

Article

A Mechanistic Diffusion–Erosion Model for Drug Release from Shrinking Cylindrical Matrices

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Abstract

Drug release from long-acting intravitreal implants is governed by the coupled effects of diffusion, hydrolysis-driven erosion, and progressive shrinkage of the polymeric matrix. To capture these mechanisms, we solve the diffusion equation in a cylindrical domain whose radius decreases according to the hydrolytic degradation kinetics of PLGA, which follow a pseudo-first-order behaviour in aqueous excess. The resulting formulation combines a modal Bessel expansion with an erosion-controlled time transformation, allowing the evolving geometry and the attenuation of the diffusion modes to be incorporated in a fully mechanistic manner. Within this framework, the shrinkage parameter p quantifies the rate of erosion-induced geometric evolution and enables an accurate reconstruction of the experimental dexamethasone release profile. The solution reproduces both the initial fast-release phase and the extended depletion tail from which the characteristic times $t_{0.50} = 264.3$ h and $t_{0.90} = 996.5$ h are extracted, providing compact and physically meaningful indicators of the transition between early and late kinetic regimes. Overall, the approach offers a robust and interpretable description of drug release from shrinking polymeric systems and is directly applicable to the design of long-acting intravitreal therapies.

Keywords: drug release modelling; polymer degradation; time-dependent diffusivity; Bessel eigenfunction expansion; intravitreal implants

1. Introduction

Intravitreal drug delivery remains a major challenge in ophthalmology, where the need for sustained therapeutic concentrations must be balanced against the anatomical and physiological constraints of the eye [1]. Biodegradable implants based on poly(lactic-co-glycolic acid) (PLGA) have emerged as clinically validated platforms for long-term treatment of retinal diseases, as demonstrated by the fluocinolone acetonide and dexamethasone devices [2,3]. These systems rely on the interplay between polymer hydration, bulk erosion, autocatalytic degradation, and drug diffusion to achieve controlled release over weeks to months [4,5]. Despite their widespread use, the mechanistic understanding of cylindrical PLGA implants remains incomplete. Classical diffusion-based models typically assume constant diffusivity, fixed geometry, or simplified empirical release laws [6,7]. Such approaches can reproduce early-time Fickian behaviour but fail to capture the evolving microstructure of degrading PLGA, including pore formation, autocatalytic cleavage, and changes in crystallinity [8,9]. Moreover, fixed-geometry formulations neglect the progressive reduction in the implant radius, which shortens the diffusion path length and



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accelerates release in the later stages. These limitations are particularly problematic in the ocular environment, where predicting the duration of therapeutic exposure is essential for treatment planning, patient compliance, and the design of next-generation intravitreal devices [1,10]. Empirical or semi-empirical models often underestimate late-stage acceleration or overestimate residence time, leading to inaccurate estimates of clinically relevant metrics such as $t_{0.5}$ and $t_{0.9}$. Recent advances in moving-boundary diffusion theory have highlighted the importance of coupling polymer erosion with transport processes. In PLGA systems, bulk hydrolysis proceeds as a pseudo-first-order reaction under a large excess of water [11], resulting in an exponential decay in the implant radius, $R(t)$. This geometric shrinkage modifies the diffusion path length and accelerates release as degradation progresses. Through the Landau transformation [12], the moving-boundary problem can be mapped onto a fixed domain, yielding a diffusion equation with a time-dependent effective diffusivity governed by the erosion profile $\rho(\tau)$. The resulting model admits a semi-analytical solution based on Bessel eigenfunction expansion. Volume integration of the modal solution yields a closed-form expression for the residual mass inside the shrinking cylinder, enabling direct comparison with experimental release data through the normalized mass fraction or the released fraction. This formulation captures both early-time diffusion-dominated release and late-time erosion-driven acceleration without resorting to empirical corrections. The erosion parameter p is identified by nonlinear least squares using experimental release data from the clinically validated dexamethasone implant [3]. To quantify parameter uncertainty, we compute the numerical Hessian of the objective function and derive the associated covariance matrix. Uncertainty is then propagated to the model prediction $F(t)$ to obtain 95% confidence bands, providing a statistically rigorous assessment of model reliability. Residual analysis and RMSE quantification further validate the adequacy of the proposed framework.

2. Materials and Methods

The dexamethasone intravitreal rod implant (Ozurdex[®]) employed in this study was obtained from a certified commercial supplier (Allergan s.p.a., Rome, Italy) and used as received. A rod with a diameter of 0.46 mm, length of 6.0 mm and mass of 1.0 mg, containing 700 µg of dexamethasone, was placed in a sealed quartz cuvette containing 1.0 mL of 2-[4-(2-hydroxyethyl)piperazin-1-yl]ethanesulfonic acid (HEPES) buffer solution (pH = 7.2). The evolution of the sample was monitored spectrophotometrically by measuring the sample's absorbance over time with a Cary 100 Varian UV-Vis, Agilent, Australia, equipped with thermostatted cells. The buffer solution and rod were placed in a rectangular quartz cell of 1 cm path length. Absorption spectra were recorded at $(30.0 \pm 0.5)^\circ\text{C}$ in the 200–800 nm wavelength region and the dexamethasone spectra were recorded at different times.

