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FORMULATION AND EVALUATION OF ORAL FAST DISSOLVING DELIVERY FOR ROSUVASTATIN

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ABSTRACT

In the present work, oral thin films of Rosuvastatin were designed with a view to enhance patient compliance by solvent casting method. In the solvent casting method, ludiflash (1,2,3,4 and 5% w/w), crospovidone (1,2,3,4 and 5% w/w) as super disintegrants were used in different concentrations with Gelatin, Poly vinyl alcohol as a film forming base for the formulation of oral disintegrating thin films of Rosuvastatin by solvent casting method. The prepared formulations of films were evaluated for film thickness measurement, folding endurance study, in-vitro disintegration time, in-vitro drug release pattern (in pH 6.8 phosphate buffer). Drug content, and drug-polymers interaction study (IR spectroscopy). Among all formulations, the formulation (F5) prepared by 5% ludiflash show good drug release (98.34%).

Keywords: Ludiflash, crospovidone; Rosuvastatin; oral disintegrating thin films

1. INTRODUCTION

Among the different routes of administration, the oral route of administration continues to be most preferred route due to various advantages including ease of administration, avoidance of pain, versatility and most importantly patient compliance. Taking the biological and physiological aspects of absorption and metabolism, not many drugs can be delivered successfully through the oral route because of the first pass effect of the drug which in turn affects the membrane permeability, absorption and bioavailability **[1]**. One such relatively new dosage form is

the oral strip, a thin film that is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity. Recently, fast dissolving drug delivery system has started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better compliance **[2, 3]**. The oral bioavailability of many drugs is poor because of the pH of the stomach, the presence of enzymes, and extensive first-pass metabolism. Traditionally, these drugs have been administered as parenteral drug delivery systems, which invariably lead to poor patient compliance. This has made the pharmaceutical industry look for alternative routes of drug delivery like film drug delivery. Intraoral fast-dissolving drug delivery system is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption **[4, 5]**. Rosuvastatin mainly used for the treatment of hyperlipidaemia which is responsible for the coronary heart disease, stroke and Miocardial infraction. Hyperlipidaemia leads to arteriosclerosis. It is the condition in which the medium or large arteries become hard (loss of elasticity). Arteriosclerosis is a Greek word; Arterio means arteries and sclerosis means hardening. It is also called as hardening of artery specifically due to the formation of athermanous plaque. Atherosclerosis is the condition in which an artery wall thickens as the result of a build-up of fatty materials such as cholesterol. It is a syndrome in which affects arterial blood vessels, a chronic inflammatory response in the walls of arteries, in large part due to the accumulation of macrophage, white blood cells and promoted by low density lipoproteins without adequate removal of fats and cholesterol from the macrophages by functional high density lipoproteins (HDL) is commonly referred to as a hardening or furring of the arteries **[6, 7]**.

1.1 Overview of the oral cavity:

Oral cavity is that area of mouth delineated by the lips, cheeks, hard palate, soft palate, and floor of the mouth. The drug administered via the oral mucosa gain access to the systemic circulation through a network of arteries and capillaries. The major artery supplying the blood to the oral cavity is the external carotid artery. The venous backflow goes through branches of capillaries and veins and finally taken up by the jugular vein **[8, 9]**.

2. MATERIALS AND METHODS

2.1 Chemical and Reagents:

Rosuvastatin drug in this study was obtained from Kekule Pharma Limited. Gelatin, PEG 400, Citric acid, Lactose was gifted from S.D.Fine chemicals Mumbai. PVA was obtained from INR Chem. Mumbai, flavour was gifted from

International flavours of fragrance India Ltd. All the other materials and reagents used were of analytical grade.

3. PREFORMULATION STUDIES

Preformulation studies are of great importance for the development of high-quality dosage formulations in the short duration. In this, physical & chemical characteristics and derived properties of API are determined and evaluated effectively. This is the first learning phase before formulation development. By this study, we can minimize errors, reduce the costing, and reduce no. of trials. Solubility studies of Rosuvastatin in different buffers **[10]**.

3.1 Solubility studies: Solubility of Rosuvastatin was carried out in different buffers. Saturated solutions were prepared by adding an excess drug to the vehicles and shaking on the shaker for 24 hrs. at 37°C under constant vibration. Filtered samples (1ml) were diluted appropriately with suitable buffer and solubility of Rosuvastatin was determined spectrophotometrically at suitable nm.

