UNIVERSITI TEKNOLOGI MARA

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

ROSLINA BINTI ALI

Thesis submitted in fulfilment of the requirements for the degree of Master of Science

Faculty of Pharmacy

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CONFIRMATION BY PANEL OF EXAMINERS

I certify that a Panel of Examiners has met on 21 December 2015 to conduct the final examination of Roslina binti Ali on her Master of Science thesis entitled “Screening For Antioxidant Activity, Toxicity and Anti-Diabetic Effect of *Erythroxylum cuneatum* Standardized Aqueous Extract” in accordance with Universiti Teknologi MARA Act 1976 (Akta 173). The Panel of Examiners recommends that the student be awarded the relevant degree. The Panel of Examiners was as follows:

Mohamed Salama Mohamed Ahmed Salama, PhD
Professor
Faculty of Pharmacy
Universiti Teknologi MARA
(Chairman)

Zabidah Binti Ismail, PhD
Professor
Faculty of Pharmacy
Universiti Teknologi MARA
(Internal Examiner)

Kamisah Yusof, PhD
Associate Professor
Faculty of Medicine
Universiti Kebangsaan Malaysia
(External Examiner)

SITI HALIJAH SHARIFF, PhD
Associate Professor
Dean
Institute of Graduates Studies
Universiti Teknologi MARA
Date: 28 March 2016
AUTHOR’S DECLARATION

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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.

Name of student : Roslina binti Ali
Student I.D. No. : 2008264836
Programme : Master of Science (Pharmacology)
Faculty : Pharmacy
Thesis Title : Screening For Antioxidant Activity, Toxicity and Anti-Diabetic Effect of Erythroxylum cuneatum Standardized Aqueous Extract.

Signature of Student : 
Date : March 2016
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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