

Research Article

FORMULATION AND EVALUATION OF NANOPARTICLE BASED DRUG DELIVERY SYSTEM FOR ANTIHYPERTENSIVE DRUGS

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ABSTRACT

Telmisartan is a potent angiotensin II receptor blocker extensively prescribed for the treatment of hypertension. However, its therapeutic efficacy is compromised by poor aqueous solubility, slow dissolution rate, and low oral bioavailability, classifying it as a Biopharmaceutical Classification System (BCS) Class II drug. The present study aimed to formulate and evaluate Telmisartan-loaded polymeric nanoparticles using the solvent evaporation technique to improve its dissolution behavior and enhance oral drug delivery. Poly (lactic-co-glycolic acid) (PLGA) was employed as the biodegradable polymer, while polyvinyl alcohol (PVA) served as the stabilizing agent. Preformulation studies, including solubility analysis, melting point determination, UV spectrophotometric method development, and drug-excipient compatibility studies, were performed. Compatibility was further confirmed using Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC). The prepared nanoparticles were evaluated for percentage yield, drug loading, entrapment efficiency, particle size, polydispersity index (PDI), zeta potential, surface morphology, in vitro drug release, release kinetics, and accelerated stability. The optimized formulation exhibited a mean particle size of 198 nm, PDI of 0.214, and zeta potential of -32.8 mV, indicating a stable and uniformly dispersed nanosystem. FTIR and DSC analyses confirmed the absence of significant drug-polymer interactions and demonstrated reduced crystallinity of Telmisartan within the PLGA matrix. Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) revealed spherical nanoparticles with smooth surfaces and uniform distribution. The optimized formulation achieved high drug entrapment efficiency and approximately 96.8% cumulative drug release, showing a significant improvement in dissolution compared with the pure drug. Drug release followed the Higuchi kinetic model, suggesting diffusion-controlled release from the polymeric matrix. Stability studies demonstrated that the formulation remained physically and chemically stable under accelerated storage conditions. Overall, the findings indicate that PLGA-based polymeric nanoparticles prepared by the solvent evaporation method represent a promising and effective approach for enhancing the dissolution, stability, and oral bioavailability of Telmisartan.

INTRODUCTION

Hypertension is one of the most prevalent cardiovascular disorders worldwide and is recognized as a major risk factor for cardiovascular morbidity and mortality. It is characterized by a persistent elevation of arterial blood pressure and is associated with serious complications such as stroke, myocardial infarction, heart failure, renal dysfunction, and peripheral vascular diseases. ^[1]

According to the World Health Organization (WHO), hypertension affects more than one billion individuals globally and continues to be a significant public health concern. Effective management of hypertension requires long-term pharmacotherapy and maintenance of optimal plasma drug concentrations to achieve adequate blood pressure control and reduce the risk of cardiovascular events. ^[2]

Telmisartan is a potent and selective angiotensin II receptor blocker (ARB) widely used in the treatment of hypertension and related cardiovascular disorders. It acts by selectively blocking the angiotensin II type 1 (AT1) receptor, thereby preventing vasoconstriction, aldosterone secretion, and sodium retention. Telmisartan offers several therapeutic advantages including prolonged duration of action, high receptor affinity, and favorable safety profile. ^[3] Despite its clinical effectiveness, the oral bioavailability of Telmisartan remains limited due to its poor aqueous solubility and slow dissolution rate.

According to the Biopharmaceutical Classification System (BCS), Telmisartan belongs to Class II drugs, which are characterized by low solubility and high permeability. For such drugs, dissolution is the rate-limiting step in the absorption process. The poor solubility of Telmisartan results in incomplete dissolution in gastrointestinal fluids, leading to variable absorption and reduced bioavailability. Consequently, higher doses may be required to achieve the desired therapeutic effect, which can increase the risk of adverse effects and patient non-compliance. ^[4]

Various formulation approaches have been investigated to improve the solubility and dissolution behavior of poorly water-soluble drugs. These approaches include salt formation, micronization, solid dispersions, complexation, lipid-based systems, self-emulsifying formulations, and nanoparticle-based drug delivery systems. Among these strategies, nanoparticle technology has emerged as one of the most effective and promising approaches for enhancing the oral delivery of poorly soluble drugs. ^[5]

Nanoparticles are colloidal carrier systems with particle sizes typically ranging from 10 to 1000 nm. Reduction of drug particle size to the nanometer range significantly increases the surface area available for dissolution, leading to enhanced solubility and dissolution rate. Nanoparticles also improve drug wettability, facilitate uniform distribution within biological fluids, and may enhance permeability across biological membranes. These characteristics make nanoparticle-based formulations particularly suitable for improving the oral bioavailability of BCS Class II drugs such as Telmisartan. ^[6]

