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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.

Introduction:

Tablet Is Defined As Solid Pharmaceutical Dosage Form Containing Drug Substance With Or Without Suitable Diluents And Prepared By Compression Or Molding Methods. They Have Been Widespread Use Since The Later Part Of The 19th Century, And Their Popularity Continues.

Usually Conventional Dosage Form Produce Wide Ranging Fluctuatio In Drug Concentration In Blood Stream And Tissues With Consequent Undesirable Toxicity And Poor Efficiency. This Factors As Well As Factors Such As Repetitive Dosing And Unpredictable Absorption Led To The Concept Of Controlled Dug Delivery Systems.

The Oral Route Of Administration Is A Very Significant Route Of Administering Drugs For Systemic Effects. The Oral Dosage Forms Are So Prolific That Their Supremacy Is Not Likely To Face My Any Serious Challenges. New Drug Entities Have the Therapeutic advantages Of Controlled Drug Delivery, Greater Attention Have Been Focused On Development Of Sustained Or Controlled Release Drug

Delivery Systems.

Tablets Remain Popular As A Dosage Form Because Of The Advantages Afforded Both To The Manufacturer(E.G.Simlicity And Economy Of The Preparation, Stability And Convenience In Packing, Shipping, And Dispensing) And The Patient (E.G. Accuracy Of Dosage, Compactness, Portability ,Blankness Of Taste, And Ease Of Administration).

Although Tablets Frequently Are Discoid In Shape, They Also May Be Round, Oval Oblong, Cylindrical Or Triangular. They May Differ Greatly In Size And Weight Depending On The Amount Of The Drug Substance Present And The Intended Method Of Administration. They Are Divided In To Two General Classes By Whether They Made By Compression Or Molding. Compressed Tablets Usually Are Prepared By Large-Scale Production Methods, While Moulded Tablets Generally Involve Small-Scale operations.

Materials and methods:

PREFORMULATION STUDIES

Preformulation may be described as a phase of formulation development process where the physicochemical and mechanical characterization of drug is done in order to develop an effective dosage form. A thorough understanding of the properties may ultimately provide a rationale for formulation design.

Organoleptic Properties:

Colour:

A small quantity of ziprasidone powder was taken in butter paper and viewed in weii illuminated place.

Taste and Odour:

Very less quantity of ziprasidone was used to get taste with the help of tongue as well as smelled to get the odour.

METHOD OF FORMULATION:

The tablets can be formulated by direct compression method by using the followingmethod.

Method

In this method the drug pass through the sieve no: 40, and retention on sieve no:60 is taken for the formulation. The polymers were weighed in require quantities. The drug and polymers are mixed well. Then finally the drug polymer mixture is compressed as tablets.

Table-6 :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 STUDIES OF THE FAST DISINTEGRATING TABLETS:

Friability:

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%.

$$F = \frac{Wo - W}{W} 100$$

Hardness test:

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.

Weight variation:

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.

Dissolution test:

Medium: 900ml of 7.4pH Potassium dihydrogen orthophosphate buffer

Apparatus : USP (paddle)

Speed : 100 rpm

Time(min) : 5, 10, 15, 20

Temperature : 37°C ± 0.5°C

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

10.1. PREFORMULATION RESULTS:

A) Organoleptic properties of the Raw Materials:

These tests were performed as per procedure given in 8.1 in material and method part. The results were illustrated in the following table.

Table-7: Organoleptic properties of the Raw Materials

S.no	Tests	Specifications/Limits	Observations
1	Colour	White	White
2	Taste	Bitter	Bitter
3	Odour	Almost odourless	Almost odourless

A) Calibration curve of the Ziprasidone:

This test was done as per procedure given in 8.3material and methods section. The results are illustrated in the following table

Table-9: Calibration curve of the ziprasidone

S.no	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	2	0.028
3	4	0.051
4	6	0.076
5	8	0.099
6	10	0.125

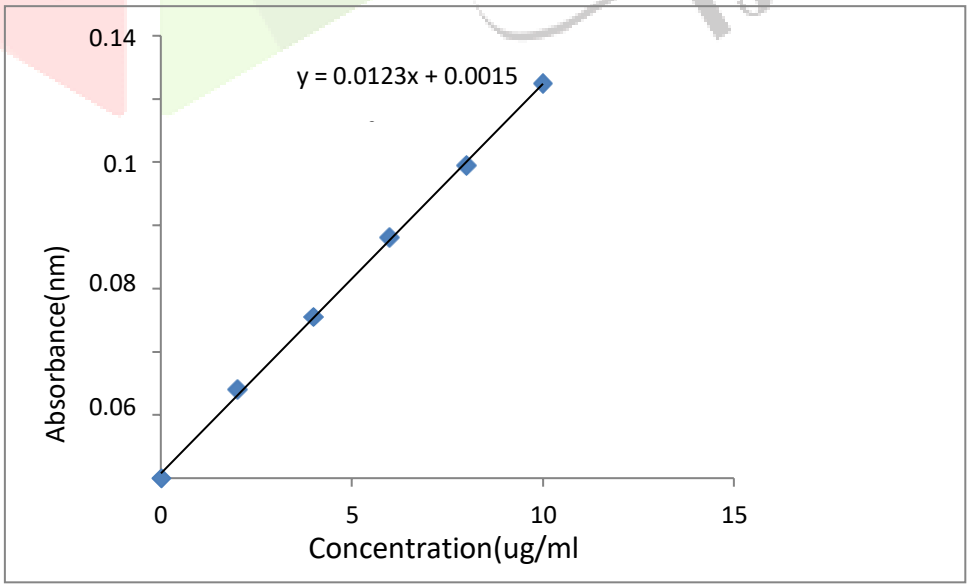

Fig1 –: Graph Showing calibration curve of Ziprasidone

B) Evaluation tests for Ziprasidone tablets:

Table-10: Evalution tests

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

IN VITRO DISSOLUTION STUDIES OF FORMULATION BATCHES:

Table -11: 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

DISSOLUTION PROFILE OF ZF1, ZF2, ZF3 FORMULATIONS:

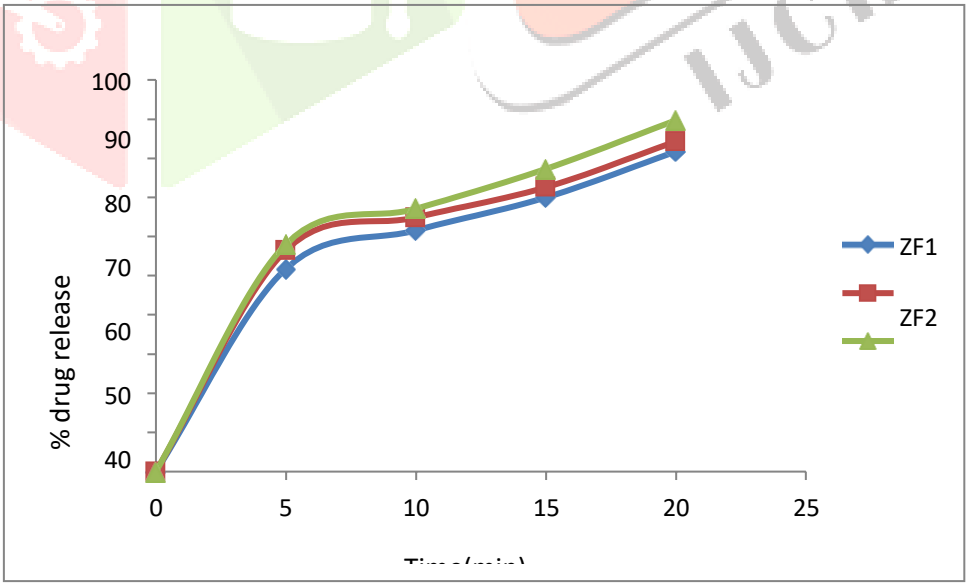

Fig1 –: Graph Showing Dissolution profile of ZF1, ZF2,ZF3 Formulations

DISSOLUTION PROFILE OF ZF4, ZF5, ZF6, FORMULATIONS:

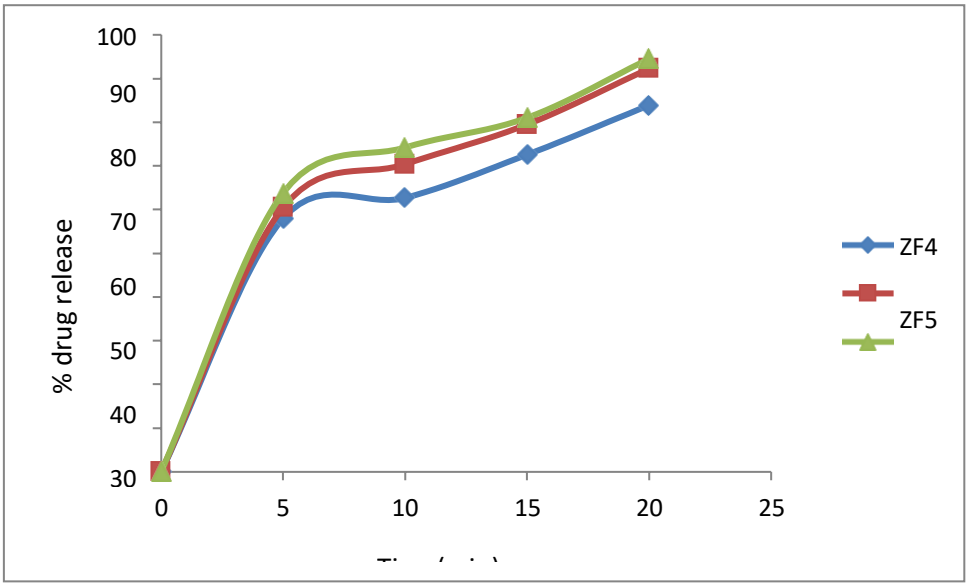

Fig3 –: Graph Showing Dissolution profile of ZF4, ZF5, ZF6 Formulations

DISSOLUTION PROFILE OF ZFC7 FORMULATION:

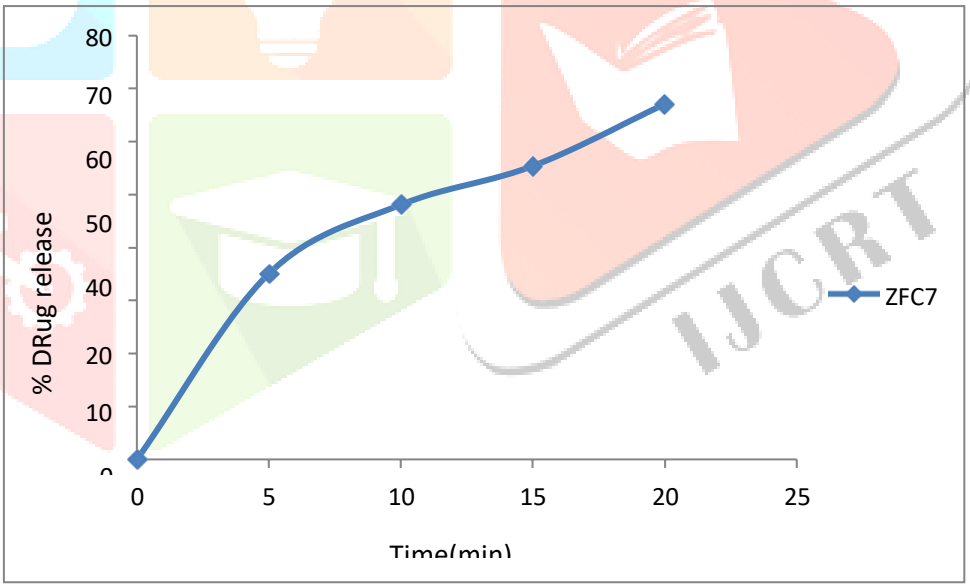

Fig4 –: Graph Showing Dissolution profile of ZFC7 Formulations

KINETICS OF DRUG RELEASE:

The order of drug release can be assessed by graphical treatment of drug release data.

Formulation-1

Cumulative % Drug Release of ZF1 Formulation of Ziprasidone fast disintegrating Tablets

Table-12: Cumulative % Drug Release of ZF1:

S.NO	TIME (MNI)	SQUARE ROOT TIME	Log Time	%DRUG RELEASE	%DRUG UN RELEASE	LOG% DRUG RELEASE	LOG%DRUG UN RELEASE
1	5	2.23	0.69	51.8	48.2	1.71	1.68
2	1 0	3.16	1.0	61.6	38.4	1.78	1.58
3	15	3.87	1.17	70.0	30.0	1.84	1.47
4	20	4.47	1.30	81.7	18.3	1.91	1.26

Graph Showing The Drug release pattern of ZF1 Formulation of Ziprasidone fast disintegrating Tablets

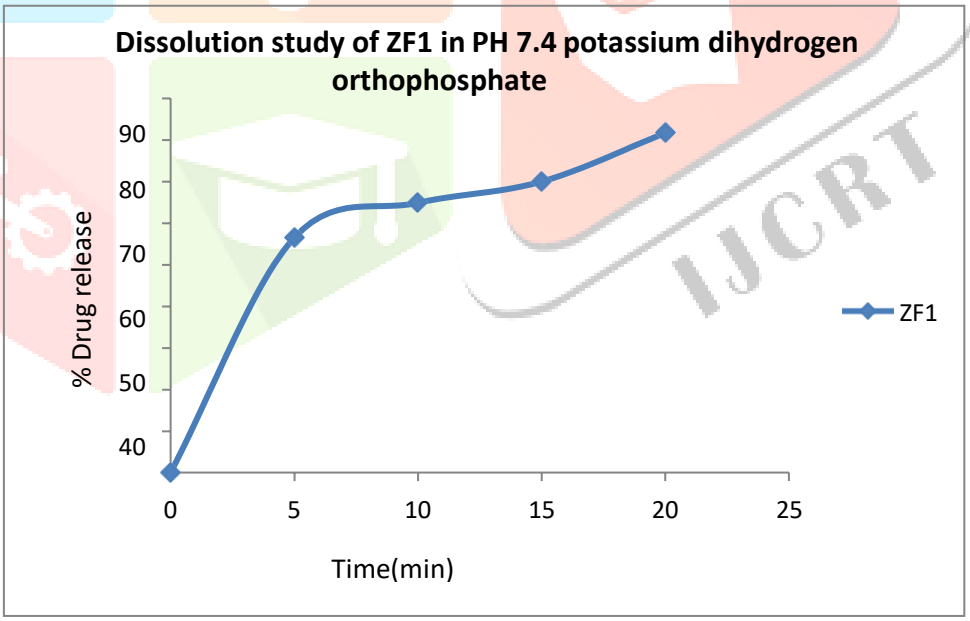

Fig5 –: Graph Showing The Drug release pattern of ZF1

FormulationFormulation-2

Cumulative % Drug Release of ZF2 Formulation ofZiprasidone fast disintegrating Tablets

Table13-: Cumulative % Drug Release of ZF2:

S.NO	TIME (MNI)	SQUARE ROOT TIME	LOG Time	%DRUG RELEASE	%DRUG UN RELEASE	LO% DRUG RELEASE	LOG%DRUG UN RELEASE
1	5	2.23	0.69	56.5	43.5	1.75	1.63
2	1 0	3.16	1.0	64.9	35.1	1.81	1.54
3	15	3.87	1.17	72.6	27.4	1.86	1.43
4	20	4.47	1.30	84.3	15.7	1.92	1.19

Graph Showing The Drug release pattern of ZF2 Formulation of Ziprasidone fast disintegrating Tablets

