



Formulation and evaluation of matrix type rosuvastatin sustained release tablets

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ABSTRACT

Sustained release tablets of Rosuvastatin were developed to prolong release of time leading to an increase in drug bioavailability. Tablets are prepared by direct compression technique using polymers HPMC K15M, HPMC K50M and ethylcellulose. Tablets were evaluated for their physical characteristics viz., hardness, thickness, friability and weight variation, drug content and floating properties. Gas generating agent plays an important role in floating lagtime and drug release. The best formulation subjected for kinetic treatment i.e., zero order, first order, pegas, Higuchi, and Hixsoncro well. The R Values are 0.9366, 0.9364, 0.9680, 0.9974 and 0.9283 respectively. The optimized batches were found to be best able at 40°C/75% RH for a period of two months.

Key words: Rosuvastatin, sustained tablets, gastric residence time, sustained drug delivery system.

INTRODUCTION

SUSTAINED RELEASE MATRIX TABLET

During the last few decades, there has been a remarkable increase in the interest in sustained release dosage form, due to prohibitive cost of developing new drug entities, discovery of the new polymers and improvement in efficiency and safety provided by these. SRDDS is a modified dosage form that prolongs the therapeutic activity of the drug. Accordingly, a prodrug or analogue modification of the drug sustains blood level is considered as sustained release system.

Sustained release tablets and capsules are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect.

Typically, sustained release products provide an immediate release of drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period. The sustained plasma drug levels provided by sustained release products often times eliminates the need for night dosing, which

benefits not only the patients but the care given as well.

The basic rationale of a sustained drug delivery system is to optimize the Biopharmaceutics, Pharmacokinetic and Pharmacodynamic properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest quantity of drug, administered by the most suitable route. The novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and / or targeting the drug to desired site. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration.

Oral route has been the most popular and successfully used for sustained delivery of drugs because of convenience and ease of administration, greater flexibility in dosage form design and ease of production and low cost of such a system. The sustained release systems for oral use are mostly solid and based on dissolution, diffusion or a combination of both mechanisms in the control of release of drugs. In this type of dosage forms, a sufficient amount of drug is initially made available to the body to cause a desired pharmacological response. The remaining fraction is released periodically and is required to maintain the maximum initial pharmacological activity for some desirable period of time in excess of time expected from usual single dose.

Several terms have been used to describe the various types of drug delivery systems intended to provide long duration of action. Today, most time-release drugs are formulated so that the active ingredient is embedded in a matrix of insoluble substance(s) such that the dissolving drug must find its way out through the holes in the matrix. Some drugs are enclosed in polymer-based tablets with a laser-drilled hole on one side and a porous membrane on the other side. GIT acids push through the porous membrane, thereby pushing the drug out through the laser-drilled hole². In time, the entire drug dose releases into the system while the polymer container remains intact, to be later excreted through normal digestion. Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral

administration, to obtain rapid and complete systemic drug absorption. Such immediate-release products result in relatively rapid drug absorption and onset of pharmacodynamic effects.

DIFFUSION SYSTEMS

In these systems, the release rate of drug is determined by its diffusion through water –insoluble polymer.

There are basically two types of diffusion devices

Reservoir devices

Matrix devices

Reservoir devices

In this a core of drug is surrounded by a polymeric membrane. Common methods used to develop reservoir-type devices include:

Micro encapsulation of drug particles

Press-coating

Micro encapsulation of drug particles method is most widely used method. Drug release usually involves a combination of dissolution and diffusion, with dissolution being the process that controls the release rate.

Some material used as the membrane barrier coat, alone or in combination, are hardened gelatin. MC, EC, polyvinyl acetate, poly hydroxyl methacrylate, HPMC and various waxes.

Matrix devices

In this dissolved or dispersed drug is distributed uniformly in an inert polymeric matrix. In this model it is assumed that solid drug dissolves from surface layer of the device first.

A) Common methods used are develop matrix -type devices include

Direct compression in case of compressible polymers

Melt granulation method in case of waxes.

OSMOTIC SYSTEMS

Osmotic pressure can be employed as the driving force to generate a constant release of drug, provided a constant osmotic pressure is maintained and a few other features of the physician Osmotically active drug, or a core of an Osmotically inactive drug, in combination with an Osmotically active salt surrounded by a semi permeable membrane containing a small orifices shown in fig.

