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(RESEARCH ARTICLE)



## Formulation and evaluation of lovastatin tablets by using liquid solid compact technique

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### Abstract

Lovastatin is a poorly soluble, highly permeable drug and the rate of its oral absorption is often controlled by the dissolution rate in the gastrointestinal tract. There are several techniques to enhance the dissolution of poorly soluble drugs. Among them, the technique of liquid-solid compacts is one of the promising techniques towards such a novel aim. Hence the objective of the present work is to formulate & evaluate tablets by liquid-solid compacts technique. The physicochemical characteristics of Lovastatin compacts such as FTIR Flow properties, Hardness, Friability, *in vitro* release, Release kinetics were evaluated. The FTIR Spectra revealed that there was no interaction between polymer and Lovastatin. The *in vitro* performance of Lovastatin compacts showed control release depends on the polymer concentrations. The diffusion exponent (n) of Korsmeyer-Peppas model was found to be non-Fickian. The results showed that liquid-solid compacts had demonstrated significantly higher drug release rates than those of conventionally made. This was due to an increase in wetting properties and surface of drug available for dissolution.

**Keywords:** Liquisolid Compacts; Lovastatin; *In vitro* studies; Drug release kinetics; Dissolution rate

### 1. Introduction

Solubility behavior of a drug is one of the key determinants of its oral bioavailability. Bioavailability of poorly water-soluble drugs is limited by their solubility and dissolution rate. Several studies have been carried out to increase the dissolution rate of drugs by decreasing the particle size, by creating nano and micro particles. However, the fine drug particles have a high tendency to agglomerate due to van-der-Waals attraction or hydrophobicity, which result in a decrease in surface area over time. Another way of increasing the dissolution rate is adsorption of the drug onto a high-surface-area carrier. In this technique, the drug is dissolved in an organic solvent followed by soaking in the solution by a high-surface-area carrier such as silica [1]. Here, agglomeration of the drug particles is prevented due to the binding of the drug to the carrier. However, due to the presence of the residual solvent in the drug formulation, it is disadvantageous to use toxic solvents.

The term liquid-solid compacts as described by Spireas et.al indicates that immediate or sustained release tablets or capsules that are prepared using the technique of “liquid-solid systems” combined with inclusion of appropriate adjuvants required for tableting or encapsulation such as lubricants and for rapid or sustained release action, such as disintegrants or binders, respectively. Liquisolid compacts prepared by using different solvents which dissolve the poorly soluble drug and gives better bioavailability [2] [3] [4].

Lovastatin is a statin natural product isolated from numerous sources including the *Pleurotus ostreatus* oyster mushroom, demonstrating hypocholesterolemic and antiproliferative properties. Lovastatin inhibits HMGR (3-

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hydroxy-3-methylglutaryl coenzyme A reductase), blocking the enzyme-catalyzed transformation of 3-hydroxy-3-methylglutaryl CoA into mevalonate [5]. Drug profile, Its Half Life 5.3 hours, and Melting Point: 174°C, Absorption: <5%, Distribution: Through Blood-Brain Barrier and Placenta, Protein binding: (>95%), Route of elimination: 83% in bile, 10% in urine, Metabolism: Metabolized mainly in Liver [6].

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## 2. Material and methods

All materials (AR Grade) used were obtained from different sources and all instruments used in work that are as given in list respectively.

### 2.1. List of materials

Micro crystalline cellulose (Nice chemicals pvt. Ltd. Cochin), Tween 80 (S D Fine Chem. Ltd. Mumbai), Ludiflash (Himedia laboratory pvt. Mumbai), Poly ethylene glycol (Loba chemicals pvt .ltd. Cochin), Propylene glycol (Nice chemicals pvt.ltd. Cochin), Magnesium stearate (Loba chemicals pvt .ltd. Cochin) and Talc (S D Fine Chem. Ltd. Mumbai).

### 2.2. List of Instruments

UV/VIS Spectrophotometer (UV-1700, Shimadzu Corporation, Japan), Electronic balance (BL-220H) (Shimadzu Corporation, Japan), Mechanical stirrer (Remi Udyog, Mumbai) and pH meter (Digisun Electronics, Mumbai).

### 2.3. Pre-formulation studies

Preformulation studies involve the determination of both physical and chemical properties of drug with the goal of producing a new drug which is safe, stable and efficacious. These preformulation studies are carried out prior to the formulation of drug. The objectives of these studies are, to establish the compatibility of drug and excipients used in the formulation and to obtain optimal drug delivery system.

### 2.4. Identification of pure drug

#### 2.4.1. Melting point determination

Melting point is the temperature at which the pure liquid and solid exist in equilibrium at an external pressure of 1 atmosphere. The Thiel's tube method of melting point determination in liquid paraffin was used in the present study [8].

#### 2.4.2. Solubility studies

Solubility studies of Lovastatin were carried out in methanol, phosphate buffer 7.4, PEG 200, Tween 80. Saturated solutions were prepared by adding excess drug to the vehicles and shaking on the shaker for 48 hr at 25 °C under constant vibration. Filtered samples (1 ml) were diluted appropriately with 0.1N hydrochloric acid solution and Lovastatin was determined spectrophotometrically at 238 nm. The average value of three trials was taken. Results are shown in Table no 2

#### 2.4.3. Physicochemical parameters

The color, odor and taste of the drug were recorded using descriptive terminology and found to be white to off-white crystalline powder, tasteless and odorless [9].

#### 2.4.4. Determination of absorption maximum ( $\lambda_{max}$ )

The wavelength at which maximum absorption of radiation takes place is called as  $\lambda_{max}$ . This  $\lambda_{max}$  is characteristic or unique for every substance and useful in identifying the substance.

Accurately weighed 100 mg of Lovastatin was dissolved in 0.1N NaOH buffer taken in a clean 100 ml volumetric flask. The volume was made up to 100 ml with the same which will give stock solution-I with concentration 1000  $\mu\text{g/ml}$ . From the stock solution-I, 5 ml was pipette out in 50 ml volumetric flask. The volume was made up to 50 ml using 0.1N NaOH buffer to obtain stock solution-II with a concentration 100  $\mu\text{g/ml}$ . From stock solution-II, 1ml was pipette out in 10 ml volumetric flask. The volume was made up to 10 ml using 0.1N NaOH buffer to get a concentration of 10  $\mu\text{g/ml}$ . This solution was then scanned at 200-400 nm in UV-Visible double beam spectrophotometer to attain the absorption maximum ( $\lambda_{max}$ ).

