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Formulation and In-Vitro Characterisation of Fast Disintegrating Tablets of Ziprosidone

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ABSTRACT

The present work investigates enhancement of dissolution profile of Ziprasidone using super disintegrants like croscaramellose sodium and sodium starch glycolate. Ziprasidone fast disintegrating tablets (FDT) can be prepared direct compression method. Effect of disintegrants on disintegration and dissolution parameters was studied. Disintegrating time and dissolution parameter (T50% and T90%) decreased with increases in the level of croscarmellose sodium and sodium starch glycolate. It was concluded that the ZF6 formulation with croscaramellose sodium (6%) as super disintegrating agent shows good drug release on ziprasidone tablet formulation.

Keywords: Fast disintegrating tablets, Ziprasidone, cross caramellose sodium, sodium starch glycolate.

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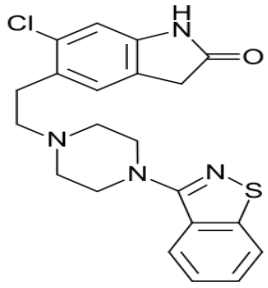
INTRODUCTION

FDTs disintegrate and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets. Solubility behaviour of a drug is one of the key determinants of its oral bioavailability. In recent years, the number of poorly soluble drugs has increased tremendously. The formulation of such drugs for oral delivery presents a challenge to the formulation scientist. Therefore, a drug with poor aqueous solubility will typically exhibit dissolution rate limited absorption. Hence, the area of pharmaceutical research that focus on improving the oral bioavailability of active agents include enhancing solubility and dissolution rate of poorly water-soluble drugs.

Ziprasidone is a novel atypical antipsychotic agent approved by FDA for the treatment of psychotic disorder. Ziprasidone is a BCS class II drug with oral bioavilability 60%. [1]The characteristics of this class of drugs are low aqueous solubility, slow dissolution and high membrane permeability



Ziprasidone acts as antagonist or inverse agonist on serotonin and dopamine receptors. Ziprasidone antipsychotic activity is likely due to a combination of its antagonistic function at D2 receptors in the mesolimbic pathways and at 5HT2A receptors in the frontal cortex. Alleviation of positive symptoms is due to antagonism at D2 receptors while relief of negative symptoms are due to 5HT2A antagonism. [4, 5]

Several attempts have been reported to improve the oral bioavilability of Ziprasidone, in this work the bioavilability of ziprasidone is increased by preparing fast disintegrating tablets by using different synthetic fast disintegrating agents.

MATERIALS AND METHODS

Materials

Ziprasidone was gifted from Natco pharma ltd. Sodium starch glycolate, croscaramellose sodium, micro crystalline, Mannitol were purchased from SDfine chemicals, Mumbai, India and all other chemicals of analytical grade.

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Preparation of ziprasidone fast disintegrating tablets

Ziprasidone fast disintegrating tablets were prepared by direct compression method. The drug and all other ingredients were passed through sieve no.4 and retain on sieve no.6. The drug, super disintegrants and diluent were mixed in proportions as shown in the table (1). Then finally the drug polymer mixture is compressed as tablets.

Table-1: Formula for the Preparation of ziprasidone tablets:

s.no	Ingredients	Formulations						
		ZF1(mg)	ZF2(mg)	ZF3(mg)	ZF4(mg)	ZF5(mg)	ZF6(mg)	ZF7(mg)
1	Ziprasidone	20	20	20	20	20	20	20
2	Sodium starch glycolate	4	8	12	-	-	-	-
3	Croscaramellose sodium	-	-	-	4	8	12	-
4	Microcrystalline cellulose	126	122	118	126	122	118	130
5	Mannitol	30	30	30	30	30	30	30
6	Camphor	10	10	10	10	10	10	10
7	Magnesium stearate	5	5	5	5	5	5	5
8	Talc	5	5	5	5	5	5	5

Evaluation of Ziprasidone fast disintegrating tablets

Weight variation [6]:

The test is considered correct if not more than 2 tablets fall outside the range, if 20 tablets are taken for the test and not more than 1 tablet fall outside the range if only 10 tablets are taken for the test.

