CHAPTER 1

1. INTRODUCTION

1.1 General

Plants produced a wide variety of secondary metabolites during hundreds of millions of years of evolution as means of defending themselves against herbivores, viruses, microorganism and other plants. Among that more than 50,000 natural products that are known today, over 12,000 are alkaloids.

Plants mostly act as food supplier due to the richness of carbohydrates, proteins, fibers and in natural products they act as traditional medicinal herbs. Malaysia is the richest and the oldest rain forest in the world. It may be attributed by the warm and nearly uniform which is suitable for the growth of the tropical rain forest. Malaysia is considered as a stable region and this has made possible for their persistence over 50 million years ago[1].

According to the World Health Organization (WHO) about three quarters of the world population relies upon traditional remedies for health care. Historian from all around the world has produced evidence to show that apparently all primitive people used herbs in sophisticated way. For instance, quinine from *Cinchona* bark was used to treat the symptoms of malaria long before the disease was identified. Most of the plant-derived drugs were originally discovered through the study of traditional cures and folk knowledge of indigenous people.

Despite the increasing interest of public in phytomedicine, very few drugs from higher plants have attained any prominence in conventional medical practice in the last

couple of decades. The most notable example is Taxol, a diterpenoid originally obtained from the bark of the pacific yew tree. Certainly we can see clear evidence of interest in phytomedicine at a global level, which has been so dramatic that sales of herbal products in the world worth over 100 billion dollar a year. There are several specific reasons for this fortunes of herbalism such as, people are aware of and frightened of the side-effects associated with chemical drugs, life-long use of expensive drugs mainly for symptomatic relief such as hypertension, asthma and diabetes. There also recognition of traditional medical systems, particularly of Asian origin and the identification of medicinal plants from indigenous that has shown to have significant healing power, either in the natural state or as the source of new pharmaceuticals.[4]

The practice of the medicinal plants found active substance, which may divided into two classes which is pharmaceutical active substance and pharmacology active substance. These active substances were classified into seven group (alkaloids, saponine, flavanoid, polyphenol, quinone, glycoside and glucoside).[2]

Herbal medicine is the most widely used system and closest to the modern medicine, in terms of application to a wide variety of disease and the way it treats disease.[3]

The chemical and the biological studies of new plants are actively studied in Malaysia. Plants were collected, extracted, and tested for the chemical contents as well as its biological activities. The author has studied the Malaysian Lauraceae plant, *Alseodaphne corneri* Kosterm. Isolation and structural elucidation of alkaloids from the bark and leaves of this species is the subject of this study.

1.2 Lauraceae: Botany and Distribution.

Kochummen (1997) reported that the Lauraceae family consists of 35 genera and 2500 species throughout the warmer parts of the world while in Malaysia it comprises about 16 genera and 213 species [5]

In Malaysia, the members of Lauraceae are known as "***Medang***" or "***Tejur***" and its growth depends on lowland or highland. In the lowland, they are typically small trees of the lower canopy except for a new species which may reach up to 30 meters tall where as in the highland the Lauraceae becomes more abundant reaching the top of the forest canopy. Therefore, the term "oaks laurels forest" is given to this vegetation which lies at 1200-1600m.

Most of Lauraceae species are evergreen, though seasonal in flowering and in the development of new leaves. There are two important features of the Lauraceae family which are the presence of aromatic substances in the tissues, the small flowers with their closely packed sepals and stamens, arranged in circles of trees, open the anters and revealed the pollen.

The leaves of plants in this family are spiral, alternate, opposite, sub-opposite, whorled, entire, and leathery. The color of the new leaves vary from nearly white to pink, purple, red, or brown as in the Kelantan, e.g. Laurel (*Litsea castanea*). The flowers are small, regular, greenish white or yellow, fragrant or with rancid smell, bisexual, or unisexual and united with six sepals in two rows.

