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Formulation and evaluation of fast dispersible Tablet of rosuvastatin using cyclodextrin Complexation method

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Abstract

Statins are the most commonly prescribed lipid lowering agents because of their effectiveness, tolerability and ease of administration. Rosuvastatin calcium is synthetic lipid lowering agent which inhibits 3-hydroxy-3-methyl-glutaryl co-enzyme-A reductase, preventing the conversion of HMG-CoA to Mevolanate. Its absolute bioavailability is 14% and coming under the class II of biopharmaceutical classification system. To enhance the solubility of Rosuvastatin cyclodextrin complexation techniques was employed. Phase solubility studies were carried out to optimize the ratio of complexing agent with drug. Drug with MβCD found to increase the solubility maximum extent evident from the higher Ks value. Further formulation prepared by spray drying displayed maximum solubility and improved release rate. Characterization such as FTIR, SEM, DSC has been found to be satisfactory. Optimized formulation was directly compressed with superdisintegrants into fast dispersible formulations, which showed immediate disintegration and faster rate of drug release compared to marketed formulation with L-HPC being optimum. Thus a fast dispersible tablet of Rosuvastatin was formulated using cyclodextrin complex resulted in enhanced solubility and faster disintegration and immediate release rate.

Keywords: Rosuvastatin, cyclodextrin and fast dispersible tablet.

Contents

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1. Introduction

An individual's specific biochemical and metabolic profile can often work against even the healthiest lifestyle. For these "biochemically challenged" patients, lipid-lowering agents such as the statins have literally provided a new lease on life. Statins are the most commonly prescribed lipid-lowering agents because they are effective, well tolerated and easy to administer. They are generally effective, are supported by favorable outcome studies and have

relatively few adverse effects. The six statins currently available are rosuvastatin (Lipitor), cerivastatin (Baycol), fluvastatin (Lescol), lovastatin (Mevacor), pravastatin (Pravachol) and simvastatin (Zocor).

There were several ways in which bioavailability of the drug can be enhanced all of which aimed at increasing the surface area of the drugs which includes. Micronization, use of salt form, use of metastable polymorphs, solvent deposition, selective adsorption on insoluble carriers, solid dispersion, solute solvent complexation, complexation with cyclodextrins. Cyclodextrins (CD's) as they are known today, were called cellulosine when first described by Villiers in 1891. Soon after, Schardinger identified the three naturally occurring cyclodextrins--alpha, beta, and gamma. These new compounds were referred to as Schardinger sugars. For 25 years between 1911 and 1935, Pringsheim in Germany was the leading researcher in this area, demonstrating that these sugars formed stable aqueous complexes with many other chemicals. By the mid 1970's, each of the natural cyclodextrins had been structurally and chemically characterized and many more complexes had been studied. Briefly, the natural cyclodextrins are produced from starch by the action of cyclodextrin glycosyltransferase (CGTase), an enzyme produced by several organisms, Bacillus macerans being the earliest source. Structurally, cyclodextrins consist of 6, 7, or 8 (α, β , and γ respectively) D-glucopyranosyl units, connected by alpha-(1,4) glycosidic linkages.

The most stable three dimensional molecular configuration for these non-reducing cyclic oligosaccharides takes the form of a toroid with the upper (larger) and lower (smaller) opening of the toroid presenting secondary and primary hydroxyl groups, respectively, to the solvent environment. The interior of the toroid is hydrophobic as a result of the electron rich environment provided in large part by the glycosidic oxygen atoms. It is the interplay of atomic (Van der Waals), thermodynamic (hydrogen bonding), and solvent (hydrophobic) forces that accounts for the stable complexes that may be formed with chemical substances. Complexes results from a Lewis acid - base reaction between two or more different chemical constituents forming compounds. Complexes are broadly classified into metal ion complexes, Organic molecular complexes and inclusion compounds. Complexes resulting from entrapment of one compound in the molecular framework of other are considered as complexes of occlusion or inclusion complexes. Monomolecular inclusion compounds involve the entrapment of a single guest molecule in the cavity of one host molecule. Most of the host molecules are cyclodextrins.

