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Research Article

Thermal Characterization and Screening of Formulation Variables of Atorvastatin Calcium Immediate Release Tablet

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Submitted: 16 May 2016

Accepted: 30 January 2017

Published: 01 February 2017

ISSN: 2334-1815

Keywords

- Atorvastatin
- Screening
- Immediate
- Mannitol
- Higuchi

Abstract

In the present investigation, the compatibility of Atorvastatin calcium was evaluated with various superdisintegrants and other solid excipients by means of FT-IR and DSC. Several batches of tablets with varying proportion of superdisintegrants were prepared by direct compression techniques. Tablets were also evaluated for different physical properties and in-vitro drug release characteristics and optimized its release comparable to marketed innovator product. Various excipients used were sodium starch glycollate, Cross carmellose sodium, Cross-povidone, lactose, Micro crystalline cellulose, mannitol, sodium alurayl sulfate, magnesium stearate, and stearic acid. From the DSC studies, the excipients such as microcrystalline cellulose (Avicel 101), magnesium stearate, mannitol, Sodium lauryl sulfate were found to have physical interactions with Atovastatin. Immediate release tablet was prepared by direct compression method and its release profile was compared with the marketed IR tablet. The prepared tablet have conform the pharmacopoeial limit for hardness, thickness, friability, weight variation and content uniformity. Formulation F11 containing two super disintegrants have shown the disintegration time less than 25 sec and better dissolution than all other formulations releasing more than 80% of the drug after 20 minutes. Kinetic data reveals that the drug release follows best order by Higuchi model, followed by korsemeyer peppas, zero order and first order mechanisms. The results of accelerated stability studies as per ICH guidelines indicated that the tablet was stable as there were no any significant physical changes after the study.

ABBREVIATIONS

ATV: Atorvastatin; DSC: Differential Scanning Calorimetry; FT-IR: Fourier Transform Infra Red Sprectroscopy; IR: Immediate Release; SSG: Sodium Starch Glycollate; CCS: Cross Carmellose Sodium; CP: Cross Povidone; MS: Magnesium Stearate; KBR: Potassium Bromide; MKT: Marketed.

INTRODUCTION

The incompatibility between drugs and excipients can alter the physicochemical properties of drugs and hence, can have an effect on its efficacy and safety profile. Therefore, drug-excipient interaction study at the initial stage of a formulation development should be treated as an imperative exercise to ensure correct selection of excipients and hereby, increasing the possibility of developing a successful dosage form [1,2]. Excipients present in solid dosage forms are composed of mixture of adjuvants, such as diluents, binders, disintegrants, lubricants, glidants, and surfactants. They permit the efficient manufacturing of capsules and tablets and affect the physical and chemical characteristics of the active ingredients as well as its bioavailability. In particular, the cost and time constraints associated with the process of pharmaceutical product development have made this type of predictability techniques even more desirable. Differential scanning calorimetry (DSC) has been widely used to assess incompatibility between formulation components, because the method is fast and versatile, and requires only a small quantity of sample [1,3]. However, caution needs to be exercised if the results of DSC alone are interpreted. Whenever possible, other techniques such as infrared spectroscopy (IR) and quantitative analysis after storage under stressed conditions should be utilized in conjunction with DSC [3]. As the thermo-analytical methods do not yield direct chemical information, Fourier transform infrared spectroscopic (FT-IR) investigations were used in this work. Oral drug delivery remains the preferred route of administration in the discovery and development of new drug candidates. The popularity of oral route is attributed to patient acceptance, ease of administration, accurate dosing, cost effective manufacturing methods and generally improve the shelf life of the product. Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release may be designed by appropriate pharmaceutically acceptable diluent or carrier, which gives rapid rate of drug release and absorption [4,5]. The basic approach used in development of

such tablets is the use of superdisintegrants like cross linked polyvinylpyrrolidone or crospovidone (polyplasdone), sodium starch glycolate (SSG), croscarmellose sodium (CCS) etc. As a drug entity reaches the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, while offering its patient population a more convenient dosage form or dosing regimen.

