Design and Optimization of PEG 6000-Based Lovastatin Solid Dispersion and Development of Orodispersible Tablets for Enhanced Dissolution

M. Ramachiruhasa Reddy[1], Dr. Y. Dastagiri Reddy[1], Dr. D. Maheswara Reddy[1*], Dr. Maheswara Reddy Mallu[2], T. Rajeswari[1], B. Nandini[1]

[1]Department of Industrial Pharmacy, Santhiram College of Pharmacy, NH-40, Nandyal- 518501, Andhra Pradesh, India

[2]Department of Biotechnology, Koneru Lakshmaiah Education Foundation, Vaddeswaram, Guntur-522302, Andhra Pradesh, India

[*]Corresponding author: Dr. D. Maheswara Reddy, Assoc. Professor, Department of Industrial Pharmacy, Santhiram College of Pharmacy, NH-40, Nandyal, Andhra Pradesh, India. Email: dagadamahesh@gmail.com

ABSTRACT

Background: Lovastatin, a BCS Class II drug, exhibits poor aqueous solubility and dissolution-limited bioavailability, which may reduce therapeutic effectiveness. Solid dispersion using hydrophilic carriers is an effective approach to enhance solubility and dissolution. Orodispersible tablets (ODTs) further improve patient compliance and provide rapid drug release.

Aim: The present study aimed to develop and optimize lovastatin solid dispersions using PEG 6000 and formulate the optimized dispersion into ODTs for improved dissolution and potential bioavailability.

Method: Solid dispersions were prepared by fusion method and optimized using Central Composite Design by studying temperature, stirring speed, and drug addition rate on drug content, drug release, and dissolution efficiency. The optimized formulation was characterized using FTIR. The optimized solid dispersion was formulated into ODTs by direct compression and evaluated for physicochemical properties, dissolution, release kinetics, and stability.

Results: The optimized formulation at 69.99°C and 499.38 rpm showed 99.23% drug content, 96.52% drug release, and 84.67% dissolution efficiency (desirability 0.904). FTIR confirmed absence of interaction, while DSC showed amorphous conversion. ODTs showed acceptable parameters with rapid disintegration (27 sec) and drug release (96.21% at 30 min). Drug release followed first-order kinetics with Fickian diffusion. Stability studies confirmed formulation stability.

Conclusion: The developed ODTs significantly improved dissolution and may enhance oral bioavailability of lovastatin.

Highlights

- Lovastatin solid dispersion optimized using Central Composite Design
- PEG 6000 significantly enhanced solubility of lovastatin
- Orodispersible tablets showed rapid disintegration (27 seconds)
- Optimized formulation achieved 96.21% drug release at 30 minutes
- Formulation remained stable under accelerated stability conditions

Keywords: Lovastatin, Solid dispersion, Orodispersible tablets, PEG 6000, Dissolution enhancement

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1. Introduction

Lovastatin is a widely prescribed lipid-lowering agent used for the treatment of hypercholesterolemia and prevention of cardiovascular diseases. It acts by inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the key enzyme involved in cholesterol biosynthesis. Despite its therapeutic importance, lovastatin belongs to Biopharmaceutics Classification System (BCS) Class II, characterized by poor aqueous solubility and high permeability. The low solubility of lovastatin results in dissolution-limited absorption, leading to low and variable oral bioavailability and reduced therapeutic efficiency. Therefore, improving the dissolution rate of lovastatin remains a significant challenge in formulation development.[1-3]

Various formulation strategies have been explored to enhance the solubility of poorly water-soluble drugs, including micronization, nanotechnology, lipid-based formulations, inclusion complexes, and solid dispersion techniques. Among these approaches, solid dispersion has gained considerable attention due to its simplicity, effectiveness, and ability to improve drug dissolution by reducing particle size, enhancing wettability, and converting crystalline drugs into amorphous forms. Polyethylene glycol (PEG 6000) is widely used as a hydrophilic carrier in solid dispersions due to its excellent solubility, low toxicity, and good compatibility with drugs. The fusion method is particularly advantageous for preparing solid dispersions as it eliminates the need for organic solvents and ensures uniform drug distribution.[4-6]

