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FORMULATION AND EVALUATION OF ROSUVASTATIN RAPIDMLETS

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ABSTRACT

The aim of the present study was to formulate and evaluate rosuvastatin rapidmelts by direct compression. As Rosuvastatin comes under BCS class II drug, the solubility of the drug should be increased before formulation. For that solid dispersions were prepared with β-CD, PEG2000, and PEG4000 by using coevaporation and kneading method. Among those solid dispersions prepared with β-CD (1:1.5) by using coevaparation method has given better drug entrapment values compared to other solid dispersions. Those solid dispersions were formulated as rapidmelts by using direct compression method. In direct compression, method rapidmelts were prepared by using super disintegrants like Ludiflash, crosscaramellosesodium, and Lycoat. Those are evaluated for both precompression and post-compression parameters. Rapidmelts prepared with Direct compression method were evaluated for weight variation, hardness, friability, %drug content and disintegration time. Among all the formulations (R1-R9) the rapidmelts prepared with Lycoat (6%)has given better dissolution and disintegration. The best formulation was subjected to stability testing for 6months at 25°C/60%RH and 40°C/75%RH. All the prepared formulations compiled with the pharmacopieal limits.

INTRODUCTION:

Oral route of administration is most convenient route for drug administration. According to the United States, Food and Drug Administration (USFDA) defined rapidmelts as "A solid dosage form containing a medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for rapidmelts generally ranges from several seconds to about a minute". Prescription Rapid melt products initially were developed to overcome the difficulty in swallowing among pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules[1]. Pediatric and geriatric patients may have difficulties in swallowing or chewing pharmaceutical dosage forms for oral administration. Tablets that rapidly

dissolve upon contact with buccal cavity could present a solution to those problems and so there is an increased interest fast dissolving dosage forms for buccal, sublingual and oral administration[2]. Many methods were reported for solubility and dissolution enhancement of poorly soluble drug such as micronization, complexation, solid dispersions, kneading method… etc. Solid dispersions are a technique that depends on melting or dissolution process to disperse one or more active ingredient in a carrier or matrix in the solid state. This ensures increased drug wettability and reduction of particle aggregation and hence increased drug dissolution[3]. Fast dissolving / disintegrating tablets immediately release the active drug when placed upon the tongue by rapid disintegration. The presence of a highly porous surface in the tablet matrix is the key factor for the rapid disintegration of rapidmelts. So, in the present investigation rapidmelts of rosuvastatin were prepared.

Rosuvastatin is widely used in the treatment of hyperlipidemia. It acts as HMG CoA reductase inhibitor. Hyperlipidemic drugs are mainly used to reduce cholesterol levels in patients at risk of cardiovascular disease[4] . Statins generally work via nuclear receptors, Statins may have benefits other than just lowering cholesterol, they have anti-inflammatory properties, which help stabilize the lining of blood vessels [5].Rosuvastatin is practically insoluble in water and crystalline compound. Dissolution is the rate-limiting step that controls oral absorption. Therefore, improvement in solubility and dissolution rate is essential to enhance drug bioavailability. As Rosuvastatin comes under BCS class II drug solid dispersions of rosuvastatin were prepared by using different polymers in different ratios by using different techniques to enhance the solubility of the drug. Then those solid dispersions were formulated as rapidmelts by using different super disintegrants using direct compression method.

MATERIALS AND METHODS:

MATERIALS: Rosuvastatin was obtained as a gift sample from Dr.Reddy's Laboratories Ltd. Hyderabad. β-cyclodextrin, PEG2000, PEG4000, Ludiflash, croscarmellose sodium, lycoat, magnesium stearate, aerosil, microcrystalline cellulose, camphor menthol, ammonium bicarbonate were kindly supplied by BMR pharma and chemicals. All the other solvents used were analytical grade.

METHODS:

Calibration procedure: Determination of λmax of Rosuvastatin using 6.8 pH buffer:A solution of Rosuvastatin containing the concentration of 10µg/ml was prepared in 6.8 pH buffer and UV spectrum was taken. The solution was scanned in the range of 200- 400nm.