For the past one decade, there has been an enhanced demand for a more patient user friendly and complaint dosage forms. As a result, the demand for developing new technologies has been increasing many folds annually. Since the development cost of a new drug molecule is very high, efforts are now made by pharmaceutical companies to focus on development of new drug dosage forms for existing drugs with an improved bioavailability and increased therapeutic efficacy together with reduced dosing frequency to minimize side effects and to make more cost effective dosage form. Oral dosage forms have always been a popular route of administration due to ease of ingestion, pain avoidance, and versatility and most importantly the patient compliance.

The physiology and psychology of the elderly are different from those of young people. Due to their decline in swallowing ability and because of their hand tremors, oral administration in elderly is a significant problem. Many patients find it difficult to swallow tablets and capsules and do not take medication as prescribed. The difficulty is experienced in particular by pediatric and geriatric patients, but it also applies to people who are ill in bed, mentally ill, developmentally disabled, uncooperative patient, patient with reduced intake regime, active working patients who are busy or traveling specially who have no access to water. In some cases such as motion sickness, sudden episode of allergic attack or coughing, swallowing tablet may become difficult. To fulfill these medical needs, pharmaceutical technologists have channelized their efforts to develop a novel oral dosage form known as Rapidly Dispersible Tablets, tables that disintegrate and dissolves rapidly in saliva without need of drinking water.

The rapid Dispersible tablets dissolve usually in oral cavity within 15 seconds to 3 minutes. The faster the drug into solution, the quicker the absorption and onset of drug effect. Many technologies available for preparation of rapid Dispersible tablets such as Zydis technology, Flash dose technology or floss technology, Mass Extrusion technique, Wet Compression Method, Spray Drying, Direct Compression Method, Wow Tab Technology and Ora Solv Technology. Advantages of rapid Dispersible tablets such as Administration to patients who cannot swallow, Convenience and patient compliance, such as disabled bed ridden patients and for traveling and busy people who do not have ready access to water, More rapid drug absorption through pregastric absorption from mouth, pharynx and oesophagus, Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety, An increase in bioavailability, New business opportunities, product differentiation, line extension and life cycle management and Exclusivity of product promotion and patent life extension. And characteristics of rapid Dispersible tablets as They should rapidly disintegrate in the mouth within few seconds without requiring water for administration, They should have a pleasing taste, They should be compatible with masking agents, They should have good compressibility characteristics and should be able to withstand transportation shocks, They should be

manufactured using conventional tablet processing and packaging equipment and should be cost effective, They should be resistant to temperature and humidity changes, They should allow for both water-soluble and water insoluble drugs to be incorporated, They should allow for maximum therapeutic efficacy and They should leave very minimal or no residue in mouth after oral administration.

2. Materials and Method

2.1 Materials

Rosuvastatin was obtained as a gift sample from DRL (Hyderabad, India). β- Cyclodextrin (βCD) and methyl-β-cyclodextrin (MβCD) were obtained as gift sample from Colorcon Asia Pvt.Ltd. (Goa, India). Super disintegrants such as Ac-Di-Sol, Low Substituted Hydroxyl Propyl cellulose (L-HPC), Avicel, Sodium Starch Glycolate were obtained from Loba Chem. (Mumbai, India). All other chemicals and reagents were of analytical grade.

2.2 Method of estimation of Rosuvastatin

A simple, fast, reproducible and precise method of estimation for Rosuvastatin was carried based on the solubility of Rosuvastatin in methanol. 10 µ/ml solution was scanned from 200-400 nm. The absorption maximum was found to be 246.5 nm. Beers range was found to be 2-26 µg/ml. Solubility measurements of Rosuvastatin were performed. An excess amount of Rosuvastatin was added to 25ml of aqueous solution of water soluble carriers like urea, Poloxamer-407, citric acid, mannitol, PVPK 30 and PEG-4000 in the various ratios such as 1:1, 1:3, 1:5 and 1:10 in screw capped bottles. Samples were shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whattman filter paper no 1. Filtered solution diluted properly with methanol. The diluted solution analyzed for the Rosuvastatin in UV 246.5 nm.

