IJPSR (2021), Volume 12, Issue 1 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 08 January 2020; received in revised form, 18 May 2020; accepted, 21 May 2020; published 01 March 2021

FORMULATION DEVELOPMENT AND EVALUATION OF ATORVASTATIN CALCIUM LIQUISOLID TABLETS

Purushottam R. Patil *, Paresh R. Mahaparale and Khalid U. Shaikh

Department of Pharmacy, Government College of Pharmacy, Osmanpura, Aurangabad - 431005, Maharashtra, India.

Keywords:

Liquisolid compacts, Atorvastatin Calcium, Dissolution rate, PEG-400

Correspondence to Author:
Dr. Purushottam R. Patil

Assistant Director on Deputation , AICTE HQ, Nelson Mandela Marg, Vasant Kunj, New Delhi 110070, India.

E-mail: prpatilgcop@gmail.com

ABSTRACT: The solubility and dissolution properties of any drug are vital determinants of its oral bioavailability. The aim of this study was to increase the dissolution rate of poorly soluble drug Atorvastatin calcium by delivering the drug as a liquisolid compact, prepared by using PEG as a solvent, Avicel PH 102 as carrier, silica, and lactose are used as coating materials. Sodium starch glycolate was used as super disintegrants and evaluated for their flow properties, drug excipient compatibility by FT-IR, DSC, respectively. Dissolution studies for liquisolid formulation and directly compressed tablet were carried out at a buffer pH 6.8 and found an increase in drug release of 101.71% and 80.09% at 45 min, respectively.

INTRODUCTION: In most of the pharmaceutical industry, major challenges in drug development is poor water solubility of drugs. New Chemical Entitles (NCE) do not enter the market due to their poor solubility. The liquisolid technique is a new method used to change the dissolution rate of poor soluble drugs. The dissolution is the rate-limiting step for the drug absorption for BCS class II (low solubility and higher permeability) drugs and BCS class IV (low solubility and low permeability) drugs in the biopharmaceutical classification system [1].

Different techniques have been reported in many literatures to improve the dissolution rate are:

- **a.** Reduce particle size *i.e.*, nanonization, micronization.
- **b.** To increase surface area.
- **c.** Use of surfactant
- **d.** Use of prodrug and drug derivatization.
- **e.** Formulation of solid solution and amorphous form.
- **f.** Microencapsulation

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(3).1849-59

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(3).1849-59

TABLE 1: BCS DRUG CLASSIFICATION [2]

BCS class	Solubility	Permeability
Class I	High	High
Class II	Low	High
Class III	High	Low
Class IV	Low	Low

Among the various techniques are used to overcome the solubility issue. Several researchers reported that the formulation of liquisolid tablet is one of the most promising techniques for drug dissolution [3].

Concept of Liquisolid Formulation: When the drug dissolved in the liquid vehicle is incorporated into a carrier material which has a porous surface and closely matted fibers in its interior as cellulose, both absorption and adsorption take place.

The liquid initially absorbed in the interior of the particle is capture by its internal structure. After

saturation, adsorption of the liquid on to the internal-external surface of the porous carrier particle occurs. Then the coating materials having high adsorption properties and a large specific surface area that provides the liquisolid system the desirable flow characteristics [4].

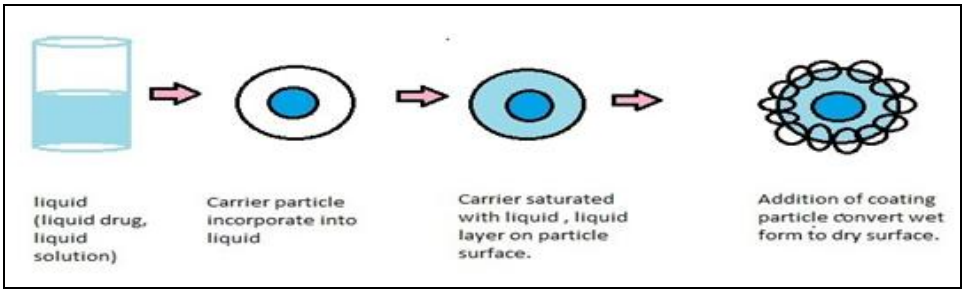

FIG. 1: CONCEPT OF LIQUISOLID SYSTEM

The non-volatile solvent present in the liquisolid system provides wetting of the drug particle by reducing the surface tension between dissolution medium and tablet surface, thus increasing in wettability and effective surface area for dissolution, which enhance the bioavailability of the drugs [5, 6].

Composition of Liquisolid Tablet:

Carrier Materials: Carrier material should possess porous surface and matted fibers in the interior, which are involved in the sorption process and improve the effective surface area for dissolution. Examples, Starch, Lactose, Sorbitol, various grades of cellulose [7].

Coating Materials: Coating material should be a material possessing fine and highly adsorptive particles, which contributes to covering the wet carrier particles and displaying a dry-looking powder by adsorbing any excess liquid. The coating material is required to cover the surface. Coating materials are very fine (10nm - 5000nm) examples colloidal silica, cab-o-sil MS, Aerosil 200, Syloid 244FFP [8].

Non-volatile Solvent: It should be inert, ability to dissolve the amount of drug, high boiling point, water-miscible, and not viscous in organic solvent system. Examples polyethylene glycol, Liquid PEG, polysorbate (Tween 80), fixed oil *etc*. [9]

Disintegrants: Which are used to solubility enhancement of drug. Examples Crospovidone, sodium starch glycolate (pumogel, Explotab).

Drugs: Drugs should be poorly soluble or insoluble in water especially BCS class II and BCS class IV drugs [10].

MATERIALS AND METHODS:

Materials: Atorvastatin calcium was a gift sample procured from Wockhardt Pvt. Ltd, Aurangabad. Avicel PH 102, Polyethylene glycol, Silica, Lactose, Sodium starch glycolate, Magnesium stearate, cross carmellose sodium are purchased from Deepa chemicals Ltd. Aurangabad.

