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Research Article

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF AMLODIPINE AND ROSUVASTATIN

Sheetal Buddhadev[1], Raval Kashyap[2], Sandip Buddhadev[3]
[1]Department of Pharmaceutics, Noble Pharmacy College, Junagadh, India
[2]Department of QA, Noble Pharmacy College, Junagadh, India
[3]Department of Dravyaguna, Gov. Ayurved College, Junagadh, India

Correspondence should be addressed to **Sheetal Buddhadev**

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ABSTRACT

Fast Dissolving Tablets (FDT)) are most accepted and exploited for the drug delivery for the patients who are having difficulty with swallowing i.e., mainly pediatric's and Geriatric's. Amlodipine besylate (ADB) is an anti-hypertensive and it is also used in many Coronary artery diseases, Whereas Rosuvastatin Calcium (RSC) is an anti-hyperlipidemia that prevents of Atheroma. The aim of the paper was to formulate a combined oral dosage form of amlodipine besylate and rosuvastatin calcium into fast dissolving tablet using three super disintegrants such as Croscarmellose Sodium (CCS), Cross povidone (CP), Sodium Starch Glycolate (SSG) at various concentrations to enhance the disintegration and dissolution of ADB and RSC to improve bioavailability of the drugs. The tablets were prepared by using direct compression method and evaluated for weight variations, Hardness, Friability, Wetting time, Disintegration time and Dissolution study. Prepared tablets are subject to FT-IR Study for Characterization and compatibility study. No Chemical interaction between drug and excipients were indicated in the FT-IR. Disintegration and dissolution profiles decreases with addition of super disintegrating agents like Croscarmellose Sodium (CCS), Cross povidone (CP), Sodium Starch Glycolate (SSG). Among all the formulation FD6 with CP in 10% and SSG 5% Concentration found to be best in drug release profile. The results showed that super disintegrants used in combinations shows better disintegrating property. Among all formulations, promising formulation FD6 showed good wetting time (26 sec), fastest disintegration time (55 sec) and maximum drug release of 99.89% within 5 minutes.

KEYWORDS: Fast Dissolving Tablets, Amlodipine besylate, Rosuvastatin Calcium, Super disintegrants, Direct compression method.

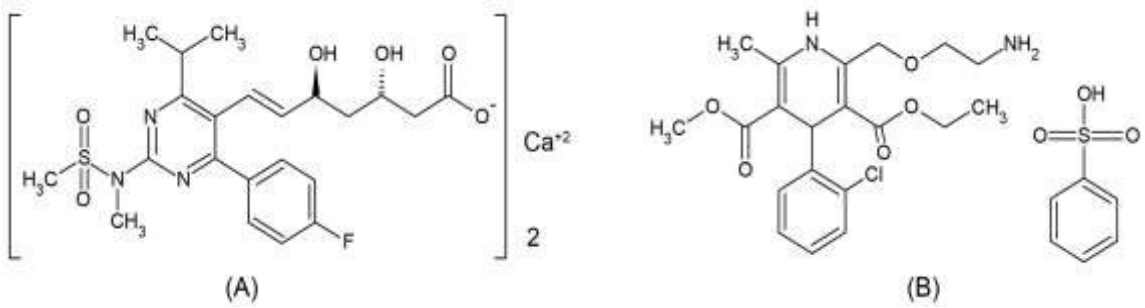
INTRODUCTION

Over a decade, the demand for development of fast dissolving tablets (FDTs) has enormously increased as it has significant impact on the patient compliance.Fast dissolving tablets offer an advantage for populations who have difficulty in swallowing. It has been reported that dysphagia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. FDTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population.[1, 2] many hypertensive symptoms of

