FORMULATION AND EVALUATION OF IMMEDIATE RELEASE TABLET OF ROSUVASTATIN CALCIUM BY LIQUISOLID COMPACT TECHNIQUE

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ABSTRACT AND KEYWORDS

i. ABSTRACT

The in-vitro dissolution property of poorly water soluble Rosuvastatin calcium was improved by exploring the potential of Liquisolid compact technique. In this technique, liquid medications of water-insoluble drugs in liquid vehicles (non-volatile solvents) can be converted into acceptably flowing and compressible powders. Different liquisolid compacts were prepared using the required quantities of powder and liquid ingredients to produce acceptably flowable and compressible admixture. To improve aqueous solubility as well as poor dissolution rate of Rosuvastatin calcium, Propylene glycol was selected as non- volatile Solvent, Anhydrous dibasic calcium phosphate and Syloid 244FP was selected as carrier and coating material respectively. The formulated liquisolid system were evaluated for their various pre-compression and post-compression parameters. From the results, it was found that solubility and drug release increased with lower drug concentration. Optimized formulation LS1 showed satisfactory results of cumulative percentage release (88.98±0.80% at 30 min., 98.27±2.0% at 60 min.). The selected formulation (LS1) was found to be stable at 40 ± 0.5 °C and 75 ± 5% RH during the test period of 1 month. From this study it concludes that, the liquisolid technique is a promising technique for improvement of dissolution property of poorly water-soluble drugs and formulating immediate release solid dosage forms.

ii. KEYWORDS

Liquisolid compacts, Rosuvastatin calcium, Immediate release, Solubility, Dissolution rate.

1. INTRODUCTION

An ideal dosage regimen in the drug therapy of any disease or the goal of any drug delivery system is the one, which immediately attains the desired therapeutic concentration of drug in plasma.[1,2] Rosuvastatin calcium is a HMG Co-A reductase inhibitor used for the treatment of the Primary hyperlipidemia, mixed dyslipidemia and hypertriglyceridemia. Rosuvastatin calcium belongs to class-II drug in BCS classification i.e. low solubility and high permeability. BCS class-II drugs pose challenging problems in their pharmaceutical product development process because of their lower solubility and dissolution rates. Therapeutic effectiveness of a drug depends on the bioavailability and ultimately upon the solubility and dissolution rate of drug molecules. Solubility and dissolution rate are the important parameters to achieve desired concentration of drug in systemic circulation for pharmaceutical response to be shown. One of the major problems with this drug is its low solubility in biological fluids, which results into poor bioavailability after oral administration. The solubility of Rosuvastatin calcium in aqueous medium was very low. The bioavailability of Rosuvastatin was approx 20 % and that results into poor bioavailability after oral administration. Thus increasing aqueous solubility and dissolution rate of Rosuvastatin calcium is of therapeutic importance.[3,4,5]

Now days, many techniques can be adapted for the solubility enhancement of poorly soluble drugs to increase dissolution rate and solve the bioavailability issue. Such methodas includes salt formation, Solid dispersion, micronisation, lyophilisation, solubilization by surfactants, solid solutions, co-solvency, micellar solubilization, inclusion complex, PH adjustment, liquisolid compact etc.[6] There are some practical limitations of the above mentioned techniques. In the Salt formation there may increase hygroscopicity which may leads to stability problems. Solubilization of drugs in aqueous media or in any organic solvents, by the use of cosolvents or surfactants leads to formulations that are usually unsuitable from patient acceptability. In complexation, if high molecular size complexing agent is used then, there is increase in size of dosage form. If the ratio of drug and complexing agent increase,

there is a chance of toxicity. In miscellar solubilization, higher amount of surfactant concentration may leads to palatability problems and toxic effects. Solid dispersion has shown good results in enhancement of solubility and dissolution rate of the drugs. However, there are only a few solid dispersion products are commercially available and solid dispersion prepared by melting technique may leads to stability problems.[7]

The liquisolid technology or powedered solution technology applied as new formulative system distinguished by its characteristics and ability to improve solubility and dissolution rate of certain poorly soluble drugs. The liquisolid compacts are acceptably flowing and compressible powdered forms of liquid medications. The term "liquid medication" comprise the solutions or the suspensions of water insoluble solid drugs incorporated in suitable nonvolatile solvent systems termed as the liquid vehicles. Using this novel formulation technique "A liquisolid compact technique", a drug in liquid form may be converted into a dry-looking, non-adherent, acceptably flowing and readily compressible powder through a simple blending with selected powder excipients termed as the carrier and coating materials.[8,9]

liquisolid technology provides a platform for solubility enhancement due to the presence of drug in a molecularly dispersed form in a non-volatile solvent as well as high effective surface area, along with better flowability and compressibility due to use of directly compressible carrier and coat material. As the vehicle used is non-volatile, the drug in solution always remains in molecularly dispersed form. Liquisolid compacts promotes dissolution rate of water insoluble drugs to a greater extent and solubilizing vehicle shows enhanced drug release due to an increased surface area of drug available for release, an increased aqueous solubility of the drug and an improved wettability of the drug particles. Accordingly, this improved drug release may result in a higher drug absorption in the gastrointestinal tract and thus, an improved oral bioavailability.[10-14]