3.2 Drug-excipient compatibility study [11]

a) Physical mixtures of drug and excipients were prepared by grinding specific ratios of drug and excipients in a mortar. A sample of 3-4 grams was loaded in a glass vial, covered with the rubber stopper, sealed with an aluminium cap and labelled properly. Samples were observed and the colour was recorded for initial evaluation and loaded into stability chambered at 40°C temperature and 75 % relative humidity for 30 days to study the Compatibility study. Samples were removed after 15 days and 30 days and observed for any change in the colour.

b) **FTIR spectroscopy**

The physical compatibility between the pure drug and polymers used in the research was tested by Infra-Red (IR) spectroscopy. FTIR absorption spectra of pure drug and physical mixture were recorded in the range of 400-4000cm-1 by KBr disc method using FTIR spectrophotometer.

c) Preparation of Standard Stock Solution:

10mg of Rosuvastatin was accurately weighed into 10 ml volumetric flask and dissolved in a small quantity of 6.8 pH Phosphate buffer solution. The volume was made up to 10 ml with the 6.8 PB solution to get a concentration of (1000 µg/ml). From this, 1 ml was withdrawn and diluted to 10 ml with 6.8 PB solution to get a concentration of (100 µg/ml) SS-II.

Determination of UV spectrum: -

From stock solution (SS-II), 1 ml was withdrawn and the volume was made up to 10 ml with 6.8 PB solution to get a concentration of 10 µg/ml. UV scan range was taken between the wavelengths 200-

400 nm. It gave a peak at 240 nm and the same was selected as λmax for Rosuvastatin.

Calibration Curve in 6.8 PB solution:

From the standard stock solution (SS-II), 0.5, 1, 1.5, 2, 2.5, 3 ml were withdrawn and volume was made up to 10 ml with PB solution to give a concentration of 5, 10 15, 20, 25 and 30 µg/ml. The absorbance of these solutions was measured against a blank of PB solution at 240 nm for Rosuvastatin and the absorbance values are summarized in **Table 1**. The calibration curve was plotted, drug concentrations versus absorbance were given in the **Figure 3**.

3.3 Preparation of mouth dissolving films:

From the preliminary physical observation of the films prepared the best compositions were used for the incorporation of Rosuvastatin. Gelatin, PVA polymers was dissolved in water with continuous stirring. The calculated amount of Rosuvastatin was dissolved in propylene glycol and add it to the polymeric solution, after complete dissolution of the drug; propylene glycol (plasticizer) was added and stirred to form a homogeneous solution and add disintegrants. The solution was cast onto mercury substrate then kept in hot air oven at 40ºC for 2 hrs. The film thus formed was cut into a size of 2 cm diameter. Each film contains 10 mg of Rosuvastatin.

The oral disintegrating thin films of Rosuvastatin were prepared by solvent casting technique. The ODT films were prepared using polymers like Gelatin, PVA. Propylene glycol is used as a plasticizer. The calculated amount of polymer was dispersed in the three-fourth volume of with continuous stirring using magnetic stirrer and the final volume was adjusted with distilled water. The calculated amount of Rosuvastatin was incorporated in the polymeric solutions after levitation with required volume of PEG. The solution was cast onto mercury substrate then kept in hot air oven at 40^0c. The films were punched into size 2cm diameter containing 10mg of Rosuvastatin. By carrying out thetrial anderror method different concentrations of film forming polymers were used like Gelatin, PVA. It has been found that 4.5%of gelatin, 3.5% of PVA shows better films. Which these concentrations of films were prepared by dissolving different quantities of film forming polymers in 10 ml of water.

NOTE: With the same procedure the films of 4.5% Gelatin, 3.5% PVA were prepared without the super disintegrating agents named as Fg, Fp respectively.

Table 1: Formulation details of Rosuvastatin Oral disintegrating thin films

Formulation	Rosuvastatin(mg)	Gelatin (%)	PVA (%)	Ludiflash (%)	Crospovidone (%)	Citric acid (mg)	Trusil flavour (mg)	PG (mg)
F g	106	4.5	--	--	--	4	8	30
F1	106	4.5	--	1	--	4	8	30
F2	106	4.5	--	2	--	4	8	30
F3	106	4.5	--	3	--	4	8	30
F4	106	4.5	--	4	--	4	8	30
F5	106	4.5	--	5	--	4	8	30
Fp	106	--	3.5	--	--	4	8	30
F6	106	--	3.5	--	1	4	8	30
F7	106	--	3.5	--	2	4	8	30
F8	106		3.5	--	3	4	8	30
F9	106	--	3.5	--	4	4	8	30
F10	106	--	3.5	--	5	4	8	30

3.4 Calculation of dose for Rosuvastatin:

The dose of Rosuvastatin is 10mg. Therefore amount of Rosuvastatin required in 2cm diameter of film is 10mg.

i. Area of film of 2cm diameter is 6.28 sq.cm.
ii. Area of petridish of 6.5cm diameter is 66.31 sq.cm.
iii. Amount of drug present in 6.28 sq.cm of film is 10mg
iv. Amount of drug present in 66.31 sq.cm of petridish is 105.58 mg.

Therefore, 66.31 sq.cm of petridish should contain 10mg of drug. It is fixed for all formulations. Therefore amount of Rosuvastatin in each film (2cm diameter) is 10mg.

