

CHAPTER 1

INTRODUCTION

“It is He who produces gardens, with trellises and without, and date palms, and crops of diverse flavour, and the olive and the pomegranate, similar (in kind) and different (in variety)” (50:11) Surah Al An’am¹.

Since ancient time people had been benefiting from the seemingly unperishable resource created by Lord Almighty which included the usage of plants for medicinal purposes, taken orally or in the form of ointments or liniments. Today, such types of treatment are referred to as “traditional medicine”. Traditional medicine imparts the usage of mixtures of various plant parts. It has been a popular method of treating diseases and is still widely practised in this region of the world. In Malaysia, this is true as can be seen by the high regard of the local community towards the “bomoh” (medicine-man), the “mak-bidan” (mid-wife) and the “mudin” (religious man who performs circumcision on boys)².

The South-east Asian region, in particular, is enriched with a significant proportion of the world’s rain forests, and Malaysia alone is the oldest home to some 15,000 species of higher plants. By 1993, Goh *et.al.* reported only more than one thousand of these species have been subjected to chemical screenings (mostly partially) and very few out of this amount have been exposed to detail chemical or pharmacological studies³.

Scientists, including the phytochemists and pharmacologists, had long been extracting and identifying the compounds present in plants and studying their biological activities. This has been able to help upgrade the standard of medication as the people become more aware of the mechanism of actions behind a certain

potions and be able to prescribe the right dose in order to avoid hazardous side effects.

In this study, the author reports the work carried out on a local medicinal plant, *Kaempferia galanga* Linn., belonging to the family of Zingiberaceae. *Kaempferia galanga* L., also known as 'cekur' in Malaysia, 'kencur' in Indonesia and 'shan-nai' in China, can be found both cultivated and wild. This plant is used traditionally for the treatment of rheumatism, asthma and hypertension⁴.

The main objectives of this study are :

- a) to investigate the compound (or mixture of compounds) present in *Kaempferia galanga* Linn. which contribute to the relaxant effect in smooth muscles of contracted rat thoracic aorta, and
- b) to study the mechanism underlying the smooth muscle relaxant activity of these isolated compounds.

1.1 ZINGIBERACEAE : DISTRIBUTION AND HABITAT

The Zingiberaceae family is largely confined to regions of the world with a warm and relatively uniform climate. It consists of not less than 45 genera and 1500 species distributed throughout the tropics, with a few species in sub-tropical regions⁵. Numerous amounts of plants of this family are found in the tropics of the Old World, scanty in the New World⁶. In Peninsular Malaysia alone, there are at least 23 genera and about 200 species found^{5,8}.

Zingiberaceae is a characteristic feature of the ground flora of the primitive forest of Malaysia. According to Holttum, they are infrequent in secondary forest and one may find them everywhere, usually as scattered plants, rarely as thickets⁷. Most members of the family are terrestrial, perennial and aromatic herbs growing naturally in shaded and damp parts of the lowland and montane forests⁹. Some species of Zingiberaceae are found throughout the country, such as *Globba pendula*, *Alpinia Javanica* and *Amomum xanthophlebium*. Other species appear to be extremely local, notably several species of *Scaphochlamys* (which are almost confined to lowland forest) and of *Geostachys* (which are nearly all mountain plants)⁷.

Species with resting rhizomes are usually adapted to a seasonal climate, and their flowering comes at a definite stage in the life-cycle. By this adaptation, such species have been enabled to invade countries beyond the uniformly moist and warm climatic regions, and have also in many cases left the forest (in which alone most Malaysian species can flourish).

1.2 GENERAL APPEARANCE AND MORPHOLOGY

Zingiberaceae are perennial herbaceous terrestrials, rarely epiphytics, and rhizomatous aromatics. The rhizome is usually fleshy and sympodial, each element of the sympodium ending in an erect shoot which bears leaves or flowers, or both. The rhizome is usually at or just below the surface of the ground. In some genera (eg. *Achasma*) it is often more deeply buried; in others (especially in *Hornstedtia* and *Geostachys*) stout unbranched stilt-roots, which may be long in some cases,

support it above the ground. Often, where there is a litter of dead leaves of some thickness, the rhizome ascends obliquely or is almost vertically supported on more slender stilt roots, as can be found in some species of *Scaphochlamys*. In many plants of other families, the rhizomes function as resting organs, persisting below ground during seasons unfavourable for growth, while the leafy shoots wither. On the contrary, under the Malaysian climate (except to some extent in the extreme north), no such unfavourable season is encountered and growth is possible at almost all time of the year. Consequently, the rhizome does not serve as a resting organ in most Malaysian Zingiberaceae. There are exceptions, however, chiefly in the genera of *Kaempferia*, *Curcuma* and *Zingiber*, whereby the rhizome is fleshy and is adapted as a resting organ.

