**RESEARCH PAPER**

# Engineering PLGA Nanocomposite Matrices: Influence of Polymer Structure on Drug Release Kinetics and Ocular Pharmacokinetics

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**Abstract:**
The study emphasizes the role of PLGA as a biodegradable polymeric matrix governing drug release through diffusion and polymer erosion mechanisms, thereby functioning as a polymer–drug nanocomposite system. The structural and physicochemical properties of the polymer matrix play a critical role in controlling drug encapsulation and release kinetics. The solvent evaporation technique was utilized to fabricate PLGA nanoparticles, and a $3^2$ factorial design was implemented for optimization. The optimized combination exhibited a zeta potential of −21.5 ± 2.6 mV, a polydispersity index of 0.182 ± 0.03, and an average particle size of 178.6 ± 12.4 nm. The drug loading was determined to be 14.6 ± 1.2%, while the drug entrapment efficiency was found to be 82.3 ± 3.7%. The biphasic release pattern was demonstrated in in vitro release studies. The initial burst release transpired within 6 hours, with a release rate of 21.4 ± 2.1%. The second burst release transpired within 72 hours, yielding a cumulative release rate of 88.7 ± 3.5%. Investigations into the permeability of nanoparticles in goat corneas revealed a 1.97-fold enhancement in the permeability coefficient, with drug infiltration from nanoparticles significantly exceeding that from drug suspension (68.2 ± 4.3% versus 34.6 ± 3.1%; $p < 0.001$). In vivo research on the pharmacokinetics of medicine absorption and ocular residence time in New Zealand albino rabbits ($n = 6$) demonstrated that PLGA nanoparticles significantly enhanced both parameters. The nanoparticle formulation exhibited a peak drug concentration (C_max) of 3.84 ± 0.42 µg/mL in aqueous humor, whereas the suspension demonstrated a concentration of 1.76 ± 0.28 µg/mL ($p < 0.001$). The extended duration to achieve maximum concentration (T_max) (4.0 ± 0.5 h vs. 1.5 ± 0.3 h) indicates a sustained release pattern. The nanoparticles exhibited a 2.2-fold enhancement in bioavailability, evidenced by a much larger area under the curve ($AUC_0$-24h) of 28.6 ± 3.2 µg·h/mL, in contrast to the suspension's 12.9 ± 2.1 µg·h/mL. The results indicate that PLGA nanoparticles offer superior therapeutic efficacy, prolonged drug release, and improved bioavailability as a carrier system for sustained ocular delivery of dexamethasone. The study emphasizes how polymer matrix density, interfacial stabilization, and crystallinity govern diffusion pathways and degradation-controlled release.

**Keywords:** Dexamethasone; ocular drug delivery; sustained release; pharmacokinetics; aqueous humor; bioavailability; corneal permeation
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## Introduction:

In the domain of controlled and sustained release medicine delivery, polymer-based systems and composite materials have emerged as critical elements in the development of new platforms. The biodegradability, mechanical strength, structural adaptability, and programmable degradation kinetics of polymers [1] are distinctive physicochemical properties that facilitate the creation of intricate delivery systems tailored for biomedical applications. Due to their ability to bypass the limitations of conventional formulation techniques, ocular delivery utilizing polymer-drug composites and polymeric nanoparticles has garnered significant attention in this field [2].

The exceptional biocompatibility, biodegradability, and regulatory approval for pharmaceutical applications of poly(lactic-co-glycolic acid) (PLGA) have resulted in its extensive examination compared to other polymers studied. PLGA is an aliphatic polyester that undergoes hydrolytic degradation into the naturally occurring metabolites lactic acid and glycolic acid within the Krebs cycle [3]. The rate of degradation and drug release dynamics are significantly influenced by the polymer's composition, encompassing characteristics such as crystallinity, molecular weight, and the lactic to glycolic acid ratio. PLGA is an excellent candidate for developing polymeric composites that facilitate regulated and sustained medication distribution due to its properties. Polymeric nanocomposites represent an advanced class of materials where the drug is integrated within a polymer matrix, forming a structured system that governs drug release through physicochemical interactions. The performance of such systems depends on polymer composition, molecular weight, crystallinity, and matrix architecture, which collectively influence diffusion pathways and degradation kinetics.[4].

The application of drug-loaded nanoparticles and polymer-drug composites demonstrates potential for enhancing the therapeutic efficacy of bioactive substances. The medication is either adsorbed onto or encapsulated inside the polymer matrix in these systems, forming a composite structure that inhibits rapid degradation of the drug and facilitates controlled diffusion [5]. In ocular applications, where rapid drug clearance is a significant challenge, the nanoscale dimensions of these composites facilitate enhanced interaction with biological membranes, improved penetration, and extended residence time [6].