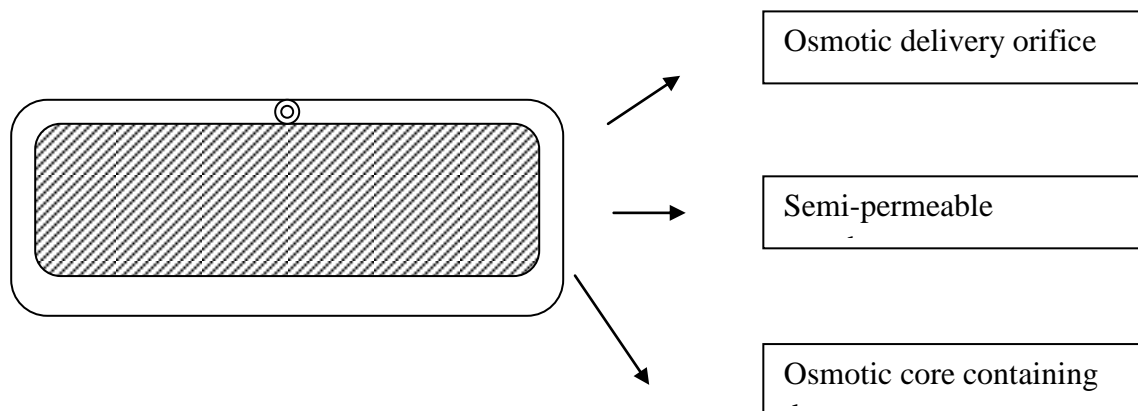


Figure-1: Osmotic System

The membrane will allow free diffusion of water but not drug. When tablet is exposed to water or any fluid in the body Water will flow into tablet because of osmotic difference.

ION EXCHANGE RESINS

Ion exchange resins are water insoluble, cross- linked polymers containing salt-forming groups in repeating positions on the polymer chain. Drug is bonded to the resin by repeated exposure of the resin to the drug in a chromatographic column or by prolonged contact of resin with the drug solution. The drug-resin then is washed to remove contamination ions and dried to form particles or beads. Drug release from the drug-resin complex depends on the ionic environment, i.e., pH and electrolyte concentration, within the GI tract as well as properties of the resin. Drug molecules attached to the resin are release by exchanging with appropriately changed ions in the GI tract followed by diffusion of free drug molecules out of the risen. Most ion-exchange resins currently employed in sustained release product contain sulfuric acid groups that exchange cationic drugs such as those with an amine functionality.

Examples: Amphetamine, phenyl-butylamine (phentermine), phenyltoloxamine, and hydrocodon.

TECHNIQUES TO FORMULATE THE TABLETS

Normally tablets are manufactured by any one of the following methods:

- Direct compression.
- Granulation.

DIRECT COMPRESSION

Direct compression is a process where the ingredients are compressed directly without going for granulation process. Direct compression offers the most expeditious method of manufacturing tablets because it utilizes the least handling of materials, involves no drying step, and is thus the most energy-efficient method, and is also the fastest, most economical method of tablet production. This process is possible if the medicaments or additives are crystalline in nature.

Manufacturing steps for direct compression

Direct compression involves comparatively few steps:

- i) Milling of drug and excipients.
- ii) Mixing of drug and excipients.
- iii) Tablet compression.

GRANULATION

It is a part of the pharmaceutical process 1.9that attempts to improve the flow of powdered materials by forming spheres like aggregates called granules.

Dry granulation

In the dry methods of granulation the primary powder particles are aggregated under high pressure and no liquid is used.

Steps in dry granulation

- i) Milling of drugs and excipients
- ii) Mixing of milled powders
- iii) Compression into large, hard tablets to make slug
- iv) Screening of slugs
- v) Mixing with lubricant and disintegrating agent
- vi) Tablet compression

Two main dry granulation processes

Slugging process

Granulation by slugging is the process of compressing dry powder of tablet formulation with tablet press having die cavity large enough in diameter to fill quickly. Only sufficient pressure to compact the powder into uniform slugs should be used. Once slugs are produced they are reduced to appropriate granule size for final compression by screening and milling.

Roller compaction

The compaction of powder by means of pressure roll can also be accomplished by a machine called chilsonator. Unlike tablet machine, the chilsonator turns out a compacted mass in a steady continuous flow. The powder is fed down between the rollers from the hopper which contains a spiral auger to feed the powder into the compaction zone. Like slugs, the aggregates are screened or milled for production into granules.

Wet granulation

Tableting by wet granulation process is the most widely used method for pharmaceutical materials. The technique involves a number of stages. During the development of a tablet formulation, all the physical variables that affect the resultant granules have to be

also considered to maximize the quality of the final product.

Wet granulation involves the massing of the mix of dry primary powder particles using a granulating fluid. The fluid contains a solvent, which can be removed by drying and it must be non-toxic.

