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FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLET OF ROSUVASTATIN USING CASSIA TORA SEEDS MUCILAGE AS NATURAL SUPERDISINTEGRANT

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ABSTRACT:

The present research work was to develop the preparation of orodispersible tablet of Rosuvastatin by Direct compression method using different concentration of Cassia tora seeds mucilage as natural superdisintegrants. A two-factor-three-level (3^2) factorial design is being used to optimize the nine formulation batches (F_1-F_9) were prepared accordingly. Two factors as independent variables (X_1- amount of β-cyclodextrine and X_2- amount of cassia tora seeds mucilage) were taken with three level (+1, 0, -1). The in-vitro drug release, Disintegration time and wetting time used as dependent variable (Response). All the active blends were evaluated for precompression parameters and the tablets were evaluated for post compression parameter (weight variation, Hardness, Thickness, Friability, Disintegration time, Drug content, wetting time, water absorption ratio and in-vitro drug studies). It was found that the drug:β-cyclodextrine inclusion complex leads to improved the dissolution characteristics and solubility of drug at optimum concentration (1:5) but as the concentration of Cassia tora seeds mucilage powder that significant effect on disintegration characteristics as well as drug release but the higher concentration of mucilage had negative impact on drug release & disintegration time. So, considered the result, it was found that the formulation F6 was found to be optimized formulation. It was observed from the F_6 which showed the disintegration time 26.05±0.249 sec and percentage cumulative drug release showed 96.8±0.629 % within a 15 minutes.

Keywords: Orodispersible Tablet, Rosuvastatin, Superdisntegrants, Cassia tora seeds, Solubility.

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INTRODUCTION

Oral delivery is current standard in the pharmaceutical industry wherever it is regarded as the safest, most suitable and most economical method of drug delivery. [1] The oral cavity is an attractive site for the administration of drugs because of ease of administration. [2]

Oro-dispersible drug delivery system are novel drug delivery techniques that make the tablets disintegrate in the mouth without chewing and water, and immediate release and enhanced bioavailability, with better patient compliance. [3, 4]

Recently, the European Pharmacopeia adopted new term that is orodispersible tablet that disintegrates/ disperses rapidly in the mouth within a minute or second without need of drinking water or chewing.

The United States Food and Drug Administration (USFDA) describe Oro-dispersible tablet as "a solid dosage form that containing active ingredient or medicinal substances which disintegrate /dissolve rapidly within the seconds when tablet placed upon the tongue. [5, 6]

Oro-dispersible tablets have a quick dissolution and rapid absorption which provide rapid onset of action. Furthermore, drug candidates that undergo pregastric absorption when formulated as ODTs may oral bioavailability of drug is improved by avoiding the hepatic first pass metabolism. It provides good stability, accurate dosing, easy of manufacturing. [7, 8]

Recent time of the market studies that indicates the more of the patient population that prefers the orodispersible tablets rather than other dosage forms and most consumers would ask their doctors for orodispersible tablets (70%), purchase ODTs (70%), or prefer ODTs to regular tablets or liquids (> 80%).[9]

MATERIAL AND METHODS

Materials

Rosuvastatin and Beta-Cyclodextrin were obtained as gift sample from Alkem Laboratories Ltd. (Mumbai). Cassia tora seeds were purchased from local market (Indore). Microcrastalline cellulose, Mannitol, Magnessium Stearate, Talc, Acetonitrile, Ethanol, Methanol, Potassium chloride and Silica gel-G were purchased from Lobachem Pvt. Ltd. And

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Aspartame, Potassium Dihydrogen phosphate, sodium hydroxide, Hydrochloric acid were purchased from Merck Pvt. Ltd.

METHOD:

PREFORMULATION STUDY

Drug Characterization:

Determination of wavelength using UV-visible spectroscopy:

10 mg was weighed and dissolved into 10 ml of Phosphate buffer solution (PH 6.8) to prepare a 1000µg/ml stock solution from which a 5µg/ml dilution was prepared. Baseline correction was performed using Phosphate buffer solution (PH 6.8) and sample was scanned between 200-400nm and wavelength of maximum absorbance (λmax) was noted. [10]

Preparation of calibration curves:

Calibration curve of rosuvastatin in phosphate buffer pH 6.8:

- **Preparation of stock solution**

  Accurately weighed 100mg of Rosuvastatin was transferred into a 100ml volumetric flask & dissolved. Then sonicated for 15 minute and the volume was made up with phosphate buffer pH 6.8 to obtain a 1000µg/ml stock solution of Rosuvastatin, From the stock solution, 1ml was taken into a 10ml volumetric flask and volume was made up with phosphate buffer pH 6.8 to obtained a 100µg/ml of solution.