Orodispersible tablets (ODTs) have emerged as an attractive dosage form that rapidly disintegrates in the oral cavity without the need for water. These formulations improve patient compliance, particularly in pediatric, geriatric, and dysphagic patients. Incorporation of solid dispersions into ODTs can further enhance dissolution and provide rapid drug release, thereby improving bioavailability of poorly soluble drugs. Additionally, ODTs offer advantages such as convenience, ease of administration, and improved therapeutic outcomes.[7,8]

Therefore, the present study aimed to develop and optimize lovastatin solid dispersions using PEG 6000 by the fusion method and evaluate formulation variables using Central Composite Design. The optimized solid dispersion was further formulated into orodispersible tablets and evaluated for physicochemical properties, dissolution behavior, release kinetics, and stability to enhance the dissolution and potential oral bioavailability of lovastatin.

2. Materials and methods

2.1. Materials

Lovastatin was procured from Yarrow Chem Products, Mumbai, India. Polyethylene glycol 6000 (PEG 6000) was obtained from Loba Chemie Pvt. Ltd., Mumbai, India. Crospovidone was purchased from BASF India Ltd., Mumbai, India. All chemicals used were of analytical grade and used as received. 69

2.2. Experimental Design (Central Composite Design)

A Central Composite Design (CCD) was employed using Design-Expert® software (Version 13, Stat-Ease Inc., USA) to optimize the formulation variables of lovastatin solid dispersion. Three independent variables were selected: temperature (X_1), stirring speed (X_2), and drug addition rate (X_3). The dependent responses evaluated were drug content (%), drug release at 30 min (%), and dissolution efficiency (%).[9,10]

A total of 15 experimental runs including factorial points, axial points, and center points were generated. Solid dispersions were prepared according to the design matrix and evaluated for selected responses. The experimental data were analyzed using analysis of variance (ANOVA), regression modeling, and response surface methodology. Optimization was performed using desirability function to obtain optimized formulation conditions.[11-13]

Table 1: Independent and dependent variables used in Central Composite Design

Independent variables		**Levels**		
Code	**Parameter**	**Low (-1)**	**Medium (0)**	**High (+1)**
X1	Temperature (°C)	60	70	80
X2	Stirring Speed (rpm)	50	75	100
X3	Drug Addition Rate (g/min)	1	2	3
Dependent variables		**Goals**		
Y1	% Drug release at 30 min	Maximum		
Y2	Drug content (%)	Acceptable		
Y3	Dissolution efficiency (%)	Maximum		

2.3. Preparation of Lovastatin Solid Dispersion

Lovastatin solid dispersions were prepared using the fusion (melt) method. Lovastatin and polyethylene glycol 6000 (PEG 6000) were accurately weighed in the required ratio. PEG 6000 was melted in a beaker at 60–80°C using a hot plate under controlled conditions. Once the polymer was completely melted, lovastatin was gradually added to the molten carrier with continuous stirring using a magnetic stirrer to obtain a homogeneous mixture.

The molten dispersion was stirred for 10–15 minutes to ensure uniform distribution of the drug within the polymer matrix. The resultant molten mass was then poured onto a clean petri dish and allowed to cool at room temperature to obtain a solidified mass. The solid dispersion was subsequently pulverized using a mortar and pestle and passed through a #60 sieve to obtain uniform particle size.

The prepared solid dispersion was stored in a desiccator until further evaluation and formulation into orodispersible tablets.

2.4 Optimization Using Response Surface Methodology

Optimization of lovastatin solid dispersion was performed using Response Surface Methodology (RSM) based on Central Composite Design (CCD). The experimental design was generated using Design-Expert® software (Version 13, Stat-Ease Inc., USA). The prepared formulations were evaluated to study the effect of selected process variables on formulation performance. The obtained responses were analyzed to determine optimal formulation conditions.

