PHYTOCHEMICAL ANALYSIS OF *Murraya koenigii* (RUTACEAE) AND *IN VITRO* CYTOTOXIC ACTIVITY OF ITS ISOLATED COMPOUNDS AND THE SYNTHETIC ANALOGUES OF GIRINIMBINE AND MAHANIMBINE

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ABSTRACT

The objectives of the study are to determine the phytochemical constituents from the bark and leaves of *Murraya koenigii*, to develop synthetic analogues from girinimbine and mahanimbine via Lewis acid-mediated reactions, and to evaluate cytotoxic activities. The isolation and purification of the chemical compounds were done by using various chromatography methodologies. These compounds were then structurally identified by various spectroscopic techniques such as NMR, IR, UV and mass spectrometry. *In vitro* cytotoxic activities were evaluated against human promyelocytic leukemia (HL-60), cervical cancer cell lines (HeLa) and the normal mouse embryonic fibroblasts (NIH/3T3) cell lines via MTT assay. As the findings, phytochemical analysis on bark and leaves of *M. koenigii* afforded a total of 36 chemical compounds included six new carbazoles, *viz.*, murrastanine-A, murrastinine-A, -B and -C, murrayatanine-A and bismahanimboline. Besides, two girinimbine analogues, *viz.*, murranimbine and epoxygirinimbine; and three mahanimbine analogues, *viz.*, bicyclomahanimbine, cyclomahanimbine and murrayazolinine, were successfully derived. Five carbazoles and two non-carbazoles have shown very strong to moderate *in vitro* cytotoxic activities (CD_{50} < 20 μg/mL) against both HL-60 and HeLa cell lines, *viz.*, murrayafoline-A, mahanine, murrayamine-J, murrastinine-C, murrayatanine-A, β-sitosterol and 2-hydroxy-4-methoxy-3,6-dimethylbenzoic acid. In conclusion, the isolated compounds from *M. koenigii* were found to possess potential *in vitro* cytotoxic activities against selected cancer cell lines. In fact, most of these results were first time reported. These findings have shown that *M. koenigii* is an important source for therapeutic discovery and may lead to the development of potential drugs.

ANALISIS FITOKIMIA *Murraya koenigii* (RUTACEAE) DAN AKTIVITI SITOTOKSIK *IN VITRO* BAGI SEBATIAN KIMIA YANG DIPENCILKAN DAN ANALOG SINTETIK GIRINIMBINA DAN MAHANIMBINA

ABSTRAK

Kajian ini bertujuan menentukan kandungan fitokimia daripada kulit kayu dan daun *Murraya koenigii*, membina analog sintetik daripada girinimbina dan mahanimbina menggunakan asid Lewis sebagai pengantara, dan menguji aktiviti sitotoksik. Pemencilan dan penulenan sebatian kimia dijalankan dengan menggunakan pelbagai kaedah kromatografi. Struktur sebatian kemudiannya dikenalpasti melalui teknik spektroskopi iaitu NMR, IR, UV dan spektrometri jisim. Aktiviti sitotoksik *in vitro* diuji ke atas sel promielositik leukemia manusia (HL-60), sel kanser servik (HeLa) dan sel normal tikus fibroblas embrio (NIH/3T3) dengan rawatan MTT. Dapatan kajian menunjukan sebanyak 36 sebatian kimia termasuk enam karbazola baharu, iaitu murrastanina-A, murrastinina-A, -B dan -C, murrayatanina-A dan bismahanimbolina telah diperolehi. Selain itu, dua analog girinimbina, iaitu murranimbina dan epoksigirinimbina dan tiga analog mahanimbina, iaitu bisiklomahanimbina, siklomahanimbina dan murrayazolinina, telah berjaya disintesiskan. Lima karbazola dan dua sebatian bukan karbazola menunjukkan aktiviti sitotoksik yang sangat aktif ke sederhana aktif (CD_{50} < 20 μg/mL) terhadap kedua-dua sel HL-60 dan sel HeLa, iaitu murrayafolina-A, mahanina, murrayamina-J, murrastinina-C, murrayatanina-A, β-sitosterol dan asid 2-hidroksi-4-metoksi-3,6-dimetilbenzoik. Kesimpulannya, sebatian yang dipencilkan daripada *M. koenigii* didapati mempunyai potensi aktiviti sitotoksik *in vitro* ke atas sel kanser yang dipilih. Malah, sebahagian besar daripada keputusan ini dilaporkan pertama kali. Hasil kajian menunjukkan *M. koenigii* merupakan sumber penting bagi penemuan terapeutik dan membawa kepada pembangunan ubat-ubatan yang berpotensi.

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