Botanically the genera of the Lauraceae are distinguished by details of the stamens which are difficult to make out. In the first six genera: *Cinnamomum. Cryptocarya*,

Phoebe, Alseodaphne, Dehaasia, and *Persea* – the flowers and also the fruits are arranged in relatively long stalked panicle produced from the leaf – axils or the end of twigs. While, in the last four genera; *Actinodaphne, Litsea, Neolitsea, and Lindera*- the flowers are grouped in the little heads which are themselves put together to form dense little clusters in the leaf-axils on the twigs behind the leaves, or on the branches and trunk.[6-8]

In Malaysia, the plants are commercialized as timbers. They are suitable for plywood manufacture and decorative works such as interior, finishing, paneling, furniture, and cabinet making. The bark of many species has commercial value such as *cinnamon* (*Cinnamomum verum, C.cassia*) and *massoy (Cryptocarya massoy*). The avocado or alligator pear (*Persea americana*), a species indigenous to Tropical America is now widely cultivated in tropical countries for its fruits. *Cinnamomum iners* (*medang teja)* is commonly planted as shade tree in Malaysia.

A high content of ethereal oils are found in many Lauraceae. Ethereal oils are important sources for spices and perfumes. Avocados are important oil-rich fruit that are now planted across tropical climates in the world.[2]

1.3 Challenges in Lauraceae Classification

The knowledge of all individuals comprising the Lauraceae is incomplete. As of 1991, approximately 25-30% of neotropical Lauraceae species had not been described. As of 2001, embryological studies had only been completed on individuals from 26 genera yielding a 38.9% level of knowledge, in terms of embryology, for this family.

Additionally, the huge amount of variation within the family for any potential defining characteristic poses a major challenge for developing a reliable classification. It is impossible to describe even one genus or tribe by a single well-defined character. For this reason, all proposed classifications rely on a set of characteristics where the combination presents the most frequently observed traits for the group.

The Lauraceae are nearly all woody trees and shrubs comprising 30 to 50 genera and about 2,000 species. An exception is the vining, leafless, parasitic genus *Cassytha.* The leaves are simple, without stipules, and usually alternate. The flowers are actinomorphic, usually bisexual, and possess a perianth of six, basally connate sepal like segments. The androecium most frequently comprises 4 whorls of 3 stamens each, although the inner whorls are often sterile. The filaments of the inner whorl usually have a pair of enlarged glandular appendages near the base. The anthers dehisce by means of commonly 4, upwardly opening flaps. The single simple pistil has a usually superior ovary with a single pendulous ovule in a solitary locule. The fruit is a berry or a drupe, often surrounded basally by the short, persistent perianth cup. Unlike other Magnoliidae, the endosperm is completely absorbed by the embryo in Lauraceae.[9, 10]

1.4 Classification of Tribes

Classification of Lauracea can be illustrated in the list below. The classification included 62 genera, mainly in Southeast Asia and Latin America.[11]

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Laurales

Family: Lauraceae

Genera:

Actinodaphne	*Adenodaphne*	*Aiouea*	*Actinodaphne*
Alseodaphne	*Anaueria*	*Aniba*	*Apollonias*
Aspidostemon	*Beilschmiedia*	*Brassiodendhron*	*Caryodaphnopsis*
Cassytha	*Chlorocardium*	*Cinnadenia*	*Clinostemon*
Cryptocarya	*Dahlgrenodendrone*	*Dehasiaa*	*Dicypellium*
Dodecadenia	*Endiandra*	*Endlicheria*	*Eusideroxylon*
Gamanthera	*Hexapora*	*Hypodaphnis*	*Iteadaphne*
Kubitzkia	*Laurus*	*Licaria*	*Lindera*
Litsea	*Machilus*	*Mezilaurus*	*Mochinnodaphne*
Mutisiopersea	*Nectandra*	*Neocinnamomum*	*Neolitsea*
Nothaphoebe	*Ocotea*	*Paraia*	*Parrasassafras*
Persea	*Phoebe*	*Phyllostemonodaphne*	*Pleurothyrium*
Potomeia	*Potoxylon*	*Povedadaphne*	*Ravensara*
Rhodostemonodaphne	*Sassafras*	*Sextonia*	*Sinosassafras*
Syndiclis	*Triododaphne*	*Umbelluraria*	*Urbanodendron*
Williamodendron	*Yushunia*		

Scheme 1.1: Classification of Tribes

1.5 Genus *Alseodaphne*: Botany and Distrubition

The genus *Alseodaphne* belongs to family Lauraceae. It comprises about 62 species, which are distributed from Yunan to West Malaysia, Sri Langka and Burma. 20 species are found in Malaysia.