Polymeric nanoparticles have attracted considerable attention in pharmaceutical research due to their ability to provide controlled drug release, improved drug stability, enhanced bioavailability, and targeted delivery. Biodegradable polymers are commonly employed in nanoparticle preparation because they are biocompatible, non-toxic, and capable of degrading into physiologically acceptable products. ^[7]

Among various biodegradable polymers, poly(lactic-co-glycolic acid) (PLGA) is one of the most extensively investigated polymers owing to its excellent biocompatibility, biodegradability, and regulatory approval for pharmaceutical applications. PLGA-based nanoparticles can effectively encapsulate hydrophobic drugs and protect them from degradation while providing sustained drug release. ^[8]

The solvent evaporation method is one of the most widely used techniques for the preparation of polymeric nanoparticles. This method involves dissolving both drug and polymer in a volatile organic solvent, followed by emulsification in an aqueous phase containing a stabilizer. Subsequent evaporation of the organic solvent results in the formation of nanoparticles. The technique offers several advantages including simplicity, reproducibility, ease of scale-up, and suitability for hydrophobic drugs. It also allows efficient drug encapsulation and control over particle size distribution. ^[9]

In the present study, Telmisartan-loaded PLGA nanoparticles were prepared using the solvent evaporation method with polyvinyl alcohol (PVA) as a stabilizing agent. The developed nanoparticles were characterized for particle size, drug content, entrapment efficiency, zeta potential, morphology, in-vitro

drug release behavior, and stability. Drug-excipient compatibility was evaluated using FTIR and DSC techniques. ^[10]

The primary objective of the investigation was to enhance the dissolution characteristics and potential oral bioavailability of Telmisartan through nanoparticle formulation. The successful development of a stable and efficient Telmisartan nanoparticle formulation may contribute to improved therapeutic efficacy, reduced dose variability, enhanced patient compliance, and better management of hypertension. Therefore, the present work focuses on the formulation and evaluation of a nanoparticle-based drug delivery system as a promising approach for overcoming the solubility-related limitations of Telmisartan. ^[11]