Atorvastatin (ATV), a HMG CoA reductase inhibitor, lipid lowering agent given in the dose ranging from 10-80 mg/day by oral route. After oral administration alone, ATV is rapidly absorbed; maximum plasma concentrations occur within 1 to 2 hours. Extent of absorption increases in proportion to atorvastatin dose. The absolute bioavailability of atorvastatin (parent drug) is approximately 14% and the systemic availability of HMG-CoA reductase inhibitory activity is approximately 30%. The low systemic availability is attributed to pre-systemic clearance in gastrointestinal mucosa and/or hepatic first-pass metabolism. Atorvastatin, a drug with low solubility and high permeability belongs to the Class II in the biopharmaceutics classification system (BCS), in which, dissolution process is the rate-limiting step for the absorption [6,7]. Hence, it is important to evaluate drug features, such as the presence of polymorphism, stability, and compatibility of the pharmaceutical formulation, since any changes can directly influence its bioavailability. Hence, the objectives of present investigation is to evaluate the compatibility of Atorvastatin with immediate release excipients and to optimize the tablet which release is best comparable with innovator product by varying different super disintegrants.

MATERIALS AND METHODS

Atorvastatin calcium was a given sample from Unichem Ltd, Ahmedabad. SSG, CCS, CP, lactose, mannitol, SLS, MCC, Magnesium stearate, Stearic acid were procured from Loba chemie pvt. Ltd. Mumbai respectively. All other chemicals used were of analytical grade.

Preparation of products and storage conditions

Binary component mixtures in 1:1 mass ratio were prepared in a porcelain mortar. The original components were investigated by means of DSC and FT-IR methods. The mixtures were investigated immediately after the preparation and after accelerated storage period (40 °C/75% RH/ 3 months). The composition of various binary mixtures for drug-excipients compatibility studies were as follows: ATV Calcium; ATV Calcium : SSG 1:1; ATV: CCS 1:1; ATV: CP 1:1; ATV Calcium : Lactose 1:1; ATV Calcium : MCC 1:1; ATV: Sodium lauryl sulfate 1:3; ATV Calcium : Mannitol 1:1; ATV Calcium : Magnesium stearate 1:0.5; ATV Calcium: Stearic acid 1:1.

Differential scanning calorimetry study

A Mettler Toledo DSC thermal analysis system (Mettler Inc., Schwerzenbach, Switzerland) was used for thermal analysis of the drug-excipient mixtures. Approximately 2–5 mg of ATV and excipient or their binary mixture was examined in the temperature range between 40 °C and 300 °C, in a normal covered Aluminium crucible (three pin holes were applied in the cover). The heating rate was 10 °C min^{-1}. Nitrogen was used as carrier gas at a flow rate of 10 Lh^{-1} during the DSC investigation [8,15].

Fourier transforms infrared spectroscopy study

FT-IR spectra of the ATV and its binary mixtures were recorded in the interval 4000–400 cm^{-1} with an Schimadzu FT-IR instrument (Japan), at 4 cm^{-1} optical resolution. Standard KBr pellets were prepared from IR grade KBr and 0.5 mg of ATV, or 1.0 mg of binary mixture. The spectra were recorded with the use of software, and all spectral interpretations were done [9,15].

Preparation of Immediate release tablet of ATV by direct compression

The weighed quantity of ATV was screened through sieve no. #40. The various excipients were accurately weighed and screened separately using sieve no. # 40. The immediate release tablets were prepared by direct compression method using the formula shown in Table (1). Different ratios of superdisintegrants, fixed amount of diluents, glidants were passed through Sieve No.60 and mixed in mortar with a pestle to obtain uniform mixing. The blended powder was compressed into tablets weighing appprox. 150 mg on a single punch tablet machine (Cadmach, Ahmadabad) using a flat-faced non-beveled punch and die set of 8-mm diameter [10,12].

Precompression parameters

Bulk density: It is a ratio of mass of powder to bulk volume. It is expressed in gm/ml and is given by the formula [8,10]. Bulk density=M/Vo Where, M = mass of the powder, Vo = bulk volume of the powder

Tapped density: It is a ratio of mass of powder to tapped volume. Ten gram of powder was introduced into a clean, dry 100 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. It is expressed in gm/ml and is given by [8,10].

Tapped density=M/Vt

Where, M = mass of the powder

Vt = final tapping volume of the powder

Angle of repose (θ): It is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. The angle of repose was then calculated using following equation [5,10]:

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

Where, h=height of the pile

r=radius of the pile

Compressibility index (Carr's index): Compressibility index is used as an important parameter to determine the flow behaviour of the powder. It is indirectly related to the relative flow property rate, cohesiveness and particle size. It is simple, fast and popular method for predicting flow characteristics.