3. Results

Intravitreal corticosteroid drugs, such as the sustained-release dexamethasone implant, play an important role in the treatment of retinal diseases, thanks to their combined anti-inflammatory and anti-edematous effects [13]. This drug is administered via intravitreal injection, as shown in Figure 1. The intravitreal implant, schematized in Figure 1, suggests the following qualitative scenario: upon initial contact with the vitreous body, which is 99% water, the polymer matrix absorbs water molecules, a fraction of which participate in hydrolytic reactions that induce chain scission [14]. Schematically, the reaction can be represented as



where R_1 and R_2 denote polymer segments of poly(lactic-co-glycolic acid) (PLGA) of variable lengths generated during the progressive degradation process.

A single hydrolytic event does not immediately dissolve the material, but it shortens the polymer chains. Only when chain-scission events accumulate to the point where the resulting fragments become sufficiently small do they become water-soluble, leading to the onset of macroscopic dissolution. Moreover, each hydrolysis event generates a carboxylic acid group, thereby increasing local acidity and accelerating further water ingress in an autocatalytic manner. As the number of reactive sites increases, the probability that an inter-crosslink chain is cleaved rises accordingly, promoting detachment and subsequent leaching of fragmented segments. This degradation behaviour is intentionally modulated in clinical implants by employing a blend of 50:50 PLGA (16.400 gmol^{-1}) with ester end-groups and 50:50 PLGA with acid end-groups [15]. The combination of these two architectures provides a controlled balance between initial stability and progressive autocatalytic erosion, enabling dexamethasone to be released over extended periods of approximately 4–6 months. The complete biodegradation of the matrix eliminates the need for surgical removal, representing a major advantage for intravitreal therapy.

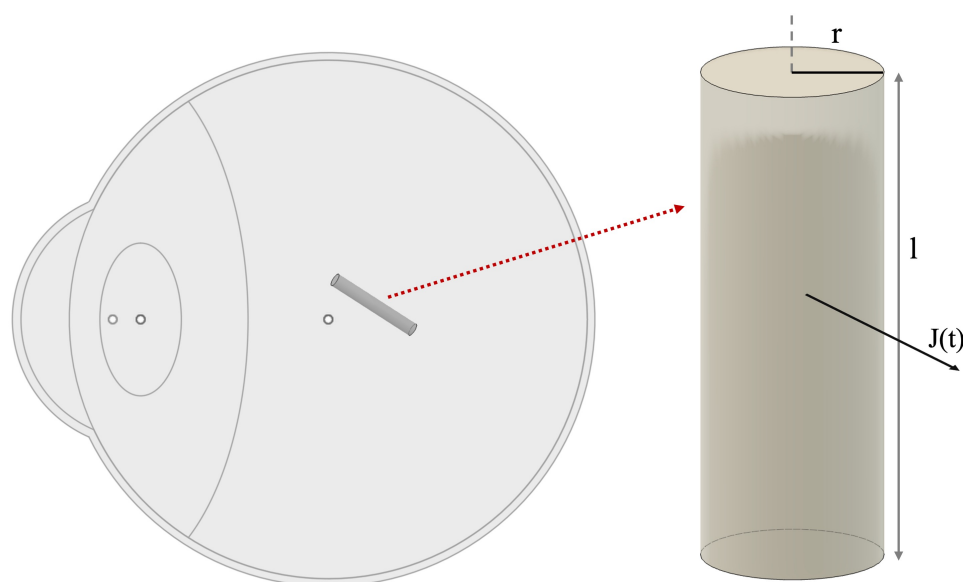


Figure 1. Minimal schematic of the eye with a PLGA cylindrical implant (**left**). The exploded view (**right**), placed well outside the eye, shows the full cylindrical geometry used in the mathematical model, including radius $R(r)$, length L , radial coordinate r , and outward flux $J(r)$ at the boundary. (Black arrow) The red dashed arrow directs the reader to a zoomed-in view of the detail.

