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The Effect of Oral Consumption of Propolis Alone and in Combination With Silver Nanoparticles on Wound Healing in Male Wistar Rats

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Abstract

Research to identify and develop compounds that facilitate wound healing is important, especially for hard-to-heal chronic wounds.

Purpose: This study was conducted to investigate the effects of orally administered propolis (a resinous substance found in beehives), alone and in combination with silver nanoparticles (SNPs), on the wound healing process in male rats.

Methods: Forty (40) male Wistar rats were randomly divided into 4 groups of 10 each: 1 control group received no treatment, and 3 study groups received a daily dose of 1) propolis (100 mg/kg), 2) propolis + 30 ppm SNPs, or 3) propolis + 60 ppm SNPs. Healing rate was determined by wound surface area reduction on days 4, 6, 8, and 10 post-surgery. On day 12 after wound creation, histological changes of wound healing, including number of new vessels, inflammatory cells (neutrophils, eosinophils, and mast cells) and fibroblasts were counted based on morphology using a 400x objective lens, and collagen deposition density was determined using hematoxylin and eosin and trichrome staining, respectively. The histological scores were based on a 0 to 4 scale from lowest to highest amount of improving tissue status and were analyzed using one-way analysis of variance, Tukey test, Kruskal-Wallis test, t test, and Mann-Whitney U test to examine differences among the groups. Significance was set at $P < .05$.

Results: The rate of wound healing was significantly different between the control and the treated groups on days 4, 6, 8, and 10 (percent change was not assessed on day 12) post-surgery, especially in the propolis + 30 ppm SNPs group compared to the control group. This difference was more significant on days 6 (wound healing percentage [WHP]: 75% and 45%) and 8 (WHP: 88% and 65%) post-surgery ($P < .001$). Mean neutrophil count on day 12 was highest in the control (34.8 ± 2.97) and lowest in the propolis + 30 ppm SNPs group (16.55 ± 2.12). The number of eosinophils on day 12 was considerably higher in the control group (1.05 ± 4) compared to those in the propolis group (3 ± 0.70), propolis + 30 ppm SNPs group (60/0 ± 1/1), and propolis + 60 ppm SNPs group (0.5 ± 0.52) ($P < .001$). Mean propolis + 30 ppm SNPs scores for epithelialization and granulation tissue formation were 3 and 4, respectively; in the propolis + 60 ppm SNPs, scores were 2 and 3, respectively; in the propolis alone group scores were 2 and 3, respectively (statistical significance

not computed for semiquantitative values). The highest fibroblast count was in the propolis + 30 ppm SNPs group (114.44 ± 3.90) compared to control group (73.2 ± 2.8); P <.001). The difference in collagen fiber density scores was also significant: 1.2 ± 0.42 in the control and 3.66 ± 0.50 in the propolis + 30 ppm SNPs group; (P <.001). The mean of collagen fiber density in the propolis + 60 ppm SNPs group was 2.63 ± 0.51.

Conclusion: Oral propolis alone and in combination with 30 ppm SNPs appears to provide anti-inflammatory effects and increase fibroblast proliferation and collagen deposition in experimental wounds, which may explain the observed differences in healing. Propolis + 60 ppm SNPs appears to have a cytotoxic effect. Research confirming these results and that examines toxicity levels in animals and humans is needed.