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1.1 General

Plants play important role as food supplier in form of carbohydrates, proteins, fibers and oils, and as sources of natural products, which can be used as traditional medicines or herbs. The dependence of early human civilization on herbs for the purpose of healing the sick is well documented in the history of Chinese, Egyptians and Romans. Even today a large number of new chemical components are isolated from plant herbs and are being used in traditional treatments among the rural communities. In fact, interests in medicinal plants throughout the world at all levels of society have grown tremendously over the past twenty years and investigations of many plant species for their biological activity on animals and human beings are still in progress.

In Malaysia, at least 500 genera and more than 5000 species were found in the flora with ca. 900 species being used by practitioners of traditional medicines¹. Less than 5% of these plants have been investigated for pharmacologically active compounds, which have been used for many generations in various traditional medicinal systems. Alkaloids have been found especially in the family of Annonaceae, Lauraceae, Apocynaceae, and several others, just to name several families. More than 10,000 alkaloids of very different structures have been isolated and some of the alkaloids possess significant pharmacological activities such as antileishmanial and cytotoxic properties²

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In the search of new medicines large number of plants is being analyzed for their secondary metabolite content. For that purpose, the author studied six species from the family of Lauraceae. The study mainly deals with isolation and structural elucidation of natural products from the bark and the leaves of *Phoebe grandis* (Nees) Merr., *Phoebe lanceolata*, *Phoebe scortechinii*, *Dehaasia longipedicellata*, *Dehaasia candolleana* and *Dehaasia incrassata*

1.2 Lauraceae: General Appearance And Morphology

Lauraceae is normally occurring in Southeast Asia and tropical America with 40 genera and over 2000 species³. It is a family of shrubs and small evergreen trees, usually with aromatic bark and leaves. In Malaysia, its contribution is about 213 species, from 16 genera.

Ecology of Lauraceae is dependent on the types of lands whether lowlands or highlands. In the lowlands, the Lauraceae are typically small trees except for a few species, which may reach 30 meters tall whereas in the highlands, like the Fagaceae (oaks, mempening) the lauraceae become more abundant reaching the top layer of the forest, which lies at 1200 - 1600 m. Such Oak-Laurel Forest is a feature of the mountains of tropical Asia from the Himalayas to New Guinea⁴. The apparent dominance of the two kinds of trees depends on the inability of other genera of lowland trees to survive at such altitudes.

In Malaysia⁵ this large Lauraceae family is known as *Medang* or *Tejur*. Most of our species are evergreen, though seasonal in flowering and in the development of

new leaves. There are two important typical features of the Lauraceae family. First, the presence of aromatic substances in the tissues makes the cut bark or the crushed leaves or fruit smell of resin, turpentine, citronella, cinnamon, cloves and essential oils. This property the laurels share with others such as *kenanga* and Eugenia families (Annonaceae and Myrtaceae). Second, the small flowers with their closely packed sepals and stamens, arranged in circles of trees, open the anthers and revealed the pollen.

The leaves of this family appear in a simple way. They are spiral, alternate, opposite, sub opposite, whorled, entire and leathery. Occasionally the secondary veins pinnate have only one pair of veins (trinerved) as in Cinnamomum. When more than one present, the basal pair is enhanced and the leaf base appears trinerved as in Lindera. The color of the new leaves vary from nearly white to pink, purple, red or brown as in the Kelantan Laurel (Litsea castanea). The leaves of many kinds are glaucous beneath and often have closely set parallel veinlets between the main veins of the leaf so as to give a spider-web effect.

The flowers are small, regular, greenish white or yellow, fragrant or with rancid smell, bisexual or unisexual, trimerous (trimerous in *Neolitsea*) and perianth free or united with six tepals in two rows (four tepals in two rows in *Neolitsea*). The flowers are pollinated chiefly by flies and beetles, which are attracted by the smell emitted from the flowers.