Important steps involved in the wet granulation

- i) Mixing of the drug(s) and excipients
- ii) Preparation of binder solution
- iii) Mixing of binder solution with powder mixture to form wet mass.
- iv) Coarse screening of wet mass using a suitable sieve (6-12 screens).
- v) Drying of moist granules.
- vi) Screening of dry granules through a suitable sieve (14-20 screen).
- vii) Mixing of screened granules with glidant, and lubricant.

MATERIALS AND METHODS

The materials and instruments used in this project are listed below.

MATERIALS

Drugs & Chemicals

1. Rosuvastatin was generously gifted by Fleming Laboratories Ltd. Hyderabad, Andhra Pradesh.
2. HPMCK15M, HPMCK50M and Ethylcellulose were gifted by Unisule Pvt.Ltd., Haryana.
3. Potassium dihydrogen orthophosphate and Disodium hydrogen orthophosphate were procured from Colorcon Pvt.Ltd. Goa.
4. Ethanol, methanol and acetone were purchased from Ranbaxy Fine Chemical Ltd., New Delhi.
5. Sodium bicarbonate Citric acid (anhydrous) Polyvinylpyrrolidone-k-30 and Hydrochloric acid LR were purchased from S.D fine chemicals, Mumbai.

Table: 1. Instruments

Equipments	Company
Electronic Balance	Shimadzu2000
Standard sieve (#60)	Ajanta Sieves, Chennai
Hardness Tester	Monsanto
Friability Tester	Roche Friabilator
USP Tablet dissolution apparatus typeII	Disso2000Lab India
UV Spectrophotometer	Shimadzu 1700, Japan
TapDensityTester(USP)	Electrolab

METHODS

Preformulation studies

It is one of the important prerequisite in development of any drug delivery system. Preformulation studies were performed on the drug, which included melting point determination, solubility and compatibility studies.

Determination of Melting Point

Melting point of Rosuvastatin was determined by capillary method. Fine powder of Rosuvastatin was filled in glass capillary tube (previously sealed on one end). The capillary tube is tied to thermometer and the thermometer was placed in fire. The powder at what temperature it will melt was noticed.

Solubility

Solubility of Rosuvastatin was determined in ethanol (95%), chloroform, acetone, ether, water and 0.1 NHCl. Solubility studies were performed by taking excess amount of Rosuvastatin in different beakers containing the solvents. The mixtures were shaken for 24 hrs at regular intervals. The solutions were filtered by using Whatmann's filter paper grade no. 41. The filtered solutions are analyzed spectrophotometrically.

Compatibility Studies

Compatibility with excipients was confirmed by carried out IR studies. The pure drug and its formulations along with excipients were subjected to IR studies. In the present study, the potassium bromide disc (pellet) method was employed.

Identification of Rosuvastatin

A solution of Rosuvastatin containing the concentration 10 µg/ml was prepared in 0.1 NHCl and UV spectrum was taken using Systronics UV/V is double beam spectrophotometer. The solution was scanned in the range of 200 – 400.

Preparation of Standard Calibration Curve of Rosuvastatin

Method

100 mg of Rosuvastatin was accurately weighed and transferred into 100 ml volumetric flask. It was dissolved and diluted to volume with 0.1 NHCl/Phosphate buffer pH 7.4 to give stock solution containing 1000 µg/ml.

The standard stock solution was then serially diluted with 0.1 NHCl/Phosphate buffer pH 7.4 to get 1 to 12 µg/ml of Rosuvastatin. The absorbance's of the solution were measured against 0.1 NHCl/ Phosphate buffer 7.4 as blank at 258.2 & 260.8 nm using UV spectrophotometer respectively. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

Evaluation of Powder Blend^{2,3,4,5}

a. Angle of repose

The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such away the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder 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 powder cone.

b. Bulk density

Both loose bulk density (LBD) and tapped bulk density¹ (TBD) was determined. A quantity of 2 gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced in to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TBD were calculated using the following equations.

LBD = $\frac{\text{Weight of the powder blend}}{\text{Untapped Volume of the packing}}$

TBD = $\frac{\text{Weight of the powder blend}}{\text{Tapped Volume of the packing}}$

c. Compressibility Index

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder

and the rate at which it packed down. The formula for Carr's Index is as below:

$$\text{Carr's Index (\%)} = [(TBD-LBD) \times 100]/TBD$$

d. Total Porosity

Total porosity was determined by measuring the volume occupied by a selected weight of a powder (V_{bulk}) and

the true volume of the powder blend (The space occupied by the powder exclusive of spaces greater than the intermolecular spaces, V).