Carr's index is determined by employing following formula [5]:

Carr's Index= [(TD-BD)x100]/ TD

Hausner's Ratio: The Hausner's ratio is a number that is correlated to the flow ability of a powder or granular material [5,15]. Hausner's ratio = TD/BD

Physical evaluation of the matrix tablets: The thickness, hardness, weight uniformity and friability were determined in a similar manner as stated for conventional oral tablets in the accredited pharmacopoeia [8,13].

Determination of Drug Content: 20 tablets from each formulation were finely powdered and a portion equal to 10 mg ATV was transferred to a 100 ml volumetric flask, dissolved in phosphate buffer (pH 6.8). Then the volume was made up with buffer and shaken for 10 minutes to ensure complete solubility of drug. The mixture was centrifuged and 10 mL of the supernatant liquid was diluted 20 times with buffer and the absorbance was determined spectrophotometrically using a UV spectrometer (UV-Visible, Perkin-Elmer, USA) at 243 nm [15].

Disintegration test: Disintegration is evaluated to ensure that the drug substance is fully available for dissolution and absorption from the gastrointestinal tract. Disintegration test was carried out using tablet disintegration test apparatus (Electrolab, India) using distilled water without disk at room temperature (37 ± 2 °C). The time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds [10,15].

In-vitro drug release studies: In vitro dissolution studies for all the tablets were carried out using USP type II Dissolution apparatus (Electrolab, Mumbai, India). The dissolution medium used was 900 ml, mixture of phosphate buffer solution pH 6.8 and water (1:1) used as dissolution medium. The tablets containing 20 mg of ATV were weighed and then introduced into the dissolution medium. 1 ml aliquots were withdrawn at every 1 hour and replaced by 1 ml of fresh dissolution media (37 ºC). The medium was stirred at 50 rpm using paddle at 37 ± 0.5 °C. The samples were collected, filtered through Whatman filter paper (0.45um) and analyzed after suitable dilution (if required) at 243 nm using UV-visible spectrophotometer against phosphate buffer (pH 6.8) as blank [13,14].

Kinetic evaluation of release data: The dissolution data from various batches of tablets were subjected to release kinetic study by fitting in to various postulated kinetic models. Drug dissolution from solid dosage form has been described by kinetic models in which the dissolved amount of drug (Q) is compared to the drug content (%) function of the test time (t). The analytical and kinetic models of the Q versus t commonly used are Zero order, First order, Higuchi and Korsmeyer-Peppas model to study the possible release mechanism [14,16].

Stability studies: The stability studies were conducted by storing the optimized tablets at 40 ± 2 ºC/75 ± 5% RH in stability chamber for 45 days. The samples were withdrawn after 45 days and analyzed for various physical tests and drug release study [5,15].

RESULTS AND DISCUSSION

Thermal characterization of ATV

DSC curve of ATV shows an endothermic event who's melting T_{onset} was 153.05 °C and Tpeak was 132.97 °C (ΔH 93.674 J g^{-1}). Then another endothermic event is observed which can be attributed to a phase transition characteristic of this polymorph with the following thermal transition of around 190-250 ° C. The melting peak of ATV according to Zhang (2009) happened to 158.8 °C and enthalpy of 86.85 J g^{-1} [9]. The melting peak of atorvastatin when disappeared, or decreased in intensity in drug-excipient binary mixtures, it was confirmed to be physical interaction. DSC curve of atorvastatin+ lactose shows only the characteristic endothermic peaks of lactose. According to the literature [9], lactose melting at 144 °C prior to the melting of ATV which promotes the solubility of ATV into the lactose and subsequent disappearance of the peak temperature of ATV. Therefore, there is no interaction with lactose. DSC curve of ATV+mannitol cause the disappearance of the melting peak characteristic of ATV or appearance of only peak of the excipient. Thus, it suggests interactions which may be physical or chemical. This was further reconfirmed by FT-IR studies. From the DSC studies, the excipients such as microcrystalline cellulose, magnesium stearate, mannitol, sodium lauryl sulfate were found to have physical interactions with ATV as shown in the Figure (1).