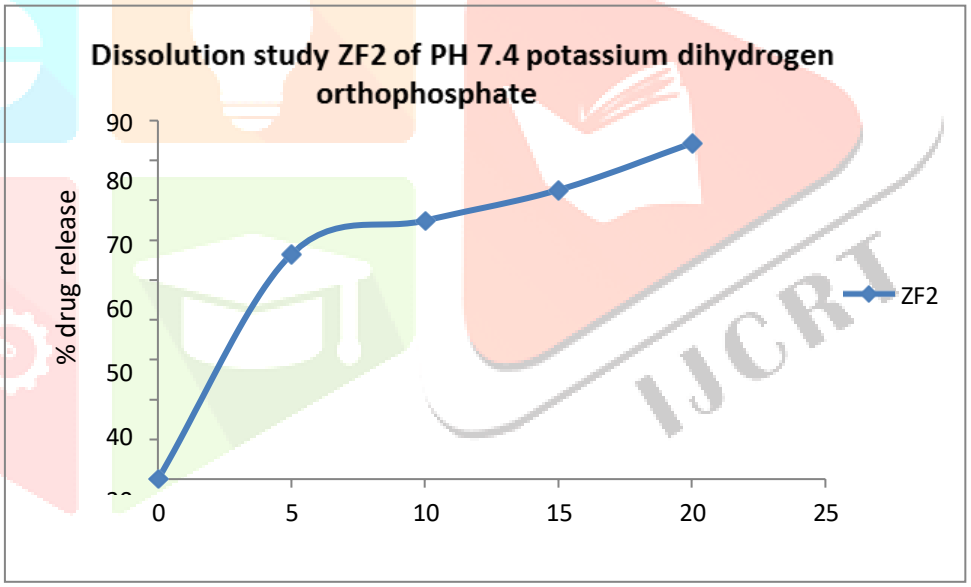

Fig6 –: Graph Showing The Drug release pattern of ZF2 Formulation

Formulation-3

Cumulative % Drug Release of ZF3 Formulation ofZiprasidone fastdisintegrating Tablets

Table14-: Cumulative % Drug Release of ZF3:

S.NO	TIME (MNI)	SQUARE ROOT TIME	LOG Time	%DRUG RELEASE	%DRUG UN RELEASE	LO% DRUG RELEASE	LOG%DRUG UN RELEASE
1	5	2.23	0.69	58.0	42.0	1.76	1.62
2	1 0	3.16	1.0	67.1	32.9	1.82	1.51
3	15	3.87	1.17	77.3	22.7	1.88	1.35
4	20	4.47	1.30	89.7	10.3	1.95	1.01

Graph Showing The Drug release pattern of ZF3 Formulation of Ziprasidone fastdisintegrating Tablets

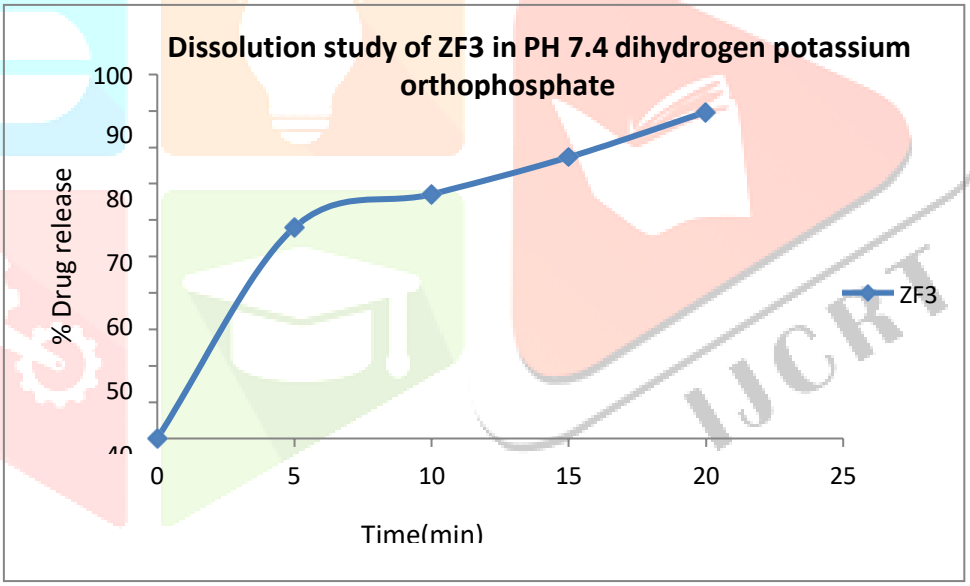

Fig7 –: Graph Showing The Drug release pattern of ZF3 Formulation

Formulation-4

Cumulative % Drug Release of ZF4 Formulation ofZiprasidone fast disintegrating Tablets

Table15-: Cumulative % Drug Release of ZF4:

S.NO	TIME (MNI)	SQUARE ROOT TIME	LOG TIME	%DRUG RELEASE	%DRUG UN RELEASE	LO% DRUG RELEASE	LOG%DRUG UN RELEASE
1	5	2.23	0.69	58.0	42.0	1.76	1.62
2	1 0	3.16	1.0	62.7	37.3	1.79	1.57
3	15	3.87	1.17	72.6	27.4	1.86	1.43
4	20	4.47	1.30	83.9	16.1	1.92	1.20

Graph Showing The Drug release pattern of ZF4 Formulation of Ziprasidone fast disintegrating Tablets