2. MATERIALS AND METHODS

2.1. Materials

Rosuvastatin calcium was obtained as a gift sample from Amneal pharmaceuticals, Ahmedabad. Aerosil 200, Propylene glycol, PEG 200, PEG 400, Castor oil, and Sodium starch glycolate were obtained from ACS chemicals, Ahmedabad. Glycerin, Span 80, Tween 20, Tween 80, and Anhydrous dibasic calcium phosphate were obtained from S.D fines,

Mumbai. Avicel PH101 and PH102 were obtained from Otto chemie private limited, Mumbai. Syloid 244FP was obtained from Loba chemie, Mumbai.

2.2. Drug-excipient compatibility study

FTIR absorption spectra of the pure drug and physical mixture of drug and excipient were recorded in the range of 4000-400 cm^{-1} by KBr disc method using FTIR spectrophotometer.

2.3. Preparation of liquisolid compacts

2.3.1. Selection of liquid vehicle

To find out the best non-volatile solvent or liquid vehicle for dissolving or suspending Rosuvastatin calcium in liquid medication, solubility studies of Rosuvastatin calcium were carried out in different non-volatile solvents. Saturated solutions were prepared in screw cap vial by adding excess drug to the non-volatile solvent and shaking on the shaker for 24 hour at 25 ^{o}C under constant vibration and speed 50 rpm. After 24 hour the solutions were centrifuged and supernant was taken and filtered, diluted with methanol and analyzed by UV-spectrophotometer (Shimadzu-1800, Japan) at a wavelength of 244 nm against blank sample.[15]

2.3.2. Flowable liquid-retention potential determination

To the 10 g of each of carrier and coating material, increasing amount of liquid vehicle was added and mix well. The corresponding Φ-value was calculated from the following equation after every addition of the non-volatile liquid:

Φ value =Weight of liquid (g) / Weight of solid (g)

The Φ-values were plotted graphically against the corresponding angle of slide. The Φ-value corresponding to 33^{o} was recorded as the flowable liquid retention potential of carrier and coating materials. The carrier and coating material with maximum liquid retention potential have been selected as optimum.[15]

2.3.3. Calculation for amount of carrier and coating material

The amount of carrier and coating material was calculated using following formula:

L_f = Φ CARRIER + Φ COATING (1/R)

Q=W/L_f

q=Q/R

Where, L_f represents liquid load factor, Φ CARRIER represents flowable retention potential for carrier material, Φ COATING represents flowable retention potential for coating material, R represents excipient ratio, W represents weight of liquid vehicle, Q represents weight of carrier material, and q represents weight of coating material.[12,17,18]

2.4. Preparation of liquisolid tablets

The drug was initially dispersed into non volatile systems termed as liquid vehicles at different concentration. To this liquid system, the calculated amount of the carrier was added by continuous mixing in the mortar. Then, coating material carefully added and mixed until mortar contents starts to look like dry powder. To above binary mixture disintegrant and lubricant are added and mixed well in mortar. All liquisolid preparations were compacted into tablets using a rotary press tablet machine with a suitable compression force that provide acceptable tablet hardness.[12,17]

2.5. Evaluation of liquisolid tablets[18,19,20]

2.5.1. Pre-compression evaluation parameters

Hausner's ratio

It is the ratio of tapped density to bulk density.

Carr's index

Carr's index was calculated as 100 times the ratio of the difference between the tapped density and bulk density to the tapped density.

Angle of repose

It is defined as the angle between the surfaces of a pile of powder and horizontal plane. Angle of repose was calculated using the following formula:

Angle of repose (θ) = $\tan^{-1}$ (h / r)

2.5.2. Post-compression evaluation parameters

Hardness

The monsanto hardness tester was used to determine the tablet hardness. The tablet was held between a fixed and moving jaw. Scale was adjusted to zero and load was gradually increased until the tablet fractured. The value of the load at that point gives a measure of hardness of the tablet. Hardness was expressed in kg/cm^2.

Weight variation

Twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. Not more than two tablets deviate from the percentage given below from the average weight and none deviate by more than twice the percentage shown.

Friability (F)

Friability of the tablet determined using roche friabilator. Roche friabilator consist of plastic chamber in which the tablets were dropped from the height of 6 inches. Pre-weighted tablets were placed in the friabilator and subjected to the 100 revolutions. After 100 revolutions tablets were dedusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage. Friability was calculated using the following formula:

$$\% \textbf{ Friability} = \frac{[(\textbf{Initial weight of the tablets} - \textbf{Final weight of the tablets})]}{\textbf{Initial weight of the tablets}} \textbf{ X 100}$$

Disintegration test

The disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus with lid on upper side and the time (seconds) taken for complete disintegration of the tablet in 0.1N HCl at 37 ±0.5 °C with no palatable mass remaining in the apparatus was measured.

