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FORMULATION AND EVALUATION OF ROSUVASTATIN (ORAL DISINTEGRATING) TABLETS BY USING NATURAL POLYMER

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ABSTRACT:
The present invention relates to the formulation of mouth disintegrating tablets of Rosuvastatin. Mouth disintegrating tablets of rosuvastatin were successfully prepared using Banana powder and Croscarmellose sodium. In the present study, mouth disintegrating tablets were prepared by direct compression method. The formulated tablets were evaluated for parameters like hardness, friability, weight variation and drug content indicate that values were within permissible limit for all formulation. The mouth disintegrating tablets of Rosuvastatin developed in this investigation releases drug within 30 minutes. Thus, we are able to achieve our objective of preparing mouth disintegrating tablets of Rosuvastatin with minimum excipients and simple method of manufacture.
Key words: Rosuvastatin (Drug), Banana powder, Croscarmellose sodium , Direct compression method.

Introduction:

An ideal dosage regimen in the drug therapy of any disease is the one, which immediately attains the desire therapeutics concentration of drug in plasma (or at the site of action) and maintains it constant for the entire duration of treatment. This is possible through administration of conventional dosage form in a particular dose and at a particular frequency. Thus drug may be administered by variety of routes in a variety of dosage forms.

Drugs are more frequently taken by oral administration. Although a few drugs taken orally are intended to be dissolved within the mouth, the vast majority of drugs taken orally are swallowed. Compared with alternate routes, the oral route of drug administration is the most popular and has been successfully used for conventional delivery of drug. It is considered most natural, uncomplicated, convenient, safe means of administering drugs, greater flexibility in dosage form design, ease of production and low cost.

Tablets and hard gelatin capsules constitute a major portion of the drug delivery systems that are currently available. However, many patient groups such as elderly, children, and patients mentally retarded, uncooperative, nauseated, or on reduced liquid intake diets have difficulty in swallowing these dosage forms. Many elderly persons face difficulties in administering conventional oral dosage forms because of hand tremors and dysphasia. Swallowing problem is common in children because of their underdeveloped muscular and nervous systems. In some cases like motion sickness, sudden episodes of allergic attack or coughing, and during unavailability of water, swallowing conventional tablets is difficult. To fulfill these medical needs, formulators have devoted considerable efforts for developing a novel type of dosage form for oral administration known as mouth dissolving tablets (MDT).

MOUTH DISSOLVING TABLET:

This is an innovative tablet technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly, usually in a matter of seconds, without the need for water, providing optimal convenience to the patient. Innovators and inventor companies have given these tablets various names such as orally disintegrating tablets (ODT), mouth dissolving (MD), fast melting, fast dissolving or Orodisperse.

The European Pharmacopoeia defines Orodisperse as a tablet that can be placed in the mouth where it disperses rapidly before swallowing. Researchers have formulated ODT for various categories of drugs, which are used for therapy in which rapid peak plasma concentration is required to achieve desired pharmacological response. These include neuroleptics, car diovascular agents, analgesics, anti-allergic and drugs for erectile dysfunction.

CHARACTERISTICS OF MOUTH DISSOLVING TABLETS:

- Convenient and easy to administer as does not require water for oral administration.
- Durable and sufficient strength to withstand the rigors of the manufacturing process and manufacturing handling.
- Pleasant mouth feel.
- Insensitive to environmental conditions such as humidity and temperature.
- Improved taste without any residue in the mouth after disintegration.
- Adaptable and amenable to existing processing and packaging machinery.
- Cost effective.

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- Compatible with taste masking.

BENEFITS OF MOUTH DISSOLVING TABLETS:

- Administered without water, anywhere, any time.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapidonset of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

LIMITATIONS OF MOUTH DISSOLVING TABLETS:

- The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

TECHNIQUES USED FOR THE FORMULATION OF MOUTH DISSOLVING TABLETS:

Direct Compression:

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied for the preparation of ODT because of the availability of improved excipients especially Superdisintegrants and sugar based excipients.

(a) Superdisintegrants:

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration.

(b) Sugar Based Excipients:

This is another approach to manufacture ODT by direct compression. The use of sugar based excipients especially bulking agents like dextrose, fructose, is malt, lactilol, maltilol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouthfeel. Mizumito et al have classified sugar-based excipients into two types on the basis of molding and dissolution rate.

Type 1- saccharides (lactose and mannitol) exhibit low mouldability but high dissolution rate.

Type 2-saccharides (maltose and maltilol) exhibit high mouldability and low dissolution rate.

AIM AND OBJECTIVE:

The aim of the present study is to formulate the Oral Mouth Dissolving tablets (ODT) of Rosuvastatin using Banana powder, Croscarmellose sodium and other directly compressible excipients by direct compression method.

The designed ODT of Rosuvastatin will be evaluated for hardness, friability, weight variation, *in-vitro* dispersion time wetting time, water absorption ratio, drug content uniformity, *in-vitro* dissolution rate.

To perform UV Analysis.

To perform IR Studies.

PLAN OF WORK:

The present research work is planned according to the following steps**:**

- Literature Survey
- Selection of Drug, Excipients
- Pre-formulation studies
- Angle of repose
- Bulk and tapped density
- Hausner ratio
- Compressible index etc.
- Manufacture of tablets
- Evaluation of tablets
- Weight variation
- Hardness
- Friability

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- Disintegration time
- Content uniformity
- In vitro dispersion time
- In-Vitro dissolution Studies

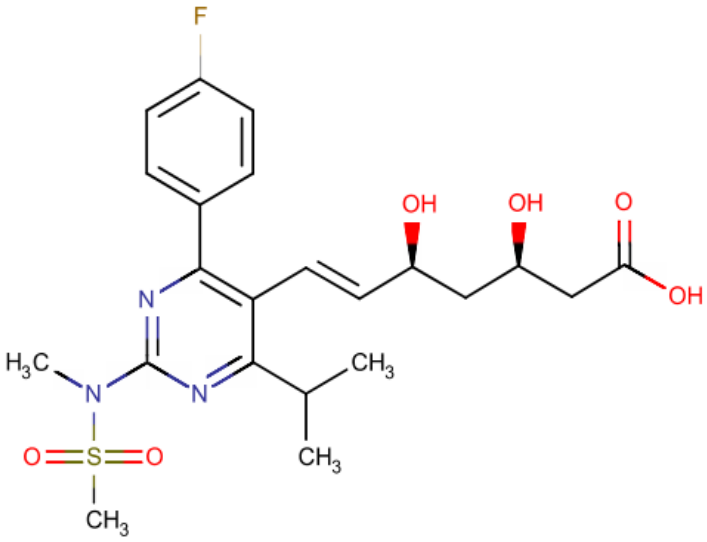
➢ Release kinetics
➢ UV studies
➢ IR studies

DRUG PROFILE

ROSUVASTATIN:

Description: Rosuvastatin is an antilipidemic agent that competitively inhibits hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase. HMG-CoA reductase catalyzes the conversion of HMG-CoA to mevalonic acid, the rate-limiting step in cholesterol biosynthesis. Rosuvastatin belongs to a class of medications called statins and is used to reduce plasma cholesterol levels and prevent cardiovascular disease.