2.4.1 Independent Variables

Three independent variables were selected for optimization: temperature (A), stirring speed (B), and drug addition rate (C). These variables were studied at three different levels (low, medium, and high) to evaluate their influence on formulation characteristics. The selected variables were chosen based on preliminary trials and their expected impact on solid dispersion formation.

2.4.2 Dependent Variables

The dependent responses selected for optimization included drug content (%), drug release at 30 minutes (%), and dissolution efficiency (%). These parameters were considered critical quality attributes for evaluating the performance of lovastatin solid dispersion and were used for optimization of formulation variables.

2.4.3 Statistical Analysis

The experimental data obtained from the design were analyzed using Design-Expert® software. Analysis of variance (ANOVA), regression analysis, and response surface plots were generated to evaluate the significance of model terms and interaction effects. Optimization was performed using desirability function to obtain the optimized formulation with maximum drug release and dissolution efficiency while maintaining acceptable drug content. The optimized formulation was validated by comparing predicted and experimental values. A p-value of less than 0.05 ($p < 0.05$) was considered statistically significant. [6]

2.5 Characterization of Solid Dispersion

The prepared lovastatin solid dispersions were evaluated for drug content, saturation solubility, in-vitro dissolution, and dissolution efficiency to assess improvement in solubility and dissolution behavior.[15,16]

2.5.1 Drug Content Determination

Accurately weighed solid dispersion equivalent to 10 mg of lovastatin was transferred into a 100 mL volumetric flask. The sample was dissolved in phosphate buffer (pH 6.8) with sonication for 10–15 minutes to ensure complete dissolution. The solution was filtered using Whatman filter paper, suitably diluted, and analyzed using a UV–Visible spectrophotometer at 238 nm. Drug content was calculated using the calibration curve.[17-19]

2.5.2 Saturation Solubility Study

Saturation solubility studies were performed by adding excess amount of pure drug and solid dispersion to separate vials containing phosphate buffer (pH 6.8). The samples were shaken for 24 hours at room temperature using a mechanical shaker. The solutions were filtered, diluted appropriately, and analyzed using UV spectrophotometer at 238 nm. The solubility values were determined and compared.[20-22]

2.5.3 *In-vitro* Dissolution Study

In-vitro dissolution studies were carried out using USP Type II (paddle) dissolution apparatus. Solid dispersion equivalent to required dose of lovastatin was placed in 900 mL phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C and stirred at 50 rpm. Samples were withdrawn at predetermined intervals, filtered, and analyzed spectrophotometrically at 238 nm. An equal volume of fresh dissolution medium was replaced after each sampling.[23-25]

2.5.4 Dissolution Efficiency

Dissolution efficiency was calculated to evaluate overall drug release performance. The percentage drug release was plotted against time, and the area under the dissolution curve was calculated using trapezoidal rule. Dissolution efficiency was determined using the following equation:[26-28]

$$\text{Dissolution Efficiency (\%)} = \frac{\text{Area under dissolution curve}}{\text{Area of rectangle } (100 \times \text{time})} X\ 100$$

2.5.5 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR analysis was performed to evaluate drug–polymer compatibility. The spectra of pure lovastatin, polymer, and physical mixture were recorded using an FTIR spectrophotometer in the range of 4000–400 cm^{-1} using KBr pellet method. The spectra were analyzed to identify possible interactions between drug and excipients.[29-31]

2.6 Formulation of Orodispersible Tablets

Orodispersible tablets containing optimized lovastatin solid dispersion were prepared by direct compression method. The required quantities of solid dispersion, microcrystalline cellulose, and superdisintegrant were accurately weighed and passed through a #60 sieve. The ingredients were blended uniformly, followed by addition of magnesium stearate and talc as lubricant and glidant. The final blend was compressed using a single punch tablet compression machine to obtain orodispersible tablets of uniform weight and hardness. The prepared tablets were stored in a desiccator until further evaluation.[32-34]

Table 2: Composition of Orodispersible Tablets Containing Lovastatin Solid Dispersion