#### 2.4.5. Preparation of standard calibration curve for lovastatin

10 mg of pure drug was accurately weight and transferred into the 10 ml volumetric flask. The volume was made up using 0.1N NaoH to get a concentration of 1000 µg/ml. From this solution 1 ml was withdrawn into 10 ml volumetric flask and it was diluted to 10 ml with distilled water to get a concentration of 100 µg/ml. From this 0.5 ml, 1 ml, 1.5 ml, 2 ml, 2.5 ml, 3.0 ml were pipetted out into a 10 ml volumetric flask and diluted to 10 ml using distilled water to get concentrations of 5 µg/ml, 10 µg/ml, 15 µg/ml, 20 µg/ml, 25 µg/ml, 30 µg/ml respectively. Absorbance of this solution was measured at 238 nm using UV Spectrophotometer against blank.

#### 2.4.6. Drug excipient compatibility

IR spectra scanning of pure drug Lovastatin, excipients 11 compacts were done in potassium bromide pellets at moderate speed between 400 to 4000 cm<sup>-1</sup>.

### 2.5. Pre-compression studies (Flow properties)

The flow ability of a powder is of critical importance in the production of pharmaceutical dosage forms in order to get a uniform feed as well as the reproducible filling of tablet dies, otherwise, high dose variations will occur. In order to ensure the flow properties of the liquid-solid systems, angle of repose measurements, Carr's index and Hausner's ratios were adopted [10].

#### 2.5.1. Angle of repose ( $\theta$ )

The angle of repose of powder blend was determined by the funnel method. The accurate weight of powder blend was taken in the funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the powder blend. The powder blend was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose ( $\theta$ ) was calculated using the following equation.

$$\theta = \tan^{-1} h/r$$

Where, h and r are the height and radius of the powder cone.

#### 2.5.2. Bulk density

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 2 gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced into 10 ml measuring cylinder. After that, the initial volume was noted and the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TDB were calculated using the following equations.

LBD= Weight of the powder blend/Untapped Volume of the packing

TBD=Weight of the powder blend/Tapped Volume of the packing

#### 2.5.3. Compressibility index

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The formula for Carr's Index is as below.

$$\text{Carr's Index (\%)} = [(TBD-LBD) \times 100]/TBD$$

#### 2.5.4. Hausner's ratio

Hausner's ratio was calculated from the equation

$$\text{Hausner's ratio} = \text{Tapped density/Bulk density.}$$

## 2.6. Preparation of conventional tablet of pure lovastatin

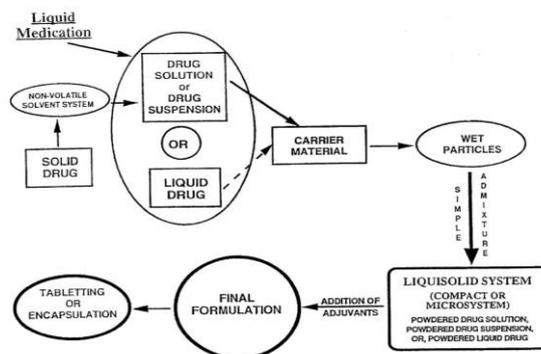
Tablet containing Lovastatin was prepared by mixing 25 mg of drug with micro crystalline cellulose (avicel 102) ludiflash 10% (w/w) as a disintegrant and mixed for 10 min. Glidant and lubricant are added and then compressed by tablet punching machine.

### 2.6.1. Preparation of liquisolid compacts

General method of preparation of liquisolid

- A Drug was initially dispersed in the non-volatile solvent systems (PEG-200, PG, Tween 80) termed as liquid vehicles with different drug vehicle ratio.
- Then a mixture of a carrier or different polymers and excipients were added to the above liquid by continuous mixing in a mortar. These amounts of the carrier and excipients are enough to maintain acceptable flow and compression properties.
- To the above binary mixture disintegrant like Ludiflash and other remaining additives are added according to their application and mixed for a period of 10 to 20 min in a mortar.
- The final mixture was compressed using the tableting machine to achieve tablet hardness.
- Characterize the final liquid-solid granules for solubility, dissolution, flowability, compressibility [11].

### 2.6.2. Depiction of liquisolid compact



**Figure 1** Depiction of liquisolid compact

### 2.6.3. Calculation of load factor

In order to address the flowability and compressibility of liquid-solid compacts, simultaneously, the "new formulation mathematical model of liquid-solid systems" was employed as follows to calculate the appropriate quantities of excipients required for producing liquid-solid systems of acceptable flowability and compressibility. This mathematical model was based on new fundamental powder properties (constants for each powder material with the liquid vehicle) called the flowable liquid retention potential ( $\Phi$ -value) and compressible liquid retention potential ( $\psi$ -number) of the constituent powders (carrier and coating materials) [1, 2, 7, 8].

According to the new theories, the carrier and coating powder materials can retain only certain amounts of liquid while maintaining acceptable flow and compression properties. Depending on the excipients ratio (R) or the carrier coating ratio of the powder system used, where

$$R=Q/q \dots (1)$$

As R represents the ratio between the weights of a carrier (Q) and coating (q) materials present in the formulation. An acceptably flowing and compressible liquid-solid system can be prepared only if a maximum liquid on the carrier material is not exceeded; such a characteristic amount of liquid is termed the liquid load factor (Lf) and defined as the ratio of the weight of liquid medication (W) over the weight of the carrier powder (Q) in the system, which should be possessed by an acceptably flowing and compressible liquid-solid system. i.e.

$$L_f=W/Q \dots (2)$$

Spireas et al. [4] used the Flowable liquid retention potentials ( $\Phi$  -values) of powder excipients used to calculate the required ingredient quantities, hence, the powder excipients ratios R and liquid load factors Lf of the formulations are related as follows

$$Lf = \Phi + \Phi (1/R) \dots (3)$$

Where  $\Phi$  and  $\Phi$  are flowable liquid retention potential of carrier and coating material respectively.