- **Preparation of dilution**

  From 100µg/ml solution the appropriate aliquot of 0.2ml, 0.4ml, 0.6ml, 0.8ml, 1.0ml, 1.2ml, 1.4ml, 1.6ml, 1.8ml and 2.0ml were taken into different volumetric flask and diluted up to 10ml with phosphate buffer pH 6.8 to get different concentration range 2-20 µg/ml. The absorbance of each dilution was noted. [11]

Determination of solubility of Rosuvastatin in various mediums:

The solubility of Rosuvastatin in various medium was determined by shake flask method. In this method 5ml of each solvent was taken into a vial and an excess amount of Rosuvastatin

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was added. The vials were sealed properly and stirred continuously at 37º ± 2 ºC. After solubilization of Rosuvastatin, an extra amount of Rosuvastatin drug was added to the vials containing drug-solvent mixture and stirred for a period of 6 hours (saturation time). The process was repeated until saturation solubility of Rosuvastatin, indicated by presence of undissolved drug. The mixtures were then kept at room temperature for 24 hrs. and the solution were filtered through what man's filter paper. Then diluted with respective solvents i.e. Acetonitrile, phosphate pH buffer 6.8 and pH 1.2 HCl buffer. The drug concentration was analyzed spectrophotometrically at 241.50nm using UV-visible spectrophotometer (Shimadzu-1800). [12, 13]

Extraction of cassia tora seeds mucilage:

The seeds of Cassia tora were dry milled in a mixer to separate the seed coat.The Cassia tora seeds (100 gm) was soaked in distilled water and shaken for 24 hours. The soaked solution was transferred to hot boiling water and boiled for 2 hours to make the solution more concentrated. The viscous solution obtained was filtered through a muslin cloth. Then transferred to an evaporating dish. The obtained mixture was dried in oven at 40–45°C. It was then powdered and passed through sieve number 60 and stored in an airtight container. [14, 15]

Preformulation study

Characterization of Cassia tora seeds mucilage: [16-19]

The prepared Mucilage powder were evaluated in terms of Organoleptic properties, Percentage yield, pH of Mucilage, Solubility of Mucilage, swelling index, Bulk density, Tapped Density , Carr's Index, Angle of Repose and Hausner's Ratio.

Drug-excipient interaction study:

The compatibility of the drug was assessed by drug-excipient interaction study. The drug was mixed with various excipients in a 1:1 ratio in glass vials which were properly sealed & labeled and kept undisturbed at 40°C temperature and 75% RH for 15 days. Physical and chemical observations of all the mixtures were done on initial day and 15th day by TLC. [20]

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Thin layer chromatography: [21]

The stationary phase was prepared by silica gel-G. The mixture of organic solvent Methanol: water (1:1 v/v) was used as mobile phase.

Calculation of Rf value:

Rf value can be calculated by following formula:

Rf= Distance travelled by solute / Distance travelled by solvent

Experimental design for optimization: [22]

A two factor three level factorial design (3^2) was used for the formulation optimization of orodispersible tablet of Rosuvastatin and experimental trials are performed at all 9 possible formulation. In which the amount of β-cyclodextrin (X_1) and cassia tora mucilage (X_2) were selected as independent variables (factor) varied at three different level: low(-1), medium(0), and high(+1) levels. The drug release and disintegration time used as dependent variables (response).

