical strength. Different commonly used superdisintagrants are 1. Modified Starches- Sodium Carboxymethyl Starch (Sodium Starch Glycolate) 2. Cross-linked polyvinylpyrrolidone (crospovidone) 3. Modified Cellulose (croscarmellose sodium). [7]

Olanzapine is hygroscopic and sensitive to heat and moisture. [8] It is metastable in nature and tends to undesirably discolor in tablet formulation. [9] Trials were taken by direct compression and wet granulation methods to study the feasibility of the processes. Direct compression was the method of choice since the impurity levels were high with wet granulation trials. Various formulations of Olanzapine tablets 20mg were prepared using the above mentioned superdisintegrants and the invitro dissolution profiles of the formulations were compared with that of marketed formulation Zyprexa 20mg. The tablets were sealed with Hypromellose (Methocel E5 Premium) to provide moisture protective barrier and film coated with Opadry White. The formulation trials were also evaluated for inprocess parameters and parameters for finished product. The invitro dissolution profiles were compared with the marketed formulation 20mg in 0.1N HCl, pH 4.5 acetate buffer and pH 6.8 phosphate buffers. Based on the dissolution results, the formula was optimized for 20mg tablets. The lower strengths 10mg and 15mg were formulated by common blend approach as that of optimized formula for 20mg strength and their dissolution profiles were compared with that of 20mg strength.

2. MATERIALS AND METHODS

Olanzapine was procured from Hetero Labs limited, Hyderabad. Other ingredients in the core formulation included directly compressible Lactose (Supertab 24AN), Lactose (powder grade), Microcrystalline Cellulose (Avicel PH112), Pregelatinised maize starch (Starch 1500), Crospovidone (Polyplasdone XL), Croscarmellose sodium (Ac-Di-Sol), Sodium starch glycollate (Primogel), Colloidal anhydrous silica (Aerosil 200) and Magnesium stearate. The coating ingredients used were Hypromellose (Methocel E5

Premium) and Opadry White, procured from Colorcon. Primojel has an average particle size of 60 microns. Ac-Di-Sol has an average particle size of 45 microns. Polyplasdone XL-10 has average particle size of 10 microns. Composition of various trials of Olanzapine tablets 20mg are given in Tables 1 and 2.

2.1 Manufacturing Process

2.1.1Direct compression

Olanzapine, Microcrystalline Celluose, Lactose (Directly compressible), Crospovidone and Pregelatinised starch were sifted through 40# mesh using vibratory sifter. The sifted raw materials were loaded into Octagonal blender and mixed for 20 minutes. Colloidal anhydrous silica was sifted through 40# and added to blender and mixed for 5 minutes. Magnesium stearate was sifted through 30# mesh and added to blender and mixed for 3 minutes at slow speed. The lubricated blend were then compressed using 10.5mm circular standard concave plain punches on Rimek 10 station single rotary "B" tooling machine at an average weight of 400mg and hardness between 150-200 N. The tablets were seal coated with non-aqueous solution of hypromellose to a weight gain of 2% to provide a moisture barrier. The seal coated tablets were further film coated to a weight gain of 4% with Opadry white suspension.

2.1.2 Wet granulation

Olanzapine, Microcrystalline Celluose, Lactose, Crospovidone and Pregelatinised starch were sifted through 40# mesh using vibratory sifter. The sifted raw materials were loaded into rapid mixer granulator and mixed for 15 minutes with impeller at slow speed and chopper off. Purified water or Isopropyl alcohol was added slowly to the dry mix over a period of 5 minutes with impeller at slow speed and chopper off. The granules were kneaded for 5 minutes with impeller at fast speed and chopper at slow speed. The granules were dried in a fluid bed dryer with inlet temperature between 35^{o}C to 45^{o}C till the LOD was between 2.0 to 3.0%. The dried granules were then sifted through 20# mesh using a vibratory sifter. The retentions were milled using multimill fitted with 1.5 mm screen in knife forward direction at medium speed. The granules were then loaded into octagonal blender. Colloidal anhydrous silica was sifted through 40# and added to blender and mixed for 5 minutes. Magnesium stearate was sifted through 30# mesh and added to blender and mixed for 3 minutes at slow speed. The lubricated blend were then compressed using 10.5mm circular standard concave plain punches on Rimek 10 station single rotary "B" tooling machine at an average weight of 400mg and hardness between 150-200 N. The tablets were seal coated with hypromellose solution to a weight gain of 2% to provide a moisture barrier. The seal coated tablets were further film coated to a weight gain of 4% with Opadry white suspension.