Methods:

Calibration Curve of Atorvastatin Calcium: Accurately weigh about 50 mg of Atorvastatin calcium and dissolved in 50 ml of Phosphate buffer pH 6.8 in 50 ml volumetric flask and finally volume is adjusted to 50 ml (µg/ml). The standard solution of Atorvastatin calcium was subsequently diluted with pH 6.8 buffer to obtain a serial dilution containing 10, 20, 30, 40, and 50 µg/ml. The absorbance of the above dilutions measured on a spectrophotometer at 246 nm using pH 6.8 buffer as blank [11]. The concentration of Atorvastatin calcium used, and the corresponding absorbance is given in **Table 6**. The absorbance was plotted against concentration, as shown in **Fig. 2**.

Determination of λ_{max} of Atorvastatin Calcium: To determine the λ max of the Atorvastatin calcium spectra run in the spectrum by the UV spectroscopy is a must. The highest concentration of the solution *i.e.,* 50µ/ml, is used to determine the λ_{max} in the range of 200-400 nm.

Method of preparation of Liquisolid Compacts: Firstly, BCS class II drug (Atorvastatin calcium) is dispersed in a non-volatile vehicle (PEG 400). Then a binary mixture of carrier coating materials (Microcrystalline cellulose *i.e.,* Avicel 102 as the carrier powder and as the coating material in a ratio of 20:1, 30:1, 40:1) was added to the mixture

containing the drug and PEG 400 under continuous triturating in a mortar and pastel. Finally, disintegrant (sodium starch glycolate) was mixed and triturate with the resultants mixture. So that by using this methodology, we get liquisolid compact of Atorvastatin calcium. Then compress the tablets of Atorvastatin calcium by using a Tablet punching machine. This is the general method for the preparation of the liquisolid compact [12, 13].

Formulation of Conventional Tablets of Atorvastatin Calcium: Conventional tablets were prepared by mixing the drug with a micro-crystalline cellulose Silica mixture (ratio MCC: Silica was 20:1) for a period of 10 min. The blend was mixed with (Soduim Starch Glycolate as disintegrants) for 10 min, and compressed using a manual tablet punching machine. Sufficient compression load was applied in order to produce tablets with the hardness 3.5 kg/cm^2. This formulation denoted as DCT [14].

Evaluation of Pre-compression Liquisolid Compact:

Angle of Repose: Fixed funnel and the free-standing cone method were employed to measure the angle of repose. A funnel was secured with its tip at a given height (H) above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the tip of the funnel. The mean radius (r) of the base of the conical pile was determined, and measured the height (h) of the pile, after that, the tangent of the angle of repose was determined. The angle of repose of powder (drug) is determined by using the following formula [15].

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

Where θ = angle of repose; h = height of pile; r = radius of the base of the pile

Bulk Density: The loose bulk density and tapped density were determined by using bulk density apparatus. Apparent bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and the weight of the powder (M) were determined. The bulk density was calculated using the formula

$$BD = M / Vb$$

Where M is the mass of powder; Vb is the bulk volume of powder.

Tapped Density: It is the ratio of the mass of the powder to the tapped volume of the powder. Volume determined using a measuring cylinder. Weight quantity of powder-filled in cylinder and volume occupied by measuring cylinder tapped for 500 times and volume occupied by measuring cylinder determined.

$$TD = M / Vt$$

Where, M is the mass of powder and Vt is the tapped volume of the powder.

TABLE 2: RELATIONSHIP BETWEEN ANGLE OF REPOSE AND FLOW PROPERTY

Angle of repose (°)	Flow Property
<25	Excellent
25 -30	Good
3 0- 40	Passable
> 40	Very Poor

Carr's Index: The compressibility index (Carr's index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities and is calculated using the formula.

$$\text{Carr's index (\%)} = (TD - BD) \times 100 / TD$$

Hausner's Ratio: A Flow property of powder mixture can be determined by Hauser's ratio. It is determined from the bulk and tapped densities and is calculated using the formula. The relationship between Hauser's ratio and flow behavior was reported in table [15].

$$\text{Hauser's Ratio} = TD/BD$$

Where, TD is the tapped density, and BD is the bulk density

TABLE 3: RELATIONSHIP BETWEEN CARR'S INDEX, FLOW CHARACTER AND HAUSER'S RATIO

Consolidation Index (%) (Carr's index)	Flow character	Hauser's ratio (%)
<10	Excellent	1.00-1.11
11 – 15	Good	1.12-1.18
16 – 25	Fair to passable	1.19-1.34
26 – 31	Poor	1.35-1.45
32 – 37	Very poor	1.46-1.59
>38	Very very poor	>1.60

Evaluation of Liquisolid Tablets:

Appearance and Shape: The general appearance of the tablets includes morphological characteristics like size, shape, color, odor, *etc*. Also, tablets may have lines, break-marks, and many symbols on the surface of tablets.

Uniformity and Thickness and Diameter: The uniformity of diameter and thickness was measured by using Vernier caliper. The average diameter and thickness of the tablets were calculated. The test passed if none of the individual diameter and thickness values deviated by >5% of the average.

Weight Variation Test: To study the weight variation, twenty tablets were taken, and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity. The percent deviation was calculated using the following formula [15].

% Deviation = (Individual weight /Average weight) × 100

Hardness Test: The hardness of formulated liquisolid tablets was assessed using a Pfizer hardness tester, and the mean hardness of three tablets was determined.

Friability Test: The friability of the prepared liquisolid tablets was measured in a Roche type apparatus, and the percentage loss in weight was calculated [1].

% Friability = (Loss in weight / Initial weight) × 100
Maximum weight loss = Less than 1%

Drug Content: Five tablets were crushed, and powder equivalent to the weight of one tablet was dissolved in solvent SLS-water (40mg/ml), and volume is made up to 100ml. The solution was filtered through Whatman filter paper no. 41. The filtrate was analyzed for drug contended at λ_{max} 246 nm by using UV spectroscopy [16].

Instrumental Analysis of Drug:

FT-IR Spectra of the Drug: FT-IR spectrometer IR 200 Thermo Electron Corporation used in Attenuated total reflectance (ATR) mode for collecting FT-IR spectra of samples. By using IR study the functional group of drug and excipients may be identified. The spectra's were collected over the range of 4000-400 cm^{-1}. [17]

Differential Scanning Calorimetry Studies: DSC thermogram of the optimized Liquisolid Compacts (10mg sample) was recorded using automatic thermal analyzer. The DSC is used to evaluate drug-excipient interaction [18].

