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Preparation and Evaluation of Nanoparticle-Based Drug Delivery System for the Management of Atherosclerosis using Atorvastatin

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ABSTRACT

Atherosclerosis remains the leading cause of cardiovascular morbidity and mortality worldwide, with conventional therapeutic approaches facing significant limitations including poor drug bioavailability at plaque sites and systemic adverse effects. This research aimed to develop and evaluate atorvastatin-loaded poly(lactic-co-glycolic acid) nanoparticles as an advanced drug delivery system for atherosclerosis management. Nanoparticles were prepared using emulsion-solvent evaporation method and systematically optimized for critical formulation parameters. The optimized formulation exhibited particle size of 186.5 ± 12.4 nm, polydispersity index of 0.21 ± 0.04, zeta potential of -22.6 ± 1.8 mV, and encapsulation efficiency of 82.6 ± 2.8%. Physicochemical characterization confirmed spherical morphology with smooth surfaces and amorphous drug dispersion within the polymer matrix. In vitro release studies demonstrated biphasic release pattern with sustained drug liberation over seven days, governed by diffusion and erosion mechanisms. Stability studies indicated satisfactory physical and chemical stability under recommended storage conditions. Cytotoxicity assessment using RAW 264.7 macrophages confirmed excellent biocompatibility at therapeutically relevant concentrations. Cellular uptake studies revealed rapid and efficient nanoparticle internalization by macrophages, with over 94% cellular uptake within 4 hours.

Keywords: Atherosclerosis, Atorvastatin, PLGA nanoparticles, Drug delivery system, Macrophage targeting

INTRODUCTION

Overview of Atherosclerosis

Atherosclerosis represents a chronic inflammatory disease of the arterial wall that remains the primary cause of cardiovascular morbidity and mortality worldwide, affecting millions of individuals across all demographics [1]. This pathological condition is characterized by the

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progressive accumulation of lipids, inflammatory cells, and fibrous elements within the intimal layer of large and medium-sized arteries, leading to the formation of atherosclerotic plaques that compromise vascular integrity and blood flow [2]. The global burden of atherosclerosis continues to escalate, with cardiovascular diseases accounting for approximately 17.9 million deaths annually, representing 31% of all global deaths according to recent epidemiological studies [3]. The development of atherosclerosis is a multifactorial process involving complex interactions between genetic predisposition, environmental factors, and metabolic abnormalities, with dyslipidemia, hypertension, diabetes mellitus, smoking, and obesity serving as major risk factors that accelerate disease progression [4].

The pathophysiology of atherosclerosis begins with endothelial dysfunction, which serves as the initial trigger for a cascade of events culminating in plaque formation [5]. Under normal physiological conditions, the vascular endothelium maintains homeostasis by regulating vascular tone, preventing thrombosis, and inhibiting inflammatory cell adhesion. However, exposure to risk factors such as oxidized low-density lipoprotein (ox-LDL), hypertension, and inflammatory mediators disrupts this delicate balance, leading to increased endothelial permeability and expression of adhesion molecules including vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) [6].

Current Therapeutic Approaches and Their Limitations

The contemporary management of atherosclerosis encompasses both pharmacological interventions and lifestyle modifications aimed at reducing cardiovascular risk factors and preventing disease progression [12]. Statins, or 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, represent the cornerstone of pharmacological therapy for atherosclerosis, effectively lowering circulating LDL cholesterol levels through inhibition of hepatic cholesterol biosynthesis and upregulation of hepatic LDL receptors [13]. Clinical trials have consistently demonstrated that statin therapy significantly reduces the incidence of major cardiovascular events, with intensive lipid-lowering strategies providing additional benefits in high-risk populations.

1.3 Nanotechnology in Drug Delivery

Nanotechnology has emerged as a revolutionary approach in pharmaceutical sciences, offering unprecedented opportunities to address the limitations of conventional drug delivery systems through the design and fabrication of nanoscale materials with unique physicochemical properties [25]. Nanoparticles, defined as particles with at least one dimension between 1 and 100 nanometers, exhibit distinctive characteristics including high surface-to-volume ratios, tunable surface properties, and the ability to interact with biological systems at the molecular and cellular levels [26]. These unique features enable nanoparticles to overcome biological barriers, achieve controlled and sustained drug release, protect therapeutic agents from degradation, and facilitate targeted delivery to specific tissues or cells, thereby enhancing therapeutic efficacy while minimizing systemic toxicity [27].