hyperlipidemia patients may be reduced using the combination formulation of antihyperlipidemic and antihypertensive agents. Combined dosage form of two or more drugs has been proven useful in multiple therapies as they offer better patient compliance than a single drug. It is well recognized that a single drug, even when used in maximal recommended dosage will control no more than 50% of a hypertensive population On the other hand, the skillful use of two or more agents in combination can improve hypertension control rates to well above 80% . Therefore, the rational for combination therapy is to encourage the use of lower doses of drug to reduce patient's blood pressure with the goal to minimize dose dependent side effects and adverse reactions [3-4]. The fixed-dose combination containing the antihypertensive agent amlodipine and the cholesterol lowering agent atorvastatin is the first combination of its kind designed to treat two risk factors for cardiovascular disease. Atorvastatin has rapid access to non-hepatic tissues due to the hydrophobicity which results in some undesirable side effects. These unwanted side effects associated with combined dosage of atorvastatin and amlodipine may be reduced when rosuvastatin is used in place of atorvastatin. An assortment of techniques has been described for the quantification of rosuvastatin alone or in combination with other products. The reverse phase-high performance liquid chromatography (RP-HPLC) methods described for simultaneous determination of rosuvastatin and amlodipine in pharmaceutical preparations however, is not developed for in vitro dissolution profile of rosuvastatin calcium and amlodipine besylate from their combination drug products. Since no systemic studies on the design and development of such a combination formulation or its in vitro dissolution study are currently available in literature, we took an attempt to develop a suitable formulation and assay method which can be used further to characterize the in vitro dissolution profile of rosuvastatin calcium and amlodipine besylate [5-9]. Rosuvastatin, chemically described as bis [(E)-7 [4-(4-fluorophenyl)-6 isopropyl-2[methyl (methyl-sulphonyl) amino] pyrimidin-5-yl] (3R, 5S) -3, 5-dihydroxyhept-6-enoic acid] (Fig. 1), is another member of the drug class statin. It is hydrophilic and this makes it hepatoselective. This drug may thus be considered as a substitute of atorvastatin to formulate a new combination of drug for dose-related reduction in systolic blood pressure, diastolic blood pressure and low density lipoprotein cholesterol in patients with co-morbid hypertension and dyslipidemia. It competitively inhibits HMG-CoA reductase enzyme that catalyzes the conversion of HMG-CoA to mevalonate, an early rate-limiting step in cholesterol biosynthesis[10].

Amlodipine besylate, chemically described as 3-ethyl-5-methyl(±)-2-[(2-amino ethoxy)methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5 pyridine di carboxy late, monobenzenesulphonate, is a long-acting dihydropyridine class of calcium channel blocker, approved for treating hypertension and both vasospastic and chronic, stable angina. It selectively inhibits the transmembrane influx of Ca^{2+} ion across L-type calcium channels, without changing serum calcium concentration. Thus it relaxes the muscles lining the arteries and lowers blood pressure. It also expands coronary arterioles which increases the flow of blood to the heart and prevents heart pain (angina) resulting from reduced flow of blood to the heart that is caused by coronary artery spasm (contraction). It is more vasoselective with lower negative inotropic effects and reflex tachycardia is less prominent since fluctuations in plasma levels are less pronounced with these agents[11].

Figure 1*: Structure of (A) Rosuvastatin calcium and (B) Amlodipine besylate*



MATERIALS AND METHODS

Materials

Amlodipine besylate, Rosuvastatin Calcium were received as gift samples from Dr. reddy Lab's, Hyderabad, Sodium Starch glycolate, Crosscarmellose sodium, Cross povidone, Microcrystalline cellulose, Aspartame, Citric acid, Aerosil, Talc and Magnesium Stearate are obtained from commercial sources Yarrow Chem. All the reagents used are of analytical grade.

Methods

Fast dissolving tablets of Amlodipine Besylate and Rosuvastatin Calcium is prepared by geometric mixing. All the ingredients were weighed according to the formula in table No. 1. Nine formulations containing Cross povidone, crosscaramellose sodium and Sodium Starch Glycolate alone, in combination and in different concentrations were prepared using 8 mm round flat punches by direct compression method in a single stage tablet punching machine.

A batch of 50 tablets was prepared in each batch for further characterization. Standard deviation (SD), averages and one way ANOVA were used to interpret the results.