Disintegration Test: Six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets Apparatus was run for 10 min, and the basket was lifted from the fluid, observe whether all of the tablets have disintegrated.

Dissolution Study: Dissolution is the process by which a solid solute enters a solution. Pharmaceutically, it may be defined as the amount of drug substance that goes into solution per unit time under standardized conditions of liquid/solid interface, temperature, and solvent composition. Dissolution kinetics is important in determining the bioavailability of a drug. The dissolution study of Atorvastatin calcium compact was performed. Dissolution study of Atorvastatin calcium is carried out in the buffer pH 6.8 by the paddle type apparatus [19].

TABLE 4: DISSOLUTION PARAMETERS

Parameters	Particulars
Dissolution Apparatus	USP-type II Apparatus (Paddle)
Agitation speed	50 rpm
Dissolution medium	Buffer PH 6.8
Volume of dissolution medium	900ml
Temperature	37± 0.5° C
Time	45 min

Comparison with Marketed Product: The developed product was quantitatively evaluated and assessed for a tablet's properties, and product quality was monitored for the various specification. The following standards and quality control tests were carried out on marketed tablets for comparative evaluation of developed and marketed product, and observation was reported in **Table 5** and comparative dissolution profile of developed and marketed product was presented in **Table 5**.

Details of Marketed Product:

Manufacturer: Sun Pharma
Brand Name: Aztor 40 mg
Batch no.: EMP230Mfg. Date: 11/2015
Exp. Date: 10/2018

RESULTS AND DISCUSSION:

TABLE 5: COMPOSITION OF DIFFERENT FORMULATION OF LIQUISOLID COMPACTS

Ingredients (mg)	Formulation Code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Atorvastatin Calcium	40	40	40	40	40	40	40	40	40
Avicel PH 102	300	280	280	260	300	260	300	280	260
Silica	15	9.3	9.3	6.5	15	6.5	15	9.3	6.5
Q/q	20	30	30	40	20	40	20	30	40
PEG 400 (ul)	81	92	70	92	92	81	70	81	70
Sodium starch glycolate	20 (5%)	20 (5%)	20 (5%)	30 (7.5%)	30 (7.5%)	30 (7.5%)	40 (10%)	40 (10%)	40 (10%)
Lactose	20.19	25.71	45.3	58.58	10.08	58.69	-	25.9	48.9
Mg. Stereate	4	4	4	4	4	4	4	4	4
Total wt of tablets (mg)	400 mg	400 mg	400 mg	400 mg	400 mg	400 mg	400 mg	400 mg	400 mg

Determination of λ_{max} by UV Spectrophotometer: Solution containing 10 µg/ml of Atorvastatin calcium was prepared and scanned over a range of 2000-400 nm against buffer pH 6.8 as blank using UV Spectrophotometer [20]. The λ_{max} was obtained at 246 nm. The plot of absorbance against wavelength is shown in **Fig. 2**.

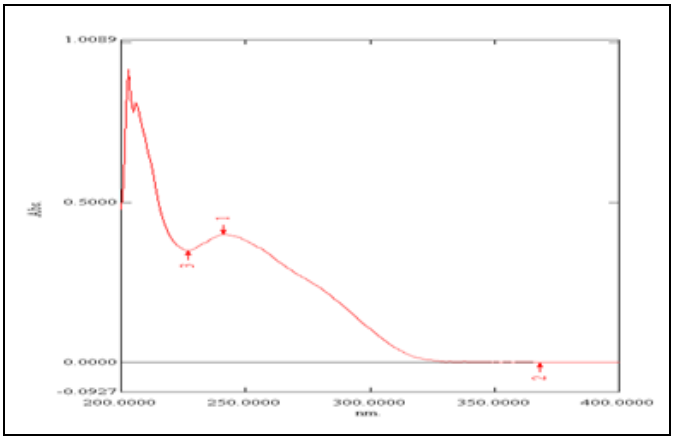

FIG. 2: SPECTRUM OF ATORVASTATIN CALCIUM DRUG

TABLE 6: CALIBRATION CURVE OF ATORVASTATIN CALCIUM IN BUFFER PH 6.8 AT λ_{max} 246 nm

S. no.	Concentration (µ/ml)	Absorbance
1	10	0.34
2	20	0.6
3	30	0.92
4	40	1.2
5	50	1.53

TABLE 7: STANDARD CALIBRATION CURVE STATISTIC

S. no.	Parameter	Observation
1	Absorbance maximum	246 nm
2	Slope	0.02971
3	Intercept	0.02924
4	Correlation coefficient (r^2)	0.998
5	Equation	Y=0.02971 X + 002924

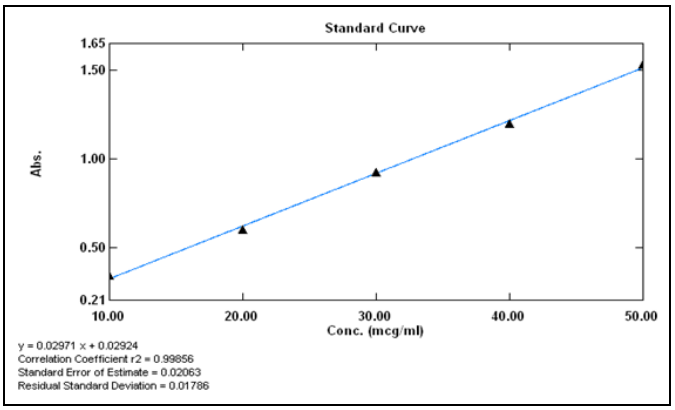

FIG. 3: CALIBRATION CURVE OF ATORVASTATIN CALCIUM IN pH 6.8 BUFFER AT λ_{max} 246 nm

Instrumental Analysis of Drug Excipients and the Liquisolid Compact:

IR Spectra of Drug Atorvastatin Calcium: The IR spectrum of Atorvastatin calcium was recorded over a range of 4000 cm^{-1} to 400 cm^{-1}. The spectrum obtained was concordant with the reference as depicted in **Fig 4**.

The assignments as shown in **Table 8** for Atorvastatin calcium. The graph shows all the ranges of the functional groups of Atorvastatin Calcium. Hence, it can be concluded that the drug was Atorvastatin calcium.

