S.Venkateswara Rao et al /J. Pharm. Sci. & Res. Vol. 13(8), 2021, 474-480

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Formulation and Evaluation of Fast Dissolving Tablets of Atorvastatin Using Novel Co-Processed Excipients

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Abstract

Atorvastatin calcium is the most preferred molecule among the statins for Hyperlipideima, used to treat Hypercholesterolemia. It acts by inhibiting the enzyme 3-hydroxy-3-methyl-glutaryl (HMG)-CoA reductase, The aim of the present investigation was to develop fast dissolving tablets of Atorvastatin Calcium. Due to its low solubility and its short absolute bioavailability of 14%, fast dissolving tablets of Atorvastatin Calcium were prepared using superdisintegrants in order to improve the dissolution rate, thereby the bioavailability. The influence of concentration of the Croscarmellose sodium was studied by a set of three formulations (F1, F2, F3) with concentrations of 2%, 4% & 8%w/w respectively. Also the influence of Sodium Starch Glycolate was studied by a set of three formulations (F4, F5 and F6) respectively. The formulation prepared with 8%w/w of superdisintegrant was offered relatively rapid release of Atorvastatin Calcium when compared with other concentrations of Croscarmellose sodium and Sodium Starch Glycolate. The formulation prepared with Croscarmellose sodium was offered relatively rapid release of Atorvastatin Calcium when compared with Sodium Starch Glycolate. Three formulations (F7, F8 and F9) were prepared incorporating a combination of superdisintegrants (Co-processed Mixtures), Croscarmellose sodium and Sodium Starch Glycolate by direct compression method. Formulation containing Co-processed mixtures had less disintegration time as compared to the individual superdisintegrants. So, we can conclude that nature, concentration of the superdisintegrant and combination of superdisintegrants (Co-processed) showed influence on the rate of dissolution.

Keywords: Atorvastatin calcium, Co-processed Mixtures, Fast dissolving tablets.

INTRODUCTION

The oral route of drug administration has wide acceptance. Tablet is the most popular among all dosage forms existing today. It offers the advantage of convenience of administration, compactness, easy manufacturing and its potential manufacturing cost savings. Many patients find it difficult to swallow tablets and hard gelatin capsules and do not take medication as prescribed. In a survey conducted by Honda and Nakano [1]. half of the patients experienced difficulty taking medication such as tablet and capsule which results in a high incidence of non compliance and ineffective therapy. The difficulty is experienced in particular by pediatrics and geriatric patients, but it also applies to people who are ill in bed and to those active working patients who are busy or travelling, especially those who have no access to water. To overcome such problems fast disintegrating, orally disintegrating tablets have emerged as an alternative dosage form. Recent advances in novel drug delivery systems aim for enhancing the safety of a drug molecule while maintaining its therapeutic efficacy so as to achieve better patient compliance. First FDT came into existence in 1980 and got approval in 1996 from the USFDA for Zydis ODT formulation of Claritin having loratidine drug [2]. Different absorption sites for drug in saliva would be mouth, pharynx, esophagus and stomach. It depends on how quickly drug comes into solution and how quickly it is absorbed [3].

MATERIALS:

The following materials of Pharma grade or the best possible Laboratory reagents were used as supplied by the manufacture.

PREFORMULATION STUDIES

The main objective of Preformulation is to generate elegant, stable, effective and safe dosage form by establishing kinetic profile, compatibility with the other ingredients and establish physico-chemical parameter of new drug substances. Preformulation is group of studies that focus on the physico-chemical properties of a new drug candidate that could affect the drug Performance and the development of a dosage form. [4]

Organoleptic Properties: Pure drug was evaluated for organoleptic properties such as appearance and colour.

Solubility Analysis: The solubility of Atorvastatin Calcium was checked in water and organic solvents. The solubility was analyzed by quantitative determination using UV spectroscopy at a wave length of 242 nm.

Melting Point Determination: Melting point determination of pure drug Atorvastatin Calcium was done by capillary tube method.

Identification of Pure Drug: FTIR spectroscopy was used for identification of pure drug Atorvastatin Calcium.

Determination of lambda Max(λ max):

Preparation of Stock solution: Weigh accurately 10mg of Atorvastatin calcium was transferred into a 100ml volumetric flask. To that flask phosphate buffer was added in a small quantity. In order to solve the drug. The volume was made upto 100ml with phosphate buffer pH 6.8 to get a overall concentration of 100µg/ml.

