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FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLETS OF ROSIGLITAZONE

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ABSTRACT
The objective of the current study was to develop and evaluate fast disintegrating tablets of Rosiglitazone which is an effective drug in the treatment of type II diabetes mellitus. Rosiglitazone containing tablets were prepared by direct compression method using different ingredients such as Cros carmellose sodium,Crospovidone, Sodium starch glycolate , Mannitol, aspartame, Magnesium stearate. The tablets were evaluated for physical properties including Hardness, Weight variation, Thickness, Friability, Drug content, Wetting time, In-vitro disintegration time, In-vitro dissolution study and also Drug release kinetic study. The Hardness, Weight variation, Thickness, Friability and Drug content of tablets were found to be acceptable according to pharmacopoeial limits. An optimized tablet formulation i.e. F6 was found, which provided short wetting time of 54 sec, In-vitro disintegration time of 29 sec. From the above results, it indicated that the amount of superdisintegrant i.e. crospovidone was significantly affected the dependent variables like wetting time and In-vitro disintegration time. The best in-vitro drug release was found to be in formulation F6 i.e.99.18% during the end of 10 min.Formulations were subjected to stability studies , Formulations are stable for 45days at different temperatures i.e 4^{o} C, 27^{o}C and 40 ^{o}C / 75 % RH with insignificant change in the hardness, disintegration time and in vitro drug release pattern. All the formulations i.e. F1 to F9 followed the first order release kinetics with diffusion mechanism.

KEYWORDS: Fast Disintegrating Tablet, Rosiglitazone, Superdisintegrants, Crospovidone.

INTRODUCTION
Oral route of drug administration have wide acceptance, up to 50-60% of solid dosage forms are popular because of natural, uncomplicated, convenient, ease of administration, accurate dosage, self medication, pain avoidance and most importantly patient compliance. The most popular solid dosage forms being tablets and capsules, one important drawback of these dosage forms for patient is the difficulty to swallow. Swallowing of solid dosage forms like tablets and capsules and improper dosing of suspension and emulsion may produce difficulty for young children because of incomplete development of muscular and nervous system and elderly patients suffering from dysphasia, Parkinson's disorder and tremor. Other groups that may experience problems using conventional oral dosage forms include the mentally ill, the mentally disabled patients, patients who are uncooperative, or on reduced liquid intake plans or nauseated, patients having a persistent cough or a gag-reflex, and travelers who may not have access to water.[1] Recent development in technology have presented viable dosage forms alternative for patients who may have difficulty in swallowing tablets or liquids, traditional tablets and capsules administered with glass of water may be inconvenient for some patients.[2]

A constant focus on Novel Drug Delivery systems that offer greater patient compliance, effective dosages and minimal chances of side effects has led to the development of Fast Disintegrating Tablets.[3] Fast Disintegrating Tablets are gaining more demand and popularity from last few years because Pharmaceutical industry has become increasingly aware of the need that elderly be considered as a separate and unique medicare population. Though geriatric patients constitute a minor proportion of the population, its growth rate is high and hence will have significant impact on development of drug delivery system.[4]

Fast Disintegrating Tablets are those when taken they disintegrate instantaneously, releasing the drug, which dissolves in gastric fluids. The faster the drug goes into solution,the quicker the absorption and the onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into

the stomach. In such cases bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.[5] Various techniques can be used to formulate rapidly disintegrating or dissolving tablets.[6-7] Direct compression is one of the techniques, requires the incorporation of a suitable super disintegrant into the formulation, or the use of highly water soluble excepients to achieve fast tablet disintegration.

Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat labile medications. Conventional equipment, commonly available excepients and a limited number of processing steps are involved in direct compression. Disintegrant efficiency is strongly affected by tablet size and hardness. Large and hard tablet have disintegration time more than that usually required. As a consequence, product with optimal disintegration properties often have medium to small size and/or high friability and low hardness. Disintegrants have major role in disintegration and dissolution of fast disintegrating tablets made by direct compression. Disintegration efficiency is based on force equivalent concept, which is combined measurement of swelling force development and amount of water absorption.

The simultaneous presence of disintegrant with high swelling force called disintegrating agent and substances with low swelling agent are claimed to be key factor for rapid disintegration of tablet; which also offer physical resistance. Rosiglitazone is an anti-diabetic drug in the thiazolidinedione class of drugs. Like other thiazolidinediones, the mechanism of action of Rosiglitazone is by activation of the intracellular receptor class of the peroxisome proliferator activated receptors (PPARs), specifically PPARγ. Rosiglitazone is a selective ligand of PPAR, and has no PPARα-binding action. Rosiglitazone and Sulfonylurea is given in combination for treatment of type 2 Diabetes Mellitus for long term therapy. During this therapy it is some time observed that there is uncontrolled increase of blood glucose level. To overcome this unusual problem fast disintegrating tablets of Rosiglitazone is preferred. The aim of this study is to formulate and evaluate Rosiglitazone Fsat Disintegrating tablet.

MATERIALS AND METHODS

Rosiglitazone Maleate was received as a gift sample from Hetero chemicals, Hyderbad. Sodium Starch Glycolate and Crosspovidone were received as a gift sample from Hetero chemicals, Hyderbad. Cross carmellose sodium from Modi Mundi chemicals, Magnesium Stearate from Yarrow Chemicals. Mannitol from LKM International. Aspartame from Micro Pharmaceutical Pvt Ltd, Hyderabad. All other materials were used of Pharma grade.