FT-IR spectroscopy of Liquisolid Compact: FT-IR spectroscopy was performed on the pure drug, and a Physical mixture of the formulations was prepared. The characteristic peak in drug and excipients vanished IR spectra Liquisolid system that which may be due to complete solubilization or amorphization of the drug in the non-volatile liquid vehicle. From the comparison of both IR spectra, that is, IR spectra of drug & IR spectra of

Liquisolid compact, results were obtained that intensity of peak decreased, so that peak of functional was shifted towards lower ranges. Results were reported in **Fig. 5.**

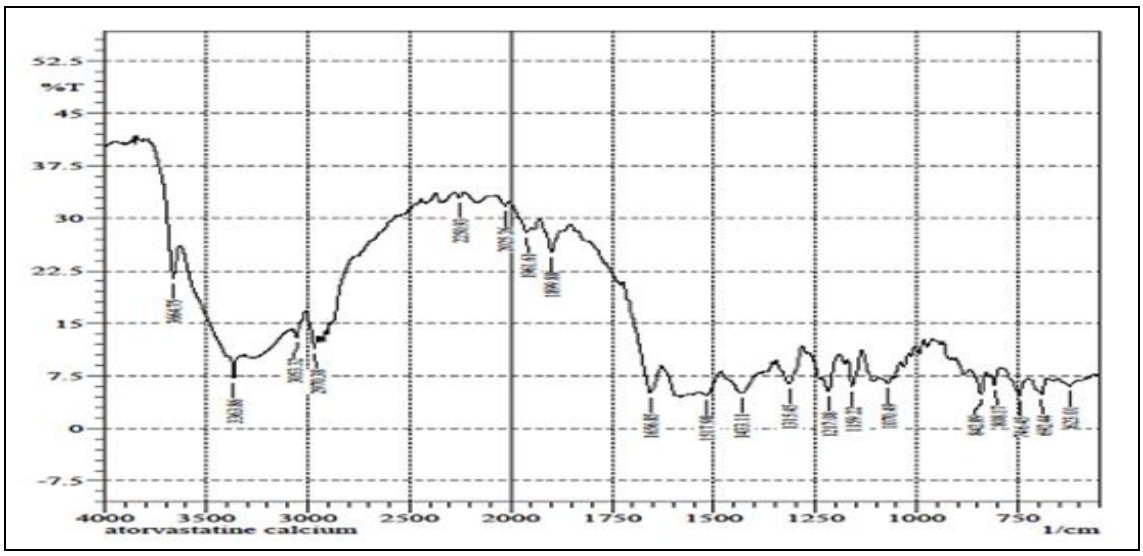

FIG. 4: IR SPECTRA OF ATORVASTATIN CALCIUM

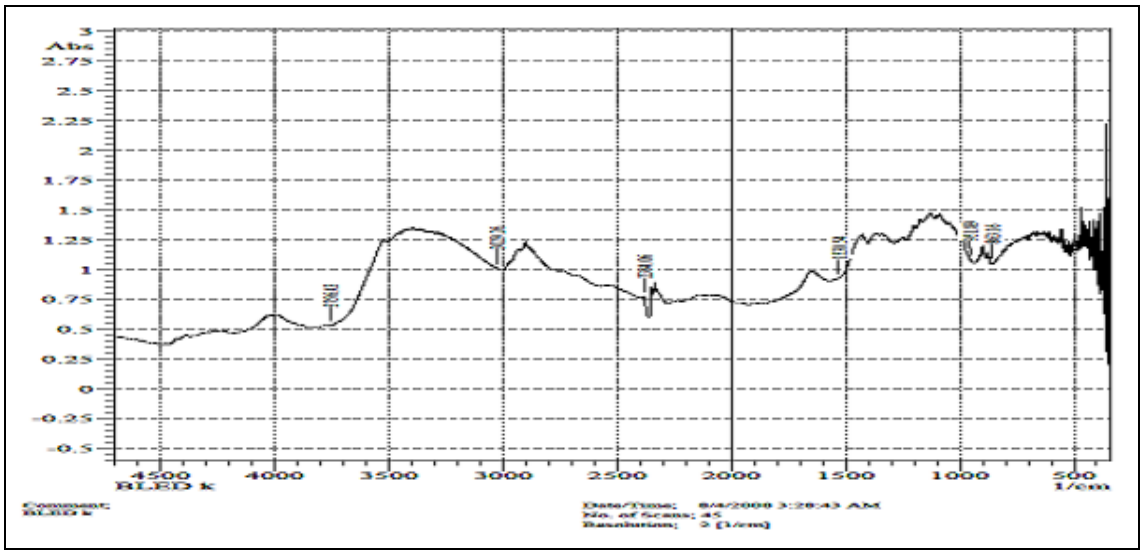

FIG. 5: IR SPECTRA OF THELIQUISOLID COMPACT

As shown in **Fig. 5** the ranges of the functional group are not changes in liquisolid compact. Therefore, the drug and excipients are compatible to each other. The IR spectra show that the excipients and drug compatible with each other. According to the following table. It proves that excipients do not interact with each other.

TABLE 8: COMPARISON OF THE PEAKS OF FUNCTIONAL GROUPS OBSERVED IN IR SPECTRA

IR SPECTRA			
Functional groups	**Range (cm^{-1})**	**Atorvastatin Calcium (Pure)**	**Liquisolid compact**
-OH	3500-3200	3365.86	3329.26
-NH	1550-1450	1517.98	1530.54
C=O	1740-1640	1656.85	1610.00
C-F	1000-800	842.89	863.89

Differential Scanning Calorimetry Study (DSC) of Drug and Liquisolid Compact:

DSC Study for the Atorvastatin Calcium: DSC thermogram of Atorvastatin calcium as shown in the thermogram in **Fig. 6**. It can be seen that endothermic peak with onset at 145.31 ºC and end set 172.87 ºC and also show the sharp peak at 161.06 ºC which corresponds to the melting point of Atorvastatin calcium (159.5 -160.5 ºC).

Fig. 6 shows that the DSC results show the appropriate melting point in the standard melting point range. Therefore, it confirms that the drug was Atorvastatin calcium.