Determination of λ_{max}: 20µg/ml concentration of solution Atorvastatin calcium was prepared in dilution. The resulting solution was scanned in UV-Visible spectrophotometer from 400-200 to determine the λ_{max}.

Calibration curve:

PH 6.8 phosphate buffer: Add 23.65ml of 0.2M NaoH to 50ml of 0.2m potassium dihydrogen phosphate & diluted to 200ml with water.

Drug Excipients Compatibility studies:

Excipients are the substances which are included along with the API in the pharmaceutical dosage forms. As most of the excipients having no direct pharmacological action but these are important for administration and modulating the accurate release of active substance and maintaining API against degradation and increasing the size of the dosage form and masking the bitter taste an increases the patient compliance and the studies of drug – excipient compatibility interactions between potential formulation excipient the API in the development stage of all dosage forms.

METHODOLOGY:

Preparation of co-processed Superdisintegrants:

Solvent evaporation method:

A blend of Croscarmellose Sodium and Sodium Starch Glycolate (in the ratio of 1:1, 1:2 & 1:3) was added to 10 ml of ethanol. The contents of the beaker (250 ml capacity) were mixed thoroughly and stirring was continued till most of ethanol evaporated. The wet coherent mass was granulated through # 60 mesh sieve. The wet granules were dried in a hot air oven at 60º C for 20 minutes. The dried granules were sifted through # 60 mesh sieve and stored in airtight container till further use [5].

Formulation of Atorvastatin calacium tablets:

Tablets containing 40 mg of drug were prepared by direct compression method. Drug was passed through sieve no 100. Drug along with other excipients were mixed in a mortar. The resulting blend was lubricated with magnesium stearate and compressed into tablets using the Karnavathi multiple punch (round shaped, 8mm thick) machine[5]. Data shown in table no-1,2&3.

Precompression parameters:

Before the compression the prepared blend was evaluated for following parameters [6].

Bulk Density:

The bulk density was determined by using bulk density apparatus.The bulk density was calculated by following formula.

$$Db = M/V_b$$

Tapped Density:

After the known mass (5g) of powder poured into the measuring cylinder it was tapped for 100times. The tapped density was calculated by following formula.

$$Dt = M/Vt$$

Carr's index:

It indicates the indirect measure of bulk density, size, shape, surface area, moisture content and cohesiveness of material. It is calculated by using the formula,

$$I = Dt\text{-}Db/Dt\times100$$

Hausner's Ratio:

It is the ratio of tapped density and bulk density. It was calculated by using the following formula.

$$\text{Hausner's ratio} = Dt/Db$$

Angle of repose:

The angle of repose physical mixtures of liquid-solid compacts was determined by fixed funnel method. The angle of repose (θ)was calculated by using the following formula.

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

Post Formulation Studies

Weight variation:

According to I.P twenty tablets were taken and their weight was determined individually with the use of digital weighing balance. The average weight of the single tablet was determined from the overall collective weight. This test is satisfactory method of determining the drug content uniformity [7].

Thickness:

The thickness of the tablet measured by using Vernier calipers with 5 tablets were taken and thickness was measured.

Hardness:

The hardness of tablet was determined by using Pfizer hardness tester. It is defined as force required breaking a tablet by Compression in a radial direction. An average of three observations was reported.

Disintegration time:

It is the process of breaking of tablet into smaller particles is referred as disintegration. One tablet from each batch 6 tubes of the basket is placed with buffer and apparatus subjected to run after it attains 37^0C. Then the assembly should be raised and lowered between 50 cycles per minute. The time taken for complete disintegration of the tablet with no sign of palpable mass remaining in the apparatus was measured and recorded.

Friability Test:

Friability of the tablets was determined using Roche Friability, before placing the tablets in the apparatus need to check the initial weight of the tablet. Tablets were de dusted using soft muslin cloth and reweighed. The % friability can be calculated by using the following formula.

$$\%\ \text{Friability} = \text{Initial weight} - \text{Final weight} / \text{Initial weight} \times100$$

Drug content Uniformity Test:

In this the tablets were weighed and powdered. An accurate amount of powder equivalent to 40mg of Atorvastatin calcium was dissolved in a 100 ml of pH 6.8 phosphate buffer which is filtered and diluted and analyzed for drug content at 242nm using UV-Visible Spectrophotometer. From the obtained absorbance values, amount of drug present in the given tablet was calculated [8].