So in order to calculate the required weights of the excipients used, first, from Eq. (3),  $\Phi$  and  $\Phi$  are constants, therefore, according to the ratio of the carrier/ coat materials (R), Lf was calculated from the linear relationship of Lf versus 1/R. next, according to the used liquid vehicle concentration, different weights of the liquid drug solution (W) will be used. So, by knowing both Lf and W, the appropriate quantities of a carrier (Qo) and coating (qo) powder materials required to convert a given amount of liquid medication (W) into an acceptably flowing and compressible liquid-solid system could be calculated from equation (1) and (2) [12].

**Table 1** Investigated formulations at a glance.

<b>Ingredients (mg)</b>	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lovastatin	10	10	10	10	10	10	10	10	10
Ludiflash	50	50	50	50	50	50	50	65	75
MCC	428	413	398	413	398	413	398	383	373
Propylene glycol	--	1:1	1:3	--	--	--	--	--	--
Tween 80	--	--	--	1:1	1:3	--	--	--	--
PEG	--	--	--	--	--	1:1	1:3	1:3	1:3
Lactose	6	6	6	6	6	6	6	6	6
Aerosil	2	2	2	2	2	2	2	2	2
Mg. stearate	4	4	4	4	4	4	4	4	4

## 2.7. Post-compression studies evaluation parameters

### 2.7.1. Weight variation test

The test was performed as per USP by weighing 20 tablets individually on electric balance, calculating the average weight, and comparing the individual tablet weight to the average. Results are shown in Table 4.

### 2.7.2. Friability test

The test was performed using Roche friability. The device was rotated at 25 rpm for 100 revolutions. Friability was calculated by using following formula.

$$\%F = 100(1-W_0/W)$$

Where, W= final weight of tablets

W<sub>0</sub>= Original weight of tablets

### 2.7.3. Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm<sup>2</sup>. Three tablets were randomly picked and hardness of the tablets was determined. Results are shown in Table no 4.

#### 2.7.4. Drug content estimation

An accurately weighed amount of each preparation was dissolved in small volume of methanol and further diluted in phosphate buffer with pH of 7.4 buffer. The content of Lovastatin was determined spectrophotometrically at 238 nm using Uv-visible spectrophotometer. Results are shown in Table no 5.

#### 2.7.5. Disintegration time

The disintegration time was determined using disintegration test apparatus at  $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ . A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time taken for complete disintegration of the tablet with no palpable mass in the apparatus was noted.

#### 2.7.6. In vitro drug release study

The dissolution study was carried out using USP XXVII Apparatus I (LAB INDIA DS8000). The dissolution medium was 900 ml of phosphate buffer with a pH of 7.4 kept at  $37 \pm 5^{\circ}\text{C}$  15 mg Lovastatin tablet were kept in the baskets of dissolution apparatus rotating at 50 rpm. Samples of 5 ml were withdrawn at specified time intervals and analyzed spectrophotometrically at 238 nm using Shimadzu 1700 UV-visible spectrophotometer, the samples withdrawn were replaced by fresh buffer solution. Each preparation was tested in triplicate and the mean values were calculated. Results are shown in table no 6 [13]

#### 2.7.7. Mathematical modeling of drug release profile

The cumulative drug release from the formulated tablets at different time Intervals were fitted to zero order kinetics, first order kinetics, Higuchi model and Korsmeyer –Peppas model to characterize mechanism of drug release [14].

#### **Zero order kinetic**

It describes the system in which the drug release rate is independent of its concentration.

$$Q_t = Q_0 + K_0 t \quad (1)$$

Where;

$Q_t$  = Amount of drug dissolved in time  $t$

$Q_0$  = Initial amount of drug in the solution, which is often zero and

$K_0$  = zero order release constant.

If the zero order drug release kinetic is obeyed, then a plot of  $Q_t$  versus  $t$  will give a straight line with a slope of  $K_0$  and an intercept at zero.

#### **First order kinetic**

It describes the drug release from the systems in which the release rate is concentration depended.

$$\log Q_t = \log Q_0 + kt / 2.303 \quad (2)$$

Where

$Q_t$  = amount of drug released in time  $t$ .

$Q_0$  = initial amount of drug in the solution

$k$  = first order release constant

If the first order drug release kinetic is obeyed, then a plot of  $\log (Q_0 - Q_t)$  versus  $t$  will be straight line with a slope of  $kt / 2.303$  and an intercept at  $t=0$  of  $\log Q_0$ .

### 2.7.8. Stability studies of lovastatin 10 mg

The International Conference of Harmonization (ICH) Guidelines titled, “stability testing of New Drug substance and products”. ICH specifies the length of study and storage conditions.

#### Method

The selected formulations were packed in bottles, which are tightly plugged with cotton and capped. They were then stored at and 40 °C / 75% RH for 3 months and evaluated for assay and *in vitro* drug release.

#### Storage conditions

Accelerated 40±2 °C/75±5% RH

Intermediate 30±2 °C/65±5% RH

Long term 25±2 °C/60±5% RH

#### Testing intervals for

Accelerated Initial, 1, 2 & 3 months.

Long term Initial, 3, 6, 9, 12, 18, 24 & 36 months.

Intermediate Initial, 3, 6, 9 & 12 months.

The optimized formula was selected for evaluation studies. Further stability study was done [15].

## 3. Results

### 3.1. API characterization

#### 3.1.1. Physical properties

For a drug substance to formulate into a dosage form, it is necessary to study the physicochemical properties of the bulk drug.

- **Colour** - white to off-white
- **State** - crystalline powder
- **Melting point** - 174 °C
- **Solubility** - Solubility of Lovastatin in methanol, phosphate buffer 7.4, propylene glycol, poly ethylene glycol 200 and Tween 80 is given in the table (8). Lovastatin solubility is very high in PEG 200 as (4.5% (w/w)) compared to other. PEG, with a large nonpolar part and several hydroxyl groups is responsible for the enhanced solubility. Thus, among the solvents tested, PEG 200 could be a better choice as a solvent [8, 9].

