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SIRTUINS IN CUTANEOUS WOUND HEALING AND SKIN REGENERATION

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Cutaneous wound healing is a natural restorative response of injured tissue consisting of 4 phases; haemostasis, inflammation, tissue growth (proliferation), and tissue remodelling (maturation). Over last few years, several studies have aimed to find out proteins as molecular targets and compounds as potential drugs for wound healing. Some of our recent studies probed Sirtuins; most of which are NAD⁺-Dependent deacetylases for their possible role(s) in cutaneous wound healing and skin regeneration *In Vitro* and *In Vivo* by using synthetic and natural sirtuin activators. Wound healing rate was measured both *In Vitro* and *In Vivo* using cultured epidermal keratinocytes and dermal fibroblasts as well as hairless mice respectively. Expression of Sirtuins, migration related proteins (Rac1, Cdc42, α-Pak) and angiogenesis related protein (VEGF) was monitored using western blot analysis. Blood vessel formation and tissue development were monitored by angiogenesis assay and haematoxylin & eosin (H & E) staining respectively on mouse skin tissue samples. Our findings suggest that activation and/or upregulation of several Sirtuins in general (Sirt1, Sirt3 and Sirt6) and Sirt1 in particular leads to faster wound healing and cell migration. Sirtuin activators increased the expression of migration related proteins both *In Vitro* and *In Vivo*. Similarly, they increased VEGF expression, tissue development and blood vessel formation in mouse skin. So the overall results showed that Sirtuin activators are effective over a wide range of concentrations for increasing the rate of wound healing. These findings are in line with some previous studies reporting activators of Sirtuins as wound healing agents and hence call for further investigation of Sirtuins and their regulators as novel targets and drugs in the important field of cutaneous wound healing.

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