Table 1: *Formulation of Fast Dissolviing tablets of Amlodipine and Rosuvastatin using direct compression technique*

Ingredients	FD1	FD2	FD3	FD4	FD5	FD6	FD7	FD8	FD9
Amlodipine	10	10	10	10	10	10	10	10	10
Rosuvastatin	10	10	10	10	10	10	10	10	10
Crosspovidone	7.5	-	-	15	7.5	15	7.5	-	-
Cross Carmellose Sodium	-	7.5	-	7.5	15	-	-	15	7.5
Sodium Starch Glycolate	-	-	7.5	-	-	7.5	15	7.5	15
Aspartame (3%)	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Citric acid (0.5%)	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Aerosil (0.5%)	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Microcrystallinecellulose	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Total Weight	150	150	150	150	150	150	150	150	150

Evaluation of Fast Dissolving Tablets of Amlodipine and Rosuvastatin

Pre- Compression Parameters

Angle of repose

Angle of repose (θ) was determined by measuring the height (h), radius of the heap(r))of the powder blend. A cut system funnel was fixed to a stand and bottom of the funnel was fixed at a height of 2 cm from the plane. Powder blend was placed in funnel and allowed to flow freely and measured the height and radius of the heap.

$$\tan \Theta = \frac{h}{r}$$

Bulk density

The bulk density of a powder is dependent on particle packing and changes as the powder consolidates. Apparent bulk density (gm/ml) was determined by pouring bulk powder into a graduated cylinder via a large funnel and measuring the volume and weight. Bulk density can be calculated by the following formula,

$$\text{Bulk density} = \frac{\text{Weight of powder}}{\text{Bulk volume}}$$

Tapped density (D_t)

Tapped density is the bulk density of a powder which has been compacted by tapping or vibration. Tapped density was determined by placing a graduated cylinder containing a known mass of powder on a mechanical tapping apparatus, which is operated for a fixed number of taps (100) or until the powder bed volume has reached a minimum. The tapped density was computed by taking the weight of drug in cylinder and final volume.

$$\text{Tapped densit } (D_t) = \frac{\text{Weight of powder}}{\text{Tapped volume}}$$

Hausner's ratio

Hausner Ratio is an indirect index of ease of powder flow. It is calculated by the following formula,

$$\text{Hausner's ratio} = \frac{\text{Tapped density of powder}}{\text{Bulk density of powder}}$$

Compressibility Index (Carr's Index)

Another indirect method of measuring powder flow form bulk densities was developed by Carr. The percentage compressibility of a powder is a direct measure of the potential powder arch or bridge strength and stability. It is calculated according to the following equation,

$$\text{Carr's Index} = \frac{\text{Tapped density} - \text{bulk density} \times 100}{\text{Tapped density}}$$

Fourier Transform Infrared Spectroscopy

To check the compatibility of drugs with each other and with superdisintegrants, Fourier transform infrared spectroscopy was conducted. Sample preparation was done in KBr disks (2 mg sample in 200 mg KBr). The scanning range was 400–4000 cm^{-1} and the resolution was 2 cm^{-1}.The hydraulic pressure was kept 150kg/cm^2

B. Post Compression Parameters[12-22]

Quality control tests for FDTs of all formulations were performed, and the average values were calculated. All the tablets were evaluated for different parameters as weight variation, hardness, friability, drug content, wetting time, water absorption ratio, disintegration time and *in vitro* dissolution study.

Weight Variation:

Twenty tablets were selected randomly from each batch and weighed individually on electronic balance (Shimadzu). The individual weighed is then compared with average weight for the weight variations.

Hardness

The strength of tablet is expressed as tensile strength (kg/cm^2). The tablet crushing load, which is the force required to break a tablet into pieces by compression. It was measured using a tablet hardness tester (Monsanto hardness tester). Three tablets from each formulation batch were tested randomly and the average readings were noted.

Friability

Friability of the tablets was determined using Roche Friabilator. This device consists of a plastic chamber that is set to revolve around 25 rpm for 4 min dropping the tablets at a distance of 6 inches with each revolution. Pre weighed sample of 20 tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F %) is given by the formula

$$\mathbf{F\ (\%) = (1 - W_0 / W) \times 100}$$

Where, W is weight of the tablets before the test

W_0 is the weight of the tablets after test.

Wetting time

A piece of tissue paper (12cmx10.75cm) folded twice was placed in a Petri dish (Internal Diameter=9cm) containing 9ml of buffer solution, which had the following to the petridish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time. Six tablets from each formulation batch were tested randomly and the average reading noted.