$$\text{Porosity (\%)} = V_{\text{bulk}} - V / V_{\text{bulk}} \times 10.$$

Table: 2: Composition of Rosuvastatin Tablet

<u>INGREDIENTS</u>	<u>FT1</u>	<u>FT2</u>	<u>FT3</u>	<u>FT4</u>	<u>FT5</u>	<u>FT6</u>	<u>FT7</u>	<u>FT8</u>	<u>FT9</u>	<u>FT10</u>
Rosuvastatin	20	20	20	20	20	20	20	20	20	20
HPMCK15M	80	-	-	90	-	-	-	45	45	35
HPMCK50M	-	85	-	-	95	-	50	-	45	30
Ethylcellulose	-	-	85	-	-	95	45	50	-	35
Sodiumbicarbonate	85	80	80	75	75	70	70	75	75	70
Citric acid (anhydrous)	25	25	20	25	20	25	25	20	25	20
PVP-K-30	25	25	30	25	25	25	25	25	25	25
MagnesiumStearate	8	8	8	8	8	8	8	8	8	8
Talc	7	7	7	7	7	7	7	7	7	7
Total wt.	250	250	250	250	250	250	250	250	250	250

Total weight of tablet =250 mg

All quantities were in milligrams.

All the batches contained 1% w/w talc and 0.5% w/w magnesium Stearate.

EVALUATION OF TABLETS

a. Weight variation test⁴

To study weight variation twenty tablets of the formulation were weighed using an Essay electronic balance and the test was performed according to the official method. Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.

b. Drug content⁶

Five tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in Phosphate buffer pH 7.4, the drug content was determined measuring the absorbance at 260.8 nm after suitable dilution using a shimadzu UV- Vis double beam spectrophotometer.

c. Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm². Three tablets were randomly picked and hardness of the tablets was determined. The thickness of the tablets was determined by using vernier³ calipers. Five tablets were used, and average values were calculated.

d. Friability Test

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed (W_0) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W). The % friability was then calculated by –

$$\%F = 100 (1 - W_0/W)$$

% Friability of tablets less than 1% are considered acceptable.

e. Tablet Density

Tablet density is an important parameter for floating tablets. The tablet will float when its density is less than that of 0.1N HCl.

The density was determined using following formula.

$$V = r^2 h d = m/v$$

Where;

- v = volume of tablet (cc)
- r = radius of tablet (cm)
- h = crown thickness of tablet (cm)
- m = mass of tablet

F. In Vitro dissolution studies¹¹

The release rate of Rosuvastatin from sustained tablets was determined using The United States Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1 N HCl, at $37 \pm 0.5^\circ\text{C}$ and 75 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 8 hours, and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 252.2 nm using a Shimadzu UV-Vis double beam spectrophotometer 1700. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve. The same is done in the phosphate buffer pH 7.4 also.

G. Swelling index¹²

The swelling index of tablets was determined in 0.1 N HCl (pH 1.2) at room temperature. The swollen weight of the tablets was determined at predefined time intervals. The swelling index was calculated by the following equation:

$$\text{Swelling index WU} = \frac{W_t - W_0}{W_0} * 100$$

Where;

W_t = Weight of tablet at time t.

W_0 = Initial weight of tablet.

STABILITY STUDIES¹⁰

In designing a solid dosage form it is necessary to know the inherent stability of the drug substance, to have an idea of what excipients to use, as well as how best to put them together with the drug and to know that no toxic substance are formed. Limits of acceptability and therefore compromises must be reasonably defined. Because the measurements of these aspects of stability as well as determination of shelf life or expiration date for the final dosage form require long term stability studies for confirmation, they can be expensive and time consuming. Consequently it is necessary to define those study designs and conditions that show the greatest probability of success. The objective therefore of a stability study is to identify and help avoid or control situations where the stability of the active ingredient may be compromised. For a drug substance to be developed into a tablet dosage form, this objective may be achieved by investigating the stability of the drug under the following three categories, (1) solid state stability of drug alone, (2) compatibility studies in presence of excipients, (3) solution phase stability.

Rationale for stability studies

There may be chemical degradation of active drug leading to a substantial lowering of the quantity of therapeutic agent in the dosage form.

Although chemical degradation of the active drug may not be expensive, a toxic product may be formed in the decomposition process.

Instability of drug product can lead to substantial lowering in the therapeutic efficiency of the dosage form.

Table. 3 ICH guidelines for stability study

Study	Storage condition		MiMinimum time
	Temperature	Relative humidity (%)	
Long term	25°C	60% 5% RH	12 Months
Intermediate	30°C	65% 5% RH	6 Months
Accelerated	40°C	75% 5% RH	6 Months

Note: The analyst can select any one of the three study conditions. Stability study was carried out at 40°C / 75%

RH for the optimized formulations. The procedure was divided into two parts,

Part one

Achieving of 60% RH

26.66 gm of sodium hydroxide was weighed and dissolved in 100 ml of distilled water to get 26.66% sodium hydroxide solution. The solution was placed in the desiccator over which a wire mesh was placed, over which the dosage form was placed and the desiccator was sealed. The desiccator was placed in the oven maintained at 25⁰C to create the Relative Humidity OF 60%.