4. EVALUATION OF FAST DISSOLVING ORAL THIN FILMS:

4.1 Post formulation studies:

The Rosuvastatin ODT films were evaluated for the following properties

a) Physical appearance and surface texture of patch:

This parameter was checked simply with visual inspection of films and evaluation of texture by feel or touch.

b) Weight uniformity of films:

Three films of the size 2cm diameter were weighed individually using digital balance and the average weights were calculated.

c) The thickness of films:

The thickness of the films was measured using screw gauge with a least count of 0.01mm at different spots of the films. The thickness was measured at three different spots of the films and average was taken.

d) Folding endurance of films:

The flexibility of films can be measured quantitatively in terms of what is known as folding endurance. Folding endurance of the films was determined by repeatedly folding a small strip of the films (approximately 2x2 cm) at the same place till it broke. The number of times films could be folded at the same place, without

breaking gives the value of folding endurance.

e) Surface pH of films:

Surface pH was determined by the films were allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of films and allowing equilibrate for 1 min.

f) In vitro disintegration time of films:

Disintegration test was performed in the USP disintegration time testing apparatus. PB (6.8)solution used as a medium. The films were placed in the tubes of the container and disintegration time was recorded.

g) Drug content uniformity study of films:

The films were tested for drug content uniformity by a UV-Spectrophotometric method. Films of 2 cm diameter were cut from three different places from the casted films. Each patch was placed in 100 ml volumetric flask and dissolved in 6.8 PB solution and 0.2 ml is taken and diluted with water up to 10 ml. The absorbance of the solution was measured at 240 nm using UV/visible spectrophotometer (Shimadzu UV-1700). The percentage drug content was determined using the standard graph and the same procedure was repeated for three films**.**

h) In-vitro Dissolution Study:

In vitro dissolution of Rosuvastatin Oral disintegrating thin films was studied in USP XXIV dissolution test apparatus 900ml 6.8 PB solution was used as dissolution medium. The stirrer was adjusted to rotate at 50rpm. The temperature of dissolution medium was maintained at 37±0.5ºC throughout the experiment. One film was used in each test. Samples of dissolution medium (5ml) were withdrawn by means of a syringe fitted with pre-filter at knownintervals oftime andanalysed for drug release by measuring the absorbance at 240nm. The volume withdrawn at each time interval was replaced with the fresh quantity of dissolution medium. Cumulative percent Rosuvastatin released was calculated and plotted against time.

i) Drug Release Kinetics:

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as:

1) Cumulative percentage drug released Vs time (In-Vitro drug release plots)

2) Log cumulative percentage drug remaining Vs Time (First order plots)

In the present study, an attempt has been made to formulate and evaluate odt films of Rosuvastatin by the solvent casting method using Crospovidone and ludiflash as super disintegrants.

5. RESULT & DISCUSSION

5.1 Solubility studies of pure drug:

Solubility

The solubility of Rosuvastatin was carried out at 25^0C using 0.1 N HCL, 6.8 phosphate buffer, and purified water **(Table 2; Figure 1)**.

From the conducted solubility studies in various buffers, we can say that 0.1 N HCL solutions have more solubility when compared to other buffer solutions.

5.2 UV spectrum of Rosuvastatin: (Figure 2)

5.3 Standard Calibration Curve of Rosuvastatin In 6.8 pH Phosphate Buffer:

Standard calibration curve of Rosuvastatin was drawn by plotting absorbance vs concentration. The λmax of Rosuvastatin in 6.8 pH phosphate buffer was determined to be 240nm as shown in **Figure 3**. The absorbance values are tabulated in **Table 3**. Standard calibration curve of Rosuvastatin in the Beer's range between 0-30 µg/ml is shown in **Figure 3**.

5.4 Compatibility Study:

Compatibility studies were performed using FT-IR spectrophotometer. When we observe the **Figure 4a, b** of FTIT spectra, the drug, exhibited the peaks at 3741 cm^{-1} , 3200-3600 $cm^{-1}$for O-H aromatic stretching, 1670-1820 cm^{-1} for C=O Stretching, 1380-1450 cm^{-1} for O=S=O stretching, 1000-1400 cm^{-1} for C-F stretching, 1400-1600 cm^{-1} for C=C stretching, 3000-3100 cm^{-1} for C-H, 1080-1360 cm^{-1} for N-C, 1640-1690 cm^{-1} for N=C Stretching. Similar peaks of the drug were observed in the drug-polymer physical mixture and thus indicate the absence of drug-polymer interaction.