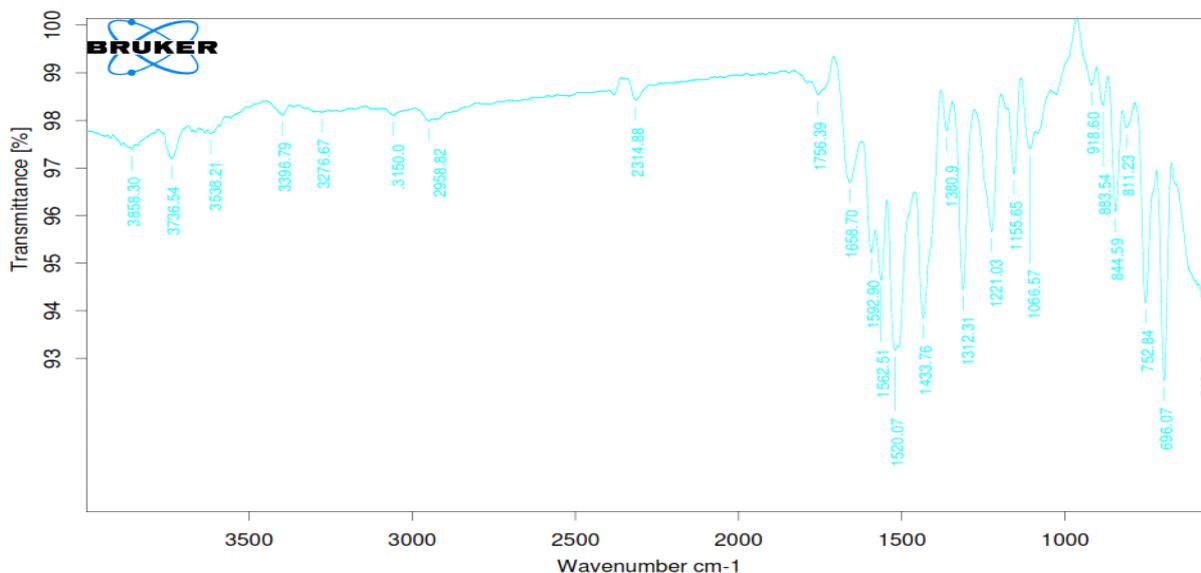
**Table 2** Solubility studies

Solvent	Solubility(mg/ml)
methanol	6238 mg/ml
Phosphate buffer solution pH 7.4	0.0013 mg/ml
Propylene glycol	0.204 mg/ml
Polyethylene glycol 200	4.5% mg/ml
Tween 80 (10%)	0.1% mg/ml

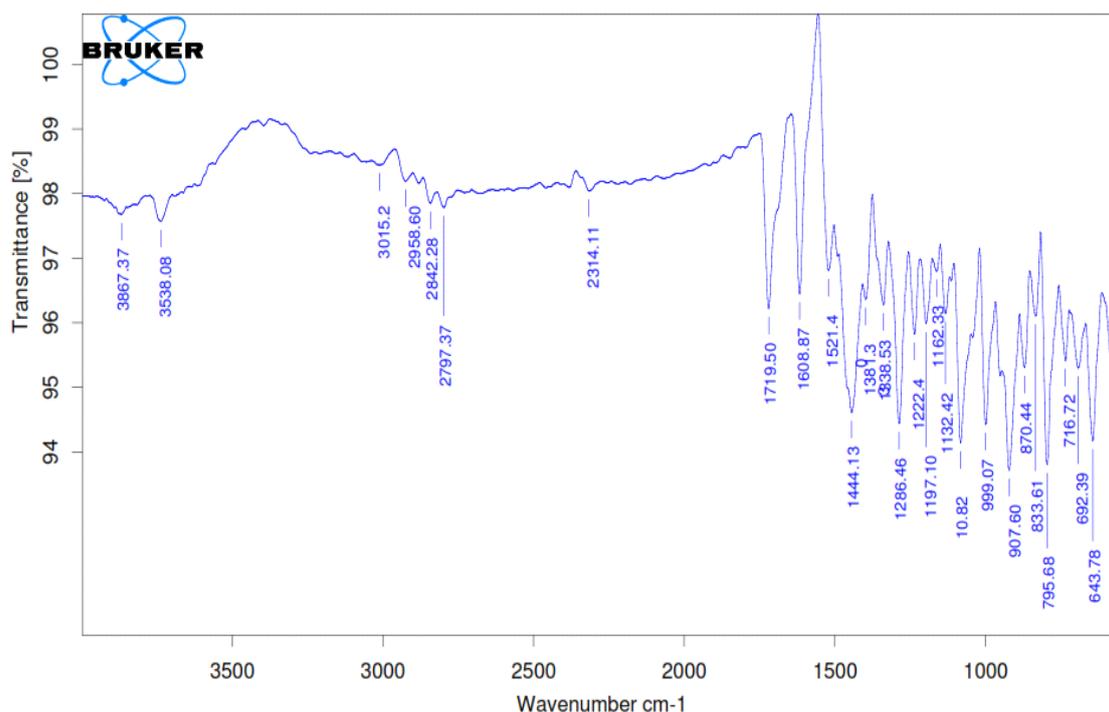
Soluble in DMSO (12 mg/mL) at 40 °C, ethanol (12 mg/mL) at 40 °C, DMF (25 mg/mL), methanol, and dilute hydrochloric acid (slightly soluble).

### 3.1.2. Drug polymer interaction study

From the spectra of Lovastatin, combination of Lovastatin with excipient. It was observed that all characteristics peak of Lovastatin were present in the combination spectrum, thus indicating compatibility of the drug and excipient IR spectra are shown in figure.