FT-IR study

The principal infra-red absorption peaks of pure ATV calcium shows characteristics peaks belonging at 1577.77, 1649, 1550, 1217.38, 1317.0, 3363 cm^{-1} corresponding to aromatic secondary N-H vibrations, C=O, C=C, C-O, C-N and O-H stretching of aromatic ring respectively (Figure 2). The identical peaks of N-H vibrations, C==O, C=C, C-O, C-N and O-H stretching were also appeared in the spectra of physical mixture of drug with SLS, mannitol, magnesium stearate , and all other excipients found compatible in DSC studies. FT-IR-spectra of drug and its physical mixture with above excipients are not exactly same, and there is slight shift of peaks or disappearance of principle peaks or modification of the principle peaks owing to physic-chemical bonding between drug and excipients indicating that there is no interaction between the drug and excipients.

Evaluation of pre-compression properties

Immediate release tablet of ATV were successfully prepared by direct compression method using superdisintgrant like croscarmellose sodium and varying the grades of microcrystalline cellulose, as per formulation Table (1). The directly compressible powder blend was evaluated for parameters like bulk density, tapped density, compressibility index, and angle of repose, Hausner ratio as shown in Table (2). The bulk density of the powder was in the range of 0.33 to 0.52 gm/ml; the tapped density was in the range of 0.47 to 0.67gm/ml, which indicates that the powder was not bulky. The angle of repose of the formulations with lactose in larger quantity was in the range of 21º to 25º, which indicated good flow of the powder. The Carr's index was found to be in the range of 22 to 30 indicating moderate to fairer compressibility of the tablet blend. The Hausner ratio lays in the range 0.758 to 0.814 confirming good flow characteristics for direct compression tablets.

Evaluation of post-compression properties

All the batches of tablets (F1-F12) were evaluated for various post compression properties such as hardness, thickness,

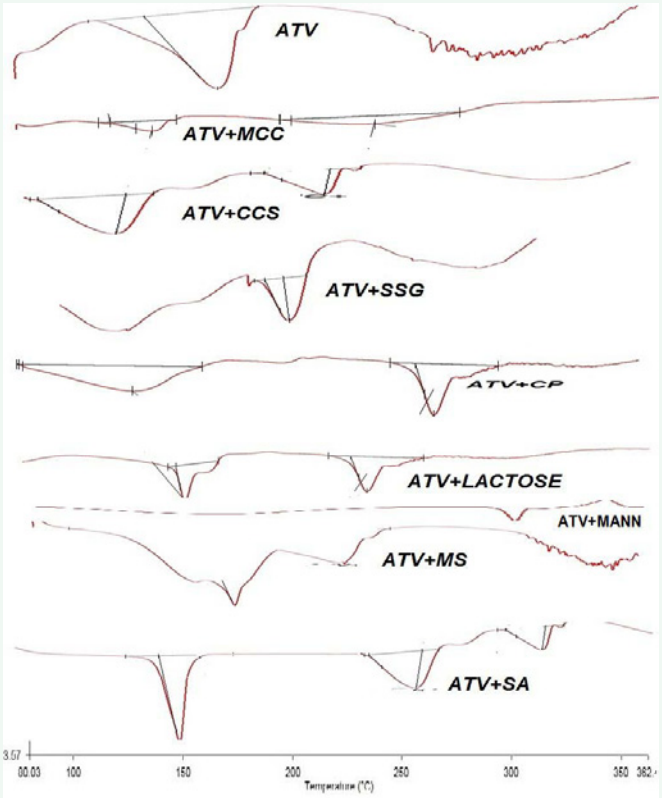

Figure 1 DSC studies of ATV with various immediate release excipients.

Table 1: Composition of various batches of atorvastatin Immediate release tablets.

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Atorvastatin Calcium	20.70	20.70	20.70	20.70	20.70	20.70	20.70	20.70	20.70	20.70	20.70	20.70
Sodium Starch Glycollate	----	----	----	4	6	8	----	----	----	----	8	8
Cross Carmellose Sodium	4	6	8	----	----	----	----	----	----	8	8	----
Cross Povidone	----	----	----	----	----	----	4	6	8	8	----	8
Sodium Lauryl Sulphate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Anhydrous Lactose	110.8	108.8	106.8	110.8	108.8	106.8	110.8	108.8	106.8	98.8	98.8	98.8
Saccharin sodium	10	10	10	10	10	v	10	10	10	10	10	10
Stearic Acid	3	3	3	3	3	3	3	3	3	3	3	3

Table 2: Physical properties of directly compressible powder blend.