I. Method of manufacturing of fast disintegrating tablets.

Fast disintegrating tablet containing Rosiglitazone was prepared by direct compression technique using varying concentration of superdisintegrants. All ingredients except magnesium stearate were blended in a glass mortar uniformly. After sufficient mixing of drug and other components, magnesium stearate was added and further mixed for additional 1-2 minutes. The mixture of drug and excepients was compressed using Cad mach(Single Rotary 16 stations) tablet punching machine with 7mm oval shapes punches and break line on one side of the tablet.

Table 1:**Composition of Roseglitazone dispersible tablets.**

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Roseglitazone	2	2	2	2	2	2	2	2	2
2	Croscarmellose sodium	6	8	10	-	-	-	-	-	-
3	Crospovidone	-	-	-	6	8	10	-	-	-
4	Sodium starch glycol ate	-	-	-	-	-	-	6	8	10
6	Mannitol	90	88	86	90	88	86	90	88	86
7	Aspartame	1	1	1	1	1	1	1	1	1
8	Magnesium stearate	1	1	1	1	1	1	1	1	1
	TOTAL (mg)	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

II. Evaluation of Roseglitazone dispersible tablets

1.Hardness

The hardness of tablets was determined by using Monsanto Hardness tester and it is expressed in Kg/cm^2. The whole experiment was performed in triplicate.

2. Friability

The friability of the tablet was determined by using Roche friabilator. It is expressed in percentage. Twenty tablets are initially weighed W1 and transferred into the friabilator. The friabilator was operated at 25 rpm for 4 minutes.The tablets were weighed again (W2). The percentage of friability was caluculated by using following formula.

$$\% \text{ Friability} = \frac{\text{Initial weight - Final weight x 100}}{\text{Initial weight}}$$

3. Weight variation

20 tablets were selected randomly and weighed accurately. The weight divided by 20 provides an average weight of tablets. Not more than two of the individual weight deviates from the average weight by 10 % and none should deviate by more than double that

percentage. Standard deviation and average weight were calculated.

4. Uniformity of Content

The drug content in each formulation was determined by mixing 10 tablets and powder equivalent to 10 mg was added in 100ml of 0.1 HCL buffer followed by stirring for 10 minutes. The solution was filtered through a 0.45µ filter paper, diluted suitably and the absorbance of resultant solution was measured by using UV-Visible spectrophotometer at 277.3 nm.

5. Disintegration Test

The test was carried out as per USP- 2008.One tablet was placed in six tubes of the basket. 0.1 HCL buffer of is used as the disintegration medium. The temperature of the liquid was maintained at 37^0 c ± 2^0 c. If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets, not less than 16 of total of 18 tablets should disintegrate completely.

6. Wetting time

A piece of filter paper folded twice and placed in a small petridish containing 5ml of distilled water. The tablet was placed on the paper, and the time for complete wetting of the tablet was measured in seconds. The wetted tablet was then weighed. Wetting time, S, was determined by using following formula.

S = 10× Wb-Wa/Wb

Where, Wa – weight of the tablet before water absorption.

Wb – weight of the tablet after water absorption.

7. In- Vitro Drug Release Study.

There are no standard methods yet developed for determining the in vitro drug release for dispersible tablets. The release rate of dispersible tablets of Roseglitazone was carried out using rotating paddle apparatus (USP Type II). The dissolution medium consisted of 900 ml of 0.1 HCL buffer. The release study was performed at 37 ^{0}C ± 0.5 ^{0}C with a rotation speed of 50 rpm. The 5ml of sample was withdrawn at time interval of 2, 4, 6,8minutes up to 10 min and replaced with 5 ml of dissolution medium The amount of Roseglitazone released was determined by UV Spectrophotometer at 277.3 nm.

8. Kinetics of In-vitro Drug Release

To study the release kinetics of in-vitro drug release, data was applied to kinetic models such as zero order, first order, Higuchi and Korsmeyer- Peppas.

Zero order

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation.

Q_0 n Q_t = K_0t

Rearrangement of equation

Qt = Q0 + K0t

Where,

Qt - is the amount of drug dissolved in time t,

Q_0 - is the initial amount of drug in the solution (most times, Q_0 = 0)

K_0 - is the zero order release constant expressed in units of concentration/time.

To study the release kinetics, data obtained from in vitro drug release studies were plotted as cumulative amount of drug released versus time.

First order

This model has also been used to describe absorption and/or elimination of some drugs, although it is difficult to conceptualize this mechanism on a theoretical basis. The release of the drug which followed first order kinetics can be expressed by the equation.

$$\frac{dC}{dt} = -Kc$$

Where,

K - is first order rate constant expressed in units of time-1.

log C = log C0 n Kt / 2.303

Where,

C0 - is the initial concentration of drug

K - is the first order constant

t - is the time in hrs.

The data obtained are plotted as log cumulative percentage of drug remaining vs. time which would yield a straight line with a slope of -K/2.303.

Higuchi

The first example of a mathematical model aimed to describe drug release from a matrix system was proposed by Huguchi in 1961. Initially conceived for planar systems, it was then extended to different geometrics and porous systems. This model is based on the hypotheses that Initial drug concentration in the matrix is much higher than drug solubility. Drug diffusion takes place only in one dimension (edge effect must be negligible).Drug diffusivity is constant. Perfect sink conditions are always attained in the release environment. Accordingly, model expression is given by the equation.

$$f_t = Q = A\sqrt{D(2C - C_s)\,C_s\,t}$$

Where,

Q- is the amount of drug released in time t per unit area A,

C -is the drug initial concentration,

Cs- is the drug solubility in the matrix media

D- is the diffusivity of the drug molecules (diffusion coefficient) in the matrix substance.

