ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Development and Evaluation of Oro dispersible tablets of Rosuvastatin calcium By β-Cyclodextrin inclusion complexes and using different Superdisintegrants.

Pilli Rohini*, Maddumala.Rajeswari [1], and Hema sekhar M[2].

Department of Pharmaceutics, Acharya Nagarjuna University College of Pharmaceutical Sciences, Nagarjuna nagar-522510, Guntur, Andhrapradesh, India.

ABSTRACT

Rosuvastatin Calcium exhibit unsatisfactory dissolution profiles and, consequently, problems of absorption and poor bioavailability. Rosuvastatin Calcium (RST), a poorly water-soluble 3-hydroxy3-methyl glutaryl CoA (HMG-CoA) Reductase inhibitor through inclusion complexation with β-cyclodextrin (β-CD). The aim of this work was to develop Rosuvastatin Calcium Orodispersible tablets by exploiting the solubilizing effect of β-cyclodextrin (β-CD). Drug–CD complex systems, prepared by different techniques, Precipitation method, Kneading method, and Co-evaporation method, they were characterized by Fourier transform infrared (FT-IR) spectroscopy. The inclusion complex containing RST: β-CD (1:1) was formulated into tablets using superdisintegrants like sodium starch glycolate, Crosspovidone and Crosscarmellose. Tablets containing RST- β-CD inclusion complex were prepared by direct compression and evaluated for various post compression parameters like hardness, friability, weight variation, thickness, drug content and in-vitro dissolution. A significant improvement of the drug dissolution profile was achieved from tablets containing drug–CD systems Kneading method products showed the best dissolution profiles, reaching more than 97.05% drug release at the end of 30 min.

Keywords: Orodispersible tablets, β-Cyclodextrin , inclusion complexes, Co-evaporation method, kneading method, Precipitation method, Rosuvastatin calcium**,**

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Oro dispersible tablets

For most therapeutic agents used to produce systemic effects, the oral route still represent the preferred way of administration owing to its several advantages and high patient compliance compared to many other routes. Oro dispersible tablets also called as orally disintegrating tablets, mouth dissolving tablets, rapid-dissolving tablets, fast disintegrating tablets, fast dissolving tablets. Oro dispersible tablets are the solid unit dosage for like conventional tablets, but are composed of super disintegrants, which help them to dissolve the tablets within a minute in the mouth in the presence of saliva without any difficulty of swallowing[1,2,3].

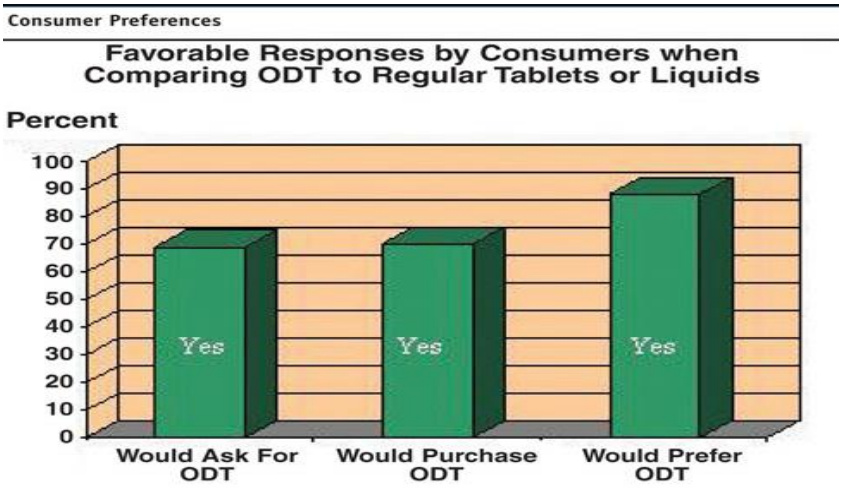

Figure 1 Consumer preferences for ODT'S

Mechanism of Superdisintegrants[4,5] :

Super disintegrants plays an important role in Oro dispersible tablets. The addition of super disintegrants principally affects the rate of disintegration and hence the dissiolution. These are four major mechanisms for tablet disintegration as follows

1. Swelling
2. Porocity and capillary action
3. Due to particle-particle repulsive forces
4. Due to deformation

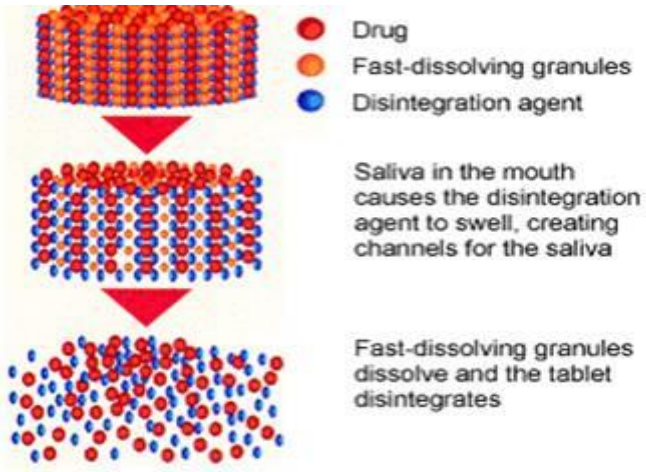

Figure 2: Mechanism of Action of Superdisintegrants

Advantages of Oro dispersible tablets[6,7,8]:

- Administration to the patients who cannot swallow, such as the elderly, stroke victims patients affected by renal failure and patients who refuse to swallow such as pediatric, geriatric and psychiatric patients.
- Rapid drug therapy intervention.
- Achieve increased bioavailability /rapid absorption through pre-gastric absorption of drugs from mouth pharynx and Oesophagus as saliva passes down.
- Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, why do not always have access to water.
- Good mouth feel properity helps to change the perception of medication as bitter pill particularly in pediatric patients.