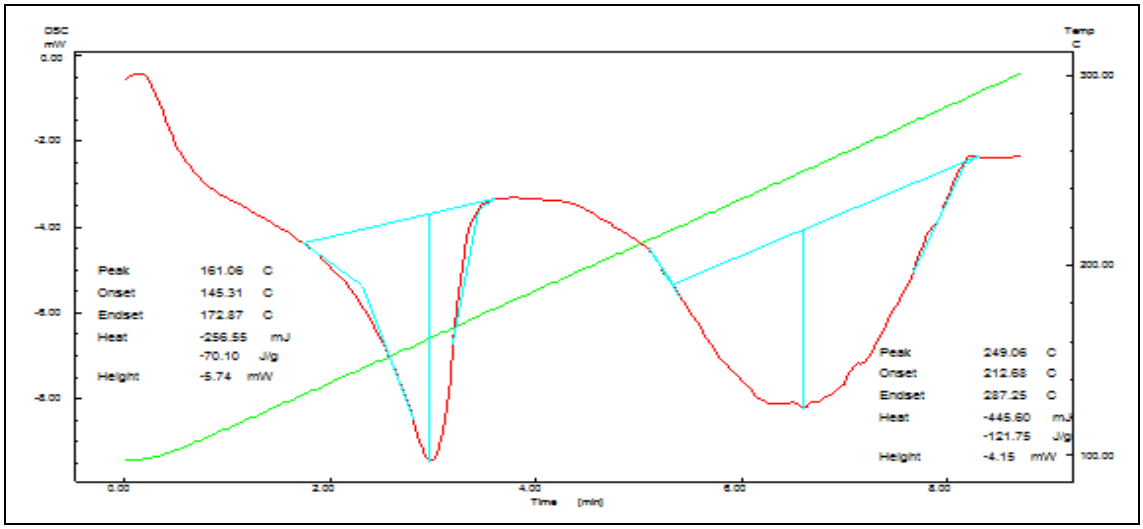

FIG. 6: DSC OF ATORVASTATIN CALCIUM

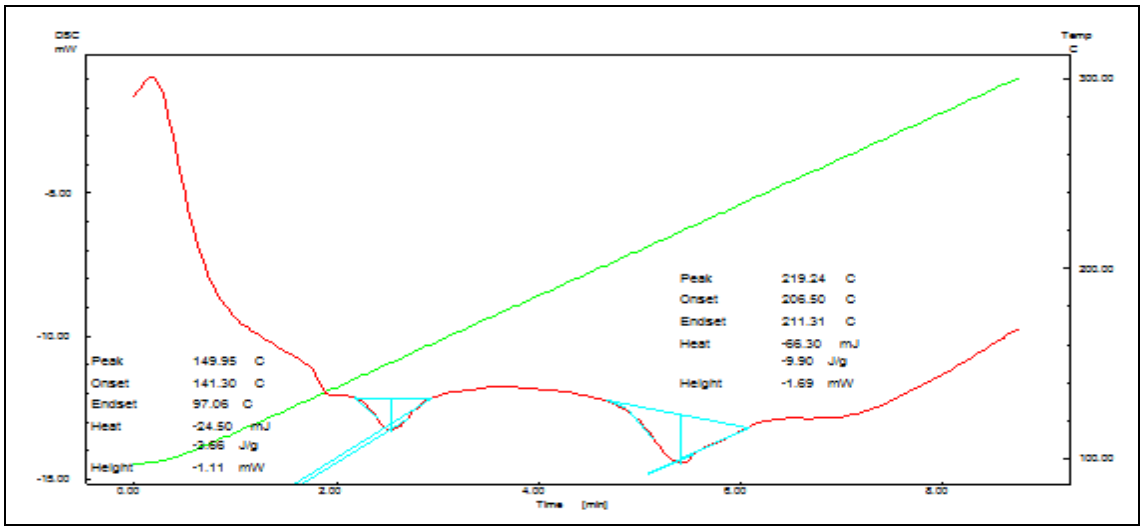

FIG. 7: DSC OF LIQUISOLID COMPACT

DSC thermogram of Atorvastatin calcium as shown in the thermogram in **Fig 6**. It can be seen from DSC thermogram of liquisolid compact shown in **Fig. 7** that endothermic peak of the pure drug at 161.06 ºC was vanished. According to the DSC results, we can conclude that there may in complete solubilization of drug in liquisolid complex.

Hence, we can conclude that there may be compatibility of the drug with excipients in liquisolid compact.

Factorial Batches:

TABLE 9: AMOUNT OF VARIABLES IN 3^2 FACTORIAL DESIGN BATCHES

Coded Value	Actual Value	
	X1 (µl)	X2 (mg)
-1	70	20
0	81	30
+1	92	40

Experimental Design:

TABLE 10: FACTORIAL BATCHES EXPERIMENTAL DESIGN

Formulation Code	Coded Value		Total Weight of Tablet (mg)
	X1	X2	
F1	0	-1	400
F2	+1	0	400
F3	-1	0	400
F4	+1	+1	400
F5	+1	-1	400
F6	0	+1	400
F7	-1	-1	400
F8	0	0	400
F9	-1	+1	400

Flow Properties of Liquisolid Compacts: Bulk density may influence the compressibility, tablet porosity, dissolution, and other properties and depends on the particle size, shape, and tendency to particle adhere together. The bulk density of

granules was found to be between 0.35-0.46 gm/cm^3. The values indicate the good packing capacity of granules. The tap density of the granules of factorial batches was found in the range of 0.43-0.56 gm/cm$^{3;}$ the bulk density and tap density was used to calculate the percent compressibility of the granules.

The carr's index of the granules observed between 13.67-17.97, indicating good compressibility of the granules. The value of the Hausner's ratio was found to be between 1.16-1.22, indicating good flowability.