Wetting time:

In this five circular tissue papers of 10cm diameter were placed in a petridish to that add 10ml of Eosin, a water soluble dye is added to that petridish kept aside for few minutes, and then tablet was gently placed on the placed on the surface of tissue paper. The time required to develop a red colour on the upper surface of the tablet was recorded as the wetting time.

In vitro Dissolution studies:

In vitro release studies for tablets of Atorvastatin calcium was studied by using dissolution testing apparatus USP paddle type, with the rotation speed of 50rpm using pH 6.8 phosphate buffer as dissolution medium maintained at a temperature of 37±0.5ºC. Samples were withdrawn at regular intervals and filtered through Whatman filter paper, diluted and analyzed at 242nm for cumulative amount of drug release using double beam UV-Visible spectrophotometer.

Accelerated Stability Study of Optimized Batch:

The optimized formulation F7 was stored in aluminum capped clear glass vials and were subjected to a storage condition of 40°C±2˚C/ 75%±5% RH for 3 months in humidity chamber. The samples were withdrawn at time intervals of 0, 1, 2, 3 months and evaluated for hardness, friability, disintegration time, drug content and *in-vitro* dissolution studies.

RESULTS AND DISCUSSION

PREFORMULATION STUDIES:

Oraganoleptic Properties: The pure drug Atorvastatin Calcium showed white to off white, unpleasant smell, very fine amorphous powder.

Solubility Studies*:* Atorvastatin Calcium was slightly soluble in water and organic solvents. The solubility in water and methanol were found to be 0.52 µg/ml and 1.84 µg/ml

Melting Point Determination: After performing capillary method melting point of Atorvastatin Calcium found in range of 160ºC.

Identification of Pure Drug: FT-IR spectroscopy was used to determine the functional group present in the pure drug sample. Spectra of Atorvastatin Calcium had shown characteristic peak at 2933.74 cm^{-1}(C-H – stretching), 1314.81 cm^{-1}(C-N – stretching), 3061.91 cm^{-1} (C-HO - stretching alcoholic group), 1568.04 cm^{-1} (C=O – stretching am idic group), 3382.29 cm^{-1} (N-H - stretching), 1651.82 cm^{-1} (C=C - bending), 752.30 cm^{-1}, 691.50 cm^{-1} (C-F- stretching), 1157.10 cm^{-1} (O-H- bending). Data is shown in fig-1

Determination of λ_{max}:

The 20µg/ml Atorvastatin calcium was scanned in UV-Visible spectrophotometer from 400-200nm to determine the λ max. The λmax was found to be at 242nm so, the calibration of Atorvastatin calcium was developed at this wavelength.Data is shown in fig-2

Calibration curve of Atorvastatin calcium:

The standard graph of Atorvastatin calcium in pH 6.8 PBS was constructed by making the concentartion range of 5-40µg/ml solutions. The absorption of solutions was examined under uv-spectrophotometer at an absorption maximum of 242nm. The standard graph was constructed by taking the absorbance on y-axis and concentration on x-axis.

The standard calibration curve of Atorvastatin calcium in pH 6.8 PBS was shown in the fig No: 19 ,drug concentration and absorbance followed linear relationship. The curve obeyed beer's Lambert's law and the correlation coefficient value (R^2) of buffer 0.9696.Data is shown in table-4 and fig no-3

Drug Excipient compatibility studies:

As the interaction studies were performed to find any kind of interaction between drug and excipients used in the liquidsolid tablets. FT-IR spectroscopy was used to determine the functional group present in the pure drug sample. Data is shown in fig no-4&5

METHODOLOGY:

Preparation of co-processed Superdisintegrants

A blend of coprocessed superdisintehrant with different ratio of Croscarmellose Sodium and Sodium Starch Glycolate (1:1, 1:2 & 1:3) was prepared by solvent evaporation method.