2.3 Phase solubility studies

Phase solubility studies were performed according to method reported by Higuchi and Connors. An excess amount of Rosuvastatin was added to aqueous solution of β- cyclodextrin (ßCD) solution (molecular weight =1135) and methyl-β-cyclodextrin (MβCD) solution (molecular weight =1190), at various concentrations (1 to 20 mM/L).The contents were stirred for 24 hours at $30^0C \pm 2^0C$. After equilibrium samples were filtered using 0.45 µ nylon disc filter and absorbance read after suitable dilutions at 246.5 nm (Shimadzu 1700 UV Visible spectrophotometer). The apparent stability constant was calculated from the initial straight portion (intrinsic solubility of Rosuvastatin) of the phase solubility diagram using the following equation. K 1:1 =Slope/Intercept (1-Slope)

2.4 Preparation of inclusion complexes: Different methods were used to formulate the cyclodextrin complex of Rosuvastatin.

2.4.1 Physical mixture methods:

Rosuvastatin and cyclodextrin (ßCD and MβCD) in the proportion of 1:1 molar concentrations were mixed in a mortar for one hour.

2.4.2 Kneading Methods: Rosuvastatin and cyclodextrin (ßCD and MβCD) in the proportion of 1:1 molar concentrations were mixed in a mortar for one hour with small quantities of methanol distilled water was added intermittently to get slurry like consistency. The paste was dried in the oven at the temperature of 45˚C for 24 hours. Dried complex were pulverized into fine powder and sifted with sieve # 80.

2.4.3 Co –Solvent Evaporation Method:

Rosuvastatin and cyclodextrin (ßCD) in a ratio of 1:1 were taken and drug was dissolved in the methanol, and the cyclodextrin dissolved in the water to get clear solution. Both the solutions were mixed at constant stirring on the magnetic stirrer. Resulting solution were evaporated at the temperature of 45˚C for 24 hours. Dried complex were pulverized into fine powder and sifted with sieve # 80.

2.4.4 Common Solvent Evaporation Methods:

Rosuvastatin and cyclodextrin (MβCD) in ratio of 1:1 were dissolved in extra pure methanol to get a clear solution. The preparation was allowed to evaporate overnight at room temperature. The cyclodextrin complexes so prepared was pulverized and sifted with sieve # 80.

2.4.5 Spray drying method:

Drug and cyclodextrins are weighed in terms of equal molar ratios (1:1). This molar ratio was selected after phase solubility studies. Drug was dissolved in methanol of 50 ml with constant stirring and this was added to a solution of Cyclodextrin (MβCD) dissolved in 50 ml of methanol. This mixture of solutions was ultrasonicated for 5 min, and this feed was fed to (Lab Ultima -222, Mumbai) mini spray drier and sprayed into the chamber from a nozzle with a diameter 0.7 mm (700µm) under the following conditions.

Inlet air temperature – 120^0c
Outlet air temperature - 70 ± 3^0C
Feed rate - 3-5 ml/min
Atomization air pressure - 2.5 kg/cm2
Aspirator - 45
Vacuum in the system - 100 mm.

2.5 Evaluation parameters for the Inclusion complexes

2.5.1 Percentage yield:

The efficiency of the process is determined by the yield obtained from the process. It is calculated as mentioned below. Practical yield *100/Theoretical yield (Weight of drug taken+ weight of Cyclodextrin)

2.5.2 Solubility analysis of the Cyclodextrin complexes:

Excess of prepared inclusion complexes were dispersed in the 25ml of distilled water in a screw capped bottles to get a supersaturated solution. These bottles were shaken continuously for 24 hours at ambient temperature until equilibrium was attained. A sample of 2ml of supersaturated solution was filtered through a 0.22µ nylon filter and 1 ml of the filtrate was further diluted suitably with methanol and the absorbance was read at 246.5 nm. Solubility studies were also performed for pure drug.

2.5.3 Drug content:

The amount of drug present in a 10 mg equivalent amount of powder was determined by, Dispersible the powder mixture in 10 ml of methanol and suitably diluted with methanol and UV absorbance was measured at 246.5 nm. Drug concentration was determined from standard graph
drug.

2.5.4 In vitro release studies:

In vitro dissolution studies were performed for all inclusion complexes in order to select the Cyclodextrin complex having maximum solubility and also to select the optimum ratio. They were further evaluated for release in the distilled water as a dissolution medium. The following conditions were maintained for the dissolution process:

Instrument	: Electro lab- USP Dissolution test apparatus.
Apparatus	: Paddle type.
Temperature	: 37±0.10C
RPM	: 75
Dissolution medium	: Distilled water
Volume of medium	: 500 ml.
Sampling intervals	: Every 10 min up to 90 minutes.
Sample volume	: 5 ml withdrawn and replaced with 5 ml of distilled water.