5.5 Evaluation of oral disintegrating thin films formulations:

a) Physical appearance and surface texture of films:

These parameters were checked simply with visual inspection of films and by feel or touch. The observation suggests that the films are having the smooth surface and they are elegant enough to see.

b) Weight uniformity of films:

The weight of prepared films was determined using digital balance and the average weight of all films was given in Table. The weight of films measured without the disintegrating agents with 4.5% Gelatin, 3.5% PVA were about 56.5, 55.50 mg respectively The films prepared from 4.5% Gelatin with different concentrations of ludiflash as 1 %, 2%, and 3% were weighed about 58.50, 60.50, 62.50 mg respectively. And with 4% and 5% ludiflash were weighed about 64.50, 66.50 mg respectively. The films prepared from 3.5% PVA with different concentrations of crospovidone as 1 %, 2% and 3% were weighed about 57.50, 59.50, and 61.50 mg and with4% and 5% of crospovidone were weighed about 63.50, 65.50 mg respectively. In all the cases the calculated standard deviation values are very low

which suggest that the prepared films were uniform in weight.

c) The thickness of films:

The thickness of the films was measured using micrometer screw gauge and the average thickness of all films was given in **Table 4**. The thickness of films measured without the disintegrating agents with 4.5% Gelatin, 3.5% PVA were about 0.120, 0.120 mm respectively. The thickness of films prepared with Gelatin the concentration 4.5% with 1%, 2%, and 3% ludiflash were about 0.122, 0.124 and 0.122 mm respectively and with 4% and 5% of ludiflash were about, 0.120 and 0.122 mm respectively. The thickness of films prepared with PVA the concentration 3.5% with 2%, 4% and 6% of crospovidone were about 0.120, 0.120 and 0.122 mm respectively and with 4% and 5% of crospovidone were about 0.124, 0.122 mm respectively. In all the cases the calculated standard deviation values are very low which suggest that the prepared films were uniform in thickness.

d) Folding endurance of films:

The folding endurance of the films was determined by repeatedly folding a small strip of the films at the same place till it broke and the average folding endurance of all films was given in **Table 4**. The folding endurance of films prepared without the disintegrating agents with 4.5% Gelatin, 3.5% PVA were about 222, 242 respectively. Gelatin the concentration of 4.5% with 12%, 2% and 3% of ludiflash were about 232, 236 and 238 respectively and with 4%, 5% of ludiflash were about 235, 240 respectively. The folding endurance of films prepared with PVA the concentration 3.5% with 1%, 2%, and 3% crospovidone were about 244, 248 and 244 respectively and with 4% and 5% of crospovidone were about 244, 245 respectively.

e) Surface pH of films:

Surface pH was determined by the films were allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH Paper near the surface of films and allowing equilibrate for 1 min and the average Surface pH of all films was given in Table. The surface pH of the films prepared without the disintegrants from 4.5% Gelatin, 3.5% PVA were about 6.61, 6.80 respectively. The films prepared from gelatin in concentration of 4.5% with 2%, 4% and 6% of crospovidone were about 6.76, 6.00 and 6.46 and with 10% and 15% of ludiflash were about 6.23, 6.66 respectively. The surface pH of the films PVA in concentration 3.5%, with 2%, 4%and 6% of cross povidone were about 6.63, 6.16 and 6.12and with 8% and 10% of ludiflash were about 6.8, 6.74 respectively.

f) In vitro disintegration time of films:

The disintegration time limit of 30s or less

for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips. Although, no official guidance is available for oral fast disintegrating films, this may be used as a qualitative guideline for quality control test or at development stage. Pharmacopoeial disintegrating test apparatus may be used for this study. Typical disintegration time for films is 5–30sec. The average disintegration time of different formulation was shown in Table

The in vitro disintegration time of the films prepared without the disintegrants with 4.5% Gelatin, 3.5% PVA were about 54, 62 sec respectively. The in vitro disintegration time of the films prepared with 4.5% Gelatin with 1%, 2% and 3% crospovidone were about, 12, 10, and 10 sec and with 4% and 5% ludiflash were about 8, 6 sec respectively. The in vitro disintegration time of the films prepared with PVA in the concentration of 3.5% with 1%, 2% and 3% were about 17, 14 and 12sec. whereas with 4% and 5% of ludiflash were about 10, 11sec. respectively. In all the cases the calculated standard deviation values are different which suggest that, the prepared films show different in-*vitro* disintegration time.

g) Drug content uniformity of films:

Rosuvastatin fast films prepared with various polymers were subjected to the uniform dispersion of drug throughout the film. In each case three films were used and the average drug content was calculated, the results were shown in **Table 5**. The drug was dispersed in the range of 95.12% to 99.88% suggesting that drug was uniformly dispersed throughout all films. The SD value calculated for such formulation is very less which suggest that the results are reproducible and accuracy in the method used to prepare the films.

h) In-vitro dissolution study:

The in-vitro drug release study of mouth dissolving films from each batch (Fg, Fp, F1 to F10) was carried out in 6.8 pH phosphate buffer solution for 30 mins and the values are shown in **Table 6**. The plot of % Cumulative drug release V/s time (mins) were plotted and depicted as shown in **Figure 5-8**.