2.1.3 Formulation trials T1 to T3

Since Olanzapine is sensitive to light, heat and moisture, trials T1 to T3 were taken to study the feasibility of different manufacturing processes-direct compression, non-aqueous granulation and aqueous granulations. Analysis of impurity levels of these trials indicated that the direct compression was the method of choice, where the impurity levels were low compared to other manufacturing processes (Trial T1). But the dissolution profile of this trial, in which Crospovidone was added 4% intragranular was slower compared to marketed product Zprexa 20mg.

2.1.4 Formulation trials T4 to T8

Trials T4 and T5 were taken with 4% Croscarmellose sodium (Ac-Di-Sol) and Sodium Starch glycollate intragranular. But the dissolution profiles of these trials were slower than T1. Trials T5 to T8 were taken with part of Crospovidone intragranular and remaining part extragranular. The dissolution profile of trial T7 was similar to marketed formulation. Two dissolution

Table 1: Compostion of formulation trials of Olanzapine tablets 20mg

Ingredients	Mg/tablet		
	T1	T2	T3
Drymix			
Olanzapine	20.0	20.0	20.0
Microcrystalline Cellulose	200.0	200.0	200.0
Lactose (Directly compressible)	136.0	---	---
Lactose	---	136.0	136.0
Crospovidone	16.0	16.0	16.0
Pregelatinised Starch	20.0	20.0	20.0
Wet granulation			
Isopropyl Alcohol	---	qs	---
Purified water	---	---	qs
Lubrication			
Colloidal anhydrous silica	4.0	4.0	4.0
Magnesium stearate	4.0	4.0	4.0
Core weight	**400.0**	**400.0**	**400.0**
Seal Coating			
Hypromellose	8.0	8.0	8.0
Isopropyl alcohol & Methlyene Chloride	q.s	q.s	---
Purified Water	---	---	qs
Seal Coated Tablet	**408.0**	**408.0**	**408.0**
Film Coating			
Opadry White	16.0	16.0	16.0
Isopropyl alcohol & Methlyene Chloride	q.s	q.s	---
Purified Water	---	---	qs
Film Coated Tablet	**424.0**	**424.0**	**424.0**

profiles are considered to be similar if the dissimilarity factor F1 lies between 0 to 15 and similarity factor F2 lies between 50 to 100. [10]

2.1.5 Formulation trials of 10mg & 15mg strengths

Among the trials taken for Olanzapine tablets 20mg, Trial T7, in which 2% Crospovidone was added intragranular and 2% extragranular was concluded as optimized formulation. The 10mg and 15mg tablets were compressed from the granules of 20mg strength (T7) at average weights of 200 mg and 300ng respectively. This was common blend approach. The tablets were seal coated to a weight of 2% and film coated to a weight gain of 4%. The dissolution profiles of 10mg (Trial A1) and 15mg (Trial B1) was similar to 20mg strength (T7). The CDER guidance states that, to claim biowaivers for lower strengths of a dosage form, an important criteria is that the dissolution profiles of the lower strengths should be similar to that of the highest strength. [11]