Disadvantages of Oro dispersible tablets:

- Hygroscopic in nature.
- Low amount of drug can be incorporated in each dose .
- Sometimes it possesses mouth feeling.
- Highly fragile some times.
- ODT requires special packaging for properly stabilization &safety of stable product.
- Eating and drinking may become restricted.

The rate of absorption and bioavailability of poor water soluble drugs is often controlled by the rate of dissolution of the drug in the gastrointestinal tract. Many technological methods of enhancing the dissolution characteristics of slightly water-soluble drugs are solid dispersions, micronization. Among the various methods, cyclodextrin complexation is an industrially accepting technique**.**

Rosuvastatin Calcium (RST), a poorly water-soluble 3-hydroxy3-methyl glut aryl CoA (HMG-CoA) Reductase inhibitor, a potent lipid-lowering agent, and used as hypo lipidemic agent. It is also used in the treatment of osteoporosis, benign prostatic hyperplasia, and Alzheimer's disease**2**. RST is crystalline nature so it reduces its aqueous solubility and finally that results in an oral bioavailability of 20%. After oral administration of RST, the peak plasma Concentration is reached within 3–5 h, the volume of distribution is 1.1-1.4 liter/Kg, and plasma protein binding is 90%. RST is extensively metabolized by oxidation, lactonisation, and glucuronidation [9,10.11,12].

Cyclodextrins are cyclic oligosaccharides, containing six, seven or eight glucopyranose units (α, β or γ respectively)obtained by the enzymatic degradation of starch. These are torus shaped molecules with a hydrophilic outer surface and lipophilic central cavity, which can accommodate a variety of lipophilic drugs. Cyclodextrins are able to form inclusion complexes with poorly water-soluble drugs and have been shown to improve pharmaceutical properties like solubility, dissolution rate, bioavailability, stability and even palatability without affecting their intrinsic lipophilicity or pharmacological properties. Natural cyclodextrins have limited water solubility. However, asignificant increase in water solubility has been obtained by alkylation of the free hydroxyl groups of the cyclodextrins resulting in hydroxyl alkyl, methyl and sulfo butyl derivatives. The objective of present study is to prepare inclusion complexes of Rosuvastatin Calcium with cyclodextrins by different methods such as physical, kneading and co-evaporation, precipitation method and increase the solubility of Rosuvastatin Calcium (RST) for improvement of dissolution rate and bioavailability of the drug[13,14,15].

EXPERIMENTAL STUDIES

MATERIALS

Rosuvastatin Calcium (RST) was gifted from MSN Laboratories. Hyderabad, India. β - cyclodextrin was obtained from Lyka laboratory, Ankleshwar, Gujarat, India. Sodium starch glycolate, Crosspovidone and Cross Carmellose Sodium were purchase from S. D. Fine chemicals ltd. Mumbai. All other chemicals and reagents used were of analytical grade.

ISSN: 0975-8585

METHODS

Compatibility studies by IR-Spectroscopy[16]

FT-IR spectroscopy was carried out to check the compatibility between drug and polymer. The FT-IR spectra of drug with polymers were compared with the standard FT-IR spectrum of the pure drug.

Calibration curve for Rosuvastatin Calcium[17]:

100 mg of drug was weighed and taken in a 100ml of volumetric flask to this add 5ml 0f methanol to dissolve the drug and then make up to water with volume it gives the 1000µg/ml and it is the stocking solution. From this 10ml solution was taken to this 90ml 0f water was added to the volume. It gives 100µg/ml acts as the working solution and prepare the concentrations according to the beer limits 5-25µg/ml and and absorbance was measured at 248 nm against reagent blank. All spectral absorbance measurement was on Shimadzu 1700 UV-visible spectrophotometer.

Preparation of β- Cyclodextrin inclusion complexes[18,19,20,21]

All the binary mixtures were prepared in a 1:1 molar ratio of drug and β-Cyclodextrin

Kneading method

RST with β-CD in 1:3 molar ratio were taken. First Cyclodextrin is added to the mortar, small quantity of 50% ethanol is added while triturating to get slurry like consistency. Then slowly drug is incorporated into the slurry and trituration is further continued for one hour. Slurry is then air dried at 25 °C for 24 hours, pulverized and passed through sieve No. 100.

Co-evaporation method:

Inclusion complex (1:3) was prepared by dissolving equimolar amount of β-CD and RST Ca in required amount of 50% aqueous ethanol. The solution was stirred till a clear solution was observed and the obtained solution was then evaporated under vacuum at a temperature of 45°C and 100 rpm. The solid residues was further dried completely at 45°C for 48 h, the dried complex was pulverized into a fine powder and sieved through sieve No. 100.