Monkeys, squirrels, bats, foxs and birds eat the fruits. However, these animals do not eat some species. The fruits are small to large one-seeded berry. They are <u>Chapter1</u> Introduction

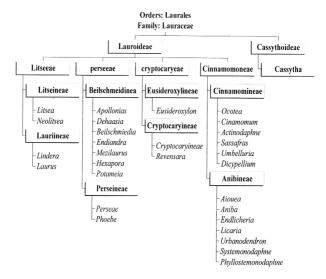
enveloped by the excrescent perianth tube (Cryptocarya) or the perianth persisting and clasping the base of fruit as in Phoebe. In some genera the perianth lobes are dropping but the tube is developing into a shallow or deep cup at base of fruit (Litsea). The fruit stalks are enlarging and becoming highly colored in some species of Dehaasia and Alseodaphne. The fruits are generally distinctive; especially those of the genera allied with Litsea, which represent a kind of forest fruit to be differed from those of any other trees.

Botanically, the genera of the Lauraceous 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 panicles produced from the leaf-axils or the end of the twigs. While, in the last four genera; Actiodaphne, Litsea, Neolitsea and Lindera- The flowers are grouped in 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.

This large family of Lauraceae provides so many useful economic products. In Malaysia, the timber is light hardwood with trademark name *Medang*. Most of the economically important species other than sources of excellent woods are spices or flavoring agents. For example, avocado (*Persea*) is one of the important tropical fruits; Camphor from the bark of an Asiatic tree (*Cinnamomum*) is extensively cultivated as the source of essential oil. In fact, ethereal oils of varied chemical composition, polyphenols, lignans and a few triterpenes and steroids have been found in the laurels, which is also rich in alkaloids⁶.

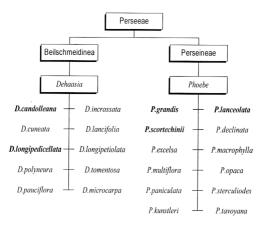
1.3 Classification of tribes

Classification of Lauraceous proposed by Hsuan Keng⁷ can be illustrated in Scheme 1.1 and Scheme 1.2. He classified that over thirty genera, mainly in tropical and sub tropical Asia and America, about sixteen are found in Malaysia. This classification is according to Malayan seed plants.



Scheme 1.1: Classification of Lauraceae

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Scheme 1. 2: Phoebe and Dehaasia species found in Malaysia.

1.4 The Genus Phoebe

Phoebe, 'the Greek Goddess' belongs to the family of Lauraceae, of the tribe of Persecae⁸. A genus of trees or shrubs can be found in Asia, Malaysia and America. In Malaysia the species are largely montane. Kochummem³ reported that there are 50 species found in Pan Tropic and 6 species in Peninsular Malaysia.

Phoebe is found most abundant in Borneo and the Malaysian Peninsula, from central Perak to Malacca. Several Malaya species with their local names are listed below: P. grandis, 'medang ketanah or tanah', P.cuneata Blume, 'medang asam' (sour-relish laurel), 'medang pasir' (shore laurel), 'medang tanah', 'medang telur'; P.

multiflora Blume, 'medang asam', 'medang ketanah', 'medang merah', 'medang pasir', 'medang burung', 'medang keserai', 'medang kunyit', 'medang jambak'; P. declinata Nees, 'medang tanah', 'medang inai', 'medang telur'; and P. tavayana Hook, 'medang rungkoi' are having a certain value as timber trees. The wood of the species mention above is used usually for house-building. As a wood of a good type soft to moderately hard, light, slightly lighter colored than the heartwood; all those species used for carving and sculpture, paneling for doors altars wardrobes, carriages and ceiling. Ridely¹⁰ reported that the wood is very durable and valued for house building and furniture.

The leaves are spirally arranged, inclined to be in rosettes at the end of the twigs. The flowers appear in bisexual and panicles from upper leaf axils. Whereas the fruits are ovoid or ellipsoid seated on a cup formed and slightly enlarged calyx.