Plants of this genus are usually trees or shrubs. Their leaves are spirally arranged often crowded at ends of branch, rarely alternate. The terminal buds are naked or covered with stiff narrow scales, inflorescence axillary's and paniculate. The Flowers are bisexual with six sub equal perianth lobes and three outer usually smaller sizes. Their fruits are ellipsoid, black, glossy, with thin juicy mesocarp or woody, seated on enlarged fleshy stalk, usually warty; perianth lobes usually deciduous. The fruits of same species are said to be highly poisonous.[5-7]

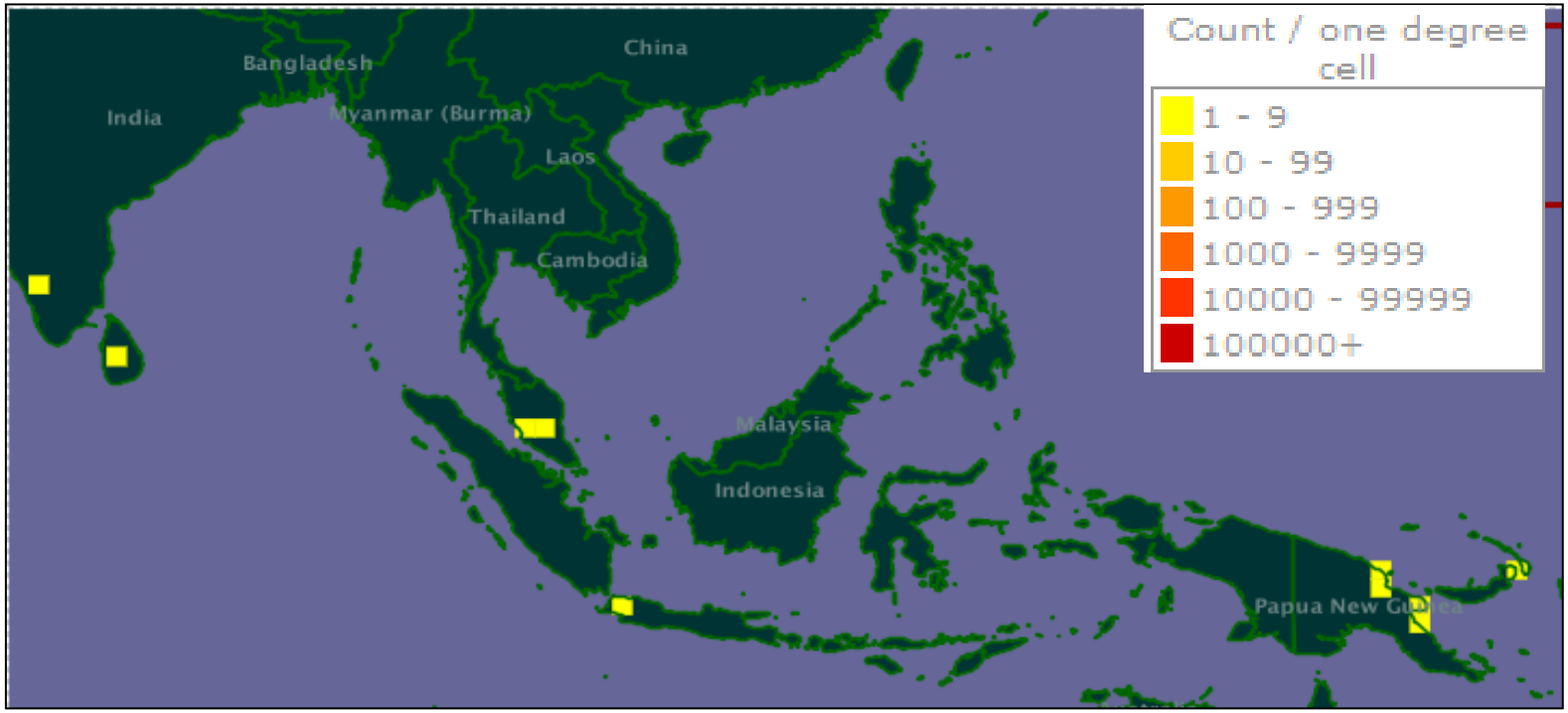

Figure 1.00: Map Distribution Occurrences of the *Alseodaphne* Species in the World[11]