The process proceeds from the outside in, eroding the rod's radius. The cylinder is much longer than it is wide, so the drug release process is effectively radially symmetric. Under these conditions, the local drug concentration C , which is a function of time t and radial coordinate r , will satisfy the diffusion equation [12]

$$\frac{\partial C}{\partial t} = D \left(\frac{\partial^2 C}{\partial r^2} + \frac{1}{r} \frac{\partial C}{\partial r} \right), \quad 0 \leq r \leq R(t) \quad (2)$$

along with the initial condition

$$C(r, 0) = C_0(r) \quad (3)$$

The choice of the initial value problem described by Equation (3) is not a serious restriction, since one can generalize this initial value problem to boundary value problems by means of the superposition integral. If the wall is a sink,

$$C(R(t), t) = 0, \quad (4)$$

and since amount of drug in the system is finite,

$$\left. \frac{\partial C}{\partial r} \right|_{r=0} = 0 \quad (5)$$

If the dimensionless quantities

$$X = \frac{r}{R_0}, \quad \tau = \frac{D_0 t}{R_0^2}, \quad \tilde{C}(x, \tau) = \frac{C(r, t)}{C_0} \quad (6)$$

are defined, Equations (2)–(5) can be rewritten as

$$\begin{cases} \frac{\partial \tilde{C}}{\partial \tau} = \frac{\partial^2 \tilde{C}}{\partial X^2} + \frac{1}{X} \frac{\partial \tilde{C}}{\partial X} & \text{for } 0 \leq X \leq \rho(\tau) \\ \tilde{C}(\rho(\tau), \tau) = 0 \\ \frac{\partial \tilde{C}(0, \tau)}{\partial X} = 0 \\ \tilde{C}(X, 0) = 1 \end{cases} \quad (7)$$

Now, to map the domain that shrinks over time onto a constant domain, the Landau transformation [12]

$$\xi = \frac{X}{\rho(\tau)}, \quad 0 \leq \xi \leq 1, \quad U(\xi, \tau) = \tilde{C}(x, \tau) \quad (8)$$

is applied, so that the model is transformed into

$$\frac{\partial U}{\partial \tau} = \frac{1}{\rho(\tau)^2} \left(\frac{\partial^2 U}{\partial \xi^2} + \frac{1}{\xi} \frac{\partial U}{\partial \xi} \right) + \xi \frac{\rho'(\tau)}{\rho(\tau)} \frac{\partial U}{\partial \xi}, \quad U(1, \tau) = 0, \quad \frac{\partial U}{\partial \xi}(0, \tau) = 0, \quad U(\xi, 0) = 1. \quad (9)$$

The solution to this equation is chosen as a superposition of the eigenfunctions of the Bessel equation [16], i.e.,

$$U(\xi, \tau) = \sum_{n=1}^{\infty} a_n(\tau) J_0(\lambda_n \xi). \quad (10)$$

If one introduces Equation (10) into Equation (9) and takes into account the orthogonality of the Bessel functions, one obtains

$$\frac{da_n(\tau)}{d\tau} = -\lambda_n^2 \left[\frac{1}{\rho(\tau)^2} + \frac{1}{\rho(\tau)} \frac{d\rho(\tau)}{d\tau} \right] a_n(\tau), \quad (11)$$

where the relationship

$$\int_0^1 \xi^2 J_0(\lambda_n \xi) \frac{\partial U}{\partial \xi} d\xi = \lambda_n^2 a_n(\tau) \quad (12)$$

is used.

The solution of Equation (11) is cast into the form

$$a_n(\tau) = a_n(0) \exp(-\lambda_n^2 E(\tau)), \quad E(\tau) = \log \rho + \int_0^\tau \frac{d\sigma}{\rho(\sigma)^2} \quad (13)$$

and

$$a_n(0) = \frac{2}{\lambda_n J_1(\lambda_n)^2} \int_0^1 \xi J_0(\lambda_n \xi) d\xi = \frac{4}{\lambda_n^2 J_1(\lambda_n)^2} \quad (14)$$

Finally, the model solution assumes the form

$$U(\xi, \tau) = \sum_{n=1}^{\infty} a_n(0) \exp(-\lambda_n^2 E_n(\tau)) J_0(\lambda_n \xi), \quad \sum_{n=1}^{\infty} a_n(0) = 1 \quad (15)$$

This expression contains all geometric and kinetic effects through erosion parameter, $\rho(\tau)$.

3.1. Selection of the Erosion Parameter

The proposed model admits an analytical solution in closed form only if the time evolution of erosion, $\rho(\tau)$, is known. On the other hand, the reaction schematized in Equation (1) proceeds with a progressive mass loss of the polymer dm_p over a time interval dt , proceeding from the outer surface toward the interior. Under typical experimental conditions, water is present in a large excess; therefore, the mass-loss kinetics can be empirically described as a first-order process [11]

$$\frac{dm_p}{dt} = -\frac{m_p}{\tau_H} \quad (16)$$

where τ_H denotes the characteristic hydrolysis lifetime [17].