Dexamethasone, a widely used anti-inflammatory corticosteroid in ophthalmic therapy, exhibits limited ocular absorption in conventional dosage forms. A potential solution to these issues is to improve drug retention at the site of action and facilitate sustained release by incorporating dexamethasone into polymeric nanoparticulate composites such as PLGA nanoparticles [7].

Polymer nanocomposites are defined by the integration of an active phase within a continuous polymer matrix, where interfacial interactions, matrix density, and phase distribution dictate macroscopic properties such as diffusion, mechanical integrity, and degradation kinetics. In polymer-based nanocomposite systems, drug delivery performance is fundamentally governed by structure–property relationships, where parameters such as polymer crystallinity, matrix density, and interfacial stabilization dictate nanoparticle formation, drug encapsulation, and release behavior. The diffusion pathways within the polymer matrix and the rate of polymer degradation collectively determine the kinetics of drug release. Furthermore, colloidal polymer behavior, including surface charge and interfacial interactions, plays a critical role in ensuring nanoparticle stability and biological interaction in ocular environments. Therefore, understanding these polymer-centric mechanisms is essential for rational design of sustained ocular drug delivery systems [8-11].

A comprehensive evaluation of the behavior of polymer-drug composites remains essential, particularly for in vivo pharmacokinetics and sustained drug release, despite significant advancements in polymer-based ocular delivery techniques. This research examines the physicochemical characteristics, release behavior, and in vivo pharmacokinetic performance of PLGA-based nanoparticulate composites containing Dexamethasone. Thus, the present work focuses not only on drug delivery performance but also on understanding the behavior of PLGA as a polymeric composite matrix controlling drug release and bioavailability..

## Material and Methods:

### Materials:

The main polymeric matrix for the creation of nanoparticles was chosen to be poly(lactic-co-glycolic acid) (PLGA; lactide:glycolide ratio 50:50, molecular weight 30,000–60,000), a biodegradable aliphatic polyester. The model medication was dexamethasone. A stabilizing ingredient for emulsion formation was polyvinyl alcohol (PVA; 1-2% w/v). The organic solvents employed to dissolve the polymer were dichloromethane (DCM) and analytical-grade acetone. Throughout the investigation, double-distilled water and analytical-grade reagents were utilized.

### Preparation of Polymer–Drug Nanocomposite System:

During solvent evaporation, polymer precipitation leads to the formation of a dense matrix, where matrix density and polymer chain organization influence drug distribution and subsequent diffusion pathways. The emulsion-solvent evaporation process was used to generate polymer-drug nanocomposites based on PLGA. To summarize, the polymer-drug composite matrix was created by dissolving 100 mg of PLGA and 10 mg of dexamethasone in 5 mL of DCM. This resulted in a homogeneous organic phase. An oil-in-water (O/W) emulsion was created by emulsifying this organic phase with 20 mL of aqueous PVA solution (1% w/v) using high-speed homogenization at 15,000 rpm for 5 minutes. To create nanoscale polymeric composite particles, the emulsion was mixed with a polymer and then stirred continuously at 800 rpm for four hours to let the solvent evaporate and the polymer precipitate. To generate a dry polymeric nanocomposite powder, the nanoparticles were first collected by centrifugation at 15,000 rpm for 20 minutes. After that, they were washed three times to remove excess stabilizer. Finally, they were lyophilized. During solvent evaporation, the polymer precipitates forming a dense matrix encapsulating the drug, thereby generating a nanocomposite structure [12].

### Experimental Design and Optimization of Polymer Composition:

Polymer concentration was selected as a critical factor due to its influence on matrix density and diffusion pathways, while stabilizer concentration was optimized to control interfacial stabilization and colloidal polymer behavior during nanoparticle formation. Polymer concentration ($X_1$) and stabilizer concentration ($X_2$), two crucial polymeric parameters impacting composite formation, were optimized using a $3^2$ factorial design. Because of their bearing on particle formation, interfacial stability, and the density of the polymer matrix, these factors were chosen. The structural and functional performance of the polymeric composite system was assessed by looking at the replies to three questions: particle size ($Y_1$), entrapment efficiency ($Y_2$), and drug release behavior ($Y_3$). In order to determine the correlations between the formulation variables and the answers, the Design-Expert® program was used for statistical analysis and model fitting. Polymer concentration influences matrix density and drug diffusion pathways, while stabilizer concentration affects interfacial characteristics of the polymeric system [13].