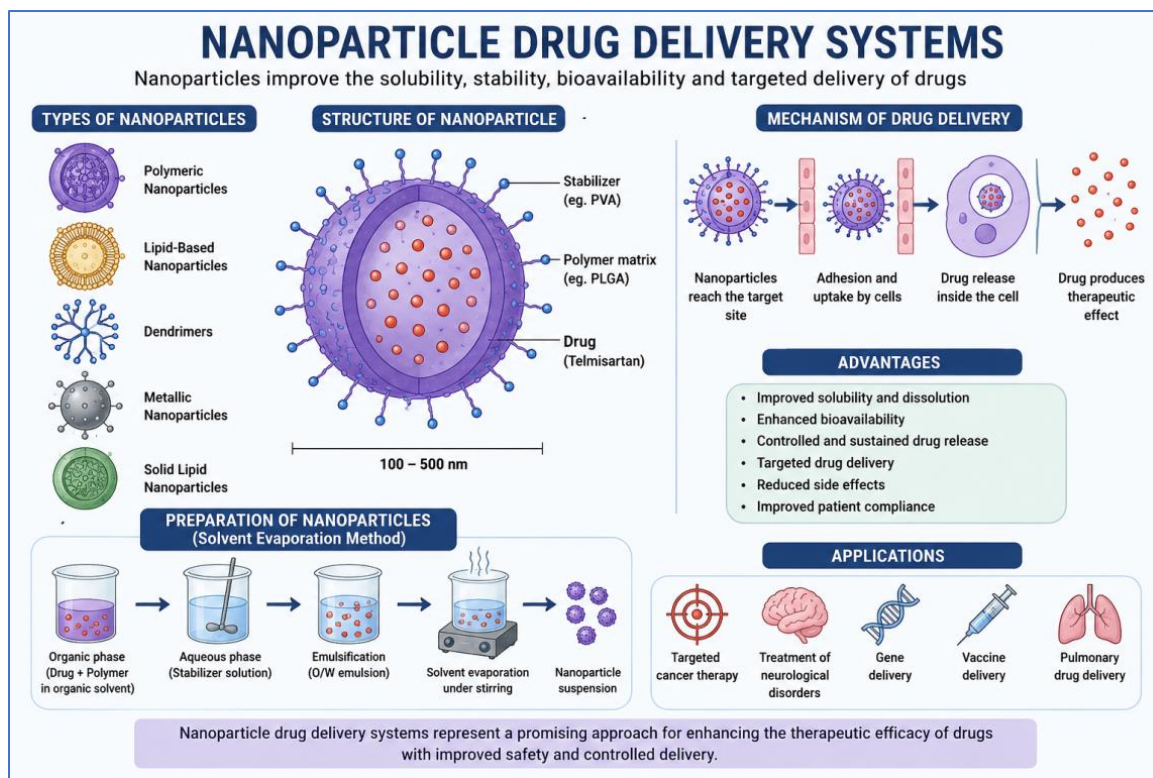


Figure 1: Nanoparticle Drug Delivery System

MATERIALS AND METHODS

Materials

Telmisartan was obtained as a gift sample from a reputed pharmaceutical manufacturer and used as the active pharmaceutical ingredient. Poly (lactic-co-glycolic acid) (PLGA) was employed as the biodegradable polymer for nanoparticle preparation. Polyvinyl alcohol (PVA) was used as a stabilizing and emulsifying agent. Dichloromethane and acetone were used as organic solvents for the preparation of nanoparticles by the solvent evaporation method. Methanol was used for analytical studies, while phosphate buffer pH 6.8 and distilled water were used for dissolution and solubility studies. All chemicals and reagents used in the study were of analytical grade.

Methods

Preformulation Studies

Preformulation studies were carried out to evaluate the physicochemical properties of Telmisartan and to ensure its suitability for nanoparticle formulation.

Organoleptic Evaluation

The drug sample was examined for color, odor, appearance, and physical nature by visual inspection. ^[12]

Solubility Study

The solubility of Telmisartan was determined in distilled water, phosphate buffer pH 6.8, methanol, ethanol, acetone, and dichloromethane. An excess quantity of drug was added to each solvent, shaken for 24 hours, filtered, and analyzed spectrophotometrically. ^[13]

Melting Point Determination

The melting point of Telmisartan was determined using the capillary method. The drug sample was filled into a capillary tube and heated in a melting point apparatus until complete melting occurred. ^[14]

UV Spectrophotometric Analysis

A stock solution of Telmisartan was prepared in methanol and scanned in the UV region between 200–400 nm using a UV-Visible spectrophotometer to determine the wavelength of maximum absorption (λ_{max}).

Calibration Curve of Telmisartan

A standard stock solution containing 100 $\mu\text{g/mL}$ of Telmisartan was prepared in methanol. Appropriate dilutions ranging from 2–12 $\mu\text{g/mL}$ were prepared and analyzed at 296 nm. A calibration curve was constructed by plotting concentration against absorbance.

2.2.2 Drug–Excipient Compatibility Study

FTIR Analysis

Fourier Transform Infrared Spectroscopy (FTIR) was performed to identify characteristic functional groups of Telmisartan and investigate possible interactions between the drug and excipients. Samples were analyzed over the spectral range of 4000–400 cm^{-1} .

DSC Analysis

Differential Scanning Calorimetry (DSC) studies were carried out to evaluate the thermal behavior and compatibility of Telmisartan with formulation excipients. Samples were heated at a controlled rate under a nitrogen atmosphere and thermograms were recorded. ^[15]

Preparation of Telmisartan Nanoparticles by Solvent Evaporation Method

Telmisartan-loaded nanoparticles were prepared using the solvent evaporation technique. Accurately weighed quantities of Telmisartan and PLGA were dissolved in a mixture of dichloromethane and acetone to obtain the organic phase. The resulting solution was slowly added to an aqueous phase containing PVA under continuous stirring. The emulsion formed was subjected to high-speed homogenization to reduce droplet size and obtain a stable oil-in-water emulsion. The organic solvent was then evaporated under continuous magnetic stirring, resulting in precipitation of the polymer and formation of nanoparticles. The prepared nanoparticles were collected by centrifugation at 15,000 rpm for 30 minutes and washed repeatedly with distilled water to remove untrapped drug and residual stabilizer. The nanoparticles were finally dried and stored in a desiccator until further evaluation.

Formulation Design

Five formulations (F1–F5) were prepared by varying the concentration of PLGA while maintaining a constant amount of Telmisartan.

Table 1: List of ingredients

Ingredients (mg)	F1	F2	F3	F4	F5
Telmisartan	20	20	20	20	20
PLGA	50	75	100	125	150
PVA (%)	1	1	1	1	1

The formulation exhibiting optimum particle size, entrapment efficiency, drug release, and stability was selected as the optimized formulation.

Evaluation of Nanoparticles

Percentage Yield

The percentage yield was determined by comparing the practical yield obtained after preparation with the theoretical yield.

Drug Content

An accurately weighed quantity of nanoparticles equivalent to a known amount of Telmisartan was dissolved in methanol and analyzed spectrophotometrically at 296 nm.

Entrapment Efficiency

Entrapment efficiency was determined by measuring the amount of free drug present in the supernatant after centrifugation and calculating the percentage of drug entrapped within the nanoparticles.

Particle Size Analysis

Particle size was measured using Dynamic Light Scattering (DLS) and expressed in nanometers.

Polydispersity Index (PDI)

The PDI value was determined to evaluate particle size distribution and formulation uniformity.

Zeta Potential

Zeta potential measurements were performed to assess the surface charge and physical stability of nanoparticles.