Since the density of the inner, non-hydrolyzed core remains constant and equal to d , and the volume at time t is $V(t) = \pi R(t)^2 L$, Equation (16) can be rewritten in terms of the time evolution of the radius $R(t)$:

$$\frac{dR}{dt} = -\frac{R(t)}{\tau_E} \quad (17)$$

where $\tau_E = 2\tau_H$ is the characteristic erosion time. The solution of Equation (17) is

$$R(t) = R_0 \exp\left(-\frac{t}{\tau_E}\right) \Rightarrow \rho(\tau) = \exp(-p\tau) \quad \text{with} \quad p = \frac{\tau_D}{\tau_E} \quad (18)$$

It is also worth noting that hydrolytic degradation in vivo is not a perfectly uniform process. Accidental cleavage of polymer chains may occur during the residence of the device in the physiological environment, and partial re-crosslinking of fragmented segments is also possible. These stochastic events contribute to a heterogeneous erosion front and modify the effective diffusional pathways within the matrix. In this way, the boundary conditions inherently account for the pseudo-first-order erosion kinetics and for the fact that the cylindrical matrix behaves as a sink, continuously reducing its radius while allowing the drug to diffuse outward without accumulation.

As $t \rightarrow \infty$, the radius $R(t)$ exponentially decays to zero, and the spatial domain of the implant collapses. In this limit, the transformed diffusion problem becomes degenerate, since the effective time $E(\tau)$ diverges and all modal contributions are fully suppressed by the factor $\exp[-\lambda_n^2 E(\tau)]$. Accordingly, the residual mass vanishes, indicating that the release process is physically complete. Furthermore, the shrinkage parameter p quantifies the erosion process in terms of diffusion lifetime [17].

3.2. Drug Release

Given the erosion profile $\rho(\tau)$, the concentration within the polymer matrix can be determined; in fact, by substituting Equation (18) into Equation (13), one finds

$$E(\tau) = -p\tau + \frac{e^{2p\tau} - 1}{2p} \quad (19)$$

which makes it possible to reconstruct the temporal evolution of the residual mass inside the cylindrical domain. In this way, the boundary conditions inherently account for the pseudo-first-order erosion kinetics and for the fact that the cylindrical matrix behaves as a sink, continuously reducing its radius while allowing the drug to diffuse outward without accumulation.

In radial geometry, the solution of the diffusion equation with a time-dependent radius can be expressed as a modal expansion over the eigenfunctions of the Bessel operator. The contribution of the n -th mode is attenuated by an exponential factor depending on the geometric eigenvalue λ_n and on the effective time $E(\tau)$. The normalized mass therefore reads

$$\frac{M(\tau)}{M_0} = \sum_{n=1}^{\infty} a_n \exp[-\lambda_n^2 E(\tau)] \quad (20)$$

where the coefficients a_n are given by Equation (13).

Generally, the concentration of a species, which changes over time, is not measured directly; instead, a property $\mathcal{P}$ that is directly proportional to the concentration is determined experimentally. Under these conditions, we can express the fraction of mass released as

$$\mathcal{P}(t) = 1 - \frac{M(t)}{M_0}. \quad (21)$$

Combining Equations (19) and (21), we obtain the final predictive form of the model

$$\mathcal{P}(t) = 1 - \sum_{n=1}^{\infty} a_n \exp\left[-\lambda_n^2 E\left(\frac{t}{\tau_D}\right)\right] \quad (22)$$

which is the quantity directly compared with the experimental release data.

3.3. Numerical Treatment of Data

The exponential erosion model contains a single free parameter, namely the ratio between the diffusive and erosive time scales which enters the solution through the effective time $E_n(\tau)$ defined in Equation (19). Given the experimental release data $\{t_i, A_i\}_{i=1}^N$, the optimal value $\hat{p}$ was obtained by minimizing the nonlinear least-squares functional

$$\mathcal{R}(p) = \sum_{i=1}^N [\mathcal{P}(t_i; p) - \mathcal{P}_i]^2, \quad (23)$$

where $A(t; p)$ is the model prediction in Equation (22). The minimization was performed using a trust-region Levenberg–Marquardt algorithm [18], which also provided the Jacobian J of the residuals with respect to p . The local uncertainty of the estimate is quantified through the covariance

$$\text{Var}(\hat{p}) = s^2 (J^\top J)^{-1} \quad (24)$$

where

$$s^2 = \frac{1}{N-1} \sum_{i=1}^N [\mathcal{P}(t_i; \hat{p}) - \mathcal{P}_i]^2 \quad (25)$$

is the unbiased estimator of the residual variance. The 95% confidence interval for p is therefore

$$\hat{p} \pm 1.96 \sqrt{\text{Var}(\hat{p})} \quad (26)$$

To quantify the uncertainty on the fitted curve, we propagate the parameter variance through the model using the sensitivity

$$G(t) = \frac{\partial \mathcal{P}}{\partial p}(t; \hat{p}) \quad (27)$$

The variance of the model prediction is then

$$\text{Var}[\mathcal{P}(t)] = G(t)^2 \text{Var}(\hat{p}) \quad (28)$$

from which the 95% confidence band follows as

$$\mathcal{P}(t) \pm 1.96 \sqrt{\text{Var}[\mathcal{P}(t)]} \quad (29)$$

Finally, the 95% prediction band, which accounts for both parameter uncertainty and measurement noise, is obtained by adding the residual variance:

$$\mathcal{P}(t) \pm 1.96 \sqrt{\text{Var}[\mathcal{P}(t)] + s^2} \quad (30)$$

These intervals provide a quantitative assessment of the reliability of the exponential erosion model and allow direct comparison between the theory and experiment.