Achieving of 75% RH

Saturated solution of sodium chloride was prepared and placed in the desiccators over which a wire mesh was placed, over which the dosage form was placed and the desiccators' was sealed. The desiccator was kept in oven maintained at 40⁰C to create the relative humidity of 75%.

Part two

The sealed formulation were placed in amber colored bottles, tightly plugged with cotton and capped. They were then stored at 25⁰C /60% RH and 40⁰C / 75% RH for two months and evaluated for their physical appearance and drug content.

RESULTS

Table: 4. Standard Curve of Rosuvastatin:

		ABSORBANCE
S.NO	CONCENTRATION (µg/ml)	In Phosphate buffer(7.4)
1.	0	0
2.	2	0.153
3.	4	0.32
4.	6	0.47
5.	8	0.614
6.	10	0.77
7.	12	0.936

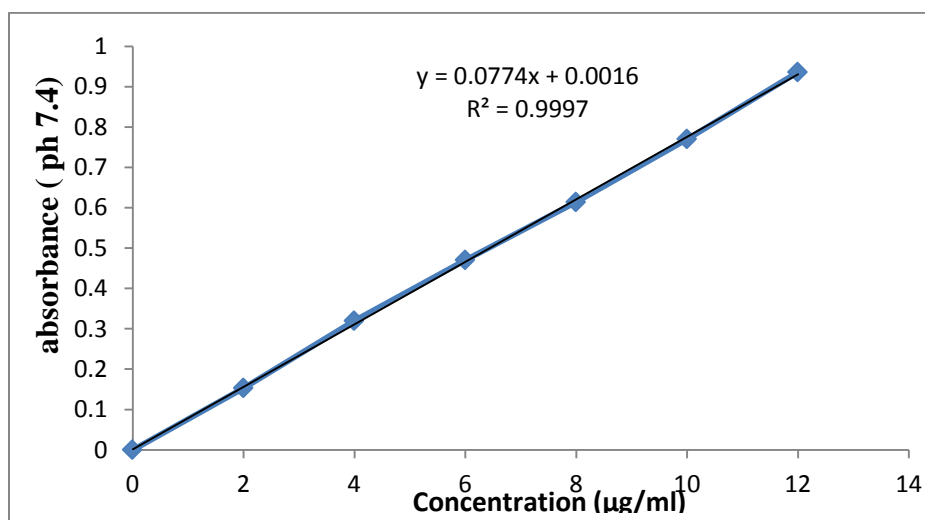


Figure 2. Standard Curve of Rosuvastatin by Phosphate buffer (7.4)