Mechanisms of Nanoparticle Targeting in Atherosclerosis

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The accumulation of nanoparticles at atherosclerotic lesion sites can occur through both passive and active targeting mechanisms, each exploiting different pathophysiological features of diseased arteries [1]. Passive targeting relies on the enhanced permeability and retention (EPR) effect observed in atherosclerotic plaques, where endothelial dysfunction and increased vascular permeability facilitate the extravasation of nanoparticles from the bloodstream into the subendothelial space [2]. The fenestrations and gaps in the dysfunctional endothelium overlying atherosclerotic lesions, ranging from 200 to 1200 nanometers, allow preferential passage of appropriately sized nanoparticles, while impaired lymphatic drainage within plaques promotes their retention [3]. However, the extent of passive accumulation depends critically on nanoparticle physicochemical properties, with size, shape, surface charge, and hydrophilicity all influencing their circulation time, margination behavior, and extravasation efficiency [4].

Types of Nanoparticles for Atherosclerosis Therapy

Polymeric nanoparticles represent one of the most extensively studied classes of nanocarriers for cardiovascular drug delivery, offering versatility in composition, surface modification, and drug release characteristics [16]. These nanoparticles can be fabricated from natural polymers such as chitosan, alginate, and hyaluronic acid, or synthetic polymers including poly(lactic-co-glycolic acid) (PLGA), polylactic acid (PLA), and polycaprolactone (PCL), each providing distinct advantages in terms of biodegradability, biocompatibility, and drug loading capacity [17]. PLGA nanoparticles have gained particular attention due to their FDA-approved status, tunable degradation kinetics achieved by varying the lactide-to-glycolide ratio, and ability to encapsulate both hydrophilic and hydrophobic drugs with high efficiency [18]. The surface of polymeric nanoparticles can be readily modified with polyethylene glycol (PEG) to create stealth particles with prolonged circulation times, or conjugated with targeting ligands to achieve site-specific delivery [19].

Therapeutic Strategies Using Nanoparticle-Based Drug Delivery

Nanoparticle-mediated delivery of conventional anti-atherosclerotic drugs offers opportunities to enhance their therapeutic efficacy while reducing systemic side effects through improved pharmacokinetics and targeted delivery [1]. Encapsulation of statins within nanoparticles has demonstrated enhanced accumulation at atherosclerotic lesion sites, prolonged drug release, and improved anti-inflammatory and plaque-stabilizing effects compared to free drug administration [2]. Similarly, nanoparticle formulations of anti-inflammatory agents such as corticosteroids, non-steroidal anti-inflammatory drugs, and specialized pro-resolving mediators have shown superior efficacy in reducing plaque inflammation and promoting resolution of atherosclerotic lesions in animal models [3]. The ability to co-deliver multiple therapeutic agents with different physicochemical properties within a single nanoparticle platform enables combination therapy targeting multiple pathogenic mechanisms simultaneously, potentially achieving synergistic effects [4].

Characterization of Nanoparticle-Based Drug Delivery Systems

Comprehensive characterization of nanoparticle-based drug delivery systems is essential to ensure their quality, reproducibility, and predictable biological performance [16]. Physicochemical characterization encompasses multiple parameters including particle size, size distribution

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(polydispersity index), morphology, surface charge (zeta potential), surface chemistry, drug loading capacity, and encapsulation efficiency [17]. Dynamic light scattering (DLS) serves as the primary technique for determining hydrodynamic diameter and size distribution in aqueous media, while nanoparticle tracking analysis (NTA) provides complementary information on particle concentration and size distribution, particularly for heterogeneous samples [18]. Electron microscopy techniques, including transmission electron microscopy (TEM) and scanning electron microscopy (SEM), enable direct visualization of nanoparticle morphology, internal structure, and aggregation state, providing essential information that cannot be obtained from light scattering methods alone [19].

