

Topical f1-protein from latex *Hevea brasiliensis* accelerates wound healing in diabetes by enhancing insulin signaling

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Introduction: Insulin binds on its receptor and activates intracellular proteins like IRS, AKT, ERK, and SHC triggering metabolic and mitogenic effects. In diabetes, the reduced expression of these proteins is mainly related to insulin deficiency or resistance. Studies have confirmed clinical efficacy in wound healing by protein fraction F1 from natural latex of *Hevea brasiliensis* rubber tree, especially in wounds compromised by diabetes, which healing is impaired. **Objectives:** To evaluate the influence of F1 in insulin signaling and this effect on wound healing in rats compromised by diabetes. **Methods:** It was used 80 Wistar rats: 40 induced to diabetes (**DM**) (streptozotocin 45 mg/Kg) and 40 non-diabetic (**N**), performed two dorsal wounds by punch (1.5 cm diameter) treated daily with carboxymethyl cellulose gel (**CMC**) 4% (**DM-sham/N-sham** groups) and 0.01% **F1** incorporated in CMC (**DM-F1/N-F1** groups). On 2, 7, 14 and 21 days post-injury 10 rats/day of follow-up/group were euthanized and evaluated the re-epithelialization by wound healing rate formula ($[\text{initial area} - \text{final area}] / \text{initial area}$) using ImageJ software to determine the wound areas from wound photos. The wound/scar was biopsied, held immunohistochemistry for IRS, AKT, ERK SHC and quantified by ImageJ the percentage of area marked by each protein. **Results:** DM-F1 showed higher re-epithelialization than the DM-sham ($p=0.0026$) and all wounds of DM groups were almost re-epithelialized on 14th day, different to wounds of N groups. Besides, N-F1 group showed the worst re-epithelialization of all groups, suggesting the F1 stimulate the wound healing especially when associated with diabetes. DM-F1 was higher expression of IRS, AKT, ERK and SHC compared to DM-sham ($p=0.0001$). **Conclusions:** F1 associated with DM appeared to increase the insulin signaling, increasing their effect on wound healing.

Keywords: wound healing, diabetes *mellitus*, *Hevea brasiliensis*, image processing computer-assisted

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