Long-term moxifloxacin release from chitosan-based antibacterial coating on polyethylene for biomedical applications

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Supplementary Material

Materials and Methods

In order to investigate the antibiotic release mechanism, the datapoints from the moxifloxacin release experiment, 0-160 days were fitted to different mathematical models: Korsmeyer-Peppas, Weibull, Higuchi, Zero order and First order, according to equations below, where *F* is the amount of drug released used as percentages and t is the time.

Korsmeyer-Peppas, where *kKP* is the Korsmeyer-Peppas constant for incorporating structural modifications and geometric characteristics of the system and *n* is the diffusional exponent that indicates the transport mechanism:

$$F = kKP(t^n) \quad (1)$$

Weibull, where *Ti* represents the release latency time, α represents the process time scale and β is the diffusional exponent that indicates the transport mechanism:

$$F = \{1 - Exp[-((t - Ti)^{\beta})/\alpha]\} \quad (2)$$

Zero-order, where *K*0 is the apparent dissolution rate constant:

$$F = K0 * t \quad (3)$$

First order, where *k*1 is the first order constant:

$$F = 1 - \exp(-k1 \times t) \quad (4)$$

Hopfenberg, where *kHB* is the Hopfenberg constant and *n* is associated with the geometry of the matrix (film, sphere or cylinder):

$$F = [1 - (1 - kHB \times t)^n] \quad (5)$$

Higuchi, where *KH* is the Higuchi constant:

$$F = KH \times t^{0.5} \quad (6)$$

The fittings were evaluated by calculating the parameters R^2, AIC (Akaike's Information Criteria) and MSC (model selection criterion). The software Microsoft Excel DDSolver add-in was used to perform the fittings and the calculations.[S1]

Statistical analysis was performed as described in the Materials and Methods section.

Post-release sample analysis

The PE-Coated samples analyzed by SEM and FTIR-ATR after 160 days correspond to the same specimens previously used in the long-term moxifloxacin release experiments. After completion of the release assay, samples were removed from the PBS medium, gently rinsed with ultrapure water to remove loosely bound buffer residues, and dried at room temperature prior to surface and chemical characterization. This approach ensures that the post-ageing analyses reflect the actual conditions experienced by the coating during prolonged drug release.

Attenuated Total Reflectance Fourier Transform Infrared (FTIR-ATR) spectroscopy was performed to evaluate the chemical structure of PE-Coated samples before and after ageing in PBS for 160 days. Spectra were acquired in absorbance mode using a Shimadzu FTIR

spectrometer equipped with an ATR accessory and diamond crystal. Measurements were collected over the spectral range of 4000–600 cm^{-1}, with a spectral resolution of 4 cm^{-1} and 32 scans per spectrum. Background spectra were recorded prior to each measurement and automatically subtracted. For each condition (before and after ageing), spectra were acquired in triplicate on independently prepared samples to ensure reproducibility. All spectra were baseline-corrected and normalized prior to comparison.

