

## **Zapping Deep-Tissue Infection With a Fast-Setting Biodegradable Hydrogel**

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**Purpose:** Wound infections have been a major challenge, especially for military medicine. As the care of casualties continues to enhance survival rates, infectious complications will remain a major cause of morbidity. When bacteria biofilm is formed at the wound site, the infection is significantly more difficult to treat while increasing the healing time and the cost of the treatment. Conventional treatment is surgical debridement combined with a cocktail of antibiotics. Because of the misuse and overuse of antibiotics, more than 50% of the bacteria are resistant against standard antibiotics. Our concept is based on targeting the bacteria synergistically on various fronts. The impact of electrical attack associated with antibacterial materials may be more significant. We designed and engineered a bioresorbable hydrogel free of antibiotics that can prevent infections, combat antibiotic resistance, and help heal infected wounds or cavities.

**Methods:** Silk fibroin (SF) aqueous solution was prepared following the protocol of Rockwood et al. Sequentially, AgNO<sub>3</sub> was added, mixed, and exposed 24 hours to incandescent light (bulb lamp 60 W) at room temperature. Different conditions (control, gel, electrical current [1mA/1 min] and combination) were performed to evaluate cytotoxicity and bacteria viability. Hydrogels were removed right after from the medium. In vitro cytotoxicity of SF/Ag-NP hydrogels and the combined effect with electrical current was verified by directly exposing Chinese hamster ovary (CHO) cells and on DH5 $\alpha$  Escherichia coli.

**Results:** Together silk hydrogel and silver nanoparticles exhibit an excellent conductivity of 1.2 S/cm allowing the electrons to flow. No cytotoxicity towards CHO cells was observed for those treated with SF/Ag-NP hydrogels or electrical current, separately or in combination. Bacterial toxicity towards E. coli was assessed. SF/Ag-NP hydrogels and electrical current did not exhibit any significant effect on bacterial killing. However, the combination of SF/Ag-NP hydrogel and current eradicated 77.8% bacteria in 1 minute. Treatments with hydrogels and combined effect presented similar Ag<sup>+</sup> release whereas a difference in ROS (reactive oxygen species) of 50% was found between treatments, showing an interesting contribution of electrical current.

**Conclusion:** An injectable antibacterial and bioresorbable composite gel was developed as a new strategy to kill bacteria without compromising wound healing. Following the demonstration of biocompatibility toward CHO cells, the gel with and without electrical current was tested against E. coli. The results confirmed the strong (80% of dead bacteria) and particularly fast (1 min) bactericidal effect of the materials when combined with short duration and low-level electrical current. This work validated the considerable potential and the superiority of using combination approaches for treating infections caused by tenacious pathogens without using antibiotics.