**Figure 2** IR spectra of Lovastatin



**Figure 3** IR spectra of optimized formulation

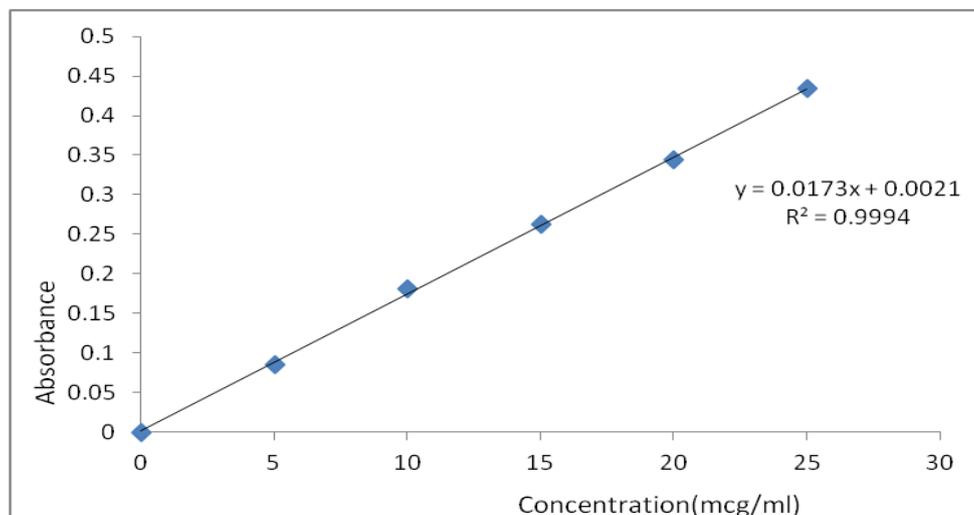
### 3.1.3. Characteristic peaks in FT-IR spectra of lovastatin

Characteristic peaks of Lovastatin appeared at 3015.2 cm<sup>-1</sup> (C=C stretching), 3538 cm<sup>-1</sup> (O-H stretching), 1221.0 cm<sup>-1</sup> (C-O-C stretching), 1066.1 cm<sup>-1</sup> (C-O stretching) and 1380.7 cm<sup>-1</sup> (C-H bending), 2958.0 cm<sup>-1</sup> (C-H stretching) were

observed. When compared with the pure drug the optimized formulation showed same Characteristic peaks .By the FT-IR studies it was confirmed that there was no interactions between pure drug and excipient.

Chemical interaction between drug and the polymeric material was studied by using FTIR. IR value of Lovastatin pure drug was observed no difference between the IR patterns of the physical mixture of Lovastatin and excipient, Lovastatin liquid-solid.

#### 3.1.4. Standard calibration curve for lovastatin in 0.1 N NaOH

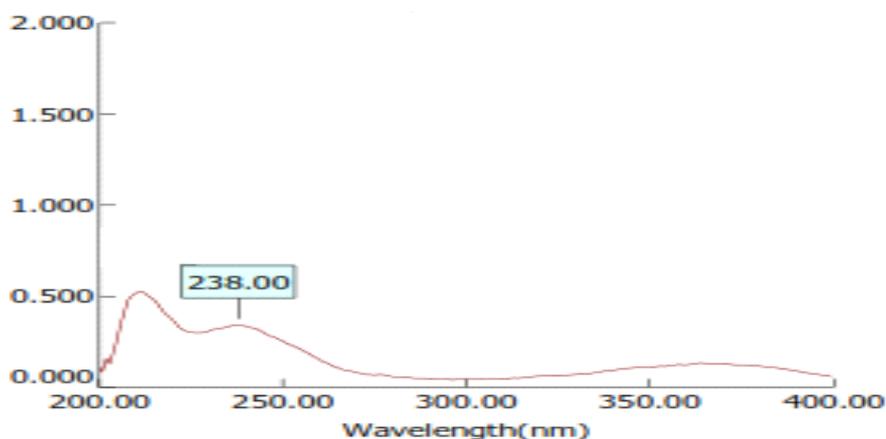


**Figure 4** standard calibration curve for lovastatin

In Preformulation studies, it was found that, the wavelength of Lovastatin by spectroscopic method at 238 nm in NaOH. This complied with IP standards thus indicating purity of obtained drug sample and plot graph of absorbance V/s concentration between 10-100  $\mu\text{g/ml}$  ranges. The Lovastatin calibration curve are shown in fig no.4

#### 3.1.5. Determination of $\lambda_{max}$

Determination of lovastatin  $\lambda$ -max was done in 0.1 N NaOH buffer medium for accurate quantitative assessment of drug dissolution rate.



**Figure 5** UV spectrum of lovastatin 238nm

The  $\lambda$ -max was found to be 238 nm, i.e., at its absorption maxima.

### 3.2. Pre-compression parameters

**Table 3** Flow properties

Formulation	Bulk density (gm/ml)	Tapped Density(gm/ml)	Carr's index (%)	Hasner ratio	Angle of Repose( $\theta$ )
F1	0.385±0.021	0.544±0.024	19.12±0.080	1.416±0.025	29.77±1.235
F2	0.363±0.031	0.435±0.033	15.87±0.045	1.186±0.035	27.16±1.423
F3	0.356±0.045	0.397±0.012	10.83±0.040	1.121±0.050	25.24±1.106
F4	0.343±0.038	0.409±0.010	14.85±0.023	1.172±0.031	26.98±1.561
F5	0.365±0.012	0.413±0.034	11.43±0.060	1.126±0.012	27.62±1.342
F6	0.314±0.024	0.394±0.025	20.28±0.012	1.257±0.026	24.55±1.566
F7	0.334±0.035	0.415±0.030	19.27±0.034	1.239±0.015	26.49±1.434
F8	0.343±0.042	0.409±0.019	14.85±0.016	1.172±0.026	26.98±1.061
F9	0.365±0.026	0.413±0.022	11.43±0.048	1.126±0.028	27.62±1.042

(n=3); ±S.D

The compressibility index ( $\leq 19.12$ ), Hausners ratio ( $\leq 1.41$ ) and angle of repose ( $\leq 29.77$ ) values indicated a fairly good flowability of granules. Results are shown in (Table 3).