Formulation of Atorvastatin calacium tablets:

Tablets containing 40 mg of Atorvastatin calacium were prepared by direct compression method. Nine different formulations of FDTs were prepared with different concentration of Crosscarmellose sodium, Sodium Starch Glycolate, and its combination as coprocessed superdisintegrants. The influence of concentration of the Crosscarmellose sodium on the performance of Atorvastatin calacium, a set of three formulations (F1, F2, F3) were prepared using three different concentrations of Crosscarmellose sodium (2%, 4% & 8%w/w) respectively. The influence of concentration of the Sodium Starch Glycolate on the performance of Atorvastatin calacium, a set of three formulations (F4, F5, F6) were prepared using three different concentrations of Sodium Starch Glycolate (2%, 4% & 8%w/w) respectively. The influence of co-processed superdisintegrants on performance of Atorvastatin calacium, a set of three formulations (F7, F8, F9) were prepared using co-processed superdisintegrants (Crospovidone :SSG) in three different ratios 1:1, 1:2, 1:3 respectively. The formulated tablets were subjected to various quality control tests and all the tablets complied with the Pharmacopoeial standards.

Precompression Parameters:

Bulk density and Tapped density:

The powdered blends of all nine formulations were evaluated for bulk density and tapped density by using bulk density apparatus. The bulk density was found in the range of 0.336±0.024 – 0.55±0.03gm/cm^3. The tapped density ranged from 0.393±0.03 – 0.620±0.04gm/cm^3. This indicates that powder is loosely packed. Data is shown in table no-5

Carr's Index & Hausner's ratio:

The compressibility index and Hausner's ratio values of all the nine formulations indicate that the prepared blends possessed minimum interparticlulate interactions and good flow property which is preliminary requirement for formulating the tablets.Data is shown in table no-6

Angle of repose:

The prepared powder blends of all the formulations were evaluated for the flow properties. The angle of repose of all formulations was within the range of 25.0 - 27.2º. These values indicate that the powder blend F1 – F9 had exhibited good flow properties.Data is shown in table no-7

Post compression Parameters:

All the formulations were prepared under similar conditions and tablets exhibited white color, convex in shape with smooth surface. The characteristic of prepared tabletss of Atorvastatin calcium are discussed below.

The hardness for the tablets of all formulations was adjusted to 3 – 3.5 Kg/cm^2 so that the effect of superdisintegrant on the dissolution rate could be evaluated accurately. The friability of all the formulated tablets was within 1%, which is an indication of good mechanical resistance of the tablet. The drug content varied between 95.93±0.46 to 98.51±0.18 for all formulations. The thickness was measured for the tablets of all formulations and was found to be within the acceptable range. The percentage variation in weight was within the range of ±7.5% complying with pharmacopoeial specification.Data is shown in table no-8

Wetting Time:

Wetting time was given the major importance in selection of the best FDT formulation among all the 9 formulations. For all the formulations, with increase in the superdisintegrant concentration from 2 – 8%, the wetting time was decreased accordingly. It is clear from the results that the formulation containing SSG had shown more wetting time than CCS and its combination. This may be due to the fact that SSG is disintegrated by swelling mechanism leading to longer wetting time and lesser water absorption ratio. The formulations that contain CCS have the shortest wetting time, which may be attributed to the strong wicking action of this super disintegrant. The result shows that all the formulations pass the test and the formulation F7 showed minimum wetting time of 18 seconds.Data is shown in Table no-9

DISINTEGRATION TIME:

Disintegration time is very important for fast dissolving tablets which are desired to be less than 60 seconds. This rapid disintegration plays a role in drug absorption in buccal cavity, which promotes the bioavailability of the drug. The *in vitro* disintegration time of prepared tablets (F1 – F9) was present between 29 to 163 sec. respectively. Out of all the formulations, F7 the tablets prepared using 1:1 ratio of CCS: SSG showed rapid disintegration in 29 sec. It was clear that the disintegration time of CCS containing tablets were comparatively lower than tablets containing SSG. This may be due to its rapid capillary activity and pronounced hydration with little tendency to form gel when comes in contact with buffer and water.Data is shown in Table no-10

EVALUATION OF *IN-VITRO* RELEASE STUDIES:

The dissolution conditions used for studying the drug release from the fast dissolving tablets of Atorvastatin calcium are:

Apparatus : USP Type II (paddle)
Agitation speed (rpm) : 50
Medium : pH 6.8 PBS
Volume : 900ml
Temperature : 37.0 ± 0.5^0 C
Time : 2, 4, 6, 8, 10 &12 minutes

The tablets formulated with 8% CCS (F3) showed greater rate of dissolution when compared to the tablets formulated with SSG. In formulation F7 containing 1:1 ratio of CCS: SSG showed better dissolution rate than those of all other formulations. This might be because of its high disintegrating nature.