Table No.1 Composition of Orodispersible table

S. No	Name of ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
1.	Drug (Rosuvastatin)	10	10	10	10	10	10	10	10	10
2.	β-cyclodextrin	0	25	50	0	25	50	0	25	50
3.	Cassia tora seed Mucilage	40	40	40	50	50	50	60	60	60
4.	Microcrystalline cellulose	130	130	130	130	130	130	130	130	130
5.	Mannitol	30	30	30	30	30	30	30	30	30
6.	Aspartame	10	10	10	10	10	10	10	10	10
7.	Magnesium Stearate	6	6	6	6	6	6	6	6	6
8.	Talc	4	4	4	4	4	4	4	4	4

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Preparation of inclusion complex by kneading method: [23, 24]

10mg of Rosuvastatin with β-CD in different ratio was taken. β-cyclodextrin was taken to the mortar-pestle in a small quantity of 50% ethanol was added while triturating to get slurry like consistency. Subsequently drug was incorporated slowly into the slurry and trituration was further continued for one hour. Slurry is then air dried at 25°C for 24 hours, pulverized and passed through sieve no. #60.

Preparation of orodispersible tablet by direct compression:

Orodispersible tablet of Rosuvastatin were prepared by direct compression method. Weighed all the ingredients accurately according to the table no.6.4. All the ingredients were mixed step by step with drug:β-cyclodextrin inclusion complex except formulation (F1, F4 and F7 i.e. only drug was mixed in it) and triturated continued for 15 minute. Then passed through sieve no. #40. Subsequently talc, magnesium stearate shifted via sieve no. 60# & mixed again[25]

The powder was compressed using multistation tablet punching machine (Aidmach Pvt. Ltd.) with 8mm flat punch, B-tooling and corresponding dies.

EVALUATION PARAMETER

Precompression Parametres of powder: [26-29]

- **Bulk Density:**

  Bulk density is defined as the total mass of the powder divided by the bulk volume and is expressed as gm/ml. This was calculated by using the formula:

  Bulk Density = weight of powder(in gm) / Bulk Volume of Powder (in ml)

- **Tapped Density:**

  It is the ratio of total mass of the powder to the tapped volume of powder. Tapped density was calculated by using the following formula:

  Tapped Density = weight of powder (in gm) / Tapped Volume of Powder (in ml)

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- **Carr's index:**

  The Carr's index of the powder blend was determined by using the formula:

  Carr's index (%) I = [(Tapped Density- Bulk Density) / Tapped Density] x 100

- **Angle of repose:**

  It was determined by the funnel method. The Weighed powder were taken in a funnel. A funnel is fitted and is secured with its tip at a height (h) of 2 cm above graph paper which is placed on a horizontal surface. The accurately weighed powder were taken and dropped in funnel. The powder blend was allowed to flow through the funnel freely onto the surface. The angle of repose was calculated by measuring the diameter and height of powder cone and putting the values to the following equation.

  $$\theta = \tan^{-1} (h/r)$$

- **Hausner's ratio:**

  If the hausner's ratio is less than 1.25 that indicates free flowing properties whereas more than 1.25 that indicates the poor flow ability. It was calculated by following formula**:**

  Hausner's ratio = Tapped density / Bulk density

Post Compression parameter of orodispersible tablet: [30-32]

- **Weight variation**

The twenty tablets were selected randomly from each formulation and the weight of their average weight was determined. Tablets were weighed individually and compared with average weight.

Percentage weight variation= Individual weight- average weight/ average weight×100

- **Hardness:**

The hardness of the tablet was determined by Monsanto hardness tester. Placed the tablet on the lower plunger and zero reading was taken from Monsanto tester scale. The range of Monsanto hardness tester is "0 to 20" kg. The screw knob was moved forward until the tablet

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breaks and the force required breaking the tablet was noted. There are three tablets of each formulation batch were tested randomly and the average reading was recorded. It is expressed in kg/cm^2.

- **Thickness:**

Thickness of the tablets was calculated by the use of vernier calliper. The scale was set to zero and placed the tablet laterally between the jaws of vernier calliper. Subsequently make certain jaws shall just touch object to be measured. The reading displayed was Record. Take out the sample, clean the jaws and keep the caliper in place. There are three tablet of each formulation batch were checked randomly and standard deviation was measured. It is expressed in mm.

- **Friability:**

Friability of the tablet was determined using Roche friabilator. Tablets were weighed before placing in friability apparatus. Tablets placed on the friabilator and subjected to 100 revolutions for 4 minute at 25 rpm and dropping the tablet at the height of 6 inches in each revolution. The tablet were reweighed and dedusted.