From the In vitro dissolution studies it was identified that the Fg formulation without disintegrant containing gelatin shows 65.12%of drug release at the end of 30mins, while Formulations containing Ludiflash in the concentration of 1%, 2% & 3% i.e., (F1-F3) shows 88.26%, 93.75%, and 95.83% at the end of 30mins.While 4% Shows 98.79% & 5% shows 98.34% release at the end of 25 mins.

while the Fp formulation without disintegrant containing PVA shows 52.52% of drug release at the end of 30mins, while Formulation (F6) containing Crospovidone in the concentration of 1% shows 76.68%

at the end of 30mins, While formulations (F7-F9) containing 2%, 3% & 4% shows 84.48%, 89.61%,& 93.06%, while the formulation (F10) containing Crospovidone 5% shows 94.82% drug release at the end of 30mins respectively.

This shows that effectiveness of super disintegrants is in the order of Ludiflash>Crospovidone. In all the formulations up to 5% w/w concentration of Ludiflash and 5% of crospovidone, there was linearly increase in dissolution rate. At higher concentration, all the formulations showed increase in dissolution rate.

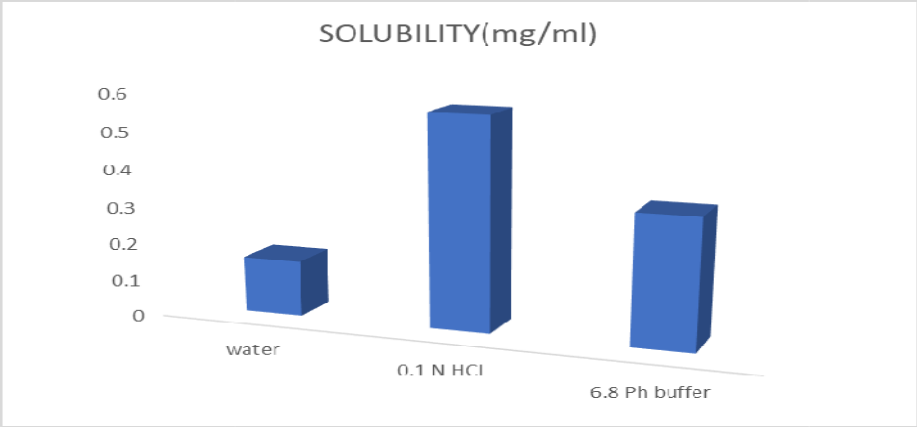
DRUG RELEASE KINETICS OF ROSUVASTATIN

Zero Order Release Kinetics (Figure 9)

First Order Release Kinetics Data (Figure 10)

Table 2: Solubility

S.NO	MEDIUM	SOLUBILITY (mg/ml)
01	Water	0.152
02	0.1 N HCL	0.568
03	6.8 Ph buffer	0.347



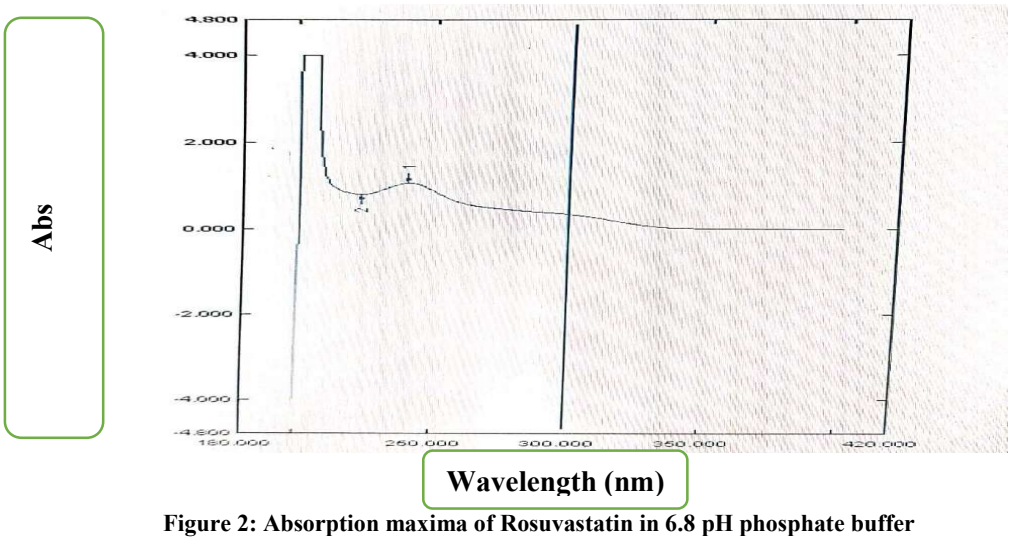


Figure 2: Absorption maxima of Rosuvastatin in 6.8 pH phosphate buffer

Table 3: Calibration data of Rosuvastatin in 6.8 PB solution at λ max 266 nm

SL.	Concentration	
1	0	0
2	5	0.176
3	10	0.346
4	15	0.518
5	20	0.703
6	25	0.871
7	30	1.035

