Electrospun PCL/zein fibers scaffolds as carriers for naringin and naringenin: a comparative physicochemical and release study for tissue engineering applications

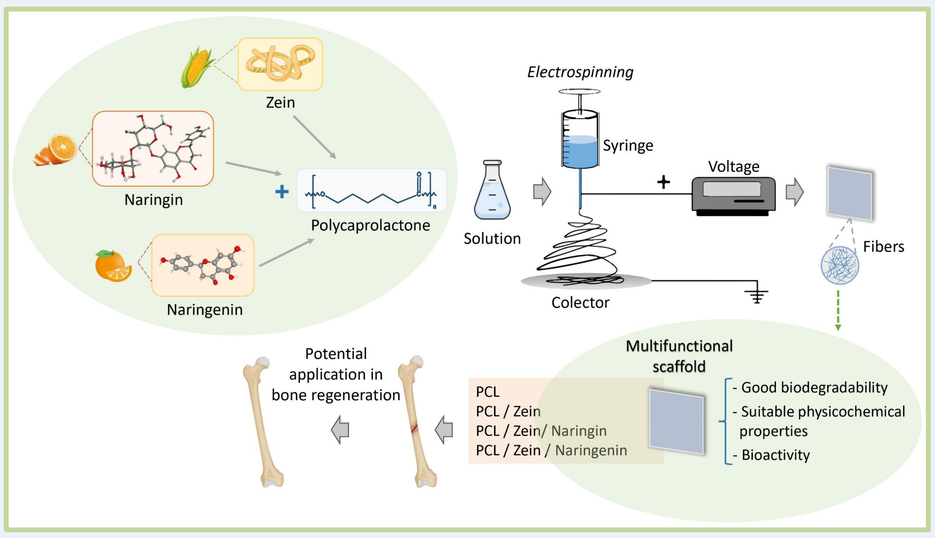
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INTRODUCTION



Electrospun fibers are promising platforms in regenerative medicine due to their ability to mimic the extracellular matrix (ECM). Polycaprolactone (PCL), a biocompatible polymer widely used for scaffold fabrication, exhibits suitable properties; however, its hydrophobicity limits cell adhesion[1]. Blending PCL with natural polymers such as zein improves hydrophilicity, biodegradability, and bioactivity[2].The incorporation of flavonoids like naringin and naringenin provides antioxidant, anti-inflammatory, and osteogenic effects[3–4], although their low aqueous solubility limits clinical application. Therefore, PCL/zein scaffolds represent promising systems for localized and bioactive compounds release.

METHODS

The scaffolds were fabricated via electrospinning from a PCL/Zein polymeric blend, incorporating naringin and naringenin as bioactive agents. The physicochemical characterization included Scanning Electron Microscopy (SEM) for morphology and porosity, and the analysis of fiber size using ImageJ software to generate diameter distribution histograms. The chemical integration and stability were verified by FTIR spectroscopy, while thermal properties were assessed through DSC. Furthermore, swelling degree, degradability (in PBS at pH 7.4 for 60 days), and in vitro release kinetics (over 168 hours) were evaluated. All results were statistically analyzed using Origin 2026 software and one-way ANOVA, with the Bonferroni test used to determine significant differences between groups (*p < 0.05, **p < 0.01, ***p < 0.001).

Table 1. Composition and formulation parameters of PCL/zein electrospun scaffolds loaded with flavonoids.

Formulation Code	Polymer ratio (wt.%)		Final solution concentration (%w/v)	Flavonoid content (wt.%)	
	PCL	zein		NI	NE
PCL	100	-	20	-	-
PZ20	80	20	40	-	-
PZ30	70	30	40	-	-
PNI	100	-	20	5	-
PZ20NI	80	20	40	5	-
PZ30NI	70	30	40	5	-
PNE	100	-	20	-	5
PZ20NE	80	20	40	-	5
PZ30NE	70	30	40	-	5

RESULTS

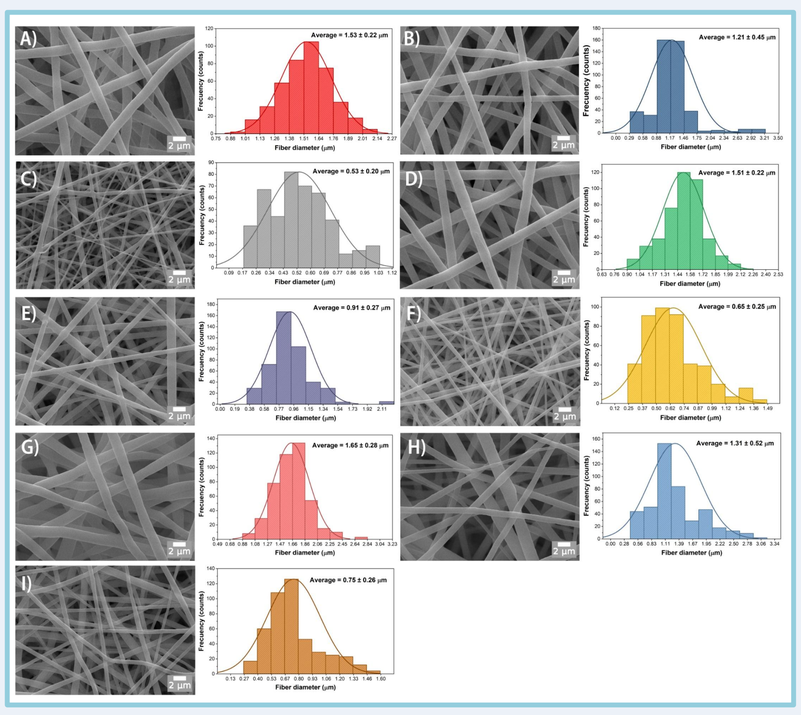


Figure 1. SEM micrographs and corresponding fiber diameter distribution histograms of electrospun scaffolds composed of (A) PCL, (B–C) PCL/Zein, (D) PCL/Naringin, (E–F) PCL/Zein/Naringin, (G) PCL/Naringenin and (H–I) PCL/Zein/Naringenin. Scale bar: 5 µm (10,000×).