Content uniformity

Twenty tablets were weighted and powdered in a mortar. Accurately weighted a quantity of the powder equivalent to about 10 mg of rosuvastatin calcium, add 10 ml methanol and

diluted to 100 ml with 0.1N HCl in 100 ml volumetric flask. It was shaken for 15 minutes and filtered. 1 ml of the filtrate was diluted to 10 ml with 0.1N HCl. The absorbance of the resulting solution was measured using UV spectrophotometric method at 244 nm wavelength and the content of rosuvastatin calcium was calculated from calibration curve.

In-vitro dissolution studies

The USP type-II paddle apparatus was used for all the in vitro dissolution studies. The rate of stirring was 50±2 rpm. The dosage forms were placed in 900 ml of 0.1 N HCl and maintained at 37±0.1°C. At appropriate intervals (10, 20, 30, 40, 50 and 60), 5ml of the samples were taken and filtered through a membrane filter. The dissolution media (0.1 N HCl) was then replaced by 5ml of fresh dissolution fluid to maintain a constant volume. After proper dilution, the samples were then analyzed at 244 nm by Shimadzu UV-1800 double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a calibration curve.

2.6. Formulation layout

2.6.1. Preliminary trials for optimization of R-value

Table 2.1: Formulation batches for optimization of R-value

Batch	Drug conc. Cd (%w/w)	R (Excipient ratio)	Lf (Liquid load factor)	W (mg) (Propylene glycol)	Q (mg) (Anhydrous DCP)	q (mg) (Syloid 244FP)	Total weight (mg)
R1	10	5	0.361	100	277.00	55.40	476.98
R2	10	10	0.315	100	317.46	31.74	495.13
R3	10	15	0.300	100	333.33	22.22	501.98
R4	10	20	0.292	100	342.46	17.12	506.33
R5	10	25	0.288	100	347.22	13.88	507.98
R6	10	30	0.285	100	350.87	11.69	509.55

***All the batches contains,** 10 mg Rosuvastatin calcium, 5% of SSG, 2% Magnesium stearate and 1% of Talc.

2.6.2. Preliminary trials for optimization of drug concentration

Table 2.2: Formulation batches for optimization of drug concentration

Batch	Drug conc. Cd (%w/w)	R (Excipient ratio)	Lf (Liquid load factor)	W (mg) (Propylene glycol)	Q (mg) (Anhydrous DCP)	q (mg) (Syloid 244FP)	Total weight (mg)
D1	10	5	0.361	100	277.00	55.40	476.98
D2	20	5	0.361	50	138.50	27.70	243.49
D3	30	5	0.361	33.3	92.32	18.46	165.60
D4	40	5	0.361	25	69.25	13.85	126.74

***All the batches contain,** 10 mg Rosuvastatin calcium, 5% of SSG, 2% Magnesium stearate and 1% of Talc.

2.6.3. Experimental layout for 3^2 full factorial design

Table 2.3: Composition of drug and excipients in 3^2 factorial design

Batch code	Drug conc. (%w/w)	R (Excipient ratio)	L_f (Liquid load factor)	W (mg) (Propylene glycol)	Q (mg) (Anhydrous DCP)	q (mg) (Syloid 244FP)	Total weight (mg)
LS1	10	5	0.361	100	277.00	55.40	476.98
LS2	13	5	0.361	77	213.29	42.65	369.55
LS3	16	5	0.361	63	174.51	34.90	304.19
LS4	10	10	0.315	100	317.46	31.74	495.13
LS5	13	10	0.315	77	244.44	24.44	383.53
LS6	16	10	0.315	63	200.00	20.00	315.64
LS7	10	15	0.300	100	333.33	22.22	501.98
LS8	13	15	0.300	77	256.66	17.11	388.81
LS9	16	15	0.300	63	210.00	14.00	319.96

All the batches contain, 10 mg Rosuvastatin calcium, 5% of SSG, 2% magnesium stearate and 1% of Talc.

2.7. Stability study of optimized batch

To determine the change in physical properties and in-vitro release profile on storage, optimized batch tablets were stored at 40 ºC ± 0.5 ºC temperature and 75% ± 5% relative humidity in stability chamber. Samples were evaluated after 1 month for in-vitro drug release study, hardness and friability.