FT-IR Studies

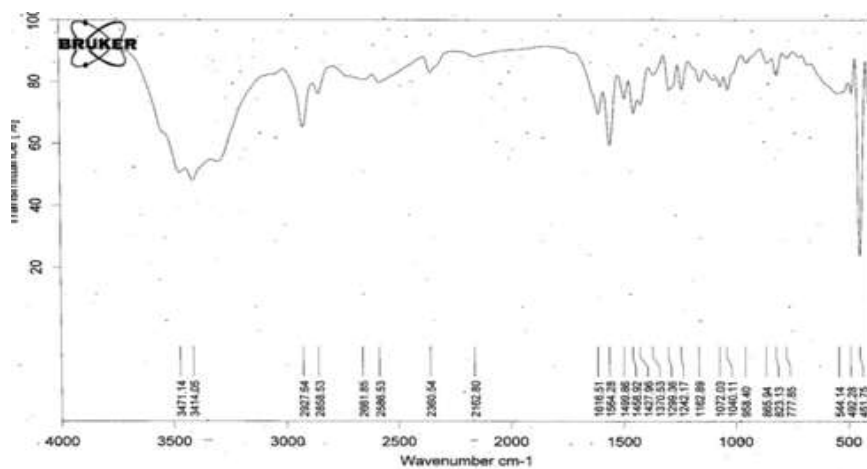


Figure (3): FT-IR Spectrum of Rosuvastatin

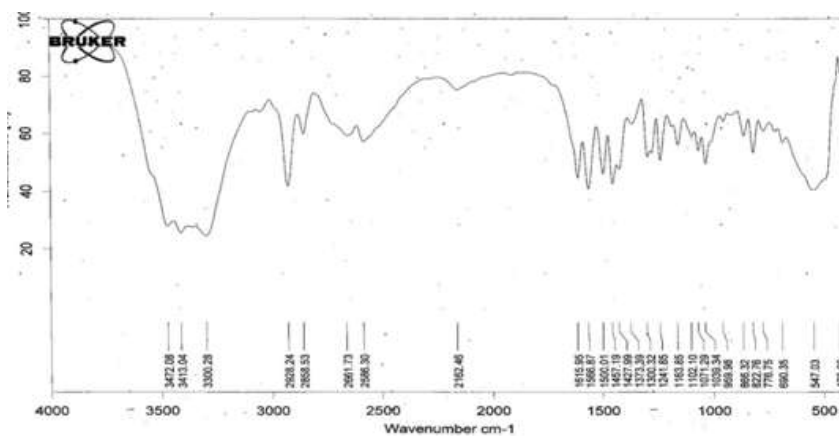


Figure (4): FT-IR Spectrum of Drug + HPMC K15 M

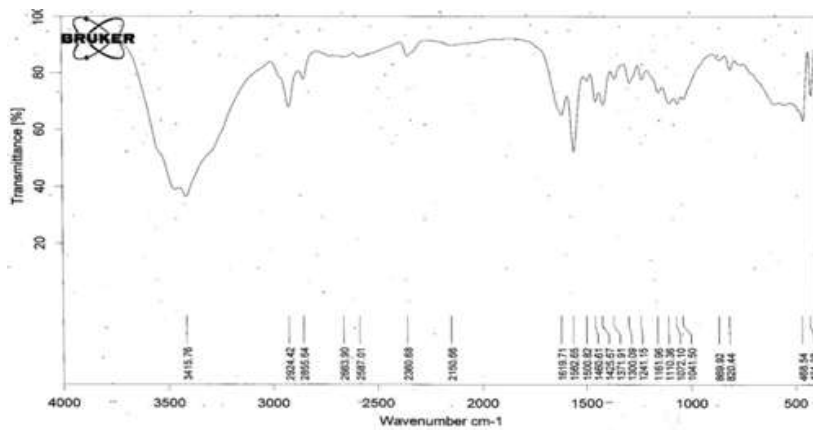


Figure (5): FT-IR Spectrum Of Rosuvastatin And HPMC K50M

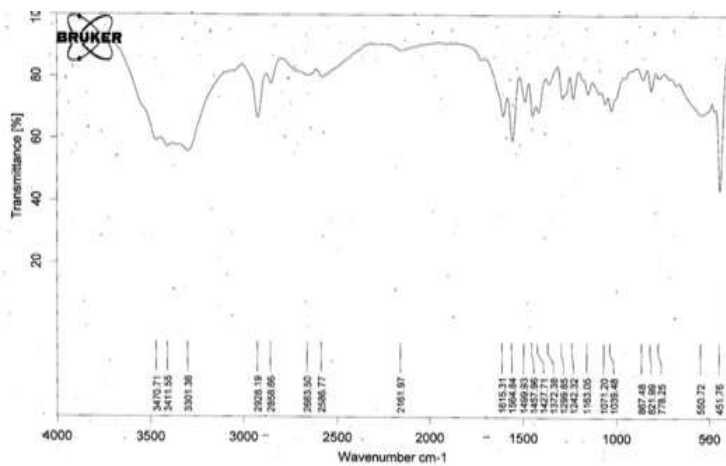


Figure (6): FT-IR Spectrum Of Rosuvastatin + Ethyl cellulose

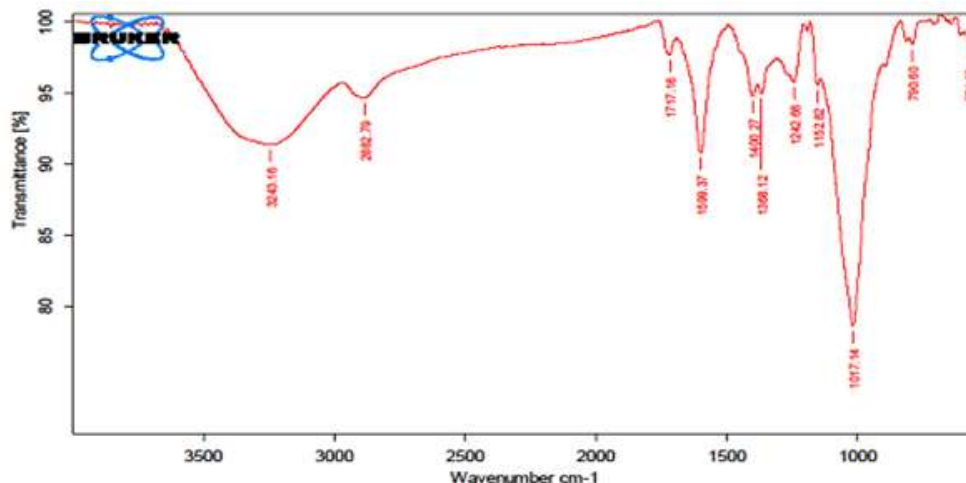


Figure (7): I.R. SPECTRUM OF ROSUVASTATIN + SODIUM BICARBONATE +Citric Acid + PVP k-30 +Mg STEARATE + Talc