This relation is valid during all the time, except when the total depletion of the drug in the therapeutic system is achieved. To study the dissolution from a planar

heterogeneous matrix system, where the drug concentration in the matrix is lower than its solubility and the release occurs through pores in the matrix, the expression is given by equation.

$$f_t = Q = \sqrt{\frac{D\delta}{\tau}(2C - \delta C_s) C_s t}$$

Where,
D- is the diffusion coefficient of the drug molecule in the solvent,
δ -is the porosity of the matrix,
τ -is the tortuisity of the matrix.
Q, A, Cs and t have the meaning assigned above.

$$f_t = Q = K_H \times t^{1/2}$$

Where,
KH is the Higuchi dissolution constant. The data obtained were plotted as cumulative percentage drug release versus square root of time.

Korsmeyer Peppas
Korsmeyer et al. (1983) derived a simple relationship which described drug release from a polymeric system equation. To find out the mechanism of drug release, first 60% drug release data were fitted in Korsmeyer Peppas model.

$$M_t / M_\infty = Kt^n$$

Where,
Mt / M∞ - is a fraction of drug released at time t,
k- Is the release rate constant and n is the release exponent.

The n value is used to characterize different release for cylindrical shaped matrices. In this model, the value of n characterizes the release mechanism of drug as described should only be used. To study the release kinetics, data obtained from in vitro drug release studies were plotted as log cumulative percentage drug release versus log time.
The value of n indicates the drug release mechanism related to the geometrical shape of the delivery system, if the exponent n = 0.5, then the drug release mechanism is Fickian diffusion. If n < 0.5 the mechanism is quasi-Fickian diffusion, and 0.5 < n < 1.0, then it is non-Fickian or anomalous diffusion and when n = 1.0 mechanism is non Fickian case II diffusion, n> 1.0 mechanism is non Fickian super case II.

9. Stability Study
Stability testing is an integral part of formulation development. It generates information on which to base proposals for the shelf lives of drug substances and products and their recommended storage conditions. Stability data also are a part of the dossier submission to regulatory agencies for licensing approval.

Stability testing ensures that a drug substance will be safe and effective throughout the shelf life of the product. However, meeting the potency and purity profiles established in the compendia can be challenging as pharmaceutical products become increasingly complex and diverse.

The optimized formulation was packed in PVC blister pack then; they were stored at three different temperatures $4^0C\pm2^0C$, $27^0C\pm2^0C$ and $45^0C\pm2^0C$ for 45 days at RH 75±5%. At 15 days intervals, the tablets were evaluated for their physical appearance, drug content and drug excipients compatibility at specified intervals of time.

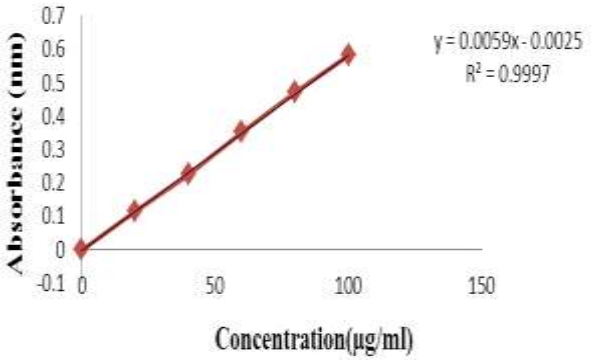
RESULTS AND DISCUSSION

1. Rosiglitazone standard calibration curve
Serial of dilutions are made from standard working solution with distilled water to get concentration from 20 to 100 microgram/ml and the absorbance was measured at 273.5nm.

Table No:2 Rosiglitazone standard calibration curve

S.No	Concentration (µg/ml)	Absorbance
1	20	0.114
2	40	0.226
3	60	0.352
4	80	0.470
5	100	0.582