A sample of 5 ml withdrawn and filtered through Whattman filter paper # 1 and 1 ml of the filtrate was made up to 10 ml with methanol in 10 ml volumetric flasks. Suitable dilutions were further made when required. The absorbance of the samples was read at 246.5 nm against blank. Dissolution studies were performed for pure drug.

2.5.5 FTIR studies:

Instrument used was Shimadzu FTIR-8700 spectrophotometer. In this study, potassium bromide disc method was employed. Both pure drug and Cyclodextrin complexes were subjected to IR studies. The powdered sample was intimately mixed with dry powdered potassium bromide. The mixture was then compressed into transparent disc under high pressure using special dies. The disc was placed in IR spectrophotometer using sample holder and spectrum was recorded

2.5.6 SEM (Scanning Electron microscope) studies:

The surface morphology of the layered sample was examined by using SEM. The small amount of powder was manually dispersed onto a carbon tab (double adhesive carbon coated tape) adhered to an aluminum stubs. These sample stubs were coated with a thin layer (30Å) of gold by employing POLARON-E 3000 sputter coater. The samples were examined by SEM and photographed under various magnifications with direct data capture of the images onto a computer.

2.5.7 DSC (Differential Scanning calorimetry) studies:

Differential scanning calorimetry was conducted using Mettler Toledo Star system, Metallurgy department, Indian Institute of Science, Bangalore, India. Sample were weighed (5.00-8.00 ± 0.5 mg) and placed in sealed aluminum pans. The coolant was liquid nitrogen. The samples were scanned at 100C/ min from 200 C to 3000 C. DSC thermo grams of pure drug, Cyclodextrin complexes were recorded.

2.6 Method of preparation of fast Dispersible tablets by direct compression method

Best formulation selected in the cyclodextrin complexes tablets were formulated employing direct compression method using 4mm biconcave punches. It is the process by which tablets are compressed directly from mixtures of the drug and excipients without preliminary treatment such as granulation. Spray dried Rosuvastatin (20 mg), superdisintegrants in different ratios (Table no 1) and excipients were blended using mortar and pestle. The drug and the disintegrants were sieved through mesh # 80 before blending. The granules were evaluated for angle of repose, bulk density and compressibility. The granules were mixed with 2% magnesium stearate as lubricant and 2% aspartame as sweetening agent. The granules were then compressed by using Cadmach rotary tablet machine using 4 mm punch. The hardness was adjusted to 2-4 kg/cm^2.

3. Results and Discussion

3.1 Phase Solubility Studies

The phase solubility profiles of Rosuvastatin ßCD complex and Rosuvastatin MβCD complex are presented in (Fig 1). The phase solubility diagram of Rosuvastatin ßCD complex Rosuvastatin MβCD could be classified as AL-type according to Higuchi and Connors. The plot shows that the aqueous solubility of drug increases linearly as a function of beta cyclodextrin and methyl beta cyclodextrin. The linear host –guest correlation with slope of less than 1 suggested the formation of 1:1 complex. Rosuvastatin- ßCD complex presented a slope of (0.0001) with an R2 value of 0.9982 and Rosuvastatin MβCD complex slope of (0.0004) with an R2of 0.9979. The apparent stability constant, Ks value obtained from the slope of linear phase solubility diagram was found to be 1.001 M-1 with beta cyclodextrin and 3.996 M-1. The K1:1 value showed that Rosuvastatin formed more stable complexes with methyl beta cyclodextrin than beta cyclodextrin.

3.2 Solubility Studies

Incase of ßCD complexes kneading method and co-evaporation method, enhanced the solubility of the drug, maximum increase in solubility was seen incase of complex prepared by kneading method (Fig 2). MßCD cyclodextrin complex prepared by kneading method, solvent evaporation & spray drying method showed a considerable increase in the solubility with maximum solubility seen in case of MßCD complex prepared by spray drying method where a 4 fold increase in solubility was observed. In case of MßCD complex prepared by kneading method 3fold increase in solubility was observed. ßCD complex of rosuvastatin could not be prepared by spray drying method because of difficulty in solvent system for the complete solubility of drug and ßCD.