Precipitation method:

Inclusion complex of RST and β-Cyclodextrin in 1:3 molar ratio was prepared by drug and CD, which dispersed in water and the solution, was heated to obtain concentrated, viscous and translucent liquid. The solution was left to give a precipitation of inclusion complex. Precipitate obtained was separated and dried to get solid inclusion complex.

Micro meritic properities:

The micromeritic properities were Angle of repose, Carr's index, Hausenars ratio for the prepared different formulations of inclusion complexes.

Drug content estimation[22,23]:

100 mg of drug β-CD complex was accurately weighed and transferred to 100 ml volumetric flask and volume was made up to the mark with water. From this 1ml was taken in 10 ml volumetric flask and the volume is adjusted up to the mark with same solvent. The absorbance of the solution was measured at 248 nm using appropriate blank. The drug content of Rosuvastatin Calcium was calculated using calibration curve

$$\text{Drug content} = \frac{\text{Estimated amount} \times 100}{\text{Label claim}}$$

ISSN: 0975-8585

FORMULATION DESIGN

Table1: Formulation design of Rosuvastatin Calcium Cyclodextrin complexes

S.No.	Formulation code	Ratio of drug and S.D
1.	F1	1:3 (RST+CCNa)
2.	F2	1:3 (RST+CP)
3.	F3	1:3 (RST +SSG)
4.	F4	1:3 (RST + CCNa)
5	F5	1:3 (RST + CP)
6	F6	1:3 (RST+SSG)
7	F7	1:3 (RST +CCNa)
8	F8	1:3 (RST+CP)
9	F9	1:3 (RST + SSG)
10	F10	1:4 (RST + CCNa)
11	F11	1:4 (RST + CP)
12	F12	1:4 (RST +SSG)
13	F13	1:4(RST +CCNa)
14	F14	1:4(RST + CP)
15	F15	1:4(RST +SSG)
16	F16	Without superdisintegrant

RST- Rosuvastatin calcium
CCNa – Cross Carmellose Sodium
C.P- Cross povidone
SSG- Sodium Starch Glycolate

In vitro dissolution studies for β-Cyclodextrin inclusion complexes24,25 :

In-vitro dissolution of RST inclusion complex was studied in USP XXIV dissolution apparatus (Electrolab) employing a paddle stirrer. 900 ml of phosphate buffer of pH 6.8 was used as dissolution medium at 50 rpm. The temperature of 37 + 0.5 °C was maintained throughout the experiment. Complex equivalent to 5 mg of RST was used in each test. 5 ml of sample of dissolution medium were withdrawn by means of syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 248 nm after suitable dilution with phosphate buffer. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. The amount of RST released was calculated and plotted against time and compared with pure drug.

Formulation of the Rosuvastatiin Calcium Oral dispersible tablets:

The complex of RST-β-CD was prepared into tablet by direct compression method containing RST-CD complex equivalent to 5mg of RST. The all excipients were passed through sieve # 85. All the above ingredients were properly mixed together for 15 mins. Talc and magnesium stearate were mixed. The mixture was then compressed in to tablet by using rotary single punch tablet machine. It was all done by Directcompression method[26,27].

Table 2: Composition of Rosuvastatin calcium Oro dispersible tablets

S.no	Ingredients	Precipitation method(mg)			Co evaporation method(mg)			Kneading method(mg)			Precipitation method(mg			Kneading method(mg)			control
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16
1	Drug-CDcomplex equivalent 5mg Rosuvastati	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20

	n Ca																
2	Cross Carmellose Sodium	**15**	-	-	**15**	-	-	**15**	-	-	**20**	-	-	**20**	-	-	-
3	Cross povidone	-	**15**	-	-	**15**	-	-	**15**	-	-	**20**	-	-	**20**	-	-
4	Sodium starch glycolate	-	-	**15**	-	-	**15**	-	-	**15**	-	-	**20**	-	-	**20**	-
5	Mannitol	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
6	Camphor	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
7	Aspartame	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**
8	Magnesium stearate	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**
9	Talc	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**
10	Avicel 102	**73**	**73**	**73**	**73**	**73**	**73**	**73**	**73**	**73**	**68**	**68**	**68**	**68**	**68**	**68**	**88**
Total weight (mg)		**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Evaluation of tablets28,29:

The prepared tablets were evaluated for weight variation, hardness, thickness, friability and disintegration time. The weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The hardness of each batch of tablet was checked by using Monsanto hardness tester. The hardness was measured in terms of kg/cm2. The hardness of 6 tablets was determined using the Monsanto hardness tester. Friability was determined by first weighing 10 tablets after dusting and placing them in a friability tester (Roche friabilator), which was rotated for 4 min at 25 rpm. After dusting, the total remaining mass of tablet was recorded and the percent friability was calculated. Disintegration test for all batches was carried out in distilled water at 37 + 0.5 °C by using USP disintegration test apparatus.