1.5 The genus Dehaasia8.

Dehaasia is a tree of moderate size, with large leaves, found almost throughout western Malaysia, Perak, Pahang to Singapore. About 35 species of Dehaasia are found in Burma, China, Thailand, Indochina, Malaysia and New Guinea. 9 species are found in Malaysia. Various Malay names are given to these species such as D. cuneata, 'medang ketanah', 'medang kunyit', 'serai tandok', D. elliptica, 'medang burong', 'medang kunyit' and generally Dehaasia itself, known as 'gajus hutan' or 'pekan'.

Bark of *Dehaasia* species is gray-brown whereas inner bark is yellow-brown, smo.:h to cracking and lenticellate. Leaves and twigs are generally drying blackish. <u>Chapter1</u> Introduction

The timber is durable and used for house building. The Orang Asli of the Tapah Hills says that the fruit is very poisonous.

1.6 Forest Key to common Phoebe and Dehaasia sp.

General: *Dehaasia* species can be characterized through their medium size to large tree with more than 90 cm girth, whereas in *Phoebe* species there are small trees or shrub and can be a medium sized tree with characteristic of leaves⁷⁻⁸:

- Small tree or shrub; leaf thinly leathery with long tip.
- Medium sized tree; leaf apex usually blunt.

Among the *Phoebe* species studied, *Phoebe grandis* is a very common species and widely distributed. Indeed, leaves of this species are characterized with less prominent in secondary nerves, which are not distinctly looping near margin. *Phoebe lanceolata* can be found mainly in riverbanks in Central Peninsular Malaysia. As comparison to other species, the young twig of *P. lanceolata* is glabrous. Description of the *Phoebe* and *Dehaasia* species, which are deposited at The University Malaya Herbarium is described below³⁻⁵.

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Figure 1.1: Phoebe grandis leaves clustered at the end of the twigs.



Figure 1.2: Dehaasia incrassata leaves and fruit with fleshy reddish stalk.

Phoebe grandis (Nees) Merr.

Phoebe grandis belongs to the tribe of Persea. This timber tree is evergreen with alternate leaves, often fascicle at the end of the twigs. The tree is medium size to 121 m tall and 150 cm girth. The bark is lenticelate and scaling off in thin papery flakes with strongly aromatic smells. The inner bark is dark brown.

The leaves are frequently clustered at the end of the twigs. The stalk may have 1.2-5 cm long with blade leathery, obovate or oblanceolate. It is also very variable and sometimes glaucous below $12.5-30 \times 3.5-12.5$ cm. The color of the flowers is normally yellowish brown. The fruits of this species may be blue in color, ellipsoid 1.5×0.75 cm seated on slightly enlarged lobed perianth. The species can be found in the lowland to the mountain forests throughout Malaysia, Java, Sumatra and Borneo.

Phoebe lanceolata (Wall. ex Nees) Nees

Lance in Latin is known as 'shaped'. It is a shrub or small riverside tree up to 9 m tall. The young twig is glabrous with the leaf stalk 1.5-4.0 cm long. The blade thinly and leathery leaves are lanceolate or elliptic, often narrow and long, 11.0-24.0 x 1.5-8.0 cm. The yellow flowers are perianth glabrous outside while the fruit is ovoid. 1.2 x 0.6 cm, seated on lobed perianth cup. This riverside tree is commonly found in lowland forests of Kelantan, Terengganu, Pahang and Selangor. This species appears in two forms; one form with very narrow, 1.0 to 1.5 cm broad lanceolate leaves and the other with 5.0 to 8.0 cm broad elliptic leaves.

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Phoebe scortechinii (Gamb.) Kochummen comb.nov.

The small tree is normally up to 15 m tall and 150 cm girth. The young twig is hairy and the leaf stalk is 1.2 cm long with blade chartaceous shape, obovate to oblanceolate, short cuspidate ca. 10-15 x 5-7 cm. Fruit unknown. Recorded from mountain forests at Maxwell's Hill, Taiping, Perak.

Phoebe scortechinii (Lauraceae) KL4886 was collected at Gunung Arong reserved forest, Johore, in April 1999. The species was identified by the phytochemical survey of Malavan Herbarium. University of Malava.

