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## Faculty of Applied Sciences

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Title :

**Phytochemical Study Of Dryobalanops From Malaysian Dipterocarpaceae, And Structure - Activity Relationship Studies**

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*Dryobalanops* is one of the genera in the Dipterocarpaceae family, which is distributed as major species in emergent canopy of Lambir Forest and Sarawak lowland dipterocarps forest. The genus is very unique, as there are only seven species available in the whole world, which confined to the tropical forests of West Malesia. The chemical constituents of Dipterocarpaceae are reported to possess various biological activities such as cytotoxicity, antiviral, antibacterial and anti-inflammatory activities. The aims of this study are to isolate secondary metabolites, to determine their antibacterial, DPPH scavenging and cytotoxic activities, to study structure-activity relationship, and to propose biogenesis pathway and chemotaxonomic significance in *Dryobalanops*. The dried powder of the stem bark of *D. aromatica*, *D. lanceolata*, *D. rappa* and *D. becarii* were macerated with acetone and evaporated under reduced pressure. The crude acetone extract was subjected to vacuum liquid chromatography to give several fractions. Purification of fraction with combination of several chromatography techniques gave four new oligostilbenoid derivatives; malaysianol A (**1**), B (**2**), C (**3**) and D (**4**), and a new galloylglucoside derivative; malaysin A (**5**), together with 15 known oligostilbenoid (**6-20**) and six known non-oligomeric compounds (**21-26**). The chemical structures of isolated compounds were elucidated

based on the spectroscopic data evidences and comparison with reported authentic data. Biogenetically, the biosynthesis routes of non-oligomeric compounds were formed from the shikimate pathway, while oligomeric compounds were from the combination of shikimate and acetate malonate pathways. Based on the radical species and their condensation types, 19 oligostilbenoids isolated from this study were formed from the oxidative coupling reaction of two radicals with active site at carbons C-8 and C-14 (**C8-C14** type), carbons C-8 and C-8 (**C8-C8** type), carbons C-3 and C-8 (**C3-C8** type), and oxygen O-13 and carbon C-8 (**C7-C14** type). The finding of oligostilbenoids with the condensation types **C3-C8** and **C7-C14** are not commonly found in Dipterocarpaceae family. Based on the chemotaxonomic study, the presence of several compounds that were only found in the tribe Dipterocarpeae and never reported in the tribe Shoreae supported the previous studies on the morphological character that suggested the placement of *Dryobalanops* under the tribe Dipterocarpeae.

In the antibacterial assay, flexuosol A (**16**) and upunaphenol D (**18**) showed moderately antibacterial activity against *S. epidermidis*, *S. aureus*, *S. xylosus* with MIC value of 50.0/16.7, 66.7/33.3 and 50.0/16.7  $\mu\text{M}$ , respectively. In the cytotoxic assay, vaticanol C (**20**) were found to be moderately active against A549 cell line ( $\text{IC}_{50}$  11.8  $\mu\text{M}$ ), as well as  $\alpha$ -viniferin (**11**) and ampelopsin E (**12**) against MCF-7 cell line ( $\text{IC}_{50}$  23.1 and 21.0  $\mu\text{M}$ , respectively), while other compounds were either weak or not active. In the DPPH assay, malaysianol A (**1**), flexuosol A (**16**) and vaticanol B (**19**) displayed great scavenging activity with  $\text{IC}_{50}$  values 15.7, 15.0 and 11.8  $\mu\text{M}$ , respectively. In the structure-activity relationship study, the scavenging activity of oligostilbenoid depend on the number of hydroxyl group and their stereochemistry, otherwise no definitive correlation between unit structures of oligostilbenoid and cytotoxicity was observed, but its conformation seem to be responsible for the cytotoxic properties.