Percentage friability = Initial weight - Final weight / Initial weight × 100

- **Disintegration time:**

First suspend the assembly in the beaker containing 6.8 pH phosphate buffer at 37±0.5°C. The tablet was placed into each of the six tubes of the disintegrating apparatus and one disc was added to each tube. Operated the apparatus until the tablet completely disintegrated. Note down the time taken for the completed disintegration of the tablet without any remitants. Removed the assembly from 6.8 pH phosphate buffer. The tablets were passed the test if all of them have disintegrated.

- **Drug content:**

The drug content was determined by calibration curve method are as follow:

Ten tablets were taken and amount of drug present in each formulation of tablet was determined. The tablet was crushed in a mortar-pestle and equivalent to 10 mg of drug

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was dissolved in phosphate buffer PH 6.8 in a 100ml volumetric flask. Volume was made up to 100ml. The sample was filtered through filter paper. From this solution 1ml were taken in a 10 ml volumetric flask & diluted with phosphate buffer pH 6.8. Further, 1ml were taken were taken and diluted up to 10ml and analyzed for drug content by UV spectrophotometer at 241.5 nm using phosphate buffer (pH 6.8).

- **Wetting time & Water absorption ratio:**

  A piece of tissue paper folded twice was placed in a small petridish containing10 ml of water. A tablet was put on the tissue paper and the time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch.

  For water absorption ratio: The wetted tablets were the reweighed. The water absorption ratio and R was determined using following equation

  $$R = 100 \times Wa\text{-}Wb/Wb \times 100$$

  Where,

  Wa = Weight of the tablet after water absorption

  Wb = Weight of the tablet before water absorption

- **In vitro Drug release study:**

  In vitro Drug release study was determined by dissolution test apparatus. Maintained the water level in the water bath up to the specific mark and adjusted or maintained temperature from heater knob. 900 ml of phosphate buffer pH 6.8 was poured in dissolution vessel and adjusted temperature between 37±0.5^{o}C. The shaft was positioned in such a way that its axis is within 2 mm of axis of the vessel and lower edge of blade was 23-27 mm from the inside of bottom of vessel. The paddles were lowered down. The tablet was put in each vessel and paddle was rotated at 50 rpm for 30 min. Withdrawn 5 ml sample at every 5 minutes interval and replaced by equal volume of fresh dissolution medium. Filtered the samples using what man's filter paper and analyzed for drug release

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of the samples by UV-visible spectrophotometer at λ max 241.5 nm using phosphate buffer pH 6.8 as blank.

6.5 Stability study:

The stability study of orodispersible tablet was studied at different storage condition. The physical stability of orodispersible tablet was observed by visual appearance and chemical stability was observed by TLC. The TLC values with solvent system methanol: water (1:1) and silica gel-G as stationary phase was determined. [33]

RESULT AND DISCUSSION

PREFORMULATION STUDY

Drug Characterization:

Determination of wavelength using UV-visible spectroscopy:

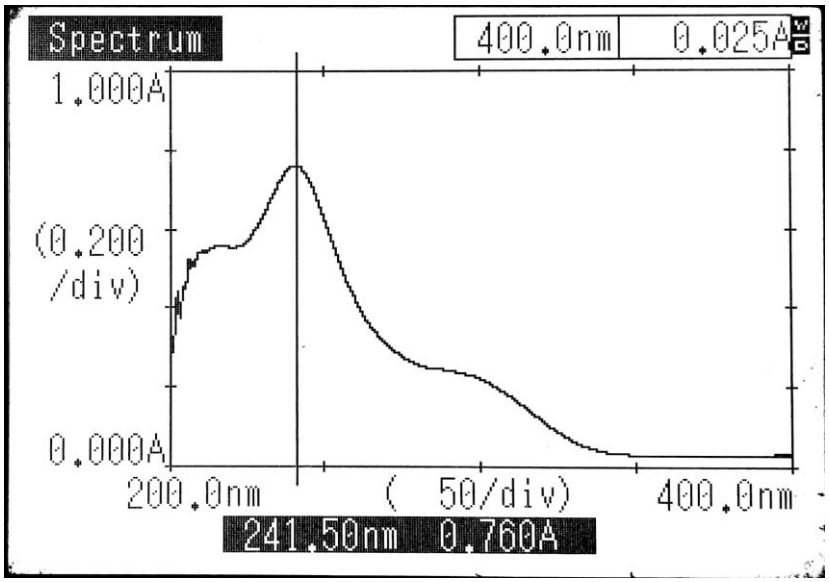

Figure 1: UV Spectrum of Rosuvastatin

The maximum wavelength of Rosuvastatin was found to be 241.5nm.