TABLE 11: EVALUATION OF PRE-COMPRESSION LIQUISOLID COMPACT

Formulation code	Bulk density mg/cm^3	Tapped density gm/cm^3	Carr's index (%)	Angle of Repose	Hausner ratio
F1	0.395±0.54	0.478±0.06	17.19±0.68	36.35±1.06	1.20±.35
F2	0.432±1.07	0.514±0.06	15.95±0.79	36.34±0.75	1.19±0.67
F3	0.456±0.67	0.555±0.23	15.98±0.76	32.65±0.89	1.02±0.12
F4	0.387±0.65	0.456±0.07	15.14±0.02	36.89±1.08	1.18±1.06
F5	0.465±0.55	0.562±0.45	17.08±0.04	35.67±0.86	1.21±0.67
F6	0.413±0.45	0.483±0.35	14.69±0.07	34.67±0.86	1.18±1.09
F7	0.437±0.51	0.512±0.96	14.69±0.13	35.89±0.67	1.17±0.75
F8	0.468±0.08	0.512±0.08	13.68±0.13	35.86±0.97	1.16±0.97
F9	0.356±0.62	0.434±0.86	17.97±0.90	35.01±0.67	1.22±0.46

Response Surface Plot for % Drug Release:

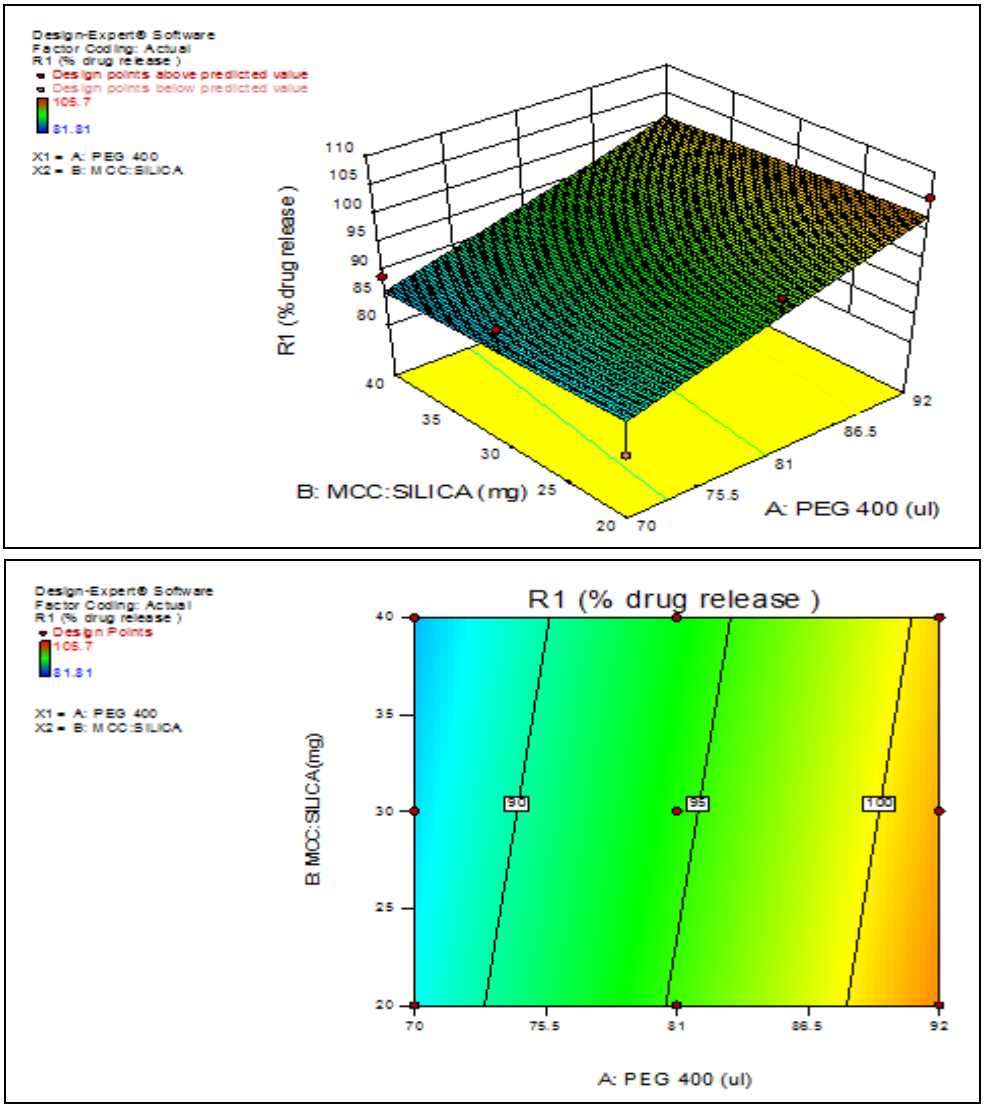

FIG. 8: RESPONSE SURFACE PLOTS

ANOVA for Response Surface Linearity Model:

TABLE12: ANOVA MODEL PREDICTION

Partial Sum of Squares Type III						
Source	**Sum of Squares**	**Df**	**Mean Square**	**F Value**	**P-Value Prob > F**	**Prediction**
Model	319.8912	2	159.9456	10.15371	0.011864	significant

TABLE 13: EVALUATION OF TABLET PROPERTIES OF FACTORIAL BATCHES

Formulation	Appearance	Thickness * (mm)	Hardness * Kg/cm^2	Weight Variation# (mg±SD)	Friability# (%)	Drug Content* (%)	D.T. (sec)
F1	Off white, circular, 10mm, flat faced	3.63±0.07	3.4±0.04	245±1.14	0.532±0.15	96.54±1.10	92
F2	Off white, circular, 10mm, flat faced	3.60±0.08	3.7±0.11	248±1.45	0.410±0.23	98.34±0.94	85
F3	Off white, circular, 10mm, flat faced	4.12±0.12	3.1±0.5	233± 1.17	0.429±0.24	100.64±0.28	87
F4	Off white, circular, 10mm, flat faced	4.05±0.45	3.9±0.08	258±1.4	0.560±0.36	99.51±1.14	90
F5	Off white, circular, 10mm,flat faced	3.39±0.48	4.3±0.13	279±1.8	0.601±0.64	99.92±0.78	94
F6	Off white, circular, 10mm, flat faced	3.35±0.69	3.3±0.58	281±1.6	0.589±0.27	102.45±0.84	88
F7	Off white, circular, 10mm, flat faced	4.08±0.58	3.7±0.12	253±1.7	0.572±0.38	97.21±0.69	91
F8	Off white, circular, 10mm, flat faced	4.42±0.46	3.8±0.19	288±1.3	0.583±0.91	98.14±0.49	87
F9	Off white, circular, 10mm, flat faced	4.23±0.71	3.6±0.07	254±1.1	0.581±0.04	100.35±1.14	92

*All values are expressed as mean ± SD, n=3; # All values are expressed as mean ± SD, n=10; # All values are expressed as mean ± SD, n=10

TABLE 14: ASSAY VALUES OF DIFFERENT FORMULATIONS (N=3±SD)

Formulation	% Drug content
F1	96.54
F2	98.34
F3	101.64
F4	99.51
F5	99.92
F6	102.45
F7	97.21
F8	98.14
F9	100.35

The *in-vitro* Dissolution Study of Atorvastatin Calcium Liquisolid Tablets: The result of *in-vitro* percentage drug amount of drug released at different time intervals plotted against time to obtain the release profile.