Ingredient	Formulation (mg)
Solid dispersion (equiv. to 10 mg drug)	40
Crospovidone	10
Avicel PH 102	95
Magnesium stearate	2
Talc	3
Total Weight (mg)	150

2.7 Evaluation of Pre-Compression Parameters

The powder blend prepared for orodispersible tablets was evaluated for pre-compression parameters including angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. For angle of repose, the powder blend was allowed to flow through a funnel fixed at a certain height onto a flat surface, and the height and radius of the formed powder heap were measured. Bulk density was determined by transferring a known weight of powder into a graduated cylinder and measuring the initial volume. The cylinder was then tapped until a constant volume was obtained to determine tapped density. Carr's index and Hausner's ratio were calculated using bulk density and tapped density values to assess flow properties and compressibility of the powder blend.[35-37]

2.8 Evaluation of Orodispersible Tablets

The prepared orodispersible tablets were evaluated for various post-compression parameters. Weight variation was determined by weighing twenty tablets individually and calculating the average weight. Tablet thickness was measured using a vernier caliper, while hardness was determined using a Monsanto hardness tester. Friability was evaluated using a Roche friabilator operated at 25 rpm for 4 minutes. Wetting time and water absorption ratio were determined by placing tablets on tissue paper soaked with water in a petri dish and recording the time required for complete wetting. Disintegration time was determined using a USP disintegration apparatus containing distilled water maintained at 37 ± 0.5°C. Drug content was determined by crushing tablets, dissolving powder equivalent to required dose in suitable medium, filtering, and analyzing using UV spectrophotometer at 238 nm.[38-40]

2.9 *In-vitro* Dissolution Study of ODTs

In-vitro dissolution studies were performed using USP Type II (paddle) dissolution apparatus containing 900 mL phosphate buffer (pH 6.8) maintained at 37 ± 0.5°C and stirred at 50 rpm. Samples were withdrawn at predetermined intervals, filtered, and analyzed using UV spectrophotometer at 238 nm. Equal volume of fresh medium was replaced after each sampling.[41-43]

2.10 Drug Release Kinetics

The dissolution data obtained from in-vitro studies were fitted to various kinetic models including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to determine the mechanism of drug release.[44-46]

2.11 Stability Studies

Stability studies were carried out according to ICH guidelines by storing optimized tablets at 40 ± 2°C and 75 ± 5% RH for three months. Samples were withdrawn at predetermined intervals and evaluated for physical appearance, drug content, and dissolution profile.[47-49]

3. Results and Discussion

3.1 Experimental Design Analysis

Central Composite Design (CCD) was employed to evaluate the effect of temperature (A), stirring speed (B), and drug addition rate (C) on drug content, drug release, and dissolution efficiency of lovastatin solid dispersion. A total of 15 experimental runs were generated and analyzed using Design-Expert® software. The developed quadratic model was found to be significant with high correlation coefficient values for drug content (R^2 = 0.9947), drug release (R^2 = 0.9989), and dissolution efficiency (R^2 = 0.9991), indicating good agreement between predicted and experimental values. The optimized formulation was obtained at 70°C temperature and 500 rpm stirring speed, with desirability value of 0.904. The predicted responses were 99.23% drug content, 96.52% drug release, and 84.67% dissolution efficiency. These results confirmed the suitability of CCD for optimization.