Structure:



IUPAC NAME: (3R,5S,6E)-7-[4-(4-fluorophenyl)-2-(N-methylmethanesulfonamido)-6-(propan-2-yl)pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoic acid

Chemical formula: $C_{22}H_{28}FN_3O_6S$

Solubility: Soluble in water (< **1 mg/ml** at 25° C), chloroform, DMSO (**100 mg/ml** at 25° C), methanol, and ethanol (< **1 mg/ml** at 25° C).

Molecular weight: 481.539 g/mol

Melting point: 173-185°C.

Pharmacology:

Indication: Used as an adjunct to dietary therapy to treat primary hyperlipidemia (heterozygous familial and nonfamilial), mixed dyslipidemia and hypertriglyceridemia. Also indicated for homozygous familial hypercholesterolemia as an adjunct to other lipid-lowering therapies or when other such therapies are not available. Furthermore, it is used to slow the progression of atherosclerosis and for primary prevention of cardiovascular disease.

Pharmacodynamics: Rosuvastatin is a synthetic, enantiomerically pure antilipemic agent. It is used to lower total cholesterol, low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apoB), non-high density lipoprotein-cholesterol (non-HDL-C), and trigleride (TG) plasma concentrations while increasing HDL-C concentrations. High LDL-C, low HDL-C and high TG concentrations in the plasma are associated with increased risk of atherosclerosis and cardiovascular disease. The total cholesterol to HDL-C ratio is a strong predictor of coronary artery disease and high ratios are associated with higher risk of disease. Increased levels of HDL-C are associated with lower cardiovascular risk. By decreasing LDL-C and TG and increasing HDL-C, rosuvastatin reduces the risk of cardiovascular morbidity and mortality.

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Mechanism of Action: 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. Rosuvastatin acts primarily in the liver. Decreased hepatic cholesterol concentrations stimulate the upregulation of hepatic low density lipoprotein (LDL) receptors which increases hepatic uptake of LDL. Rosuvastatin also inhibits hepatic synthesis of very low density lipoprotein (VLDL). The overall effect is a decrease in plasma LDL and VLDL. In vitro and in vivo animal studies also demonstrate that rosuvastatin exerts vasculoprotective effects independent of its lipid-lowering properties. Rosuvastatin exerts an anti-inflammatory effect on rat mesenteric microvascular endothelium by attenuating leukocyte rolling, adherence and transmigration (PMID: 11375257). The drug also modulates nitric oxide synthase (NOS) expression and reduces ischemic-reperfusion injuries in rat hearts (PMID: 15914111). Rosuvastatin increases the bioavailability of nitric oxide (PMID: 11375257, 12031849, 15914111) by upregulating NOS (PMID: 12354446) and by increasing the stability of NOS through post-transcriptional polyadenylation (PMID: 17916773). It is unclear as to how rosuvastatin brings about these effects though they may be due to decreased concentrations of mevalonic acid.

Absorption: Bioavailability is approximately 20%. Peak plasma concentrations were reached 3 to 5 hours following oral dosing. Both Cmax and AUC increased in approximate proportion to CRESTOR dose. Food has no effect on the AUC of rosuvastatin

Protein binding: 88% bound to plasma proteins (mostly albumin). Binding is reversible and independent of plasma concentrations.

Metabolism: Not extensively metabolized. Only ~10% is excreted as metabolite. Cytochrome P450 (CYP) 2C9 is primarily responsible for the formation of rosuvastatin's major metabolite, N-desmethylrosuvastatin. N-desmethylrosuvastatin has approximately 50% of the pharmacological activity of its parent compound in vitro. Rosuvastatin clearance is not dependent on metabolism by cytochrome P450 3A4 to a clinically significant extent. Rosuvastatin accounts for greater than 90% of the pharmacologic action. Inhibitors of CYP2C9 increase the AUC by less than 2-fold. This interaction does not appear to be clinically significant.

Route of elimination: Rosuvastatin is not extensively metabolized; approximately 10% of a radiolabeled dose is recovered as metabolite. Following oral administration, rosuvastatin and its metabolites are primarily excreted in the feces (90%). After an intravenous dose, approximately 28% of total body clearance was via the renal route, and 72% by the hepatic route.

Half-life: 19 hours

Toxicity: Generally well-tolerated. Side effects may include myalgia, constipation, asthenia, abdominal pain, and nausea. Other possible side effects include myotoxicity (myopathy, myositis, rhabdomyolysis) and hepatotoxicity. To avoid toxicity in Asian patients, lower doses should be considered. Pharmacokinetic studies show an approximately two-fold increase in peak plasma concentration and AUC in Asian patients (Philippino, Chinese, Japanese, Korean, Vietnamese, or Asian-Indian descent) compared to Caucasians patients.

Affected organisms:

- Humans and other mammals.

METHODOLOGY

Table No – 1: Ingredients and Manufactures

S.NO.	INGREDIENTS	SUPPLIER
	ROSUVASTATIN	SUPPLIED BY PHARMA TRAIN
	BANANA POWDER	SD FINE CHEMICALS, MUMBAI
	CROSCARMELLOSE SODIUM	SD FINE CHEMICALS, MUMBAI
	AVICEL PH102	SD FINE CHEMICALS,MUMBAI

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	PEPPERMINT FLAVOUR	NIHAL PHARMA,HYD
	AEROSIL	SD FINE CHEMICALS,MUMBAI
	MAGNESIUM STERATE	SD FINE CHEMICALS,MUMBAI

Table No – 2: Equipment and Companies

S.NO.	NAME OF THE EQUIPMENT	MODEL
1	ELECTRONIC WEIGHING BALANCE	SCALE-TEC
2	FRIABILATOR	ROCHE FRIABILATOR, ELECTROLAB, MUMBAI.
3	COMPRESSION MACHINE	CMD(CADMACH)
4	TABLET HARDNESS TESTER	PFIZER HARDNESS TESTER, MUMBAI
5	UV	LABINDIAUV 3000+
6	DISSOLUTION APPARATUS	ELECTROLAB TDT-08L
7	VERNIERCALLIPERS	CD-6"CS

I. Analytical Method Development:

Preparation of 6.8 phosphate buffer:

6.8gms of potassium di hydrogen ortho phosphate was taken in a 1000ml volumetric flask and dissolved with distilled water and make up to 1000 ml with distilled water and adjust pH upto 6.8 with Sodium hydroxide solution.

Determination of λ_{max} of Rosuvastatin in 6.8 phosphate buffer:

Procedure:

Working standard: 100mg of Rosuvastatin was weighed and dissolved in 10ml methanol and then make up to a volume of 100ml with 6.8 phosphate buffer it give 1000µg/ml concentrated stock solution.

Dilution 1: From the working standard solution 10ml was diluted to 100ml with 6.8 phosphate buffer it will give 100µg/ml concentrated solution.

Dilution 2: From the dilution-1 10ml was diluted to 100ml with 6.8 phosphate buffer it will give 10µg/ml concentrated solution.

This solutions was scanned at range of 200-400nm wavelength light corresponding scan spectrum curve was noted .the corresponding wavelength having highest absorbance is noted as $\lambda_{max..}$

II. Construction of calibration curve of Rosuvastatin in 6.8 phosphate buffer:

Procedure:

Working standard: 100mg of Rosuvastatin was weighed and dissolved in 10ml methanol and then make up to a volume of 100ml with 6.8 phosphate buffer it give 1000µg/ml concentrated stock solution.

