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| **Abstract Title:** | **Mitigating Burn Injury Severity And Infection By Using A Novel Dressing That Targets Oxidative Stress Pathways** |
| **Author and Co-authors:** | Jahnabi Roy, PhD, Christine J. Kowalczewski, PhD, Angela R. Jockheck-Clark, PhD, Robert J. Christy, United States Army Institute of Surgical Research, San Antonio, TX<br>Cortes Williams, PhD, Luis A. Martinez, John W. Simecek, NAMRU-SA |
| **Objective:** | 1) Describe the role of antioxidants on burn wound injuries.<br>2) Describe the incorporation of antioxidants into biocompatible materials by electrospinning as well as the activity of antioxidants incorporated into biomaterials. |
| **Abstract:** | **Background:** Delays in hospital care and surgical interventions impede healing of battlefield burn wound injuries. Burned tissue exhibits lowered levels of superoxide dismutases, glutathione, and other antioxidants, resulting in high levels of oxidative stress. This environment drastically hinders the cell's reactive oxygen species (ROS) scavenging mechanisms, resulting in DNA damage and an increase in necrotic tissue. The use of topical and systemic antioxidants, particularly N-acetylcysteine, has improved burn wound healing in rodent models and human clinical trials. The aim of this study was to generate a biomaterial dressing that could restore the redox balance within potentially salvageable tissue, to reduce the acute and systemic burn-related pathophysiologies.<br><br>Electrospinning is a cost-effective fiber production method that uses electrostatic forces to cast a nanofibrous mesh. It can be used to generate scaffolds with porosities and large surface area-to-volume ratios. This allows for absorption of wound exudate, prevention of dehydration, and improved permeability. Moreover, electrospun fibers can have controlled release of their incorporated bioactive components. Therefore, the development of electropun wound dressings containing antioxidants could stabilize the tissue damaged by burns and prevent tissue loss that accompanies delayed surgical care. Here we report on the chemical, physical and biological properties of antioxidant-containing wound dressings generated by electrospinning.<br><br>**Methods:** Electrospun polymeric biomaterials, including polyethylene oxide and poly (lactic-co-glycolic acid), were used to encapsulate different antioxidants, including ascorbic acid, α-tocopherol and melatonin. The effect of these antioxidants on cell viability of human dermal fibroblasts (hDFs) was determined by PrestoBlue and CyQuant |

assays. The total antioxidant capacity of all three antioxidants was determined by measuring the reduction of copper (II) to copper (I). Additionally, the effect of the antioxidants and the antioxidant containing dressings was measured in a cell based assay by measuring total ROS.

**Results:** Ascorbic acid, α-tocopherol and melatonin reduced ROS in cultured hDFs in a dose-dependent manner. Furthermore, the concentrations of these antioxidants required for bioactivity did not affect the hDF viability. These antioxidants were compatible with electrospinning solvent systems and maintained functional capacity after electrospinning. The electrospun fibers were characterized for their fiber size and porosity as well as the release kinetics of the various antioxidants. Current efforts are being directed towards co-encapsulation of antioxidants with antimicrobials into the dressing to moderate infection related complications in burn wounds and modulate burn progression. These dressings will be applied to in vivo models of thermal injury to investigate their effects on wound healing.

**Conclusions:** Preliminary findings indicate that antioxidants can scavenge ROS from fibroblasts in cell culture. Additionally, antioxidant molecules retain their activity after being electrospun into polymeric scaffolds. Future in vivo studies will indicate if the oxidative stress in burned tissue is alleviated and we hypothesize that restoration of redox balance can improve thermal injury wound healing outcomes.

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