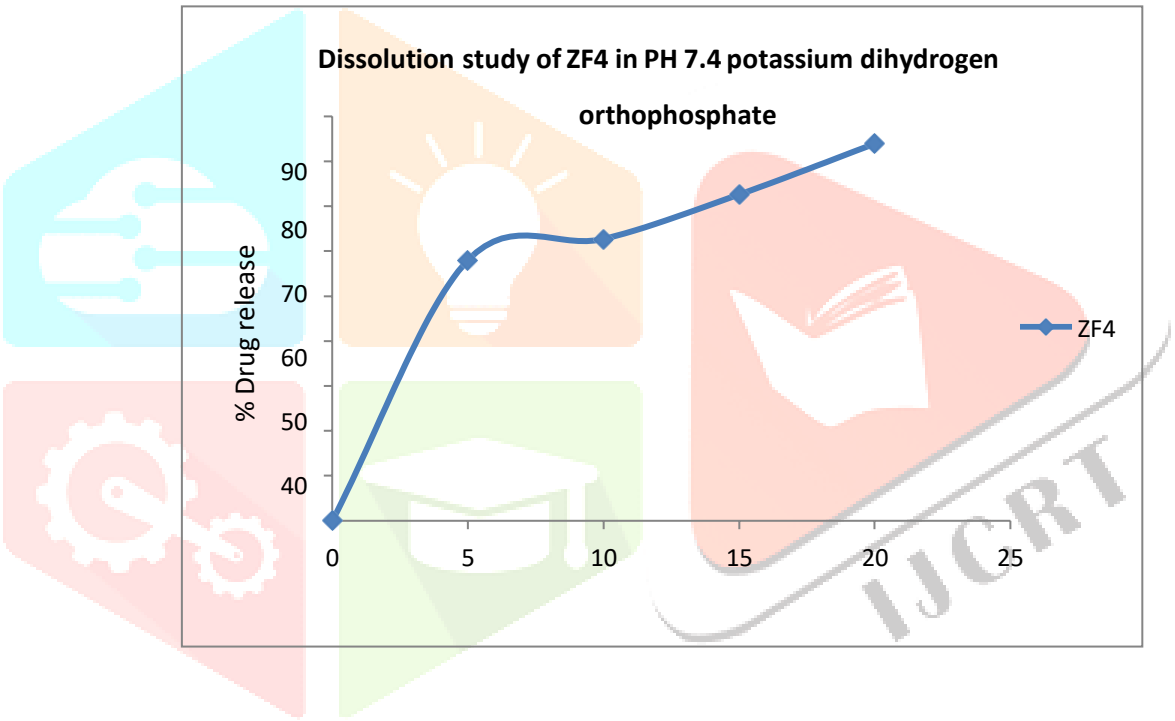

Fig8 –: Graph Showing The Drug release pattern of ZF4 Formulation

Formulation-5

Cumulative % Drug Release of ZF5 Formulation ofZiprasidone fast disintegrating Tablets

Table16-: Cumulative % Drug Release of ZF5:

S.NO	TIME (MNI)	SQUARE ROOT TIME	LOG TIME	%DRUG RELEASE	%DRUG UN RELEASE	LO% DRUG RELEASE	LOG%DRUG UN RELEASE
1	5	2.23	0.69	60.5	39.5	1.78	1.59
2	1 0	3.16	1.0	70.4	29.6	1.84	1.47
3	15	3.87	1.17	79.5	20.5	1.90	1.31
4	20	4.47	1.30	92.3	7.7	1.96	0.88

Graph Showing The Drug release pattern of ZF5 Formulation of Ziprasidone fast disintegrating Tablets

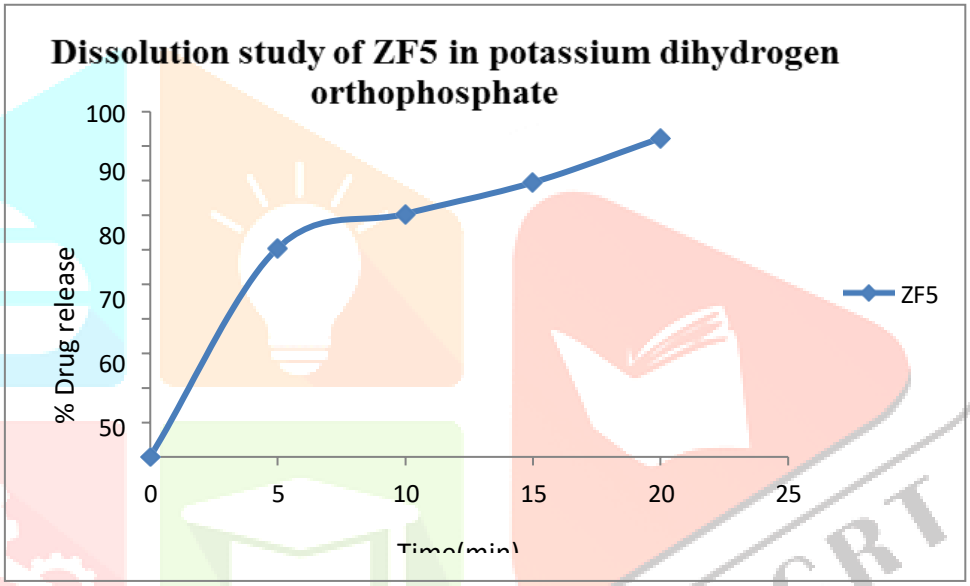

Fig9 –: Graph Showing The Drug release pattern of ZF5 Formulation

Formulation-6

Cumulative % Drug Release of ZF6 Formulation ofZiprasidone fastdisintegrating Tablets

Table17-: Cumulative % Drug Release of ZF6:

S.NO	TIME (MNI)	SQUARE ROOT TIME	LOG Time	%DRUG RELEASE	%DRUG UN RELEASE	LO% DRUG RELEASE	LOG%DRUG UN RELEASE
1	5	2.23	0.69	63.8	36.2	1.80	1.55
2	1 0	3.16	1.0	74.2	25.8	1.87	1.41
3	15	3.87	1.17	81.0	19.0	1.90	1.27
4	20	4.47	1.30	94.5	5.5	1.97	0.74