Dilution 1: From the working standard solution 10ml was diluted to 100ml with 6.8 phosphate buffer it will give 100µg/ml concentrated solution.

From dilution 1, take 0.2, 0.4, 0.6, 0.8 and 1ml of solution and was diluted up to mark in 10ml volumetric flask to obtain 2, 4, 6, 8 and 10 µg/ml concentrated solutions. This solutions absorbance was noted at $\lambda_{max=257}$

PREPARATION OF ORAL DISINTEGRATING TABLETS

Direct compression method:

Mouth disintegrating tablets of Rosuvastatin were prepared by direct compression method.

All the ingredients were powdered separately and passed through # 40 mesh sieve separately. The drug and directly compressible excipient were mixed by adding small portion of each at a time and blending it to get a uniform mixture and keptaside. Then the other ingredients were mixed in geometrical order, in an inflated polyethylene

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pouch magnesium stearate and talc were added last and mixed for further two minutes and the tablets were compressed using 6 mm flat round punches to get tablets of 100 mg weight.

Table No – 3: Formulation of Mouth Disintegrating Tablets of Rosuvastatin

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8
Rosuvastatin	10	10	10	10	10	10	10	10
CCS	10	20	30	40	-	-	-	-
Banana powder	-	-	-	-	10	20	30	40
MCC	125	115	105	95	125	115	105	95
Pipperment flavor	1	1	1	1	1	1	1	1
Sodium lauryl sulphate	2	2	2	2	2	2	2	2
Mg. stearate	2	2	2	2	2	2	2	2
Total wt (mg)	150	150	150	150	150	150	150	150

EVALUATION OF TABLETS

The formulated tablets were evaluated for the following Pre, post compression quality control studies and dissolution studies

A) Pre Compression studies:

1. **Angle of Repose:** It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.

Angle of Repose of granules was determined by the funnel method. Accurately weighed powder blend was taken in the funnel. Height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. Powder blend was allowed to flow through the funnel freely on to the surface. Diameter of the powder cone was measured and angle of repose was calculated using the following equation[17].

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

Where:

θ = angle of repose

h = height in cms

r = radius in cms

The angle of repose has been used to characterize the flow properties of solids. It is a characteristic related to inter particulate friction or resistance to movement between particles.

Table No – 4: Angle of Repose Limits

Flow Properties and Corresponding Angles of Repose

Flow Property	Angle of Repose (degrees)
Excellent	25–30
Good	31–35
Fair—aid not needed	36–40
Passable—may hang up	41–45
Poor—must agitate, vibrate	46–55
Very poor	56–65
Very, very poor	>66

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2. Density:

Bulk density (BD): It is the ratio of total mass of powder to the bulk volume of powder Weigh accurately 25 g of granules, which was previously passed through 22#sieve and transferred in 100 ml graduated cylinder. Carefully level the powder without compacting, and read the unsettled apparent volume. Calculate the apparent bulk density in gm/ml by the following formula[18].

Bulk density = weight of powder/ Bulk volume.

$$BD = \frac{M}{V0}$$

M = mass of the powder

V_0 = bulk volume of the powder.

a. Tapped density (TD): It is the ratio of total mass of powder to the tapped volume of powder.

Weigh accurately 25 g of granules, which was previously passed through 22# sieve and transferred in 100 ml graduated cylinder of tap density tester which was operated for fixed number of taps until the powder bed volume has reached a minimum, thus was calculated by formula[18] .

Tapped density = Weigh of powder / Tapped volume

$$Dt = \frac{M}{Vf}$$

M = mass of the powder

V_f = tapped volume of the powder.

2. Carr's Index:

Compressibility index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the BD and TD of a powder and the rate at which it packed down[19]. The formula for Carr's index is as below:

$$\textbf{Compressibility index} = 100 \times \frac{\text{Tapped density - Bulk density}}{\text{Tapped density}}$$

3. Hausner's Ratio:

Hausner's Ratio is a number that is correlated to the flow ability of a powder[19] .

$$\textbf{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Table No – 5: Compressibility Index Limits

Scale of Flow ability (USP29-NF34)

Compressibility Index (%)	Flow Character	Hausner's Ratio
≤ 10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very Poor	1.46-1.59
> 38	Very, very Poor	> 1.60

B) Post compression studies:

1. **General appearance:** The formulated tablets were assessed for its general appearance and observations were made for shape, colour, texture and odour.
2. **Average weight/Weight Variation:** 20 tablets were selected and weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to

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assure whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 300 mg tablets and none by more than double that percentage.

Average weight = weight of 20 tablets
20

%weight variation = average weight - weight of each tablet ×100
Average weight

Table No – 6: Weight Variation Tolerance For Uncoated Tablets
Acceptance criteria for tablet weight variation (USP 29-NF 34)

Average weight of tablet(mg)	% difference allowed
130 or Less than	± 10
130-324	± 7.5
More than 324	± 5

3. **Thickness:** Thickness of the tablets (n=3) was determined using a Verniercalipers.
4. **Hardness test:** Hardness of the tablet was determined by using the Monsanto hardness tester (n=3) the lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.
5. **Friability test:** This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting.
   Initial weight of 20 tablets is taken and these are placed in the Friabilator, rotating at 25rpm for 4min.
   The difference in the weight is noted and expressed as percentage.
   It should be preferably between 0.5 to 1.0%.
   %Friability = [(W_1-W_2)/W_1] X 100
   Where, W_1= weight of tablets before test,
   W_2 = weight of tablets after test
6. **Wetting time**: Five circular tissue papers were placed in a petridish of 10cm diameter. Ten millimeters of water was added to the petridish. A tablet was carefully placed on the surface of the tissue paper in the petridish at 25^0C. The time required for water to reach the upper surface of the tablets and to completely wet them was noted as the wetting time. These measurements were carried out in replicates of six. Wetting time was recorded using a stopwatch.
7. In- Vitro Dispersion Time: In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of 6.8 phosphate buffer. Tablets from each formulation were randomly selected and in vitro dispersion time was performed.
8. Water absorption ratio(%): A piece of tissue paper folded twice was placed in a small petridish (Internal diameter=6.5 cm) containing 6ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) wasw determined using the following equation.

$$Water\ absorption\ ratio\ (R) = \frac{Wa - Wb}{Wb} * 100$$

Where, Wb is the weight of the tablet before water absorption and Wa is the weight of the tablet after absorption.