Hardness test [7]:

This is to force required to break a tablet in diametric compression. Hardness of the tablet is determined by Monsanto or Pfizer hardness tester. The hardness of 5 kg considered as suitable for handling the tablets.

Friability [7]:

This test performed to evaluate the ability to withstand abrasion in packing, handling and transporting. Initial weight of 20 tablets is taken and these are placed in the friabilator, rotating at 25 rpm for 4 min. the difference in the weight is noted and expressed as 1%. It should be preferably between 0.5 to 1.0%.

ISSN: 0975-8585

In-vitro Disintegration Test [8]:

The test was carried out on 6 tablets using Tablet disintegration tester ED-20 (Electrolab, Mumbai, India) distilled water at 37°C±2°C was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

Water Absorption Ratio [9]:

A piece of tissue paper folded twice was placed in a small Petri dish containing 6ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighted. Water absorption ratio, R was determined using following equation.

$$R = 100 \times \_Wa - Wb/Wa$$

Where, Wa = Weight of tablet after water absorption
Wb = Weight of tablet before water absorption.

Dissolution test [10]:

Dissolution test for tablets were done by USP paddle type apparatus using 900 ml of 7.4 pH of potassium dihydrogen orthophosphate buffer. The paddle speed was maintained at 100 rpm, and temperature of the medium was maintained at 370 c ± 0.5 0 c. the samples are withdrawn at an interval of 0.5,1,2,3,6,9,12 hours. The withdrawn samples are observed at UV spectrophotometer at λ max 223 nm**.**

Preparation of Dissolution Medium:

The 7.4 gm of Potassium dihydrogen orthophosphate was accurately weighed and dissolved in 1000ml of water.

RESULTS AND DISCUSSION

Drug content and physical evaluation of Ziprosidone fast disintegrating tablets of the proposed formulations were subjected to various evaluation tests such as hardness, uniformity of weight, drug content and friability, the results are shown in table(3).

Table-2: Micrometric properties

Formulation code	Bulk density	Tapped density	Angle of repose	Cars index	Hausner's ratio
ZF1	0.515	0.619	26.8	16.8	1.201
ZF2	0.519	0.621	26.4	16.4	1.196
ZF3	0.525	0.627	26.49	16.2	1.194
ZF4	0.470	0.571	26.43	17.6	1.214
ZF5	0.460	0.615	25.83	23.8	1.336

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ZF6	0.470	0.620	31.97	24.1	1.319
ZFC7	0.480	0.640	35.37	25.0	1.333

Table-3: Evalution tests for Ziprasidone tablets

FORMULATION CODE	HARDNESS (KP)	% FRIABILITY	% WEIGHT VARIATION	DISINTEGRATION TIME (min:sec)	Water absoption ratio(R)
ZF1	4.5	0.56	1.6	90	86
ZF2	4.6	0.58	2.4	87	93
ZF3	4.4	0.49	2.2	70	95
ZF4	4.8	0.71	2.0	85	99
ZF5	4.9	0.45	2.1	80	99
ZF6	4.3	0.51	2.0	65	103
ZFC7	3.8	0.75	1.7	120	80

The dissolution studies were carried out for the formulations ZF1 to ZF7 from the results, the formulations ZF1, ZF2 & ZF3 are formulated by using sodium starch glycolate as super disintegrating agent with polymer concentration 2%, 4%, 6% shows percentage drug release 81.7%, 84.3%, 89.7% respectively, the formulations ZF4, ZF5 & ZF6 are formulated by using croscaramellose sodium as super disintegrating agent with polymer concentration 2%, 4%, 6% shows percentage drug release 83.9%, 92.3%, 94.5% respectively at 20 min. The ZFC7 formulation without any super disintegrant shows 67.1% drug release at 20 min.