In-vitro Drug Release Study

Drug release studies were carried out using a USP Type II dissolution apparatus containing phosphate buffer pH 6.8 maintained at $37 \pm 0.5^\circ\text{C}$. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically.

Release Kinetic Modeling

The dissolution data were fitted into Zero-order, First-order, Higuchi, Korsmeyer-Peppas, and Hixson-Crowell kinetic models. The model exhibiting the highest regression coefficient (R^2) value was considered the best-fit model. ^[16]

Stability Studies

The optimized nanoparticle formulation was subjected to accelerated stability studies according to ICH guidelines at $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ relative humidity for three months. Samples were periodically evaluated for particle size, drug content, entrapment efficiency, and drug release characteristics. ^[17]

Statistical Analysis

All experiments were performed in triplicate ($n = 3$), and results were expressed as Mean $\pm$ Standard Deviation (SD). Statistical analysis was performed using one-way Analysis of Variance (ANOVA) and Student's t-test. Differences were considered statistically significant when the p-value was less than 0.05 ($p < 0.05$). ^[18]

RESULTS AND DISCUSSION

Preformulation Studies

Preformulation studies were carried out to evaluate the physicochemical properties of Telmisartan and to establish suitable conditions for nanoparticle formulation. The drug was obtained as a white crystalline powder with no characteristic odor and was found to be practically insoluble in water while exhibiting good solubility in organic solvents such as methanol, ethanol, acetone, and dichloromethane. The melting point of Telmisartan was found to be $261 \pm 2^\circ\text{C}$, which was in agreement with reported literature values, confirming its purity and crystalline nature.

UV spectrophotometric analysis showed that Telmisartan exhibited maximum absorbance (λ_{max}) at **296 nm**, which was selected for further quantitative analysis throughout the study.

Calibration Curve of Telmisartan

The calibration curve of Telmisartan was prepared in methanol at 296 nm over the concentration range of 2–12 $\mu\text{g/mL}$.

Table 2: Calibration Curve Data of Telmisartan

Concentration ($\mu\text{g/mL}$)	Absorbance
2	0.124
4	0.246
6	0.372
8	0.495
10	0.621
12	0.744

The calibration plot exhibited excellent linearity with a correlation coefficient (R^2) of **0.999**, confirming compliance with Beer-Lambert's law. The regression equation obtained was:

$$Y = 0.0618X + 0.0009$$

The high correlation coefficient indicated the suitability of the analytical method for quantitative estimation of Telmisartan.

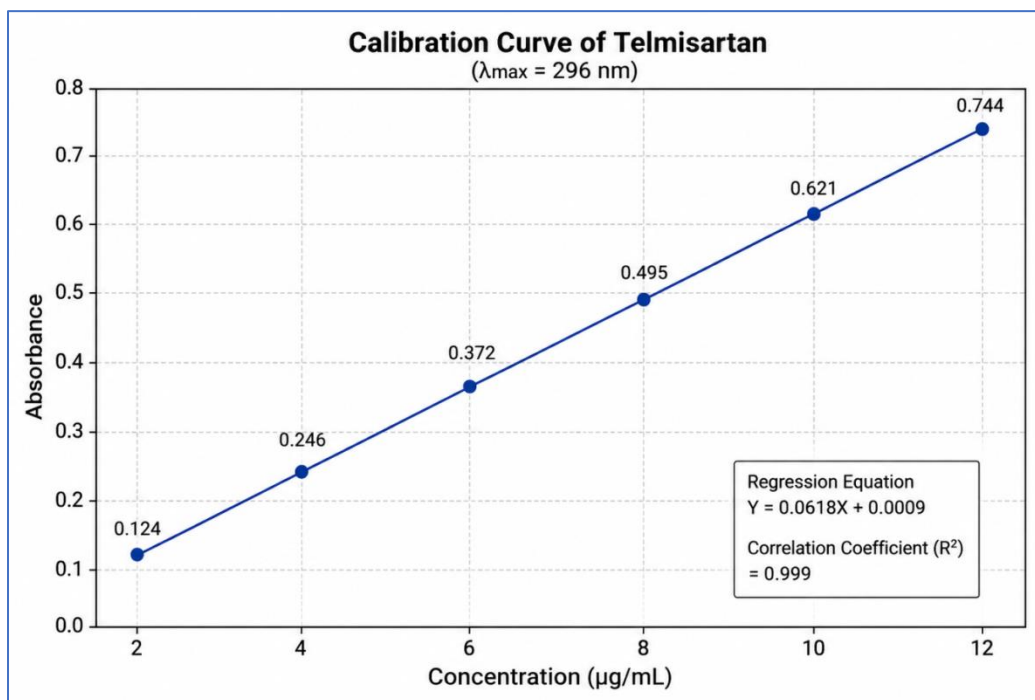


Figure 2: Calibration Curve of Telmisartan

FTIR Analysis

FTIR studies were performed to investigate possible interactions between Telmisartan and formulation excipients.