Results

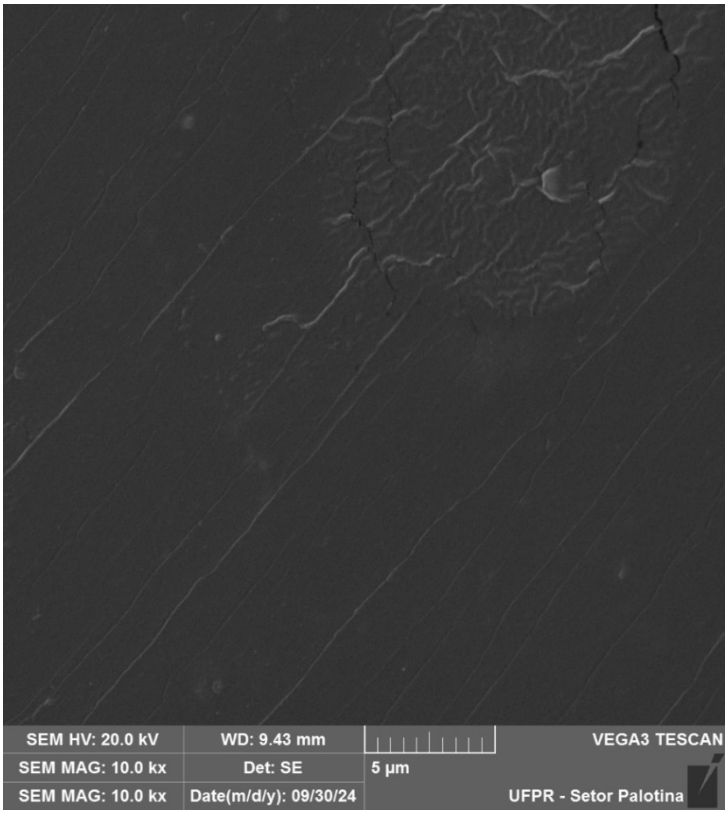

Figure S1. SEM images at 10,000x magnification of PE-Coated

PE-Coated surface at 10,000x magnification exhibits a continuous surface morphology, with the original polyethylene processing marks largely suppressed. The absence of exposed substrate features and the homogeneous texture observed at the micrometric scale indicate effective surface coverage by the chitosan-based layer. Minor topographical variations and shallow undulations are attributed to the drying and film-forming behavior of the polysaccharide coating rather than coating discontinuities. These high-resolution observations complement the low-magnification SEM and cross-sectional analyses presented in Figure 1, providing additional evidence of coating continuity and uniformity across the PE surface.

Table S1 presents the statistical comparison of cumulative moxifloxacin release between Film and PE-Coated systems over time. At very early time points, statistically significant differences are observed; however, these differences occur within an initial transient release regime, where small absolute variations are amplified by low cumulative release values. At intermediate time points, the cumulative release profiles are statistically indistinguishable, indicating convergence toward a common steady-state behavior. At prolonged times (>140 days), statistically significant differences re-emerge, reflecting differences in the asymptotic release levels. Importantly, these statistical differences do not translate into changes in the

underlying release mechanism, as both systems exhibit diffusion-dominated, non-ideal transport behavior, as demonstrated by the kinetic modeling analyses presented in Tables S2 and S3.

Table S1. Statistical comparison (ANOVA followed by Tukey's post hoc test) of cumulative moxifloxacin release between Film and PE-Coated samples

Time (days)	**Film (mean ± SD, %)**	**PE-Coated (mean ± SD, %)**	**p-value**	Statistically different?
0.0	0.97 ± 0.06	0.47 ± 0.06	0.000	Y
0.04	6.00 ± 0.55	2.47 ± 0.45	0.001	Y
0.17	12.03 ± 0.46	9.53 ± 1.25	0.035	Y
1.0	20.10 ± 0.70	19.10 ± 1.05	0.236	N
3.0	29.07 ± 0.65	28.43 ± 0.57	0.283	N
7.0	39.70 ± 0.44	38.63 ± 0.29	0.024	Y
14.0	49.07 ± 0.49	48.77 ± 0.49	0.489	N
21.0	56.67 ± 0.87	55.33 ± 0.45	0.086	N
28.0	60.10 ± 1.72	57.90 ± 1.15	0.144	N
35.0	64.30 ± 2.25	61.63 ± 1.07	0.145	N
43.0	66.93 ± 2.94	63.87 ± 0.90	0.176	N
49.0	70.23 ± 3.35	66.53 ± 0.90	0.161	N
56.0	73.20 ± 3.87	68.97 ± 1.17	0.162	N
63.0	76.40 ± 4.33	71.33 ± 1.16	0.136	N
70.0	79.10 ± 4.63	73.27 ± 1.25	0.113	N
77.0	81.30 ± 4.79	75.13 ± 1.28	0.131	N
84.0	82.87 ± 4.93	77.20 ± 1.56	0.128	N
91.0	84.43 ± 5.00	78.07 ± 1.55	0.127	N
98.0	84.43 ± 5.00	78.07 ± 1.55	0.127	N
105.0	86.30 ± 5.32	79.33 ± 1.27	0.106	N
112.0	87.37 ± 5.47	79.60 ± 1.33	0.087	N
119.0	88.37 ± 5.62	79.87 ± 1.40	0.074	N
126.0	89.30 ± 5.77	80.13 ± 1.32	0.061	N
133.0	90.20 ± 5.90	80.37 ± 1.33	0.056	N
141.0	91.07 ± 6.04	80.63 ± 1.27	0.050	N
148.0	91.93 ± 6.18	80.83 ± 1.21	0.045	Y
155.0	92.00 ± 6.22	81.23 ± 1.19	0.048	Y
162.0	92.23 ± 6.26	81.30 ± 1.20	0.047	Y
169.0	92.37 ± 6.28	81.37 ± 1.21	0.047	Y
176.0	92.50 ± 6.30	81.43 ± 1.21	0.046	Y
183.0	92.63 ± 6.32	81.50 ± 1.22	0.045	Y
190.0	92.73 ± 6.34	81.57 ± 1.22	0.044	Y
197.0	92.73 ± 6.36	81.57 ± 1.22	0.044	Y

Differences were considered statistically significant at $p \leq 0.05$.