In Vitro dissolution study:

In-vitro dissolution of Oro dispersible tablet was studied in dissolution apparatus (Electrolab) employing a paddle stirrer. 900 ml of phosphate buffer of pH 6.8 was used as dissolution medium. The stirrer was adjusted rotate at 50 rpm. The temperature of dissolution media was previously warmed to 37 + 0.5 °C and was maintained throughout the experiment. 5 ml of sample of dissolution medium were withdrawn by means of syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 248 nm after suitable dilution with phosphate buffer pH 6.8. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Percentage amount of Rosuvastatin released was calculated and plotted against time. For comparison, the dissolution of marketed tablet was studied and observed[30].

Wetting Time:

Wetting time was measured using a simple procedure. a piece of tissue paper cut circularly (6.5 cm diameter) and placed on a petri dish containing 6ml of water at room temperature.A tablet is placed on the surface of the tissue paper and the time required for complete wetting of the tablet was noted.

Water Absorption:

A piece of tissue paper folded twice was placed in a small petridish (internal diameter = 6.5 cm) Containing 6 ml of water. A tablet was placed on the paper, and allowed to wet completely. The wetted tablet was removed and reweighted. Water absorption ratio, R, was determined according to following equation.

$$R = \{(Wa - Wb)/ Wa\} X100$$

ISSN: 0975-8585

RESULTS

Drug – polymer interaction studies:

From the spectrum of Rosuvastatin Calcium, physical mixture of Rosuvastatin Calcium and polymers observed that all characteristic peaks of Rosuvasatin Calcium were present in the combination spectrum, thus indicating compatibility Rosuvastatin Calcium and polymer. As clearly seen from the spectra, the characteristics peaks of Rosuvastatin calcium and β-Cyclodextrin combination the peaks were found to be 3375,293,1907,& 576 it shows that strong interaction between the drug and polymer compared with the standard. It shown in figure

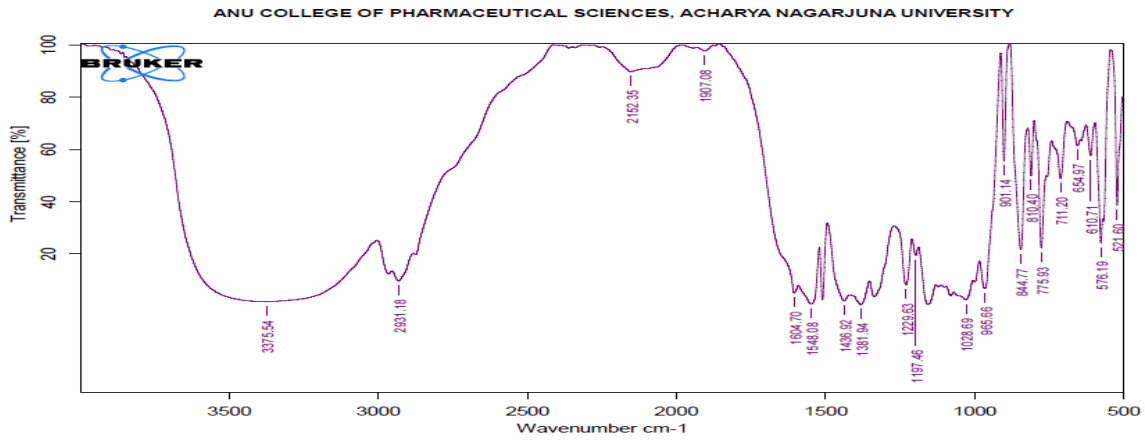

Figure 3: FT- IR Spectra of Rosuvastatin calcium and β- Cyclodextrin

Calibration curve of Rosuvastatin Calcium

Data for the standard calibration curve of Rosuvastatin Calcium at *λ max* 248nm in water it was shows that linear curve it was shown in figure.

Table no 3: Calibration curve of Rosuvastatin Calcium

S.NO	Concentration (µg/ml)	Absorbance
1	5	0.224
2	10	0.464
3	15	0.587
4	20	0.818
5	25	0.967

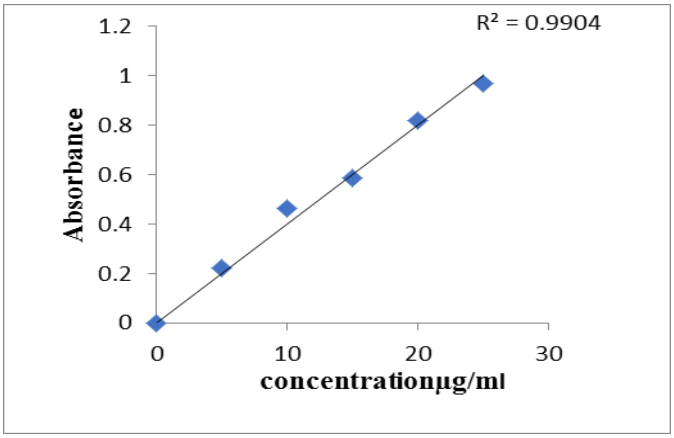

Figure 4: Calibration curve of Rosuvastatin calcium

ISSN: 0975-8585

In vitro dissolution studies for inclusion complexes:

Since the presence of cyclodextrin showed that there was decreased in extinction coefficient of the drug, since the hydroxy propyl β-cyclodextrin is highly water soluble it was expected to instantly dissolve in the medium under the condition of dissolution test .The release rate profile was drawn as the cumulative percent release on y-axis and time on x-axis which showed in figure 2. It showed that 44.69% of the pure Rosuvastatin was released in 20 min, and up to 64.28% after 30 min. Physical mixture shows release up to 49.29% of the drug in 20 min and up to 67.04% after 30 min whereas 69.79% and 80.26% drug release after 30 min from precipitated and co-evaporated respectively. Kneaded products showed highest dissolution profile among all complex 89.46% drug release in 20 min. that shows that there was improvement in dissolution rate of drug from inclusion complex as compared to physical mixture and pure drug.