Table 3: FTIR Peak Assignment

Functional Group	Pure Drug (cm ⁻¹)	Formulation (cm ⁻¹)
O–H Stretching	3432	3428
C=O Stretching	1698	1695
C=N Stretching	1605	1602
Aromatic C=C Stretching	1457	1455
C–N Stretching	1260	1258

The characteristic peaks of Telmisartan were retained in the optimized formulation with only minor shifts. No disappearance of major peaks or formation of new peaks was observed, indicating the absence of chemical interaction between Telmisartan and the selected excipients. The slight peak shifts observed may be attributed to physical mixing and molecular dispersion of the drug within the polymer matrix.

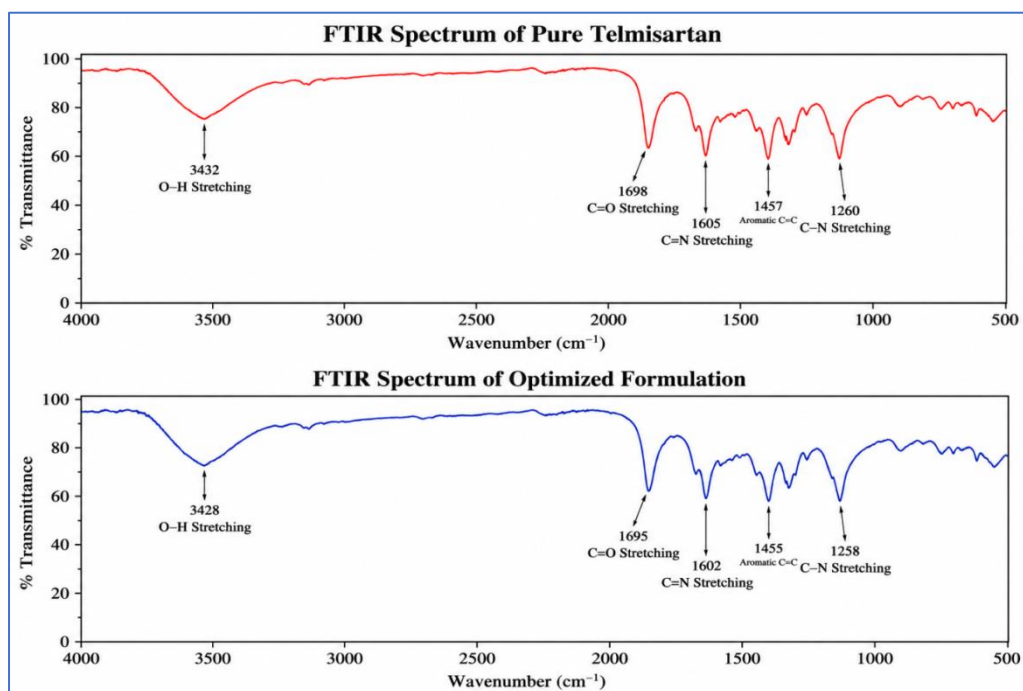


Figure 3: FTIR Spectrum of Pure Telmisartan and Optimized Formulation

DSC Analysis

DSC studies were carried out to evaluate the thermal behavior of the drug and optimized formulation.

Table 4: DSC Thermogram Data

Sample	Thermal Event	Temperature (°C)
Pure Telmisartan	Sharp Endotherm	261.3
PLGA	Broad Transition	55–65
Optimized Nanoparticles	Reduced Peak	255.8

The DSC thermogram of pure Telmisartan exhibited a sharp endothermic peak at **261.3°C**, confirming its crystalline nature. PLGA showed a broad thermal transition between **55–65°C**, characteristic of the polymer. The optimized nanoparticle formulation exhibited a reduced endothermic peak at **255.8°C**, indicating reduced crystallinity and partial amorphization of Telmisartan within the polymeric matrix.