Table 3: ANOVA results for responses

Source	Sum of Squares	df	Mean Square	F-value	p-value	
ANOVA for Drug content %						
Model	19.89	9	2.21	104.14	< 0.0001	significant
A-Temperature	0.2250	1	0.2250	10.60	0.0225	
B-Stirring Speed	1.22	1	1.22	57.72	0.0006	
C-Drug Addition Rate	0.1960	1	0.1960	9.24	0.0288	
AB	0.9800	1	0.9800	46.18	0.0011	
AC	0.5000	1	0.5000	23.56	0.0047	
BC	0.4050	1	0.4050	19.08	0.0072	
A²	4.09	1	4.09	192.70	< 0.0001	
B²	1.49	1	1.49	70.19	0.0004	
C²	1.69	1	1.69	79.72	0.0003	
ANOVA for Drug Release %						
Model	652.80	9	72.53	516.78	< 0.0001	significant
A-Temperature	46.22	1	46.22	329.34	< 0.0001	
B-Stirring Speed	13.00	1	13.00	92.59	0.0002	
C-Drug Addition Rate	2.21	1	2.21	15.74	0.0107	
AB	14.58	1	14.58	103.88	0.0002	
AC	8.00	1	8.00	57.00	0.0006	
BC	5.12	1	5.12	36.48	0.0018	
A²	140.60	1	140.60	1001.74	< 0.0001	
B²	57.88	1	57.88	412.40	< 0.0001	
C²	51.94	1	51.94	370.08	< 0.0001	
ANOVA for Dissolution efficiency %						
Model	523.58	9	58.18	605.68	< 0.0001	significant
A-Temperature	44.94	1	44.94	467.92	< 0.0001	
B-Stirring Speed	12.32	1	12.32	128.28	< 0.0001	
C-Drug Addition Rate	2.03	1	2.03	21.08	0.0059	
AB	12.75	1	12.75	132.76	< 0.0001	
AC	7.80	1	7.80	81.22	0.0003	
BC	5.95	1	5.95	61.96	0.0005	
A²	100.98	1	100.98	1051.36	< 0.0001	
B²	45.72	1	45.72	476.01	< 0.0001	
C²	45.72	1	45.72	476.01	< 0.0001	

Table 4. Model summary statistics and polynomial equations for responses obtained from Central Composite Design

Response	r^2	Adjusted r^2	Predicted r^2	SD	% CV	Adequate precision
Y1	0.9947	0.9851	0.9270	0.1457	0.1495	36.1368
Y2	0.9989	0.9970	0.9905	0.3746	0.4930	76.9660

Y3	0.9991	0.9974	0.9918	0.3099	0.4374	84.9345
Equation						
Y1=99.35+0.1500A+0.3500B+0.1400C−0.3500AB−0.2500AC−0.2250BC−1.26A^2−0.7611B^2−0.8111C^2						
Y2=87.08+2.15A+1.14B+0.47C−1.35AB−1.00AC−0.80BC−7.39A^2−4.74B^2−4.49C^2						
Y3 = 80.65+2.12A+1.11B+0.45C−1.26AB−0.9875AC−0.8625BC−6.27A^2−4.22B^2−4.22C^2						

3.2 Effect of Variables on Drug Content

The drug content of solid dispersions ranged from 96.85% to 99.35%. ANOVA analysis showed that stirring speed (B) had the most significant effect ($p = 0.0006$), followed by temperature ($p = 0.0225$) and drug addition rate ($p = 0.0288$). Increasing stirring speed improved drug content due to enhanced mixing and uniform drug distribution. However, at higher temperature levels, slight reduction in drug content was observed due to possible degradation. The optimized formulation showed 99.23% drug content, indicating uniform dispersion of lovastatin within PEG 6000.

3.3 Effect of Variables on Drug Release

Drug release at 30 minutes ranged from 72.45% to 96.52%. Temperature showed the highest influence ($F = 329.34$, $p < 0.0001$), followed by stirring speed ($F = 92.59$, $p = 0.0002$) and drug addition rate ($p = 0.0107$). Increasing temperature enhanced drug release due to improved amorphization and solubility of lovastatin in PEG 6000. The optimized formulation exhibited 96.52% drug release at 30 minutes, confirming improved dissolution behavior.

3.4 Effect of Variables on Dissolution Efficiency

Dissolution efficiency values ranged from 65.32% to 84.67%. Temperature showed the most significant effect ($F = 467.92$, $p < 0.0001$), followed by stirring speed ($F = 128.28$, $p < 0.0001$) and drug addition rate ($p = 0.0059$). Increasing temperature improved drug solubilization and dispersion, resulting in enhanced dissolution efficiency. The optimized formulation showed 84.67% dissolution efficiency, confirming improved dissolution performance of lovastatin solid dispersion.

