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QUANTIFICATION OF WOUND PARAMETERS IN ANIMALS TREATED WITH PROLYL-4-HYDROXYLASE INIHIBITORS

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We are investigating the effect of inhibitors of prolyl-4-hydroxylase on wound healing in rats. The compounds under study are phenanthrolinones, which act as competitive inhibitors of prolyl-4-hydroxylase. Cell based studies have shown the ability of these compounds to block collagen synthesis by cultured fibroblasts. One of these compounds (FG1648) was applied topically to punch wounds made in the back of rats. Wounds that were treated with the compound had a significant delay in contraction. To assess the quality of the tissue deposited in the wounds of the animals treated with FG1648, we created linear incisional wound in the backs of rats and gave some of the animals FG1648 (50mg/kg/bid) by oral gavage. The rats were sacrifices of day 14 and the breaking strength of the wounds from the control and treated animals were assessed utilizing the Biomechanical Tissue Characterization System (BTC 2000). The BTC 2000 uses a vacuum to deform the wound and a laser to measure the deformation and breaking strength of the wounds in the treated animals and a greater degree of elasticity. These studies indicate that collagen synthesis inhibitors can modulate the physical qualities of wound healing without interfering with critical events such as closure and epithelialization of the wound.