

***Senecio serratuloides* var. in Wound Healing: Efficacy and Mechanistic Investigations in a Porcine Wound Model**

Introduction

Senecio serratuloides is widely used for wound healing in South Africa but minimal information regarding its efficacy is available. Furthermore toxic pyrrolizidine alkaloids may be present. The following investigation sought firstly to evaluate the efficacy and safety of *Senecio serratuloides* in a porcine wound model; secondly to assess for a potential mechanism and finally isolate and identify fractions in *in-vitro* assays.

Assessment of Efficacy and Safety

Materials and Methods: Deep partial thickness and full thickness wounds were created on 9 pigs. Treatment included an occlusive dressing (negative control), activated carbon, or the *Senecio* preparation. Wounds were monitored using photographic documentation, pH measurement and histological analysis (skin thickness and collagen content). Toxicity was monitored on blood and liver samples.

Results and Discussion: Efficacy of *Senecio serratuloides* was established with a significantly thicker epidermis, maximal at day 7 post-operative, 2 days before the controls. Effects on collagen content was negligible with no toxicity detected.

Mechanistic investigation

Materials and Methods: Wound fluid was analysed for IL-10, IL-12, IL-1 β , IL-6, IL-8, TNF- α using flow cytometry based assays. Tyrosine phosphorylation and cellular proliferation was assessed using dual immunofluorescence staining.

Results and Discussion: IL-1 β levels were significantly greater in the *Senecio* treatment. Tyrosine phosphorylation increased to day 9 post-operative where it stabilised in all groups. In the same period, cellular proliferation was sustained in the *Senecio* treated wounds but not in the controls. Keratinocyte proliferation was identified as the target for *in-vitro* assays.

Extraction, Isolation and Partial Identification using In-vitro Proliferation Assays.

Materials and Methods: The plant was fractionated using solid phase extraction cartridges. Keratinocytes were grown under standard conditions in 96-well plates.

Cellular proliferation was assessed spectrophotometrically using a resazurin dye technique. Active fractions were analysed using gas chromatography and mass spectrometry.

Results and Discussion: Identified fractions increased the rate of proliferation by 300-400%. Potential lead compounds were identified. Importantly, pyrrolizidine alkaloids could not be detected.

Conclusion

Senecio serratuloides is efficacious in treating deep partial thickness wounds without inducing liver toxicity. Sustained keratinocyte proliferation linked to tyrosine phosphorylation may be an underlying mechanism. Although successful, *in-vitro* detection of active fractions requires further characterisation.