9. Assay Procedure: Ten tablets were weighed and powdered, a quantity of powder equivalent to 100 mg of Rosuvastatin was transferred to a 100 ml volumetric flask and 10 ml methanol is added. The drug is extracted in methanol by vigorously shaking the stoppered flask for 15 minutes. Then the volume is adjusted to the mark with 6.8 phosphate buffer and the liquid is filtered. From prepared solution take 0.1ml soluion in 10ml volumetric flask and make up to mark with 0.1 N HCL. The Rosuvastatin content was determined by measuring the absorbance at 257 nm after appropriate dilution. The drug content was calculated using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations.
   Calculate the quantity in mg of drug in the portion taken by the formula
   Assay = test absorbance/standard absorbance*standard concentration/sample concentration*purity of drug/100*100
10. In vitro Dissolution Study: 900 ml of 6.8 phosphate buffer was placed in the vessel and the USP-II apparatus (Paddle method) was assembled. The medium was allowed to equilibrate to temperature of 37^0C±0.5^0C. A tablet was placed in the vessel and was covered; the apparatus was operated up to 30mins at 50 rpm. At definite time intervals, 5 ml of dissolution medium was withdrawn; filtered and again replaced with 5 ml of fresh medium to maintain sink conditions. Suitable dilutions were done with dissolution medium and were analyzed spectrophotometrically at λ_{max}=257 nm using a UV-spectrophotometer (Lab India).

Table No – 7: Dissolution Parameters

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Parameter	Details
Dissolution apparatus	USP -Type II (paddle)
Medium	6.8 phosphate buffer
Volume	900 ml
Speed	50rpm
Temperature	37± 0.5 ºC
Sample volume withdrawn	5ml
Time points	2, 4, 6, 8, 10, 15, 20 and 30mins
Analytical method	Ultraviolet Visible Spectroscopy
Λmax	257 nm

11. **RELEASE KINETICS**: The analysis of drug release mechanism from a pharmaceutical dosage form is an important but complicated process and it is practically evident in case of matrix system. As a model dependent approach the dissolution data are fitted to three popular release models such as zero order, first order, diffusion equations which have been described in the literature. The order of drug release from matrix system was described by zero order kinetics or first order kinetics. The mechanism of drug release from matrix system was studied by Higuchi equation.
12. **ZERO ORDER RELEASE:**

It defines a linear relationship between the fraction of drug release

Q=KoT

Q=Fraction of drug release at time t.

A plot of fraction drug release against time will be linear if the release obeys zero order release kinetics.

13. **FIRST ORDER RELEASE KINETICS:**

Wagner assuming that the exposed surface area of the tablet decreased exponentially with time during dissolution process suggested that drug release from most slow release tablets could be described adequately by apparent first order kinetics.

The equation used is

Log (1-Q)= -K1T

Thus a plot of logarithm of fraction of drug remained against time will belinear if the release obeys first order kinetics.

12 . IR SPECTROSCOPY:

Infrared spectroscopy or used in vibrational spectroscopy is concerned with the study of absorption of infrared radiation which results in vibrational transitions .IR spectra is mainly used in structural elucidation to determine the functional groups.

Energy of a molecule =Electronic energy+vibrational energy+Rotational energy

ABSORPTIONS OF COMMON FUNCTIONAL GROUPS

GROUP	RANGE (cm^-1)
C-H Stretching (alkane)	2960-2850
C-H Stretching(alkene)	3040-3010
C-H Stretching(aromatic)	3030
C-H Bending(alkane)	1340
C-H Bending(aromatic)	700-850
C=C Stretching(alkene)	1680-1620

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C=C Stretching (aromatic)	1450-1600
C=O Stretching(ketone)	1705-1725
C=O Stretching(aldehyde)	1720-1740
C=O Stretching(acid)	1600-1725
C=O Stretching(amide)	1650-1700
O-H Stretching(free)	1650-1700
O-H Bending(alcohols)	3590-3650
O-H Bending(phenols)	1050-1150
C-O Stretching(alcohols)	1250-1350
C-O Stretching(phenols)	1310-1410
N-H Stretching	3400-3500
N-H Bending	1500-1650
C=N Stretching	1630-1690
S-H Stretching	2500-2600

PROCEDURE:

Take few mg of sample to be estimated. Then wipe the sample cell glass with chloroform and apply the sample powder to be estimated uniformly and observe the results.

SOLUBILITY:

Solubility is a property of a solid, liquid or gaseous chemical substances called solute to dissolve in a solid, liquid or gaseous solvent.

Different solvents are used like organic & inorganic to test the solubility of the Rosuvastatin.

Organic Solvents- acetone, alcohol, chloroform, carbon tetrachloride ,phenol, formic acid.

Inorganic Solvents- hydrochloric acid, sodium hydroxide, sulphuric acid, ammonia,

ANTIOXIDANTS:

A substance that inhibits oxidation, especially one used to counteract the deterioration of stored products.

In this formulation BHA & BHT are used as antioxidants to prevent the oxidation of the banana powder.

Some other antioxidants are ascorbicacid, tocopherol.

RESULTS AND DISCUSSION

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1. Construction of Standard Calibration Curve of Rosuvastatin in 6.8 phosphate buffer

The absorbance of the solution was measured at 257nm, using UV spectrometer with 0.1N HCL as blank. The values are shown in table. A graph of absorbance Vs Concentration was plotted which indicated in compliance to Beer's law in the concentration range 2 to 10 µg/ml

Table No – 8: Standard Calibration Graph Values of Rosuvastatin in 6.8 phosphate buffer

Concentration (µg/ml)	Absorbance
0	0
2	0.153
4	0.267
6	0.382
8	0.505
10	0.632

Standard plot of Rosuvastatin by taking absorbance on Y – axis and concentration (µg/ml) on X – axis, the plot is shown fig.

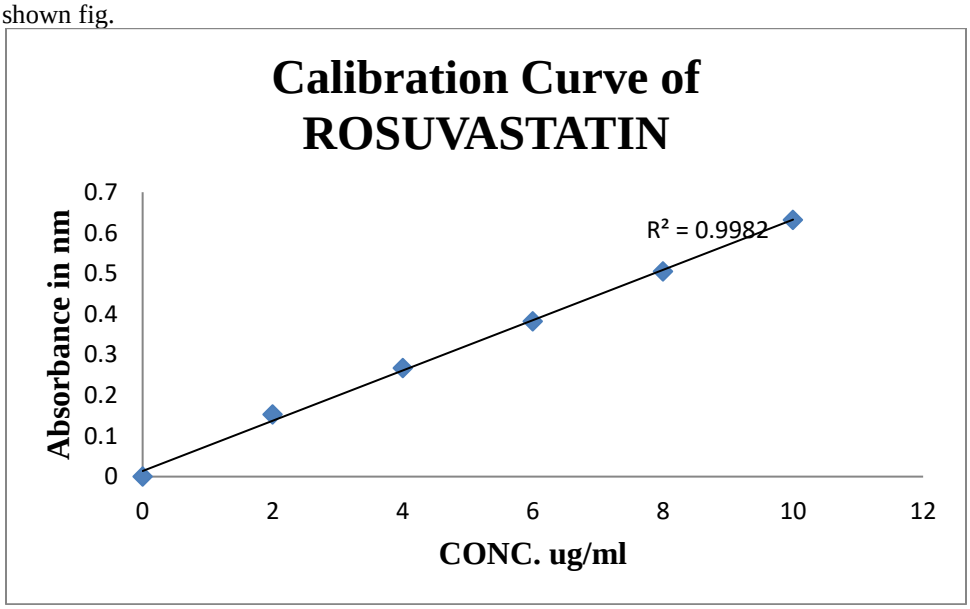

Figure No – 4: Standard Calibration Curve of Rosuvastatin in 6.8 phosphate buffer