3. RESULTS AND DISCUSSION

3.1. Drug-Excipient compatibility study

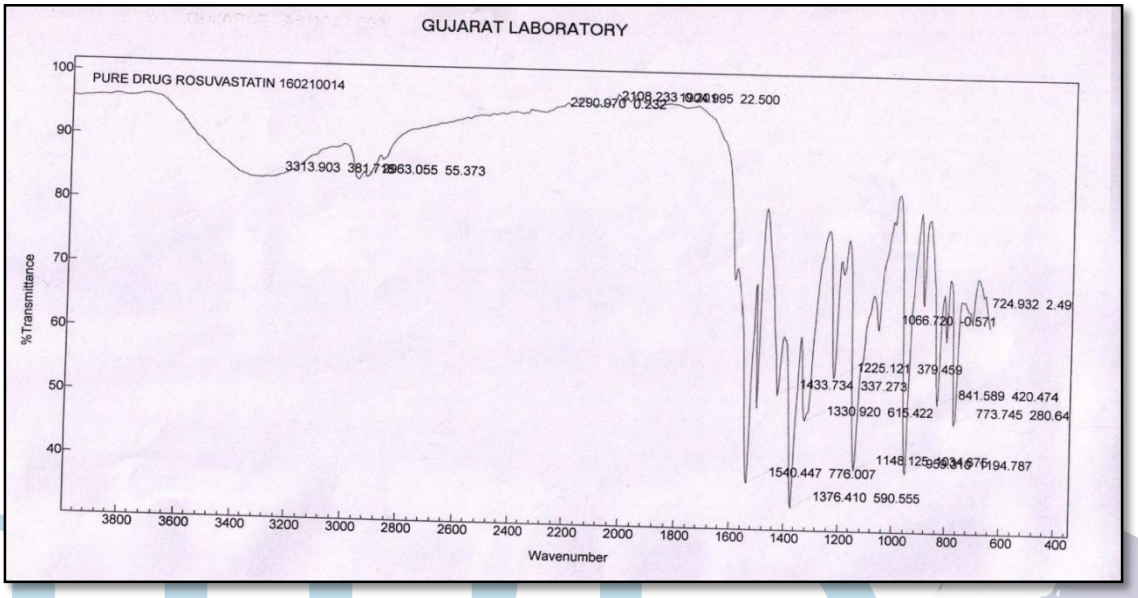

Figure 3.1: FT-IR spectrum of Rosuvastatin calcium

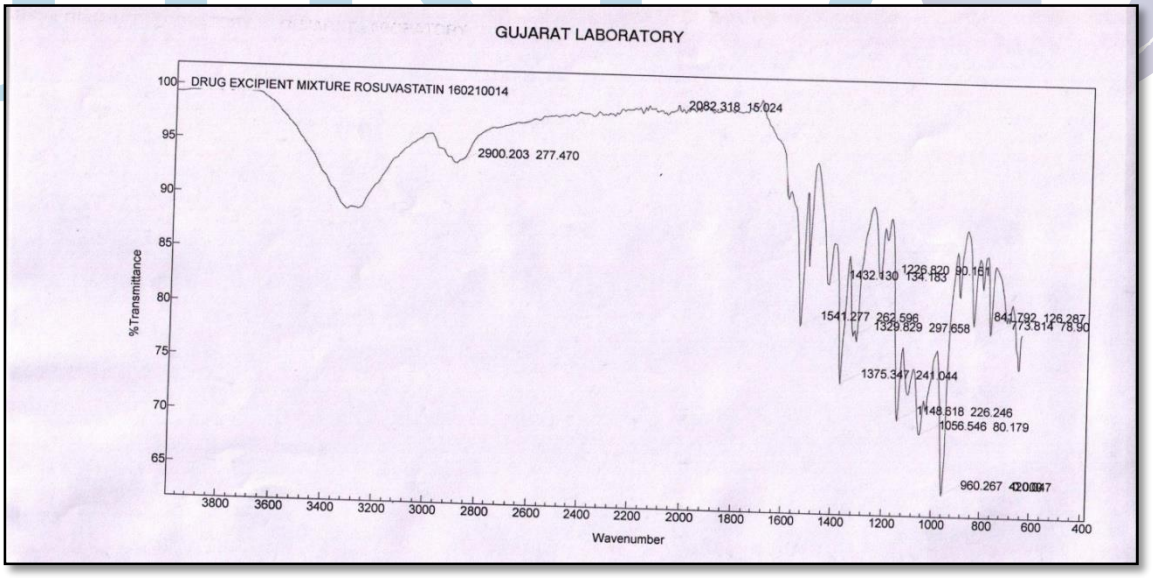

Figure 3.2: FT-IR spectrum of physical mixture of excipients and Rosuvastatin calcium

From the IR spectrum of pure rosuvastatin calcium, an absorption band was observed at the peaks 2963.055 cm^{-1} (C-H, str), 1376.410 cm^{-1} (C=F, str), 1066.720 cm^{-1} (S=O, str) which are the characteristic peaks of rosuvastatin calcium and were not affected and prominently observed in IR spectra of rosuvastatin calcium along with liquid vehicle and carrier materials.

Characteristic peak of the individual excipients were also retained, also no new peak was found in drug loaded mixture of the excipients to be formulated in liquisolid compacts. This indicates that there is no interaction between the drug and excipients.

