UNIVERSITI TEKNOLOGI MARA

CHEMICAL CONSTITUENTS FROM *Diospyros discolor* Willd. AND THEIR ACETYLCHOLINESTERASE INHIBITORY ACTIVITY

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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.

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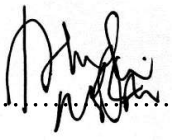
Signature of Student	:	
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ABSTRACT

Diospyros discolor Willd. (Ebenaceae), also known as 'buah mentega' in Malay, is widely distributed in South East Asia. Traditionally, the plant was used for various health complaints such as diarrhea, dysentery, stomatitis, snake bites, spider bites, diabetes, and eczema in South East Asia. Many compounds, especially triterpenes in *Diospyros* sp. were reported to inhibit acetylcholinesterase and butrylcholinesterase enzyme *in vitro* and *in vivo*. *D. discolor* was reported to contain triterpenes, yet to be investigated for their AChE inhibitory activity. *D. discolor* leaves extract showed high (95.80 ± 1.57 %) AChE inhibitory activity at the concentration of 100 µg/mL. Therefore, *D. discolor* was further evaluated for its chemical constituents and bioactivities. The leaves and stem barks of *D. discolor* were air-dried, powdered, and successively extracted using *n*-hexane, dichloromethane, and methanol. The solvents were evaporated off to obtain dried crude extracts. Exhaustive purification employing various chromatographic techniques including vacuum liquid chromatography (VLC), column chromatography (CC), radial chromatography (RC), and preparative thin layer chromatography (PTLC) afforded a new flavonol, 7,4'-dihydroxy-5,3',5'-trimethoxyflavonol (**149**), along with seven known triterpenes; betulin (**2**), betulinic acid (**3**), ursolic acid (**27**), *β*-sitosterol (**91**), *β*-sitosterol-3-*O*-glucopyranoside (**92**), stigmasterol (**94**), stigmast-4-en-3-one (**95**), four flavonols; kaempferol (**109**), hyperin (**116**), astragalin (**122**), isoquercitrin (**123**) and a flavan-3-ol; (+)-epicatechin (**140**) from the leaves and stem bark of *D. discolor*. Their structures were determined by comprehensive NMR, FTIR and MS analysis. The methanol extracts of leaves and stem barks of *D. discolor* did not show significant antiproliferation against SH-SY5Y cell when incubated at different sample concentration ranging from 1000 to 3.90625 ppm at 24-, 48- and 72-hours incubation time. However, the methanol extract of stem barks exhibit significant antiproliferative activity at 125, 500 and 1000 ppm concentration at 72 hours incubation. The compounds (**2**, **3**, **91**, **92**, **94**, **95**, **122**) were tested for AChE inhibitory activity, but only stigmast-4-en-3-one (**95**) showed the highest AChE inhibitory activity among the compounds tested with an IC_{50} value of 11.77 ± 2.11 µM. Compound (**95**) was previously isolated from *D. maritima* stem and *D. eriantha* heartwood, but this is the first time reported from *D. discolor* and studied against AChE. In conclusion, the phytochemical study on *D. discolor* resulted in a new flavonol (**149**) and twelve known compounds of triterpenes and flavonoids previously reported in *Diospyros* sp. Even though *D. discolor* extracts showed high percent inhibition against AChE enzyme, the compounds isolated showed moderate inhibition.

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