Table 1.1: Data Set Coordinates of *Alseodaphne Species*[11]

Scientific Name	Dataset	Coordinates	Country
Alseodaphne	Plants of Papua New Guinea	8.925°S, 143.258°E	Papua New Guinea
Alseodaphne	Plants of Papua New Guinea	7.175°S, 147.508°E	Papua New Guinea
Alseodaphne	Missouri Botanical Garden	6.6199°S, 106.53°E	Indonesia
Alseodaphne	Plants of Papua New Guinea	6.425°S, 147.258°E	Papua New Guinea
Alseodaphne	Plants of Papua New Guinea	6.7583°S, 147.008°E	Papua New Guinea
Alseodaphne	Missouri Botanical Garden	5.17°S, 145.8°E	Papua New Guinea
Alseodaphne	Plants of Papua New Guinea	5.175°S, 145.425°E	Papua New Guinea
Alseodaphne archboldiana	NSW herbarium collection	4.9°S, 145.1°E	Papua New Guinea
Alseodaphne	Plants of Papua New Guinea	4.3416°S, 152.008°E	Papua New Guinea
Alseodaphne peduncularis	Missouri Botanical Garden	3.97°N, 101.63°E	Malaysia
Alseodaphne	Missouri Botanical Garden	3.0°N, 102.33°E	Malaysia
Alseodaphne semicarpifolia	Missouri Botanical Garden	7.27°N, 80.59°E	Sri Lanka
Alseodaphne	Missouri Botanical Garden	11.3°N, 76.58°E	India

Table 1.2: *Alseodaphne* Species Found in Malaysia

Genus: *Alseodaphne*	
A. peduncularis	***A. corneri***
A. oblanceolata	*A. rubrolignea*
A. bancana	*A. dura*
A. nigrescens	*A. insignis*
A. micrantha	*A. intermedia*
A. obovata	*A. albifrons*
A. ridleyi	*A. macrantha*
A. paludosa	*A. wrayi*
A. pendulifolia	*A. foxiana*
A. garciniaecarpa	*A. perakensis*

1.6 *Alseodaphne corneri* Kosterm

Alseodaphne corneri Kosterm exists as small trees with about 6m tall. Terminal bud covered with 1cm long scales. Their twigs are stout, grey with prominent leaf scars. Leaves are closely spirally arranged at ends of twigs with stalk about 3-4cm long, blade thickly leathery, abovate to elliptic shape with the size 28-52 × 12-16 cm. The leaves closely spirally arranged at end of twigs. They are apex pointed; midrib raised on the upper surface, secondary nerves about 22 pairs, raised on both surfaces, tertiary nerves reticulate, visible on both surfaces. Inflorescence in particles clustered below the apical bud and axillaries up to 14cm long, unbranched, glabrous, axes glaucuous, bracts up to 8mm long and persistent. The flowers are up to 14mm long, perianth lobes equal, oblong and 5mm long. The fruit of this species are ellipsoid; up to 3×2cm seated on very thick, rough, warded, obconical 2-3cm long pedicles with persistent perianth lobes.[6]

Figure 1.01: Pictures of *Alseodaphne corneri* Kosterm

1.7 Objectives of Study

The main objectives of this study are;

1. To extract and isolate alkaloid from the barks and leaves of *Alseodaphne corneri*.

2. To elucidate the structure of new and known alkaloids by using spectroscopic methods mainly 1D-NMR (^{1}H and ^{13}C), 2D-NMR (COSY, HMQC, HMBC, NOESY), Ultraviolet (UV), Infrared and HR-MS.

3. To study the biological activities such as antihypertensive and antiplasmodial activities of the known and new alkaloids isolated from *Alseodaphne corneri.*