Fig .1:Standard graph of Rosiglitazone



FTIR STUDIES

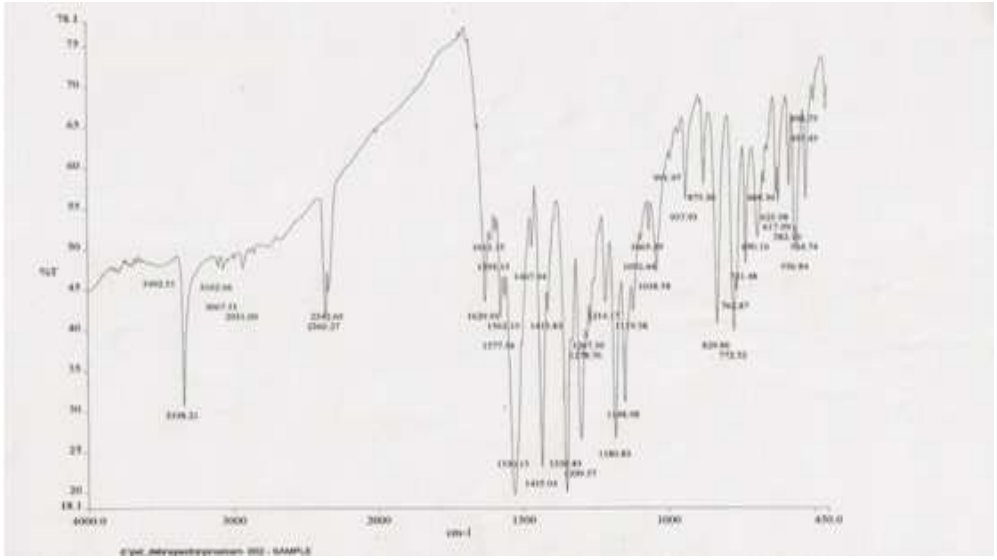


Fig-2 Infra Red Spectrum of Pure Rosiglitazone

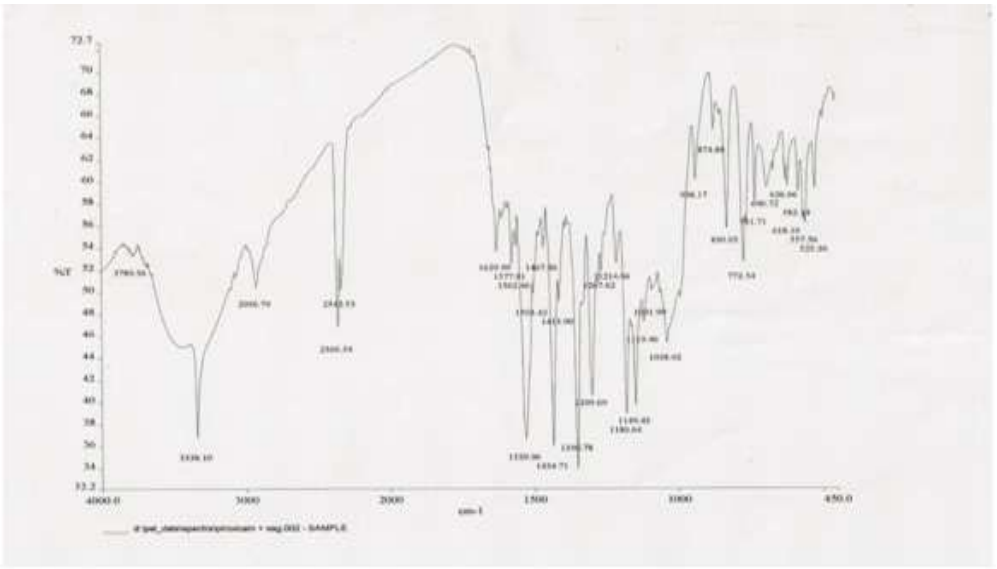


Fig-3 : Infra Red Spectrum of Rosiglitazone with Sodium Starch Glycolate

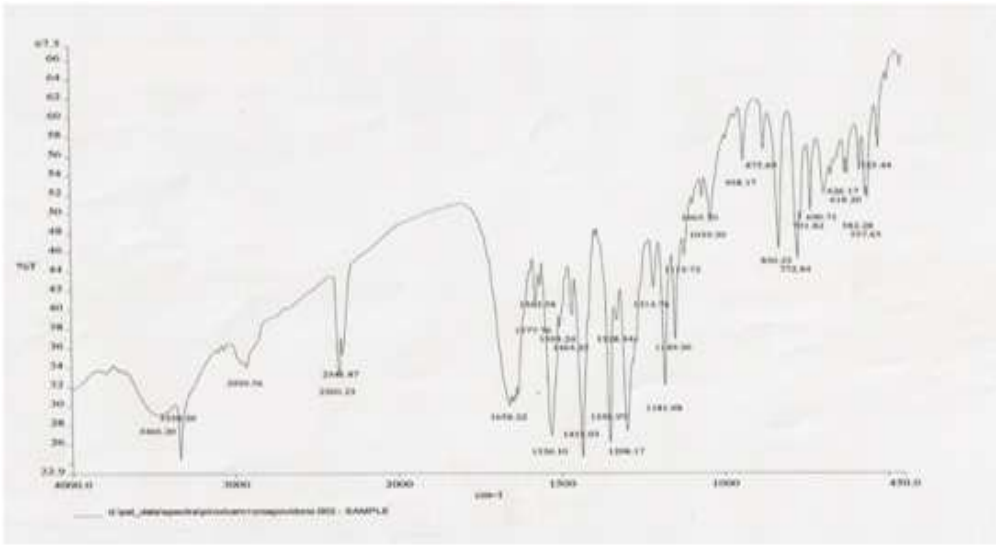


Fig-4: Infra Red Spectrum of Rosiglitazone with Crospovidone

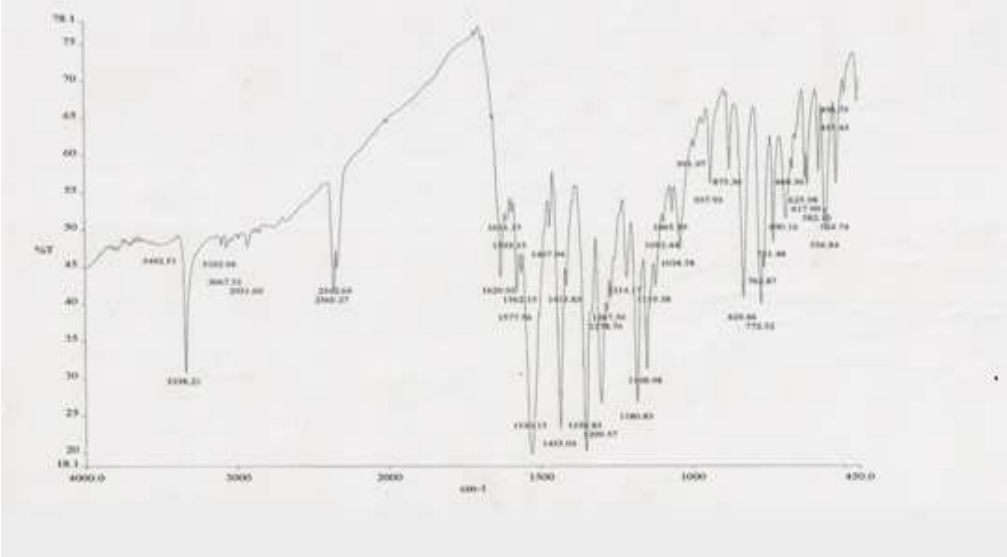


Fig-5: Infra Red Spectrum of Rosiglitazone with Croscarmellose Sodium

From the above figure 2-5, it can be seen that, the major functional group peaks observed in spectras of Drug with all the polymers remains unchanged as compared with spectra of Rosiglitazone. So from the above IR spectra it can be observed that there is no interaction between Rosiglitazone and Polymers used in the formulations.

2. Micromeritic properties to the Rosiglitazone: The results of the Micromeritic properties of the granules are presented in table No:3.

Table No:3 Micromeritic properties to the Rosiglitazone

Form. No	Bulk density (gm/cm^3)*	Tapped density (gm/cm^3)*	Compressi-bility Index (%)*	Hausner Ratio*	Angle of repose (θ°)*
F1	0.425±0.001	0.464±0.001	8.60±0.001	1.094±0.002	22.33±0.635
F2	0.416±0.006	0.459±0.004	9.36±0.003	1.103±0.001	22.29±1.028
F3	0.425±0.009	0.465±0.002	8.60±0.005	1.094±0.003	24.15±0.350
F4	0.421±0.001	0.459±0.001	8.27±0.007	1.090±0.005	23.48±0.330
F5	0.431±0.004	0.470±0.005	9.57±0.002	1.105±0.002	25.26±0.426
F6	0.425±0.001	0.481±0.002	10.60±0.004	1.118±0.005	22.78±0.203
F7	0.401±0.002	0.462±0.001	9.5±0.002	1.201±0.007	22.48±0.801
F8	0.412±0.006	0.458±0.005	9.06±0.002	1.082±0.002	24.72±0.720
F9	0.419±0.005	0.424±0.004	8.07±0.007	1.063±0.004	21.78±0.210

*All the values are expressed as mean± SD, n=3.

The Bulk density of various powder mixed blends prepared with different super disintegrants, was measured by graduated cylinder. The bulk density was found in the range **0.401– 0.431 kg/cm^3.**