Formulation Code	Angle of Repose (degree)	Tapped Density (g/cm^3)	Bulk Density (gm/cm^3)	Hausner ratio	Compressi-bility Index (%)
F-1	21.88±1.10	0.435±0.04	0.543±0.06	0.801±0.21	24.82±0.02
F-2	23.76±0.05	0.414±0.02	0.546±0.04	0.758±0.18	31.88v0.05
F-3	24.32±0.21	0.455±0.03	0.567±1.09	0.802±0.10	24.61±0.02
F-4	22.66±0.24	0.476±0.04	0.597±0.07	0.797±0.08	25.42±0.06
F-5	23.98±0.31	0.422±0.01	0.518±0.03	0.814±0.09	22.74±0.01
F-6	24.12±0.08	0.458±0.04	0.562±0.08	0.814±1.10	22.70±0.04
F-7	23.50±0.18	0.436±0.05	0.564±1.10	0.773±1.05	29.35±0.06
F-8	23.61±0.14	0.421±0.05	0.548±1.13	0.768±1.07	30.16±0.02
F-9	25.34±0.11	0.431±0.07	0.553±1.14	0.779±1.10	28.30±0.08
F-10	24.78±0.07	0.464±0.05	0.578±0.09	0.802±1.02	24.56±0.03
F-11	24.08±0.15	0.430±0.03	0.558±0.06	0.770±0.91	28.57±0.05
F-12	25.30±0.13	0.453±0.06	0.578±1.10	0.783±0.88	27.59±0.06

Values are mean ± SD, n=3 in case of study.

friability, weight variation, content uniformity as shown in Table (3). The tablets were compressed at the average weight of 150 mg. The weight variation of all batches in the ranges of 147 ± 0.34 to 154 ± 0.34 mg. The pharmacopoeial limit for percent deviation in weight variation for 100 mg tablet is ± 7.5%. The average percent deviation for all tablets was found to be within the limit and hence it passes the weight variation test. The tablets thickness was 3.5 ± 0.03 to 3.8 ± 0.03 mm. The tablets hardness was 3.5 ± 0.15 to 4.1 ± 0.13 kg/cm^2.

In-vitro drug release behavior of prepared tablets

The in-vitro dissolution profiles of all formulations are depicted in Figure (3a-3d). Release a data revealed that formulation F1, F2 and F3 released 72.3%, 74.37% and 76.50% drug respectively within 20 minutes. Formulation F4, F5 and F6 released 71.2%, 73.37% and 74.7% drug respectively within 20 minutes. Formulation F7, F8 and F9 released 67.17%, 69.30% and 71.21% drug respectively within 20 minutes. Results also reveals that the batches F10, F11 and F12 released 72.4%, 82.7%, 77.8% and 72.4% of drug within 20 minutes demonstrating the immediate release pattern. Among all the formulations F3 containing cross carmellose sodium, F6 containing sodium starch glycollate and F12 containing 1:1 ratio of CCS:SSG, F11 containing 1:1 ratio of CCS: cross povidone have shown increased drug release in 20 minutes as compared to CP. Formulation F11have shown the disintegration time less than 25 sec and better dissolution than

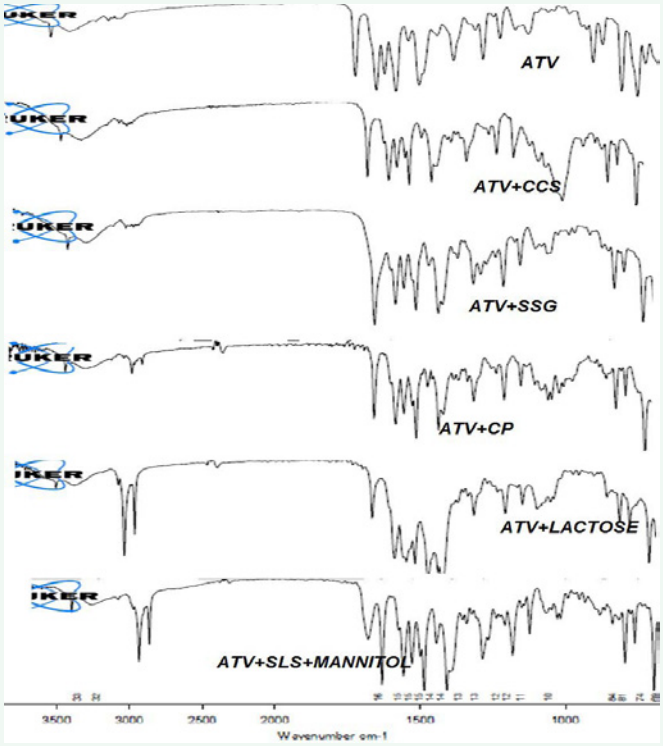

Figure 2 FT-IR spectrum of pure ATV and drug-excipient physical mixtures.

