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THE EFFECT OF *MIKANIA MICRANTHA* ETHANOLIC LEAVES EXTRACT ON WOUND HEALING

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ABSTRACT

Consideration of the important on wound healing treatment in human health and more than 75% of the population rely mainly on plants and plant extract. *Mikania micrantha* Kunth is a perennial creeping vine commonly known as "*selaput tunggul*" in Malaysia and "*sembungrambat*" in Indonesia, possesses several pharmacological properties and can be used to prevent and cure several diseases. Traditionally it is used in healing of sores and for wound dressing. This study was conducted to investigate the effectiveness of *M. micrantha* ethanolic extract (MELE) in wound healing, *in vitro* and *in vivo* as well as its phytochemical content. Acute dermal toxicity of MELE was also conducted to determine its safety. Total phenolic compound and antioxidant content in MELE were quantified using pyrogallol, gallic acid and stigmasterol. The plates were derivatised with ferric chloride, DPPH and anisaldehyde solutions that were freshly prepared and determined by densitometric chromatogram of HPTLC, scanned at 200 nm and 300 nm. Acute dermal toxicity study of MELE was conducted based on OECD guidelines on female and male Sprague-Dawley rats. At the end of study, blood was drawn for biochemistry and haematology analysis and the liver and kidney was excised for histology examination using H&E stain. For the *in vitro* study, cytotoxicity study was conducted on human dermal fibroblasts (HDF) using MTT assay. The acceleration of wound healing via scratch assay was carried out. HDF were treated with various concentration of MELE (7, 15, 30, and 60 µg/ml) with 100 µM of trolox as reference. Cell distribution was measured using flow cytometry analysis. In the *in vivo* study, male Sprague-Dawley rats were topically administered (0.2 ml of treatment twice daily) with MELE (10, 20 and 40 mg/ml), normal saline (vehicle control) and solcoceryl gel (positive control) on an excision wound area (2 cm in diameter) at the nape of the dorsal of the rat. The wound closure rate was calculated. Then, the rats were sacrificed, and blood collected for cytokine analysis. The skins were excised for histology evaluation. Our results showed that MELE has high content of phenolic and antioxidant properties. Rats treated with MELE showed no dermal toxicity with no significant physical and behavioural changes. No abnormalities were observed in the liver and kidney of the rats. Moreover, MELE was not cytotoxic against HDF cells with IC_{50} >100 µg/ml after 24 and 48 hours of incubation. In the scratch assay, MELE demonstrated potential wound healing properties compared to solcosery gel. MELE did not affect the cell cycle distribution and progressively underwent DNA synthesis and mitotic division in fibroblast cells. In the *in vivo* study, MELE-treated rats showed significant acceleration of wound closure with appropriate regulation of the cytokines. Histology examination of the skin showed little scar formation with less inflammatory cells, more collagen disposition and more granulation tissue in MELE-treated rats compared to control rats. The ability of MELE to accelerate wound healing may be due to the high polyphenol content in the extract. In conclusion, MELE has the potential to accelerate wound healing process with no toxicity observed due to its high phenolic and antioxidant properties.

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