3.3 Dissolution Studies.

Dissolution profiles of the Rosuvastatin particle and cyclodextrin complexes are shown in the (Fig 3). The rate of dissolution was found to be increased in all the cyclodextrin complexes as shown by time taken for 50% of drug to be released (t50%) . Cyclodextrin complexes prepared with spray drying showed fastest release with t50% of 30 minutes. While cyclodextrin complexes prepared by kneading method using beta cyclodextrin and methyl beta cyclodextrin had t50% of 65 and 53 minutes respectively, where as pure drug had taken 228 minutes. Thus it was observed that cyclodextrin complexes prepared by spray drying method with the drug to carrier ratio 1:1 had maximum solubility of Rosuvastatin with enhanced dissolution rate.

3.4 FTIR Studies

Spectra of ßCD and MβCD complexes presents the prominent peaks in the region of 3400.0cm-1,2929.11cm-1,1604cm-1and3402.20cm-1,2925.81cm-1,1650cm-1, respectively. The prominent peaks of Rosuvastatin was observed the region of 3365.84 cm-1 due to the (-OH stretching), a peak at 3200.12 cm-1 due to the N-H stretching and a peak at 1650 cm-1 observed due to the carbonyl group. At the lower frequencies 1315.36 (C-N stretching), 1108 (C-O stretching) 1218 for (C-F stretching) observed. In the physical mixtures of ßCD and drug as well as MβCD and drug there seemed to be no change only the summation of parent drug and polymer peaks. In case of complexes prepared using ßCD, MβCD show considerable differences such as overlapping of O-H and N-H group peak resulting broadening of the peak was observed. These modifications clearly indicate the presence of host guest interaction suggesting the formation of stable hydrogen bonds between Rosuvastatin and cyclodextrins. However other peaks corresponding pure drug such as C-H, C-O, C-N, stretching, can be clearly detected at the lower frequencies. This indicates that overall symmetry of the molecule might not be significantly changed. In the complexes of spray dried MβCD there is interaction between the drug and cyclodextrin observed it was clear that some of IR absorption peaks in inclusion complexes were different from that of corresponding physical mixtures the shape and location of the peaks in the region 3365.84 cm-1(-OH stretching), a peak at 3200.12 cm-1 due to the N-H stretching of had dramatically changed. This suggests that host guest interactions were dominated by stable hydrogen bonding among the groups mentioned above.

3.5 SEM studies

SEM study indicated that pure drug particles were irregular in shape, while the physical mixture of the drug and carrier shows that drug particle remains dispersed and physically adsorbed on the surface of carrier particles. SEM of ßCD has presented a parallelogram shape. In case physical mixture of the drug and ßCD shows adherence of drug particle on the carrier system. The cyclodextrin ßCD complex appeared in the form of irregular particles in which original morphology of both the components disappeared. But the tiny aggregates of amorphous pieces of irregular size were present. Results in the reduced particle size, there by increased surface area eventually responsible for the increased solubility**.** In case of physical mixtures of drug with MβCD the drug characteristic drug molecules adhered on to the MβCD surfaces were clearly detectable thus confirming the presence of drug. Similarly in drug MβCD complexes appeared in the form in which the original morphology of both the components has lost, and minute aggregates of amorphous pieces were found. Therefore reduced particle size, increased surface area which could be responsible for the enhanced drug solubility found in drug complexes. With spray dried MβCD complexes shows discrete separate particle, the aggregation may be due to increase in the concentration of cyclodextrin complexes. Spray dried complex appeared in the spherical in shape. By this it could be interpreted that reduced particle size,

increased effective surface area and close contact of the drug particle with cyclodextrin responsible for the enhanced drug solubility.