Standard calibration curve of Rosuvastatin using 6.8 pH buffer Method:10 mg drug was taken accurately in 10ml volumetric flask. It was dissolved in 6.8 pH buffer to gives 1000 µg /ml. the standard stock solution stock solution was then serially diluted with 6.8 pH buffer to get 5 to 30 µg/ml of Rosuvastatin. The absorbance was measured against 6.8 pH buffer as blank at 246 nm using UV spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

Phase solubility studies for Rosuvastatin: The aqueous solubility of pure drug powder was determined at 37±0.5 ºC in distilled water, various buffers, and water. Solubility was measured by shaking an excess amount of pure drug in 100mL of water until equilibrium was attained. Solute and solvent

were placed in a stopper conical flask immersed in a thermostated water bath and agitated continuously for 24 hrs. The temperature during agitation was kept at 37±0.5 ºC. After 24 hrs, the solution was filtered through a Millipore filter (0.22µm). It was diluted sufficiently with water and absorbance was recorded at 243nm by UV-Visible spectrophotometry.

Preparation of solid dispersions:

Solvent evaporation method: Drug and polymers were mixed in different ratios (1:0.5,1:1,1:1.5) in a mortar. Methanol was added in proportion wise with constant and continuous stirring until the mixture was completely dissolved. Methanol was evaporated under constant stirring and resultant solid dispersions were collected.

Kneading method:

In a mortar, 50% solvent was taken to that add the calculated amount of polymer and is triturated to get slurry-like consistency. Then the drug was incorporated, remaining solvent was added and trituration is continued for 1hr, air dried at 40 ºC for 48hrs and the resulting dried product was pulverized and passed through a mesh sieve. **Drug entrapment efficiency:** Percentage yield was determined by weighing the dried solid dispersion and calculated with respect to the weight of the initial components according to the following formula;

%Yield = [mass of solid dispersion / (mass of drug + mass of lipid substances)] ×100.

Ten milligrams of each solid dispersion were weighed in glass Stoppard tubes and redispersed in 3 ml distilled water. The dispersion was then lysed with 1ml chloroform to allow for the complete release of the entrapped drug. Complete extraction of the drug was facilitated by shaking the tubes for 6 hrs in water bath shaker at 37 ºC. The samples were centrifuged at 6000 rpm for 5 min and then allowed to stand for complete separation of the two phases. The collected aqueous solutions were analyzed for determining the drug concentration as previously described. Drug concentration was also used for determining % encapsulation efficiency according to the following formula

% Encapsulation efficiency = (actual drug loading/ theoretical drug loading) × 100.

Preparation of Rosuvastatin Rapidmelts:

Rosuvastatin rapidmelts were prepared by using direct compression and sublimation methods.

Direct compression method: Solid dispersions equivalent to10mg were taken. Rapidmelts were prepared by using superdisintegrants CCS, Ludiflash, Lycoat (2,4,6%). All the ingredients were passed through the mesh. Then all the ingredients were mixed in geometric order and the tablets were compressed with 12mm size round Punch.

Pre compression Parameters: The various characteristics of blends to be conducted before compression are as follows:

Angle of Repose: Angle of repose (θ) was determined using the fixed funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the granular cone was measured and angle of repose was calculated using the following equation:

$\tan \theta = h/r$

Where h and r are the height and radius of the cone.

Bulk density and Tapped density: A suitable amount of powder from each formulation, previously lightly shaken to break agglomerates formed, was introduced into a 10 ml measuring cylinder. After initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from a height of 2.5 cm at 2-second intervals. The tapping was continued until no further change in volume was noted. Bulk density = weight of the powder/volume of the packing

Tapped density = weight of the powder / tapped volume of the packing

Carr's index: The compressibility index of the powder blend was determined by the Carr's index. It is a simple test to evaluate the bulk density and tapped density of a powder and the rate at which its packed down. Carr's index = (tapped density – bulk density/tapped density) X 100

Hausner's ratio:Hausner's ratio was calculated from the bulk and tapped density of Rosuvastatin blend powder formulation and it is expressed as: Hausner's ratio = tapped density / bulk density

Post Compression Parameters:

Hardness: Hardness is defined as the resistance of the tablet against the applied force till it breaks.Hardness indicates the ability of a tablet to withstand mechanical shocks while packaging, handling, and transportation. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2.

Weight Variation: To ensure the uniformity of tablets weight variation test was carried out. Twenty tablets were randomly selected from each formulation and separately weighed. Their average weight and (±SD) were calculated.

