

UNIVERSITI TEKNOLOGI MARA

**BIOLOGICAL AND PHYTOCHEMICAL STUDIES
OF FIVE MALAYSIAN *UNCARIA* SPECIES**

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ABSTRACT

In this study, five species of *Uncaria* (family Rubiaceae) also known as “Gambir” widely used as traditional medicine in Malaysia were evaluated for their biological activities as well as phytochemical and total phenolic contents. They are *U. calophylla*, *U. acida*, *U. lucida*, *U. cordata* and *U. longiflora* var *pteropoda*. The methanolic extracts of the plants are subjected to various bioassays including antioxidant, radical scavenging (by 1,1-diphenyl-2-picrylhydrazyl or DPPH) method, antimicrobial (by hole-plate diffusion method) and antihyperglycemic assay (*in-vitro* inhibition of α -glucosidase enzyme and *in-vivo* assay). The total phenolic content (TPC) of the plants was evaluated by the Folin-Ciocalteu method. All tested extracts exhibited very strong antioxidant potential (>85% inhibition) in the FTC and TBA assays. In the DPPH assay, *U. longiflora* (stems and leaves) showed strong radical-scavenging properties with IC_{50} values of 8-10 μ g/ml comparable to vitamin C. In the antimicrobial assay, most extracts displayed good antimicrobial activity against Gram-positive bacteria. *U. longiflora* was found to inhibit *Candida albicans* with MIC value of <1.0 μ g/ml for both leaves and stems comparable to cyclohexamide. In the *in-vitro* and *in-vivo* assays, *U. longiflora* (stems), *U. acida* (leaves) and *U. cordata* (stems) showed very good antihyperglycemic potential. On the basis of chemical and biological screening, *U. longiflora* (stems) was selected for phytochemical investigation. Repeated chromatographic techniques on the bioactive fraction resulted in the isolation of two major compounds **ULs1** and **ULs2** identified as pentacyclic alkaloids isomitraphylline and isopteropodine based on 1H and ^{13}C NMR spectroscopic data. **ULs1** exhibited stronger antioxidant and α -glucosidase activities than **ULs2** which could relate to better immuno-modulatory properties of isomitraphylline. In the α -glucosidase inhibitory assay, these two compounds also showed dose-dependent activities indicating their potential as antihyperglycemic agents for type II diabetes.

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In the name of Allah, the Most Compassionate, the Most Merciful

Based from the Quranic in Surah Al-Alaq: 1-5

“Proclaim! In the name of thy Lord and Cherisher, who created man, out of a (mere clot of congealed blood). Proclaim! And thy Lord is Most Bountiful. He who taught (the use of) the pen. Taught man that which he knew not”.

This holy verse emphasized on the need for mankind to sep knowledge as much as possible. With that in mind as well as accepting the government’s urge for the younger generations to do researches, I decided to embark on this journey. My deepest gratitude goes to my two supervisors: Associate Professor Dr Rohaya Ahmad and Associate Professor Dr Zainon Mohd Noor for their invaluable advices. I thanked my husband for his support and encouragements, my lovely children namely Along, Mimi, Aqilah and Ariff Luqman, who have been my strength in this challenging path towards excellence. My thanks also go to the Ministry of Education, who financed my study and the principal of Sekolah Menengah Kebangsaan Meru, Klang for the support given. Last but not least are my peers in the Natural Product Lab, G Block and to all my students whom I encountered at Universiti Teknologi MARA, Shah Alam, Selangor. I sincerely hope that this research will benefit the society.

TABLE OF CONTENTS

TITLE PAGE	PAGE
ABSTRACT	iii
ACKNOWLEDGEMENT	iv
TABLE OF CONTENTS	v
LIST OF TABLES	x
LIST OF FIGURES	xi
LIST OF ABBREVIATIONS	xii
CHAPTER 1: INTRODUCTION	
1.1. Natural Products and Phytochemistry	1
1.2. The Genus <i>Uncaria</i>	2
1.3. Problem Statement	2
1.4. Objectives of Study	3
1.5. Scope of Study	3
CHAPTER 2: LITERATURE REVIEW	
2.1. Malaysian Medicinal Plants	4
2.2. Genus <i>Uncaria</i>	5
2.3. Traditional and Pharmacological Uses of <i>Uncaria</i>	8
2.4. Indole Alkaloids	10
2.5. Phytochemical and Biological Studies of <i>Uncaria</i>	13
2.6. Phytochemical and Biological Studies of Malaysian <i>Uncaria</i>	14
2.7. Antimicrobial Agents	15
2.8. Antioxidants	16

CHAPTER 1

INTRODUCTION

1.1 Natural Products and Phytochemistry

What is natural product? A natural product can be defined as a product that is derived from plants, animals or microbial sources, primarily through physical processing, sometimes, facilitated by simple chemical reactions such as acidification, basification, ion exchange, hydrolysis and salt formation as well as microbial fermentation (Hezberg, 1996). Natural compounds mainly originate from three sources; plants, animals and microorganisms. Natural products, also referred to as secondary metabolites, are important in many aspects of life, imparting taste, aroma and colour to most of our foods and providing a vast number of pharmacoactive chemicals used in medicine and agriculture (Mahady, 2001).

Plants have been used as food, dyes, fragrances (perfumes) and insect repellents (Heath, 1981). Phytochemistry is an understanding of plant metabolites and their constituents. Knowledge of structures and relationships helps us to understand how botanical medicines function in the human body (Mahady, 2001). Most of the plant-derived drugs were originally discovered through the study of traditional cures and folk knowledge of indigenous people (Gilani, 2005). Researchers have been interested in biologically-active compounds isolated from plants species; for example, the elimination of pathogenic microorganisms because of the resistance that microorganisms have built against antibiotics (Essawi & Srour, 2000). Some of the important medicines are plant-derived; for example, reserpine from *Rauwolfia serpentina* and digitoxin from *Digitalis purpurea* used as cardiovascular drugs, quinine from *Cinchona* used as an antimalarial