### Characterization of Polymeric Nanocomposites:

### Physicochemical Characterization of Polymer Matrix:

To understand polymer‑drug interactions and structural characteristics of the composite system, advanced analytical techniques such as Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC), and X-ray Diffraction (XRD) are recommended. These techniques help evaluate chemical compatibility, thermal transitions, and crystallinity changes within the PLGA matrix [13].

### Crystallinity Analysis (XRD):

The crystalline nature of pure dexamethasone, PLGA, and the prepared nanocomposite formulation was analyzed using X-ray diffraction. The samples were scanned over a 2θ range of 5° to 60° using Cu-Kα radiation (λ = 1.5406 Å) at a fixed voltage and current. The diffraction patterns were recorded to identify characteristic peaks corresponding to crystalline phases. Changes in peak intensity and the presence of amorphous halos were used to assess the physical state of the drug and its dispersion within the polymer matrix [14].

**Thermal Analysis and Glass Transition Temperature (DSC):**
Differential Scanning Calorimetry was employed to determine the thermal transitions of the polymer, drug, and nanocomposite system. Accurately weighed samples were sealed in aluminum pans and heated over a temperature range of 25°C to 250°C at a constant heating rate (typically 10°C/min) under a nitrogen atmosphere to prevent oxidative degradation. The glass transition temperature (Tg) of PLGA and the melting endotherm of dexamethasone were recorded. Variations in thermal events were analyzed to assess changes in polymer chain mobility and the physical state of the drug within the matrix [14].

**Polymer–Drug Compatibility (FTIR):**
Fourier Transform Infrared Spectroscopy was performed to evaluate chemical compatibility and possible interactions between PLGA and dexamethasone. Samples of pure components and nanocomposites were prepared using the KBr pellet method and scanned over a wavenumber range of 4000–500 $cm^{-1}$. The characteristic functional group peaks of the polymer and drug were identified and compared. Any shifts, disappearance, or appearance of peaks were analyzed to detect potential interactions or chemical modifications during formulation [14].

**Particle Size, Polydispersity Index (PDI), and Surface Charge:**
To determine the zeta potential, size distribution, and hydrodynamic diameter of the polymeric nanoparticles, dynamic light scattering (DLS) was used. These parameters have a crucial role in determining the stability of polymer dispersion and the interactions between particles. The data were shown as the mean ± standard deviation of three duplicates, and the measurements were taken at 25°C following the proper dilution [14].

**Morphological and Structural Analysis:**
We used scanning electron microscopy (SEM) to look at the polymeric nanocomposites' surface shape and how well they were made. Particle form, surface smoothness, and aggregation behaviour which indicate properties of the polymer matrix during solidification were evaluated by seeing samples that had been sputter-coated with gold to increase conductivity [15].

**Drug–Polymer Interaction and Loading Efficiency:**
The efficiency of drug integration inside the polymer matrix was evaluated by determining the entrapment efficiency (EE%) and drug loading (DL%). In order to liberate the imprisoned Dexamethasone, the polymeric network was disrupted by dissolving the nanoparticles in acetone. The amount of drug was measured using spectrophotometry at a wavelength of 242 nm. Composite formation efficiency and polymer-drug compatibility can be understood with the help of these characteristics [16].

***In-Vitro* Drug Release from Polymeric Matrix:**
The dialysis bag diffusion method was used to assess the dexamethasone release behavior from the PLGA polymeric composite system. The solution was maintained at 37 ± 0.5°C with steady stirring while nanoparticles containing 2 mg of medication were immersed in phosphate-buffered saline (PBS, pH 7.4) and deposited in a dialysis membrane (MWCO 12,000-14,000 Da). Spectrophotometric analysis was performed on samples taken at pre-arranged intervals up to 72 hours. Two intrinsic release mechanisms of PLGA composites, one regulated by diffusion and the other by polymer breakdown, were evaluated using the release profile [17].

***Ex-Vivo* Corneal Permeation Study:**
Using a Franz diffusion cell and an excised goat cornea, we tested the polymeric nanocomposite system's permeability properties. The receptor compartment was kept at physiological temperature and filled with PBS (pH 7.4). After 8 hours of applying the nanoparticle formulation and medication suspension to the donor compartment, samples were taken. The effect of polymeric carriers on transcorneal drug transport was assessed by determining the drug concentration and calculating the apparent permeability coefficient [18].