4. Discussion

In Figure 2 the full set of UV-Vis spectra collected over the entire monitoring period is reported as a three-dimensional surface plot. Each curve represents the absorbance profile at a given time, while the time axis spans the whole duration of the experiment.

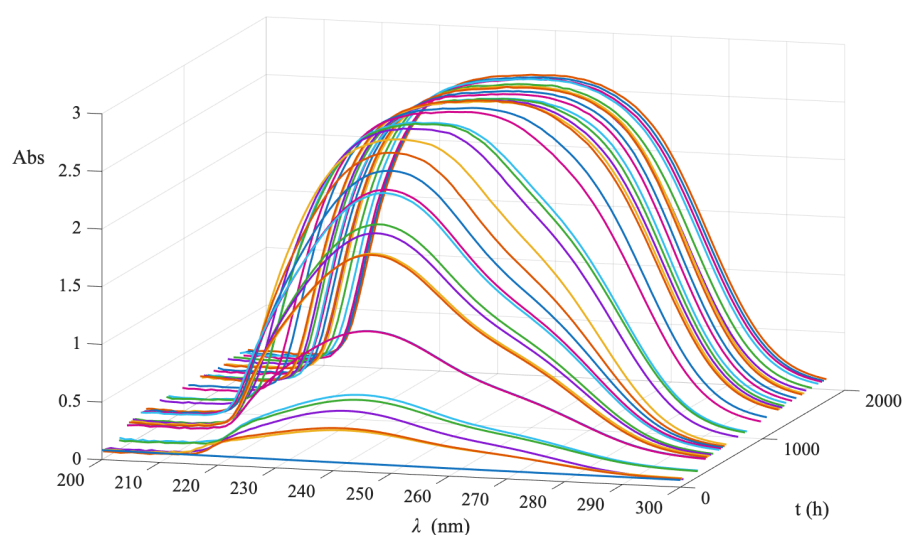


Figure 2. Three-dimensional representation of the UV-Vis spectra recorded throughout the entire monitoring period. Each curve corresponds to the absorbance profile at a given time, while the time axis spans the full duration of the experiment. The plot highlights the progressive decrease in overall absorbance and the subtle reshaping of the spectral band in the 200–300 nm region, providing a comprehensive visual overview of the temporal evolution of the system.

This representation highlights the progressive evolution of the spectral features, showing both the gradual decrease in overall absorbance and the subtle reshaping of the band in the 200–300 nm region. The 3D view provides an immediate visual impression of the kinetic trend, allowing one to appreciate how the spectral signature changes continuously as the system undergoes degradation and release. This plot serves as the experimental foundation upon which the quantitative modelling developed in the following sections is built.

In order to extract information on drug release kinetics from the experimental results in Figure 2, the physical property analyzed was the integral absorbance [19]. In other words, for each acquisition time, the area under the peak was computed and recorded [20].

The corresponding asymptotic value at long periods of time, A_∞ , was obtained from the plateau of the experimental dataset. The normalized absorbance

$$\hat{\mathcal{P}}(t) = \frac{A_{\text{area}}(t)}{A_\infty} \quad (31)$$

thus provides a direct measure of the fraction of material released into the medium. This scalar observable constitutes the experimental kinetic curve against which the theoretical is quantitatively compared. As suggested in Ref. [21], we first examined the applicability of Fickian diffusion by analyzing the release curve in the two classical regimes. Following the standard approach, the quantity $1 - M(t)/M_0$ was plotted in semi-logarithmic coordinates for the range $0 \leq M(t)/M_0 \leq 0.4$ (Figure 3a), and in log–log coordinates for $0.4 \leq M(t)/M_0 \leq 1$ (Figure 3b).

