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Novel nano-insulin formulation modulates cytokine secretion and remodeling to accelerate diabetic wound healing



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## **ACCEPTED MANUSCRIPT**

#### Novel nano-insulin formulation modulates cytokine secretion and remodelling to accelerate diabetic wound healing

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#### Abstract

Little is known about insulin's wound healing capability in normal as well as diabetic conditions. We here report specific interaction of silver nanoparticles (AgNPs) with insulin by making a ~ 2 nm thick coat around the AgNPs and its potent wound healing efficacy. Characterization of the interaction of human insulin with silver nanoparticles showed confirmed alteration of amide-I in insulin whereas amide-II and III remained unaltered. Further, Nanoparticles protein interaction kinetics showed spontaneous interaction at physiological temperature with  $\Delta G$ ,  $\Delta S$ , Ea and Ka values -7.48, 0.076, 3.84 Kcal mole<sup>-1</sup> and 6 x 10<sup>5</sup> s<sup>-1</sup> respectively. Insulin loaded AgNPs (IAgNPs) showed significant improvement in healing activity *in vitro* (HEKa cells) and *in vivo* (Wister Rats) in comparison with the control in both normal and diabetic conditions. The underlying mechanism was attributed to a regulation of the balance between pro (IL-6, TNF $\alpha$ ) and anti-inflammatory cytokines (IL-10) at the wound site to promote faster wound remodeling.

**Key Words:** Insulin, Wound Healing, Protein-Nanoparticles Interactions, Diabetes, Inflammation, Silver nanoparticles.

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