Friability: Friability of the tablet determined using Roche friabilator. This device subjects the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablet at the height of 6 inches in each revolution. A preweighed sample of tablets was placed in friabilator and was subjected to 100 revolutions. Tablets were dusted. After 100 revolutions the tablets were reweighed.

Then calculate friability by the given equation.

$$F= (1-Wo/W)\ 100$$

Wo = weight of the tablet before the test,
W = weight of the tablet after the test.

In vitro disintegration time: The in vitro disintegration studies were carried out using a digital tablet disintegration test apparatus. One tablet was placed in each of the 6 tubes of the basket assembly and the disk was added to each tube. This assembly was then suspended in a 1-liter beaker containing water with its temperature being maintained at 37±2℃. The basket was then moved up and down through a distance of 5 to 6 cm, at the frequency of 28 to 32 cycles per minute. The time required for the complete disintegration of the tablet was recorded. It is expressed in seconds.

In vitro dissolution studies: The dissolution profiles of rapidmelts were determined in a dissolution tester, apparatus II. All tests were conducted in 900ml phosphate buffer pH6.8 containing 0.5%SLS at a temperature of 37±0.5 ºC with a paddle rotation speed at 50rpm. At specified time intervals 1,5,10,15,20,25, 30,35,40,45 and 50min; 5mlof dissolution medium was withdrawn and replaced with an equal Volume of medium to maintain a constant total volume. Samples were filtered through a 0.45 µm Milliporefilter and assayed for

drug content spectrophotometrically at 243nm.

Drug – Excipient compatibility study:

DSC: The DSC can be used to obtain the thermal critical points like melting point, enthalpy specific heat or glass transition temperature of substances. The sample and an empty reference crucible is heated at constant heat flow. A difference of the temperature of both crucibles is caused by the thermal critical points of the sample and can be detected.

FT-IR studies:Sample/KBr ratio: The concentration of the sample in KBr should be in the range of 0.2% to 1%. The pellet is much thicker than a liquid film, hence a lower concentration in the sample is required (Beer's Law). Too high a concentration usually causes difficulties obtaining clear pellets. The IR beam is absorbed completely or scattered from the sample which results in very noisy spectra.

Sample preparation: Completely dried potassium bromide was transferred into a mortar. About 2 % of drug sample was weighed in digital balance, mixed and grind to a fine powder. Two stainless steel disks were taken out of the desiccator. A piece of the precut cardboard (in the tin can next to the oven) on top of one disk was placed and cutout hole was filled with the finely ground mixture. The second stainless steel disk was kept on top and transfers the sandwich onto the pistil in the hydraulic press. With a pumping movement, hydraulic pump handle moved downward. The pistil will start to move upward until it reaches the top of the pump chamber. Then, the pump handle moved upwards and continued pumping until the pressure reaches 20,000 prf. Rest for a few seconds and with the small lever on the left side, the pressure was released. Removing of the disks and pulling apart. Obtained film was homogenous and transparent in appearance. Than inserted into the IR sample holder and attach with scotch tape and run the spectrum.The physical mixtures of drugs were prepared in 1:1 ratio and then passed through sieve # 30. The compatibility of drugs with excipients was studied by FT-IR.

Stability Studies: In order to study the stability of the rapidmelts, representative samples of the were packed in amber colored airtight glass containers and they were stored in stability chambers maintained at 25°C/60 % RH and 40°C/75 % RH. The physicochemical properties of these samples were analyzed at 0, 3 and 6 months. At each time point, one container was taken out from the respective storage conditions and subjected to content uniformity and dissolution rate studies.

RESULTS & DISCUSSION:

Calibration curve for Rosuvastatin:

The method obeyed Beer's law in the concentration range of 5-30µg/ml. The value of 'r' was found to be 0.9994, indicating a positive correlation between the concentration of Rosuvastatin and the corresponding absorbance values. The values of m and C were found to be 0.0285, 0.0119. The values were given in Table 1 were found to be very low which indicated that the method used for the study was reproducible. The amount of Rosuvastatin in formulations or dissolution fluids was calculated using the corresponding m values or directly from the respective standard graph, shown in **Fig1.**

Phase solubility studies: The phase solubility studies of the pure drug were done in different solvents (water,0.1N HCl, pH6.8 phosphate buffer) given in **Table 2**. From the result, it was concluded that Rosuvastatin drug is more soluble in phosphate buffer.