The Tapped density of various powder mixed blends prepared with different super disintegrants, was measured by graduated cylinder. The Tapped density was found in the range **0.424 – 0.481 gm/cm^3.**

The Compressibility index of various powder mixed blends, prepared with different super disintegrants, using bulk density and tapped density data, compressibility index was calculated. It was found in the range **8.07 – 10.60%.**

The Hausner's ratio of various powder mixed blends, prepared with different superdisintegrants, using bulk density and tapped density data, Hausner's ratio was calculated. It was found in the range **1.082 – 1.201.**

Angle of repose ranged from **22.29±1.028 to 25.26±0.426.** The flow properties of powder blend in all formulations exhibit good flow characteristics.

3. Physical Evaluation of the tablets

The result of the Physico-chemical properties of the prepared tablets was done as per the procedure and presented in the table no: 4.

Table No -4 Physical Evaluation of the tablets

Form. No	Wetting time (sec)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Disintegration time (sec)	Weight variation
F1	54.54±0.003	2.7±0.005	3.50±0.25	0.293±0.03	33.47±0.02	100±2.20
F2	55.56±0.006	2.4±0.002	3.48±0.15	0.293±0.04	31.56±0.02	100±1.44
F3	54.46±0.002	2.0±0.002	3.42±0.14	0.291±0.08	29.91±0.03	100±2.34
F4	56.37±0.007	2.8±0.003	3.58±0.21	0.428±0.06	35.42±0.06	100±0.94
F5	59.35±0.008	2.7±0.004	3.68±0.21	0.426±0.02	33.45±0.02	100±0.84
F6	54.25±0.006	2.2±0.003	3.71.±0.15	0.426±0.02	29.25±0.04	100±1.98
F7	59.90±0.005	2.6±0.003	3.45±0.16	0.521±0.03	33.25±0.05	100±1.45
F8	56.08±0.003	2.4±0.006	3.36±0.19	0.431±0.01	31.24±0.07	100±1.68
F9	59.45±0.004	2.2±0.004	3.64±0.27	0.530±0.02	30.25±0.05	100±1.88

4. Evaluation of tablets

Tablets were prepared using direct compression technique. Since the material was free flowing, tablets were obtained of uniform weight due to uniform die fill tablets were obtained in the range with acceptable weight variations as per pharmacopoeia specifications, less than 5%.