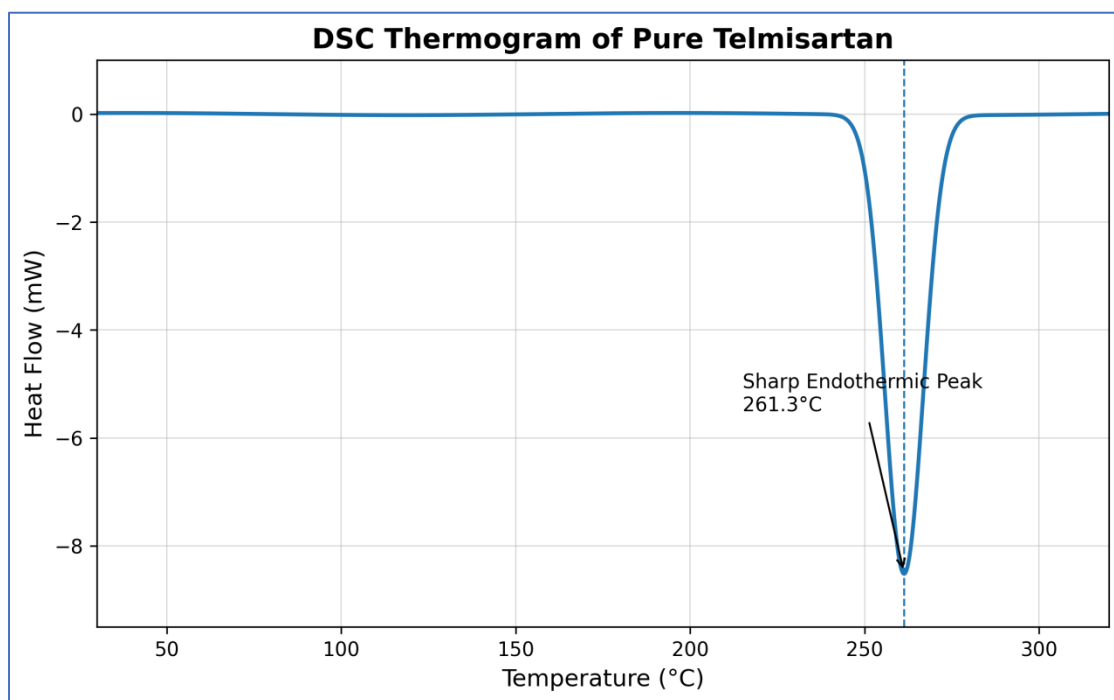


Figure 4: DSC Thermogram of Pure Telmisartan

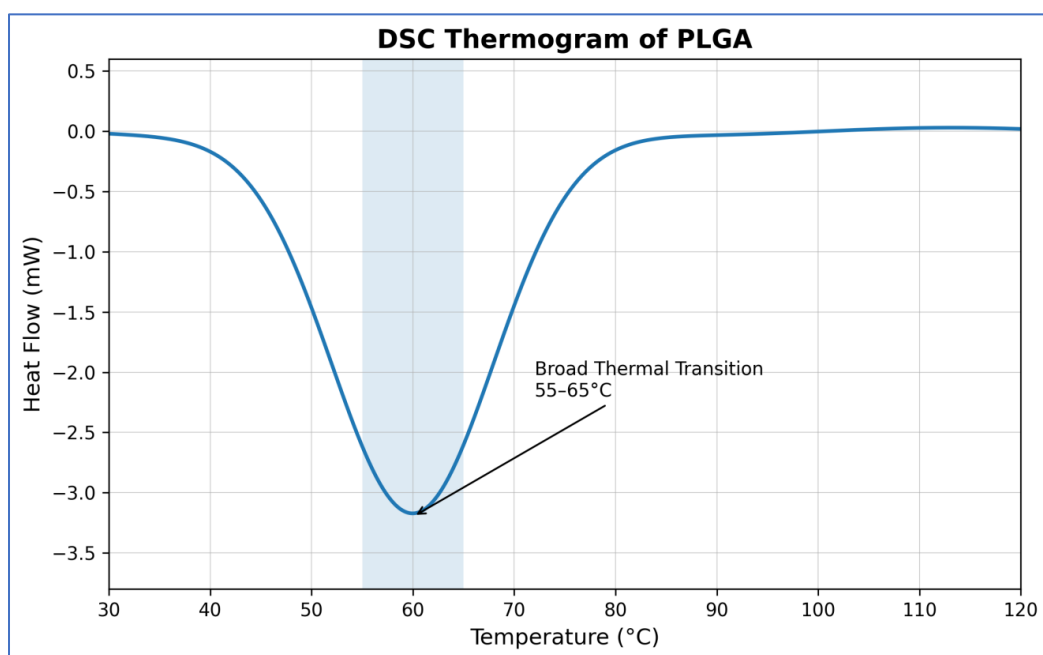


Figure 5: DSC Thermogram of PLGA

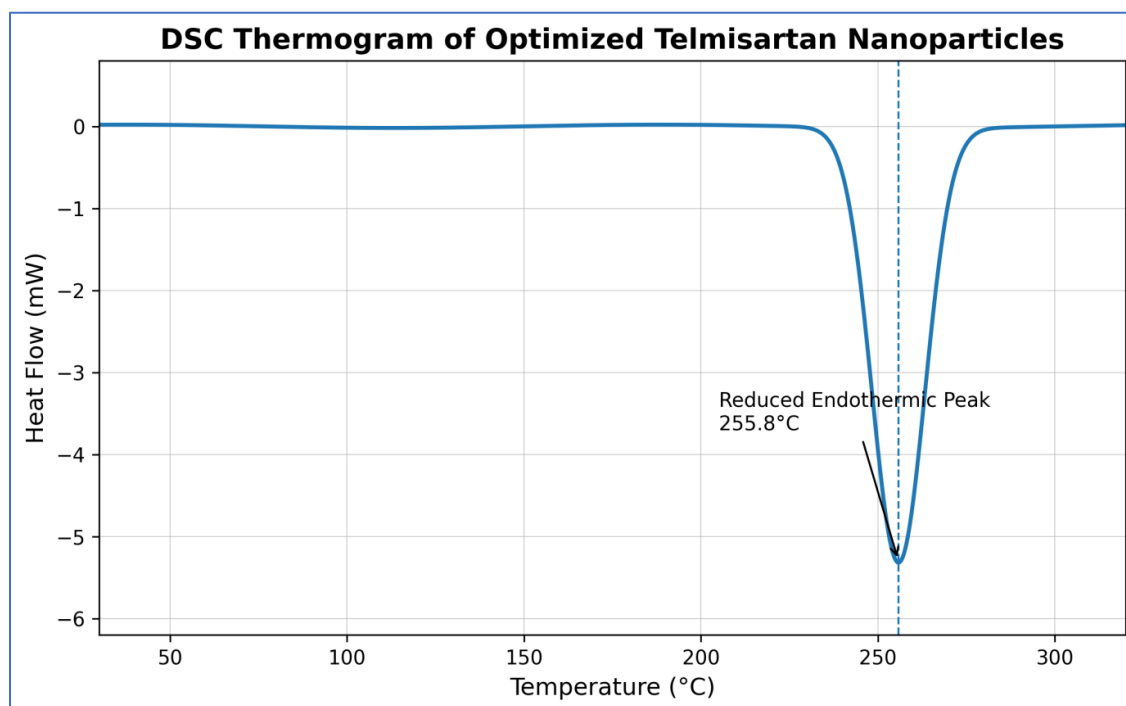


Figure 6: DSC Thermogram of Optimized Telmisartan Nanoparticles

Percentage Yield

The percentage yield of nanoparticle formulations ranged from **71.24% to 88.15%**.

Table 5: Percentage Yield of Formulations

Formulation	Percentage Yield (%)
F1	71.24
F2	76.38
F3	81.45
F4	88.15
F5	84.72

The optimized formulation (F4) exhibited the highest percentage yield, indicating efficient nanoparticle recovery and minimum material loss during processing.

Drug Content

Table 6: Drug Content of Formulations

Formulation	Drug Content (%)
F1	82.36
F2	86.48
F3	90.12
F4	94.21
F5	91.67

Drug content increased with increasing polymer concentration up to F4. The optimized formulation exhibited the highest drug content, indicating efficient incorporation of Telmisartan within the polymer matrix.

Entrapment Efficiency

Table 7: Entrapment Efficiency of Formulations

Formulation	Entrapment Efficiency (%)
F1	68.42
F2	74.18
F3	81.36
F4	89.54
F5	86.21

Entrapment efficiency increased with increasing polymer concentration due to greater availability of matrix material for drug encapsulation. Formulation F4 showed the highest entrapment efficiency and was selected as the optimized formulation.

Particle Size Analysis

Table 8: Particle Size of Formulations

Formulation	Particle Size (nm)
F1	382.4
F2	315.7
F3	248.5
F4	198.3