3.2. Solubility studies

Table 3.1: Solubility study of Rosuvastatin calcium

Sr. no.	Name of solvent	Solubility (mg/ml) ± SD*
1	Tween 80	8.46 ± 1.98
2	Tween 20	4.86 ± 1.81
3	Span 80	11.37 ± 1.40
4	Propylene glycol	20.74 ± 0.2
5	PEG 200	16.57 ± 1.07
6	glycerin	7.56 ± 1.11
7	PEG 400	9.52 ± 1.16
8	Water	0.44 ± 0.23
9	Castor oil	3.71 ± 0.9

*** Values are mean ± SD, (n=3)**

The solubility of Rosuvastatin calcium in various non-volatile solvent is given in Table 5.6. The results shows that the solubility of Rosuvastatin calcium in Propylene glycol is higher in comparison with other solvent. For this reason, Propylene glycol was selected to be the suitable solvents for preparing Rosuvastatin calcium liquisolid compacts.

3.3. Selection of carrier and coating material

Angle of slide for carrier and coating material was used to determine flowable liquid retention potential, which are needed for calculation of the liquid load factor (Lf). Angle of slide had preferred over the other methods, e.g. angle of repose, to determine the flow properties of powder excipients and liquid/powder admixtures. The validity of angle of slide has been proven to be effective.

Table 3.2. Flowable liquid retention potential

Carrier materials	Flowable liquid retention potential (Φ-value at 33º)	Coating materials	Flowable liquid retention potential (Φ-value at 33º)
Avicel 101	0.210	**Syloid 244FP**	**0.455**
Avicel 102	0.146	Aerosil 200	0.410
Anhydrous DCP	**0.270**	-	-

The results shows that Phi-value corresponding to an angle of slide of 33° was higher for anhydrous dibasic calcium phosphate and syloid 244FP as carrier and coating material, respectively. So, anhydrous dibasic calcium phosphate and syloid 244FP was selected as carrier and coating material respectively for the formulation of rosuvastatin calcium liquisolid compacts.

3.4. Evaluation of preliminary trials and factorial batches

3.4.1. Evaluation of preliminary trials for optimization of R-value

To optimize R value i.e. ratio of carrier and coating material, different batches R1, R2, R3, R4, R5 and R6 were prepared which contain different value of R. In this preparation the drug concentration was remained same as i.e. 10 %. The prepared batches were evaluated for various pre and post-compression parameters.

Table 3.3: Evaluation parameter for optimize R-value

Batch	Angle of Repose *	Carr's Index *	Hardness (kg/cm2) *	Friability (%)*	Disinteg-ration time (sec)*	% Drug Content *	Weight Variation *	% CPR at 30 min	% CPR at 60 min
R1	22.69 ±0.80	11.12 ±0.44	4.5±0.4	0.48 ±0.03	82±0.2	98.81 ±1.12	PASS	88.98± 0.80	98.27 ±2.0
R2	26.26 ±1.06	13.56 ±0.50	4.6±0.4	0.55±0.02	88±0.2	98.25 ±1.56	PASS	86.93± 2.45	96.89 ±2.03
R3	28.45 ±0.05	13.11 ±0.12	4.6±0.5	0.66±0.02	94±0.4	96.66 ±2.45	PASS	85.48± 0.65	93.11 ±0.04
R4	31.52 ±1.23	14.81 ±0.49	4.8±0.4	0.55±0.02	112±0.5	96.90 ±1.89	PASS	79.25± 0.12	87.73 ±0.6
R5	37.76 ±1.55	16.57 ±0.52	4.5±0.2	0.61±0.02	117±0.6	98.02 ±1.74	PASS	71.78± 0.22	82.70 ±0.05
R6	41.40 ±1.06	19.53 ±0.37	4.6±0.4	0.60±0.01	126±0.4	94.12 ±1.45	PASS	65.24± 0.52	75.53 ±1.45

*** Values are mean ± SD, (n=3)**

The results shows that the highest drug release were obtained with **R1** batch which was prepared by taking R-value 5. The cumulative percentage release of all batches at different time interval were depicted in figure 3.3.

3.4.2. Evaluation of preliminary trials for optimization of Drug concentration

To optimize the drug concentration, different batches D1, D2, D3, D4 were prepared which contain different percentage of drug concentration. In this preparation the R value was remained same. The prepared batches were evaluated for various pre and post-compression parameters. Here in the 5 % of drug concentration, the tablet with sufficient hardness was not formed, hence the range of drug concentration was selected from 10 to 40.

Table 3.4: Evaluation parameters for optimize Drug concentration

Batch	Angle of Repose * (θ)	Carr's Index*	Hardness (kg/cm2) *	Friability (%)*	Disinteg-ration time (sec)*	% Drug content *	Weight variation *	% CPR at 30 min	% CPR at 60 min
D1	22.69 ±0.20	11.12 ±0.44	4.5±0.4	0.48 ±0.03	82±0.2	98.81 ±1.12	PASS	88.98 ±0.80	98.27 ±2.40
D2	25.50 ±0.50	13.3 ±0.37	4.6±0.3	0.55±0.02	90±0.6	96.25 ±1.56	PASS	81.93 ±2.45	95.89 ±2.03
D3	30.30 ±0.70	15.2 ±0.12	4.5±0.2	0.67±0.01	96±0.8	94.06 ±2.45	PASS	71.48 ±0.65	88.11 ±0.04
D4	31.08 ±0.92	14.4 ±0.49	4.2±0.3	0.68±0.1	105±0.5	89.90 ±1.89	PASS	66.25 ±0.12	78.73 ±0.60

*** Values are mean ± SD, (n=3)**

The results shows that the highest drug release were obtained with **D1** batch which was prepared by taking drug concentration 10% w/w. The cumulative percentage release of all batches at different time interval were depicted in figure 3.4.