DRUG PROFILE

Introduction to Therapeutic Agents for Atherosclerosis

The selection of appropriate therapeutic agents for incorporation into nanoparticle-based drug delivery systems represents a critical decision that fundamentally influences the therapeutic potential and clinical applicability of the final formulation. An ideal anti-atherosclerotic drug for nanoparticle encapsulation should possess several key characteristics including proven efficacy in reducing atherosclerotic plaque progression or promoting plaque regression, well-established mechanisms of action targeting relevant pathophysiological pathways, favorable physicochemical properties compatible with nanoparticle formulation techniques, and documented safety profiles from existing clinical use or preclinical studies. The drug profile provides comprehensive information about the selected therapeutic agent, encompassing its chemical structure, physicochemical properties, pharmacological actions, pharmacokinetics, therapeutic applications, adverse effects, and rationale for selection in the context of nanoparticle-based delivery for atherosclerosis management.

Chemical Structure and Nomenclature

The selected drug for this research is atorvastatin calcium, a synthetic lipid-lowering agent belonging to the statin class of medications. The chemical name of atorvastatin is [R-(R*,R*)]-2-(4-fluorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate. The molecular formula of atorvastatin calcium trihydrate is $(C_{33}H_{34}FN_2O_5)_2Ca \cdot 3H_2O$, and it has a molecular weight of 1209.42 grams per mole for the trihydrate form, with the anhydrous calcium salt having a molecular weight of 1155.36 grams per mole.

Physicochemical Properties

Understanding the physicochemical properties of atorvastatin is essential for rational formulation design and predicting its behavior in biological systems. Atorvastatin calcium trihydrate appears as a white to off-white crystalline powder that is very slightly soluble in water and phosphate buffer at neutral pH, slightly soluble in ethanol, and freely soluble in methanol. The aqueous solubility of atorvastatin is pH-dependent due to the presence of ionizable groups, with increased solubility observed under acidic or basic conditions compared to neutral pH. At pH 7.4, the solubility of atorvastatin is approximately 0.1 to 0.2 milligrams per milliliter, which classifies it as a poorly water-soluble drug according to the Biopharmaceutics Classification System.

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LITERATURE REVIEW

Evolution of Nanoparticle-Based Drug Delivery Systems

The development of nanoparticle-based drug delivery systems represents a paradigm shift in pharmaceutical sciences, with research over the past three decades demonstrating their potential to overcome fundamental limitations of conventional therapeutics [31]. Early investigations into colloidal drug carriers in the 1970s and 1980s laid the groundwork for modern nanotechnology applications, with pioneering studies demonstrating that particles in the nanometer size range could exhibit unique biological behaviors including prolonged circulation times, enhanced tissue penetration, and the ability to evade rapid clearance by the reticuloendothelial system [32].

Nanoparticle Targeting Strategies in Atherosclerosis

The successful application of nanoparticle-based therapeutics in atherosclerosis management critically depends on achieving preferential accumulation of drug carriers within atherosclerotic plaques while minimizing uptake by non-diseased tissues [40]. Passive targeting exploits the pathophysiological characteristics of atherosclerotic lesions, particularly the disrupted endothelial barrier integrity, increased vascular permeability, and enhanced retention of macromolecules within the inflamed arterial wall, to promote nanoparticle extravasation and accumulation at disease sites [41]. Studies utilizing intravital microscopy and radiolabeled nanoparticles have demonstrated that particles in the size range of 50 to 200 nanometers exhibit optimal passive targeting to atherosclerotic plaques, with smaller particles showing insufficient retention and larger particles experiencing limited extravasation through the compromised endothelium [42].

Polymeric Nanoparticles for Cardiovascular Applications

Poly(lactic-co-glycolic acid) has established itself as the gold standard biodegradable polymer for nanoparticle fabrication in cardiovascular applications, supported by extensive safety data, FDA approval for various clinical applications, and well-characterized degradation kinetics that can be modulated through variation of lactic acid to glycolic acid ratios [49]. The hydrolytic degradation of PLGA into lactic acid and glycolic acid, both naturally occurring metabolites that enter the tricarboxylic acid cycle, ensures complete biodegradation without accumulation of toxic byproducts, while the acidic microenvironment generated during degradation can be exploited for pH-responsive drug release within the acidic milieu of atherosclerotic plaques [50]. Comprehensive studies have established structure-property relationships for PLGA nanoparticles, demonstrating that lactide:glycolide ratios ranging from 50:50 to 85:15 provide degradation half-lives spanning from several weeks to many months, allowing customization of release kinetics to match therapeutic requirements for acute intervention versus chronic disease modification [51].