### 3.3. Post compression parameters

#### 3.3.1. Hardness and friability

**Table 4** Hardness and friability

Formulation	Friability test (Fines %)	Hardness±SD (Kg/cm <sup>2</sup> )	Weight variation %RDS	Disintegration time
F1	0.048	4.7± 0.74	1.9±0.76	258
F2	0.019	3.4±0.96	2.0±0.17	312
F3	0.242	4.0±0.83	1.3±0.36	268
F4	0.134	3.2±0.35	1.6±0.48	309
F5	0.246	3.9±0.13	2.1±0.98	226
F6	0.146	3.3±0.22	1.1±0.68	268
F7	0.214	3.6±0.46	1.0±0.19	148
F8	0.312	3.4±0.13	1.2±0.12	89
F9	0.126	3.7±0.22	1.6±0.26	76

As the granules were free flowing, tablets produced were uniform weight with acceptable weight variation ( $\leq 2.1$ ) due to uniform filling in the die. Hardness (3.2-4.0kg/cm<sup>2</sup>) and friability values (0.019-0.24) indicated that tablets had a good mechanical strength. Results are shown in (Table 4).

## 3.3.2. Drug content

**Table 5** Estimation of drug content

Formula	Drug content (%)
F1	95.23±2.2
F2	97.18±1.9
F3	96.19±1.7
F4	99.58±2.6
F5	96.21±1.1
F6	97.69±1.9
F7	98.59±1.2
F8	98.41±1.6
F9	99.06±1.5

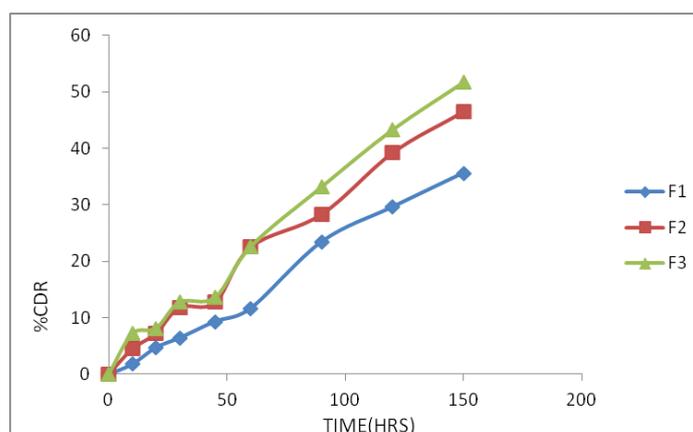
Drug content of formulation F1-F9 were found to be in the range of 95.23-99.06%

3.4. *In vitro* dissolution study

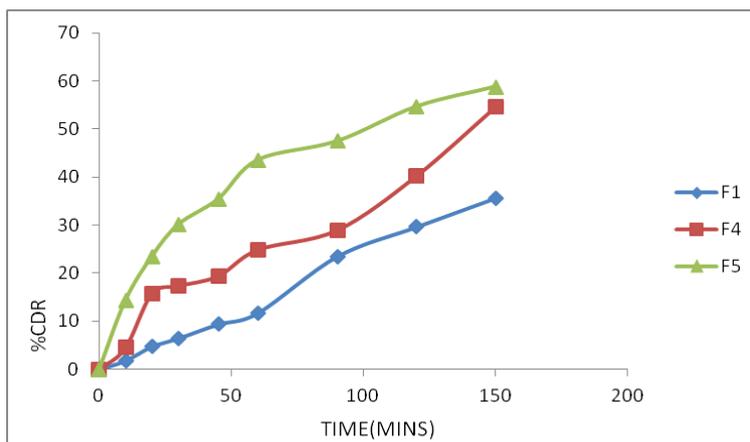
Apparatus II, solvent phosphate buffer pH 7.4 medium, volume 900 ml, rpm 100, temperature  $37 \pm 5$  °C and  $\lambda_{\max}$  238 nm.

**Table 6** *In vitro* release data of lovastatin compacts

Time (mins)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
10	1.8	4.5	7.2	4.5	14.4	18.72	23.26	28.21	29.14
20	4.74	7.25	8.16	15.75	23.53	27.63	33.63	35.02	38.45
30	6.45	11.85	12.78	17.37	30.16	35.54	37.89	40.56	41.26
45	9.36	12.75	13.66	19.38	35.43	43.35	47.55	49.21	50.24
60	11.69	22.56	22.65	24.86	43.56	48.42	54.85	56.28	58.15
90	23.46	28.36	33.24	28.92	47.46	53.68	62.56	65.19	67.15
120	29.63	39.28	43.35	40.2	54.63	60.79	71.15	73.02	75.21
150	35.63	46.56	51.78	54.58	58.76	77.68	84.42	86.24	89.25

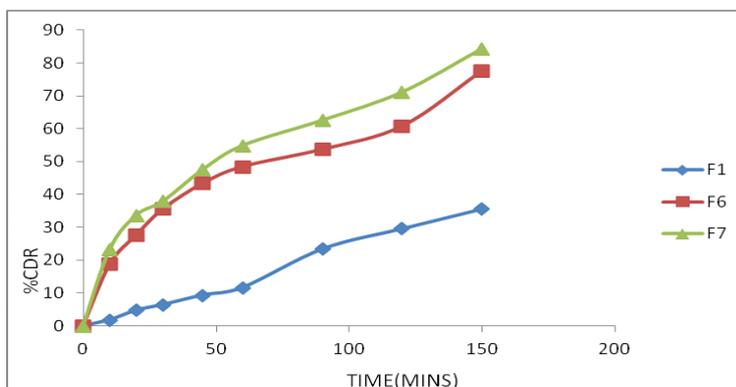
3.4.1. Comparison of *in vitro* drug release of conventional tablet with the liquid solid compacts**Figure 6** Comparative *in vitro* drug release of F1, F2, F3

Formulations F1, F2 and F3 containing Propylene Glycol (1:1, 1:3) in the above comparative in-vitro drug release formulation F3 (PG 1:3) shows better drug release i.e. 43.35% in 120 min.