***In-Vivo* Pharmacokinetic Evaluation of Polymeric System:**
The polymeric nanocomposite system was tested in live animals using six New Zealand albino rabbits weighing 2.0-2.5 kg. The Institutional Animal Ethics Committee gave their stamp of approval to the research plan. Experimental

groups included animals given either a standard medication suspension or a nanoparticulate composite formulation based on PLGA. The lower conjunctival sac was injected with a single dose, which was 50 µL. Under a light anesthetic, aqueous humor samples were taken at predetermined intervals ranging from half an hour to twenty-four hours. Using a proven HPLC method, the drug concentration was measured. To evaluate the effect of polymeric encapsulation on the ocular drug disposal, pharmacokinetic parameters such as C_max, T_max, and AUC$_0$-24h were computed using non-compartmental analysis [19].

## Statistical Analysis:

Statistical methods such as Student's t-test and one-way analysis of variance (ANOVA) followed by Tukey's post hoc test were utilized to examine all of the experimental data. The mean and standard deviation (SD) were the statistical measures that were utilized to assess the data. At a significance level of $p < 0.05$, differences were deemed to be statistically significant.

## Results:

### Characterization of Polymeric Nanocomposites:

FTIR analysis was conducted to investigate the chemical compatibility and intermolecular interactions between PLGA and dexamethasone. Spectra were recorded over a wavenumber range of 4000–500 cm$^{-1}$ using the KBr pellet method. The presence, shift, or disappearance of characteristic functional group peaks was analyzed to assess potential interactions and confirm successful incorporation of the drug into the polymer matrix. DSC analysis was performed to evaluate the thermal properties and phase behavior of the polymeric nanocomposite. Samples of pure polymer, drug, and nanocomposite were heated over a temperature range of 25–250°C at a controlled heating rate under a nitrogen atmosphere. The glass transition temperature (Tg) of PLGA and melting endotherms of dexamethasone were analyzed to determine changes in crystallinity and molecular dispersion within the composite system. XRD analysis was carried out to assess the crystalline or amorphous nature of the components and the final nanocomposite formulation. Diffraction patterns were recorded over a 2θ range of 5°–60° using Cu-Kα radiation. The disappearance or reduction of characteristic crystalline peaks of dexamethasone in the nanocomposite was used as an indicator of amorphization and successful dispersion within the PLGA matrix.

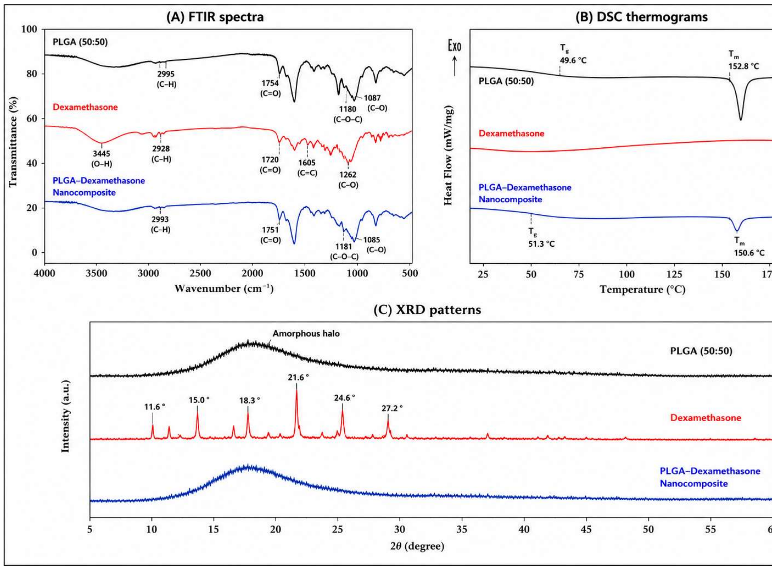

**Figure 1: Physicochemical characterization of PLGA-based polymeric nanocomposites using FTIR, DSC, and XRD analysis.**

### Particle Size, Polydispersity Index (PDI), and Surface Charge:

The observed surface charge reflects colloidal polymer behavior, where electrostatic repulsion contributes to interfacial stabilization and prevents aggregation, thereby maintaining dispersion stability. The emulsion-solvent evaporation process was used to successfully synthesize the PLGA-based polymer-drug nanocomposite system. The optimization process using a factorial design revealed that the concentration of polymers had a substantial impact on drug encapsulation and particle size, whereas the concentration of stabilizers affected the stability of the dispersion. The uniform size distribution was shown by the improved formulation's low polydispersity index (0.182 ± 0.03) and an average particle size of 178.6 ± 12.4 nm. Electrostatic repulsion likely contributed to the good colloidal stability, as indicated by the zeta potential measurement of −21.5 ± 2.6 mV. Drug loading was 14.6 ± 1.2% and entrapment efficiency was 82.3 ± 3.7%, respectively, indicating that Dexamethasone was effectively incorporated into the polymer matrix (Table 1). Particle size and drug encapsulation were influenced by polymer matrix density and polymer–drug interactions within the composite structure.