Graph Showing The Drug release pattern of ZF6 Formulation of Ziprasidone fastdisintegrating Tablets

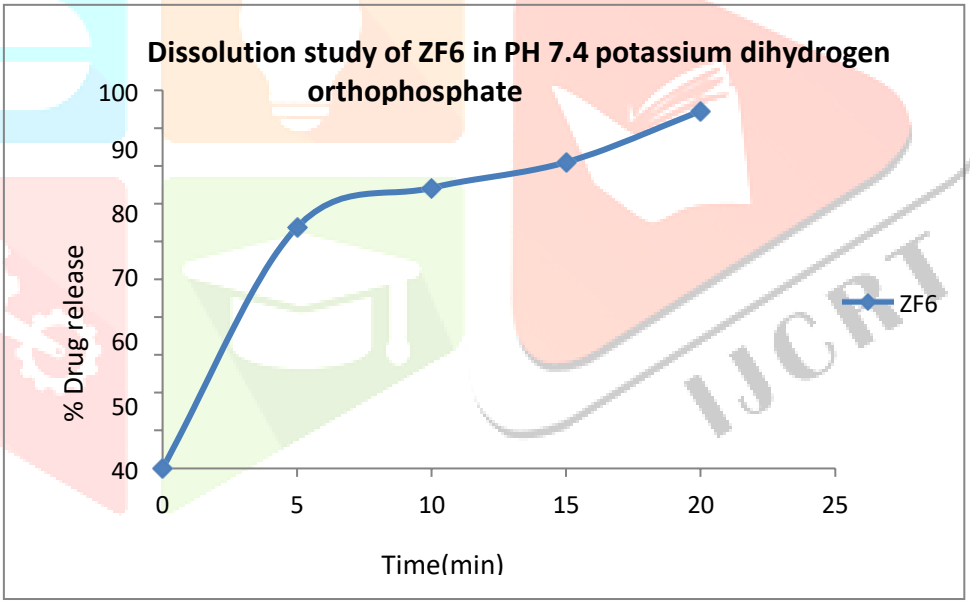

Fig10 –: Graph Showing The Drug release pattern of ZF6 Formulation

Formulation-7

Cumulative % Drug Release of ZFC7 Formulation ofZiprasidone fast disintegrating Tablets

Table18-: Cumulative % Drug Release of ZFC7:

S.NO	TIME (Min)	SQUARE ROOT TIME	LOG TIME	%DRUG RELEASE	%DRUG UN RELEASE	LO% DRUG RELEASE	LOG%DRUG UN RELEASE
1	5	2.23	0.69	35.1	64.9	1.54	1.55
2	1 0	3.16	1.0	48.1	51.9	1.68	1.41
3	15	3.87	1.17	55.4	44.6	1.74	1.64
4	20	4.47	1.30	67.1	32.9	1.82	1.51

Graph Showing The Drug release pattern of ZFC7 Formulation of Ziprasidone fastdisintegrating tablets

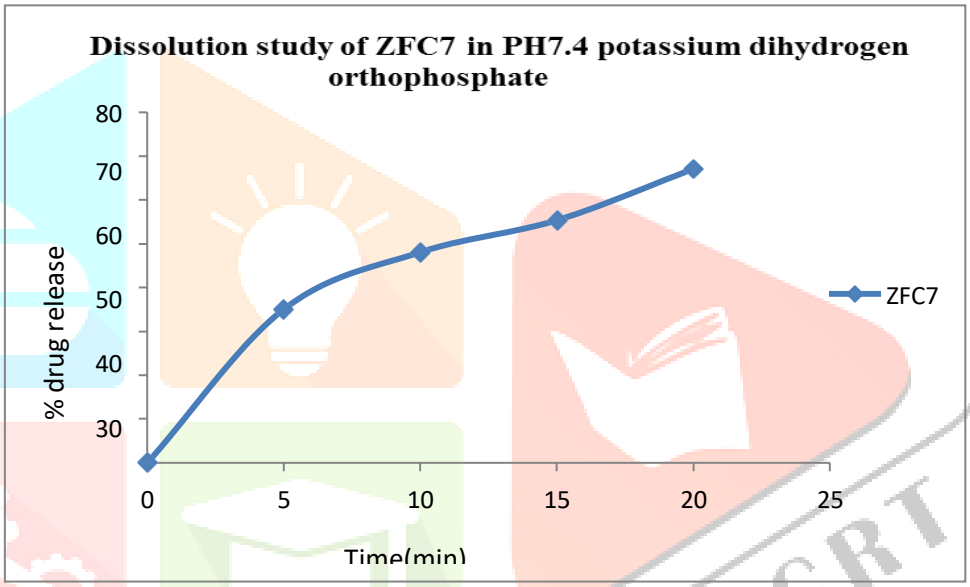

Fig11 –: Graph Showing The Drug release pattern of ZFcC7 Formulation

First order release profile of ZF1, ZF2 Formulations:

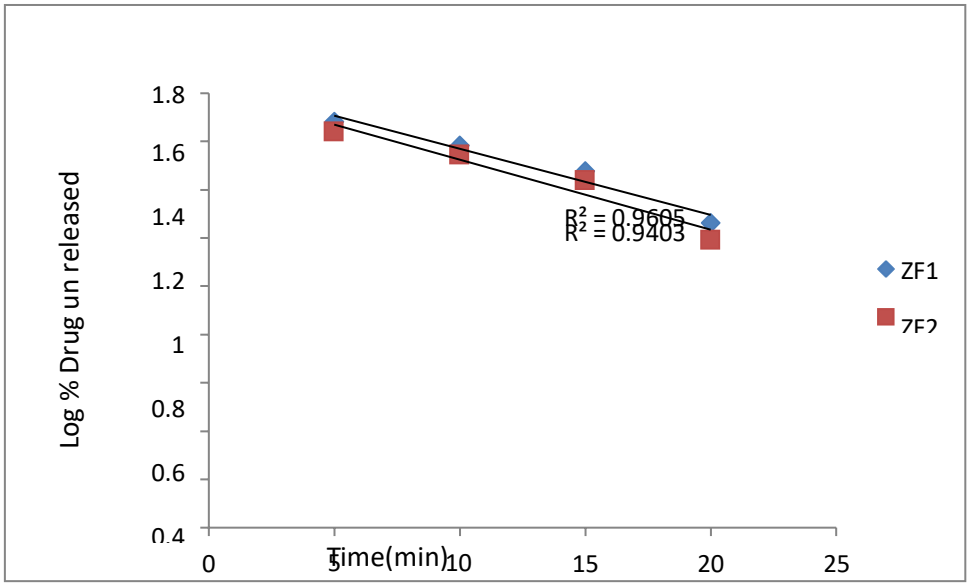

Fig -12: Graph Showing the Drug release pattern of ZF1, ZF2formulations

First order release profile of ZF4, ZF5 Formulations:

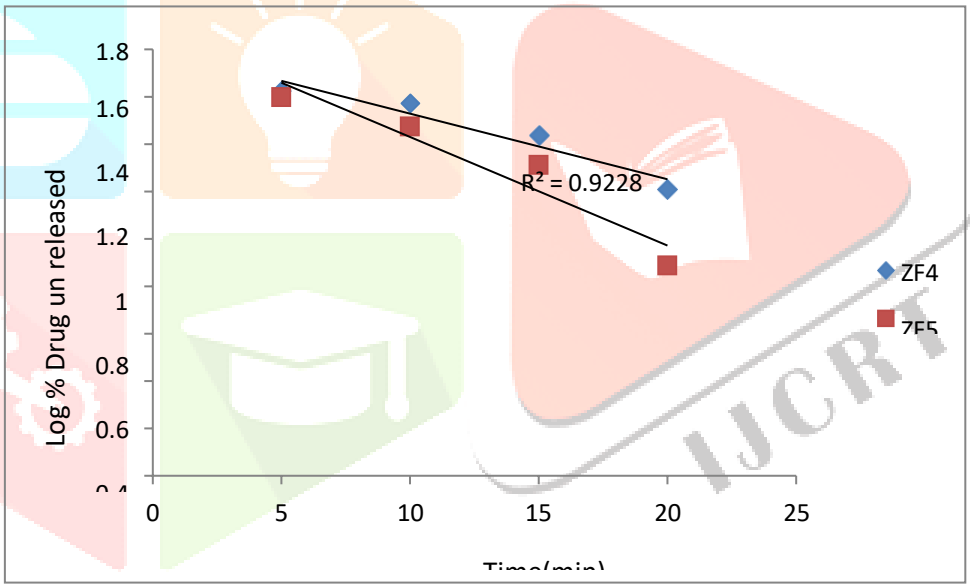

Fig13 -: Graph Showing the Drug release pattern of ZF4, ZF5 formulations

First order release profile of ZF3, ZF6 Formulations:

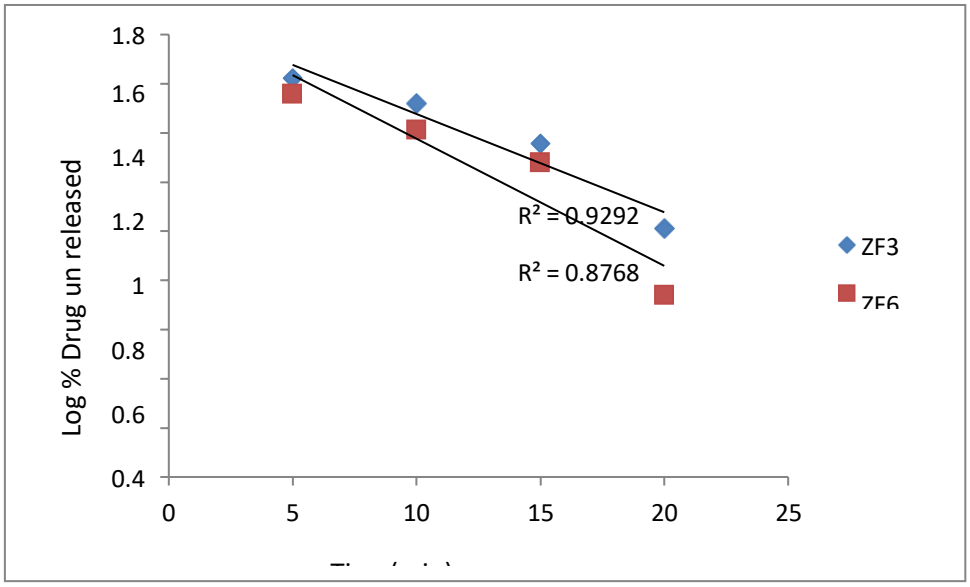

Fig 14 -: Graph Showing the Drug release pattern of ZF3, ZF6 formulationsFirst order release profile of ZFC7 Formulation:

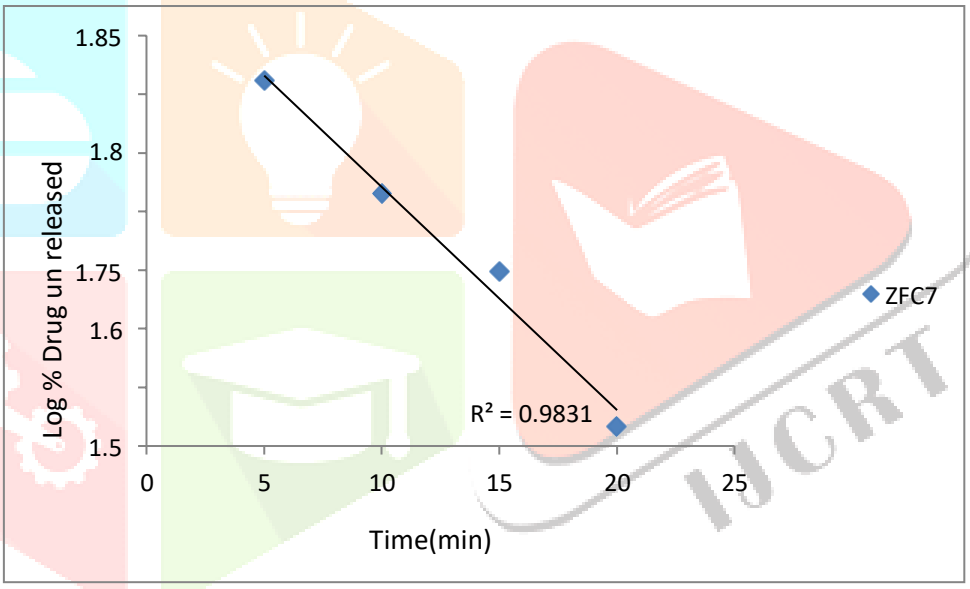

Fig15 -: Graph Showing the Drug release pattern of ZFC7formulation

T50 VALUES OF ZF1, ZF2, ZF3, ZF4, ZF5, ZF6, ZFC7 FORMULATIONS:

Table-33:T50 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	ZFC7	7.1	26.8

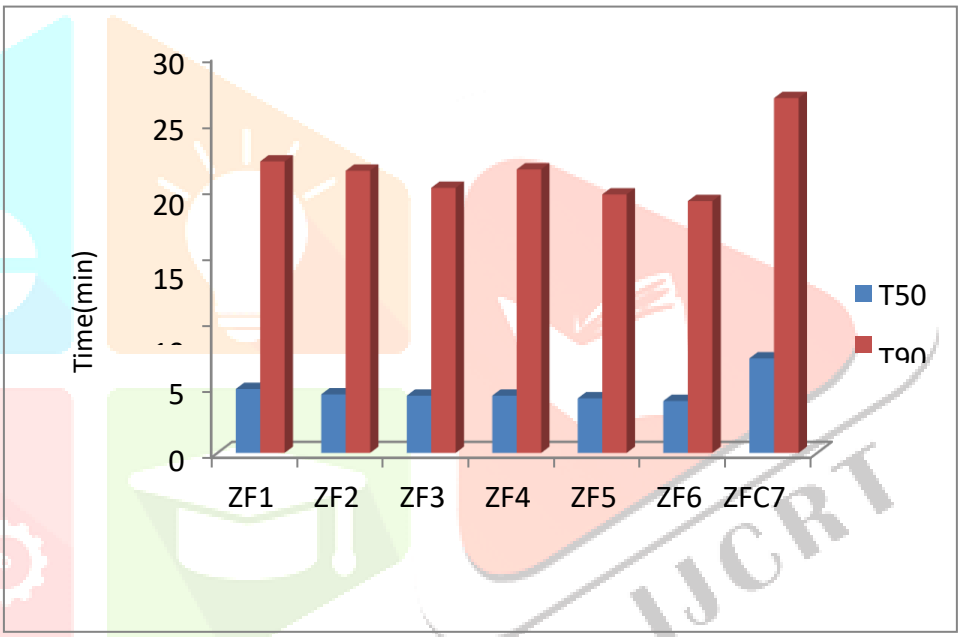

Fig 22-: Graph showing T_{50} values of all formulations

Table -34 :Correlation coefficient values of All Formulations:

s.no	Formulation code	Zero order R^2	First order R^2
1	ZF1	0.770	0.940
2	ZF2	0.795	0.960
3	ZF3	0.818	0.929
4	ZF4	0.785	0.913
5	ZF5	0.808	0.922
6	ZF6	0.785	0.876
7	ZFC7	0.899	0.983

Discussion:

The Preformulation studies were done for the raw materials and from the results the flow property of the raw materials were found to be passable. The polymers used in the formulations were in the specified concentration range. The polymer drug interaction studies also done and there is a minimal interaction between the drug and polymers was found.

The micrometrical studies for the powder were carried out and the results show that,the flow property of formulations ZF1 to ZF7 were passable.

The hardness, weight variation, of the tablets was evaluated and all the formulations were compiled within the pharmacopoeial limits.

The friability test was carried out and was found that all of the formulations were compiled within the pharmacopoeial limits.

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.

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%) shows good drug release on Ziprasidone tablet formulation and can be used for successful development of super disintegrating tablets.

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