Dehaasia longipedicellata (Ridl.) Kosterm

Dehaasia longipedicellata is a small tree with 12 m tall and 30 cm girth. Leaves are apex pointed; blade softy hairy on the undersurface, broadly elliptic to obovate, $13 - 27.5 \times 6.5 - 13.5$ cm and stalk is about 1.0 - 2.5 cm long. The leaves also have 10 - 14 pairs of secondary nerves, raised below; faint above and tertiary nerves scalar form. They are also having reticulations visible on both surfaces. Flowers of this species are unknown but the fruit is globosely with depressed or flattened apex. 5.5 cm across on 3.5 long swollen stalks.

Dehaasia candolleana (Meisn.) Kosterm

This species is a small tree with 8 m tall and 10 cm in diameter. The bark is whittish grey; inner bark is white and grey twigs with lark: leaf-scars; leaves spirally <u>Chapter l</u> Introduction

simple, crowded at the end of the twigs, elliptic, apex shortly acuminate or acute, base obtuse, 17.5-25.0 cm x 5.5-13.5 cm, bright green and rugose above, paler below, nerves 8-11 pairs, distinct below; petioles 2.5 cm long; in flourescence in axillary panicles, flowers dark red, densely hairy.

Dehaasia incrassata (Jack) Kosterm

This species is a small tree with 5 m tall and 10 cm in diameter. The bark is grey-brown, smooth and lenticellate while the inner bark is yellow. Leaves are spirally simple, leathery, from elliptic-oblong to oblanceolate or obovate, apex acuminate acute, base cuneate, 8.0-15.0 cm x 5.5-10.0 cm, bright green above, polar below, nerves 8-11 pairs, curving and joining near the margin; petioles 3 cm long, grooved above; fruit terminal, oblong, 5 cm x 2 cm, brigt green, ripening shyny purplish black; stalks 3 cm long.

1.7 Medicinal Value

Traditional medicine is widespread throughout the world and Malaysia is no exception. It has been with Malaysians of all ethnics for the last hundreds of years of recorded history. In fact, Malaysians of various communities show a tendency to favour the growth of traditional medicine. Ethno botanical surveys carried out among various Malaysians communities revealed that many plants species are extensively being used as remedies for various symptomatic diseases or illness¹¹.

Table 1.2: The medicinal values of *Phoebe* species 12.

Phoebe Species	Part of Plant	Treatment
P. nanmu	Twigs	A decoction is used in treating cholera trouble.
	Bark	As a fomentation on sprains swellings.
P. henryi	Fruit	A decoction is a remedy for stomachache.
P. excelsa	Bark	A bitter alkaloid poisonous to toads.
P. forbesii	Bark	Positive to treat Anti-tumor

Several medicinal values of *Phoebe* species are shown in Table 1.2 and no medicinal record are found for *Dehaasia* species. Some species of *Phoebe* are used for treatment against several diseases in China, Indonesia, Indochina, Japan, Philiphine and Malay Penisula. The twigs, bark, inner bark, leaves and also seeds of the species are used in treating several diseases including anti-tumor as described in

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Table 1.2. Methods such as decoction and fomentation of the twigs and bark are likely applied.

1.8 Objectives of Study

The main objectives of this study are:-

- 1. to elucidate the structure of both novel and known compounds emphasizing on the alkaloids from the *Phoebe* and *Dehaasia* species. The novel compounds will then be analyzed using spectroscopic methods mainly 2D NMR (COSY, HMBC, HMQC and NOESY), Ultra violet, Infra Red and Mass Spectroscopy. These instruments are widely used in hospitals, research laboratories, and forensic sciences and so on. The methods are under constant development and the study is to extend this rapid development into characterizing and determining the structure of alkaloids.
- 2. to study in detail naturally occurring compounds from the *Phoebe* and *Dehaasia* species and to classify the alkaloids especially a rare proaporphine-tryptamine dimers with other isoquinoline type (proaporphine, aporphine, morphine and bisbenzylisoquinoline) which have a good bioactivity and very interesting structures.
- to investigate the bioactivity of the crude alkaloids and major compounds toward antimalarial activity and receptor-binding assays.