The formulation prepared with 8%w/w of superdisintegrant was offered relatively rapid release of Atorvastatin Calcium when compared with other concentrations of Croscarmellose sodium and Sodium Starch Glycolate. The formulation prepared with Croscarmellose sodium was offered relatively rapid release of Atorvastatin Calcium when compared with Sodium Starch Glycolate. Formulation containing Co-processed mixtures had less disintegration time as compared to the individual superdisintegrants. So, we can conclude that nature, concentration of the superdisintegrant and combination of superdisintegrants (Co-processed) showed influence on the rate of dissolution.Data is shown in Table no-11 and fig no-6,7,8&9

STABILITY STUDIES:

The stability studies were conducted on the selected formulation F7 as per the ICH guidelines. The stability studies were done at the intervals of 0, 30, 60 and 90 days. The parameters studied were weight variation, percentage drug content and percentage of drug release. The results are shown in **Table-12.** From the results it was concluded that there were no significant changes in any values. Hence this formulation was considered to be stable after three months stability study.Data is shown in Table no-12.

Table No- 1: Composition of fast dissolving tablets formulated with CCS

S.No	Ingredients (mg)	F1	F2	F3
1	Drug	40	40	40
2	MCC	104	101	95
3	CCS	3 (2%)	6 (4%)	12 (8%)
4	Talc	1.5	1.5	1.5
5	Mg. stearate	1.5	1.5	1.5
	Total Weight	150	150	150

Table No- 2: Composition of fast dissolving tablets formulated with SSG

S.No	Ingredients (mg)	F4	F5	F6
1	Drug	40	40	40
2	MCC	104	101	95
3	SSG	3 (2%)	6 (4%)	12 (8%)
4	Talc	1.5	1.5	1.5
5	Mg. stearate	1.5	1.5	1.5
	Total Weight	150	150	150

Table No-3: Composition of fast dissolving tablets formulated with coprocessed superdisintegrants (CCS: SSG)

S.No	Ingredients (mg)	F7 (1:1)	F8 (1:2)	F9 (1:3)
1	Drug	40	40	40
2	MCC	95	95	95
3	**CCS: SSG**	12	12	12
4	Talc	1.5	1.5	1.5
5	Mg. stearate	1.5	1.5	1.5
	Total Weight	150	150	150

Table No -4: Standard Calibration Curve of Atorvastatin Calcium in pH 6.8 PBS

S.No	Concentration(µg/ml)	Absorbance in pH 6.8 PBS
1	0	0.00
2	5	0.214
3	10	0.340
4	15	0.470
5	20	0.568
6	25	0.792
7	30	0.852
8	35	1.173
9	40	1.414

Table No-5: Bulk density & Tapped density of all the formulations F1-F9

S.No	Formulation code	Bulk density(gmcm$^{3)}$	Tapped density(Gm/cm^3)
1	F1	0.526±0.01	0.590±0.02
2	F2	0.456±0.02	0.483±0.49
3	F3	0.336±0.024	0.393±0.03
4	F4	0.420±0.11	0.46±0.05
5	F5	0.370±0.05	0.443±0.07
6	F6	0.480±0.04	0.520±0.09
7	F7	0.395±0.02	0.420±0.03
8	F8	0.550±0.03	0.620±0.04
9	F9	0.531±0.05	0.608±0.07

Mean ± S.D of three determination

Table No-6: Carr's Index and Hausner's ratio

S.No	Formulations	Carr's index	Hausner's ratio
1	F1	10.1±0.65	1.03±0.041
2	F2	6.26±0.5	1.40±0.54
3	F3	14.3±0.26	1.14±0.24
4	F4	17.9±0.20	1.27±0.19
5	F5	10.4±0.11	1.18±0.04
6	F6	11.03±0.62	1.11±0.06
7	F7	9.32±0.45	1.05±0.03
8	F8	14.5±0.3	1.28±0.27
9	F9	12.6±0.23	1.45±0.52

Mean ± S.D. of three determinations

Table No-7:Angle of Repose

S.No	Formulation code	Angle of repose
1	F1	26.6±0.31
2	F2	25.2±0.41
3	F3	27.2±0.44
4	F4	26.5±0.55
5	F5	25.0±0.98
6	F6	26.9±0.51
7	F7	25.4±0.16
8	F8	25.1±0.80
9	F9	26.4±0.53