3.4.3. Evaluation of factorial batches

The carrier : coating ratio and drug concentration play a crucial role in the preparation of liquisolid compacts. Three level two factor full factorial design (3^2 factorial design) useful to study the effect of independent variables (Anhydrous DCP : Syloid 244FP ratio and drug concentration) on responses such as angle of repose, carr's index, hausner's ratio, %friability, solubility, dissolution and disintegration Time. Based on preliminary trials, two factors and their levels were determined as follows: Drug concentration (X1): 10-16 and Anhydrous DCP : Syloid 244FP (X2): 5-15% w/w.

From the evalution of various pre and post compression parameters, it is conclude that **LS1** is comes under the standard value of above mention parameter as well as it has highest cumulative percentage release at 30 min and 60 min obtained were 88.98±0.80 and

98.27±2.0, respectively. The cumulative percentage release of all factorial batches at different time interval were depicted in figure 3.5.

Table 3.5: Evaluation Parameters of batches LS1 to LS9

Batch	Carr's Index *	Hausner's ratio*	Angle of repose (θ)*	Hardness* (kg/cm2)	Weight variation*
LS1	11.12±0.44	1.22±0.23	22.69±0.80	4.5±0.4	PASS
LS2	13.78±0.25	1.30±0.54	29.40±0.65	4.5±0.5	PASS
LS3	18.68±1.54	1.34±0.87	33.12±0.84	4.5±0.3	PASS
LS4	12.56±0.50	1.24±0.32	26.26±1.06	4.6±0.4	PASS
LS5	20.02±0.54	1.32±0.87	31.12±0.25	4.6±0.1	PASS
LS6	21.05±0.74	1.40±0.21	39.28±0.04	4.6±0.6	PASS
LS7	13.11±0.12	1.26±0.39	28.45±0.05	4.6±0.5	PASS
LS8	22.23±0.32	1.36±0.58	36.32±0.21	4.6±0.2	PASS
LS9	23.05±0.11	1.42±0.32	43.25±0.08	4.32±0.2	PASS

*** Values are mean ± SD, (n=3)**

Table 3.6: Evaluation Parameters of batches LS1 to LS9

Batch	% friability*	Drug content* (%)	Disintegration time* (sec)	% CPR at 30 min	% CPR at 60 min
LS1	0.48±0.03	98.81±1.12	82±0.2	88.98±0.80	98.27±2.0
LS2	0.53±0.05	97.35±1.32	97±0.5	82.48±0.81	91.11±0.98
LS3	0.74±0.07	95.32±0.80	106±0.32	75.39±0.64	85.77±0.24
LS4	0.55±0.02	98.25±1.56	88±0.4	86.93±2.45	96.89±2.03
LS5	0.37±0.07	96.41±0.32	101±0.45	76.84±0.53	87.32±0.64
LS6	0.48±0.02	98.19±0.11	121±0.32	72.22±0.32	81.21±1.21
LS7	0.66±0.02	96.66±2.45	94±0.2	85.48±0.65	93.11±0.04
LS8	0.64±0.09	97.32±0.87	113±0.2	74.45±0.36	84.21±0.65
LS9	0.53±0.07	94.32±1.02	127±0.61	70.84±0.74	77.14±0.54