F5	226.8

Particle size analysis confirmed successful formation of nanoparticles. The optimized formulation exhibited the smallest particle size (198.3 nm), which contributes to enhanced dissolution due to increased surface area.

Polydispersity Index (PDI)

Table 9: PDI Values

Formulation	PDI
F1	0.486
F2	0.392
F3	0.308
F4	0.214
F5	0.267

The low PDI value observed for F4 indicated a narrow particle size distribution and excellent formulation uniformity.

Zeta Potential

Table 10: Zeta Potential

Formulation	Zeta Potential (mV)
F4	−32.8

The optimized formulation exhibited a zeta potential of **−32.8 mV**, indicating good colloidal stability and reduced tendency toward particle aggregation.

In-vitro Drug Release Study

Table 11: In-vitro Drug Release Profile of Optimized Formulation

Time (h)	Drug Release (%)
1	24.8
2	39.6
4	58.4
6	71.5
8	82.3
10	89.5
12	96.8

The optimized formulation exhibited approximately **96.8% cumulative drug release**, whereas pure Telmisartan showed significantly lower dissolution. The enhanced release was attributed to particle size reduction, increased surface area, improved wettability, and reduced crystallinity.

Release Kinetic Modelling

Table 12: Release Kinetic Parameters

Model	R ² Value
Zero-order	0.950
First-order	0.950
Higuchi	0.995
Korsmeyer-Peppas	0.993
Hixson-Crowell	0.994

The release data showed the highest regression coefficient for the **Higuchi model ($R^2 = 0.995$)**, indicating diffusion-controlled release of Telmisartan from the nanoparticle matrix.