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Preparation of calibration curve:

Calibration curve of Rosuvastatin in phosphate buffer pH 6.8

The calibration curves of rosuvastatin in phosphate buffer pH 6.8 were prepared and shown below:

Table no.2: Absorbance data of Rosuvastatin in phosphate buffer pH 6.8 for preparation of calibration curve, at 241.5nm

S.No.	Concentration (µg/ml)	Absorbance (mean ± standard deviation)
1	2	0.075±0.021
2	4	0.179±0.017
3	6	0.241±0.026
4	8	0.324±0.017
5	10	0.454±0.023
6	12	0.598±0.033
7	14	0.6320.023
8	16	0.754±0.030
9	18	0.825±0.025
10	20	0.994±0.023

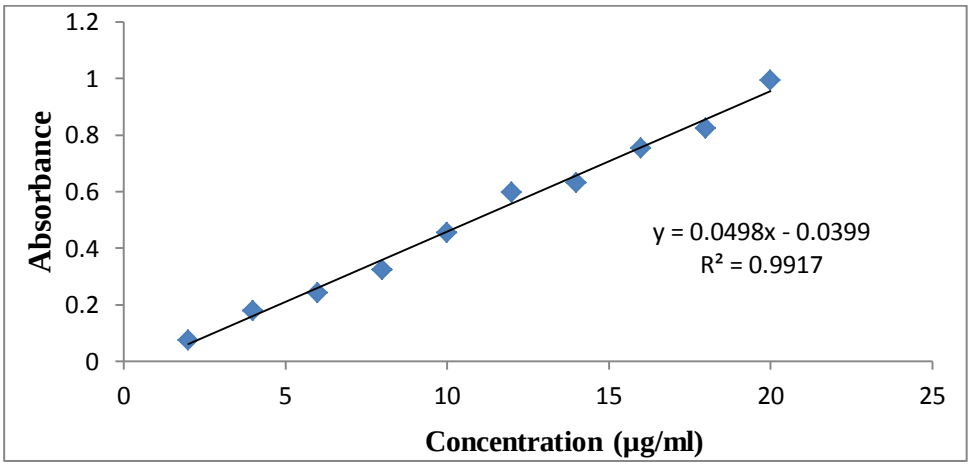

Figure 2: Calibration graph of Rosuvastatin in phosphate buffer pH 6.8 at 241.5nm

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Rosuvastatin in phosphate buffer pH 6.8 follows the Beer–Lambert's law in the concentration range of 2-20 µg/ml.

Determination of solubility of Rosuvastatin in various medium:

The solubility of Rosuvastatin in various mediums was studied and the results of study were shown in below table:

Table no.3: Solubility data of Rosuvastatin in different mediums

S.NO.	Solvent	Solubility (mg/ml) Mean±SD
1	Acetonitrile	127.06±1.721
2	Phosphate buffer pH 6.8	15.41±2.72
3	pH 1.2 HCl buffer	0.527±0.054

Determination of solubility of inclusion complex:

The solubility of inclusion complex in phosphate buffer pH 6.8 was studied and the results of study were shown in below table:

Table no.4: Solubility data of inclusion complex:

S.No.	Phosphate buffer pH 6.8	Solubility (mg/ml) Mean±SD
1	Pure drug	15.41±2.72
2	Drug:β-CD (1:2.5)	34.46±0.802
3	Drug:β-CD (1:5)	46.18±0.776

Characterization of cassia tora mucilage powder: The prepared mucilage powder was evaluated as follows:

Table no.5: Characterization of cassia tora seeds mucilage powder:

S.No.	Parameters	Result
1	Color	Brown
2	Odor	Odorless

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3	Taste	Characteristics
4	Percentage Yield	12.6%±0.416
5	pH of Mucilage	7.2±0.057Ph
6	Solubility of Mucilage	Soluble in hot water and insoluble in organic solvents
7	Swelling Index	11.1±0.795
8	Bulk density	0.357±0.005
9	Tapped density	0.418±0.005
10	Carr's index	14.5±0.208
11	Angle of repose	28.8±0.854
12	Hausner's ratio	1.16±0.005

Drug-excipient interaction study:

The drug (Rosuvastatin) was found to be compatible with various excipients which were selected for formulation of orodispersible tablet. The compatibility was assessed by TLC and the retention factors of all ratios found similar.