Table no 5: In-vitro % Drug Release Profile of Inclusion complexes and pure drug

Time (mins)	% Drug release			
	PPT	COE	KM	PURE
5	36.45	24.5	28.08	11.3
10	52.73	28.12	40.56	17.58
15	70.82	35.78	53.31	30.20
20	77.89	50.3	63.1	44.69
25	82.46	62.89	72.64	52.87
30	87.12	69.79	80.67	64.28

Micro meretic properities:

The pre compression studies were done for the prepared formulations of different ratios of inclusion complexes like Angle of Repose , Bulk density, Tapped density , Compressibility index and Hausenar's ratio the results were observed and shows that they were within the limits and good flow properities.it Was shown in Table no 6

Table no 6: Pre-Compression Parameters for inclusion complexes

Formulation	Angle of Repose (0)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner's Ratio
F1	22.15	0.270	0.360	25	1.33
F2	29.79	0.257	0.335	23.28	1.3
F3	26.34	0.243	0.300	22.89	1.23
F4	23.98	0.271	0.350	18.14	1.29
F5	25.67	0.262	0.320	17.71	1.22
F6	23.68	0.252	0.305	16.11	1.21
F7	28.90	0.250	0.298	15.52	1.19
F8	27.74	0.245	0.290	14.74	1.18
F9	24.60	0.243	0.285	15.31	1.172
F10	24.16	0.258	0.291	22.13	1.12
F11	23.13	0.231	0.289	16.15	1.20
F12	26.78	0.267	0.295	24.31	1.181
F13	28.56	0.289	0.287	17.12	1.14
F14	27.89	0.243	0.292	16.23	1.23
F15	25.37	0.238	0.287	13.17	1.24
F16	20.12	0.213	0.256	15.36	1.12

Post compression parameters for prepared tablets:

After compression of tablets the post compression parameters were done for the tablets weight variation, Hardness, Friability, and Drug content was observed they were within the ranges and it was shown in Table no 7

ISSN: 0975-8585

Table no 7: Post-Compression Parameters of Designed Formulations.

Formulation	Weight Variation (%)	Hardness (kg/cm²)	Frability (%)	% Drug content
F1	2.35	3.0	0.678	89.92
F2	2.65	3.5	0.420	92.03
F3	2.78	4.0	0.399	95.56
F4	3.12	3.0	0.606	87.95
F5	3.56	3.0	0.455	93.29
F6	3.26	4.0	0.504	95.0
F7	4.5	2.5	0.367	97.25
F8	2.3	2.5	0.84	98.81
F9	2.35	3.0	0.359	93.75
F10	3.12	2.5	0.781	91.23
F11	2.21	2.2	0.564	89.16
F12	4.02	2.0	0.783	92.78
F13	2.65	2.1	0.679	86.15
F14	2.16	2.3	0.891	88.13
F15	2.67	2.1	0.927	96.56
F16	2.13	2.4	0.345	82.16

In vitro dissolution studies for prepared tablets:

The dissolution studies were conducted for the prepared tablets at sink conditions it shows that the precipitation method and kneading method give the best results with less time increasing in Superdisintegrants ratio when compared with the marketed formulation. The precipitation method gives 95% at the end of 30 mins and kneading method gives the 97% at the end of the 30 mins. The results were shown in Table no 8

Table no 8: Dissolution profile for F1 - F9 formulations

Time (mins)	% Drug dissolved								
	Precipitation method			Co evaporation method			Kneading method		
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	14.0	54.0	12.6	25.82	20.66	9.8	12.6	38.03	9.39
10	27.23	73.18	18.78	29	44.54	12.6	23.47	46.95	15.49
15	40.84	83.11	22.06	32.4	47.42	15.96	29.58	64.8	21.13
20	44.13	90.15	28.17	32.86	55.87	16.90	35.68	75.13	22.06
30	61.98	95.32	42.73	36.6	80.76	17.84	38.97	87.10	31.46
45	69.02	99.54	46.8	66.2	94.28	20.19	54.0	94.38	38.50
60	76.06	100	83.11	86.86	98.6	25.82	70.43	100	46