TABLE 15: % OF CUMULATIVE DRUG RELEASE OF FORMULATION F1-F3

Time (min)	Cumulative drug release %		
	F1	F2	F3
1	22.57875	20.17575	24.09525
5	54.945	27.03525	39.03525
10	64.05975	34.569	65.4655
15	79.02675	40.06125	80.59725
20	83.3625	56.2045	84.18375
25	93.2625	81.41175	92.6635
30	90.5355	89.4915	97.8815
45	99.48375	90.31525	101.712

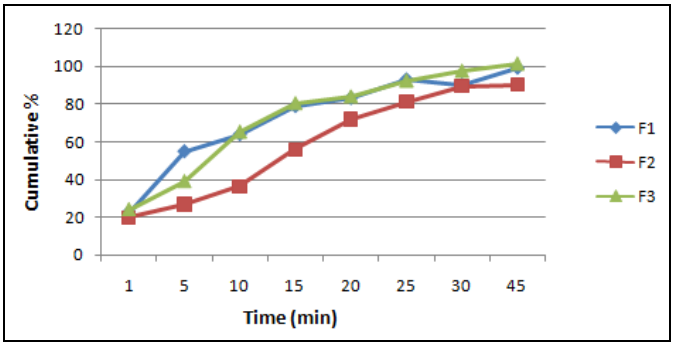

FIG. 9: % OF CUMULATIVE DRUG RELEASE OF FORMULATION F1- F3

TABLE 16: % OF CUMULATIVE DRUG RELEASE OF FORMULATION F4- F6

Time (min)	Cumulative Drug Release %		
	F4	F5	F6
1	15.59025	12.99375	26.5095
5	25.5555	28.64475	43.00875
10	37.37025	39.77325	49.07475
15	43.5825	47.59475	56.1825
20	49.783	57.2085	61.776
25	62.34075	74.3025	71.76825
30	72.94275	80.6502	78.702
45	81.81675	88.974	91.2195

All the liquisolid tablets show thee higher drug release than the (DCT) Direct compressed tablets due to the fact that the drug is already in a solution of PEG 400 while at the same time it is carried by

the powder particles (microcrystalline cellulose and silica), thus its release is accelerated due to its increased wettability and surface availability to the dissolution medium.

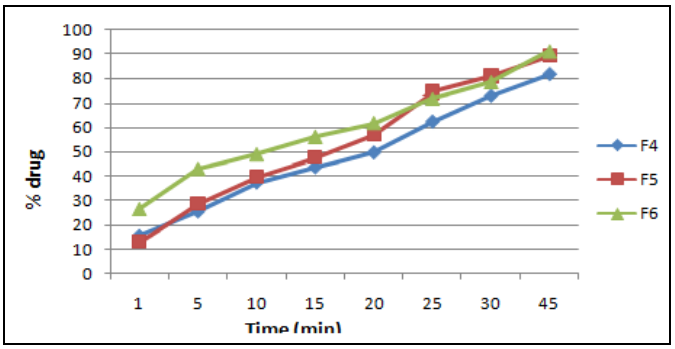

FIG. 10: % OF CUMULATIVE DRUG RELEASE OF FORMULATION F4- F6

TABLE 17: % OF CUMULATIVE DRUG RELEASE OF FORMULATION F7-F9

Time (min)	Cumulative Drug Release %		
	F7	F8	F9
1	25.48	13.806	15.6285
5	58.5502	37.37025	20.65725
10	77.14875	56.988	33.0255
15	87.01425	71.09325	43.362
20	89.91775	81.882	57.051
25	93.69675	89.81325	64.60425
30	97.6635	94.72425	77.04675
45	105.732	100.2983	98.3385

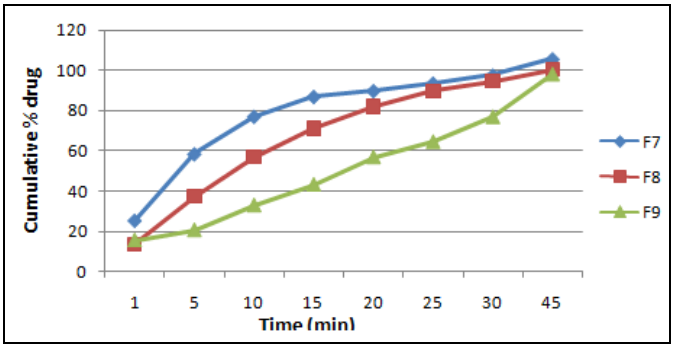

FIG. 11: % CUMULATIVE DRUG RELEASE OF FORMULATION OF F7-F9

TABLE 18: COMPARATIVE EVALUATION OF DEVELOPED AND MARKETED PRODUCT

Evaluation parameter	Developed product	Marketed Product
Appearance	409.7mg, white coloured,10 mm, round flat faced	275 mg off white coloured, 8mm, round biconvex faced
Hardness (Kg/cm^2)	3.1±0.5	2.5± 0.06
Thickness (mm)	4.12±0.12	3.12±0.013
Friability (%)	0.429±0.24	0.321±0.52
Drug Content (%)	101.64 %	102.21%
In-vitro DT (sec)	87 sec	85 sec.
Cumulative % drug release	101.71±0.37	103.16±1.03