Table no.6: Data of drug-excipient interaction study

S.No.	Drug/ drug+ Excipient Ratio (1:1)	Physical appearance (initial)	Present Day (Rf)	Physical appearance (final)	After15 Days (Rf)	Inference
1.	Drug (Rosuvastatin)	White	0.84	White	0.85	No Change
2.	Pure Drug + β-cyclodextrin	White	0.83	White	0.86	No Change
3.	Pure Drug + Mucilage	Light brown	0.89	Light brown	0.80	No Change
4.	Pure Drug + MCC	White	0.87	White	0.89	No Change
5.	Pure Drug + Mannitol	White	0.83	White	0.83	No Change

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6.	Pure Drug+ Aspartame	White	0.88	White	0.87	No Change
7.	Pure Drug + Magnesium stearate	White	0.86	White	0.87	No Change
8.	Pure Drug + Talc	White	0.74	White	0.72	No Change
9.	Pure drug + Mixture	Whitish brown	0.85	Whitish brown	0.87	No Change

Evaluation of post-compression parameters of orodispersible tablet:

The orodispersible tablet of Rosuvastatin were evaluated like weight variation, hardness, thickness, friability, disintegration time, drug content, wetting time and water absorption ratio. The results of the studies were shown in below table:

Table no.7: Weight variation, Hardness, Thickness, and Friability of Formulation F1-F9

Formulation	Weight variation (mg) Mean±SD	Hardness (Kg/cm^2) Mean±SD	Thickness (mm) Mean±SD	Friability (%) Mean±SD
F1	229.5±5.616	2.8±0.057	3.5±0.057	0.442±0.004
F2	259.5±6.86	2.9±0.115	3.7±0.057	0.389±0.002
F3	278.5±5.87	3.0±0.057	3.9±0.1	0.360±0.001
F4	238±6.155	2.9±0.152	3.6±0.115	0.421±0.002
F5	267.5±4.442	3.0±0.1	3.8±0.057	0.374±0.004
F6	289±4.472	3.0±0.057	4.0±0.057	0.348±0.001
F7	250±6.488	3.0±0.057	3.8±0.1	0.405±0.002
F8	279±5.52	3.1±0.1	3.9±0.057	0.360±0.001
F9	299.5±5.104	3.1±0.057	4.1±0.1	0.337±0.002

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Table no.8: Disintegration Time, Drug Content, Wetting time & water absorption Ratio of Formulation F1-F9.

Formu-lation	Disintegration Time (sec) Mean±SD	Drug Content (%) Mean±SD	Wetting time (sec) Mean±SD	water absorption Ratio (%) Mean±SD
F1	32.34±0.307	96.4±1.300	38.97±0.537	21.69±4.30
F2	36.18±0.688	97.87±0.692	41.77±0.309	25.60±2.25
F3	34.02±0.588	98.44±0.722	35.48±0.176	28.54±3.57
F4	30.69±0.578	97.65±0.665	34.47±0.512	33.3±4.2
F5	32.52±0.567	99.37±0.398	39.34±0.686	34.4±2.22
F6	26.24±0.559	98.51±0.843	29.11±0.130	40.9±3.05
F7	29.603±0.511	98.05±0.961	32.04±0.065	41.3±2.30
F8	39.77±0.523	98.33±0.907	47.43±0.691	45.2±2.04
F9	30.57±0.380	97.96±0.057	35.21±0.249	47.76±3.86

In-vitro drug release study of orodispersible tablet:

The percentage cumulative drug release from formulations F1 to F9. The formulation F6 was shows the highest release (96.2%) within 15 minutes

Table no.9: Percentage cumulative drug release data of F1 to F9 formulation of orodispersible tablets:

Time (in min	% Cumulative drug Release (Mean±SD)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	22.2± 0.584	26.7± 0.665	54.3± 0.928	24.4± 0.991	42.0± 0.928	72.2± 0.546	12.9± 0.680	16.4± 0.762	20.3± 1.201
10	32.3± 0.694	41.3± 1.363	63.1± 0.408	34.7± 1.411	51.9± 0.520	85.2± 0.859	22.0± 0.564	26.1± 0.906	30.7± 0.840