EVALUATION OF BLEND

A) Pre Compression studies

Table No – 12: Pre Compression Studies Of Rosuvastatin Oral Disintegrating Tablets

Formulation code	Bulkdensity (Kg/cm^3)	Tappeddensity (Kg/cm^3)	Carsindex	Hausnersratio	Angleof repose (°)
F1	0.40	0.48	16	1.2	32.73
F2	0.39	0.48	18	1.23	34.96
F3	0.50	0.58	13	1.16	28.58
F4	0.44	0.50	12	1.1	27.92
F5	0.37	0.41	9.75	1.1	25.35
F6	0.37	0.41	9.75	1.1	33.14
F7	0.36	0.39	7.6	1.0	27.03
F8	0.41	0.45	8.8	1.0	31.85

B) Post Compression Studies:

Table No – 9: Post Compression Studies For Oral Disintigrating Tablets of Rosuvastatin

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Batch	Hardness (kg/cm2)	Friability (%)	Drug Content (%)	Thickness (mm)	Disintegration Time (sec)	Wetting Time (sec)	In vitro dispersion time	Weight variation	Water absorption ratio
F1	3.1	0.45	99.12	2.5	30	45	29	pass	61.3
F2	2.9	0.62	100.73	2.8	25	42	34	pass	69.8
F3	3.3	0.71	99.74	2.6	20	35	25	pass	73.4
F4	2.5	0.32	98.98	2.5	31	31	32	pass	86.2
F5	2.8	0.51	99.67	2.6	27	36	31	pass	84.12
F6	2.8	0.52	99.83	2.8	25	43	33	pass	93.4
F7	2.9	0.38	101.32	2.8	31	41	36	pass	64.3
F8	3.2	0.48	100.87	2.5	26	36	33	pass	74.8

SOLUBILITY: The prepared formulation of Rosuvastatin was found to be soluble in some organic and inorganic solvents.Soluble in- Sulphuric acid(CONC.), sodium hydroxide(CONC.), phenol.Insoluble in- acetone alcohol, chloroform, carbon tetrachloride, ammonia, formic acid.

INVITRO DISSOLUTION STUDIES OF ROSUVASTATIN TABLETS:

Table No – 10: Dissolution Data of Oral Disintegrating Tablets of Rosuvastatin

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	**0**	0	0
2	17.1	65.1	32.7	47.2	36.8	**28.4**	37.7	38.3
4	49.7	73	40.5	53	42.6	**38.3**	52.5	49.7
6	56.6	79.4	49.6	64.6	51	**51**	66.8	58.2
8	80.7	83.9	52.5	68.9	56.6	**80.8**	79.3	67.9
10	90	86.5	56.9	81.2	73.6	**83.5**	82.2	83.6
15	90.7	92.1	73.6	92.4	80	**92**	87.7	84.9
20	95.9	97.8	83.5	94.8	92.1	**94.8**	90.6	89.7
30	100	99	92.1	98.6	98.8	**99.2**	95.8	94.8

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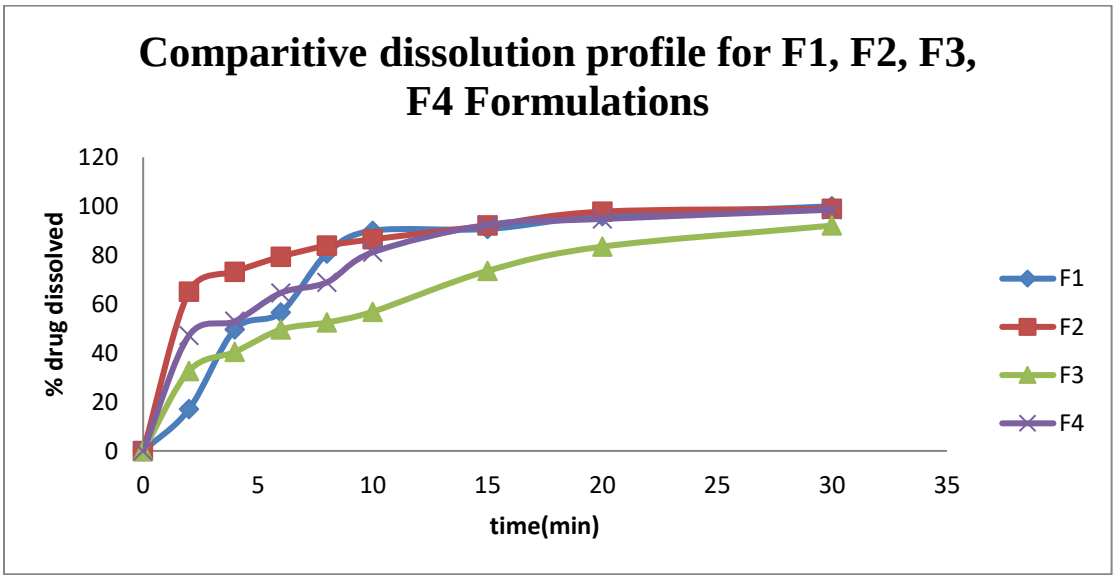

Figure No – 5: Comparative dissolution profiles for F1, F2, F3 and F4 Formulations

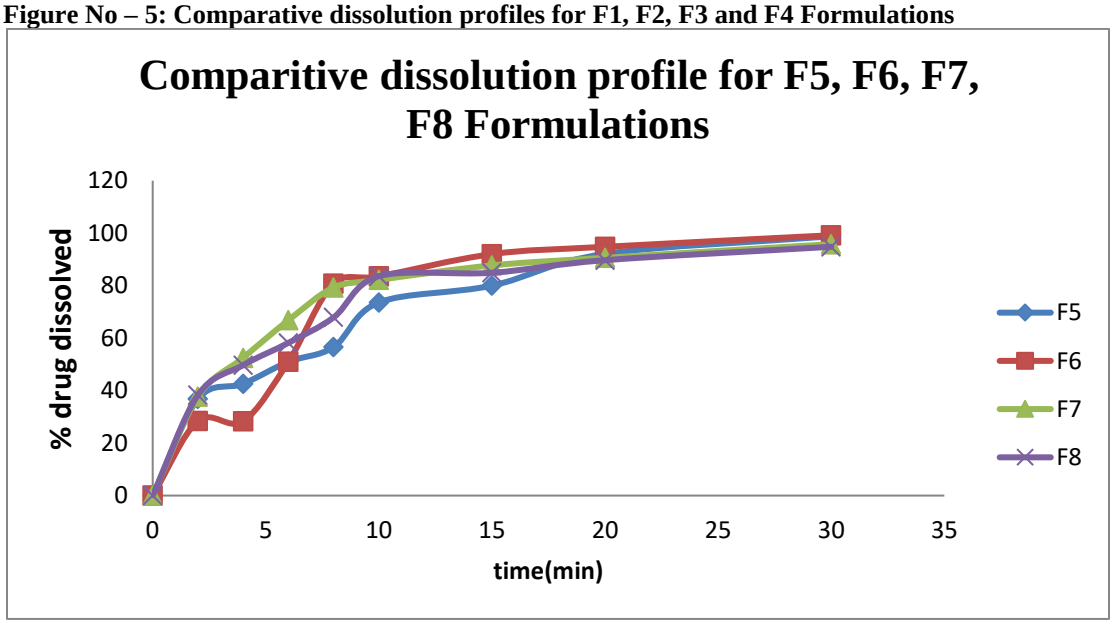

Figure No – 6: Comparative dissolution profiles for F5, F6, F7 and F8 Formulations