Table -4: Dissolution studies of formulations

Formulation code	%drug release			
	05 (min)	10 (min)	15(min)	20(min)
ZF1	51.8	61.6	70.2	81.7
ZF2	56.5	64.9	72.6	84.3
ZF3	58.1	67.1	77.3	89.7
ZF4	58.0	62.7	72.6	83.9
ZF5	60.5	70.4	79.5	92.3
ZF6	63.8	74.0	81.0	94.5
ZFC7	35.1	48.1	55.4	67.1

Table-5:T50 & T90 values of ZF1, ZF2, ZF3, ZF4, ZF5, ZF6, ZFC7

S.no	Formulation code	T_{50} values(min)	T90 values(min)
1	ZF1	4.8	22
2	ZF2	4.4	21.3
3	ZF3	4.3	20
4	ZF4	4.3	21.4
5	ZF5	4.1	19.5
6	ZF6	3.9	19
7	ZF7	7.1	26.8

ISSN: 0975-8585

Fig1 –: Graph Showing Dissolution profile of ZF1, ZF2,ZF3 Formulations

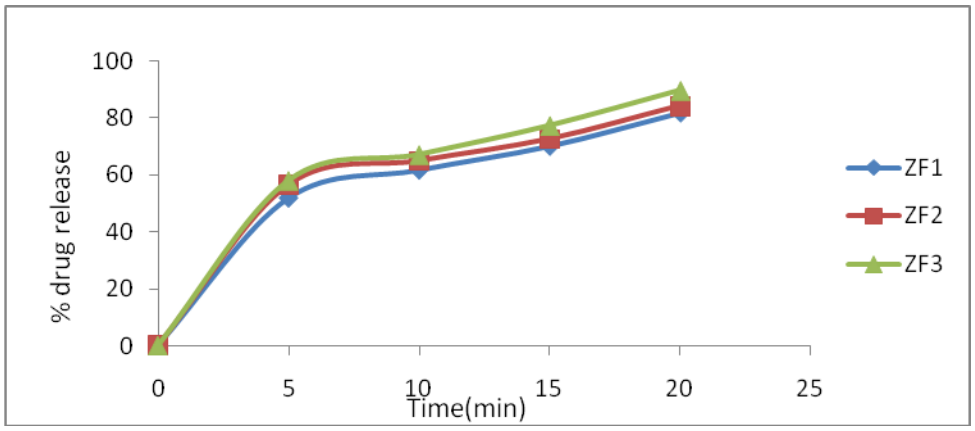


Fig2 –: Graph Showing Dissolution profile of ZF4, ZF5, ZF6 Formulations

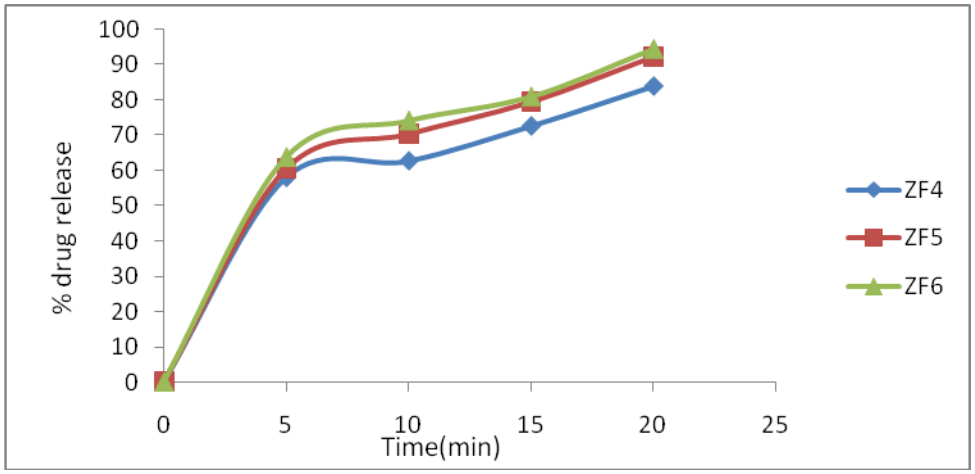


Fig3 –: Graph Showing Dissolution profile of ZFC7 Formulations

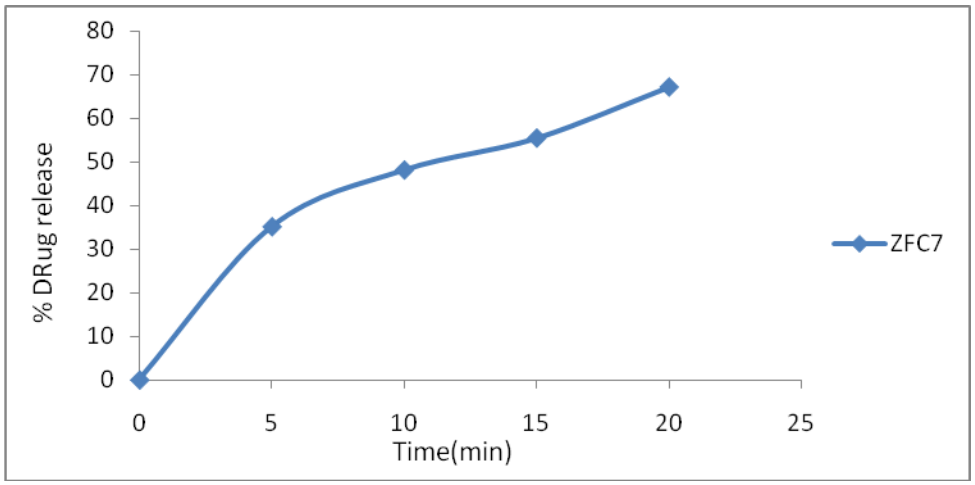
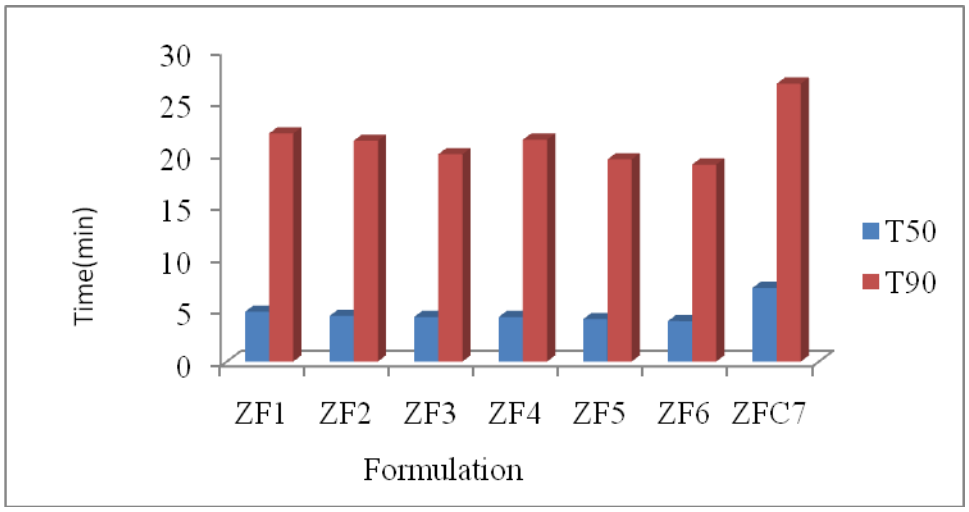


Fig-4: Graph showing T_{50}, T_{90} values of all formulations

ISSN: 0975-8585



The drug profile of ZF6 with 6% croscaramellose sodium as super disintegrating agent shows the good percentage drug release and it shows maximum percentage drug release at 20 min 94.5%.

CONCLUSION

From the above study we inferred that, The super disintegrating agents like croscaramellose sodium and sodium starch glycolate fastens the release of ziprasidone from the tablet.The higher concentration of the polymer (super disintegrant) used, the greater the fastness of the drug release.

Finally we concluded that the ZF6 polymer with higher polymer concentration (6%), croscaramellose sodium as super disintegrating agent shows good drug release on Ziprasidone tablet formulation and can be used for successful development of super disintegrating tablets.

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ISSN: 0975-8585

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