Table 3: Physical properties of various batches of immediate release tablets.

Batch Code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight Variation (mg)	Drug Content (%)	DT(sec)
F1	3.5±0.03	3.5±0.15	0.68±0.23	148±0.45	98.67±0.05	45±0.04
F2	3.8±0.06	3.4±0.16	0.57±0.28	147±0.34	96.54±0.03	40±0.06
F3	3.6±0.04	3.5±0.13	0.54±0.31	151±0.08	98.45±0.02	35±0.03
F4	3.5±0.02	3.6±0.16	0.72±0.38	150±0.25	96.08±0.04	34±0.01
F5	3.8±0.05	3.8±0.12	0.64±0.21	148±0.56	97.32±0.03	30±0.06
F6	3.5±0.05	4.0±0.10	0.52±0.25	149±0.65	96.54±0.04	28±0.03
F7	3.8±0.02	4.1±0.13	0.54±0.28	152±0.60	97.81±0.06	46±0.02
F8	3.7±0.04	4.2±0.08	0.65±0.18	154±0.34	98.74±0.03	41±0.06
F9	3.8±0.05	4.0±0.12	0.63±0.11	151±0.71	95.56±0.07	38±0.02
F10	3.8±0.03	3.6±0.13	0.69±0.24	153±.46	96.71±0.03	28±0.10
F11	3.6±0.05	3.5±0.08	0.75±0.21	148±.05	98.10±0.02	24±0.19
F12	3.8±0.03	3.8±0.10	0.72±0.16	150±0.90	96.72±0.05	34±0.12

Values are mean ± SD, n=3 in case of study.

all other formulations. Hence, formulation F11 is considered to be the best formulation among the other.

Drug Release mechanism

The results of in-vitro release data after kinetic evaluation are presented in Table (4). Kinetic evaluation of the release data reveals that the r^2 value of optimized batch F11for zero order and first order were obtained as 0.853 and 0.866 respectively. Based on the results it was confirmed that the optimized formulation followed first order release. However, the highest co-relation of F11 was found in Higuchi's model as evidenced by linearity closer R^2 value (0.982) indicating that drug release from the immediate release tablets occurs through diffusion process. The in-vitro release data was further fitted to Krosmeyer-Peppas model which is generally used to analyze the release mechanism when more than one type of release phenomenon is operational. Good linearity was observed with high 'r' values. The value of release exponent 'n' is an indicative of release mechanism. The value of 'n' obtained for the optimized formulation F11 was found to be 0.4 suggesting probable release by case-I transport. The results

Table 4: Kinetic model evaluation of in-vitro release data.

Formulation code	Zero order		1st order		Higuchi		Korsemeyer peppas	
	K_0	R^2	K_1	R^2	K_H	R^2	n	R^2
MKT	2.804	0.808	0.064	0.856	19.18	0.076	-1.88	0.674
F1	2.922	0.899	0.050	0.844	18.51	0.978	-1.41	0.641
F2	2.866	0.869	0.055	0.853	18.63	0.971	-1.62	0.577
F3	2.860	0.844	0.071	0.791	18.90	0.962	-2.16	0.646
F4	2.768	0.887	0.037	0.919	16.82	0.990	0.453	0.980
F5	2.815	0.882	0.043	0.894	17.15	0.990	0.441	0.979
F6	2.824	0.868	0.051	0.851	17.29	0.985	0.414	0.968
F7	2.254	0.773	0.020	0.861	14.32	0.945	0.274	0.927
F8	2.310	0.758	0.022	0.827	14.76	0.936	0.264	0.921
F9	2.373	0.754	0.026	0.727	15.17	0.933	0.258	0.898
F10	2.633	0.867	0.032	0.930	16.14	0.985	0.381	0.966
F11	2.915	0.853	0.069	0.866	17.98	0.982	0.383	0.961
F12	2.715	0.857	0.037	0.930	16.74	0.986	0.373	0.967