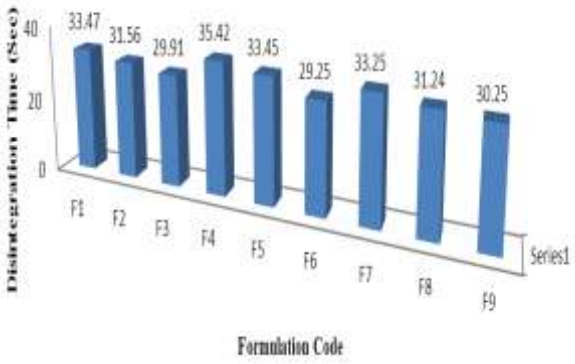
Tablets were evaluated by using Vernier calliper. The thickness of the tablets was found in the range **2.0 – 2.8 mm**. Uniformity thickness was obtained due to uniform die fill. Tablets were evaluated by using Pfizer Hardness tester. Hardness of the tablets was found in the range **3.36 – 3.71 Kg/cm^2.** Uniform hardness was obtained due to equal compression force.

Tablets were evaluated by using Roche Friabilator and friability of tablets was observed in the range **0.291 - 0.530.**

Tablets were evaluated for disintegration time in the IP disintegration apparatus. The disintegration time was found in the range **29 – 33 sec.**

The tablets are evaluated for the uniformity dispersion in which all the tablets were dispersed in few seconds in purified water and all the formulations were under the IP limits. Tablets were evaluated for wetting time test. The wetting time was found in the range **54 – 59 sec.**Tablets are evaluated for the content uniformity test all the formulations are under the IP specifications.

Fig.6 : Disintegration Time of Rosiglitazone



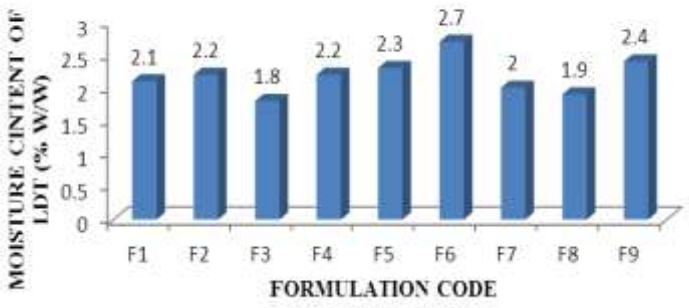
5. Moisture content of the prepared Tablets

The result of the moisture content of the prepared Rosiglitazone was done as per the procedure and presented in the table no: 5.

Table No: 5 Moisture content of the prepared Tablets

FORMULATION CODE	F1	F2	F3	F4	F5	F6	F7	F8	F9
MOISTURE CONTENT(%W/W)	2.1	2.2	1.8	2.2	2.3	2.7	2.0	1.9	2.4

Fig.7 : Moisture Content of Rosiglitazone Tablets



6. Assay of prepared Rosiglitazone Tablets

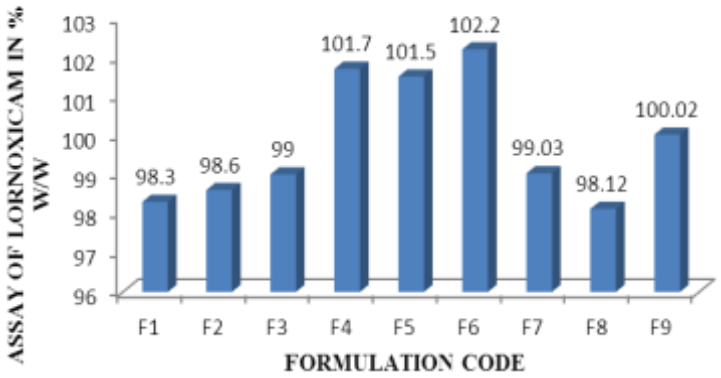
The results of the assay of Rosiglitazone were done as per procedure and presented in the table no: 6.

Table No: 6 Assay of prepared Rosiglitazone Tablets

FORMULATION CODE	F1	F2	F3	F4	F5	F6	F7	F8	F9
Assay of Tablets in % w/w	98.3	98.6	99.0	101.7	101.5	102.2	99.03	98.12	100.02

Tablets were evaluated by using assay method. The drug was obtained in the acceptable limit. The drug content was found in the range **98.3 – 102.2%.**

Fig 8 : Assay of Rosiglitazone

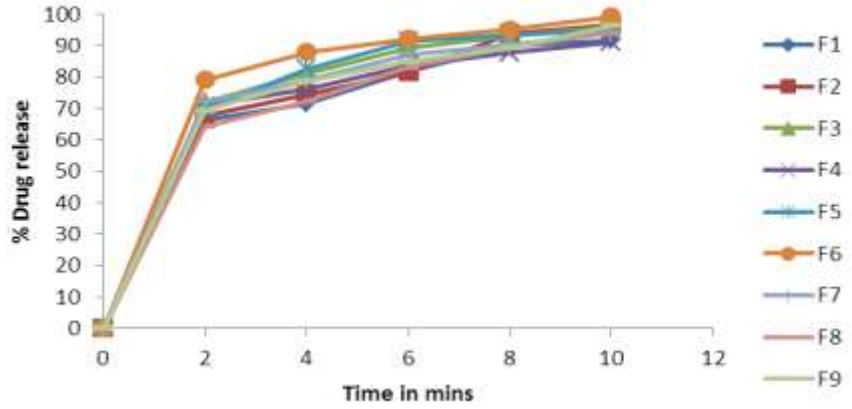


7. In–vitro drug release studies

Table No: 7: Comparative Dissolution Profile of Rosiglitazone dispersible tablets in 0.1 HCL Buffer Solution