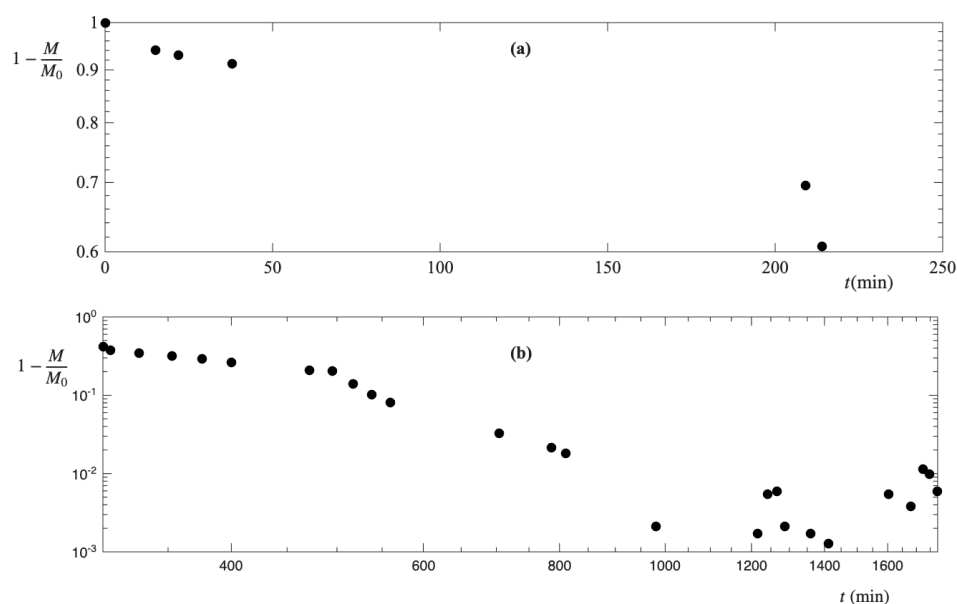


Figure 3. Verification of Fickian release asymptotics through classical linearization methods. Panel (a) shows the quantity $1 - M(t)/M_0$ plotted in semi-logarithmic coordinates for the short-time regime ($0 \leq M(t)/M_0 \leq 0.4$), while panel (b) reports the same quantity in log–log coordinates for the long-time regime ($0.4 \leq M(t)/M_0 \leq 1$).

According to the Fickian theory, these representations should yield straight lines corresponding to the short-time and long-time asymptotic limits of the diffusion solution. However, except for very small values of $M(t)/M_0$, the experimental data do not exhibit linear behaviour in either representation. This deviation suggests that additional physical mechanisms—such as geometry evolution, erosion-driven acceleration, and mode-dependent attenuation—play a significant role in shaping the release profile. These observations motivate the use of our full modal framework, which naturally incorporates the shrinking geometry and the time-dependent attenuation of the Bessel modes. The resulting solution captures both the early-time dynamics and the long diffusional tail, providing a physically consistent description of the release process across the entire experimental time window.

To determine an appropriate truncation level, we computed the partial sums $U_N(\zeta, \tau)$ of Equation (10) for two representative radial positions: $\zeta = 0.3$ and $\zeta = 0.6$. Figure 4a,b display the curves obtained for $N = 1, 2, \dots, 10$.

As shown in both panels, the partial sums rapidly converge: already for $N = 3$ the curves collapse onto a common profile, and further increasing N produces negligible changes in the solution. This analysis confirms that only the lowest-order modes contribute appreciably to the mass evolution, whereas higher-order terms are strongly attenuated by

the exponential factor $\exp[-\lambda_n^2 E_n(\tau)]$. Therefore, truncating the modal expansion at $N = 5$ provides an excellent balance between computational efficiency and accuracy, ensuring full convergence of the predicted release curve while avoiding unnecessary numerical cost. The corresponding eigenvalues λ_n and modal coefficients a_n were computed from the eigenfunction expansion of the radial diffusion operator, and the effective times $E_n(\tau)$ were evaluated according to Equation (19) for the exponential erosion law. With these ingredients, the model prediction $\hat{\mathcal{P}}(t)$ was obtained by direct evaluation of Equation (22). The optimal value of the parameter p was then determined by nonlinear least-squares minimization of the residual functional in Equation (23).