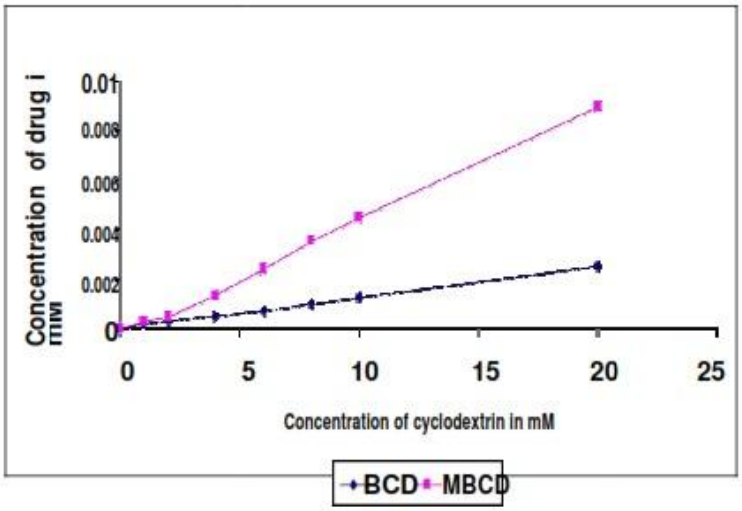

Figure 1: Phase solubility studies of Rosuvastatin with the β-CD and Methyl β-CD

BCD is β-CD, y = 0.0001x, R^2 value= 0.9982
MBCD is Methyl β-CD, y = 0.0004x, R^2 value= 0.9975.

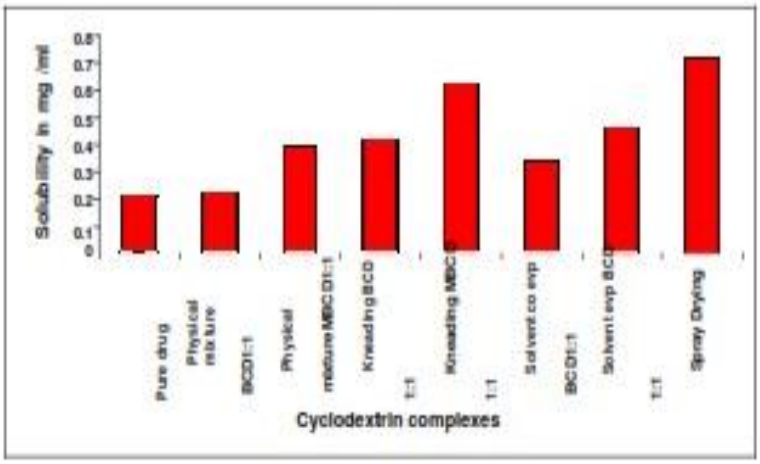

Figure 2: Solubility study profile various Cyclodextrin complexes in distilled water