Table 2: Composition of formulation trials of Olanzapine tablets 20mg

Ingredients	Mg/tablet					
	T1	T4	T5	T6	T7	T8
Drymix						
Olanzapine	20.0	20.0	20.0	20.0	20.0	20.0
Microcrystalline Cellulose	200.0	200.0	200.0	200.0	200.0	200.0
Lactose (Directly compressible)	136.0	136.0	136.0	136.0	136.0	136.0
Crospovidone	16.0	---	---	12.0	8.0	4.00
Croscarmellose Sodium	---	16.0	---	---	---	---
Sodium starch glycollate	---	---	16.0	---	---	---
Pregelatinised Starch	20.0	20.0	20.0	20.0	20.0	20.0
Lubrication						
Crospovidone	---	---	---	4.0	8.0	12.0
Colloidal anhydrous silica	4.0	4.0	4.0	4.0	4.0	4.0
Magnesium stearate	4.0	4.0	4.0	4.0	4.0	4.0
Core Weight	400.0	400.0	400.0	400.0	400.0	400.0
Seal Coating						
Hypromellose	8.0	8.0	8.0	8.0	8.0	8.0
Isopropyl alcohol & Methlyene Chloride	q.s	q.s	q.s	q.s	q.s	q.s
Seal Coated Tablet	408.0	408.0	408.0	408.0	408.0	408.0
Film Coating						
Opadry White	16.0	16.0	16.0	16.0	16.0	16.0
Isopropyl alcohol & Methlyene Chloride	q.s	q.s	q.s	q.s	q.s	q.s
Film Coated Tablet	424.0	424.0	424.0	424.0	424.0	424.0

2.2 Evaluation of In Process Parameters 0f Granules

The lubricated granules were evaluated for loss on drying, bulk density, tapped density, compressibility index, Hausner's ratio and particle size distribution. Loss on drying was determined at 105°C for 5 minutes using IR moisture analyzer. Bulk density and tapped

density was estimated using Bulk density apparatus (Electro lab, Mumbai).

Table 3: Evaluation of inprocess parameters of lubricated granules of formulation trials

S.No	Parameters	T1	T2	T3	T4	T5	T6	T7	T8
1	Loss on drying (%w/w)	---	2.8	2.9	3.4	3.1	2.7	2.8	2.8
2	Bulk density (g/cc)	0.556	0.532	0.581	0.543	0.521	0.510	0.562	0.554
3	Tapped density (g/cc)	0.658	0.625	0.694	0.641	0.610	0.595	0.638	0.652
4	Compressibility index	15.55	14.89	16.27	15.22	14.58	14.29	13.59	14.58
5	Hausner's ratio	1.18	1.17	1.19	1.18	1.17	1.17	1.19	1.14

Table 4: Evaluation of Olanzapine tablets 20mg

S.No	Parameters	Specifications	T1	T2	T3	T4	T5	T6	T7	T8
1	Average weight	424.0mg±2.0%	425.2	422.6	426.8	425.7	423.9	422.7	421.9	422.4
2	Weight variation	424.0mg±7.5%	419-434	418-427	417-431	415-429	414-431	416-430	417-429	418-431
3	Hardness	150-200 N	161 - 184	159-176	164 - 185	165 - 190	162 - 187	168-189	164-188	166-182
4	Disintegration time	NMT 15 minutes	5'55'	8'45'	9'30'	6'15'	6'22'	4'25'	3'32'	2'35'
5	Thickness	3.50±0.20 mm	3.38-3.62	3.43-3.58	3.45-3.61	3.41-3.61	3.42-3.56	3.43-3.59	3.48-3.65	3.51-3.61
6	Friability	NMT 1% w/w	0.22	0.31	0.29	0.22	0.28	0.27	0.21	0.24
7	Assay	90.0 to110.0%	99.5	98.7	98.2	99.8	100.1	99.4	99.2	99.6
8	Related substances									
	Lactam	NMT 0.5%	0.01	0.02	0.02	0.01	0.01	0.01	0.01	0.02
	Rel.compound B	NMT 0.5%	0.02	0.02	0.03	0.02	0.01	0.02	0.02	0.02
	Thiolactam	NMT 0.5%	0.01	0.02	0.02	0.02	0.01	0.02	0.01	0.02
	Rel. compound C	NMT 0.5%	0.01	0.01	0.02	0.01	0.01	0.01	0.01	0.01
	Ind.impurity	NMT 0.2%	0.02	0.11	0.25	0.02	0.02	0.02	0.02	0.02
	Total	NMT 1.5%	0.07	0.18	0.34	0.08	0.06	0.08	0.07	0.09

Table 5: Evaluation of Olanzapine tablets 10mg (Trial A1)