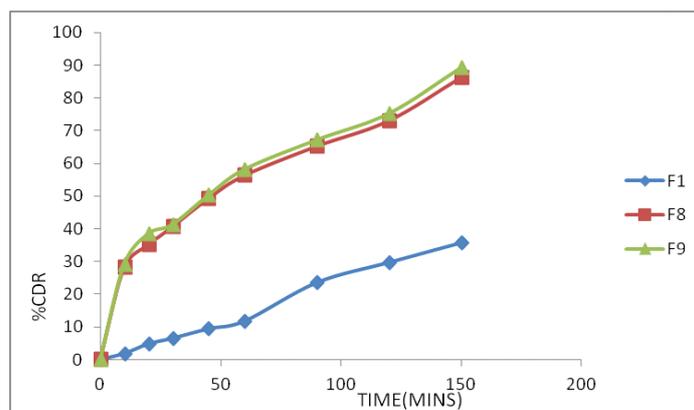
**Figure 7** Comparative *in vitro* drug release of F1, F4, F5

Formulations F1, F4 and F5 containing Tween 80 (1:1, 1:3) in the above comparative in-vitro drug release formulation F3 (Tween<sup>80</sup> 1:3) shows better drug release i.e. 43.56% within 1 hr.



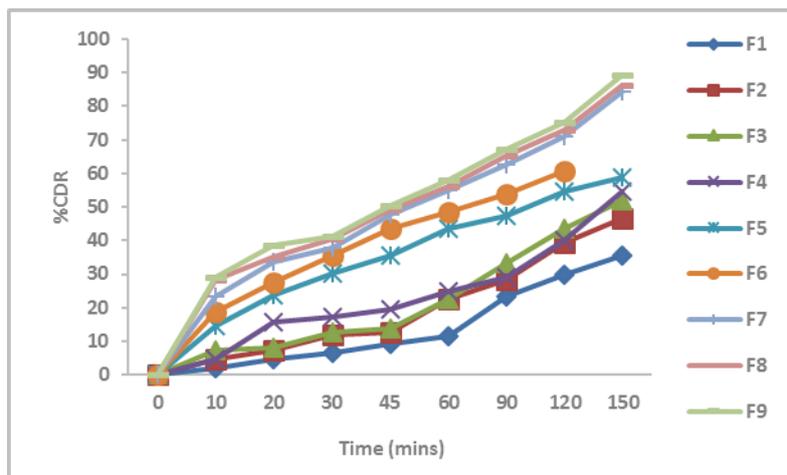
**Figure 8** Comparative *in vitro* drug release of F1, F6, F7

Formulations F1, F6 and F6 containing Polyethylene Glycol (1:1, 1:3) in the above comparative in-vitro drug release formulation F7 (PEG 1:3) shows better drug release i.e. 23.26% and 33.63% in 10 and 30 min.



**Figure 9** Comparative *in vitro* drug release of F1, F8, F9

Formulations F1, F8 and F9 containing Polyethylene Glycol (1:3, 1:3) in the above comparative *in-vitro* drug release formulation F9 (PEG 1:3, MCC 373 mg) shows better drug release i.e. 89.25% in 150 min.



**Figure 10** % CDR= cumulative percentage drug release

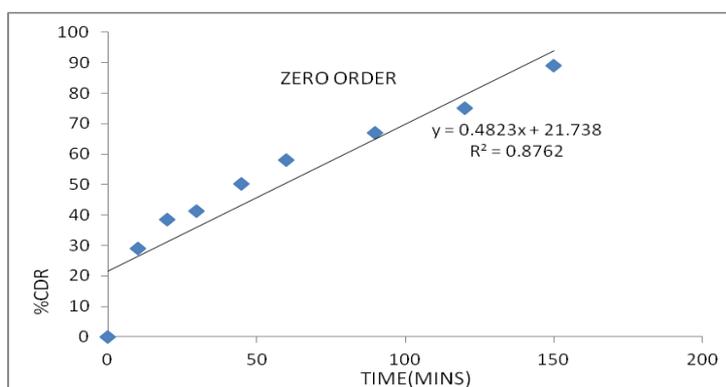
Among all the formulations F9 displays good drug release of 89.25% in 150 min. So F9 is considered as the optimized formulation.

### 3.4.2. Release kinetics

**Table 7** Release kinetics of optimized formulation

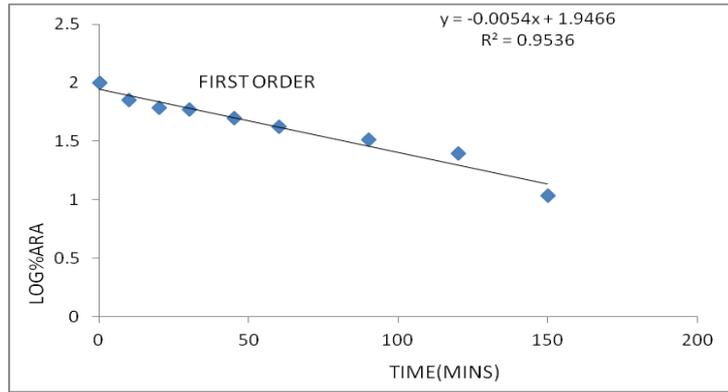
Order	Zero	First	Higuchi	Peppas	n Value
R <sup>2</sup> value	0.8762	0.9536	0.9888	0.8909	0.831

Zero order release kinetic data of optimized formulation of Lovastatin compacts



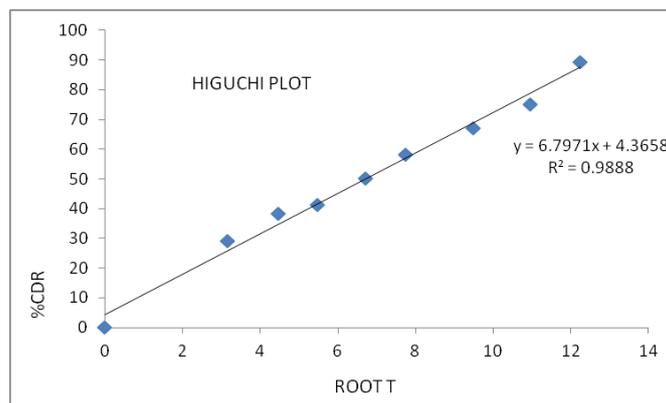
**Figure 11** Zero order F9

First order release kinetic data of optimized formulation of Lovastatin compacts.