All formulations exhibited homogeneous, continuous fibers free of defects (beads). The addition of zein significantly reduced the fiber diameter (up to 65% in PZ30), facilitating the spinnability of the solution.

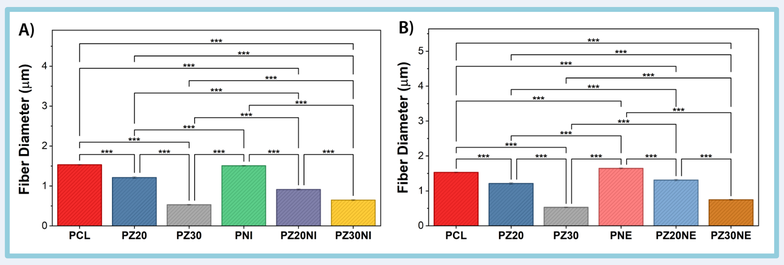
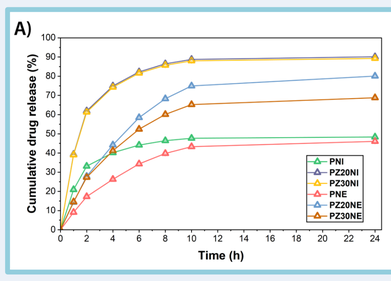


Figure 2. Comparison of the average fiber diameters of electrospun scaffolds: (A) PCL, PZ20, PZ30, PNI, PZ20NI and PZ30NI, (B) PCL, PZ20, PZ30, PNE, PZ20NE and PZ30NE.

The PCL/zein ratio is the dominant factor in morphology. Naringenin (NE) had a greater impact on increasing diameter than naringin (NI), suggesting a stronger interaction with the polymer matrix during electrospinning.



B)

Sample	First order		Higuchi		Korsmeyer-Peppas		
	k_1	R^2	k_H	R^2	k_p	R^2	n
PNI	-0.0512	0.878	13.260	0.920	0.229	0.935	0.370
PZ20NI	-0.2040	0.9587	24.506	0.919	0.423	0.935	0.366
PZ30NI	-0.1980	0.9566	24.316	0.920	0.426	0.934	0.366
PNE	-0.0579	0.9881	16.694	0.998	0.097	0.987	0.701
PZ20NE	-0.1406	0.9991	29.505	0.991	0.153	0.991	0.744
PZ30NE	-0.1073	0.9930	24.792	0.996	0.156	0.989	0.674

Figure 3. Cumulative release profiles of naringin- and naringenin-loaded electrospun scaffolds in PBS: (A) release during the first 24 h and (B) Kinetic parameters derived from in vitro cumulative release model fitting.

An initial rapid release was observed, followed by a sustained phase. Matrices with higher zein content (PZ30) favored a greater release of the active compounds

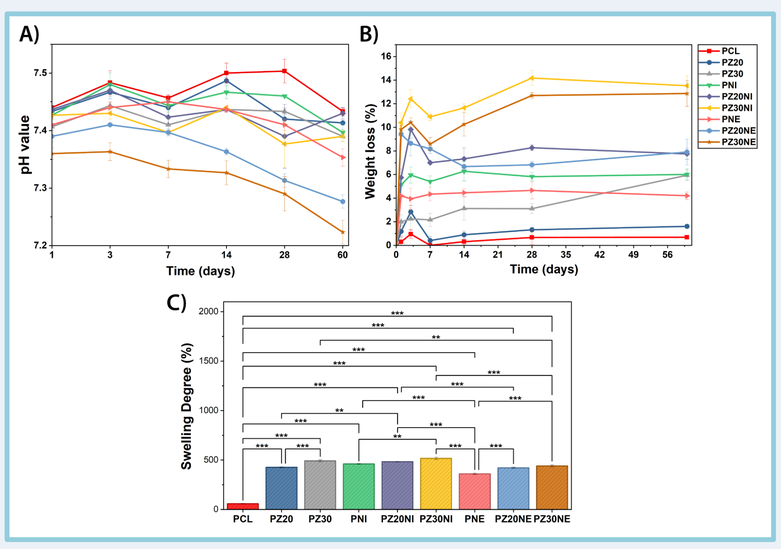


Figure 4. Evaluation of the physicochemical and degradation properties of the scaffolds: A) pH value, B) Weight loss percentage over 60 days in PBS, and C) Swelling degree after 24 hours.

All samples maintained physiological pH (7.2–7.5), confirming the material's biocompatibility. Weight loss increased proportionally with zein content, reaching 13% in PZ30NE due to the larger surface area and higher hydrophilicity of thin fibers. This accelerated degradation correlates with the gradual release of acidic by-products, observed as a downward pH trend after day 28. This correlates with the swelling data, zein incorporation significantly enhances water absorption compared to pure PCL, a key factor for nutrient diffusion and cell anchorage.

CONCLUSIONS

- Flavonoid-loaded PCL/zein fibrous scaffolds were successfully developed by electrospinning, yielding structures that mimic the extracellular matrix.
- The polymer ratio controls the morphology: higher zein content results in thinner fibers and faster degradation.
- Naringenin (NE) exhibits a more pronounced interaction with the matrix than naringin (NI), significantly affecting the crystallinity and thermal transitions of the system.
- The combination of 30% zein with naringenin optimizes degradation and release profile, positioning it as the most promising formulation for guided bone regeneration applications.

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