Water Absorption Ratio

A Petri dish with inner diameter of 6.5 cm and having 6 ml water in it was used for this test. A tissue paper folded twice was put in the Petri dish. A pre-weighed tablet was positioned in it, after complete wetting the tablet was re-weighed

$$\mathbf{R = (Wa - Wb / Wb) \times 100}$$

Wa = Weight of the tablet before wetting

Wb = Weight of tablet after Wetting

Content Uniformity Test

The drug contents of each formulation was determined and found tobe between 97%-105% which was within the legal limits. Equal quantities of powder and standards were taken and assayed at respective wavelengths after suitable dilutions and filtration.

The standard solutions of Amlodipine and Rosuvastatin were scanned separately in the range of 200 to 400 nm against 1 N Phosphate buffer (PH 6.8) as blank and wavelengths of maximum absorbance were determined. Amlodipine and Rosuvastatin showed absorbance maxima at 237nm (λ_1) and 244 nm (λ_2) respectively. The concentrations of drugs were determined using following equations.

$$\mathbf{Cx} = (\mathbf{A2} \times \mathbf{ay1} - \mathbf{A1} \times \mathbf{ay2}) / (\mathbf{ax2} \times \mathbf{ay1} - \mathbf{ax1} \times \mathbf{ay2})$$

$$\mathbf{Cy} = (\mathbf{A1} \times \mathbf{ax2} - \mathbf{A2} \times \mathbf{ax1}) / (\mathbf{ax2} \times \mathbf{ay1} - \mathbf{ax1} \times \mathbf{ay2})$$

Where, Cx = Concentration of Amlodipine in gms/lit

Cy = Concentration of Rosuvastatin in gms/lit

A_1 = Absorbance at 244nm

A_2 = Absorbance at 237nm

ax1= absorptivity of Amlodipine at 244 nm

ay1= absorptivity of Rosuvastatin at 244 nm

ax2= absorptivity of Amlodipine at 237 nm

ay2= absorptivity of Rosuvastatin at 237nm

The absorbance of the solution was measured at 237nm and 244nm and concentration of the two drugs were calculated using this equation.

In Vitro Disintegration Time

One tablet was placed in each tube of disintegration apparatus (Pharma Test Germany). Buffer solution of pH 6.8 was used for disintegration and temperature was maintained at 37°C ± 2°C. The time required for complete disintegration of the tablets was noted.

Invitro Drug Release Studies

Dissolution studies were performed in phosphate buffer of pH 6.8 using USP type-2 apparatus [Electrolab Tablet Dissolution Tester] with a speed of 50 rpm at 37°C. Aliquots of 5ml of dissolution medium were withdrawn at specific time intervals (5, 10, 15, 20, 25, 30, 45 and 60 minutes), filtered and the amount of drug released was determined using UV Visible spectrophotometrically. Three trials for each batch were performed and average percentage drug release with standard deviation was calculated and recorded.

Stability Studies

Stability studies were carried out for the optimized formulation according to ICH guidelines. An optimize formulation were sealed in aluminium packaging coated inside with polyethylene, and samples were kept in humidity chamber (Remi, India) at 40°C and 75% RH for three month. At the end of the three month, samples were analyzed for drug physical changes, properties, drug content and in vitro release studies.

RESULTS AND DISCUSSION

Fast Dissolving tablets of Amlodipine besylate and Rosuvastatin Calcium of Strength 10,10 mg were prepared by using direct compression method with three superdisintegrant such as Croscarmellose Sodium(CCS) ,Cross Povidone(CP) and Sodium Starch Glycolate(SSG). Nine formulations containing Cross povidone, crosscaramellose sodium and Sodium Starch Glycolate alone, in combination and in different concentrations 5%,

10% used to study the effect of concentration on formulation Dissolution profile.