Table 9: Dissolution profile of F10 - F17 formulations

Time (min)	% Drug dissolved							
	Precipitation method			Kneading method			CONTROL	MARKET
	F10	F11	F12	F13	F14	F15	F16	F17
0	0	0	0	0	0	0	0	0
5	35.87	74.05	26.2	79.44	37.25	18.85	7.35	78.19
10	85.55	83.7	74.05	83.17	84.17	40.47	14.25	93.83
15	86.93	85.55	85.56	86.93	87.85	49.212	15.638	94.05
20	89.69	90.6	86.47	88.313	94.75	70.314	22.99	95.34
30	97.5	95.67	88.43	96.13	97.05	74.5	37.71	97.67
45	98.43	99.812	94.13	97.05	97.05	83.71	49.216	-
60	-	100	95.21	97.512	97.512	85.55	60.71	-

ISSN: 0975-8585

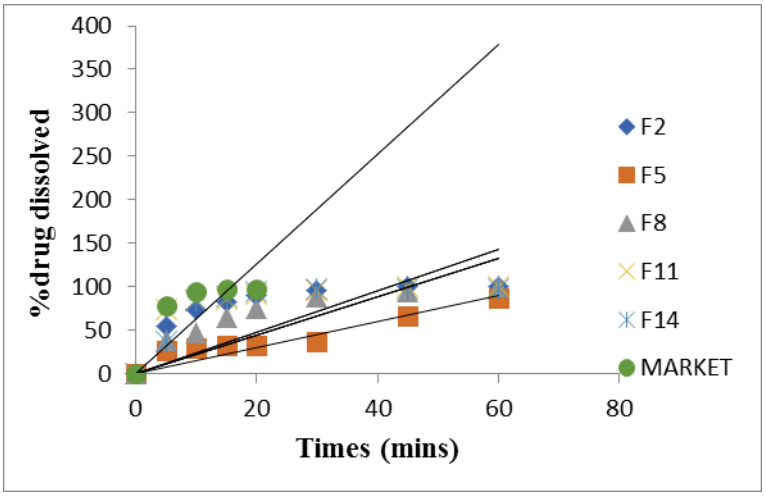

Figure 5: Comparison graph F2, F5 , F8, F11, F14 With market Formulation(zero order)

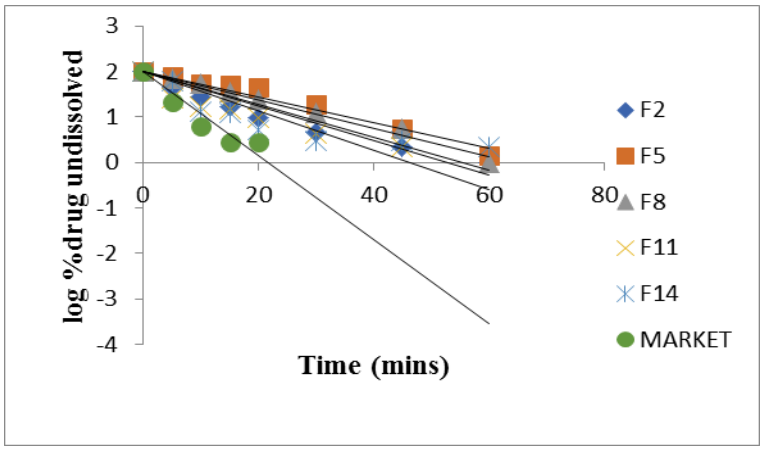

Figure 6: Comparison graph F2, F5, F8, F11, F14 With Market Formulation (First order)

Table 10: Wetting time, Water absorption ratio, Disintegration time of Designed Formulations.

Formulation code	Wetting time(sec)	Water absorption Ratio	Disintegration time(sec)
F1	23	68.7	58
F2	21	62.2	51
F3	20	71.7	45
F4	18	79.4	52
F5	38	62.3	50
F6	35	59.8	48
F7	33	55.3	60
F8	31	52.9	54
F9	41	48.5	40
F10	19	78.9	54