Time (min)	PERCENTAGE DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
2	66.42±0.65	67.89±0.28	72.05±0.89	70.74±0.91	69.77±0.62	79.00±0.38	72.02±0.85	64.32±1.21	69.32±0.95
4	71.69±0.85	74.49±0.28	81.01±0.62	76.24±1.54	82.59±1.27	87.91±0.28	79.19±0.68	72.41±0.48	78.61±0.74
6	81.72±1.25	81.66±0.62	89.12±1.28	83.62±0.87	91.48±0.62	92.14±0.75	87.14±1.07	83.12±0.62	84.91±0.87
8	89.83±0.35	93.89±0.98	93.12±1.35	87.78±0.75	93.40±1.18	95.13±0.97	90.25±1.49	89.63±0.47	89.39±0.76
10	90.12±1.34	94.90±0.87	96.21±0.34	94.12±1.28	94.45±0.75	99.18±1.08	90.12±0.97	94.16±0.34	96.45±0.67

Fig 9 :Percentage Drug Release of Rosiglitazone



In-vitro drug release studies were conducted for the formulation using USP dissolution apparatus type-II (paddle), at 25 rpm. The percentage drug release at the end of 10 min was found in the range **90 – 99 %.**

Cross carmellose sodium is used as the super disintegrant in the formulation F1 – F3 at the concentrations of the 6, 8, 10 % ratio was 1:3, 1:4, 1:5 respectively.

Crospovidone is used as the super disintegrant in the formulation F4 – F6 at the concentrations of 6, 8, 10 % and ratio was 1:3, 1:4, 1:5 respectively.

Sodium starch glycolate is used as the super disintegrant in the formulation F7 – F9 at the concentrations of 6, 8, 10 % ratio was 1:3, 1:4 , 1:5 respectively.

F6 was showing good drug release in with in 10mins,and Crospovidone is used as F6 formulation 10% and 1:5 ratio was release good, So, F6 was optimized formulation.

8. Kinetics study

Table 8: Dissolution Kinetics of optimized batch F6.

Time mins	Square root of time	Log time	% drug released	Log % drug released	% drug remaining	Log % drug remaining
0	0	-	0	-	100	2
2	1.414214	0.30103	79	1.897627091	21	1.322219295
4	2	0.60206	87.91	1.94403828	12.09	1.082426301
6	2.44949	0.778151	92.14	1.964448208	7.86	0.895422546
8	2.828427	0.90309	95.13	1.978317497	4.87	0.687528961
10	3.162278	1	99.18	1.996424104	0.82	0.086186148

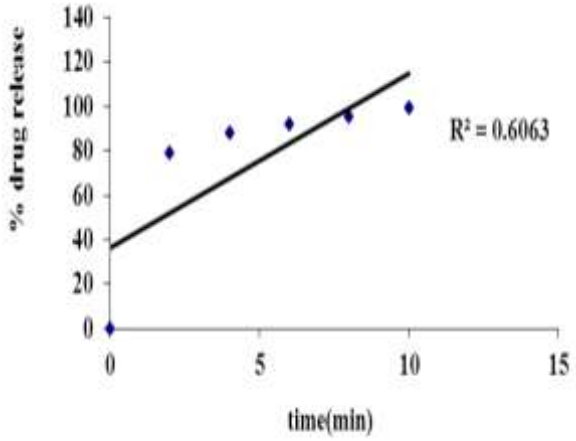


Fig 10: Zero order plot for optimized batch F6

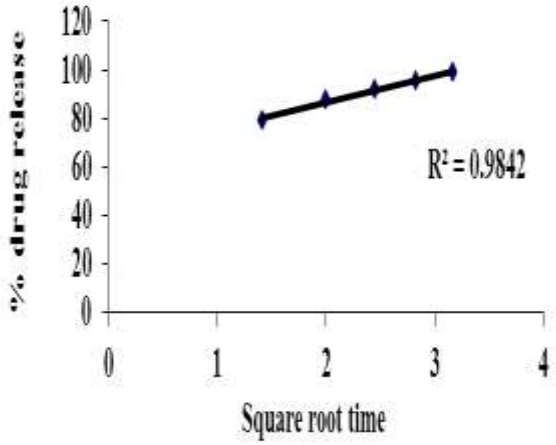


Fig 12: Higuchi plot for optimized batch F6

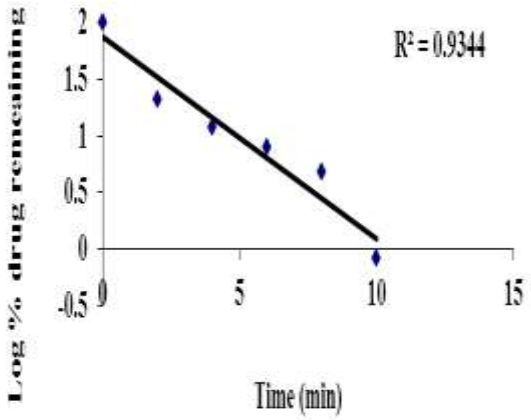


Fig 11: First order plot for optimized batch F6

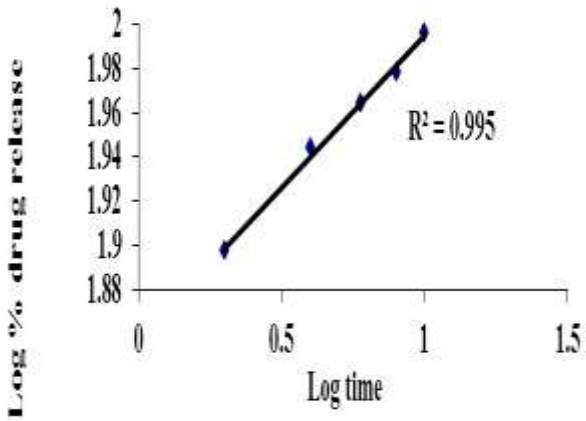


Fig 13: Korsemeyer peppa's plot for optimized batch F6

DISCUSSION

The release profile of the optimized formula F6 was fallowing first order kinetics and best fitted to Korsmeyer-Peppas model with R^2 value of 0.995. As the n value for the Korsmeyer-Peppas model was found to be less than 1, it follows case-2 transport(non-fickian).

