UNIVERSITI PUTRA MALAYSIA

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

MAIZATULAKMAL BINTI YAHAYU

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

By

MAIZATULAKMAL BINTI YAHAYU

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May 2012

Chairman: Profesor Mawardi Rahmani, PhD
Faculty: Science

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, xanthones, 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, β-sitosterol (119). Similar isolation work on *Cratoxylum arborescens* has yielded three xanthones, α-mangostin (36), β-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$_{50}$ values 63.3 and 80.2 µg/ml, respectively. The study on antiproliferative activity against human breast cancer (MCF7) cell line displayed that α-mangostin (36) and β-mangostin (37) exhibited significant activity with IC$_{50}$ values of 12.48 µg/ml and 28.42 µg/ml respectively. Meanwhile, only α-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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alkaloid, xanthone, flavonoid dan triterpenoid. Ekstrak mentah dan sebahagian sebatian yang telah dipencilkkan telah diuji aktiviti antioksidan, sitotoksik dan antimikrob dengan masing-masing menggunakan kaedah DPPH, MTT dan peresapan cakera. Sel yang digunakan untuk uji 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 albicans*.

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, β-sitosterol (119). Kajian yang sama ke atas *Cratoxylum arborescens* telah menghasilkan tiga xanthone, α-mangostin (36), β-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 IC₅₀ 63.3 dan 80.2 µg/ml. Kajian ke atas aktiviti antiproliferatif terhadap sel kanser payudara manusia (MCF7) menunjukkan α-mangostin (36) dan β-mangostin (37) memiliki aktiviti yang menarik dengan nilai IC₅₀ 12.48 dan 28.42 µg/ml. Namun begitu, hanya α-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\textsuperscript{th} May 2012 to conduct the final examination of Maizatulakmal on her thesis entitled “Chemical Constituents and Biological Activities of *Glycosmis macrantha* Merr. and *Cratoxylum arborescens* (Vhal) 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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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

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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: 30th May 2012
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