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15	45.1± 0.992	52.5± 2.377	72.0± 0.676	45.4± 0.497	61.1± 0.503	96.2± 0.614	31.2± 0.861	35.4± 0.889	40.9± 1.246
20	52.8± 0.664	63.5± 3.065	83.5± 0.620	56.8± 0.688	72.8± 0.534		39.7± 0.577	45.6± 0.828	51.5± 1.050
25	64.7± 0.892	75.1± 1.998	92.1± 0.909	67.76 ±0.59 8	81.9± 0.681		49.6± 0.579	56.2± 0.706	62.6± 0.691
30	75.0± 0.829	85.1± 1.956		78.9± 0.361	91.8± 0.516		58.6± 0.621	66.3± 1.129	73.2± 0.789

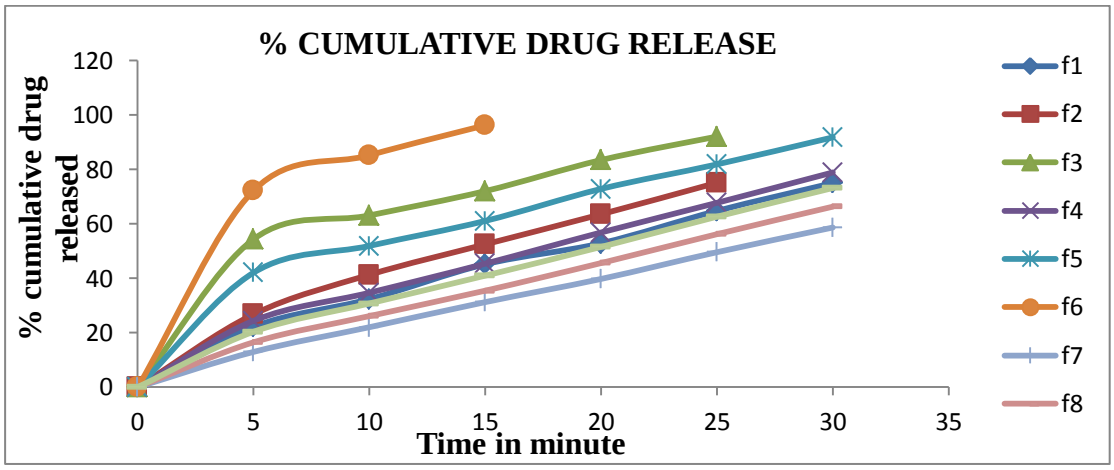

Figure 3: Percentage cumulative drug release graph from formulation F1-F9

Formulation and evaluation of optimized tablet:

Evaluation of precompression parameters of powder of optimized tablet (F6):

The bulk density, tapped density, Carr's index, angle of repose and Hausner's ratio of optimized formulations ware performed and shown in table no. 10. All the results shown that the optimized formulations possess a good flow property.

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Table no.10: Evaluation of precompression parameters of powder of optimize tablet (F6):

Formulat-ion	Bulk density (gm/ml) Mean±SD	Tapped density (gm/ml) Mean±SD	Carr's index (%) Mean±SD	Angle of repose (^{o}) Mean±SD	Hausner's ratio Mean±SD
F6	0.368 ±0.011	0.423±0.010	12.93±0.416	23.6±0.793	1.14±0.005

Evaluation of Post-compression Parameters of optimized tablet (F6):

The orodispersible tablet of Rosuvastatin were evaluated like weight variation, hardness, thickness, friability, disintegration time, drug content, wetting time and water absorption ratio and in vitro drug release study. The results of the study were shown in below table:

Table no.11: Weight variation, Hardness, Thickness, and Friability of Formulation F6

Formulation	Weight variation(mg) Mean±SD	Hardness (Kg/cm^2) Mean±SD	Thickness (mm) Mean±SD	Friability (%) Mean±SD
F6	289.5±3.940	3.0±0.057	4.0±0.057	0.347±0.001

Table no.12: Disintegration Time, Drug Content, Wetting time & water absorption Ratio, and of optimized tablet (F6):

Formulation	Disintegration Time(sec) Mean±SD	Drug Content (%) Mean±SD	Wetting time (sec) Mean±SD	Water absorption Ratio(%) Mean±SD
F6	26.05±0.249	99.12±0.646	29.35±0.321	40.22±1.986

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In-vitro drug release study of optimized tablet (F_6):

The percentage cumulative drug release from formulations F6 was found to be 96.8% drug within 15 minutes.