Mean ± S.D. of three determinations

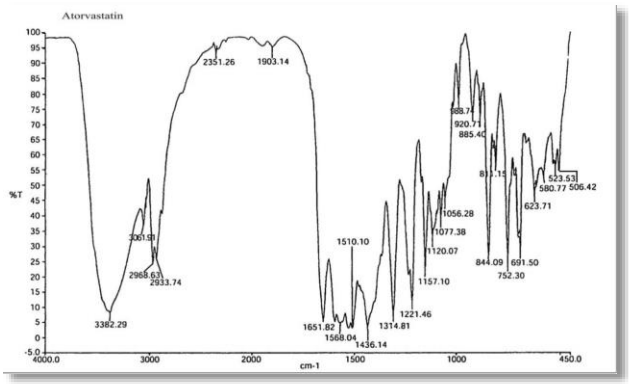


Fig-1: IR Spectra of Pure Atorvastatin Calcium

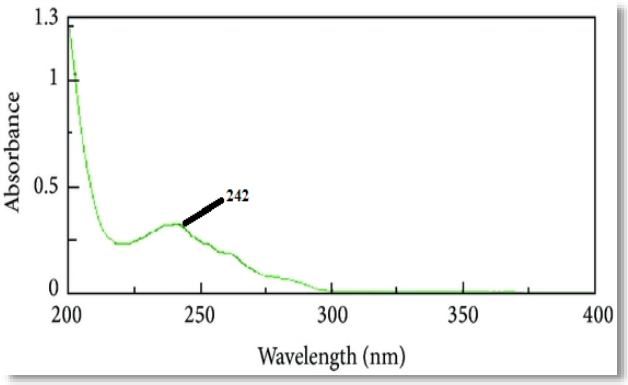


Fig-2 : λ Max of Atorvastatin Calcium

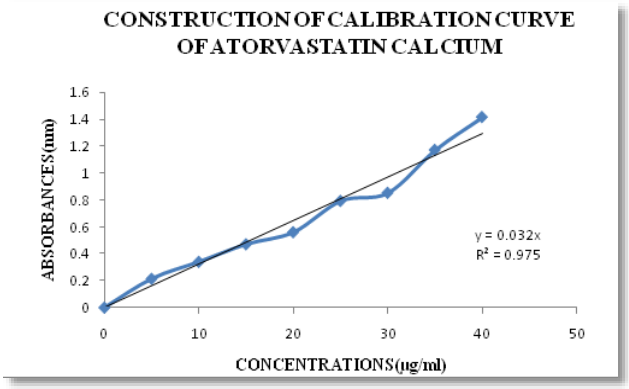


Fig No-3: Calibration Curve of Atorvastatin calcium in pH 6.8 PB

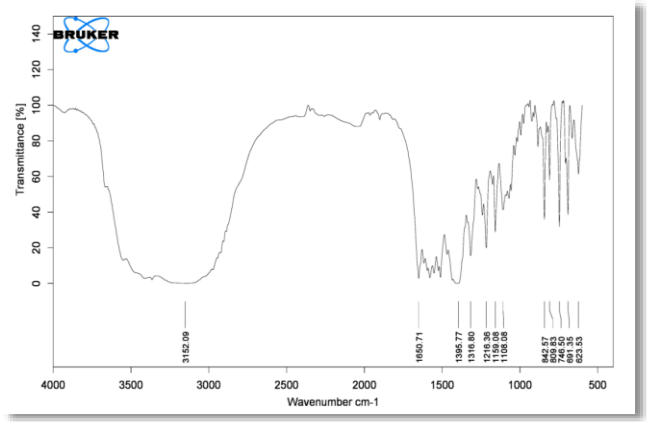


Fig No- 4:FT-IR spectra for Atorvastatin calcium + CCS

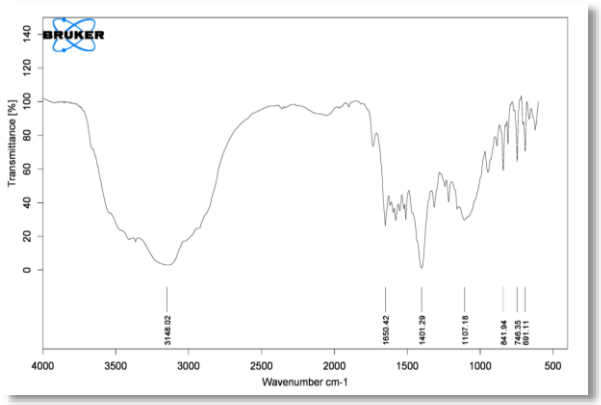
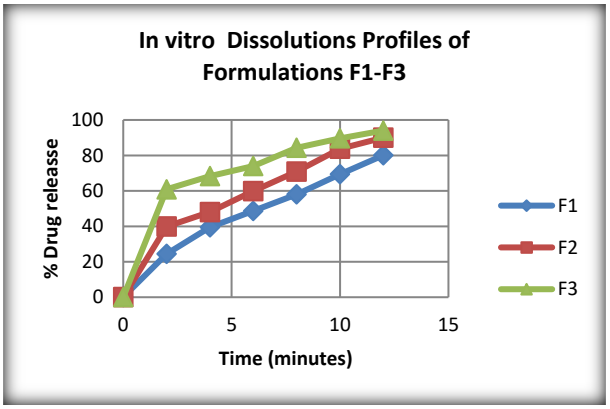


Fig No- 5:FT-IR spectra for Atorvastatin calcium + SSG



FigureNo-6: Comparative Dissolution Profiles of the Formulations F1-F3

Table No-8: Evaluation Parameters of Atorvastatin Calcium FDTs

Formulation Code	Hardness (kg/cm^2)	Friability (%)	Weight variation (%)	Thickness (mm)	Drug content (%)
F1	3.0±0.23	0.238±0.019	3.4±0.48	3.2±0.007	97.90±0.09
F2	3.2±0.21	0.433±0.006	2.5±0.62	3.1±0.001	96,51±0.38