Table: 5. Micrometric properties of powder blend

Powder blend	Angle of Repose (o)	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Compressibility Index (%)	Hansner Ratio
FT1	24.50'	0.131	0.156	16.02	1.19
FT2	26.40'	0.112	0.128	15.62	1.14
FT3	25.35'	0.092	0.108	14.81	1.20
FT4	28.60'	0.110	0.132	16.66	1.20
FT5	29.50'	0.123	0.145	15.17	1.17
FT6	25.40'	0.113	0.132	14.39	1.16
FT7	26.50'	0.133	0.152	12.50	1.14
FT8	24.32'	0.135	0.154	13.47	1.14
FT9	26.68'	0.140	0.160	12.35	1.42
FT10	28.82'	0.110	0.130	15.38	1.18

Table 6. Effect of different polymers on drug release by paddle method Cumulative % Drug release in 7.4 Phosphate Buffer

Time (hrs)	FT1	FT2	FT3	FT4	FT5	FT6	FT7	FT8	FT9	FT10
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	2.48	4.32	1.54	3.41	1.94	2.24	2.48	3.86	1.24	2.36
2	4.36	6.86	2.26	5.80	3.78	3.94	4.78	5.24	2.58	5.48
3	6.41	6.46	4.80	7.68	5.24	6.52	6.58	7.94	5.91	8.32
4	9.43	12.9	6.48	10.2	8.40	8.40	8.60	10.3	8.24	10.6
5	13.88	18.4	9.42	14.8	11.8	11.8	12.3	14.3	10.2	13.4
6	17.34	20.1	10.3	16.3	14.8	14.8	16.6	17.4	12.2	16.8
7	20.15	25.3	14.7	22.4	18.8	18.8	20.2	22.2	16.2	20.3
8	25.28	30.4	19.3	28.8	22.4	22.4	26.2	28.6	20.9	24.3
9	29.38	37.2	22.6	32.5	24.4	24.3	30.4	32.5	22.3	27.4
10	32.46	39.4	25.8	35.9	28.5	28.5	32.1	35.3	26.2	30.2
24	60.58	49.4	30.8	45.3	35.4	35.4	44.2	47.2	32.2	38.8
FLT (sec.)	175	102	NO	95	136	NO	100	78	190	45
TFT (hrs)	8	8	NO	12	12	NO	>12	6	8	>12

FLT= Floating lag time

TFT=Totalfloatingtime

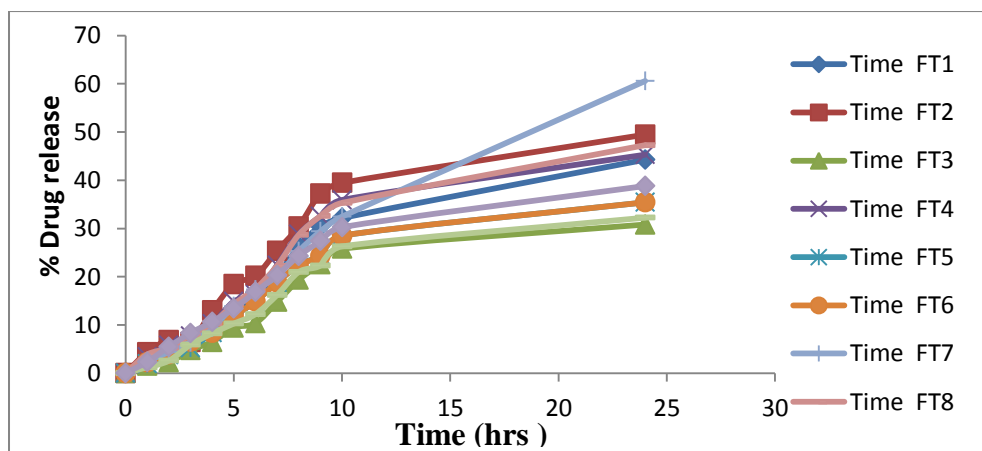


Figure:8 Dissolution study of Cumulative % Drug release in 7.4 Phosphate Buffer F1-F10

