



**UNIVERSITI PUTRA MALAYSIA**

***CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF  
GLYCOSMIS MACRANTHA MERR. AND CRATOXYLUM ARBORESCENS  
(VAHL) BLUME***

**MAIZATULAKMAL BINTI YAHAYU**

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MACRANTHA* MERR. AND *CRATOXYLUM ARBORESCENS* (VAHL) BLUME**

By

**MAIZATULAKMAL BINTI YAHAYU**

**This thesis submitted to the School of Graduate Studies, Universiti Putra Malaysia, in  
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**May 2012**

**Chairman: Profesor Mawardi Rahmani, PhD**

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Phytochemical and biological activity studies of *Glycosmis macrantha* (family Rutaceae) and *Cratoxylum arborescens* (family Guttiferae) were carried out. The stem barks of *Glycosmis macrantha* and *Cratoxylum arborescens* were collected from Sabah and Sarawak, respectively. These two species were subjected to detail phytochemical investigation which involved extraction using three organic solvents of different polarity and isolation of the compounds by using common chromatographic techniques such as gravity column chromatography, vacuum column chromatography, chromatotron, preparative thin layer chromatography and gel filtration column chromatography using Sephadex LH20. The structural elucidations of the isolated compounds were carried out using spectroscopic techniques such as NMR, MS, IR, UV and by comparison with literature data. The phytochemical investigations have led to the isolation of several compounds of different classes including alkaloids, xanthenes, flavonoids and

triterpenoids. The crude extracts and some of the isolated compounds were tested for antioxidant, cytotoxic and antimicrobial activity using DPPH, MTT and disc diffusion methods, respectively. The cell line used in cytotoxic assay was the human breast cancer (MCF7) cell line. The antimicrobial activity was tested against eight microbes namely *Bacillus subtilis*, *Bacillus cereus*, *Escherichia coli*, *Klebsiella pneumonia*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Enterobacter aerogenes* and *Candida albican*.

The phytochemical study of *Glycosmis macrantha* has led to the isolation of two new acridone alkaloids, macranthanine (**116**), 7-hydroxynoracronycine (**117**); one known acridone alkaloid, namely atalaphyllidine (**118**), two flavonoids, dihydroglychalcone A (**32**) and epicatechin (**58**); and a sterol,  $\beta$ -sitosterol (**119**). Similar isolation work on *Cratoxylum arborescens* has yielded three xanthenes,  $\alpha$ -mangostin (**36**),  $\beta$ -mangostin (**37**) and fuscaxanthone C (**103**) together with stigmasterol (**120**). Among the pure compounds, only macranthanine (**116**) and 7-hydroxynoracronycine (**117**) exhibited significant activities towards antioxidant assay with IC<sub>50</sub> values 63.3 and 80.2  $\mu$ g/ml, respectively. The study on antiproliferative activity against human breast cancer (MCF7) cell line displayed that  $\alpha$ -mangostin (**36**) and  $\beta$ -mangostin (**37**) exhibited significant activity with IC<sub>50</sub> values of 12.48  $\mu$ g/ml and 28.42  $\mu$ g/ml respectively. Meanwhile, only  $\alpha$ -mangostin (**36**) exhibited strong inhibition on the growth of *B. subtilis*, *B. cereus*, *S. typhimurium* and *S. aureus* with inhibition zone 16, 20, 17 and 20 mm, respectively.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk Ijazah Master Sains

**KANDUNGAN KIMIA DAN AKTIVITI BIOLOGI DARIPADA *GLYCOSMIS MACRANTHA* MERR. DAN *CRATOXYLUM ARBORESCENS* (VAHL) BLUME**

Oleh

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Kajian fitokimia dan aktiviti biologi ke atas tumbuhan Rutaceae, *Glycosmis macrantha* dan tumbuhan Guttiferae, *Cratoxylum arborescens* telah dijalankan. Kulit batang *Glycosmis macrantha* dan *Cratoxylum arborescens* masing-masing telah diperoleh dari Sabah dan Sarawak. Kedua-dua species tersebut digunakan untuk kajian fitokimia yang lebih mendalam yang melibatkan pengekstrakan dengan menggunakan tiga pelarut organik yang berbeza kecutubannya dan pemencilan sebatian dengan menggunakan teknik kromatografi biasa seperti kromatografi turus graviti, kromatografi turus vakum, kromatografi radial, kromatografi lapisan nipis penyediaan dan kromatografi turasan gel menggunakan Sephadex LH 20. Pengenalpastian struktur sebatian yang telah dipencilkan ini telah dijalankan dengan menggunakan kaedah spektroskopi seperti NMR, MS, IR, UV dan juga perbandingan dengan data literatur. Kajian fitokimia ini telah membawa kepada pemencilan beberapa sebatian yang berbeza kelas termasuk

alkaloid, xanthon, flavonoid dan triterpenoid. Ekstrak mentah dan sebahagian sebatian yang telah dipencilkan telah diuji aktiviti antioksidan, sitotoksik dan antimikrob dengan masing-masing menggunakan kaedah DPPH, MTT dan peresapan cakera. Sel yang digunakan untuk ujikaji sitotoksik adalah sel kanser payudara manusia (MCF7). Aktiviti mikrob telah diuji ke atas lapan mikrob seperti *Bacillus subtilis*, *Bacillus cereus*, *Escherichia coli*, *Klebsiella pneumonia*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Enterobacter aerogenes* dan *Candida albican*.

Kajian fitokimia ke atas *Glycosmis macrantha* telah membawa kepada pemencilan dua sebatian baru alkaloid akridon, makranthanina (**116**), 7-hidroksinorakronisina (**117**); satu alkaloid akridon yang telah diketahui iaitu atalafilidina (**118**), dua flavonoid, dihidroglicalkon A (**32**) dan epikatekin (**58**); serta satu sterol,  $\beta$ -sitosterol (**119**). Kajian yang sama ke atas *Cratoxylum arborescens* telah menghasilkan tiga xanthon,  $\alpha$ -mangostin (**36**),  $\beta$ -mangostin (**37**) dan fuscaxanthon C (**103**) bersama stigmasterol (**120**). Di antara sebatian tulen tersebut, hanya makranthanina (**116**) dan 7-hidroksinorakronisina (**117**) menunjukkan aktiviti yang berpotensi terhadap ujian antioksidan dengan nilai  $IC_{50}$  63.3 dan 80.2  $\mu\text{g/ml}$ . Kajian ke atas aktiviti antiproliferatif terhadap sel kanser payudara manusia (MCF7) menunjukkan  $\alpha$ -mangostin (**36**) dan  $\beta$ -mangostin (**37**) memiliki aktiviti yang menarik dengan nilai  $IC_{50}$  12.48 dan 28.42  $\mu\text{g/ml}$ . Namun begitu, hanya  $\alpha$ -mangostin (**36**) sahaja yang memiliki perencatan yang kuat ke atas pertumbuhan *B. subtilis*, *B. cereus*, *S. typhimurium* dan *S. aureus* dengan zon perencatan 16, 20, 17 dan 20 mm.

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I certify that a Thesis Examination Committee has met on 30<sup>th</sup> May 2012 to conduct the final examination of **Maizatulkmal** on her thesis entitled “**Chemical Constituents and Biological Activities of *Glycosmis macrantha* Merr. and *Cratoxylum arborescens* (Vahl) Bl.**” in accordance with Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The committee recommends that the student be awarded the degree of Master of Science.

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## DECLARATION

I declare that the thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institutions.



MAIZATULAKMAL BT. YAHAYU  
Date: 30<sup>th</sup> May 2012

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