**Table 1. Physicochemical Characterization of PLGA Nanocomposites**

| Parameter | Value |
|---|---|
| Particle Size (nm) | 178.6 ± 12.4 |
| PDI | 0.182 ± 0.03 |
| Zeta Potential (mV) | −21.5 ± 2.6 |
| Entrapment Efficiency (%) | 82.3 ± 3.7 |
| Drug Loading (%) | 14.6 ± 1.2 |

**Morphological Analysis:**

The spherical morphology and smooth surface indicate uniform polymer precipitation, suggesting controlled interfacial stabilization and matrix formation, which are critical for defining internal diffusion pathways. The nanoparticles were found to be spherical, with smooth surfaces and minimal aggregation, as demonstrated by scanning electron microscopy. This finding provides evidence that the nanoparticles successfully formed a polymeric composite structure that was uniform through its composition. Figure 1 is a scanning electron micrograph that demonstrates PLGA-based polymeric nanocomposites that are spherical and uniformly dispersed throughout the nanocomposites.

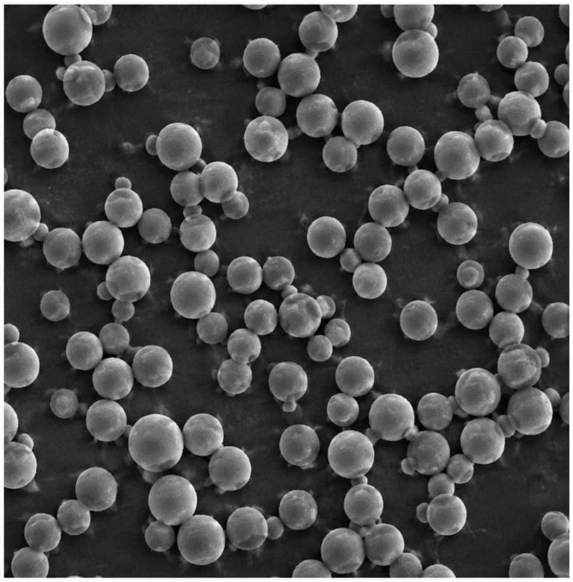

**Figure 2. SEM Image of PLGA Nanocomposites**

**Polymer Matrix Behavior and Drug Release Mechanism:**

The PLGA nanocomposite system exhibited a biphasic drug release pattern governed by polymer matrix characteristics. The initial burst release is attributed to surface-associated drug, whereas the sustained phase is controlled by diffusion through the polymer matrix followed by gradual polymer degradation. This confirms that drug release is matrix-controlled rather than purely diffusion-driven.

***In-Vitro* Drug Release Study:**

The biphasic release pattern can be attributed to structure–property relationships within the polymer matrix, where the initial burst release is governed by drug located near the surface, while the sustained phase is controlled by diffusion through the polymer matrix and gradual polymer degradation. The matrix density and polymer crystallinity influence the tortuosity of diffusion pathways, thereby regulating drug release kinetics. Dexamethasone released in two distinct phases from PLGA nanocomposites in vitro. There was a rapid release of 21.4 ± 2.1% in the first 6 hours, and then a steady release of 88.7 ± 3.5% in the subsequent 72 hours. The rate of release was indicative of a process that involved both polymer degradation and diffusion-controlled release. The In-Vitro Drug Release Profile is displayed in Table 2. Dexamethasone is released continuously from PLGA polymeric nanocomposites, as seen in Figure 2 of the Cumulative release profile. Sustained release was governed by diffusion through the PLGA polymer matrix and its subsequent degradation.