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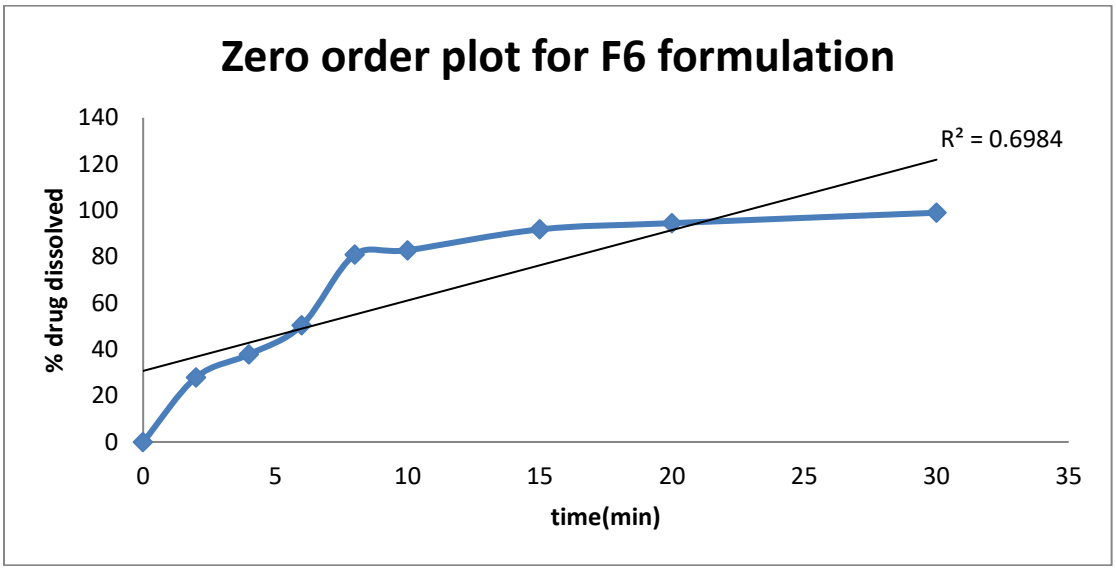

Figure No – 7: Zero order plot for best formulation F6

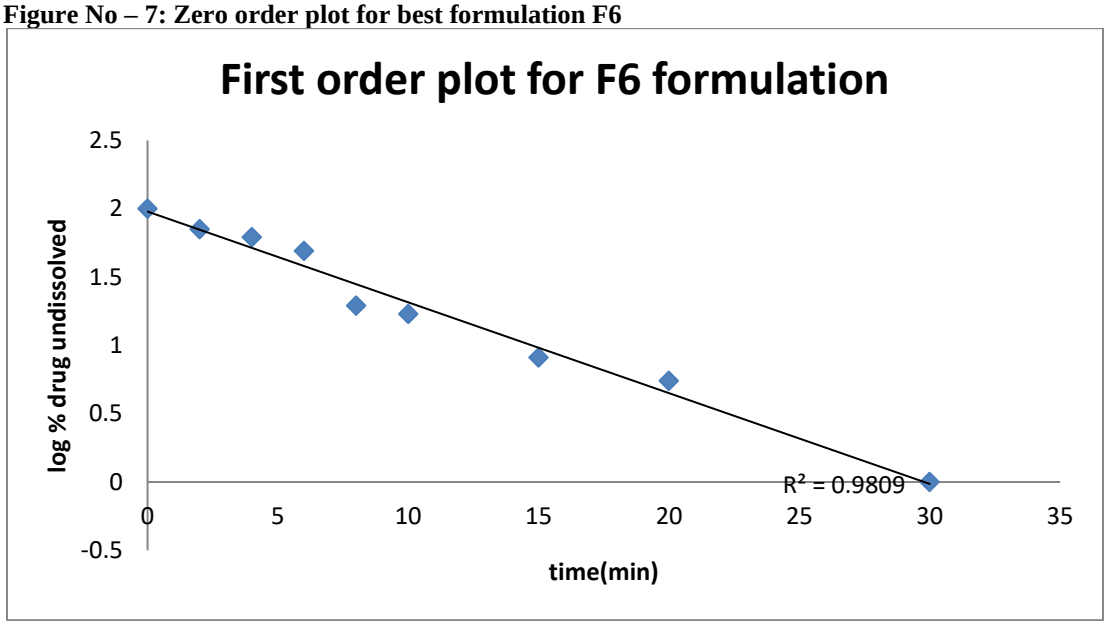

Figure No – 8: First order plot for best formulation F2

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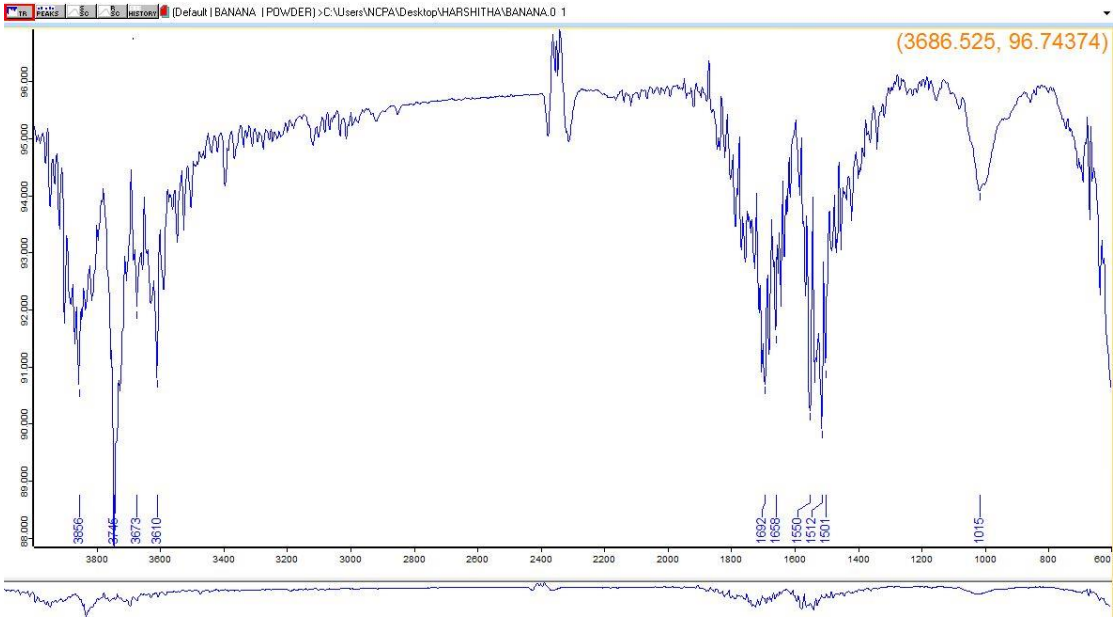
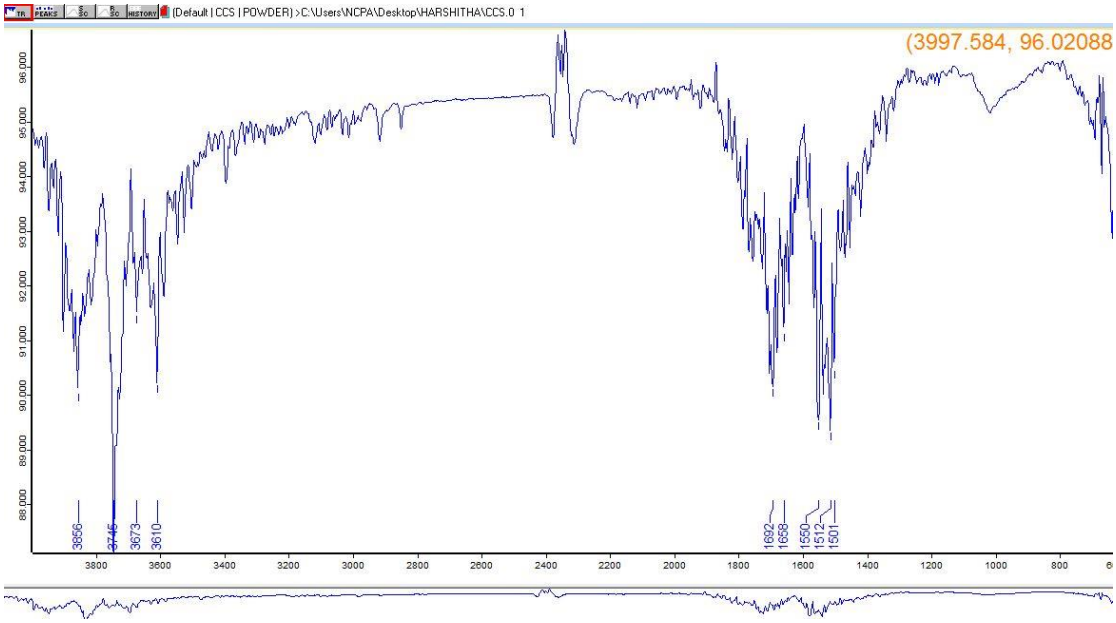
IR SPECTROSCOPIC ANALYSIS