9. Stability studies.

Table 9: Stability studies of Rosiglitazone tablets.

Parameters	After 15 days	After 30 days	After 45 days
Physical appearance	No change	No change	No change
Weight variation (mg)	100±3.34	100±2.55	100±4.23
Thickness (mm)	2.1±1.87	2.53±2.86	2.4±3.98
Hardness (kg/cm^2)	3.6±0.23	3.3±0.64	3.2±0.99
Friability (%)	0.41±0.05	0.43±0.08	0.45±0.06
Drug content (%/tablet)	100.34±0.34	99.81±0.29	99.01±0.87
Wetting time (sec)	55.21±0.02	56.12±0.15	58.51±0.59
Disintegration time (sec)	34.19±0.15	39.13±0.45	45.05±0.61
Percentage drug release	99.08±1.08	98.68±1.2	98.1±0.7

DISCUSSION

According to ICH guidelines, 45 days stability study at 4^0C ±2^0C, 27^0C ±2^0C and 45^0C ±2^0C for 45 days at RH 75±5% of optimized formulation (F6) was carried out. It showed negligible change over time for parameters like appearance, drug content, dissolution and assay etc., No significant difference in the drug content between initial and formulations stored at 4^0C ±2^0C, 27^0C ±2^0C and 45^0C ±2^0C for 45 days at RH 75±5% for 45 days.

CONCLUSION

The Present study was undertaken with an aim to formulate and evaluated Fast Disintegrating tablets of Rosiglitazone using direct compression method with the addition of super disintegrating agents Crospovidone. Pre-formulation study was carried out initially with study of selection of superdisintegrants was done and different formulations were prepared using superdisintegrants Crospovidone and different excipients. Results of all the physical and in-vitro dissolution data, In-vitro disintegration study was performed and from all evaluation data concluded that the F-6 formulation was the best one. From the present study it may be concluded that formulation of Fast Disintegrating tablets of Rosiglitazone containing superdisintegrants Crospovidone and mannitol is suitable and can be taken as an ideal formulation.

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REFERENCES

1. Indurwade NH., Rajyaguru TH., Nakhat PD, Novel approach-fast dissolving tablets. Indian drugs, 2002; 39(8): 405-7.
2. Robin HB, Meghan FW. Fast dissolving tablets. US.Pharmacist (online).2002 Sep (cited 2006dec25); (1screen). Available from:http://www.uspharmacist.com/oldformat.asp?url=newlook/files/feat/fastdissolving.ht
3. http://www.drug delivery technology .com/cgi-bin/articles.
4. Bushan SY, Sambaji SP, Anant RP, New drug delivery system for elderly. Indian Drugs, 2000; 37(7): 312-18.
5. Kuchekar BS, Badhan AC, Mahajan HS, Mouth dissolving tablets. A Novel Drug Delivery System. Pharma Times., 2003; 35: 7-9.
6. Allen LV, Rapid-dissolve technology: An interview with loyd V. Allen. Int J Pharm Technol, 2003; 7: 449-50.
7. Fu Y. Yang s, Jeong SH, Kimura S, Park K , Orally fast disintegrating tablets: developments, technologies, tast-making and clinical studies.Crit Rev Ther Drug Carrier Syst, 2004; 21: 433-76.
8. AHFS Drug information American society of Health – System pharmacist., 2002; 68: 20.92:3070.
9. J Mendham, R. C. Denney, D. J. Bares, M. Thamos. Vogel's Textbook of Quantitative Chemicals Analysis, 6thEdn, Pearson Education Ltd., 2001.
10. Schmidt P, Simone S, Fast dispersible Ibuprofen tablets. Eur J Pharma Sci, 2002; 15: 295-305.
11. L. Lachman, H. A. Liberman, J. L. Kanig .The Theory and practice of Industrial Pharmacy, 3rd Edn, Varghese Publishing House., 1991; 296-301.
12. Amin P, Gupta S, Prabhu N, Wadhwani A, Fast disintegrating Dosage Form of Oflaxacin and Metranidazolebenzoate. Indian Drugs, 2005; 42(9): 614-7.
13. In vitro Dissolution The united States Pharmacopoeia, United States Pharmacy convention. Asian edition, 2000; 1941-46.
14. Natalie MC, Clure. Stability Studies in overview of ICH Guidelines for drug products. Matrix Pharmaceutical Inc. 1997.
15. Gazzi S, Chegonda KK, Chandra SRG, Kumar BV, Reddy P. Formulation and evaluation of dispersible tablets of paracetamol. AAPS. Pharm. Sci. Tech., 2009; 10: 530-539.
16. Edmund J. Elder. Et al., Preparation, Chracterisation and Scale-up of Ketoconazole with enhanced dissolution and Bioavailability. Drug Dev. and Ind. Pharmacy., 2007; 33: 755-765.
17. Brain R Matthews. Regulatory aspects of stability testing in Europe. Drug dev Ind Pharm., 1999; 25(7): 831-856.