UNIVERSITI TEKNOLOGI MARA

PHYTOCHEMICAL STUDIES AND BIOLOGICAL EVALUATION OF *Artocarpus odoratissimus* AND *Artocarpus sarawakensis*, AND SOME SYNTHESIS OF PINOSTROBIN AND PINOCEMBRIN DERIVATIVES

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Perkara di atas di rujuk.

2. Sehubungan dengan itu, pihak kami menyerahkan buku hard bound thesis yang telah diserahkan oleh Dr. Nyotia Anak Nyokat untuk simpanan dan rujukan di Perpustakaan UiTM Sarawak.

3. Disertakan Borang Pengesahan Penerimaan yang perlu dikembalikan kepada kami untuk tujuan rekod.

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WAN FAKHRURRAZI BIN WAN DAHLAN

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TABLE OF CONTENTS

ABSTRACT

Phytochemical study and biological evaluation were conducted on stem bark and roots of *A. odoratissimus*, and stem bark and leaves of *A. sarawakensis*. Previous studies revealed that *Artocarpus* species possess various biological activities such as cytotoxicity, antioxidant, antibacterial and anti-inflammatory. However, there are very few reports on the *Artocarpus* species from Sarawak. Besides, *A. odoratissimus* has not been studied intensively, and *A. sarawakensis* has not been reported before. Thus, this study aimed to develop a chemical profile of these species as well as to explore the potential of both plants against microbial and other bioassays. Various chromatographic methods such as vacuum liquid chromatography, column chromatography, and radial chromatography were used to isolate and purify compounds from the extracts of both plants. Structural elucidation was accomplished using spectroscopic methods such as ultraviolet, infrared, mass spectroscopy, 1D nuclear magnetic resonance, and comparison with reported authentic data. The phytochemical study resulted in the isolation of two flavonoids; pinocembrin and pinostrobin, together with ten triterpenoids. Six compounds were isolated from *A. odoratissimus*. Taraxsteryl acetate and hexyl laurate were found in the stem bark, while, pinocembrin, pinostrobin, α-amyrin acetate, and β-amyrin acetate were isolated from the root extract. All compounds except taraxsteryl acetate were identified for the first time from *A. odoratissiumus*. Nine compounds were isolated from *A. sarawakensis*. α-Amyrin, ß-amyrin, stigmasterol, α-amyrin acetate, ß-amyrin acetate, and hexyl laurate were isolated from the stem bark, while, *β*-sitosterol, lupeol, friedelin and stigmasterol were isolated from the leaves extract. Two flavonoids, namely pinostrobin and pinocembrin were synthesized and derived. The extracts for both species and some of the isolated pure compounds were tested for its antioxidant and antimicrobial activities. The antioxidant properties showed that the leaves methanolic extract of *A. sarawakensis* demonstrated the strongest free radical scavenging activity with IC_{50} value of 17.0 μg/mL and contained the highest phenolic content (2695.5 mg GAE/g). As for synthesized compounds, 3'-nitro-2-hydroxy-4, 6-dimethoxychalcone showed the highest antioxidant activity with IC_{50} value of 132.4 μg/mL. The microbial activity was carried out by disc diffusion and microdilution method for determination of the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). The stem bark methanolic extract of *A. odoratissimus* displayed very good activities towards *S. pyogenes* with MBC values 28.13 μg/mL and towards *P. aeruginosa* and *E. coli* 56.25 μg/mL followed by the stem bark ethyl acetate extract of *A. odoratissimus* towards *S. pyogenes* with MBC values of 56.25 μg/mL. All the synthesized compounds showed strong activity towards *S. pyogenes* and *P. mirabilis* with MIC values less than 100 μg/ mL. In the Lipoxygenase assay, the result showed a high inhibition of enzyme activity with 100.00 % inhibition for the stem bark and root ethyl acetate extracts of *A. odoratissimus*. Meanwhile, *A. sarawakensis* extracts revealed a moderate enzyme activity with 67.09 ± 3.85 % and 64.19 ± 2.37 inhibition for the leaves and stem bark ethyl acetate extracts. A total of 21 synthesized compounds were evaluated for the anticancer activity against the human breast cancer (MCF-7). Chalcones derivatives were found to have stronger activity than derivatives of pinostrobin and pinocembrin. Compound 2-hydroxy-4,6-dimethoxychalcone showed the most potent activity against MCF-7 with the percentage of inhibition value of 11.96 %.

CHAPTER ONE
INTRODUCTION

1.1 Background of Study

The healing potential in plants has been well documented long before humankind understood the presence of microbes and its relationship with plants in medicinal uses. Since ancient times, plants were used to treat common infectious diseases in man. Knowledge of the benefits of these traditional plant medicines have been passed down the generations and is still used these days habitually to treat various maladies (Rios and Recio, 2005). Based on a report by The World Health Organization, more than 80% of the populations in developing countries derive their primary healthcare needs from plants or plant-based derivatives (Canter, Thomas, and Ernst, 2005).

Herbal products are the oldest form of medicine used in healthcare. This knowledge was crucial to the expansion of modern civilization. A primitive man observed, appreciated and utilized to their advantage the great diversity of plants available to them as sources of food, clothing, shelter, and medicine. The use of medicinal plants in the treatment of common diseases was acquired over time through the observations of wild animal behavior and by trial and error. Over time, each tribe developed their own 'pharmacopeia' based on this knowledge acquired. Environmental, geographical, ethnic and religious differences of each civilization further influenced the practices and the philosophy of traditional medicine leading to many different systems (World Health Organization, 2005).

Natural products are a renewable source of chemicals derived from living things such as plants, microbes, and animals. Multidisciplinary approaches which consist of botany, ethnobotany, phytochemistry, and biological techniques are often involved in the study of natural products. Recently, the use of natural base products as nutraceuticals for improving human health has become preferable; even as a potential chemotherapeutic agent. Plant products and their derivatives contribute to about 50% of all drugs used in clinical medicine. In the last decade alone, at least a dozen potent drugs found from flowering plants. For example, the derivatives of *Dioscorea* species,