S.No	Parameters	Specifications	Results
1	Average weight	212.0 mg ±2.0%	214.2
2	Weight variation	212.0mg ±7.5%	205.8 - 215.4
3	Hardness	70-100 N	78-91
4	Disintegration time	NMT 15 minutes	2'45''
5	Assay	90.0 to 110.0%w/w	99.8
6	Related substances		
	Lactam	NMT 0.5%	0.01
	Rel.compound B	NMT 0.5%	0.02
	Thiolactam	NMT 0.5%	0.01
	Rel. compound C	NMT 0.5%	0.01
	Ind.impurity	NMT 0.2%	0.02
	Total	NMT 1.5%	0.07

Table 6: Evaluation of Olanzapine tablets 15mg (Trial B1)

S.No	Parameters	Specifications	Results
1	Average weight	318.0 mg ±2.0%	319.7
2	Weight variation	318.0mg ±5%	311.5 – 326.2
3	Hardness	110-150 N	126-142
4	Disintegration time	NMT 15 minutes	3’05’’
5	Assay	90.0 to 110.0%w/w	99.8
6	Related substances		
	Lactam	NMT 0.5%	0.02
	Rel.compound B	NMT 0.5%	0.02
	Thiolactam	NMT 0.5%	0.01
	Rel. compound C	NMT 0.5%	0.01
	Ind.impurity	NMT 0.2%	0.02
	Total	NMT 1.5%	0.08

Table 7: Comparative dissolution profiles of formulation trials (20 mg) vs marketed formulation Zyprexa 20mg in 0.1N HCl

Time (Minutes)	% Drug release in 0.1N HCl								
	Zyprexa 20mg	T1	T2	T3	T4	T5	T6	T7	T8
5	35.7	25.6	13.4	13.2	24.6	23.6	30.4	34.7	40.2
10	62.1	51.6	22.5	24.8	50.1	48.7	55.4	60.4	66.8
15	86.5	75.4	37.8	36.4	71.8	69.5	79.2	83.7	90.2
20	93.5	88.7	51.6	48.7	84.7	80.7	90.5	91.9	97.9
30	99.2	97.4	75.8	70.4	95.7	94.7	95.4	98.4	99.8
45	100.8	99.5	90.8	88.7	99.8	99.7	99.1	99.7	100.2
60	101.1	100.2	99.7	98.6	100.1	100.2	99.8	100.5	100.8
F1		7.0	32.4	51.3	9.0	10.7	5.0	1.7	2.9
F2		56.7	25.2	14.9	52.0	48.4	65.9	86.9	73.1

Table 8: Comparative dissolution profiles of formulation trials (20 mg) vs marketed formulation Zyprexa 20mg in pH 4.5 acetate buffer

Time (Minutes)	% Drug release in pH 4.5 acetate buffer								
	Zyprexa 20mg	T1	T2	T3	T4	T5	T6	T7	T8
5	33.8	24.1	14.2	15.8	22.1	21.9	28.4	32.5	38.7
10	60.9	50.7	24.5	24.9	49.4	47.4	52.4	60.1	66.8
15	85.7	76.1	39.4	38.7	69.8	68.4	76.8	84.9	91.2
20	94.8	85.7	53.8	48.4	82.4	81.4	90.7	92.7	94.8
30	98.2	96.7	78.7	74.8	93.7	94.8	97.4	98.9	98.3
45	99.7	99.1	92.7	91.4	99.1	99.2	99.0	99.2	99.8
60	100.6	100.8	100.4	100.5	100.8	99.9	99.2	100.2	100.2
F1		7.0	29.6	31.1	9.8	10.6	5.2	0.9	2.8
F2		56.5	26.7	25.6	49.9	48.3	63.2	91.5	71.5

Table 9: Comparative dissolution profiles of formulation trials (20 mg) vs marketed formulation Zyprexa 20mg in pH 6.8 phosphate buffer