Before compressing, powder blend was first assessed for rheological properties Table 2. The results had shown that all the parameters were present within the specified limits. It indicates that powder has good flow properties. This powder blend was used to make Fast dissolving tablets. The weight of tablets was present between 148.60 to 151.92 mg. This indicates that tablets have no weight variation. Friability of all 9 formulations was less than 1% which indicates that tablets had good mechanical strength to bear any sort of stress during transport and storage. One way ANOVA was used to evaluate results statistically. P-value was 0.0289 which indicate that results were significant. It means that friability was significantly affected by the concentration of superdisintegrants and method of preparation.

Disintegration time (55 to 180 sec), wetting time (25 to 46 sec) and dispersion time (55 to 184 sec) were calculated for each formulation. Tablets should disintegrate completely in oral cavity in less than 3 minutes. The fast disintegration may be due to the rapid uptake of water from the medium which results in swelling and bursting effect is produced. Disintegration time, wetting time and dispersion time all were less for FD6 formulation containing both Crosspovidone and sodium starch glycolate in combination. P-value for these parameters was less than 0.05 which indicates that results were significant. It suggests that disintegration time, wetting time and dispersion time were affected by nature of superdisintegrant and method of preparation. Statistically by one way ANOVA results of in vitro dispersion were significant between the groups. Water Absorption ratio was used to determine that how much water is absorbed by the tablets. As value of water absorption ratio increases it indicates that rapid breaking of tablets and therefore faster disintegration as table 4. This disintegration ultimately affect dissolution rate of tablets. It was more for the formulations containing crosscaramellose sodium than cross povidone. The results of one way ANOVA had shown that water absorption ratio within groups were significant which indicates that concentration of superdisintegrants affect the tablet disintegration. The drug release studies were performed up to 45 minutes at 237 and 244nm for Amlodipine and Rosuvastatin respectively using UV- visible spectrophotometer after appropriate dilution and filtration. Drug release was rapid for FD6 formulation that was 99.10% for amlodipine and 98.96% for atorvastatin within 5 min. Three best formulations were chosen for stability studies. No significant changes were occurred in various parameters at the end of three months when stability studies were performed under zone 4 according to ICH (International Conference on Harmonization) guidelines.

CONCLUSION

Fast Dissolving tablets of Amlodipine and Rosuvastatin were prepared by direct compression method using crospovidone (CP), croscarmellose (CCS) and sodium starch glycolate (SSG) in combined form as CP and CCS in combination of 10:5 and 5:10 ratios, CP and SSG in combination of 10:5 and 5:10 ratios and CCS and SSG in combination of 10:5 and 5:10 ratios respectively. From the observed parameters it was concluded that the formulation (FD6) containing 10% crosspovidone and 5% sodium starch glycolate satisfied all the official requirements. It shows *In-vitro* disintegration time 55 secs and greater rate of dissolution at 5 minutes which gives 99.89% drug release. Results from stability studies also indicate that the formulated fast dissolving tablets are stable for a period of 3 months 40±2 °c and 75±5%RH. There were no remarkable changes were observed during the period of storage. There is no change in physical appearance and % drug release for the period of 3 months, so it is continue for the next three month as per ICH guidelines for stability studies. Cross povidone swell 4-10 folds in less than 10 seconds and it has excellent swelling properties and its high wicking property than Sodium Starch Glycolate at that concentration and Sodium Starch Glycolate show better disintegration time and Swelling of time thus increase the rate of dissolution of formulation. Hence it can be concluded that using a combination of synthetic superdisintegrants would be quite effective in providing faster onset of action without the need of water for swallowing

Table 2: Pre-compression studies parameters of Fast Dissolving Tablet of Amlodipine and Rosuvastatin tablet

Formulation	Angle of Repose (θ)*	Bulk Density (g/ml)*	Tapped Density (g/ml)*	Carr's index (%)*	Hausner Ratio*
FD1	25.8± 0.28	0.701± 0.02	0.828± 0.04	15.338± 0.04	1.181± 0.01
FD2	26.7± 0.19	0.698± 0.00	0.822± 0.01	15.085± 0.11	1.178±0.02
FD3	26.0± 0.16	0.695± 0.01	0.818± 0.01	15.037± 0.15	1.177± 0.01
FD4	26.0± 0.21	0.696± 0.01	0.820± 0.00	15.122± 0.05	1.178±0.02
FD5	26.5± 0.23	0.696± 0.01	0.820± 0.01	15.122±0.13	1.178±0.02
FD6	25.4± 0.17	0.694± 0.02	0.824± 0.02	15.777± 0.14	1.187± 0.01
FD7	27.3± 0.08	0.698± 0.01	0.812± 0.01	14.039± 0.14	1.163± 0.01
FD8	28.0± 0.22	0.702± 0.00	0.800± 0.01	12.250± 0.08	1.140± 0.01
FD9	25.8± 0.21	0.696± 0.01	0.820± 0.00	15.122± 0.05	1.178±0.02