F3	3.1±0.16	0.210±0.003	2.7±0.11	3.2±0.003	96.81±0.14
F4	3.4±0.14	0.644±0.010	3.2±0.34	2.9±0.005	95.93±0.46
F5	3.2±0.21	0.817±0.004	1.6±0.26	3.1±0.002	97.45±0.26
F6	3.3±0.22	0.437±0.012	2.1±0.31	3.0±0.008	96.64±0.31
F7	3.2±0.14	0.377±0.0085	2.8±0.13	3.1±0.002	98.51±0.18
F8	3.2±0.16	0.524±0.002	3.3±0.64	3.2±0.002	98.29±0.51
F9	3.4±0.15	0.644±0.010	2.7±0.15	3.1±0.001	97.43±0.25

Mean ± S.D. of three determinations

Table No - 9: Wetting time of Atorvastatin calcium FDTs

S. No	Formulation code	Wetting time (sec)
1	F1	63.32±2.21
2	F2	39.40±1.43
3	F3	28.30±0.94
4	F4	80.56±2.23
5	F5	66.20±1.43
6	F6	44.30±0.94
7	F7	18.48±1.52
8	F8	25.32±3.05
9	F9	39.00±1.43

Mean ± S.D. of three determinations

Table No -10: *In-vitro* Drug disintegration time

S.NO	Formulation Code	*In-vitro* disintegration time(Sec)
1	F1	128±0.1
2	F2	106±0.3
	F3	53±0.53
4	F4	163±0.51
5	F5	120±0.25
6	F6	81±0.35
7	F7	29±0.58
8	F8	42±0.94
9	F9	56±0.43

