



# Topical Application of Propolis Enhances Cutaneous Wound Healing by Promoting TGF-Beta/Smad-Mediated Collagen Production in a Streptozotocin-Induced Type I Diabetic Mouse Model.

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## Abstract:

**BACKGROUND/AIMS:** Impaired wound healing is considered to be one of the most serious complications associated with diabetes as it significantly increases the susceptibility of patients to infection. Propolis is a natural bee product used extensively in foods and beverages that has significant benefits to human health. In particular, propolis has antioxidant, anti-inflammatory and analgesic effects that could be useful for improving wound healing. In this study, we investigated the effects of topical application of propolis on the healing and closure of diabetic wounds in a streptozotocin (STZ)-induced type I diabetic mouse model. **METHODS:** Sixty male mice were distributed equally into 3 experimental groups: group 1, non-diabetic control mice; group 2, diabetic mice; and group 3, diabetic mice treated daily with a topical application of propolis. **RESULTS:** We found that diabetic mice exhibited delayed wound closure characterized by a significant decrease in the levels of TGF- $\beta$ 1 and a prolonged elevation of the levels of inflammatory cytokines (IL-1 $\alpha$ , IL-6 and TNF- $\alpha$ ) and MMP9 in wound tissues compared with control non-diabetic mice. Moreover, the wound tissues of diabetic mice showed a marked reduction in the phosphorylation of Smad2 and Smad3 as well as a marked reduction in collagen production. Interestingly, compared with untreated diabetic mice, topical application of propolis significantly enhanced the closure of diabetic wounds and decreased the levels of IL-1 $\alpha$ , IL-6, TNF- $\alpha$  and MMP9 to near normal levels. Most importantly, compared with untreated diabetic mice, the treatment of diabetic mice with propolis significantly enhanced the production of collagen via the TGF- $\beta$ 1/Smad2,3 signaling axis in wounded tissues. **CONCLUSION:** Our findings reveal the molecular mechanisms underlying the improved healing and closure of diabetic wounds following topical propolis application

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