3.5 Optimization and Validation of Model

Optimization of lovastatin solid dispersion was performed using Response Surface Methodology based on Central Composite Design. The optimization aimed to maximize drug content, drug release, and dissolution efficiency. The optimized formulation was obtained at temperature of 70°C and stirring speed of 500 rpm with a desirability value of 0.904. The predicted responses were 99.23% drug content, 96.52% drug release, and 84.67% dissolution efficiency. The experimental values were found to be 99.18%, 96.21%, and 84.33%, respectively, showing good agreement with predicted values and confirming model validity.

3.5.1 ANOVA Analysis

Analysis of variance (ANOVA) confirmed that the developed quadratic model was statistically significant for all responses. For drug content, the model showed F-value of 104.14 with p-value < 0.0001 and R^2 value of 0.9947. Drug release showed F-value of 516.78 with R^2 value of 0.9989, while dissolution efficiency exhibited F-value of 605.68 with R^2 value of 0.9991. The high F-values and low p-values indicated that the model was significant and suitable for optimization. The low residual error further confirmed model accuracy.

3.5.2 Response Surface Plots

Response surface and contour plots were generated to study the effect of formulation variables. The plots indicated that drug content, drug release, and dissolution efficiency increased with increasing temperature and stirring speed up to an optimum level. The response surface plots showed dome-shaped curves indicating the presence of optimum region. The optimum values were observed around 70°C temperature and moderate stirring speed, where maximum responses were achieved.

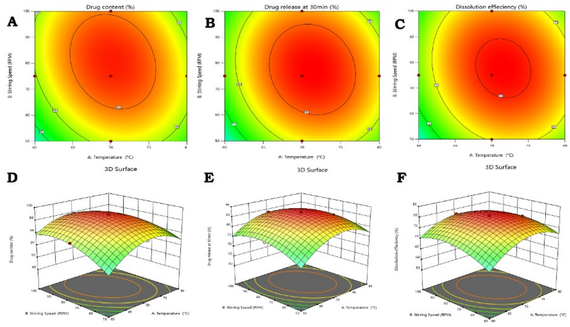

Figure 1: Contour plots of Responses & 3D plots of the responses: A) & D) Drug content (%) B) & E) Drug Release at 30 min (%) C) & F) Dissolution Efficiency (%)

3.5.3 Desirability Function

Numerical optimization using desirability function identified the optimized formulation with desirability value of 0.904. The optimized conditions predicted 99.23% drug content, 96.52% drug release, and 84.67% dissolution efficiency. The experimental values were found close to predicted values with less than 1% error, confirming reliability of optimization model and successful validation of formulation.

3.6 Characterization of Optimized Solid Dispersion

The optimized lovastatin solid dispersion was characterized for drug content, saturation solubility, dissolution behavior, and drug–polymer compatibility to confirm improvement in solubility and dissolution performance.

3.6.1 Drug Content

The optimized solid dispersion showed drug content of 99.23 ± 0.15%, indicating uniform distribution of lovastatin within the PEG 6000 matrix. The results were within acceptable limits (95–105%), confirming the suitability of the formulation and effectiveness of the optimization process.

3.6.2 Saturation Solubility Study

The saturation solubility of pure lovastatin was found to be 18.7 ± 1.6 µg/mL in phosphate buffer (pH 6.8), whereas optimized solid dispersion showed significantly improved solubility of 74.3 ± 2.4 µg/mL. The increase in solubility was attributed to conversion of crystalline drug into amorphous form and improved wettability provided by PEG 6000. These results confirmed enhancement in solubility of lovastatin after solid dispersion formation.

3.6.3 Dissolution Study

The optimized solid dispersion showed enhanced dissolution compared to pure drug. Pure lovastatin exhibited 68.4 ± 1.6% drug release at 30 minutes, whereas optimized solid dispersion showed 91.7 ± 1.3% drug release at 30 minutes. The improved dissolution was attributed to reduced particle size, improved wettability, and amorphous drug dispersion in PEG 6000.