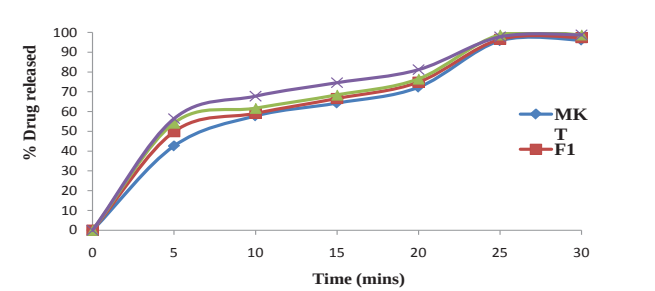

Figure 3a In vitro drug release rate curve for different immediate release tablets containing different proportion of super disintegrants . Marketed (-♦-), F1 (-■-), F2 (-▲-), F3 (-¥-) showing release of drug from prepared formulations.

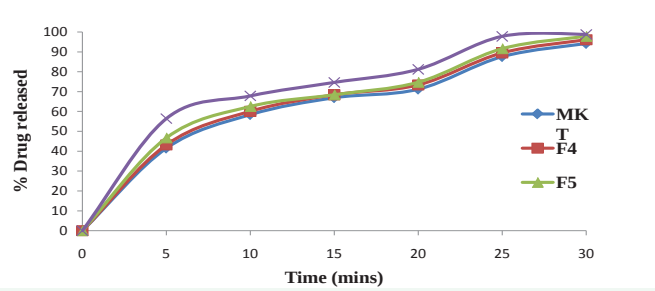

Figure 3b In vitro drug release rate curve for different immediate release tablets containing different proportion of super disintegrants. Marketed (-♦-), F4 (-■-), F5 (-▲-), F6 (-¥-) showing release of drug from prepared formulations.

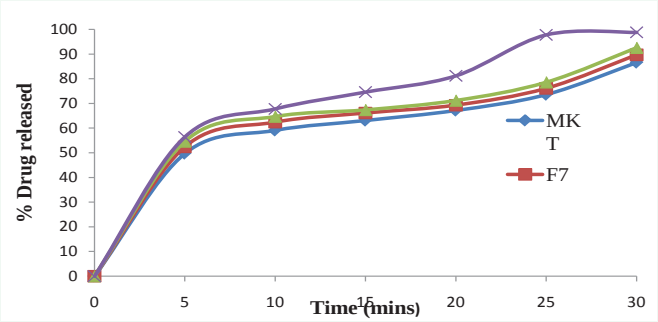

Figure 3c In vitro drug release rate curve for different immediate release tablets containing different proportion of super disintegrants. Marketed (-♦-), F7 (-■-), F8 (-▲-), F9 (-¥-) showing release of drug from prepared formulations.

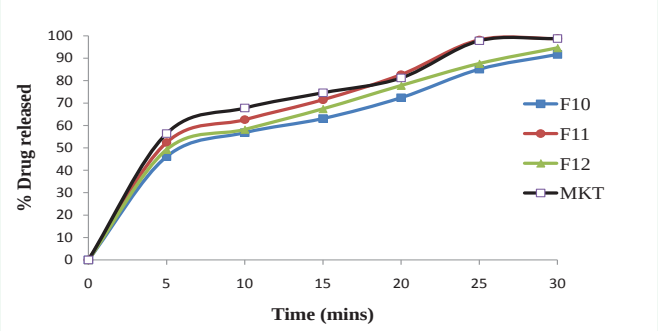

Figure 3d In vitro drug release rate curve for different immediate release tablets containing different proportion of super disintegrants. Marketed (-□-), F10 (-■-), F11 (-●-), F12 (-▲-) showing release of drug from prepared formulations.

of accelerated stability studies as per ICH guidelines indicated that the tablets did not show any significant physical changes (color change, friability and hardness), assay and dissolution characteristics during the study period.