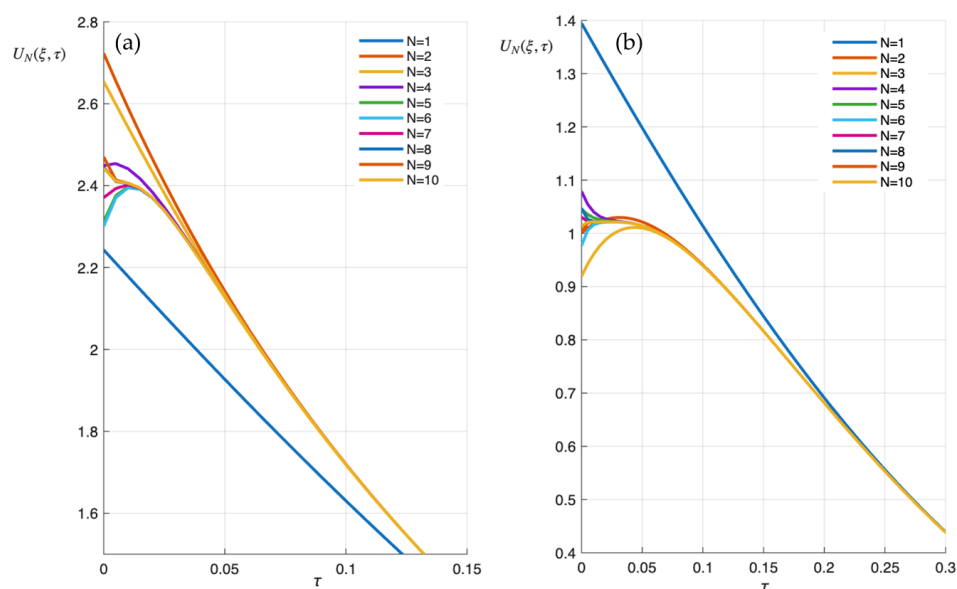


Figure 4. Partial sums of the modal expansion $U_N(\xi, \tau)$ evaluated at two fixed radial positions. Panel (a) shows the curves computed at $\xi = 0.3$ for truncation orders $N = 1, 2, \dots, 10$, while panel (b) reports the corresponding results at $\xi = 0.6$.

Figure 5 shows the experimental release kinetics together with the best fit of the exponential erosion model. The agreement between the measured data and the theoretical curve is excellent over the entire time window, confirming that the model captures both the initial rapid increase and the subsequent approach to the asymptotic plateau. The fitted value of the parameter is $\hat{p} = 1.16$, with a standard deviation of 0.03 and a 95% confidence interval of $[1.11, 1.21]$, indicating a well-resolved and statistically robust estimate. The shaded region around the fitted curve represents the 95% confidence band, while the outer envelope corresponds to the 95% prediction band. The narrow width of both bands reflects the low residual variance and the high reproducibility of the experimental dataset, further supporting the validity of the exponential erosion model in describing the release process. Although the early- and late-time release regimes are governed by different modal contributions [22], the full Bessel-series solution consistently integrates both dynamics. Higher-order modes, characterized by larger eigenvalues λ_n , decay rapidly and therefore dominate the initial fast-release phase. Conversely, the fundamental mode controls the long-time behaviour, giving rise to the extended diffusional tail observed experimentally. The combined effect of these modal contributions enables the model to accurately reproduce the entire release profile, including the characteristic times $t_{0.50}$ and $t_{0.90}$ extracted from Figure 5. Both the experimental measurements and the model predictions were evaluated up to $t > 1000$ h, since intravitreal implants are clinically expected to remain in the eye for approximately 3–4 months. The long-time behaviour is therefore essential not only for assessing the structural integrity of the device but also for verifying the sustained

therapeutic exposure required for effective treatment. The agreement between the model and the experimental data over this extended time window confirms the robustness of the proposed framework and its relevance for predicting the performance of long-acting intravitreal therapies.

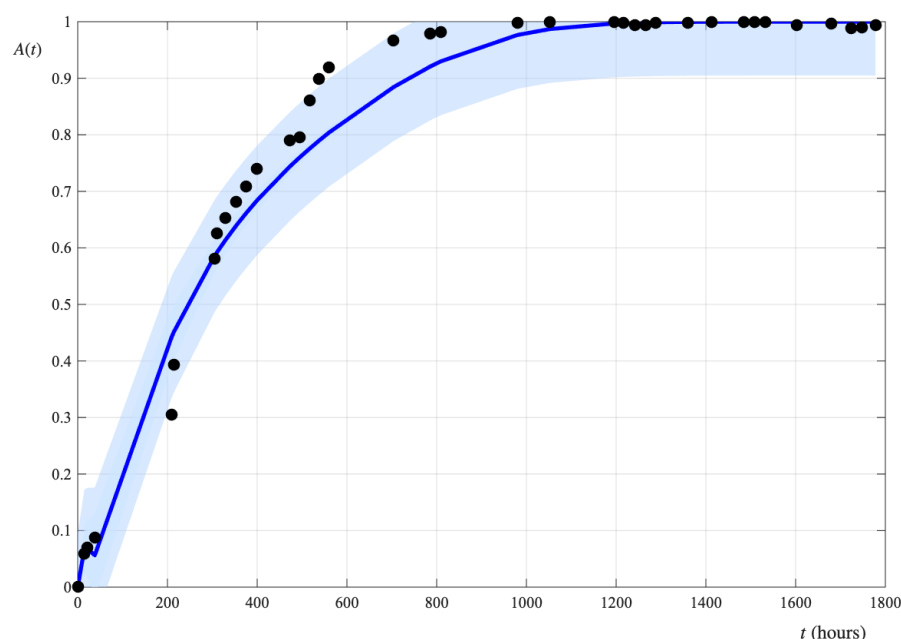


Figure 5. Modelled release profile of dexamethasone from the shrinking cylindrical matrix. The solid line represents the theoretical curve obtained from the calibrated model, while the symbols denote the experimental data. The model accurately reproduces both the initial fast release phase and the long depletion tail, yielding the characteristic times $t_{0.50} = 264.3$ h and $t_{0.90} = 996.5$ h, which quantify the transition between the early and late kinetic regimes. These values highlight the ability of the system to sustain drug release over extended periods, confirming the predictive capability of the proposed framework.