BANANA POWDER



MAGNESIUM STEARATE

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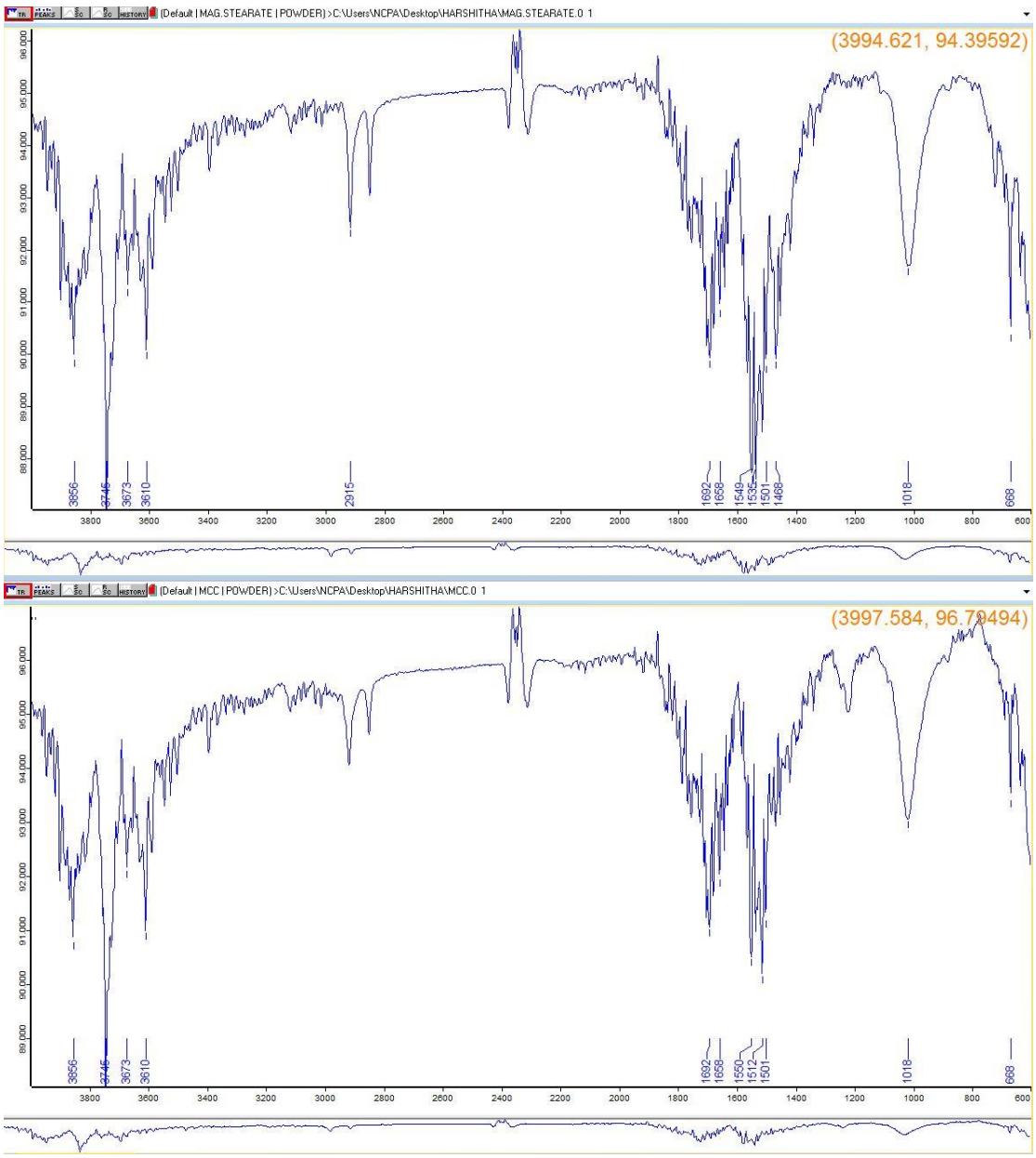

