

UNIVERSITI TEKNOLOGI MARA

**ISOLATION, ABSOLUTE
CONFIGURATION
DETERMINATION AND ALPHA
GLUCOSIDASE INHIBITORY
ACTIVITY OF LABDANE
DITERPENOIDS FROM
HEDYCHIUM CORONARIUM J.
KOENIG RHIZOMES AND LCMS
PROFILING OF *ALPINIA
PURPURATA* (VIEILL.) K. SCHUM
RHIZOMES**

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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.

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Thesis Title	:	Isolation, Absolute Configuration Determination and Alpha Glucosidase Inhibitory Activity of Labdane Diterpenoids from <i>Hedychium coronarium</i> J. Koenig Rhizomes and LCMS Profiling of <i>Alpinia purpurata</i> (Vieill.) K. Schum Rhizomes
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ABSTRACT

The necessitation of stereochemical study of chiral drugs to ensure their safety before manufacturing have spurred the need to determine the absolute configuration (AC) of labdane diterpenoids isolated from rhizomes of *Hedychium coronarium* J. Koenig. Literature has revealed that NMR data alone are insufficient for stereochemical study of these compounds. The employment of CD technique such as vibrational circular dichroism (VCD) along with density functional theory (DFT) calculations has helped to unequivocally assign AC of stereogenic centers of labdane diterpenoids from other plants. Labdane diterpenoids are known to possess α -glucosidase inhibitory activity but there is no report of this activity of the labdane diterpenoids isolated from the rhizomes of the *Hedychium coronarium*. *Alpinia purpurata* (Vieill.) K. Schum rhizomes have been reported to contained few labdane diterpenoids. However, no report on LCMS profile of fractions from rhizomes of this plant with a view of identifying more labdane diterpenoids. This study was aimed at the isolation, purification and characterization of labdane diterpenoids from *Hedychium coronarium* rhizomes through RHPLC method, NMR, FT-IR, OR and MS analyses, and the determination of the distribution of labdane diterpenoids in *Alpinia purpurata* rhizomes by qualitative LCMS profiling of its Hexane and DCM fractions. Experimental and theoretical vibrational circular dichroism (VCD) analyses were conducted on the isolated labdane diterpenoids. Conformational analysis was carried out by MMFF94 as implemented in Spartan 14 software. The stable conformers of less than 10 kcal and higher than 1.5% Boltzmann population were geometrical optimized at DFT/B3LYP/6-31+G(d,p) level of theory as implemented in Gaussian 16. Two new C-15 diastereotopic labdane diterpenoids; H α -15 (15*R*) and H β -15 (15*S*) Coronarin D methyl ethers (Compound I and II) were successfully separated and their absolute configurations were unequivocally established as (+)-(5*S*,9*S*,10*S*,15*R*) and (-)-(5*R*,9*R*,10*S*,15*S*), respectively. The two compounds gave four theoretical stable conformers each along with their relative energies and Boltzmann populations at 298K. Nine other known labdane diterpenoids; Compound III to X and XII were also isolated and absolute configurations of four of them (Compound IV, V, VIII and XII) were established as (+)-(5*S*,9*S*,10*S*)-labda-8(17),13(14)-diene-16,15-olide, (+)-(5*S*,9*S*,10*S*)-labda-8(17),12-diene-15(16)-olide, (-)-(5*R*,9*S*,10*S*,11*S*,15*S*)-15-hydroxy-16-formyl-labda-8(17),12-dien-11,15-peroxide and (+)-(5*S*,9*S*,10*S*)-15,16-bisnorlabda-8(17),11-diene-13-one, respectively. Compound III and IX; Coronarin D C-15 epimers and 15-hydroxy-labda-8(17),13(14)-diene-16,15-olide or Coronarin C epimers were established by VCD as C-15 epimeric mixtures. The two new labdane diterpenoids along with seven others from *Hedychium coronarium* rhizomes were subjected to α -glucosidase inhibitory assay. Six compounds; I, II, IV, VIII, IX and X showed the most significant α -glucosidase inhibitory activity with compound II being the most active with IC₅₀ of 22 μ M; twice as effective as than acarbose with IC₅₀ of 46 μ M. All the compounds (I, II, IV, VIII, IX and X) are hits for α -glucosidase inhibitors for management of diabetes mellitus. The qualitative LCMS profiling of the *Alpinia purpurata* rhizomes fractions revealed ten and eleven possible labdane diterpenoids from hexane and DCM fractions, respectively.

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