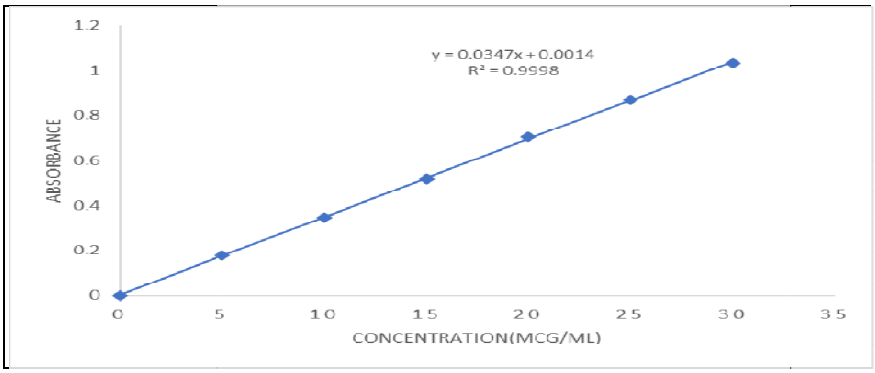


Figure 3: Standard calibration curve for Rosuvastatinin 6.8 PB solution at λmax 240 nm

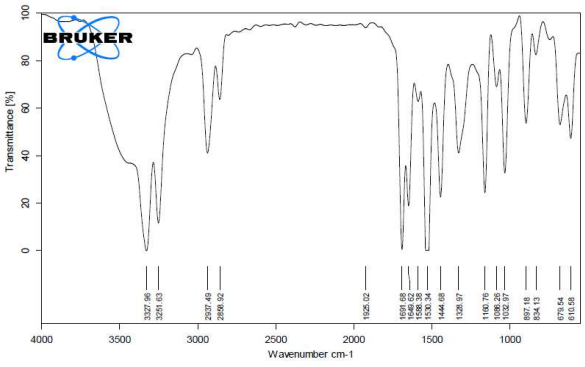


Figure 4(a): FTIR spectrum of Pure Rosuvastatin

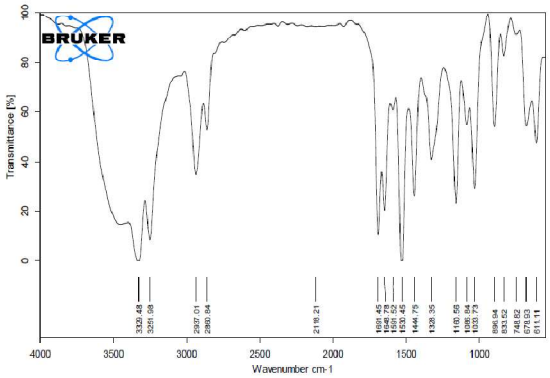


Figure 4(b): I.R. Spectra of optimized formulation

Table 4: Evaluation of Fast Dissolving Films of Rosuvastatin

Formulation Code	Avg. Weight (mg)	Avg. Thickness (mm)	Avg. Folding Endurance
Fg	56.50	0.120	222
F_1	58.50	0.120	232
F_2	60.50	0.122	236
F_3	62.50	0.124	238
F_4	64.50	0.122	235
F_5	66.50	0.120	240
F_P	55.50	0.122	242
F_6	57.50	0.120	244
F_7	59.50	0.120	248
F_8	61.50	0.122	244
F_9	63.50	0.124	245
F_{10}	65.50	0.122	244

Table 5: Evaluation of ODT films of Rosuvastatin

Formulation Code	Avg. Drug Content Uniformity (%)	Avg. In Vitro Disintegration (sec)	Avg. Surface pH
Fg	95.12	54	6.67
Fp	96.08	62	6.89
F1	98.24	12	6.76
F2	96.22	10	6.00
F3	97.48	10	6.46
F4	98.20	8	6.23
F5	97.42	6	6.66
F6	98.88	17	6.06
F7	98.88	14	6.83
F8	98.26	12	6.06
F9	97.48	10	6.33
F10	97.55	11	6.76