**Table 2. *In-Vitro* Drug Release Profile**

| Time (h) | % Drug Released |
|---|---|
| 1 | 8.2 ± 1.1 |
| 2 | 14.5 ± 1.6 |
| 6 | 21.4 ± 2.1 |
| 12 | 38.7 ± 2.8 |
| 24 | 56.3 ± 3.2 |
| 48 | 72.5 ± 3.6 |
| 72 | 88.7 ± 3.5 |

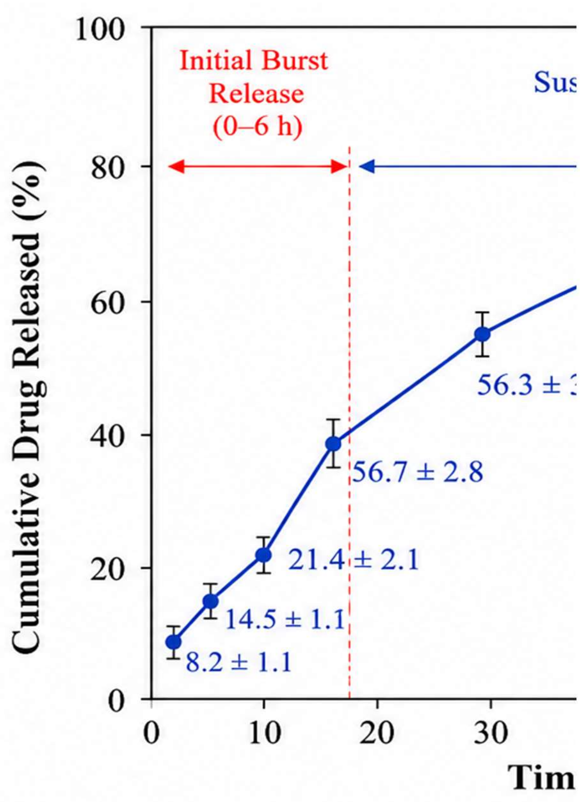

**Figure 3.** ***In-Vitro*** **Release Profile of Dexamethasone from PLGA Nanocomposites**

The observed biphasic release profile can be mechanistically explained based on polymer matrix architecture and structure–property relationships. The initial burst release is attributed to the rapid diffusion of drug molecules weakly associated with or adsorbed onto the nanoparticle surface, reflecting short and less tortuous diffusion pathways. In contrast, the sustained release phase is governed by a combination of diffusion through the dense polymer matrix and progressive polymer degradation. The matrix density of PLGA plays a crucial role in restricting drug mobility by increasing diffusional path length, while polymer crystallinity influences water penetration and hydrolytic degradation rates, thereby modulating release kinetics. As the polymer undergoes bulk erosion, the formation of microvoids and channels further facilitates controlled drug diffusion. This interplay between diffusion and degradation mechanisms confirms that drug release is predominantly matrix-controlled rather than purely diffusion-driven.

### *Ex-Vivo* Corneal Permeation Study:

The enhanced permeation may also be associated with colloidal polymer behavior and interfacial interactions, facilitating closer contact with the corneal surface and improving drug transport. There was a discernible improvement in the corneal penetration of the polymeric nanocomposite formulation when compared to the normal suspension. On the other hand, when compared to the suspension, which shown a cumulative drug permeation of 34.6 ± 3.1% ($p < 0.001$), nanoparticles demonstrated a value of 68.2 ± 4.3%. Because of the interaction between the nanoscale size and the polymer, the apparent permeability coefficient (P_app) increased by approximately 1.97 times, which indicates that there was an increase in the amount of molecules that were able to pass through the ocular barrier (Table 3).

**Table 3.** ***Ex-Vivo*** **Corneal Permeation Parameters**

| Parameter | Suspension | Nanocomposite |
|---|---|---|
| % Drug Permeated | 34.6 ± 3.1 | 68.2 ± 4.3 |
| P_app (cm/s ×$10^{-6}$) | 2.1 ± 0.3 | 4.1 ± 0.5 |

### *In-Vivo* Pharmacokinetic Study:

The prolonged T_max and enhanced AUC are indicative of controlled drug release governed by polymer degradation and diffusion pathways, highlighting the role of polymer matrix architecture in modulating pharmacokinetic behavior. The PLGA nanocomposite formulation greatly enhanced the ocular drug bioavailability, as demonstrated by the in-vivo pharmacokinetic study. The nanoparticles had a C_max of 3.84 ± 0.42 µg/mL, while the suspension had a C_max of 1.76 ± 0.28 µg/mL ($p < 0.001$). A longer T_max (4.0 ± 0.5 h vs. 1.5 ± 0.3 h) suggests that the medication was released gradually over time. In addition, the nanoparticles had a considerably larger $AUC_0$-24h (28.6 ± 3.2 µg·h/mL) compared to the solution (12.9 ± 2.1 µg·h/mL), showing a bioavailability increase of 2.2 times. As shown in Table 4 Figure 3, the plasma concentration-time profile demonstrates that the drug levels are improved and sustained when formulated with PLGA nanocomposite.