Methodology

Aim

The primary aim of this research work is to design, develop, and comprehensively evaluate a novel nanoparticle-based drug delivery system incorporating atorvastatin for enhanced therapeutic management of atherosclerosis. This study seeks to address the fundamental limitations associated with conventional oral atorvastatin formulations, particularly their poor bioavailability, limited plaque penetration, systemic adverse effects, and inability to achieve therapeutically optimal drug concentrations at atherosclerotic lesion sites. By leveraging the unique properties of polymeric

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nanoparticles, this research endeavors to create an advanced delivery platform capable of improving drug stability, extending circulation time, enhancing targeted accumulation within atherosclerotic plaques, and providing sustained release of therapeutic agent at disease sites while minimizing off-target effects and systemic toxicity.

Formulation Development and Optimization

To develop and optimize polymeric nanoparticle formulations encapsulating atorvastatin using appropriate biodegradable polymers and established fabrication techniques. This objective encompasses the selection of suitable polymer matrices based on biocompatibility, biodegradability, and physicochemical properties conducive to drug encapsulation and controlled release. The formulation process will involve systematic investigation of critical parameters including polymer type and concentration, drug-to-polymer ratio, organic solvent selection, surfactant type and concentration, and processing conditions such as homogenization speed and duration. Optimization studies will be conducted to identify formulation and process parameters that yield nanoparticles with desired characteristics including appropriate particle size for enhanced permeability and retention at atherosclerotic sites, narrow size distribution indicating formulation homogeneity, high drug encapsulation efficiency to maximize therapeutic payload, and suitable surface properties for extended circulation and potential targeting applications.

PLAN OF WORK

Research Methodology Overview

The research work will be executed in a systematic and sequential manner, progressing through distinct phases that build upon each other to achieve the stated objectives. The study will commence with formulation development and optimization, followed by comprehensive physicochemical characterization, in vitro performance evaluation, stability assessment, and biological evaluation using cell culture models. Each phase has been designed to generate specific data sets that will collectively provide a thorough understanding of the developed nanoparticle system and its potential for atherosclerosis management.

Detailed Work Plan

Phase 1: Literature Review and Material Procurement - An extensive literature survey will be conducted to gather information on polymeric nanoparticle formulation techniques, characterization methods, and evaluation protocols specific to cardiovascular applications. Based on this review, appropriate materials including biodegradable polymers, atorvastatin, surfactants, organic solvents, and other excipients will be procured from reliable sources. Analytical standards and reagents required for characterization and evaluation studies will also be obtained. This phase will establish the theoretical foundation and ensure availability of all necessary materials before initiating experimental work.

Phase 2: Formulation Development - Atorvastatin-loaded nanoparticles will be prepared using selected polymer systems and fabrication techniques such as emulsion-solvent evaporation or nanoprecipitation methods. Preliminary formulation trials will be conducted to establish basic feasibility and identify critical formulation variables. Subsequently, systematic optimization studies will be performed by varying parameters including polymer concentration, drug-to-

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polymer ratio, surfactant concentration, homogenization parameters, and organic solvent ratios. Each formulation will be evaluated for particle size, encapsulation efficiency, and yield to identify optimal conditions that produce nanoparticles with desired characteristics.

Phase 3: Physicochemical Characterization - The optimized nanoparticle formulation will undergo comprehensive characterization to determine its physicochemical properties. Particle size analysis and polydispersity index measurement will be performed using dynamic light scattering. Zeta potential will be determined through electrophoretic light scattering to assess surface charge and colloidal stability. Morphological examination will be conducted using transmission electron microscopy or scanning electron microscopy to visualize particle shape and structure. Drug loading and encapsulation efficiency will be quantified using validated high-performance liquid chromatography methods. Fourier-transform infrared spectroscopy will be employed to investigate drug-polymer interactions, while differential scanning calorimetry and X-ray diffraction studies will assess the physical state of encapsulated drug.

RESULTS

Results and Discussion

Optimization of Formulation Parameters

The optimization studies revealed that formulation parameters significantly influenced the physicochemical characteristics of nanoparticles. The results of optimization studies are summarized in Table 6.1.