3.6.4 FTIR Analysis

FTIR analysis of pure lovastatin and optimized solid dispersion showed characteristic peaks without significant shifts. The major peaks corresponding to O–H stretching (~3540 cm^{-1}), C=O stretching (~1725 cm^{-1}), and C–H stretching (~2925 cm^{-1}) were retained in optimized formulation. The absence of new peaks indicated no chemical interaction between lovastatin and PEG 6000, confirming compatibility of drug and polymer.

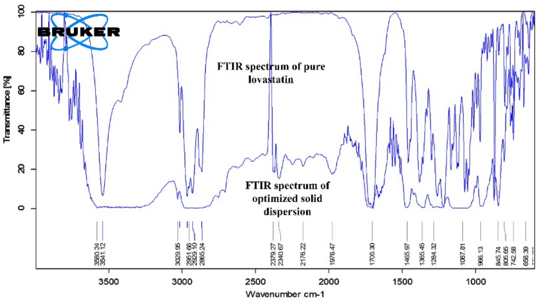

Figure 2: FTIR Spectrum of Pure Lovastatin and Optimized solid dispersion

3.7 Pre-Compression Parameters

The powder blend prepared for orodispersible tablets was evaluated for pre-compression parameters including angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio. The angle of repose was found to be 27.35 ± 0.82°, indicating good flow properties. Bulk density and tapped density were found to be 0.42 ± 0.02 g/cm³ and 0.48 ± 0.03 g/cm³, respectively. Carr's index and Hausner's ratio were calculated as 12.50% and 1.14, respectively. These values indicated good flowability and compressibility of the powder blend suitable for direct compression.

3.8 Evaluation of Orodispersible Tablets

3.8.1 Physical Parameters

The prepared orodispersible tablets showed uniform physical properties. The average tablet weight was found to be 182 ± 2.0 mg. The hardness of tablets was 3.3 ± 0.2 kg/cm², indicating adequate mechanical strength. Friability was found to be 0.41 ± 0.04%, which was within acceptable limits (<1%), confirming good mechanical resistance of tablets.

3.8.2 Wetting Time and Disintegration Time

The wetting time of optimized tablets was found to be 23 ± 2 seconds, indicating rapid water penetration. The disintegration time was found to be 27 ± 3 seconds, which is suitable for orodispersible tablets. Rapid disintegration was attributed to presence of superdisintegrant and improved wettability of solid dispersion.

3.8.3 Drug Content

The drug content of optimized orodispersible tablets was found to be 99.18 ± 0.46%, indicating uniform drug distribution within tablets and compliance with pharmacopeial limits.

3.9 *In-vitro* Dissolution Study of ODTs

The optimized orodispersible tablets showed rapid drug release with 62.4 ± 1.8% release at 5 minutes and 96.21 ± 1.12% drug release at 30 minutes. The rapid dissolution was attributed to fast tablet disintegration and improved solubility of lovastatin from solid dispersion.

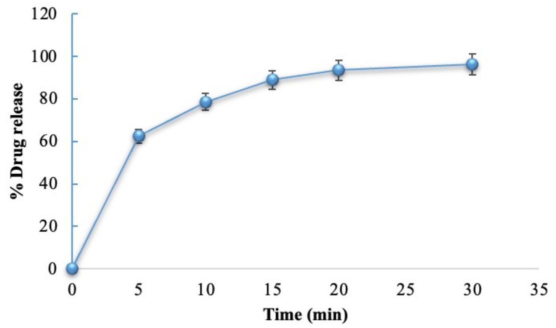

Figure 3: ***In-vitro*** **dissolution profile of optimized lovastatin orodispersible tablets**

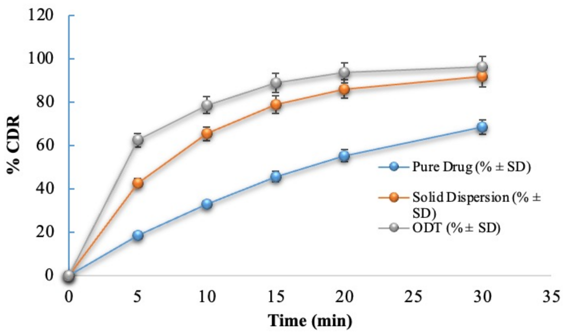

Figure 4: Dissolution comparison (Pure drug vs Solid dispersion vs ODT)