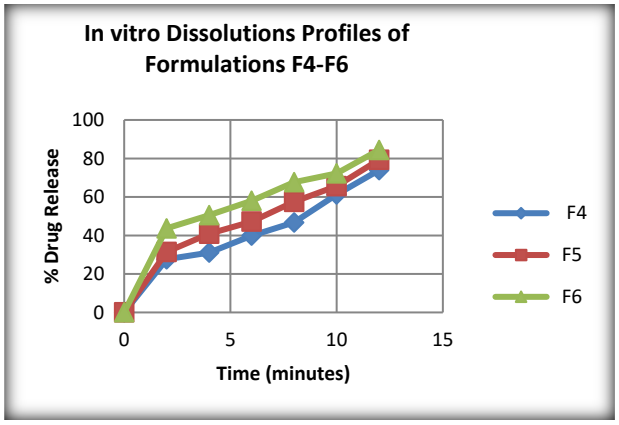
Mean ± S.D. of three determinations

Table No-11: Cumulative Percent Drug release of Atorvastatin calcium FDTs

Time (min)	% Drug Release								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
2	24.47	39.89	60.9	27.63	31.44	43.68	65.54	41.39	31.25
4	39.50	48.05	68.31	31.09	40.89	50.55	75.32	56.43	44.65
6	48.68	59.9	74	39.91	47.23	58.04	80.7	64.9	52.7
8	58.04	70.89	84.31	46.77	57.49	67.68	89.63	72.63	64.61
10	69.40	83.75	89.66	61.25	65.62	72.24	94.49	85.71	76.11
12	80.07	90.03	94.02	73.95	79.35	84.44	99.81	90.1	85.32

Table-12: Stability Studies of Formulation F9

Parameter	Time (days)			
	0	**30**	**60**	90
Disintegration Time	29 ± 0.17	28 ± 0.34	27 ± 0.56	28 ± 0.42
Hardness (Kg/Cm^2)	3.2 ± 0.15	3.2 ± 0.52	3.0 ± 0.43	3.0 ± 0.44
Friability (%)	0.37 ± 0.008	0.37 ± 0.005	0.38 ± 0.004	0.36 ± 0.005
Drug Content (%)	98.51%±0.26	98.51%±0.80	97.21%±0.68	97.12%±0.70
Drug release %	99.81±0.37	98.20±0.69	97.89±0.65	98.62±1.22



FigureNo-7: Comparative Dissolution Profiles of the Formulations F4-F6

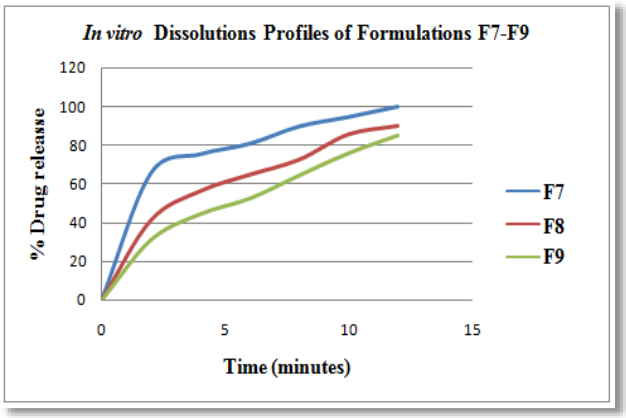


Figure No - 8: Comparative Dissolution Profiles of the Formulations F7 – F9

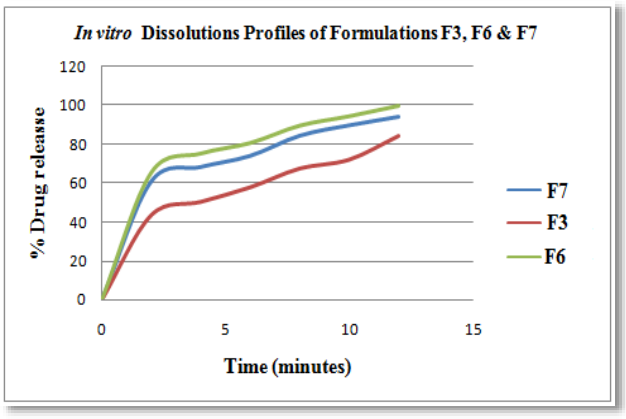


Figure No - 9: Comparison of Dissolution Profiles of Formulations F3, F6, F7

CONCLUSION

In the present research work, to study the influence of pharmaceutical excipients on performance of Atorvastatin Calcium, two superdisintegrants and its combination of at different concentrations were used to prepare fast dissolving tablets. An increased superdisintegrant associated with enhanced wicking, disintegration and thus, enhanced drug release. Formulation containing Co-processed mixtures had less disintegration time and rapid drug release as compared to the individual superdisintegrants. So, we can conclude that nature, concentration of the superdisintegrant and combination of superdisintegrants (Co-processed) showed influence on the rate of dissolution. The optimized formulation F7 revealed a percentage cumulative drug release (CDR) of 99.81% at the end of 12min. Thus the objective of Atorvastatin calcium with co-processed superdisintegrants to achieve faster dissolution rates was met with success.

Acknowledgment

The presenting authors are thankful to management and principal of Vijaya institute of pharmaceutical sciences for women, Vijayawada for their valuable support in carrying out this work.

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