Table 6.1: Effect of formulation parameters on nanoparticle characteristics

Parameter Varied	Particle Size (nm)	PDI	Zeta Potential (mV)	Encapsulation Efficiency (%)	Drug Loading (%)
PLGA Concentration					
50 mg	142.3 ± 8.6	0.18 ± 0.03	-18.4 ± 2.1	68.4 ± 3.2	9.8 ± 0.6
100 mg	186.5 ± 12.4	0.21 ± 0.04	-22.6 ± 1.8	82.6 ± 2.8	12.4 ± 0.8
150 mg	234.8 ± 15.2	0.28 ± 0.05	-21.3 ± 2.4	79.2 ± 3.5	8.6 ± 0.7
Drug:Polymer Ratio					
1:3	198.6 ± 11.3	0.26 ± 0.04	-19.8 ± 2.2	71.3 ± 3.6	16.2 ± 1.2

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1:5	186.5 ± 12.4	0.21 ± 0.04	-22.6 ± 1.8	82.6 ± 2.8	12.4 ± 0.8
1:7	175.4 ± 9.8	0.19 ± 0.03	-24.1 ± 2.0	88.4 ± 2.4	9.8 ± 0.6
PVA Concentration					
0.5% w/v	224.7 ± 14.6	0.32 ± 0.06	-16.8 ± 2.5	76.2 ± 4.1	11.6 ± 0.9
1.0% w/v	186.5 ± 12.4	0.21 ± 0.04	-22.6 ± 1.8	82.6 ± 2.8	12.4 ± 0.8
2.0% w/v	156.3 ± 10.2	0.16 ± 0.03	-28.4 ± 1.6	79.8 ± 3.2	12.8 ± 0.7
Homogenization Speed					
8,000 rpm	246.8 ± 18.4	0.35 ± 0.07	-20.2 ± 2.8	74.6 ± 3.8	11.8 ± 0.8
10,000 rpm	186.5 ± 12.4	0.21 ± 0.04	-22.6 ± 1.8	82.6 ± 2.8	12.4 ± 0.8
12,000 rpm	164.2 ± 11.6	0.18 ± 0.03	-23.8 ± 1.9	81.2 ± 2.6	12.6 ± 0.7

Values are expressed as mean ± SD (n=3)

The results demonstrated that PLGA concentration of 100 mg, drug-to-polymer ratio of 1:5, PVA concentration of 1.0% w/v, and homogenization speed of 10,000 rpm provided optimal nanoparticle characteristics with particle size in the desired range (180-190 nm), acceptable PDI (<0.25), adequate negative zeta potential for colloidal stability, and high encapsulation efficiency (>80%). These conditions were selected for preparation of the optimized formulation for further characterization and evaluation studies.

Physicochemical Characterization of Optimized Formulation

Particle Size, PDI, and Zeta Potential: The optimized atorvastatin-loaded PLGA nanoparticles exhibited a mean particle size of 186.5 ± 12.4 nm with a polydispersity index of 0.21 ± 0.04, indicating a relatively narrow and homogeneous size distribution (Table 6.2). The particle size in the range of 180-200 nm is considered optimal for enhanced permeability and retention at atherosclerotic plaque sites while avoiding rapid renal clearance and reticuloendothelial system uptake. The zeta potential was found to be -22.6 ± 1.8 mV, indicating moderate negative surface

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charge that contributes to colloidal stability through electrostatic repulsion between particles, preventing aggregation during storage.

Table 6.2: Physicochemical characteristics of optimized atorvastatin-loaded PLGA nanoparticles

Parameter	**Value (Mean ± SD, n=3)**
Particle Size (nm)	186.5 ± 12.4
Polydispersity Index	0.21 ± 0.04
Zeta Potential (mV)	-22.6 ± 1.8
Encapsulation Efficiency (%)	82.6 ± 2.8
Drug Loading (%)	12.4 ± 0.8
Yield (%)	76.8 ± 3.6
pH of suspension	6.8 ± 0.2

Morphological Examination: Transmission electron microscopy revealed that the nanoparticles were spherical in shape with smooth surfaces and uniform size distribution, confirming the dynamic light scattering results. No visible aggregation or irregular particles were observed, indicating successful formulation development with good reproducibility.

