UNIVERSITI TEKNOLOGI MARA

SCREENING FOR ANTIOXIDANT ACTIVITY, TOXICITY AND ANTI-DIABETIC EFFECT OF *ERYTHROXYLUM CUNEATUM* STANDARDIZED AQUEOUS EXTRACT

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of the requirements for the degree of
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CONFIRMATION BY PANEL OF EXAMINERS

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I declare that the work in this thesis was carried out in accordance with the regulation of Universiti Teknologi MARA. It is an original and is the result of my own work, unless otherwise indicated or acknowledgements as referenced work were made accordingly. This thesis has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

I, hereby, acknowledge that I have been acknowledged with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, with respect to the conduct of my study and research.

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ABSTRACT

Erythroxylum cuneatum (Erythroxylaceae) standardized aqueous extract was investigated for its antioxidant and antihyperglycemic activities for its safety *in vivo*. Dried extract was provided by Forest Research Institute of Malaysia (FRIM). Antioxidant activity was evaluated via total phenolic content assay, 1, 1-diphenyl-2-picrylhydrazyl (DPPH) scavenging activity assay, ferric reducing antioxidant power (FRAP) assay, and via inhibitory effect of extract against lipid peroxidation in liver microsomes induced by *tert*-butylhydroperoxide (*tert*-BOOH). Safety of extract was determined using Organization for Economic Co-operation and Development (OECD) guidelines acutely and subacutely in mice. Total phenolic content of extract was 0.38 ± 0.15 mg gallic acid equivalent (GAE)/mg dry weight of extract. DPPH assay showed *E. cuneatum* extract had an EC_{50} of 6.17 ± 0.02 µg/mL, while the antioxidant references were trolox, gallic acid and quercetin which elicited EC_{50} values of 3.89 ± 0.09, 0.3 ± 0.07 and 2.69 ± 0.07 µg/mL, respectively. EC_{50} values for *E. cuneatum* extract, trolox and gallic acid in the FRAP assay were 3.72 ± 0.28, 12.09 ± 0.44 and 18.59 ± 0.21 µmol Fe^{2+}/ mg dry weight, respectively. IC_{50} value for *E. cuneatum* extract, trolox and gallic acid for inhibition of *tert*-BOOH-induced lipid peroxidation were 31.62 ± 0.10, 10.00 ± 0.21 and 12.59 ± 0.12 mg/mL, respectively. Antioxidant activity of extract was correlated to total phenolic content. Based on Organization for Economic Co-operation and Development (OECD) guidelines, oral *E. cuneatum* extract is non-toxic as no adverse effect were seen at levels of more than 5 g/kg following acute oral administration and 1 g/kg following subacute administration in male and female mice. However, when administered acutely via intraperitoneal route, a dose of 300 mg/kg extract was moderately toxic, thus was harmful. In the streptozotocin induced hyperglycemic rat model, *E. cuneatum* extract (100 and 300 mg/kg, p.o.) administered twice daily elicited a significant decrease in serum glucose level after 3 weeks of treatment. In summary, *E. cuneatum* standardized aqueous extract given orally was safe in acute and subacute treatment. It has glucose-lowering effect in hyperglycaemic condition and showed high antioxidant activities in four different antioxidant assays.

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