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Sirt1 Activators Promote Skin Cell Regeneration and Cutaneous Wound Healing

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Abstract : Skin acts as a barrier against the harmful environmental factors. Integrity and timely recovery of the skin from injuries and harmful effects of radiations is thus very important. This study aimed to investigate the importance of Sirt1 in the recovery of skin from UVB-induced damage and cutaneous wounds by using natural and synthetic novel Sirt1 activators. Juglone, known as a natural Pin1 inhibitor, and NED416 a novel synthetic Sirt1 activator were checked for their ability to regulate the expression and activity of Sirt1 and hence photo-damage and wound healing in cultured skin cells (NHDF and HaCaT cells) and mouse model by using Sirt1 siRNA knockdown, cell migration assay, GST-Pulldown assay, western blot analysis, tube formation assay, and immunohistochemistry. Interestingly, Sirt1 knockdown inhibited skin cell migration in vitro. Juglone up regulated the expression of Sirt1 in both the cell lines under normal and UVB irradiated conditions, enhanced Sirt1 activity and increased the cell viability by reducing reactive oxygen species synthesis and apoptosis. Juglone promoted wound healing by increasing cell migration and angiogenesis through Cdc42/Rac1/PAK, MAPKs and Smad pathways in skin cells. NED416 upregulated Sirt1 expression in HaCaT and NHDF cells as well as increased Sirt1 activity. NED416 promoted the process of wound healing in early as well as later stages by increasing macrophage recruitment, skin cell migration, and angiogenesis through Cdc42/Rac1 and MAPKs pathways. So, both these compounds activated Sirt1 and promoted the process of wound healing thus pointing towards the possible role of Sirt1 in skin regeneration and wound healing.

Keywords : skin regeneration, wound healing, Sirt1, UVB light
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