

Title THE DEVELOPMENT OF NANOEMULSION
FORMULATION CONTAINING ARTOCARPUS INCISUS
EXTRACT FOR APPLICATION IN WHITENING PRODUCT

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ABSTRACT

The purposes of this study were to determine melanogenesis inhibitory, antioxidant, anti-inflammatory activities and to develop nanoemulsion formulation containing *Artocarpus incisus*'s heartwood extract using PIT method for application in whitening product. The heartwood of *A. incisus* grown in Phitsanulok Province, Thailand was extracted by using diethyl ether. HPLC analysis showed that *A. incisus* contained high amount of artocarpin ($44.5 \pm 0.1\%$ w/w). Melanocyte B16F1 melanoma cells were used for determination of the melanogenesis inhibitory activity of the extract comparing with kojic acid. The IC_{50} value of melanogenesis inhibition of the extract was 43.5 ± 2.3 $\mu\text{g/mL}$ while kojic acid exhibited IC_{50} of 57.6 ± 1.3 $\mu\text{g/mL}$. The obtained micrograph also confirmed that the extract did not change cell morphology but reduced the melanin content by inhibiting melanin synthesis, whereas kojic acid caused changes in cell morphology by losing dendrites at the same concentration. Additionally, the extract exhibited the antioxidant activity in a dose-dependent manner at the EC_{50} of 168.6 ± 6.8 $\mu\text{g/mL}$, according to DPPH assay. For anti-inflammatory activity, the inhibitory effect of the extract on $\text{TNF-}\alpha$ release was less than that of prednisolone about 8 folds.

In this study, nanoemulsion formulations containing *A. incisus* extract were prepared by the phase inversion temperature (PIT) method. The optimal formula containing 0.02% w/w *A. incisus* extract, 41.62% w/w isopropyl myristate, 8% w/w cetareth-10, 5% w/w glyceryl monostearate and 0.03% w/w carbopol 940 provided homogeneous o/w emulsion. The droplet size was 325 ± 15 nm with polydispersity of 0.31 ± 0.02 . The nanoemulsion formulations containing *A. incisus* extract obtained were physically and chemically stable. *In vitro* permeation studies were carried out across excised mouse skin using a Franze diffusion cell. The percentage of cumulative artocarpin released within 24 hours from nanoemulsion formulations was $87.2 \pm 1.6\%$. Furthermore, an efficient lightening effect was observed following topical application of nanoemulsion formulations containing *A. incisus* extract to UVB-stimulated hyperpigmented dorsal skin of C57BL/6 mice. The results suggest that *A. incisus*'s heartwood extract may be a candidate for an efficient whitening agent. In addition, nanoemulsions using PIT method are potential vehicles for improving transdermal delivery of the compounds from *A. incisus*'s heartwood extract.