In the context of diffusional and erosion-controlled systems, the identification of characteristic times such as $t_{0.50}$ (the time required to release 50% of the payload) and $t_{0.90}$ (the time required to reach 90% release) represents a fundamental step in the quantitative description of the release kinetics. These two indicators condense all dynamical behaviour into physically interpretable quantities: $t_{0.50}$ captures the initial rate of release, whereas $t_{0.90}$ reflects the long-tail behaviour associated with the depletion regime. Their combined use enables a direct comparison between materials, operating conditions, and theoretical models without relying on the full shape of the release curve. From the modelled release profile reported in Figure 5, the characteristic times are found to be $t_{0.50} = 264.3$ h and $t_{0.90} = 996.5$ h. These values clearly indicate that the system exhibits a relatively rapid initial phase, with half of the total release occurring within approximately 11 days, followed by a markedly slower depletion regime that extends over nearly 42 days. The large separation between $t_{0.50}$ and $t_{0.90}$ reveals that, after the initial phase, the kinetics become strongly diffusion-limited, with the system entering a regime dominated by a progressive reduction in the active surface and the long-tail behaviour typical of cylindrical, erodible matrices. The fact that $t_{0.90}$ is nearly four times larger than $t_{0.50}$ highlights the ability of the material to retain a significant fraction of the payload well beyond the midpoint of the release process, ensuring sustained and prolonged delivery. This behaviour is particularly advantageous in applications requiring long-term release stability, such as transdermal patches, hydrogel matrices, or implantable systems. Overall, the extracted characteristic times confirm that the

proposed model captures both the fast initial response and the extended tail of the release curve, providing a robust and physically meaningful description of the system's kinetics.

Beyond the specific case of dexamethasone, the calibrated model provides a powerful predictive framework for exploring how different physicochemical properties influence the release kinetics of other therapeutic agents. Because the formulation is expressed in a dimensionless form and the fitted parameter p encapsulates the effective interplay between diffusion, erosion, and geometry, the model can be readily adapted to alternative drugs by appropriately rescaling the characteristic time τ_D and redefining the drug-specific transport parameters. In practical terms, extending the model to a new molecule requires (i) estimating or measuring its intrinsic diffusivity within the polymer matrix, (ii) adjusting the erosion-related parameter p to reflect its interaction with the degrading material, and (iii) recalculating the modal coefficients to account for any change in geometry or loading conditions. Once these quantities are specified, the same analytical structure used for dexamethasone directly yields the corresponding release curve and the associated characteristic times. This generalizability is particularly advantageous in early-stage formulation design, where rapid screening of candidate drugs is essential. By predicting how modifications in molecular size, solubility, or affinity for the matrix affect the release profile, the model enables rational planning of long-acting delivery strategies without the need for extensive empirical testing.

5. Conclusions

In this work, we developed and validated a mechanistic model capable of describing the release kinetics of dexamethasone from a shrinking cylindrical matrix. By combining a modal Bessel expansion with an erosion-controlled time transformation, the model successfully reproduced both the initial fast release phase and the extended depletion tail observed experimentally. The excellent agreement between the theoretical curve and the experimental data confirms that the single fitted parameter p effectively captures the interplay between diffusion, geometry evolution, and matrix erosion. From the modelled release profile, the characteristic times extracted from Figure 5—namely $t_{0.50} = 264.3$ h and $t_{0.90} = 996.5$ h—provide a compact and physically meaningful summary of the kinetics. The large separation between these two times highlights the presence of a long diffusional tail, indicating that the system retains a significant fraction of the payload well beyond the midpoint of the release process. These characteristic times therefore offer a practical and quantitative way to compare different formulations or operating conditions, and they serve as robust indicators of the system's performance. Beyond the specific case of dexamethasone, the structure of the model is general and can be readily adapted to other therapeutic agents. Because the formulation is expressed in a dimensionless framework, extending the model to a new drug only requires the redefinition of a limited set of quantities: the intrinsic diffusivity of the molecule within the matrix, the erosion-related parameter p reflecting its interaction with the degrading material, and the characteristic time τ_D associated with the new transport regime. Once these parameters are specified, the same analytical formulation directly yields the predicted release curve and the corresponding characteristic times. This makes the model particularly valuable for early-stage formulation design, where rapid screening of candidate molecules is essential.

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Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

PLGA	Poly(lactic-co-glycolic) acid
UPW	Ultra-Pure Water
RMSE	Root Mean Square Error

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