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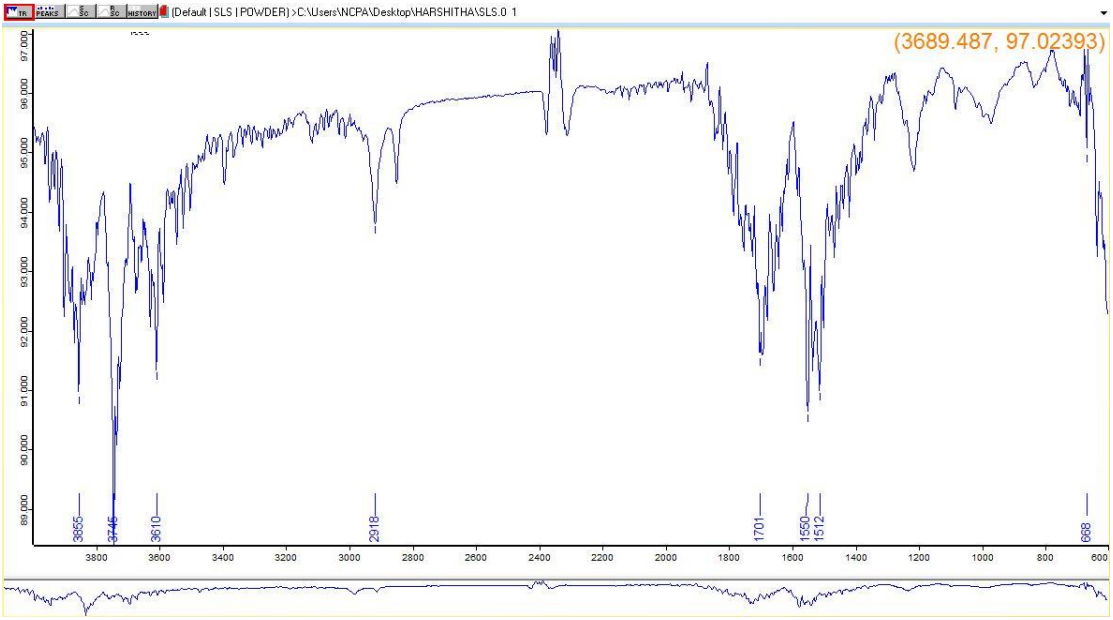
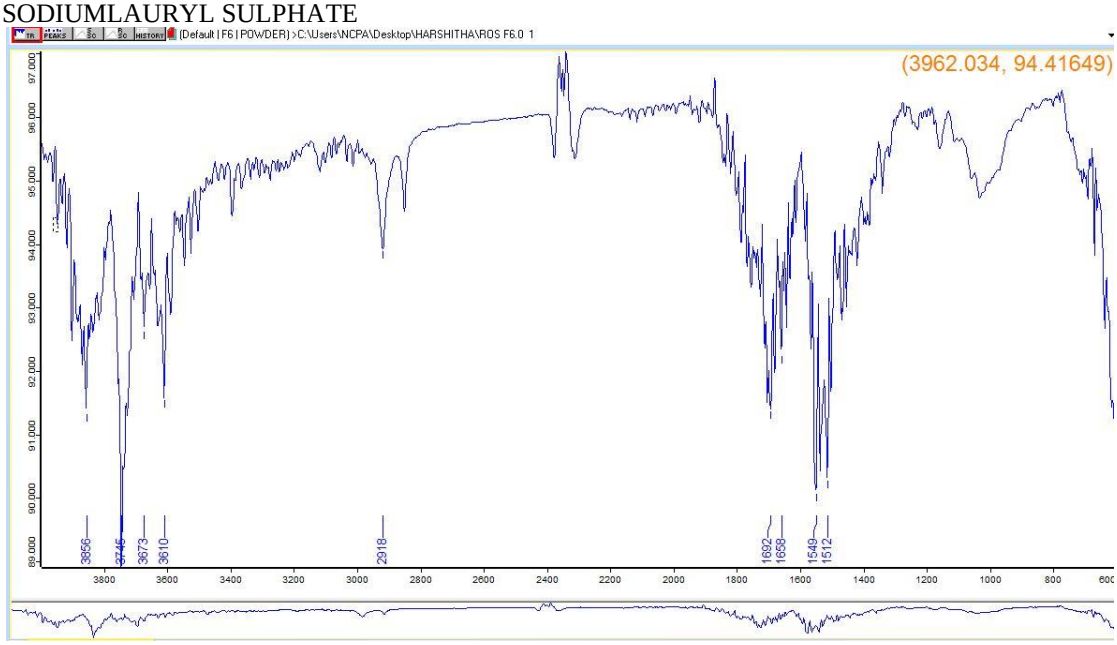
MICROCRYSTALLINE CELLULOSE



SODIUMLAURYL SULPHATE



F6 ROSUVASTATIN

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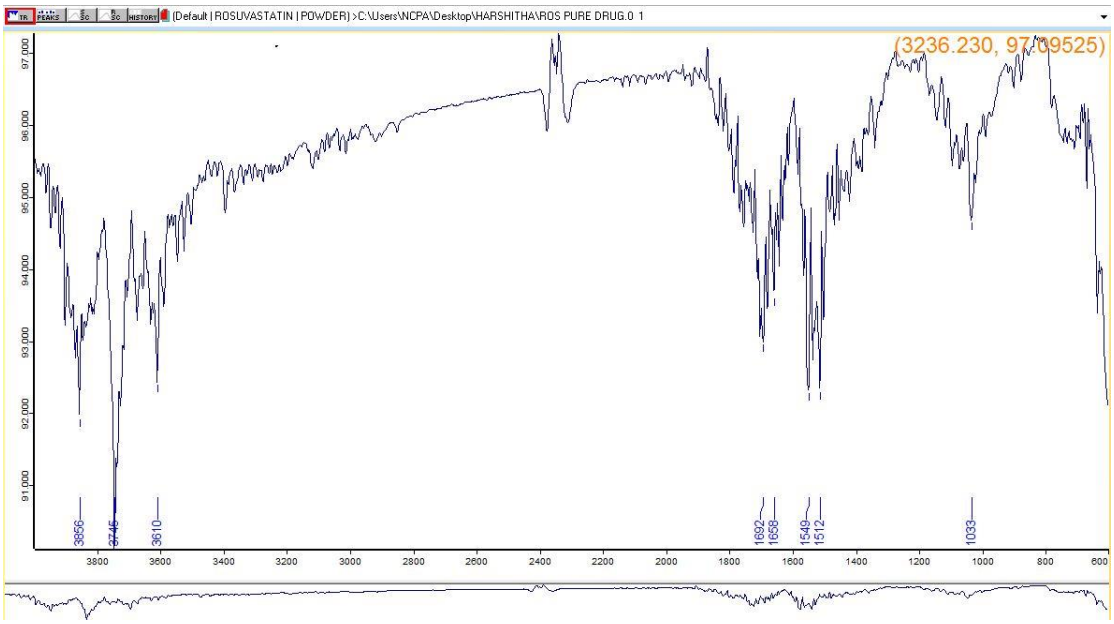

ROSUVASTATIN

SUMMAY AND CONCLUSION

1. Suitable analytical method based on UV-Visible spectrophotometer was developed for Rosuvastatin. λ_{max} of 257 nm was identified in 0.1N HCL.
2. Direct compression method was established to manufacture mouth disintegating tablets of Rosuvastatin.
3. Mouth disintegrating tablets of Rosuvastatin were successfully prepared using Banana powder and Croscarmellose sodium.
4. In the present study, mouth disintegating tablets were prepared by direct compression method.
5. Evaluation parameters like hardness, friability, weight variation and drug content indicate that values were within permissible limit for all formulations.
6. *In vitro* drug release study was carried out and based on the results; F-6 was identified as the best formulation among all the other formulations and *In vitro* release profiles was 99% within 30 minutes.
7. The Bananapowder used formulation has shown better release profile than compared with other formulations.

The mouth disintegating tablets of Rosuvastatin developed in this investigation releases drug within 30 minutes. Thus, we are able to achieve our objective of preparing mouth disintegating tablets of Rosuvastatin with minimum excipients and simple method of manufacture.

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