Table no.13: Percentage cumulative drug release data of optimized tablet (F6):

S. No.	Time (in min)	% Cumulative drug release (Mean±SD)
		Optimized formulation F_6
1	0	0.00±0.000
2	5	72.7±0.719
3	10	86.2±0.628
4	15	96.8±0.629

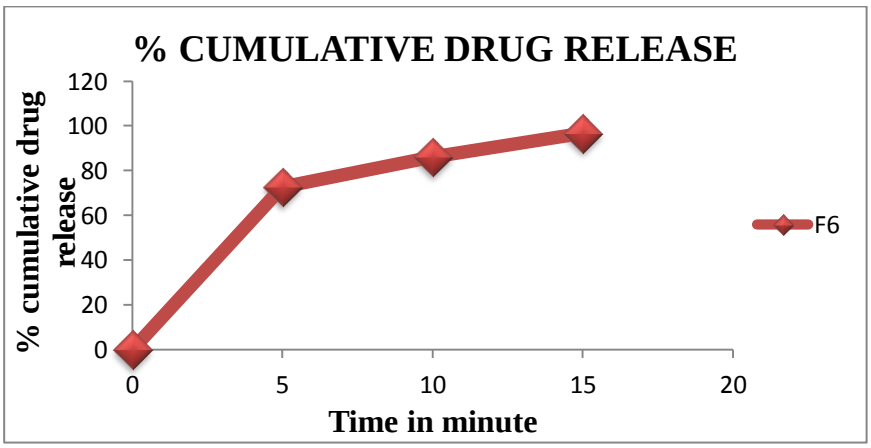

Figure 4: Cumulative % drug release graph of optimized formulation (F_6)

Stability study:

Stability studies for three month were performed at different storage condition for optimized orodispersible tablet (F6). The optimized orodispersible tablet were found to be stable with no change in physical appearance and TLC values (Rf) were found similar at different storage condition at different time interval. It was concluded that the formulation is stable at different storage conditions.

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Table no.14: Stability data of optimized formulation (F6):

S. No.	Time	Physical appearance	Result	Storage condition	Rf value
1	Initial Day	Light brown	No change in appearance	2-8ºC	0.81
		Light brown	No change in appearance	Room temperature	0.83
		Light brown	No change in appearance	50°C	0.81
2	1 month	Light brown	No change in appearance	2-8ºC	0.80
		Light brown	No change in appearance	Room temperature	0.85
		Light brown	No change in appearance	50ºC	0.82
3	3 month	Light brown	No change in appearance	2-8ºC	0.81
		Light brown	No change in appearance	Room temperature	0.83
		Light brown	No change in appearance	50ºC	0.80

8. Summary and Conclusion:

In the present research work an attempt has been made to optimized, formulate and evaluate orodispersible tablet of Rosuvastatin.

Rosuvastatin is an antihyperlipidemic drug belongs to BCS class-II (Low Solubility and high permeability). It has poor bioavailability and low solubility.

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In the present work solubility and bioavailability of drug was enhanced using inclusion complex. The inclusion complex of Drug: β-cyclodextrin was prepared in different ratio by kneading method.

The direct compression method was used to formulate and evaluate orodispersible tablet of Rosuvastatin.

The cassia tora seeds mucilage powder used as superdisintegrants in the formulation at different concentrations (40, 50, & 60mg) respectively. And inclusion complex of Drug: β-cyclodextrin was used in the formulation F2, F3, F5, F6, F8 & F9 except formulation F1, F4 & F7.

As the concentration of superdisintegrant cassia tora seeds mucilage powder that significant effect on disintegration characteristics as well as drug release. But the higher concentration of mucilage had negative impact on drug release & disintegration time.

Addition of Drug: β-cyclodextrin inclusion complex leads to improved dissolution characteristics and solubility of drug at optimum concentration (1:5). So, considering the above results it was found that the formulation f6 was found to be optimized formulation from the data obtained. It is observed from the formulation F6 which shown disintegration time 26.24 sec. and percentage cumulative drug release shown 96.8% within 15 minute.

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