Table 3: Post-compression studies of Fast Dissolving Tablet of Amlodipine and Rosuvastatin

Formulation	Wt variation (mg) (Avg.±SD)	Hardness (kg/cm^2) (Avg.±SD)	Friability (%) (Avg.±SD)	Thickness (mm) (Avg.±SD)	Drug content (%) (Avg.±SD)At 237 nm
FD1	151.92 ±3.85	3.82±1.7	0.48	3.26±0.01	98.3±0.21
FD2	149.06 ±2.50	3.50± 1.4	054	3.34±0.06	98.8±0.19
FD3	149.86 ±3.05	3.35±1.4	0.56	3.26±0.04	96.9±0.16
FD4	150.63±1.50	3.96±1.8	0.42	3.25±0.06	99.5±0.16

FD5	148.60 ±1.75	3.98±1.3	0.50	3.21±0.01	97.6±0.23
FD6	151.15 ±1.50	3.70±2.1	0.45	3.18±0.03	98.3±0.21
FD7	149.44±2.50	3.65±1.5	0.48	3.23±0.01	97.6±0.23
FD8	148.89 ±2.50	3.50±1.6	0.50	3.19±0.05	99.5±0.16
FD9	151.92 ±1.50	3.56±1.8	0.54	3.30±0.01	96.8±0.16

Table 4: Post-compression studies of Fast Dissolving Tablet of Amlodipine and Rosuvastatin

Formulation	Wetting time (sec)(Avg.±SD)	Water absorption ratio (Avg.±SD)	Moisture uptake study (Avg.±SD)	Disintegration time (min. sec) (Avg.±SD)	pH of Tablet sol
FD1	38.43±0.02	38.55±0.03	3.62±0.11	3.04±0.01	6.8
FD2	46.30±0.01	38.55±0.03	4.14±0.13	2.52±0.01	6.6
FD3	29.15±0.05	37.39±0.01	4.28±0.16	2.38±0.01	7.1
FD4	28.59±0.01	36.71±0.03	5.06±0.12	2.15±0.01	7.0
FD5	30.57±0.01	42.76±0.01	3.62±0.12	1.39±0.01	6.8
FD6	25.98±0.02	34.19±0.05	2.14±0.11	0.55±0.01	6.9
FD7	28.98±0.01	38.32±0.03	3.72±0.12	2.00±0.01	7.0
FD8	30.59±0.01	36.86±0.01	4.51±0.12	1.46±0.01	7.1
FD9	28.59±0.01	35.41±0.02	3.94±0.11	1.16±0.01	6.9

Table 5: Drug content of Fast Dissolving Tablets of Amlodipine and Rosuvastatin at 237 nm and 244 nm

Formulation	Drug content (%) (Avg.±SD)At 237 nm	Drug content (%) (Avg.±SD)AT 244 nm
FD1	98.13±0.71	98.4±3.16
FD2	97.03±0.54	98.4±0.16
FD3	98.04±0.34	101.3±0.19
FD4	98.00±0.55	97.3±0.21
FD5	98.08±0.64	99.3±0.23
FD6	99.04±0.11	101.2±0.21
FD7	98..02±0.21	97.6±0.23
FD8	98.52±0.79	99.2±0.21
FD9	99.02±0.21	98.9±0.16

Table 6: Dissolution profile and percentage of drug release of Fast Dissolving Tablet of Amlodipine and Rosuvastatin