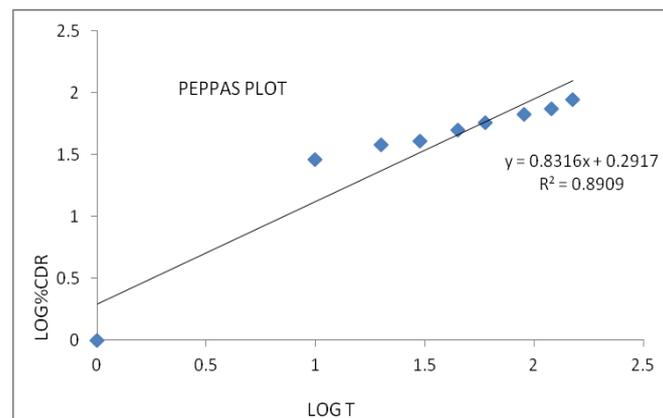
**Figure 12** First order

Higuchi plot of optimized formulation of Lovastatin compacts



**Figure 13** Higuchi plot

Peppas Plot of optimized formulation of Lovastatin compacts



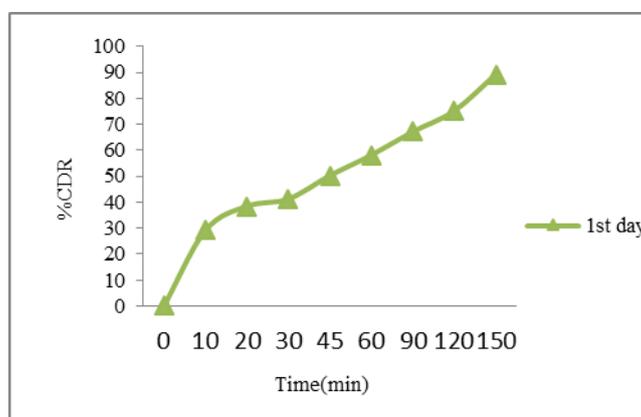
**Figure 14** Peppas plot

The *in vitro* dissolution data for best formulation F9 were fitted in different kinetic models i.e., zero order, first order, Higuchi and korsmeyer-peppas equation. Optimized formulation F9 shows R2 value 0.9536. As its value nearer to the '1' it is conformed as it follows the first order release. The release kinetics for the optimized formula is shown in table.

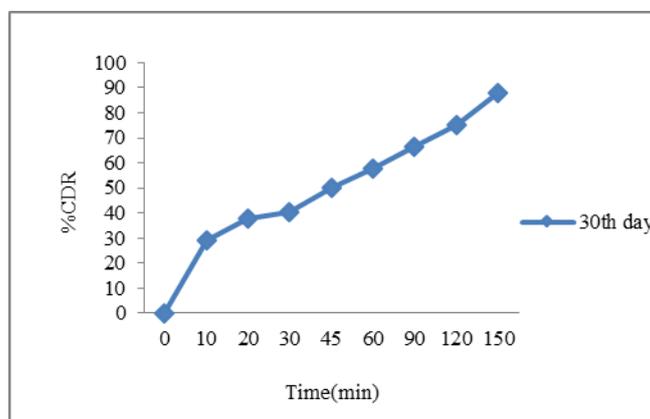
### 3.5. Stability studies

**Table 8** *In-vitro* drug release data of the stability formulation (F9)

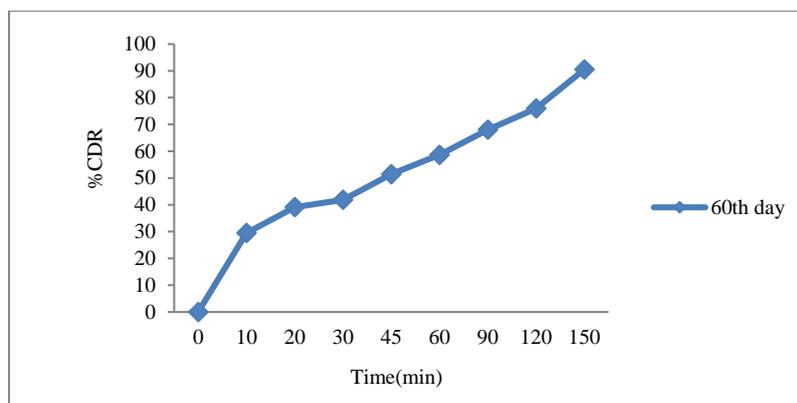
Time (min)	Cumulative* % drug released* ± SD at 40± 1 °C		
	1 <sup>st</sup> day	30 <sup>th</sup> day	60 <sup>th</sup> day
0	0	0	0
10	29.14	29.03	29.46
20	38.45	37.92	39.12
30	41.26	40.56	41.86
45	50.24	50.06	51.42
60	58.15	57.84	58.64
90	67.15	66.42	68.02
120	75.21	75.10	75.96
150	89.25	88.16	90.52



**Figure 15** Stability studies for 1<sup>st</sup> day



**Figure 16** Stability studies for 30<sup>th</sup> day



**Figure 17** Stability studies for 60<sup>th</sup> day

From the above conducted stability studies of optimized formulation for about 90 days by comparing the results we can say that there is no change in the optimized formula on storage which indicates that it passes the stability studies.

#### 4. Conclusion

The aim of this study was to improve the dissolution profile thereby increase solubility. From the results obtained from executed experiments, it can be concluded that the preformulation studies like melting point, flow properties UV-analysis of lovastatin complied with IP standards. The FTIR spectra revealed that there was no interaction between polymer and drug. Polymers used were compatible with Lovastatin. *In vitro* drug release of Lovastatin, compacts showed an increase in dissolution rate of Lovastatin. So PEG 200, Tween 80, PG could be an economic substitute as dissolution enhancing agent. Based on mathematical data revealed from models, it was concluded that the release data was best fitted with first order kinetics. Higuchi equation explains the diffusion controlled release mechanism, the diffusion exponent 'n' values were found to be in the range of 0.5 to 1.0 for the Lovastatin compacts indicating Non-Fickian diffusion. Among the PEG 200, Tween 80, PG PEG 200 in 13 ratios with the higher concentration of ludiflash (75mg) shows better drug release than the other formulations. The stability studies indicate that the optimized formulation was stable at the end of 90<sup>th</sup> day.

#### Compliance with ethical standards

##### *Acknowledgments*

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##### *Disclosure of conflict of interest*

The authors declare no conflict of interest.

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