**Table 4. Pharmacokinetic Parameters**

| Parameter | Suspension | Nanocomposite | p-value |
|---|---|---|---|
| C_max (µg/mL) | 1.76 ± 0.28 | 3.84 ± 0.42 | < 0.001 |
| T_max | 1.5 ± 0.3 | 4.0 ± 0.5 | < |

| | | | |
|---|---|---|---|
| (h) | | | 0.01 |
| $AUC_0$–24h (µg·h/mL) | 12.9 ± 2.1 | 28.6 ± 3.2 | < 0.001 |

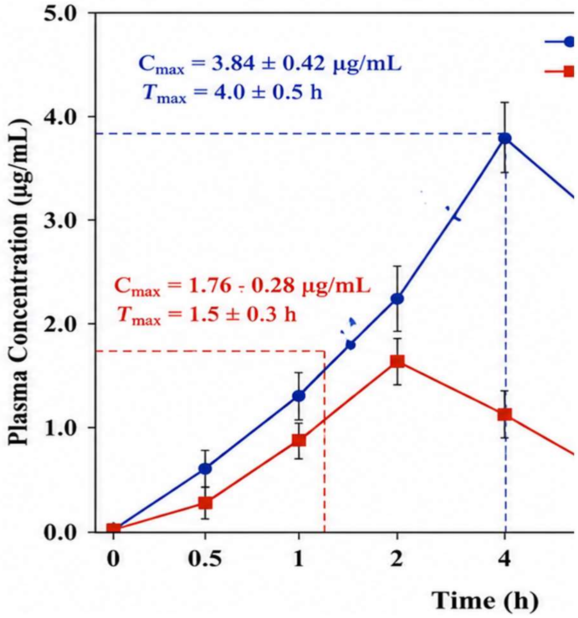

**Figure 4. Plasma Concentration–Time Profile**

**Discussion:**

The present study demonstrates that the performance of PLGA-based nanocomposites is strongly governed by structure–property relationships, where polymer degradation, matrix density, diffusion pathways, and polymer crystallinity collectively influence drug release behavior and pharmacokinetic performance. Highlighting the crucial significance of polymer engineering in improved polymeric nanocomposite matrixs, the focus on polymer and composite design allowed controlled manipulation of physicochemical properties, drug release behavior, and in vivo performance [20]. From a polymer science perspective, the observed behavior can be explained by the degradation kinetics of PLGA, which involves hydrolysis of ester linkages leading to gradual erosion of the polymer matrix. This process significantly contributes to sustained drug release. From a mechanistic perspective, matrix density plays a critical role in defining diffusion pathways, where densely packed polymer networks restrict drug mobility, resulting in sustained release. Additionally, polymer crystallinity influences water penetration and degradation kinetics, thereby modulating drug release profiles. The interplay between these factors establishes a controlled release system governed by both diffusion and polymer erosion mechanisms. The optimized nanoparticles were ideal for use in the eye since their size distribution was narrow and their mean particle size was less than 200 nm. The effective stability and emulsification of the polymeric phase during production is responsible, from a polymer science standpoint, for this nanoscale size [21].

Reducing aggregation and improving formulation stability, the observed negative zeta potential suggests electrostatic stabilization of the colloidal system. In addition, the excellent compatibility between PLGA and dexamethasone is evident from the high entrapment efficiency, which indicates that the polymer-drug interactions inside the composite matrix are beneficial [22].

The structure–property relationship of the polymeric composite system plays a crucial role in determining drug release kinetics, where matrix porosity, polymer crystallinity, and molecular weight influence diffusion and degradation behavior. The presence of homogenous polymer precipitation and matrix formation was supported by morphological examination, which verified the creation of spherical nanoparticles with smooth surfaces. Because it affects the drug's diffusion paths and release kinetics directly, structural integrity is crucial in polymeric composites. Nanoparticles synthesized with a high concentration of stabilizers and a dispersion of polymers do not aggregate, lending credence to this claim [23].