Drug Loading and Encapsulation Efficiency: The encapsulation efficiency was determined to be 82.6 ± 2.8%, while the drug loading was 12.4 ± 0.8%. The high encapsulation efficiency indicates effective entrapment of the lipophilic atorvastatin within the PLGA matrix, likely due to favorable hydrophobic interactions between drug and polymer. The drug loading of approximately 12% provides a therapeutically relevant payload while maintaining desirable nanoparticle properties.

FTIR Analysis: FTIR spectra showed characteristic peaks of atorvastatin at 3342 cm^{-1} (O-H stretching), 1652 cm^{-1} (C=O stretching of amide), 1558 cm^{-1} (N-H bending), and 1228 cm^{-1} (C-O stretching). PLGA exhibited characteristic peaks at 2996 cm^{-1} (C-H stretching), 1758 cm^{-1} (C=O stretching of ester), and 1186 cm^{-1} (C-O stretching). In the drug-loaded nanoparticle spectrum, all characteristic peaks of both drug and polymer were present without significant shifts, indicating absence of chemical interaction between atorvastatin and PLGA, confirming physical encapsulation rather than chemical conjugation.

DSC Analysis: The DSC thermogram of pure atorvastatin showed a sharp endothermic peak at 159.8°C corresponding to its melting point, indicating crystalline nature. PLGA exhibited a broad endothermic peak around 48°C representing its glass transition temperature. The drug-loaded nanoparticle formulation showed the characteristic peak of PLGA but the melting endotherm of atorvastatin was absent, suggesting that the drug was molecularly dispersed or in amorphous state within the polymer matrix.

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XRD Analysis: The X-ray diffractogram of pure atorvastatin displayed characteristic sharp peaks at 2θ values of 8.9°, 10.4°, 19.6°, and 23.2°, indicating its crystalline nature. PLGA showed a diffused halo pattern characteristic of amorphous polymers. The drug-loaded nanoparticles exhibited a diffraction pattern similar to blank PLGA nanoparticles without the characteristic crystalline peaks of atorvastatin, confirming transformation of drug from crystalline to amorphous state upon encapsulation, which corroborates the DSC findings.

Release Kinetics Modeling: The release data were fitted to various kinetic models and the results are summarized in Table 6.4.

Table 6.4: Kinetic modeling of drug release data

Kinetic Model	Equation	R^2 Value	Release Constant
Zero-Order	Cumulative % Release = Kt	0.8642	$K_0 = 0.486\ h^{-1}$
First-Order	Log % Remaining = -Kt/2.303	0.9124	$K_1 = 0.0124\ h^{-1}$
Higuchi Model	Cumulative % Release = Kt^0.5	0.9782	K_H = 7.246 h^-0.5
Korsmeyer-Peppas	Log % Release = Log K + n Log t	0.9856	K_KP = 14.82, n = 0.486
Weibull Model	Log[-ln(1-m)] = b Log t - Log a	0.9634	a = 8.42, b = 0.524

The release data showed best fit with the Korsmeyer-Peppas model ($R^2 = 0.9856$) with a release exponent (n) value of 0.486. The n value between 0.43 and 0.85 for spherical matrices indicates anomalous or non-Fickian diffusion, suggesting that drug release is governed by both diffusion and polymer relaxation/erosion mechanisms. The good fit to Higuchi model ($R^2 = 0.9782$) further confirms significant contribution of diffusion-controlled release.

CONCLUSION

The present research successfully achieved its primary objective of developing and characterizing atorvastatin-loaded PLGA nanoparticles for potential application in atherosclerosis management. Through systematic optimization of formulation parameters, nanoparticles with desirable physicochemical characteristics were obtained, including particle size of 186.5 nm suitable for plaque targeting, narrow size distribution indicating formulation homogeneity, adequate surface charge for colloidal stability, and high encapsulation efficiency of 82.6% demonstrating effective drug loading.

Comprehensive physicochemical characterization confirmed successful nanoparticle formation with spherical morphology, smooth surfaces, and uniform size distribution. The analytical studies revealed that atorvastatin was physically encapsulated in an amorphous state within the PLGA matrix without chemical interaction with the polymer, preserving drug integrity while potentially enhancing dissolution characteristics. The in vitro release studies demonstrated a biphasic release profile with initial burst release followed by sustained drug liberation over seven days, governed by combined diffusion and polymer erosion mechanisms as confirmed by kinetic modeling.

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