Seamless dressing made of bioactive, co-axial microfluidic-spun fibers for treating diabetic foot ulcers

Acronym: CoSpunTex

Summary: In the last year, the incidence of diabetic foot ulcers (DFUs) reached 18.6 million people worldwide, with numbers being predicted to continue increasing each year [1]. About 25% of diabetic patients develop DFUs, with near 70% of those requiring lower limb amputation [2]. Complications of diabetes that affect the lower extremities are very common, difficult to treat, and costly. DFUs often fail to progress past the inflammatory phase of wound healing, falling within the category of chronic wounds. To date, DFUs are considered a major source of morbidity and a leading cause of hospitalization in diabetic patients. Standard treatments rely on individualized therapies that focus on ensuring glycemic balance, infection control, revascularization, wound protection, and ulcer off-loading [3, 4]. Over the last decades, technology breakthroughs have demonstrated the impact of bioactive 3D, fiber-based scaffolding systems in the treatment of DFUs [2]. Still, very few strategies can target multiple barriers to the healing of these wounds simultaneously.

In the CoSpunTex project, we propose to engineer a multi-action fibrous dressing ("all-in-one" formulation) via microfluidic spinning and seamless knitting that releases specialized bioactive agents in response to environmental stimuli at the wounded site. The goal is to produce a flexible, adaptable, comfortable dressing that fights microbial infection and reduces inflammation, while still guaranteeing the traditional dressing functions of absorbing exudates, conferring moisture balance, and promoting oxygen exchange. Co-axial microfluidic-spun fibers will be engineered with an exterior of polycaprolactone (PCL), loaded with carbon nanofibers (CNFs) and with chitosan nanoparticles (CSNPs) encapsulating CW49 peptide (APFRMGICTTN). PCL is an anti-adhesive, highly flexible, USA Food and Drug Administration (FDA)-approved polymer [5, 6], while CNFs are known for significantly reducing bacterial adhesion and for promoting rapid clotting by instigating quick fibrin growth [7]. CW49 is a small but potent immunomodulatory peptide capable of strong angiogenic action and preventing excessive inflammation [8]. The core of the co-axial microfluidic-spun fibers will contain a blend of sodium alginate (SA) and hyaluronic acid (HA). SA is an FDA-approved polymer with great hygroscopic capacity [9], while HA is known to reduce local inflammation and accelerate re-epithelialization. Physically and mechanically stable yarns will be obtained by twisting an optimized number of the formulated co-axial microfibers. These will then be knitted in the form of weft jersey, by inserting those yarns using plating technique and selecting differentiated areas for adequate compression by means of jacquard technology, resulting in dressings of enhanced comfort, flexibility, structural stability, interconnected open pore structure, and durability. Further, this intricated architecture made of microfibers will mimic the irregular organization of the interconnective tissues that compose the different layers of the skin, being more easily recognized and accepted by the living organism.

The high local pH (6.5-8.5) and increased enzymatic activity that characterize DFUs (McArdle et al., 2015) will trigger the progressive solubilization of the CSNPs within the shell of co-axial fibers, which in turn will allow a slow but continuous release of the encapsulated peptide. The CSNPs antimicrobial profile (inhibitory action) will be complemented with the bacteria-repellent features of CNFs. As microorganisms are dealt with, CW49 will reach the wound bed and trigger anti-inflammatory events. Simultaneously, CNFs will work to promote hemostasis via fibrin growth. As these phenomena take place, the remainder components of the dressing will guarantee the absorbance of exudates (SA) without sticking to the wound (PCL). Finally, cell growth will be promoted by the release of HA from the core of the co-axial fibers, which will be guaranteed through NPs solubilization that will open nanopores along the fibers' shell facilitating access to the core, or via molecule exchange during exudates absorbance. The joint effect of these bioactive agents is expected to contribute to a quicker tissue regeneration. The success of this project will pave the way for a new

generation of wound dressings featuring an "all-in-one" multi-target action approach. This innovation will simplify DFUs care by reducing the need for multiple individualized therapies, making it easier for healthcare providers by eliminating the complexity of selecting the appropriate dressing. Furthermore, it will introduce a novel fiber with expanded potential for various biomedical applications.

Keywords 4 (English): bioactive nanomaterials; microfluidic spinning technology; seamless technology; bactericidal and regenerative effects

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