*** Values are mean ± SD, (n=3)**

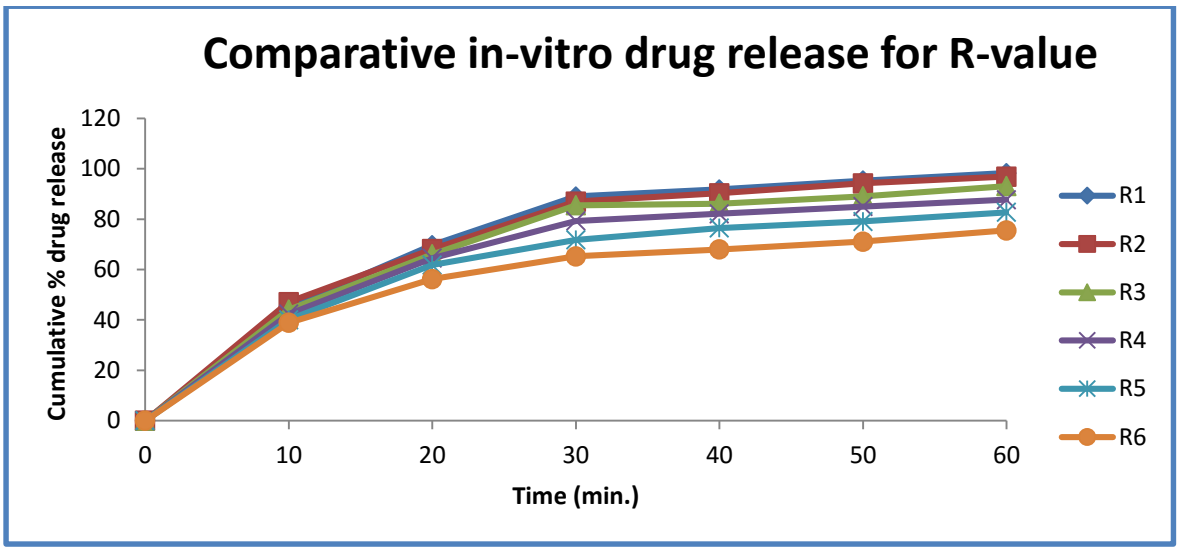

Figure 3.3: Dissolution profile of Rosuvastatin calcium with different R-value.

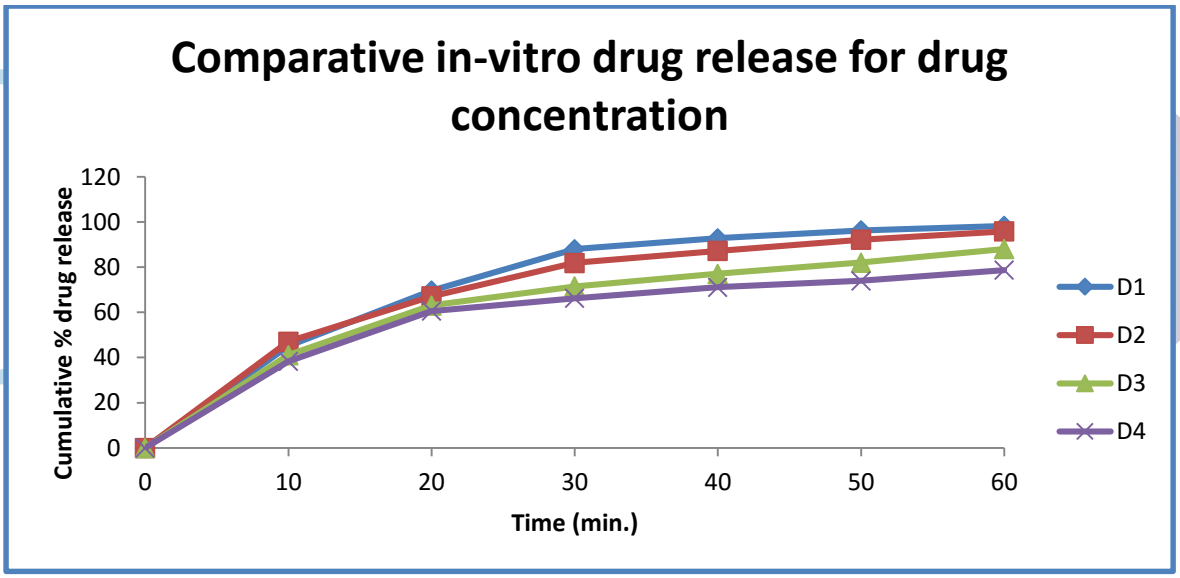

Figure 3.4: Dissolution profile of Rosuvastatin calcium with different drug concentration

