UNIVERSITI TEKNOLOGI MARA

DISCRIMINATIVE ANALYSIS OF *FICUS DELTOIDEA* JACK VARIETIES USING MULTIPLATFORM METABOLOMICS AND DEVELOPMENT OF BIOACTIVITY PREDICTION MODEL

NORAINI BINTI KASIM

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AUTHOR'S DECLARATION

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

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

Name of Student	:	Noraini binti Kasim
Student I.D. No.	:	2012497394
Programme	:	Doctor of Philosophy – AS990
Faculty	:	Applied Sciences
Thesis Title	:	Discriminative Analysis of Ficus Deltoidea Jack Varieties using Multiplatform Metabolomics and Development of Bioactivity Prediction Model
Signature of Student	:	 ……..
Date	:	April 2020

ABSTRACT

Ficus deltoidea Jack (Moraceae) or locally known as *'mas cotek'* is a popular herb possessing various medicinal attributes. Ethnobotanically, *Ficus deltoidea* has been claimed to possess antidiabetic properties, the leaf decoction is commonly used as an alternative for type 2 diabetes management. Morphology distinction of the seven main varieties (var. *angustifolia*, var. *bilobata*, var. *deltoidea*, var. *intermedia*, var. *kunstleri*, var. *motleyana* and var. *trengganuensis*) is challenging due to the extreme leaf heterophylly and unclear varietal boundaries. This study aims to establish an analytical method for distinguishing the seven varieties found in Peninsular Malaysia based on comprehensive metabolite analysis. The seven varieties were fingerprinted and profiled using HPLC, MS and NMR. Mass-based dereplication identified 26 compounds comprising of flavanols, proanthocyanidins, hydrocinnamic acids, furanocoumarins and flavone glycosides. In addition, high resolution MS in this work was able to detect new hydrocinnamic acids; 2-*O*-acetyl-3-*O*-*trans*-*p*-coumaroyltartaric acid and 2-*O*-acetyl-3-*O*-*cis*-*p*-coumaroyltartaric acid in *F. deltoidea* with high confidence. Interestingly, var. *intermedia* was found to contain a unique compound, absent in all other varieties, oxypeucedanin hydrate. Apart for that, generally the varieties contain the same set of metabolites but differ in the quantity. The chemical markers of *F. deltoidea,* vitexin and isovitexin, were quantified in all varieties using UHPLC analysis. Their content were significantly different across the varieties. Isovitexin content was highest in var. *angustifolia* with 12.97 µg/g of dry plant material while vitexin content was highest in var. *deltoidea* with 27.21 µg/g of dry plant material. Multivariate data analysis PLSDA and HCA revealed the existence of three groups based on the differentiation in the metabolite content. Group 1 consists of var. *bilobata*, group 2 consists of var. *intermedia* and *angustifolia,* and group 3 consists of var. *motleyana*, var. *deltoidea*, var. *kunstleri* and var. *trengganuensis*. Intra-variety analysis of var. *trengganuensis* from several locations revealed that they are not significantly different. The chemical profiles were quite consistent regardless of nature the plants, cultivated or wild. Even plants growing among bushes on sandy soils and the ones growing on palm trees were similar. At 100 ppm, α-glucosidase inhibitory activity of all collected 112 samples ranges from no inhibition to 71.50%, indicating the varied biological properties. Consequently, PLS predictive model for α-glucosidase inhibitory activity based on the metabolite profiles was constructed. The findings suggest that varieties *intermedia* (CH), *trengganuensis* and *kunstleri* are more superior in terms of α-glucosidase inhibitory activity. Metabolites correlated to α-glucosidase inhibitory activity were identified as 4-aminobutyrate, malic acid, epicatechin, catechin, afzelechin and isoleucine. The validated predictive model was found to be very accurate with the root mean squared error of prediction (RMSEP); 5.4. The correlation model can be useful tool in quality control of *F. deltoidea* herbal products especially for identification of correct varieties possessing optimal biological properties, eliminating the need for routine bioactivity testing for all samples.

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TABLE OF CONTENTS