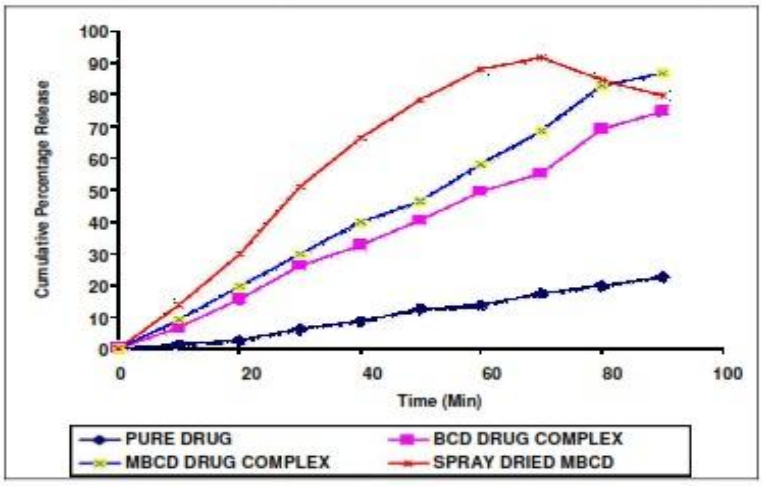

Figure 3: In vitro release studies of cyclodextrin complexes

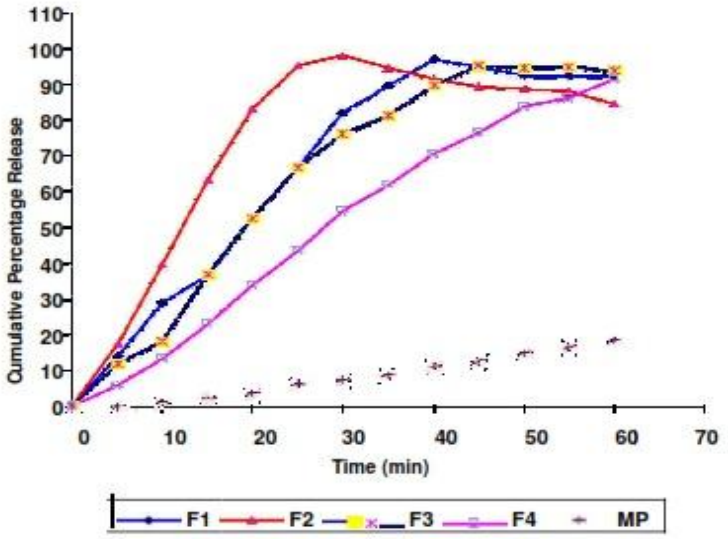

Figure 4: Comparison of *In- vitro* dissolution studies of formulation with marketed

Table 1: Formulation of fast dissolving tablets using Spray dried cyclodexterine complex

S. No	Ingredients	F1	F2	F3	F4
1	SPD drug MBDCD complex	20	20	20	20
2	AC-DI-SOL	6.32	-	-	-
3	L-HPC	-	31.25	-	-
4	AVICEL	-	-	18.9	-
5	Sodium Starch Glycolate	-	-	-	10.08
6	Dicalcium Phosphate	85.12	60.19	72.6	81.4
7	Aspartame	5	5	5	5
8	Flavour	1	1	1	1
9	Magnasium Sterate	1.26	1.26	1.26	1.26
10	TALC	6.3	6.3	6.3	6.3
	Total In mg	126	126	126	126

Table 2: Comparison between Disintegration Time, Disintegration Time in Oral Cavity and Wetting Time of Formulations.

S.No	Parameters	F1	F2	F3	F4
1	Disintegration time(s)	12	7	15	28
2	DT in oral cavity(s)	15	8	14	26
3	Wetting time (s)	14	8	15	25

3.6 DSC Studies.

DSC thermo grams of Rosuvastatin showing two endothermic peak one of which at 151.48˚C corresponding to the melting point of the Rosuvastatin and another at 63.81˚C due to loss of water or dehydration was shown in . In case of physical mixture of ßCD Rosuvastatin showed the spectra corresponding to the superposition of their parent products. Drug endothermic melting peak shifted to lower temperature with more or less reduced intensity. Traces of beta cyclodextrin showed an endothermic effect ranging from 50-100˚C attaining the maximum around 80˚C, corresponding to dehydration process, followed by an irreversible solid –solid phase transition at 232.87˚C and finally a degradation process, which took place around 230˚C.Incase of the ßCD Rosuvastatin complexes endothermic peak at 151.48˚C disappeared but presented a new peak at 82.60˚C was observed with reduced intensity as a consequences of interaction between the components. In case of physical mixture of MβCD and Rosuvastatin (Fig 9) showed the persistence of endothermic peak of the both the constituents. Here the drug endothermic peak shifted to 165.29˚C more or less with reduced intensity.

A very broad endothermic effect from 40-100˚C at a peak of 62.75˚C corresponding to dehydration process and at peak around 230.61˚C may be due to solid –solid phase transition was observed. In case of MβCD drug complexes (Fig 9) all the prominent peaks of Rosuvastatin lost in the inclusion complex with MβCD the disappearance of the thermal features of the drug indicated that the drug penetrated in to the cyclodextrin cavity replacing the water molecules. This phenomenon is indicative of a stronger interaction between Rosuvastatin and MβCD in the solid state However in the MβCD drug complex prepared by spray drying complete disappearance of the thermal behavior of Rosuvastatin showing a broad endothermic peak ranging 45-120˚C with a peak at 87.44˚C resulting in the major interaction between the drug and cyclodextrin. These results indicated the existence of interaction between Rosuvastatin and MβCD by spray drying method to form the inclusion complex.