CONCLUSION

With all the above observations it was found that, ATV Calcium immediate release tablet can be successfully prepared with selected superdisintegrants which are found compatible in FT-IR and DSC studies. ATV was found incompatible with mannitol, Magnesium stearate, MCC. So, DSC and FT-IR was successful tool to screen the interactions with ATV and immediate release tablet can be developed by direct compression method. All formulations were found to be satisfactory when evaluated for thickness, weight uniformity, hardness, friability, drug content uniformity, disintegration time and in-vitro drug release. Formulation F11 containing two super disintegrants have shown the disintegration time less than 25 sec and better dissolution than all other formulations releasing more than 80% of the drug after 20 minutes. Evaluation of the release kinetic data reveals that tablets containing 1:1 ration of two super disintegrants (CCS:SSG) exhibit Higuchi spherical matrix release indicating that drug release from the tablet was diffusion controlled followed by case I transport. Stability study revealed that, the selected formulation F11 was stable over the period of three months of stability study.

ACKNOWLEDGMENTS

The authors greatly acknowledge GIPS, Shrimanta Shankar Academy Society, SSA, Guwahati to carry out DSC and FT-IR studies free of cost. The authors are also thankful to Loba Chemie Pvt. Ltd. Mumbai, India for providing Atorvastatin calcium research sample.

REFERENCES

1. Bruni G, Berbenni V, Milanese C, Girella A, Marini A. Drug-excipient compatibility studies in binary and ternary mixtures by physico-chemical techniques. J Therm Anal Cal. 2010; 102: 193-201.
2. Freire FD, Aragão CF, Lima TFA, Raffim FN. Compatibility study between chlorpropamide and excipients in their physical mixtures. J Therm Anal Calorim. 2009; 97: 355–357.
3. Carvalho KP, Rocha TC and Leles MIG. Characterization of atorvastatin by TG and DSC. Braz J Ther Ana. 2012; 1: 79-83.
4. Rowe RC, Sheskey PJ, Quinn ME. Hand Book of Pharmaceutical Excipients. 6th edn, London: Pharmaceutical Press. 2009; 80.
5. Sinko PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences, 5th edn, New Delhi, Wolters Kluwar Healthcare Pvt. Ltd, 2007; 553-558.
6. Jivraj M, Martini LG and Thomson CM. An overview of the different excipients useful for the direct compression of tablets. Pharm Sci Technol Today. 2000; 2: 58-63.
7. Oliveira MA, Yoshida MI, Belinelo VJ, Valotto RS. Degradation Kinetics of Atorvastatin under Stress Conditions and Chemical Analysis by HPLC. Molecules. 2013; 18: 1447-1456.
8. Patel JA. Formulation and evaluation of immediate release tablet of azithromycin by dry granulation method using super disintegrants. Am J PharmTech Res. 2011; 1: 211-218.

9. Zhang HX, Wang JX, Zhang ZB, Le Y, Shen ZG, Chen JF. Micronization of atorvastatin calcium by antisolvent precipitation process. Int J Pharm. 2009; 374: 106-113.

10. Nyol Sandeep, Gupta MM. Immediate drug release dosage form: a review. J Drug Deliv Ther. 2013; 3: 155-161.

11. Palanisamy P, Jayakar B, Chandira R. Margret, Venkateshwarlu BS, Pasupathi A. Formulation, Evaluation and Development of Immediate Release Film Coated Tablets of Atorvastatin and Sustained Release Film Coated Tablets of Ezetimibe in Capsules Form USP. Int J Med Pharm. 2013; l: 1-10.

12. Dokala GK, Pallavi Ch. Direct Compression - An Overview. Int J Res Pharm Biomed Sci. 2013; 4: 155-158.

13. Sharma B, Saini V, Arvind S. Preparation, Characterization and In-Vitro Evaluation of Atorvastatin Calcium Solid Dispersions with Various Hydrophilic Polymers and Its FDT Formulation. Curr Phar Res. 2012; 2: 620-630.

14. Karimban JA. Formulation and Evaluation of Immediate Release Venlafaxine HCl Tablets: Comparative Study of Super Disintegrant and Diluents. Int Res J Pharm. 2012; 3: 324-329.

15. Kotta KK, Suma P, Srikrishna T. Formulation and Evaluation of Atorvastatin Calcium Immediate Release Tablets. Ind J Nov Drug Deliv. 2013; 5: 130-141.

16. Kumar S, Garg SK, Aseri A. Design, optimization and in-vitro evaluation of Atorvastatin fast dissolving tablets by using solid dispersion technique. World J Pharm Pharm Sci. 2014; 3: 1217-1239.

Cite this article

Nath B, Roy TK (2017) Thermal Characterization and Screening of Formulation Variables of Atorvastatin Calcium Immediate Release Tablet. JSM Nanotechnol Nanomed 5(1): 1044.