



Original article

In vitro wound healing activity of 1-hydroxy-5,7-dimethoxy-2-naphthalene-carboxaldehyde (HDNC) and other isolates of *Aegle marmelos* L.: Enhances keratinocytes motility via Wnt/ β -catenin and RAS-ERK pathways

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ABSTRACT

Wound healing is a complex process in which injured skin and tissues repaired by interaction of a complex cascade of cellular events that generates resurfacing, reconstitution and restoration of the tensile strength of injured skin. It follows β -catenin, extracellular signal regulated kinase (ERK) and Akt signaling pathways. *Aegle marmelos* L., generally known as bael is found to act as anti-inflammatory, antioxidant and anti-ulcer agent. Furthermore, studies have demonstrated that this Indian traditional medicinal plant, *A. marmelos* flower extract (AMF) was used for wound injury. Henceforth, the current study was investigated to ascertain the effect of its active constituents *in vitro* wound healing with mechanism involve in migration of cells and activation of β -catenin in keratinocytes, inhibition of PGE₂ in macrophages and production of collagen in fibroblasts. We have taken full thickness wound of rats and applied AMF for 2 weeks. Cutaneous wound healing activity was performed using HaCaT keratinocytes, Hs68 dermal fibroblasts and RAW264.7 macrophages to determine cell viability, nitric oxide production, collagen expression, cell migration and β -catenin activation. Results shows that AMF treated rats demonstrated reduced wound size and epithelisation was improved, involved in keratinocytes migration by regulation of Akt signaling, beta-catenin and extracellular signal-regulated kinase (ERK) pathways. AMF and its active constituent's increased mRNA expression, inhibited nitric oxide, PGE₂ release, mRNA expression of mediators in RAW 264.7 macrophages and enhances the motility of HaCaT keratinocytes *in vitro* wound healing of rats.

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1. Introduction

A variety of inflammatory cells, parenchymal cells, soluble mediators and extracellular matrix molecules undergo complex

interactions to accomplish the process wound healing and it is constituted of three stages, first is inflammatory followed by proliferative and final stage is remodeling (Mendonca and Coutinho-Netto, 2009). Wound healing process create extracellular signal-regulated kinase (ERK) pathways Akt signaling and beta-catenin (Squarize et al., 2010; Mi, et al., 2018). Embryonic development majorly involves beta-catenin signalling pathway for migration and proliferation of cells (Widelitz, 2008). In wound healing process, both β -catenin dependent pathway and β -catenin independent pathway are important (Mendonca and Coutinho-Netto, 2009). Growth factors like fibroblast growth factor and epidermal growth factor activates ERK and Akt signaling pathways, which in turn induce

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