Table S2. Statistical comparison of kinetic models fitted to the complete drug-release profiles (0–160 days)

	Film			**PE-Coated**		
Model	**R^2**	**MSC**	**AIC**	**R^2**	**MSC**	**AIC**
Korsmeyer–Peppas	0.993	4.86	43.84	0.978	3.65	70.82
Weibull	0.994	4.94	41.61	0.997	5.58	18.62
Higuchi	0.823	1.66	130.26	0.737	1.26	135.27
First order	0.845	1.79	126.65	0.685	1.08	140.13

Zero order	0.043	−0.03	175.85	−0.167	−0.23	175.46

Table S3. Kinetic parameters obtained from Korsmeyer–Peppas and Weibull models (mean ± SD)

Model	Parameter	Film	PE-Coated
Korsmeyer–Peppas	*n*	0.28 ± 0.02	0.25 ± 0.01
Weibull	β	0.51 ± 0.08	0.42 ± 0.02

The release kinetics were evaluated using the coefficient of determination (R^2), the model selection criterion (MSC), and the Akaike information criterion (AIC). Although R^2 indicates the goodness of fit, it does not account for model complexity. Therefore, MSC and AIC were used as complementary criteria, as they penalize overparameterization and enable a more reliable comparison between models.[S2]

Among the evaluated models, the Weibull equation provided the best global description of the release profiles (0–160 days) for both Film and PE-Coated systems, as indicated by the highest MSC and lowest AIC values. This suggests a non-ideal release behavior governed by heterogeneous and time-dependent transport processes.

The Korsmeyer–Peppas model, while not statistically superior for the complete release profile, was retained for mechanistic interpretation. The release exponent *n* derived from this model is commonly used to qualitatively assess diffusion-controlled and anomalous (non-Fickian) transport mechanisms. Accordingly, Weibull was selected to describe the overall kinetics, whereas Korsmeyer–Peppas was employed to support the discussion of the release mechanism. The release mechanism is diffusion-dominated, as indicated by $n < 0.5$, but occurs under non-ideal conditions, as evidenced by $\beta < 1$ in the Weibull model, reflecting matrix heterogeneity and time-dependent diffusion pathways.

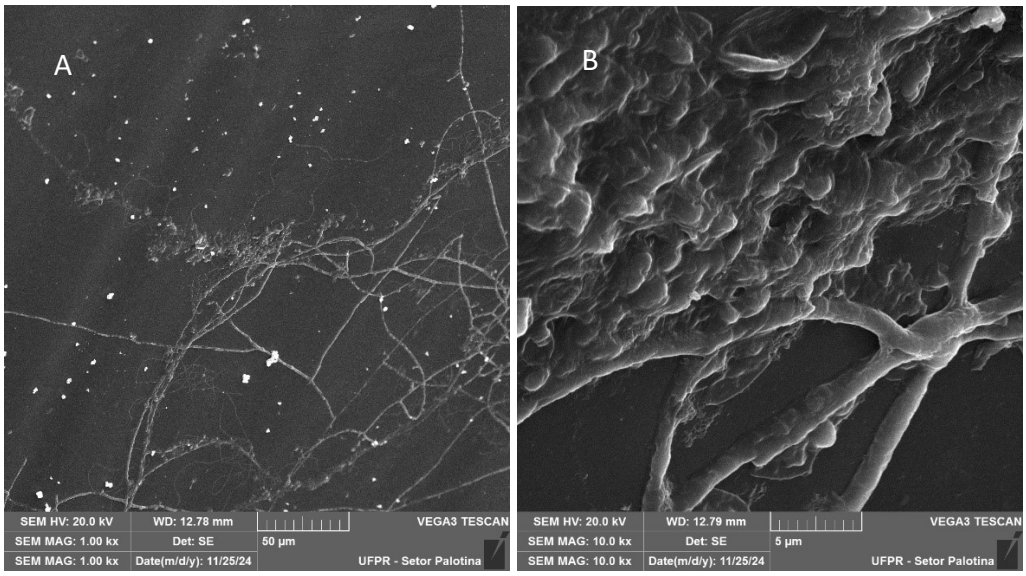

Figure S2. Scanning electron microscopy images of PE-Coated samples aged for 160 days in PBS at 1000x magnification (A) and 10,000x magnification (B).