The comparative dissolution study demonstrated significant improvement in drug release from solid dispersion and orodispersible tablets compared to pure lovastatin. Pure drug showed only 18.5% release at 5 minutes, whereas solid dispersion and ODT exhibited 42.6% and 62.4% drug release, respectively. At 30 minutes, pure drug showed 68.4% release, while solid dispersion and ODT achieved 91.7% and 96.21% drug release, respectively. The enhanced dissolution of solid dispersion was attributed to improved wettability, reduced particle size, and conversion of crystalline drug into amorphous form. Further improvement in ODT formulation was due to rapid tablet disintegration and increased surface area for dissolution. These results confirmed that incorporation of optimized solid dispersion into orodispersible tablets significantly enhanced dissolution behavior of lovastatin.

3.10 Drug Release Kinetics

The dissolution data were fitted into various kinetic models. The first-order model showed highest correlation coefficient (R^2 = 0.992), indicating concentration-dependent drug release. The Higuchi model showed R^2 value of 0.971, suggesting diffusion-based release mechanism. Korsmeyer–Peppas model showed R^2 value of 0.983 with release exponent (n = 0.41), indicating Fickian diffusion mechanism.

3.11 Stability Studies

Stability studies were conducted at 40 ± 2°C and 75 ± 5% RH for three months. The optimized formulation showed no significant change in physical appearance. Drug content decreased slightly from 99.18% to 98.54%, while drug release decreased from 96.21% to 95.02%. These results indicated that the optimized formulation remained stable under accelerated conditions.

Table 5: Stability Study Results of Optimized ODT (n = 3)

Time (Months)	Physical Appearance	Drug Content (%) (Mean ± SD)	Drug Release at 30 min (%) (Mean ± SD)
0	No change	99.18 ± 0.46	96.21 ± 1.12
1	No change	99.05 ± 0.52	95.88 ± 1.18
2	No change	98.82 ± 0.61	95.36 ± 1.24
3	No change	98.54 ± 0.66	95.02 ± 1.31

CONCLUSION

The present study successfully developed and optimized lovastatin solid dispersions using PEG 6000 to enhance dissolution of poorly soluble lovastatin. Solid dispersions were prepared using the fusion method and optimized using Central Composite Design by evaluating temperature, stirring speed, and drug addition rate. The optimized formulation was obtained at 69.997°C and 499.38 rpm, showing 99.23% drug content, 96.52% drug release at 30 minutes, and 84.67% dissolution efficiency, with a desirability value of 0.904, indicating successful optimization.

Characterization studies confirmed the formation of solid dispersion. FTIR analysis revealed no significant drug–polymer interaction, while DSC analysis indicated conversion of crystalline lovastatin into amorphous form, contributing to improved dissolution behavior.

The optimized solid dispersion was successfully formulated into orodispersible tablets using direct compression. The tablets exhibited acceptable physical properties with weight variation of 182 ± 2.0 mg, hardness of 3.3 ± 0.2 kg/cm², friability of 0.41 ± 0.04%, wetting time of 23 ± 2 seconds, and disintegration time of 27 ± 3 seconds. Drug content was 99.18 ± 0.46%.

The optimized ODT formulation showed rapid drug release with 62.4% release at 5 minutes and 96.21% at 30 minutes. Drug release followed first-order kinetics (R^2 = 0.992) with Fickian diffusion mechanism (n = 0.41). Stability studies demonstrated no significant changes, with drug content of 98.54% and drug release of 95.02% after three months.

Overall, the developed lovastatin solid dispersion-based orodispersible tablets significantly improved dissolution and stability, suggesting potential enhancement in oral bioavailability of lovastatin.

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6. Conflict of Interest

The authors declare no conflict of interest.

7. Funding Statement

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