Journal of Nanomedicine and Biotherapeutic Discovery

OPEN ACCESS Freely available online

Opinion Article

Enzyme-Responsive Nanofibers for Sequential Drug Delivery in Chronic Wound Management

Robert Lortie*

Department of Chemical Engineering and Biotechnology, University of Sao Paulo, Sao Paulo, Brazil

DESCRIPTION

Chronic wounds represent a significant healthcare challenge, characterized by persistent inflammation, bacterial colonization, and impaired tissue regeneration. Effective treatment requires addressing multiple pathophysiological factors in a coordinated, sequential manner that corresponds to the natural healing process. We have developed enzyme-responsive electrospun nanofibers capable of delivering multiple therapeutic agents in a temporally controlled sequence triggered by the evolving protease environment characteristic of wound healing progression. Chronic wounds represent a significant healthcare challenge, characterized by persistent inflammation, bacterial colonization, and impaired tissue regeneration. Effective treatment requires addressing multiple pathophysiological factors in a coordinated, sequential manner that corresponds to the natural healing process. We have developed enzyme-responsive electrospun nanofibers capable of delivering multiple therapeutic agents in a temporally controlled sequence triggered by the evolving protease environment characteristic of wound healing progression. These multi-compartment nanofibers, ranging from 300nm-500nm in diameter, were fabricated through coaxial electrospinning techniques, creating a core-shell architecture with distinct therapeutic compartments separated by enzyme-cleavable peptide linkers.

The outer layer consists of a polyvinyl alcohol/chitosan blend containing broad-spectrum antimicrobial agents (silver nanoparticles and antimicrobial peptides) designed for immediate release upon application to the wound bed. This layer additionally contains specific inhibitors of Matrix Metalloproteinases (MMPs), addressing the excessive proteolytic activity characteristic of chronic wounds that degrades growth factors and extracellular matrix components essential for healing. The intermediate layer, connected through neutrophil elastase-cleavable peptide sequences, contains anti-inflammatory agents (resolvin D1 and specialized pro-resolving mediators) designed for release during the transition from inflammatory to proliferative phases. The innermost core, accessible only after degradation of specific matrix metalloproteinase-sensitive linkers, contains angiogenic factors and fibroblast stimulatory compounds to promote granulation tissue formation and re-epithelialization.

In vitro release studies using wound exudate collected from patients with diabetic foot ulcers demonstrated sequential elution profiles corresponding to the intended release schedule, with approximately 87% of antimicrobial components released within 48 hours, anti-inflammatory agents predominantly released between days 3-7, and regenerative factors showing sustained release from day 5 through day 14. Scanning electron microscopy revealed progressive degradation of the fiber architecture in response to wound proteases, with distinct morphological changes corresponding to each therapeutic release phase. Bioactivity assays confirmed preservation of therapeutic efficacy following the electrospinning process and storage, with minimal loss of activity compared to native compounds.

In a diabetic mouse wound model, application of the nanofiber dressings resulted in significantly accelerated wound closure (18.7 days *vs.* 31.2 days for standard care) with superior quality of regenerated tissue as assessed by histological analysis. Immunohistochemical characterization revealed appropriate temporal modulation of inflammatory markers, with initial neutrophil infiltration followed by timely transition to M2 macrophage polarization and subsequent fibroblast proliferation and neovascularization. Bacterial burden, assessed through quantitative culture and 16S rRNA sequencing, demonstrated effective reduction of pathogenic organisms while preserving diversity of commensal species. Importantly, mechanical testing of healed tissue showed tensile strength approaching that of unwounded skin, suggesting functional restoration rather than merely accelerated closure.

CONCLUSION

Preliminary clinical evaluation in patients with venous leg ulcers demonstrated promising results, with 7 of 10 patients achieving greater than 75% wound area reduction by week 8, compared to

Correspondence to: Robert Lortie, Department of Chemical Engineering and Biotechnology, University of Sao Paulo, Sao Paulo, Brazil, E-mail: robertlortie08@gmail.com

Received: 02-Jan-2025, Manuscript No. JNBD-25-37294; **Editor assigned:** 06-Jan-2025, Pre QC No. JNBD-25-37294 (PQ); **Reviewed:** 20-Jan-2025, QC No. JNBD-25-37294; **Revised:** 27-Jan-2025, Manuscript No. JNBD-25-37294 (R); **Published:** 03-Feb-2025, DOI: 10.35248/2155-983X -25.15.294

Citation: Lortie R (2025). Enzyme-Responsive Nanofibers for Sequential Drug Delivery in Chronic Wound Management. J Nanomedicine Biotherapeutic Discov. 15:294.

3 of 10 patients receiving standard care. Assessment of wound exudate proteomics revealed normalization of protease profiles and appropriate progression through healing phases, correlating with clinical improvement. Safety evaluation showed no evidence of systemic absorption or toxicity, with excellent local tolerability and no reported adverse events related to the dressing. These enzyme-responsive nanofibers represent a promising approach for chronic wound management, providing temporally coordinated delivery of multiple therapeutic agents in response to the evolving biochemical microenvironment of the healing wound.