Table: 7. Effect of hardness on Buoyancy Lag Time

Hardness in kg/cm ²	Buoyancy Lag Time (sec)
4	52
5	61
6	79
7	94
8	190

Table: 8 Kinetic values obtained from vitreleaseddata of Formulation F7

Kinetic Model	Slope	R ²
Zero-order plot	8.3466	0.9366
First-order plot	0.0041	0.9364
Higuchi plot	29.935	0.9974
Korsmeyer-Peppas	0.7212	0.9680
Hixson- crowell	0.0298	0.9283

RESULTS OF STABILITY STUDIES

The results of the stability studies for formulation FT7 are in the following table.

Table: 9. Results of stability studies

Time in day	At 25 ^o C		At 40 ^o C (75% RH)		At 50 ^o c	
	PA	HD%DC	PA	HD%DC	PA	HD%DC
0	+++	4.2 99.05	+++	4.2 101.5	+++	4.0 97.65
30	+++	4.1 99.02	+++	4.2 100.2	+++	4.1 97.54
60	+++	4.1 98.04	+++	4.3 100.4	+++	4.2 97.64

Where,

PA=physical appearance

HD=Hardness (Kg/cm²)

SUMMARY

Rosuvastatin is a competitive inhibitor of HMG-CoA reductase. HMG-CoA reductase catalyzes the conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol biosynthesis. Review of literature indicated that floating drug delivery system can minimize the fluctuation of plasma level and can be used to maintain drug concentration at a therapeutic level by means of controlled drug release.

The aim of the study was to develop and physico-chemically characterized sustained release matrix tablet of Rosuvastatin based on a matrix polymer. Rosuvastatin has a biological half-life (19 hours). Development of sustained release formulation of Rosuvastatin can be advantageous. A traditional oral sustained release formulation releases most of the drug at the colon, thus the drug should have absorption window either in the colon or throughout the gastrointestinal tract. Being weak acid, pKa – 4.55, the Rosuvastatin well absorbed from the upper portion of the duodenum. Moreover, less solubility in alkaline pH of Rosuvastatin is partly

responsible for the poor bioavailability of Rosuvastatin from the colon. These properties of Rosuvastatin favor the traditional approach to sustained release delivery. Hence, clinically acceptable sustained release dosage forms of Rosuvastatin prepared with conventional technology may not be successful.

Different types of matrix forming polymers were studied: HPMC k15m, HPMC k50m, ethyl cellulose, for the study. The tablets eroded upon contact with the release medium, and the relative importance of drug diffusion, polymer swelling and tablet erosion for the resulting release patterns varied significantly with the type of matrix former. the release rate could effectively be modified by varying the “matrix-form.polymer”, the tablet geometry (radius), the type of matrix forming polymer. The use of polymer blends. The controlled behavior of the matrix drug delivery systems could successfully be combined with accurate control of the drug release patterns. The batch optimization was done using HPMC K15M, HPMC K50M and Ethyl cellulose as matrix polymers as they gave optimum SDDS as well

as long acting affect and no / least eroding effect. It was also found that the tablet formulations released more than 90 % drug in 12 hours as desired.

The use of HPMC K15M, HPMC K50M polymer in matrix tablets as density reducing agent has given a different look while Ethyl cellulose used as release retardant polymer. During the study with the polymer various characteristics of the material were observed; like highly porous spherical structure, good compressibility, good flow property with drug and other polymers, no significant effect on drug release and compatibility with drug and other polymers as seen through IR spectra.

Thus it is summarized and concluded that HPMC K15M, HPMC K50 M and Ethyl cellulose can be successfully used in the formulation of Rosuvastatin sustained release drug delivery system.

CONCLUSION

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From the compatibility studies, it was concluded that HPMC K15M, HPMC K50M, and Ethyl cellulose were compatible with Rosuvastatin and thus suitable for the formulation of Rosuvastatin sustained tablets.

In vitro buoyancy studies were performed for all the formulations, FT 1 to FT 10 by using 0.1 N HCl solutions at 37°C. All the formulations were floated except FT 3 and FT 6. The formulation FT 7 containing 90 mg of HPMC K15M, 45 mg of HPMC K50M and 45 mg of Ethyl cellulose showed more sustained drug release time (12 hours) than other formulations. In vitro dissolution studies were also performed for all formulations. The formulation FT 7 showed the controlled release for 24 hours. Thus FT 7 was identified as ideal batch based on its results.

Finally, it was concluded that HPMC K15M, HPMC K50 M and Ethyl cellulose can be successfully used in the formulation of Rosuvastatin sustained release drug delivery system.