TABLE 19: COMPARATIVE DISSOLUTION PROFILE OF DEVELOPED AND MARKETED PRODUCT

Time (min)	Cumulative % drug release	
	Developed Product (F3)	Marketed Product
1	24.09±0.34	42.07±0.08
5	39.03±0.15	54.93±1.32
10	65.46±0.26	61.15±0.03
15	80.59±0.48	69.92±0.25
20	84.18±0.31	76.83±0.48
25	92.66±0.30	82.57±0.38
30	97.88±0.45	97.16±0.53
45	101.71±0.37	103.16±1.03

All values are mean ± SD, N=3

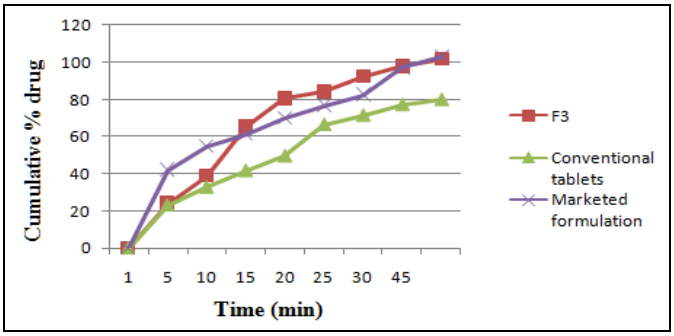

FIG. 12: DISSOLUTION PROFILE OF F3, CONVENTIONAL TABLET, AND MARKETED FORMULATION

CONCLUSION: In this present work, nine formulations of Atorvastatin calcium tablets were successfully prepared by using liquisolid compact technique. Cumulative percentage drug release of Atorvastatin calcium liquisolid tablets is faster than conventional tablets. Liquisolid technique changes the properties of Atorvastatin calcium particle by simply dispersing the drug particles in non-volatile solvent PEG 400, which increases the wetting property and surface area of the drug particle to improve the dissolution profile and might be oral bioavailability of the drug.

ACKNOWLEDGEMENT: Authors are thankful to Dr. V. K. Mourya, Principal Government College of Pharmacy, Aurangabad, for providing the necessary facilities to carry out this work.

CONFLICTS OF INTEREST: There is no conflict of interest amongst the authors and coauthors.

REFERENCES:

1. Hamsanandini J, Parthiban S and Vikneswari A: Dissolution enhancement techniques of poorly soluble drugs by liquisolid compacts. Int J Res Pharm Nano Sci 2014; 3(3): 177-85.
2. Korni R: Liquisolid technique: an approach to enhance the dissolution rate of olanzapine. Indian J Pharm Sci 2018; 80(6): 1003-10.

3. Cherukuri S, Chappidi SR, Dindigala A and Vadla A: Liquisolid Technique : A novel approach to enhance solubility and bioavailability of BCS-II drugs. Int J Pharm Res Sch 2012; 3(7): 108-15.
4. Panda S, Varaprasad R, Priyanka K and Swain RP: Liquisolid technique: a novel approach for dosage form design. Int J Appl Pharm 2017; 9(3): 8-14.
5. Derle DV: Solubility enhancement of nifedipine by using liquisolid compact technique. Indo American Journal of Pharmaceutical Research 2017: 7(02): 7740-55.
6. Pravala K and Nagabandi VK: Solubility enhancement of poorly soluble drugs by using novel technique: a comprehensive review. International Journal of PharmTech Research 2020; 13(2): 80-93.
7. Sinkar NB and Gondkar SB: Liquisolid systems: solubility enhancement of poor soluble drugs. World J Pharm Res 2015; 4(3): 1748-65.
8. Vadlamudi MK and Dhanaraj S: Disparate practical way of doing solubility enhancement study to improve the bioavailability of poorly soluble drugs, Journal of Chemical and Pharmaceutical Res 2016; 8(1): 208-35.
9. Nash RA: Suspensions. In: J Swarbrick, JC Boylan (ed). Encyclopedia of pharmaceutical technology, Marcel Dekker, 2002 Second ed Vol. 3 New York; 2045-3032.
10. Kumar JK, Kumar GYS and Kumar PS: Liquisolid compacts : an effective approach towards enhancement of dissolution rate of poorly soluble drugs. Int J Pharma Chem Res 2015; 1(1): 38-45.
11. Koteswari P, Sunium S, Srinivasababu P, Babu GK and Nithya PD: Formulation development and evaluation of fast disintegrating tablets of lamotrigine using liqui-solid. Int J Pharm Investig 2014; 4(4): 207-14.
12. Mohammed AM and Al- Akkam EJ: preparation *and in-vitro* evaluation of clopidogrel bisulfate liquisolid compact. Iraqi J Pharm Sci 2018; 27(2): 135-49.
13. Sravana M, Srivalli P and Rajeev T: A novel approach for improvement of solubility and bioavailability of poorly soluble drugs : liquisolid compact technique. Int J Res Pharm Biomed Sci 2012; 3(4): 1621-32.
14. Wang D, Xing H, Jiang J, Chen X, Yang T and Wang D: Liquisolid technique and its applications in pharmaceutics. Asian J Pharm Sci 2017; 12(2): 115-23.
15. Indian Pharmacopoeia Commission, Ministry of Health & Family Welfare, Government of India. The Indian Pharmacopoeia 2010; 138.
16. Rajesh K: Formulation and evaluation of bilayer liquisolid tablets of atorvastatin calcium and felodipine. Int Res J Pharm 2013; 4(1): 138-45.
17. Savkare AD and Bhavsar MR: Liquisolid techniques: a review. Int J Pharma Sci Res 2017; 8(7): 2768-75.
18. Jabbar ASA and Hussein AA: Formulation and evaluation of piroxicam liquisolid compacts. Int J Pharm Pharm Sci 2013; 5(1): 132-41.
19. Shah D and Patel MM: Formulation and evaluation of liquisolid compacts of olanzepine. Journal of Drug Delivery and Therapeutics 2019, 9(4): 189-02.
20. Wankhede NB, Walekar SS and Sadgir PS: Liquisolid: A novel technique for dissolution enhancement of poorly water soluble drugs. Asian J Pharm Technol Innov 2014; 2(8): 77-90.

How to cite this article:
Patil PR, Mahaparale PR and Shaikh KU: Formulation development and evaluation of atorvastatin calcium liquisolid tablets. Int J Pharm Sci & Res 2021; 12(3): 1849-59. doi: 10.13040/IJPSR.0975-8232.12(3).1849-59.

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