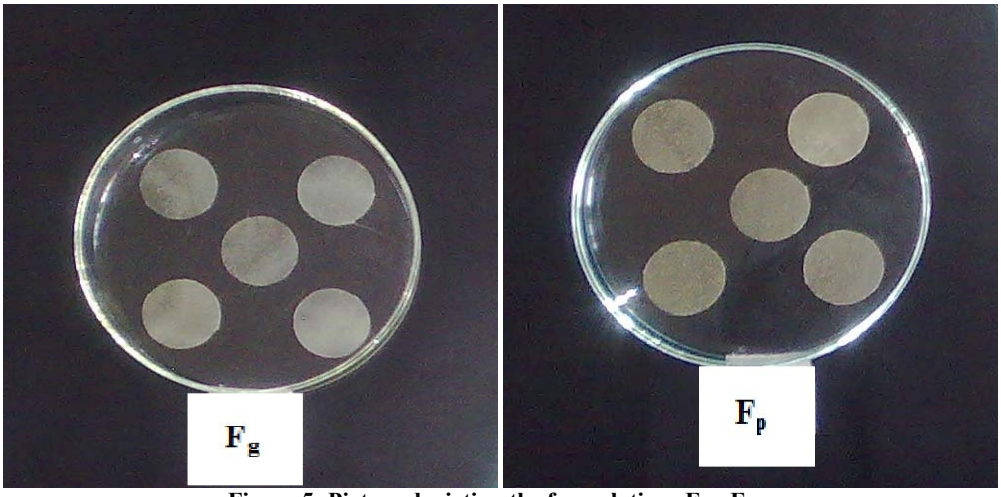


Figure 5: Picture depicting the formulations Fg , Fp .

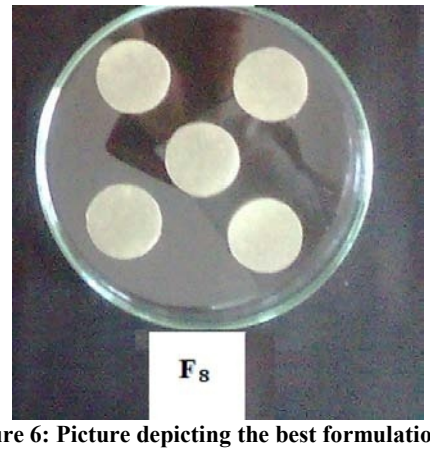


Figure 6: Picture depicting the best formulation F8

Table 6: In vitro dissolution studies:

Time(min)	Fg	FP	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0	0	0
5	22.58	15.46	42.95	65.42	67.91	69.93	67.49	41.27	48.87	54.78	56.87	58.45
10	36.54	26.24	57.31	69.37	72.43	74.86	74.04	45.96	54.08	59.85	60.98	64.94
15	41.21	31.81	66.72	73.07	76.48	79.13	79.19	49.97	58.36	64.19	65.39	70.51
20	50.22	39.38	72.05	79.19	82.49	84.78	88.06	58.05	66.16	70.69	72.68	77.93
25	56.24	48.16	81.66	86.83	89.97	92.53	98.34	67.34	75.76	79.71	82.96	83.50
30	65.12	52.52	88.26	93.75	95.83	98.79		76.68	84.48	89.61	93.06	94.82

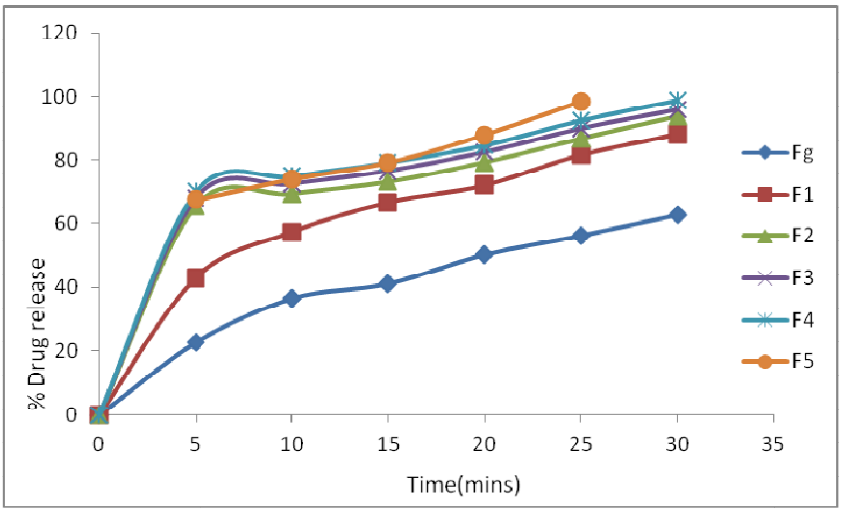


Figure 7: *In-vitro* drug release of formulations (Fg, F1-F5)