ISSN: 0975-8585

F11	32	46.67	50
F12	26	54.87	43
F13	30	43.46	63
F14	41	78.91	58
F15	19	63.22	46
F16	29	67.64	79

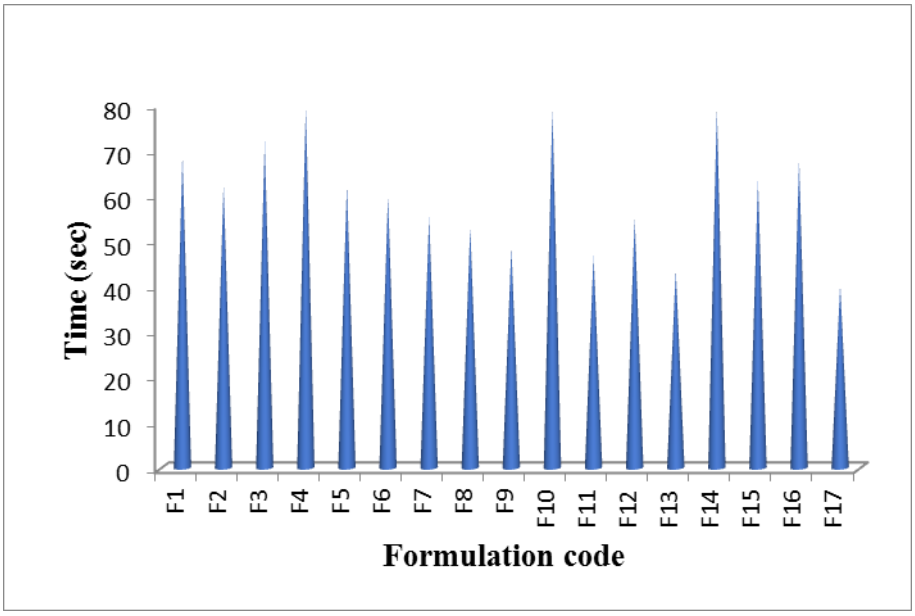

Figure 7: water absorption time For Tablets

DISCUSSION

The present work was to determine "Development and Evaluation of Oro dispersible tablets of Rosuvastatin calcium by β-Cyclodextrin inclusion complexes by using different super disintegrants " in achieving the objectives in the preformulation studies the micromeritic proprieties were determine and Angle of Repose was found to be excellent and it's been varying with different formulations shown in the Table 6.

The formulation design was made with three methods by using different ratios of super disintegrant and it was shown in the Table 1&2. Formulation F1 to F3 precipitation method was selected using three different superdisintegrants.F4 to F6 Co-evaporation method was done using three different superdisintegrants.F7 to F9 kneading method was selected three different super disintegrants, F10- F12 the concentrations of the super disintigrants was enhanced by using precipitation method was followed. Similarly F13-F15 kneading method with enhanced concentrations of super disintegrant was taken. F16 is stands for control and F17 is stands for market formulation with 5mg .In post compression studies the weight variation was calculated and found to be with in the limits .

Hardness, friability was shown in the Table7.The standard calibration curve was plotted to compare with the in vitro dissolution profile shown in Table 8&9. In vitro dissolution studies was performed and it was absorbed for the drug release rate in precipitation method F2 formulation showing 100% release at the end of 60mins, whereas 86% in F3 and 76% in F1.When the concentration of super disintegrant was enhance it was observed 97% release in case of F10 and 95% at F11 and 88.4% in F12 at the end of 30mins only shown in the Table 17&18. The formulations F4-F6 was done by co-evaporation method and the observed release profile

98.6% in F5 and 88.6% in F4 and 25% at the end of 60min in F6 as the low release profile being observed, so it is not further continued in the enhance of super disintegrants.

The formulations F7-F9 was done by kneading method it was observed 100% at F8, 74.3% in F7 and 46% in F9 and it's been further extended with the increase of super disintegrants. The formulations F13-F15 was taken and it was observed 97% for F13, 96% for F14 and 74% for F15 at the end of 30mins only. Comparision of the kinetical graph were plotted for the shown in the Figure5&6.

The obtained values were compare with the controlled value in and it was observe the enhance of drug release with the increase of super disintegrants .In the case of control 60% of drug was released at the end of 60mins, whereas the best formulations were observed at 97% F10 the end of 30mins hence the influence of super disintegrant was more. The best fit obtained values from different methods, where considered with marketed product and it was observed the values are similar with the market product.In precipitation method among the F1-F3 and F10-F12 it was observed 100%drug released at the end of 60mins in F2 the best formulation was optimized to F10.In kneading method the formulations F7-F9 and F13-F15 was observed 100% drug was released in F8 at the end of 60mins and 97.3%in F14 at the end of 30 min .Hence F14 formulation is the best fit formulation to optimize.In co evaporation method F4-F6 was considered 98.6% in F5 formulation at the end of 60mins

CONCLUSION

This study shows that there is formation of a β-CD Rosuvastatin calcium complex in aqueous solution and this complex, prepared by the various inclusion complexation methods, also exist in the solid state. The inclusion complex prepared with β-CD by kneading method showed highest solubility and fastest dissolution profile (more than 97% drug release in 30 min). The relative efficiency of different superdisintegrants to improve the disintegration and dissolution rate of tablets was in the order, sodium starch glycolate > Crosspovidone >Crosscarmellose. The improved dissolution rate may be as a result of the increase in solubility, brought about by complexation. From the results we can assume that the aqueous solubility and dissolution rate of Rosuvastatin calcium can be significantly increased by forming complexes.

ACKNOWLEDGEMENT

At first, I consider it as a great privilege to express my heartfelt gratitude and sincere thanks to my esteemed guide Mrs. **Dr. P. Rohini**, **M.Pharm, Ph.D** Assistant professor, Department of Pharmaceutics, University College of Pharmaceutical Sciences, Acharya Nagarjuna University, Guntur, for her valuable suggestions, encouragement, motivation, guidance and co-operation during my dissertation work.I express my profound thanks to MSN Laboratories Hyderabad for providing Rosuvastatin Calcium