Drug entrapment efficiency: From the drug entrapment values it was observed that

solid dispersions prepared with coevaporation method were better entrapped compared to kneading method. The solid dispersions prepared with Rosuvastatin and β-CD (1:1.5) has given better entrapment in all the solid dispersions. So that solid dispersion was selected for the formulation of drug using direct compression method. The drug entrapment values were given in the **Table5.** Among both the methods cosolvent evaporation was found to be good compared to kneading method.

Formulation of tablets using Direct compression method: The solid dispersions prepared using solvent evaporation method was collected and formulated as rapid melts using excipients by Direct compression. The formulation of rosuvastatin rapid melts using direct compression was given in **Tables6.**

Evaluation of rapidmelts:

Precompression parameters: These parameters are important for the measurement of flow properties of powders. The powder has shown the angle of repose values between 25-28 º. It indicates the excellent flow of a powder. Carr's index was found to be between 8-14(%) and Hausner's ratio values are between 1.09-1.16. These indicate good flow of powder. The results were shown in the **Table 7**.

Post-compression parameters:

Hardness: All the formulations were evaluated for hardness using Monsanto hardness tester and the data was given in the**Table8**.The average hardness was found to be between 3-5.5kg/cm^2, which was found to be within the IPlimits.

Weight variation*:* All the formulations were evaluated for uniformity of weight and the results were given in the **Table8**. The average weight of all the formulations was found to be in the range of 196.58±0.20to 199.36±0.05mg.

Drug content: All the formulations were evaluated for drug content according to the procedure described in methodology. Assay values of the formulations prepared by using direct compression method were found to be in the range of 96.23±0.20 to 99.65±0.10(%).According to IP standards, the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all rapid melt formulations comply with the standards given in IP.

Friability: Rapidmelts were evaluated for their %friability using Roche friabilator. The friability of the formulations prepared by using direct compression method was found to be in the range 0.15±0.10to 0.61±0.11(%). The average %friability was found to be less than1%. It indicates the good mechanical strength of tablets.

In-vitro **Disintegration time:** Disintegration time was found to be between 45-120sec.The disintegration time of the formulations prepared by using direct compression method was found to be in the range 46±5 to 94±3(sec). These results indicate that increasing the concentration of superdisintegrants disintegrating time of the tablet was decreased. According to the pharmacopieal standards, the dispersible tablet must disintegrate within 3 min. All the formulation has shown disintegration time less than 3min.so these formulations are suitable for formulating rapidmelts.

In-vitrodissolutionstudies:

Formulations from R1-R9 were prepared using superdisintegrants (Ludiflash, CCS, Lycoat) by direct compression methodwere evaluated for *invitro* dissolution studies and the results were shown in the **Table9**. The result exhibit a direct relationship between concentration of superdisintegrants and drug release. Among the various formulations R7 prepared with Ludiflash(6%) has given 100%drug release in 25min.

Calibration curve for Rosuvastatin:

Concentration (µg/ml)	Absorbance
0	0
5	0.120
10	0.275
15	0.412
20	0.554
25	0.702
30	0.851

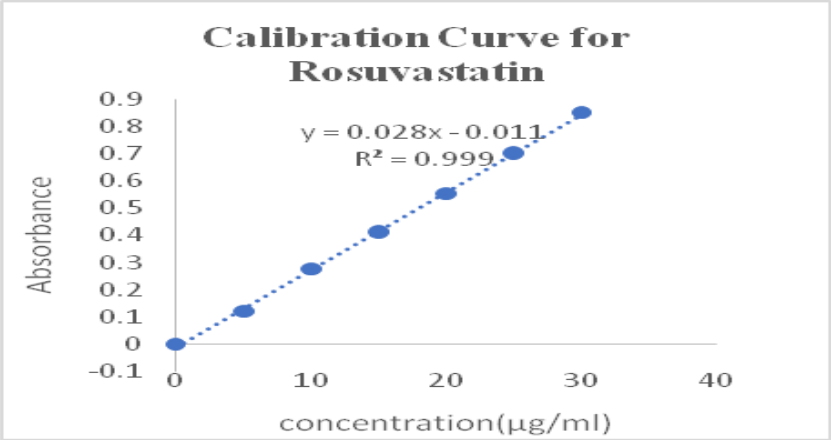

Table 1 & Fig 1: Calibration Curve For Rosuvastatin

Table2: Phase solubility studies for Rosuvastatin:

Solvent	Solubility (mg/ml)
Water	0.047
0.1 N HCl	0.148
P^H 6.8 Phosphate buffer	0.216

Table 3: Preparation of solid dispersions of Rosuvastatin by using Cosolvent evaporation method:

Excipients	**1:0.5(ROS1)**	**1:1(ROS2)**	**1:1.5(ROS3)**	**1:0.5(ROS4)**	**1:1(ROS5)**	**1:1.5(ROS6)**
Drug(mg)	500	500	500	500	500	500
β-cyclodextrin(mg)	250	500	750	--	--	--
PEG -2000(mg)	--	--	--	250	500	750
Water and ethanol	Quantity sufficient					

Table 4: Preparation of solid dispersions of Rosuvastatin by using kneading method:

Excipients	**1:0.5(ROS1)**	**1:1(ROS2)**	**1:1.5(ROS3)**	**1:0.5(ROS4)**	**1:1(ROS5)**	**1:1.5(ROS6)**
Drug(mg)	500	500	500	500	500	500
β-cyclodextrin(mg)	250	500	750	--	--	--
PEG4000(mg)	--	--	--	250	500	750
Water and ethanol	Quantity sufficient for paste formation					

Table 5: Drug Entrapment efficiency values:

Solid Dispersion	Cosolvent method	Kneading method
ROS1	76.50	71.63
ROS2	78.26	73.30
ROS3	79.98	75.59
ROS4	65.11	59.94
ROS5	67.02	62.23
ROS6	70.20	64.97

Table 6: Formulation of Rosuvastatin rapid melts by Direct compression method:

Excipient name	R1	R2	R3	R4	R5	R6	R7	R8	R9
Equivalent SD(mg)	50.01	50.01	50.01	50.01	50.01	50.01	50.01	50.01	50.01
Ludiflash(mg)	4	--	--	8	--	--	12	--	--
CCS(mg)	--	4	--	--	8	--	--	12	--
Lycoat(mg)	--	--	4	--	--	8	--	--	12
Mg Stearate(mg)	3	3	3	3	3	3	3	3	3
Aerosil(mg)	2	2	2	2	2	2	2	2	2
MCC(mg)	QS	QS	QS	QS	QS	QS	QS	QS	QS
Total weight(mg)	200	200	200	200	200	200	200	200	200

Table7: Preformulation parameters for rapidmelts by direct compression method:

Formulation code	Angle of repose(°)	Bulk density(mg/cm^3)	Tapped Density(mg/cm^3)	Carr'sIndex(%)	Hausner's ratio
R1	27.41±0.01	0.54±0.01	0.62±0.10	12.90±0.01	1.14±0.01
R2	26.48±0.11	0.52±0.05	0.58±0.01	10.34±0.21	1.11±0.20
R3	26.61±0.05	0.51±0.10	0.58±0.05	12.06±0.11	1.13±0.03
R4	25.20±0.11	0.55±0.06	0.64±0.021	14.06±0.05	1.16±0.05
R5	26.99±0.06	0.53±0.02	0.61±0.06	13.11±0.08	1.15±0.15
R6	27.74±0.02	0.58±0.04	0.66±0.21	12.12±0.10	1.13±0.20
R7	27.88±0.10	0.57±0.10	0.65±0.24	12.30±0.20	1.14±0.11
R8	26.56±0.20	0.51±0.20	0.56±0.20	8.92±0.15	1.09±0.12
R9	28.80±0.04	0.55±0.11	0.62±0.10	11.29±0.11	1.12±0.10

Table 8: Post compression parameters for rapidmelts by direct compression method:

Formulation code	Hardness (kg\cm^2)	Weight variation(mg)	Drug content(%)	Friability(%)	Disintegration time(sec)
R1	3.96±0.01	199.36±0.05	96.78±0.01	0.25±0.10	79±2
R2	4.02±0.10	198.30±0.02	97.13±0.02	0.31±0.02	85±5
R3	4.10±0.11	198.89±0.14	96.23±0.20	0.19±0.06	94±3
R4	3.88±0.05	199.12±0.11	98.45±0.14	0.36±0.01	62±6
R5	3.95±0.02	197.82±0.15	97.60±0.11	0.49±0.08	70±8
R6	4.05±0.15	199.02±0.06	99.65±0.16	0.22±0.09	82±1
R7	4.23±0.12	198.56±0.02	98.54±0.11	0.15±0.10	46±5
R8	3.87±0.05	197.78±0.20	97.02±0.13	0.30±0.12	65±2
R9	3.99±0.20	198.80±0.03	99.23±0.11	0.61±0.11	77±1