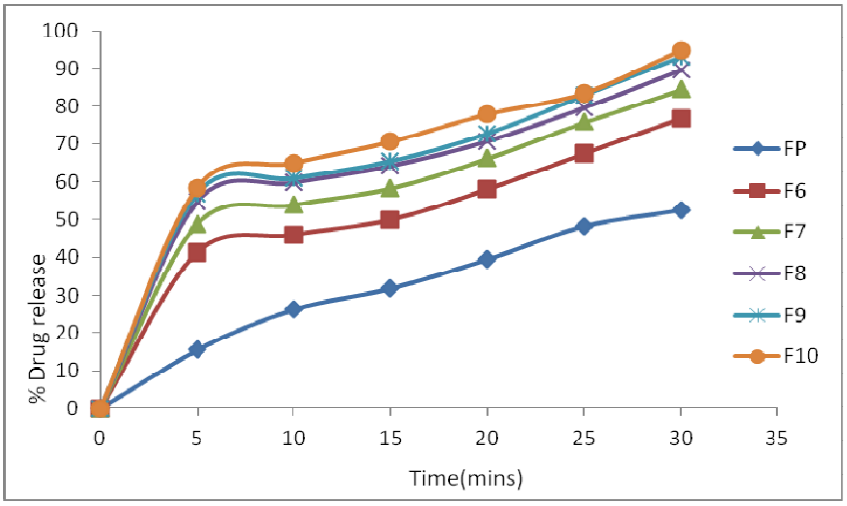


Figure 8: *In-vitro* drug release of formulations (Fp, F6-F10)

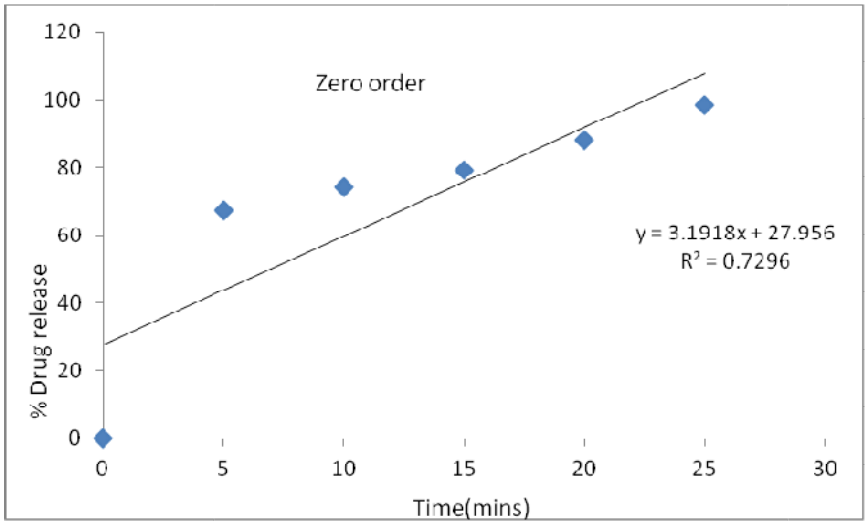


Figure 9: Zero order release profile of Rosuvastatin Best formulation (F5)

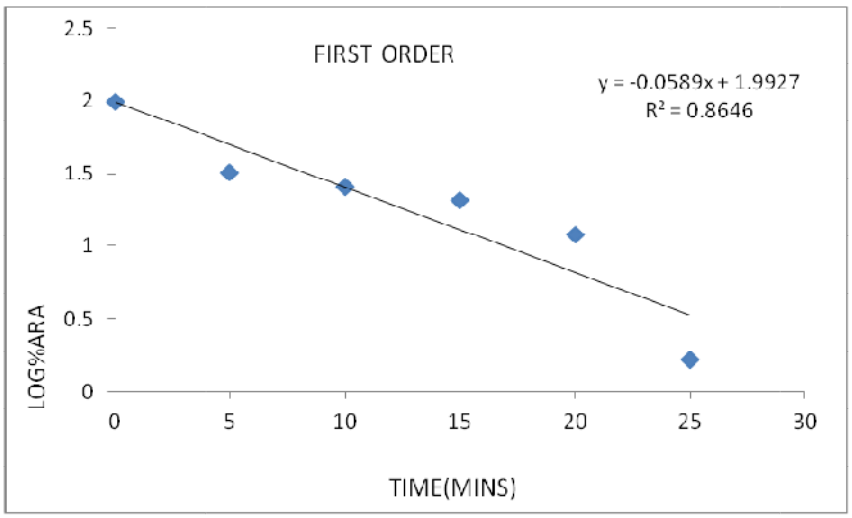


Figure 10: First order release profile of Rosuvastatin Best formulation (F5)

Table 7: Regression coefficients fit to different drug release kinetics models of Rosuvastatin Best formulation (F5)

Formulation code	Zero order	First order
	r^2	r^2
F5	0.729	0.864

The *in vitro* dissolution data for best formulation F5 were fitted in different kinetic models i.e, zero order, first order. Optimized formulation F5 follows first order.

6. CONCLUSION

The final suitable formulation (F5) was achieved fruitfully by the solvent casting method using polyvinyl alcohol and ludiflash as disintegrant which exhibited a rapid disintegration time (6sec) and in vitro drug release (98.34%).

Considering the results of batches containing ludiflash and crospovidone as disintegrant it can be concluded that the formulation F5 was meeting the higher in-vitro correlation limits and in less instance of time when subjected to the comparison with other formulation with crospovidone as the disintegrating agent. It was also observed that solvent casting method was the best suitable method used for immediate drug release. Based on all the above considerations these formulas will be subjected to bioavailability studies and if it complies with all the requirement of those studies the same formula will be commercialized

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