Electrospun chitosan-elastin for improved wound healing

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Statement of Purpose: Skin tissue is subject to many external forces and agents that could potentially cause injury. Minor injuries like cuts are usually resolved quickly by the natural healing ability of skin. In the case of patients with compromised wound healing, like diabetics, minor injuries can evolve to chronic wounds that severely impact quality of life and require professional attention. Current treatments, including grafting and skin substitutes, are met with high infection rates, lack of vascularization/tissue integration, and poor mechanical properties which result in lackluster healing capabilities.

We propose a novel electrospun membrane consisting of a chitosan-elastin copolymer to address these issues.

Chitosan is a biodegradable, biocompatible polycationic polysaccharide that has been shown to exhibit good mechanical and anti-microbial properties. Our previous work has shown that electrospun chitosan membranes were successful when used for guided bone regeneration. With some slight modifications, we believe that these membranes can also be used to treat chronic skin wounds. Incorporation of elastin will work to further improve mechanical properties and induce neovascularization, both of which improve tissue integration.

The inclusion of elastin may produce a synergistic effect that leads to improved healing and diminishing of the chronic wound state.

Methods: Fabrication of electrospun chitosan-elastin membrane - The chitosan-elastin electrospun membranes were fabricated as previously described [1]. Briefly, a 5.5wt% 70% DDA Chitosan (Primex, Siglyfjordur, Iceland) in trifluoroacetic acid/dichloromethane (TFA/DCM) (7:3) was mixed overnight. Soluble elastin (4 wt%) (ES12, Elastin Products Company, Inc. Owensville, MO, USA) was added the day after, before spinning, and manually mixed. Solution was loaded in a syringe and charged with a high voltage. Electrospun fibers were collected on a grounded, stainless steel rotating plate. Following spinning, the electrospun fibers were treated for removal of TFA salts and attachment of a hydrophobic tert-butyloxycarbonyl (tBOC) group to prevent fiber swelling, as previously described [2]

Incorporation of elastin, removal of TFA salts, and attachment of hydrophobic tBOC group was verified via ATR-FTIR.

Fiber morphology was examined via scanning electron microscopy (SEM).

Fiber diameter was measured using Image J – Fiji image analysis software.

Results: ATR-FTIR spectra confirmed removal of TFA salts via decreased peaks in chitosan-elastin (CE) membrane (*). Decreased peaks at 2980 (C-H bend), 1688 (C=O stretch), 1529 (CO-NH_2), and 1370 (C-H bend) cm^{-1} signify attachment of hydrophobic tBOC group (black arrow). Incorporation of elastin is verified by peaks at 1535 (amide II band) and 1655 (amide I band) cm^{-1} (red arrow) (Figure 1A).

SEM images confirmed optimization of modified electrospinning protocol from standard chitosan membranes to chitosan-elastin (CE) membranes. Images also confirmed retention of fiber morphology after TFA salt removal and tBOC attachment treatment (Figure 1B).

CE membranes saw larger average fiber diameter compared to electrospun chitosan membranes (491 ± 79 nm and 230 ± 58 nm, respectively).

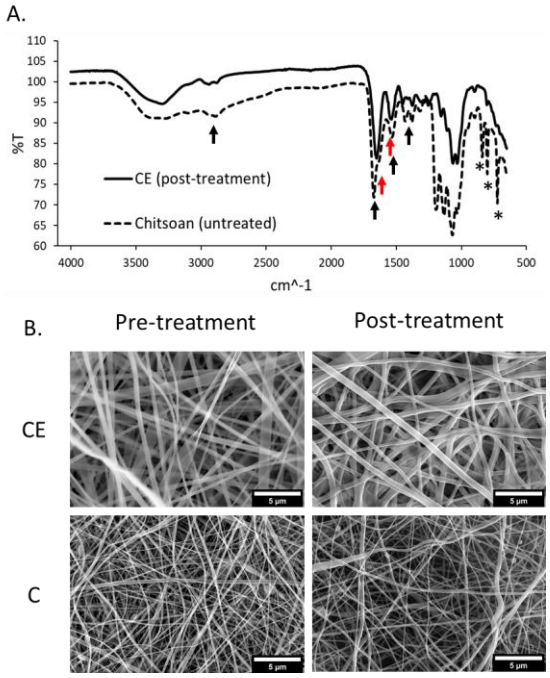

Figure 1: (A) ATR-FTIR spectra of treated, electrospun chitosan-elastin (black) and untreated, electrospun chitosan (dashed). (B) SEM images of pre- and post-treated electrospun chitosan-elastin (CE) and chitosan (C) membranes).

Conclusions: These findings confirm the successful incorporation of elastin into our electrospun chitosan membranes. Currently ongoing/planned studies include tensile tests, quantification of elastin incorporation, addition of magnesium-substituted hydroxyapatite gel coating, and *in vitro* cell attachment/viability assays.

References:

[1] V. P. Murali *et al.*, "Modified electrospun chitosan membranes for controlled release of simvastatin," *Int. J. Pharm.*, vol. 584, Jun. 2020.

[2] H. Su *et al.*, "In vitro and in vivo evaluations of a novel post-electrospinning treatment to improve the fibrous structure of chitosan membranes for guided bone regeneration," *Biomed. Mater.*, vol. 12, no. 1, p. 015003, Feb. 2017.