Formulation	5min	10min	15min	20min	25min	30min	45min	60min
FD1	19.72	21.65	46.50	80.36	94.58			
FD2	18.12	25.02	30.8	36.1	47.5	65.8	82.9	93.75
FD3	25.05	28.98	68.64	75.50	85.05	94.50		
FD4	47.32	72.56	90.89	98.00				
FD5	38.45	66.35	88.12	96.21				

FD6	99.89			
FD7	96.20	98.85	99.90	
FD8	89.20	92.25	98.85	99.90
FD9	94.50	97.25	99.90	

Table 7: Stability study (40 °C/75%RH) of Optimized Formulation (FD6) of Fast Dissolving Tablet of Amlodipine and Rosuvastatin

Parameters	Before stability studies	After stability studies
Weight variation(mg))	151.15±2.50	150.85±1.24
Hardness (kg/cm^2)	3.70±1.6	3.35±0.15
Friability(% w/w)	0.45	0.50
Invitro disintegrating time(sec)	55± 0.03	45±0.50
Wetting time(sec)	25.98±0.02	24.05± 1.5
Drug content (%)	97.6±1.65	97.50±1.10
In vitro release (%) at 5 min	99.89±0.50	98.59±0.50

Figure 2: *FTIR spectra of (A) Amlodipine (B) Rosuvastatin (C) Amlodipine and Rosuvastatin (D) Crosscarmellose sodium (E) Cross povidone (F) Sodiumstarch glycolate (G) Amlodipine, Rosuvastatin, Crosspovidone and Sodium starch glycolate*

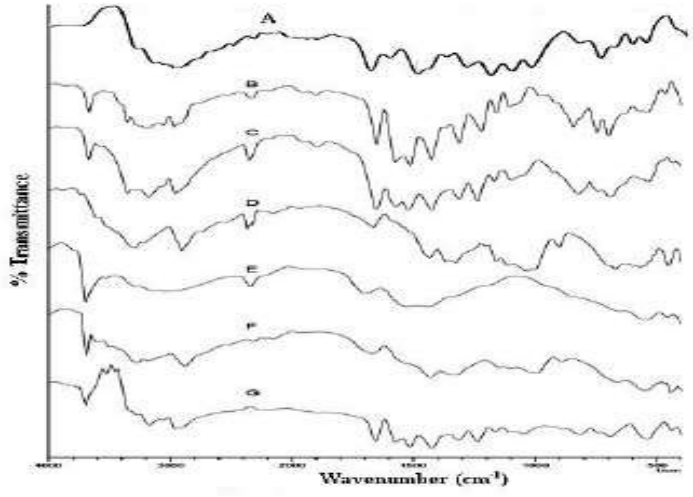
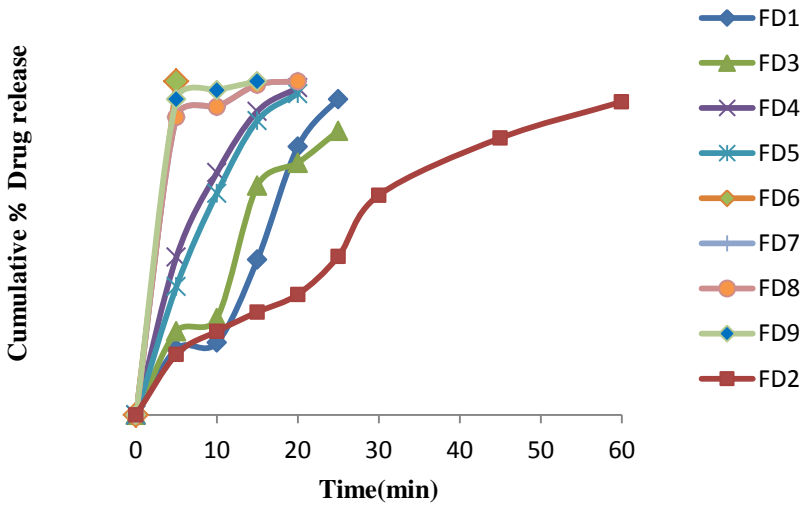


Figure 3*: Invitro drug release of Fast Dissolving Tablet of Amlodipine and Rosuvastatinglipizide in formulation FD1 to FD9 in phosphate buffer of pH 6.8*



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