The role of interfacial stabilization and colloidal polymer behavior is equally important in determining nanoparticle stability and biological interaction. The presence of stabilizer ensures proper dispersion by reducing interfacial tension, while the surface charge contributes to electrostatic stabilization. These properties enhance nanoparticle interaction with ocular tissues, thereby improving drug retention and permeation. There was an initial burst release and then sustained drug release over 72 hours in the in vitro release profile, indicating a biphasic pattern. Two separate mechanisms, one involving the quick release of the drug linked with the surface and the other involving diffusion-controlled release from the polymer core, account for this characteristic behavior of PLGA-based polymeric systems. Another way that polymer composition controls drug delivery kinetics is through the slow breakdown of polylactic acid (PLGA), which adds to sustained release. These results prove that the nanocomposite matrix serves its intended purpose as a controlled-release device [24].

Research on the drug's permeability outside of living organisms showed that it was much more effectively transported into the cornea than the standard suspension method. The enhanced performance is because the polymeric composites are able to contact with the corneal epithelium more closely due to their nanoscale size and larger surface area. In addition, PLGA's polymeric structure may facilitate the short-term alteration of epithelial barrier characteristics, leading to an improvement in drug penetration. To overcome obstacles to ocular delivery, polymer-based nanocomposites are advantageous, as shown by the nearly twofold increase in permeability coefficient [25].

The drug release behavior from PLGA nanocomposites can be interpreted using classical polymer-controlled release models. The observed biphasic profile indicates a combination of diffusion-controlled and erosion-controlled mechanisms, typical of biodegradable polymers. The initial burst release is governed by rapid diffusion of surface-associated drug, consistent with the Higuchi model (Fickian diffusion). In contrast, the sustained phase arises from coupled matrix diffusion and polymer degradation, reflecting non-Fickian transport as described by the Korsmeyer–Peppas model. In PLGA systems, hydrolytic cleavage of ester bonds leads to bulk erosion, increasing matrix porosity and facilitating drug diffusion over time. Limited polymer hydration and swelling further contribute by enabling water penetration and pore formation. The release profile deviates from zero-order kinetics and more closely follows first-order behavior, where release depends on residual drug concentration. Overall, drug release is governed by a coupled diffusion–degradation mechanism, controlled by matrix density, degradation kinetics, and evolving diffusion pathways.

Additional confirmation of the polymeric nanocomposite system's superiority comes from the in vivo pharmacokinetic studies. Improved drug absorption and sustained release in ocular tissues are suggested by the observed increases in C_max and AUC, as well as a longer T_max. From a polymer-composite perspective, this is because the PLGA matrix slowly erodes and degrades over time, allowing for continuous drug release over a long duration. Polymer encapsulation is efficient in minimizing precorneal drug loss and prolonging residence time, as demonstrated by the considerable improvement in bioavailability [26]. However, detailed polymer characterization studies such as FTIR, DSC, and XRD were not performed, which could further elucidate molecular interactions and structural properties of the composite system. The observed pharmacokinetic enhancement can be directly linked to polymer-controlled drug release, where the gradual degradation of the polymer matrix sustains drug availability, while structured diffusion pathways regulate release rate.

This work emphasizes the importance of integrating polymer science with pharmaceutical design in order to obtain desired therapeutic effects through the tailoring of composite systems. An adaptable framework for improving medication delivery performance is provided by the capacity to alter polymer composition, particle size, and drug-polymer interactions. But there are some restrictions that need to be thought about. Molecular drug-polymer interactions could not be further understood in this work since advanced polymer characterisation methods including FTIR, DSC, and XRD were not utilized. Further research is also needed to determine the polymeric system's scalability and long-term durability. To further improve ocular targeting and treatment efficacy, future studies may investigate the use of composite coatings or surface-functionalized polymers [27-30].

## Conclusion:

The findings emphasize that polymer structure–property relationships, including matrix density, diffusion pathways, and degradation kinetics, are key determinants of sustained drug delivery performance. This study highlights the importance of PLGA as a polymeric matrix in designing nanocomposite polymeric nanocomposite matrixs. As a result of efficient polymer-drug integration into the composite matrix, the optimized nanocomposite system displayed desirable physicochemical properties, such as stable surface charge, high entrapment efficiency, and nanoscale particle size. An early burst followed by extended drug release characterizes the biphasic in vitro release profile, confirming that the PLGA polymer matrix may provide regulated and sustained administration through combination diffusion and degradation mechanisms. Nanoscale polymeric systems have the added benefit of improving corneal permeability, which allows them to bypass ocular obstacles. Drug bioavailability was significantly improved in vivo pharmacokinetic evaluation compared to standard suspension, with higher C_max, longer T_max, and enhanced AUC values. Both the ocular residence time and the sustained therapeutic drug levels are improved by polymeric encapsulation, according to these results. The findings emphasize the potential of polymer and composite engineering in developing advanced biomedical delivery systems.

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None

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