Time	% Drug release in pH 6.8 phosphate buffer								
(Minutes)	Zyprexa 20mg	T1	T2	T3	T4	T5	T6	T7	T8
5	16.7	12.4	7.5	7.9	11.5	10.4	14.7	16.4	20.7
10	33.2	25.8	15.8	14.7	23.4	20.5	27.4	33.9	39.8
15	60.8	49.5	23.7	23.9	48.9	47.9	51.7	61.4	68.4
20	83.5	75.7	40.4	39.7	70.4	69.7	75.9	82.7	92.4
30	92.7	86.8	52.7	50.4	81.9	82.4	91.4	91.4	95.8
45	98.6	97.5	77.9	75.4	92.4	92.7	96.8	99.2	99.4
60	99.9	100.2	93.4	92.7	99.8	99.4	99.8	100.5	99.8
F1		7.7	35.8	37.2	11.8	12.9	5.1	0.5	6.4
F2		59.0	27.2	26.5	51.7	49.9	64.3	95.1	62.9

Table 10: Comparative dissolution profiles of formulation trials A1(10mg) and B1(15mg) vs formulation trial T7 (20mg) in 0.1N HCl

Time	% Drug Release in 0.1N HCl		
(Minutes)	20 mg (T7)	10 mg (A1)	15 mg (B1)
5	34.7	39.7	37.2
10	60.4	68.5	65.7
15	83.7	87.9	85.4
20	91.9	94.7	93.2
30	98.4	99.4	99.1
45	99.7	100.5	100.1
60	100.5	100.8	100.4
F1		4.1	2.1
F2		68.5	79.4

Table 11: Comparative dissolution profiles of formulation trials A1(10mg) and B1(15mg) vs formulation trial T7 (20mg) in pH 4.5 acetate buffer

Time	% Drug Release in pH 4.5 acetate buffer		
(Minutes)	20 mg (T7)	10 mg (A1)	15 mg (B1)
5	32.5	34.5	33.7
10	60.1	62.4	61.9
15	84.9	87.8	85.7
20	92.7	94.6	93.5
30	98.9	99.4	98.7
45	99.2	100.1	99.4
60	100.2	100.5	100.1
F1		2.0	0.8
F2		84.1	93.2

Table 12: Comparative dissolution profiles of formulation trials A1(10mg) and B1(15mg) vs formulation trial T7 (20mg) in pH 6.8 phosphate buffer

Time (Minutes)	% Drug Release in pH 6.8 phosphate buffer		
	20 mg (T7)	10 mg (A1)	15 mg (B1)
5	16.4	19.4	18.1
10	33.9	37.5	35.9
15	61.4	65.4	63.4
20	82.7	85.7	83.8
30	91.4	93.4	92.4
45	99.2	99.8	99.5
60	100.5	100.2	99.9
F1		3.3	1.5
F2		76.9	88.3

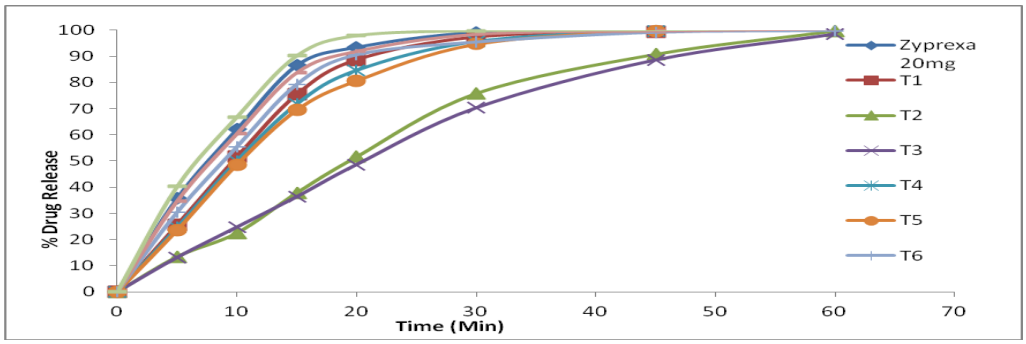

Fig 2: Comparative dissolution profiles of formulation trials (20mg) vs marketed formulation Zyprexa 20mg in 0.1N HCl

