

Abstract

Healing with honey is known through ages. Its growing importance in mainstream medicine is also remarkable. Anti-inflammatory, anti-bacterial, anti-oxidant, angiogenic and anti-scarring impacts of honey especially in wound repair is noteworthy. However, possible variation of its healing impacts as per floral origin, anti-oxidant potential and dilution needs in depth characterization. Present study physico-chemically screened sixteen honeys and Jamun honey (JH) selected for detailed study particularly considering remarkable antioxidant potential. Polyphenolics of JH (JHEP) analyzed by chromatography and mass spectrometry. JHEP doses in modulating hypoxic assaults on Keratinocytes (HaCaT) studied with cadherin-catenin-cytoskeleton complex (F-actin, E-cadherin and β -catenin), HIF 1 α , Ki67 and p63 expressions employing immuno-cytochemistry (ICC), western blot and qRT-PCR. Influence of JH dilutions on HaCaT wound model under hypoxia and normoxia also explored along with documenting epithelial gene expressions and epithelio-mesenchymal transition (EMT) markers. Topical effects of JH on full thickness (diabetic/non-diabetic) wounds in comparison Manuka honey (MH) studied with semi-quantitative histopathology and collagen (I and III) expressions. Their implications on primary cutaneous fibroblasts from diabetic/non-diabetic mice also evaluated. JH impacts on diabetic wounds again assessed for angiogenic markers *viz.* HIF-1 α , VEGF, VEGFR-II. Tested honey samples satisfied criteria of Indian standard and Codex Alimentarius standard. The JH showed optimum pH (3.55), low water and hydroxy methyl furfural, highest catalase activity, phenolics and proline contents. JHEP mass spectrometry identified phytochemicals and plant secondary metabolites *viz.* *hesperetin*, *quercetin*, *ellagic acid* having anti-oxidative potential. Under hypoxia, 0.063 mg/ml JHEP dose on HaCaT showed reduction of ROS, membrane damage, HIF 1 α expression and restoration of membranous cadherin-catenin-cytoskeleton complex as well as p63 and Ki67 expressions. JH dilution (0.1% v/v) depicted reduced hypoxic impact on *in vitro* wound repair and EMT. JH and MH demonstrated enhanced collagen I expression in diabetic/non-diabetic wounds, *in vitro* wound healing of fibroblast population with α -SMA positive cell migration. Topical application of JH significantly enhanced angiogenic markers in promoting diabetic wound healing. Multi-dimensional characterization of varied honey and Jamun honey selection having potent antioxidant components and dilution effects on wound repair including diabetic wounds hence facilitated relevant therapeutic applications and indicated its applicability in appropriate dilutions for developing tissue engineering biomaterial scaffold.

Keywords: Honey characterization, Jamun honey, Antioxidants, Hypoxic assaults, Gene expression, Diabetic wound healing.