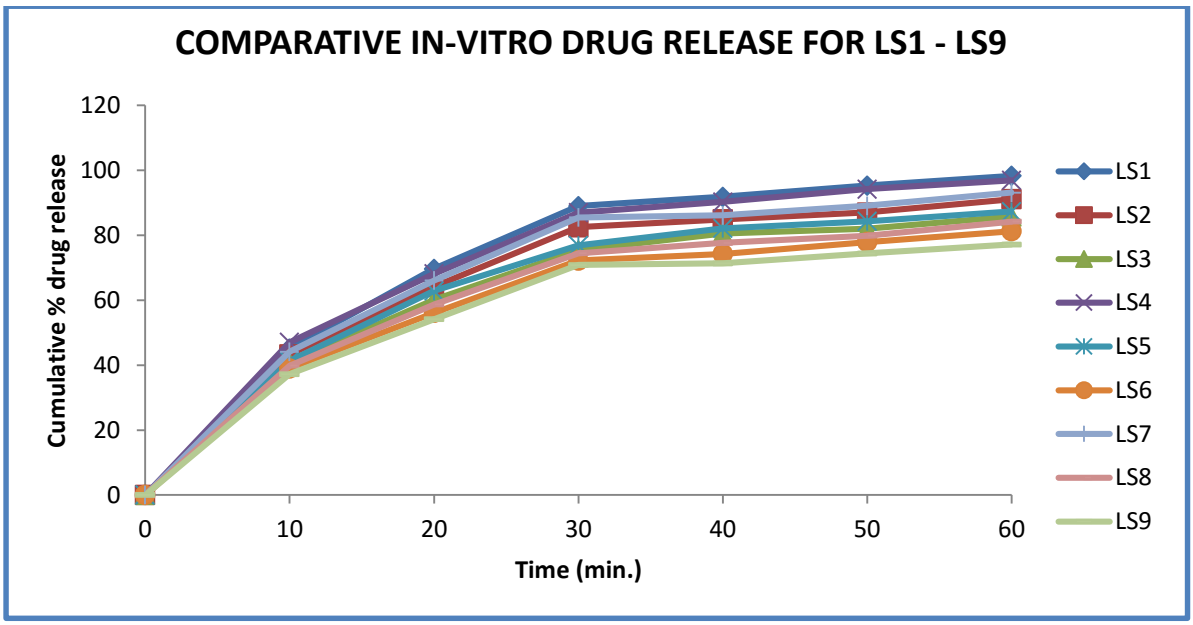

Figure 3.5: Dissolution profile of different factorial batches

3.5. Stability study

The tablets were stored for 1 month at 40ºC ± 0.5 ºC temperature and 75% ± 5% relative humidity. The result do not show any significant change in physical appearance, hardness, %friability and cumulative percentage release in comparison with initial values. The results of initial value and after 1 month are shown in table 3.7. Comparison of in-vitro drug release between initial results and results after 1 monts were depicted in figure 3.6.

Table 3.7: Evaluation of optimize formulation kept for stability study at 40ºC and 75% RH

Parameters	Initial	After 1 months
Friability	0.48±0.03	0.52±0.17
CPR at 30 min	88.98±0.80	85.93±0.83
CPR at 60 min	98.27±2.0	94.05±0.89
Hardness	4.5±0.4	4.1±0.5

*** Values are mean ± SD, (n=3)**

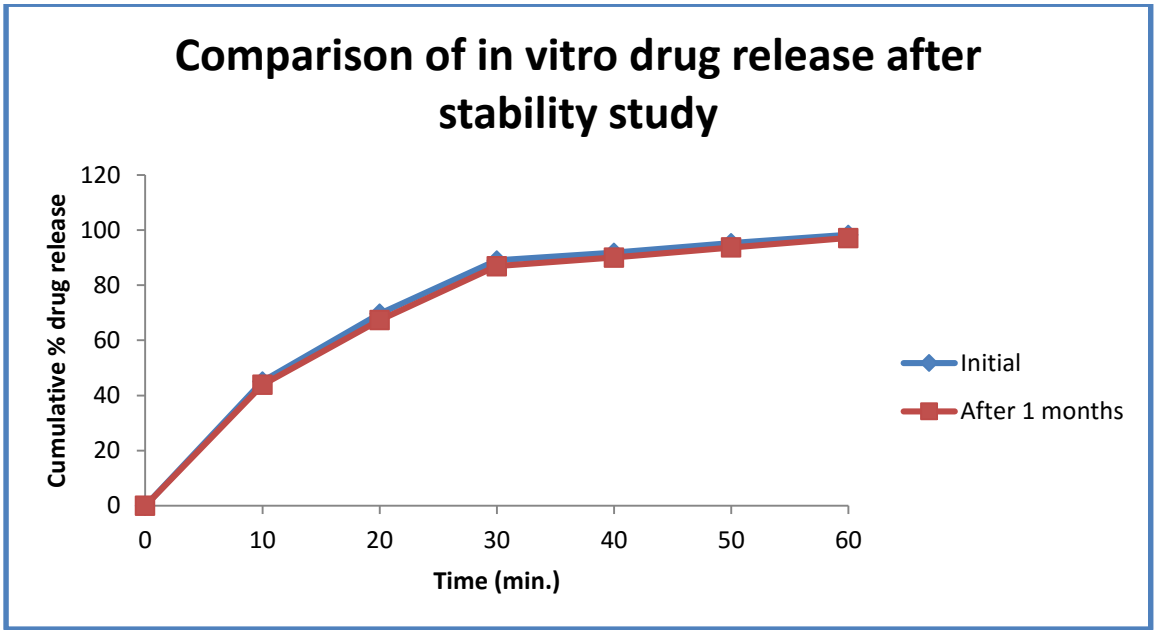

Figure 3.6: Comparison of in-vitro drug release after stability study

4. CONCLUSION

The present study has been satisfactory attempt to prepare immediate release tablets of rosuvastatin calcium by using liquisolid compact technique as well as to improve flow characteristics, solubility and dissolution characteristics of rosuvastatin calcium as it has low aqueous solubility. Liquisolid compacts of rosuvastatin calcium were prepared by using propylene glycol, anhydrous dibasic calcium phosphate and syloid 244FP showed improved flow characteristics, solubility and dissolution profiles. The solubility of the rosuvastatin calcium higher with lower drug concentration. The flow property, angle of repose were improved at R value of 5. The optimized LS1 batch showed highest in-vitro dissolution compared to other batches. The formulation remained stable when checked effect of storage condition through stability study.

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