Table 9: Cumulative %drug release for formulations prepared using direct compression:

Time(min)	R1	R2	R3	R4	R5	R6	R7	R8	R9
0	0	0	0	0	0	0	0	0	0
5	30.21±0.01	16.36±0.02	18.50±0.01	28.9±0.10	21.65±0.10	25.98±0.20	42.5±0.01	38.58±0.02	38.98±0.01
10	49.25±0.05	44.24±0.03	25.25±0.12	48.54±0.15	51.15±0.12	33.65±0.01	58.90±0.05	58.98±0.20	47.65±0.10
15	65.55±0.10	50.54±0.04	30.54±0.20	55.65±0.05	60.25±0.11	48.96±0.15	73.66±0.06	65.55±0.03	55.52±0.23
20	70.62±.05	60.54±0.20	45.23±0.05	68.72±0.20	65.33±0.20	52.25±0.10	88.38±0.20	72.73±0.10	65.56±0.15
25	78.11±0.15	70.30±.12	56.35±0.10	78.29±0.03	72.34±0.15	63.5±0.13	100.26±0.05	85.59±0.15	70.54±0.12
30	85.25±0.20	78.64±0.10	67.59±0.13	91.95±0.15	85.81±0.13	72.56±0.05	---	99.55±0.06	75.96±0.11
35	99.89±0.06	85.39±0.01	78.50±0.05	99.69±0.11	96.55±0.12	83.65±0.12	---	---	----
/40	----	98.88±0.03	87.54±0.04	----	99.59±0.02	95.95±0.03	-----	---	---
45	----	----	93.5±0.01	----	----	99.99±0.05	---	----	----
50	----	---	98.98±0.20	----	----	----	----	---	----

Table 10: Percent drug dissolved at 10 min (D_{10}) and Dissolution Efficiency (DE) values of Rosuvastatin from various formulations and in comparison, with the pure drug:

Formulation code	D10 (%)	DE5%	DE10%
R1	49.25±0.05	15.105	27.41
R2	44.24±0.03	8.18	14.49
R3	25.25±0.12	9.25	15.56
R4	48.54±0.15	14.45	26.58
R5	51.45±0.12	10.825	23.31
R6	33.65±0.01	12.99	21.40
R7	58.90±0.05	21.25	35.97
R8	58.98±0.20	19.29	34.04
R9	47.65±0.10	19.49	31.40

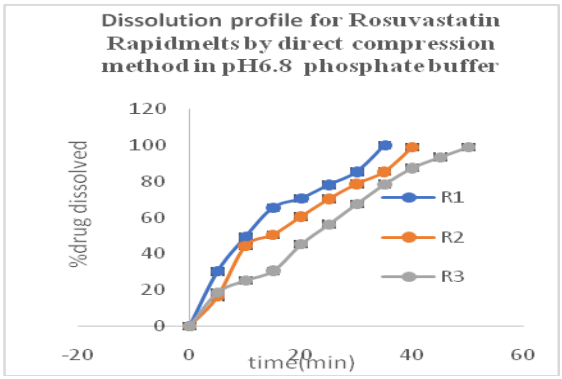

Fig2: Dissolution profile for Rosuvastatin rapidmelts using Ludiflash, CCS and lycoat (2%) by direct compression method

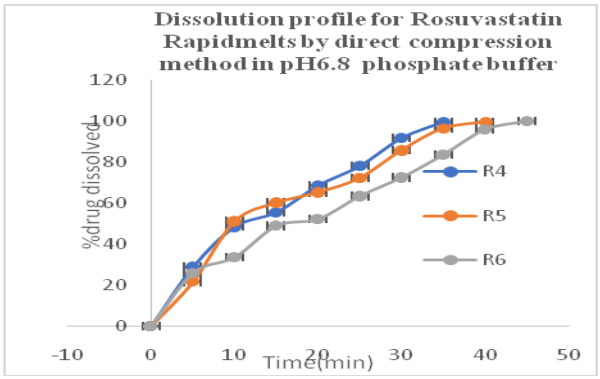

Fig3: Dissolution profile for Rosuvastatin Rapidmelts using ludiflash, CCS, Lycoat(4%) by direct compression method