REFERENCE

[1] Kaushik D., 2004 'Mouth dissolving tablets: A review Indian Drugs" 41: Page no- 187-193.
[2] Shastry C.S., Srinath M.S.,2004 'Pharmaceutical approaches of taste masking oral dosage forms', Indian Drug 41: Page no- 253, 257.
[3] Adel M.,Semreen M.K., Qato M.K., 2005. 'Fast dissolving dosage forms – technique' Pharma Tech., 25: Page no- 68-75.
[4] Laila J.K., Sharma A.H., 1993 'Freeze drying and its application', Indian drugs, 31: Page no- 503-513.
[5] Lachmann L., Liebermann H.A., Kiang J.L., 1998 'The theory and practice of industrial pharmacy', 3rd Edition, Vargese publishing House, Bombay, Page no- 430-440.
[6] Allen L.V wang B., 1986 'Method of making a rapidly dissolving tablet'. US patent, 43: Page no- 123-131.
[7] Bhagwati S., Hiremath S N., 2005 'Comparative evaluation of disintegrates by formulating cefixime dispersible tablets' Indian Journal of Pharmaceutical sciences. 39:40, Page no- 194-197.
[8] Lew, 2007 'Rapidly disintegrating tablets of selegiline' Indian Journal of Pharmaceutical Education. Research 41: Page no- 174-175.
[9] Sreenivas S A.,Gadad AP.,Patil MB.,2006 'Formulation and evaluation of ondasetron hydrochloride directly compressed mouth disintegrating tablets' Indian Drug 43: Page no- 35-37.

[10] Mishra D N, 2006 'Rapidly disintegrating oral tablets of meloxicam by direct compression method', Indian Drugs 43: Page no- 117-121.
[11] Shirwaikar A. A., Ramesh A., 2004 'Fast disintegrating tablets of atenolol by dry granulation method', Indian Journal of Pharmaceutical sciences, 66: Page no- 422-426.
[12] Halakatti P.K.,Mastiholimath V.M.,2006 'Rapidly disintegrating Domperidone tablets'. Indian Drug, 43: Page no- 594-597.
[13] Shishu and Bhatti A., 2006 'Fast disintegrating tablets of diazepam', Indian Drugs, 43: Page no- 643-648.
[14] Kuchekar B.S., Petkat K.C., Desai S.A., 2006 "Orodisolving tablets of promethazine hydrochloride' Indian Journal of Pharmaceutical Education& Research 40: Page no- 172-173.
[15] Mishra B., Panigrahi D.,2005 'Mouth dissolving tablets an overview of preparation techniques, evaluation and patented technologies', Indian Journal of Pharmaceutical sciences.
[16] Chaudhari P.D., Kolhe K.V., 2005 'Formulation and evaluation of fast dissolving tablet of famotidine' Indian Drugs 42: Page no- 641-649.
[17] Mishra D N, 2005 'Rapidly disintegrating oral tablets of valdecoxib by direct compression method', Indian Drugs 43: Page no- 117-121.
[18] Henmann H Rothe W., 1975 'Preparation of porous tablets US patents no 3,885,026'.
[19] Dangagi P.M., Sreenivas S.A.,Mastiholimath V.S 'Orodispersible tablets: New fangled drug delivery system a review', Indian Journal of Pharmaceutical Education &. Research. 39:4.
[20] Mahajan H.S., Kuchekar B.S., Badhan C.,2004 'Mouth dissolving tablets of sumtriptan succinate', Indian Journal of Pharmaceutical sciences, Page no- 238-240.
[21] Shirwaikar A. A., Ramesh A., 2004 'Fast disintegrating tablets of atenolol by dry granulation method', Indian Journal of Pharmaceutical sciences, 66: Page no- 422-426.
[22] santhosh r iyeret al. formulation and evaluation of fast dissolving tablets of risperidone solid dispersion international journal of pharmaceutical, chemical and biological sciences issn: 2249-9504 ijpcbs 2013, 3(2),Page no. 388-397
[23] D.v.r.n.Bhikshapathi , v. durga madhuri preparation and evaluation of fast dissolving oral films containing naratriptan Hcl research article American . Journal of. Pharm tech research. 2014; 4(2) issn: 2249-3387
[24] Kshirasagar, senthil kk, formulation and evaluation of naratriptan orodispersible tablets using superdisintergrants by direct compression method international journal for pharmaceutical Research scholars (ijprs) v-2, i-2, 2013 issn no: 2277 - 7873
[25] Biju SS, Taleganokar S, Misra PR and Khar RK, Vesicular systems: An overview. Indian J.Pharm. Sci, 68: 2006, 141-153
[26] Y. Jin, Li Tong, Ping Ai, Miao Li, Xinpu Hou "Self-Assembled Drug Delivery Systems Properties and *In Vitro –In Vivo* Behaviour of Acyclovir Self-Assembled Nanoparticles (san)," Int. J. Pharm. 309 (1–2), 2006, 199–207.
[27] P. Goyal et al., "Liposomal Drug Delivery Systems: Clinical Applications," Acta Pharm. 55, 2005, 1–25.
[28] .H.A. Lieberman, M.M. Rieger, and G.S. Banker,Pharmaceutical Dosage Forms: Disperse Systems (Informa Healthcare, London, England, 1998), p. 163.
[29] Kaur and Kanwar.M., "Ocular Preparations: The Formulation Approach," Drug Dev. Ind. Pharm, 28(5), 2002,473–493
[30] M.O. Vaizoglu and P.P. Speiser, "Pharmacosomes—A Novel Drug Delivery System," Acta Pharm. Suec. 23, 1986, 163–172.
[31] N.K. Jain, Advances In Controlled and Novel Drug Delivery(CBS Publishers, New Delhi, India, 2003)276.