UNIVERSITI TEKNOLOGI MARA

ISOLATION OF STILBENOID COMPOUNDS FROM *MACARANGA HEYNEI* I.M. JOHNSON AND *SHOREA LEPROSULA* MIQ., BIOSYNTHETIC PATHWAY, SYNTHESIS OF STILBENOID ANALOGUES, AND THEIR BIOACTIVITIES

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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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ABSTRACT

The phytochemical investigations were conducted on two plants namely *Macaranga heynei* I.M. Johnson (Euphorbiaceae) and *Shorea leprosula* Miq. (Dipterocarpaceae). The aim of this study are to isolate the secondary metabolites from two plants as mentioned, to propose the biosynthetic pathway of new isolated compounds, to synthesize the stilbene analogues, to evaluate the bioactivities of isolated and synthesised compounds as well as to discuss the structure-activity relationship (SAR) of the results from bioassays. The isolation process was conducted by using several chromatographic techniques such as thin layer, vacuum liquid, radial, column and preparative thin layer chromatographies. The structures of the isolated compounds were elucidated by means of various spectroscopic analyses namely infrared (IR), ultraviolet-visible (UV-Vis), mass (MS) and nuclear magnetic resonance (NMR) spectroscopies; optical rotation, melting point, polarimeter and comparison with the previous literature studies. Ten dihydrostilbenes were isolated from the leaves of *M. heynei* which seven of them are new compounds characterised as malayheyneiins A-G **(230-236)** and three known compounds namely laevifolins A **(148)** and B **(149)** as well as macarubiginosin C **(152)**. Six oligostilbenoids were obtained from the purification on the stem bark of *S. leprosula*; (-)-roxburghiol A **(179)**, (-)-laevifonol **(167)**, (+)-α-viniferin **(156)**, (-)-hopeaphenol **(213)**, (+)-isohopeaphenol **(214)** and (-)-hemsleyanol D **(223)**. (-)-Roxburghiol A **(179)**, (+)-isohopeaphenol **(214)** and (-)-hemsleyanol D **(223)** were firstly reported in this species. In DPPH radical scavenging activity, malayheyneiins A **(230)** and C **(232)**, laevifolins A **(148)** and B **(149)**, macarubiginosin C **(152)**, (+)-α-viniferin **(156)**, (-)-hopeaphenol **(213)** and (-)-hemsleyanol D **(223)** are good DPPH scavengers (IC_{50} = 4.56-10.25 μM). Both dihydrostilbenes and oligostilbenoids were derived from phenylpropanoid pathway but the route of dihydrostilbenes has its own special network. It is being separated from stilbenes by the action of double bond reductase (DBR) on *p*-coumaroyl CoA prior to the action of stilbene synthase (STS) enzyme. In acetylcholinesterase inhibitory assay, malayheyneiins B **(231)** and C **(232)**, macarubiginosin C **(152)** and hopeaphenol **(213)** showed significant activity (IC_{50} = 5.06 – 10.00 μM). In the antibacterial assay, laevifolins A **(148)** and B **(149)** displayed moderate activity against *Staphylococcus cohnii*. Interestingly, laevifolin B **(149)** demonstrated strong inhibition (IC_{50} = 1.64 μM) against *S. aureus* whilst laevifolin A **(148)** showed moderate activity. Laevifolin A **(148)** and macarubiginosin C **(152)** displayed significant inhibition against HT-29 cancer cell line with the IC_{50} values of 21.20 and 55.30 μM respectively. In addition, three deoxybenzoin and twelve stilbene analogues were synthesised using Fridel-Craft acylation and Wittig reactions respectively. All major compound were examined for DPPH radical scavenging, acetylcholinesterase inhibitory and antibacterial activities. 2,3',4,4'-Tetrahydroxy deoxybenzoin **(238)** gave moderate scavenging activity (IC_{50} = 22.34 μM). Interestingly, 2,4,4'-trihydroxy deoxybenzoin **(237)** displayed excellent activity against acetylcholinesterase inhibitory (IC_{50} = 1.02 μM). Structure-activity relationship studies on the assays revealed the presence of prenyl group and catechol moiety in the compounds as one of the factors that contributed to the good activity.

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