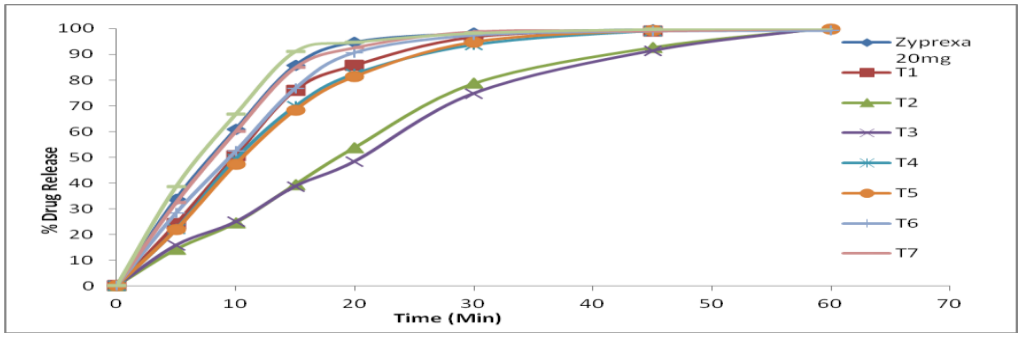

Fig 3: Comparative dissolution profiles of formulation trials (20mg) vs marketed formulation Zyprexa 20mg in pH 4.5 acetate buffer

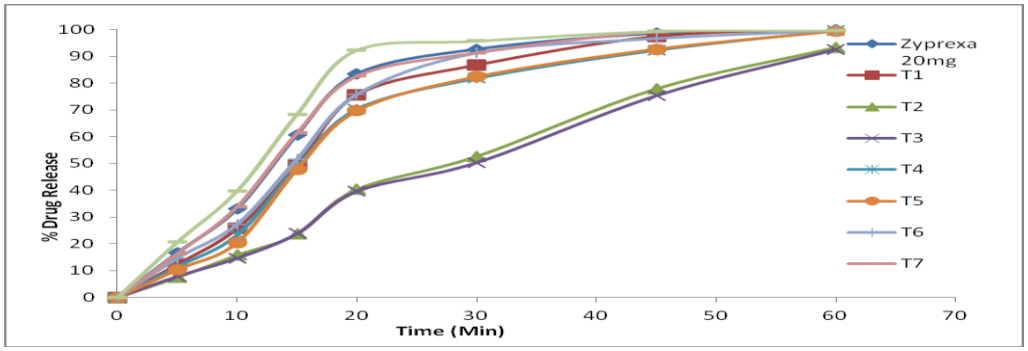

Fig 4: Comparative dissolution profiles of formulation trials (20mg) vs marketed formulation Zyprexa 20mg in pH 6.8 phosphate buffer

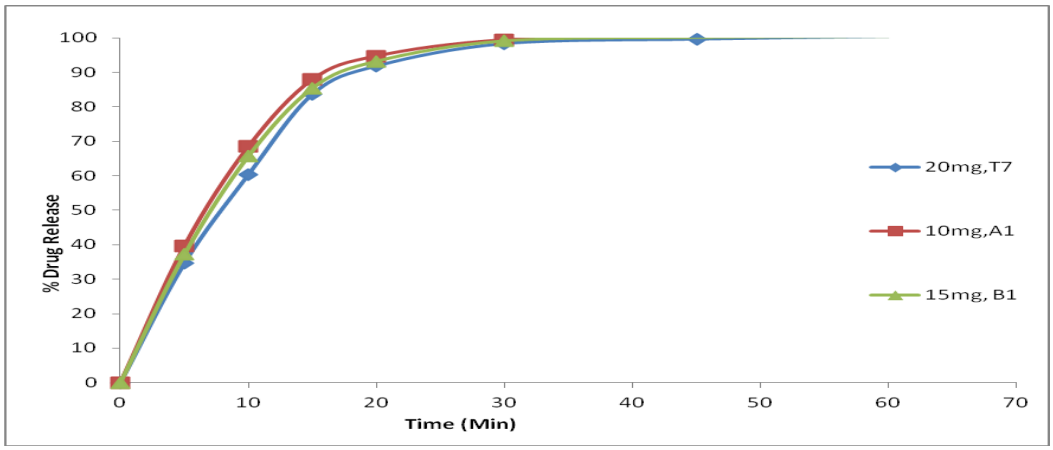

Fig 5: Comparative dissolution profiles of formulation trials T7(20mg) vs formulation trial A1(10mg) and B1 (15mg) in 0.1N HCl