SEM analysis of PE-Coated samples after prolonged ageing (160 days in PBS) reveals a heterogeneous surface morphology characterized by fibril-like elongated structures and locally swollen regions distributed across the surface. These features indicate partial surface reorganization of the chitosan-based coating during long-term exposure to an aqueous environment. Importantly, no evidence of macroscopic delamination or large-area coating

failure is observed, suggesting that the coating remains adherent to the polyethylene substrate despite ageing. The origin of the fibrillar structures cannot be conclusively assigned and may be related to swelling-induced rearrangement of the polymeric network and/or deposition of residual buffer components. Overall, the SEM observations support coating stability under prolonged immersion conditions, while indicating dynamic structural reorganization rather than static surface preservation.

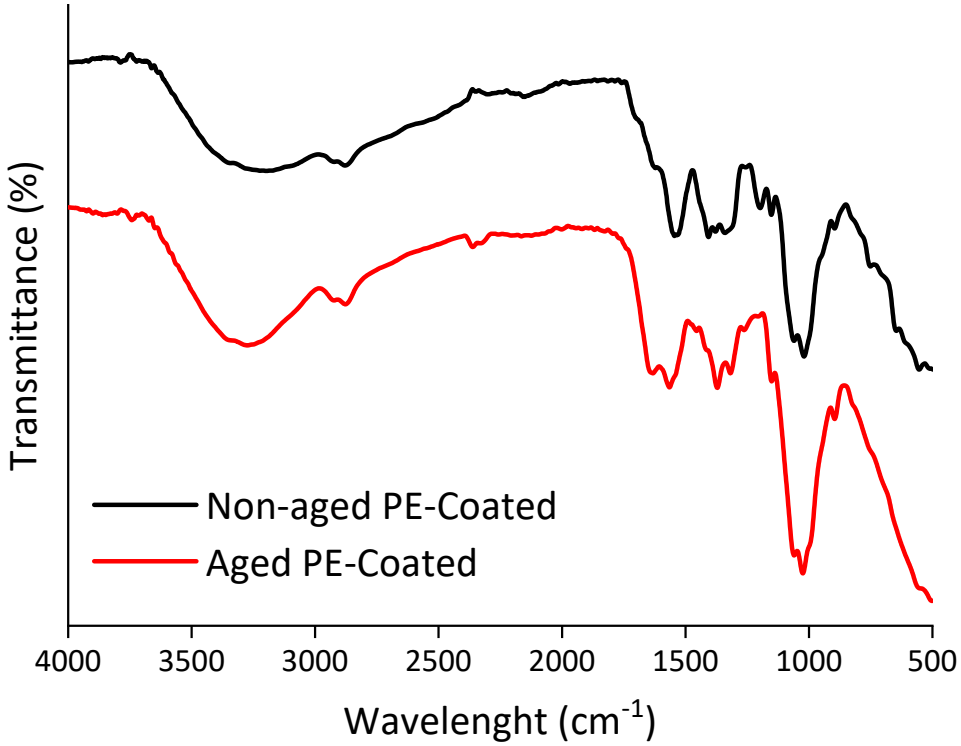

Figure S3. Fourier transformed infrared spectroscopy-attenuated total reflectance (FTIR-ATR) analysis of PE-Coated samples before and after ageing in PBS solution for 160 days.

FTIR-ATR analysis reveals noticeable spectral differences between fresh and aged PE-Coated samples, particularly in the 1600–1700 cm^{-1} region and within the 1200–900 cm^{-1} fingerprint range. The 1600–1700 cm^{-1} region, dominated by the amide I vibration of chitosan, is sensitive to hydration state, hydrogen bonding, and ageing-related chain rearrangements. Changes observed after prolonged PBS exposure are consistent with structural reorganization of the chitosan network rather than polymer backbone degradation. Similar spectral evolutions have been reported for aged chitosan-based systems and for chitosan undergoing hydration- and ageing-induced rearrangements without loss of chemical integrity. Taken together, FTIR-ATR results indicate that the coating does not remain chemically static during long-term immersion but undergoes reversible or semi-reversible structural adaptations associated with aqueous ageing.[S3,S4]

Figure S4. 35 days aged PE-Coated samples after adhesion strength test.

Figure S4 shows representative photographs of PE-Coated samples after the adhesion strength test performed following 35 days of ageing. The images indicate that coating failure occurs locally at the stressed region, while large areas of the coating remain attached to the polyethylene substrate. No evidence of spontaneous delamination or widespread coating detachment is observed outside the mechanically tested area. These visual observations are consistent with the pull-off adhesion results and support the conclusion that the chitosan-based coating maintains interfacial integrity after prolonged aqueous ageing, with failure predominantly governed by the applied mechanical load rather than by interfacial degradation.

References (Supporting Information)

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