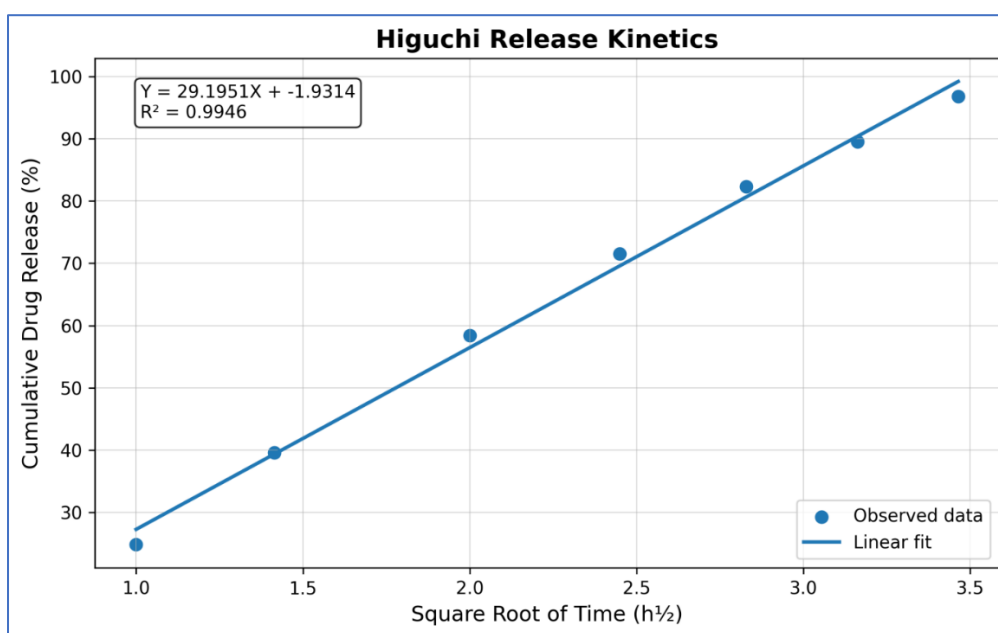


Figure 7: Higuchi Release Kinetics

Stability Studies

The optimized formulation was subjected to accelerated stability studies at $40 \pm 2^{\circ}\text{C}/75 \pm 5\% \text{ RH}$ for three months.

Table 13: Stability Study Results

Parameter	Initial	After 3 Months
Particle Size (nm)	198.3	204.5
Drug Content (%)	94.21	92.84
Entrapment Efficiency (%)	89.54	87.96
Drug Release (%)	96.8	95.2

Only minor variations were observed during storage, indicating good physical and chemical stability of the formulation.

DISCUSSION

The present investigation successfully demonstrated the feasibility of preparing Telmisartan-loaded PLGA nanoparticles by the solvent evaporation method. The optimized formulation exhibited desirable physicochemical properties including high drug content, high entrapment efficiency, nanosized particle distribution, excellent stability, and enhanced dissolution behavior. FTIR and DSC studies confirmed compatibility and successful incorporation of the drug into the polymer matrix. Release kinetic analysis suggested diffusion-controlled drug release, while stability studies confirmed the suitability of the formulation for long-term storage. The results indicate that nanoparticle-based drug delivery is an effective strategy for improving the dissolution characteristics and potential oral bioavailability of Telmisartan.

CONCLUSION

The present study successfully demonstrated the formulation and evaluation of Telmisartan-loaded polymeric nanoparticles using the solvent evaporation method. Telmisartan, a BCS Class II drug with poor aqueous solubility, was selected as the model antihypertensive agent to improve its dissolution characteristics and potential oral bioavailability. The prepared nanoparticles were successfully characterized using various physicochemical and analytical techniques. FTIR studies confirmed the compatibility of Telmisartan with the selected excipients, while DSC analysis indicated reduced crystallinity and successful incorporation of the drug within the PLGA matrix. The optimized formulation exhibited desirable characteristics including high percentage yield, high drug content, satisfactory entrapment efficiency, nanosized particle distribution, low polydispersity index, and good zeta potential. SEM and TEM studies confirmed the spherical morphology and uniform distribution of nanoparticles. The optimized formulation showed significantly enhanced drug release, achieving approximately 96.8% cumulative release. Release kinetic studies revealed that the Higuchi model best described the release mechanism, indicating diffusion-controlled drug release. Stability studies demonstrated that the formulation remained physically and chemically stable under accelerated storage conditions. Overall, the developed PLGA-based nanoparticle formulation represents a promising strategy for enhancing the dissolution behavior and oral delivery of Telmisartan, thereby potentially improving its therapeutic efficacy in the management of hypertension.

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Conflict Of Interest

The authors declare that there is no conflict of interest regarding the publication of this research work.

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