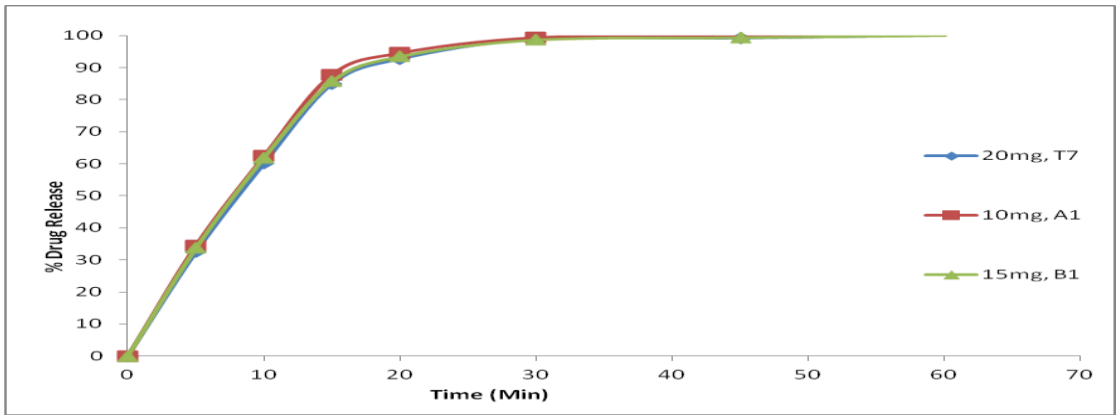

Fig 6: Comparative dissolution profiles of formulation trials T7(20mg) vs formulation trial A1(10mg) and B1 (15mg) in pH 4.5 acetate buffer

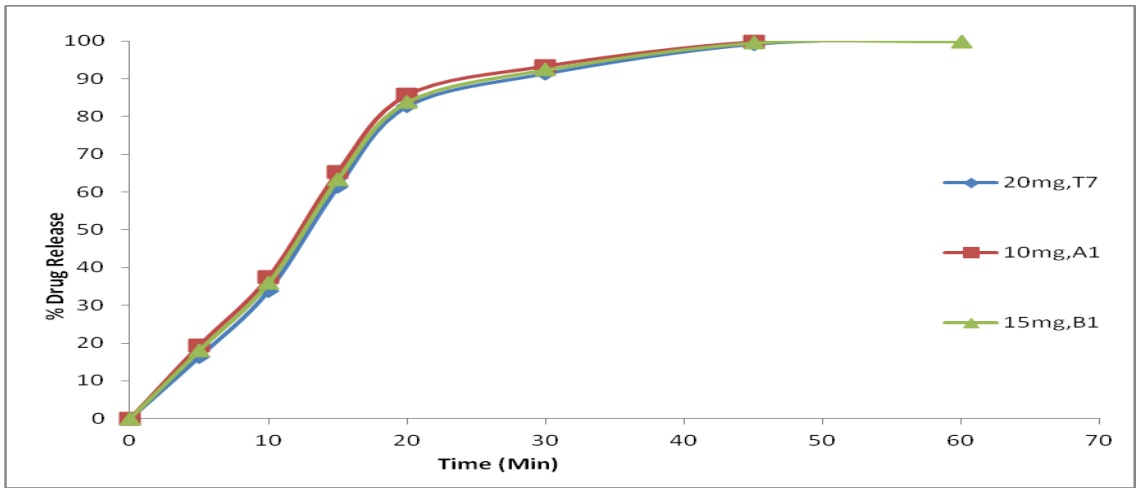

Fig 7: Comparative dissolution profiles of formulation trials T7(20mg) vs formulation trial A1(10mg) and B1 (15mg) in pH 6.8 phosphate buffer

2.3 Evaluation of Tablets

The finished tablets were tested as per standard procedure.

2.3.1 Average Weight

20 tablets were weighed together and the average weight was determined.