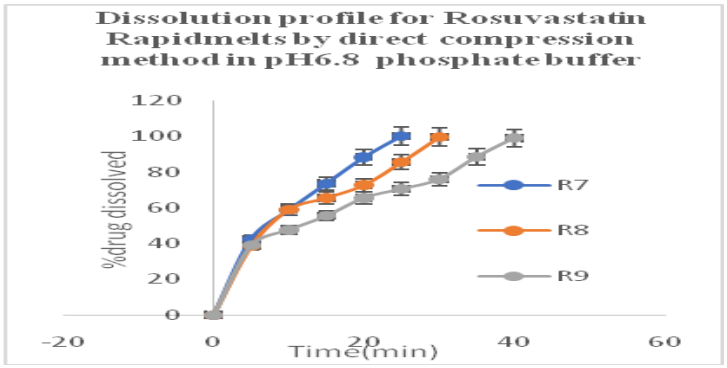

Fig4:Dissolution profile for Rosuvastatin rapidmelts using ludiflash,CCS,lycoat (6%) by direct compression method

Table 11: Stability studies:

Time(Min)	%Dissolution rate	25^0C/60 % RH (Dissolution rate after storage) %		40^0C/75 % RH (Dissolution rate after storage) %	
		3Months	6Months	3Months	6Months
0	0	0	0	0	0
5	42.5±0.01	42.7±0.02	42.7±0.05	43.0±0.01	43.5±0.02
10	58.90±0.05	57.91±0.02	58.94±0.05	57.9±0.07	58.8±0.02
15	73.66±0.06	73.65±0.05	73.62±0.05	72.06±0.06	71.05±0.08
20	88.38±0.20	88.34±0.05	87.35±0.02	88.31±0.08	87.31±0.01
25	100.26±0.05	100.24±0.02	100.06±0.05	101.02±0.06	100.21±0.08

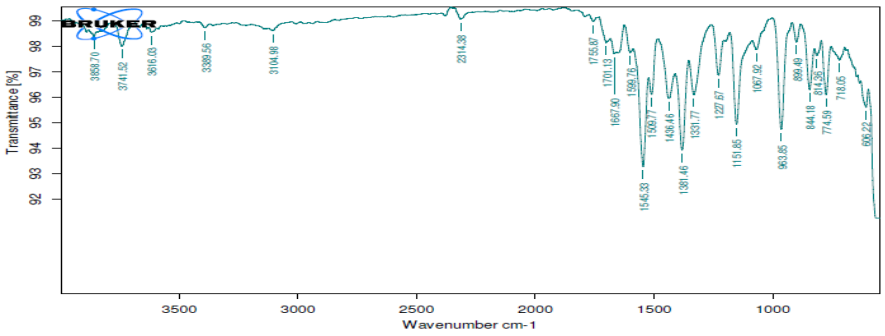

Fig 5: FTIR PURE ROSUVASTATIN

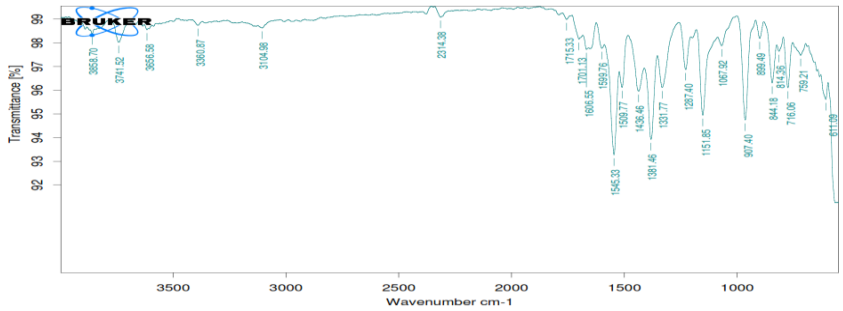

Fig 6: FTIR OPTIMIZED ROSUVASTATIN

DSC Studies:

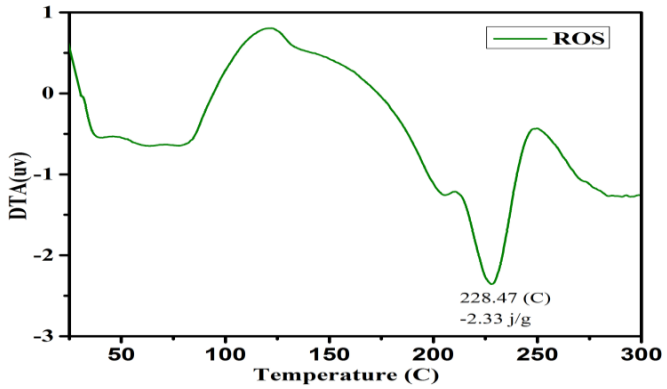

Fig 7: DSC for rosuvastatin pure drug

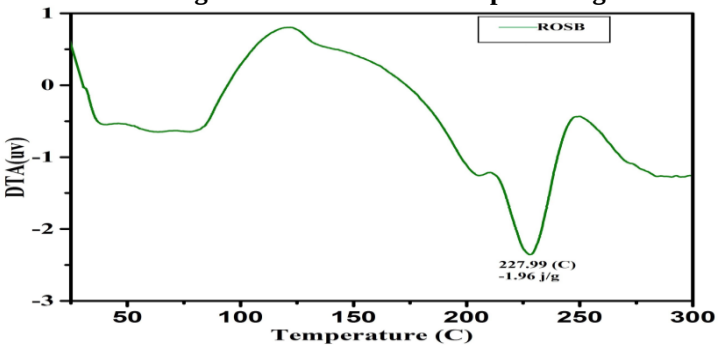

Fig 8: DSC for rosuvastatin optimized formulation

Stability studies: Hence, based upon evaluation parameters and drug release profiles R12 was selected as optimized and subjected to stability studies and stored at 25°C/60 % RH and 40°C/75 % RH (ICH,2003). The samples were withdrawn at 0, 3, 6 months and Rosuvastatin rapidmelts were found to be stable. When the samples were withdrawn after 3 and 6 months (for both conditions) no color change was observed. The amounts of Rosuvastatin (%) in the rapidmelts stored under conditions according to ICH guidelines are given in **Table11.** Stability studies revealed that there is no significant changes were observed throughout the study. So we can say that formulation has good stability.

FTIR studies:

When we observe the **Fig.13** FTIR spectra, the drug, exhibited peaks at 3858$cm^{-1}$for amide N-H stretch,3104cm^{-1} for =C-H,1545$cm^{-1}$for C=C stretching,1331.77$cm^{-1}$for C-N stretching,,774cm^{-1} for aromatic C=H bending. The same peaks of the drug were observed in the FTIR spectra of the rapidmelts **fig6**. Thereby ruling the absence of drug-polymer interaction from the obtained results. So further studies were performed based on these results. Fourier transform infrared spectroscopy analysis was performed to pure drug and optimized formulation and presented in **Fig 5&6**.

DSC studies:

The thermogram of pure drug Rosuvastatin has given endothermic peak at 227.9ºC.The Thermogram of rapidmelts has given endothermic peak at 228.47ºC.DSC thermograms for pure drug and optimized formulation were given in **Fig 7 and 8**. Peaks indicating that there were no interactions between drug and excipients.

CONCLUSION:

In the present work an attempt was made to formulate rapidmelts of Rosuvastatin using direct compression and sublimation methods. The IR spectra and DSC studies revealed that there is no interaction between superdisintegrants and drug. As Rosuvastatin comes under BCS class II solubility of Rosuvastatin was enhanced by preparing solid dispersions. The prepared solid dispersions were formulated as rapidmelts with superdisintegrants (Ludiflash, CCS and Lycoat) using direct compression method. The prepared blends were evaluated for precompression studies such as bulk density, tapped density, Carr's index, Hausner's ratio, the angle of repose. They were found to be within limits. After completion of precompression studies required powder blend was weighed and compressed using tablet compression machine. They were kept for post-compression studies such as weight variation, hardness, friability, *in-vitro* disintegration and dissolution studies.

The result of physical parameters by direct compression has shown good flow properties. Various concentrations of superdisintegrants have given quicker disintegration. Formulation R7 optimized formulation having least disintegration time and 100%dissolution in 25min.From the result it was concluded that formulated tablets(R7) were more effective.

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