3.7 Formulation of tablets.

Spray dried Rosuvastatin was taken to formulate the fast dispersible tablet so as to disintegrate with in the mouth of the patient especially for the elderly patients. Tablet was formulated by using the different super disintegrants such as Ac-Di-Sol, L-HPC, Avicel, Glycolys in the specified quantities as shown in the (Table No 1) represented by F1,F2,F3, F4 respectively .These formulation evaluated for the pre compression and post compression parameters. Tapped density of the formulations was in between 0.62-0.68 gm/ml, where as the untapped density was in the range of 0.53-0.59 gm /ml. The compressibility values varied from 10.77%-14.52%.The angle of repose values of the formulations varied from 39˚to 40˚. From these values, it was evident that these blends had excellent flow properties. Physical parameters confirmed to the requirements such as taste, and color. weight variation was found within the specification of I.P 1996.Avarage weight of the all four formulation was found in the range of 116.3-135.7 mg. Hardness of the F1 formulation found to be 2.5 Kg/cm2 comparatively less than other formulation such as F4 having 4 Kg/cm2 where as F2 and F3 formulation 3.4 Kg/cm^2 3.0 Kg/cm2 respectively. Thickness of the all the four formulation was found to be in the range of 0.53 to 0.59 mm. Friability of the F1, F2 found to be 0.63,0.62% respectively where as F3, F4 found to have 0.41,0.58 % respectively . Drug content of the all the four formulations was fond to be in the range of 94 to 102%.

3.8 Disintegration Time Study

Disintegration time of different formulations was shown in the (Table 2). All the formulation shown disintegration time less than 30 seconds. Among the 4 formulations F2 had shown very less time to disintegrate. Hence the formulation F2 made of super disintegrant such as L- HPC shown the faster disintegration compared to other super disintegrants.

3.9 In vitro dissolution study

In vitro dissolution of various formulations at different time interval is reported in the. All the formulations released drug comparatively faster rate than that of the marketed conventional tablet of Rosuvastatin. Formulation with L-

HPC showed maximum dissolution rates with 40 % of the drug released in10 minutes. Formulation with Ac-Di-Sol released the 28% of the drug in 10 minutes. Formulation with Avicel, Glycolys released at a very slow rate compared to L-HPC formulation that is19%, 12% respectively in the 10 minutes.

4. Conclusion

Enhancement of solubility of Rosuvastatin was observed in the ßCD and complex, where Rosuvastatin form 1:1 molar inclusion complex. Kneading and spray drying methods improved dissolution rate as well as solubility of the drug. Methyl beta cyclodextrin complex showed a greater increase in solubility when compared to beta cyclodextrin complex. Spray drying method was found to produce small uniform size spherical particles, which resulted in increased dissolution rate, and increased solubility. It may be concluded that the fast disintegrating tablets can be prepared by direct compression of spray dried MβCD-drug complex using superdisintegrants. All the formulations apart from fulfilling official and other specifications shown quicker disintegration and faster rate of drug release compared to the marketed formulation. Among which L-HPC formulation exhibited excellent disintegrating as well as release characteristic.

5. References

1. Brukert, E., J Am Med Assoc. **1990**, 263, 35-36.
2. Victoria, F. R., AJPS **2005**, 69, 546-560.
3. Shewale, B. D., Sapkal, N. P., Raut, N. A., Gaikwad, N. J., Fursule, R. A., Indian J. Pharm Sci., **2008**, 70, 255–257.
4. Subrahmanyam, C. V. S., Text book of physical pharmaceutics, New Delhi **2000**.
5. Michael, S. H., Jinxiu, L., Yevgeniy, I., Andrew, P. S., Wendy, T., Linda, L. D., Yin, T., Journal of Bone and Mineral Research. **2008**, 23, 1672–1679.
6. Habib, W., Khankari, R., Critical Reviews therapeutic drug carrier systems. **2000**, 17: 61- 67.
7. Kuchekar, B. S., Atul, C. B., Mahajan, H. S., Pharm time. **2003**, 35: 1-7.
8. Reddy, L. H., Ghose, B. R., Indian J Pharm Sci. **2002**, 64: 331-336.
9. Parakh, S. R., Gothoskar, A. V., Pharma Tech. **2003**, 27, 92-100.
10. Indurwad, N., Rajyaguru, T., Ind drug. **2002**, 39, 405-409.
11. Higuchi, T., Connors, K., Adv Anal Chem Instrum. **1965**, 4, 117-212.
12. Palem, C. R., Patel, S., Pokharkar, V. B., PDA J Pharm Sci Technol. **2009**, 63, 217-25.
13. Milind, P. W., Chetan, P. Y., Santosh, U. Z., Paresh, I. K., Ganesh, H. M., Journal of Pharmacy and Pharmaceutical Sciences. **2010**, 2, 154-157.