2.3.2 Weight Variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated.

2.3.3 Thickness

Ten tablets were randomly selected from each batch and their thickness was measured by using digital vernier caliper. The average thickness and standard deviation was determined.

2.3.4 Hardness

The hardness was determined for 10 tablets of each batch by using Erweka tablet hardness tester. The average hardness and standard deviation was determined.

2.3.5 Friability

Twenty tablets were weighed and placed in the Electrolab friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions the tablets were deducted and weighed again. The percentage friability was measured using the formula, % F = {1-(Wt/W)} ×100

Where, % F = friability in percentage, W = Initial weight, Wt = weight after revolution.

2.3.6 Disintegration time

The disintegration test was done on 6 units using the apparatus as per British pharmacopoeia method.

2.3.7 Assay of tablets

The assay of Olanzapine tablets was estimated as per the United States Pharmacoepial method 2012.

Chromatographic conditions

Mode: Liquid chromatography

Detector: UV 260 nm

Column: 15-cm x 4.6-cm; 15-µm packing.

Procedure:

5 tablets were powdered and weight equivalent to 25 mg of Olanzapine and dissolved in mobile phase to obtain a concentration of 0.1mg/mL of Olanzapine.

Buffer 1: 6.9 g/L of monobasic sodium phosphate. Adjust with phosphoric acid to pH 2.5.

Buffer 2: 12 g/L of sodium dodecyl sulfate in Buffer 1

Mobile phase: Acetonitrile and Buffer 2 (1:1)

In-Vitro Dissolution Studies

In Vitro dissolution study was done as per United States Pharmacoepial method 2012.

Number of units: 6

Medium: 0.1 N HCl, 900 mL.

Apparatus: Paddle

Rpm: 50 rpm.

Time: 60 min

Mobile phase: 10 g/L of ammonium acetate in a mixture of methanol and water (2:3). Adjust with hydrochloric acid to a pH of 4.0.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
20	0	100
25	0	100
27	100	0
35	100	0

Related Substances:

Chromatographic conditions

Mode: Liquid chromatography

Detector: UV 220 nm

Column: 25-cm x 4.6-cm; 5-µm packing.

Procedure:

Buffer 1: 3.3 mL/L of phosphoric acid. Adjust with 50% sodium hydroxide to a pH of 2.5.

Buffer 2: 8.7 g/L of sodium dodecyl sulfate in Buffer 1

Buffer 3: 18.6 mg/L of edetate disodium (EDTA) in Buffer 2

Solution A: Acetonitrile and Buffer 2 (12:13)

Solution B: Acetonitrile and Buffer 2 (7:3)

Diluent: Acetonitrile and Buffer 3 (2:3)

Mobile phase:

3. RESULTS AND DISCUSSION

The lubricated granules were evaluated for in process parameters like loss on drying, bulk density, tapped density, compressibility index and Hausner's ratio. These results were found to be satisfactory and are presented in Table 3.

The tablets after compression were evaluated for parameters like average weight, weight variation, hardness, thickness, disintegration time and friability. The results were satisfactory and are presented in Table 4.

4. CONCLUSION

Olanzapine tablets 10mg, 15mg and 20mg were formulated by direct compression process since the impurity levels were high with wet granulation methods. A prerequisite to demonstrate bioequivalence of generic formulation with that of marketed formulation is that the dissolution profile of generic formulation should be similar to marketed formulation. The bioavailability of the drug is influenced by the solubility of the drug from the dosage form. Three different superdisintegrants, crospovidone, croscarmellose sodium and sodium starch glycolate were selected for matching the dissolution profile with the marketed formulation. The dissolution profile of trial T7, which contained Crospovidone 2% intragranular and 2% extragranular was similar to marketed formulation Zyprexa 20mg. The 10mg and 15mg strengths were formulated based on common blend approach to Trial T7 of 20mg tablets. The dissolution profiles of 10mg and 15mg strengths were similar to 20mg strength, which is an essential criteria to claim biowaivers for lower strengths of generic formulation. The inprocess and finished product quality control parameters of all strengths were found to be satisfactory. Thus it can be concluded that the formulations of Olazapine tablets 10mg, 15mg and 20mg are suitable for intended use.

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