In general, the leaves of the Zingiberaceae family are thinly membranous or rather fleshy, large ovate or lanceolate, usually petioled shortly, and ligulate, sheathing below. The leaf-shoot is erect (about 1 - 5 m tall) with the apex curving over a little and unbranched; except that is found in *Costus*. In the *Hedychium* tribe, short leaf-shoots were found in several genera such as *Kaempferia* and *Scaphochlamys*. The petiole, or base of the leaf-blade, is joined to a sheath. At the intersection of petiole and sheath is the ligule, which is almost always conspicuous; it forms a narrow or broad lamina passing across the base of the petiole, and sometimes has raised auricles on either side. Leaf-shoots which do not bear terminal inflorescences are usually termed false-stems; they consist of only a series of concentric leaf-sheaths, the inner sheaths longer and larger with no true stem present. This situation is found in young banana shoot that has not flowered yet. But

in all Zingiberaceae of the *Alpinia* or *Phaeomeria* habit a true central stem is present.

In the short-stemmed genera such as *Kaempferia*, the structure of the leaf-shoot is exactly as in *Alpinia* or *Phaeomeria*, but the stem proper is very short, the leaves few on each shoot, their blades almost erect instead of horizontal, and their petioles longer. The sizes of the leaves of the Zingiberaceae family vary with different genera, some quite huge (to about a metre long); however, they are never less than a few centimetres long. The leaves are often asymmetric in shape in the *Kaempferia* group, the lamina on the two sides of the midrib being of unequal width; in the *Alpinia* group the asymmetry is obviously observed in an unequal base to the lamina.

The flowers of Zingiberaceae are bisexual, in spikes or solitary, usually with conspicuous bracts: sepals 3; petals 3, unequal; stamen 1, staminoda 2, one much larger than the other; carpels 3, the style 1, the ovary 1- or 3-chambered. The flowers are reported to last less than 24 hours. In most cases, they open in the morning and fade by the next. In some species of Zingiber, they open in the afternoon and last a few hours. The flowers range from medium to large in size and are showy and irregular; in panicles or dense cymes or heads, bracteate, terminal or from the rhizome, rarely falsely lateral. The flowers are all tubular and contain nectar. The form of the flower is surprisingly constant throughout the family and it is the character which separates Zingiberaceae from all other plants. As a result, it is difficult to divide the family into groups on the basis of floral characters.

The flowers are based on the ancestral liliiflorous type of 3 sepals, 3 petals, 3+3 stamens and a gynaecium of 3 parts. In most cases, the sepals are joined to form a tube and are relatively inconspicuous. The petals are also partly joined to form a tube and usually look like the sepals of a lily or an orchid as they are the conspicuous outer components of the flower. The lip or labellum represents the stamens, either whole or in part; is usually broad and differently coloured, entire or trilobed. The stamen is the modified section of the flower. The one functional stamen is on the same radius as the dorsal petal, and hence belongs to the inner whorl, whereas the two adjacent stamens of the outer whorl are often clearly present as staminodes, small or large. A unique feature of the stamen is the way it holds the style between the swollen pollen-sacs. The style has slender filiform and bears cup-shaped stigma.

The ovary of Zingiberaceae is either trilocular with axile placentation (in most genera) or unilocular with parietal placentation (the *Globba* group); or in some genera (*Kaempferia* and allies) there is a tendency to the reduction or elimination of the septa. The axile ovules are confined to a small basal group or to a larger or smaller columnar placenta.

The fruit of this family is capsular or sub-baccate (berry) with seed usually numerous aromatic, often arillate, albumen floury. In the *Hedychium*, *Zingiber*, *Roscoeia* and the *Globba* groups, the fruits are fully dehiscent, with three valves separating to the apex and spreading apart. In *Costus*, dehiscence occurs, with extrusion of the groups of seeds. However, splitting does not reach the apex of the ovary, which is crowned by the calyx. In *Catimbium*, the fruits do not break open

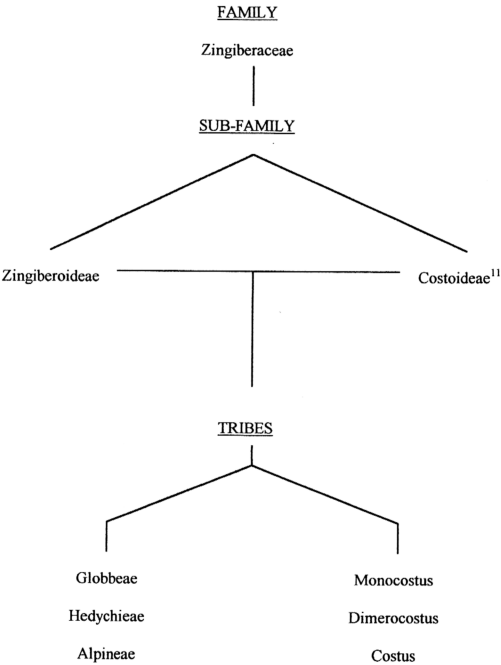
naturally. In *Hornstedtia*, the fruits break open irregularly in their basal parts, whilst still enclosed within the involucre bracts. In some species of *Amomum*, and other genera, the fruits are near to fleshy and indehiscent, while in other, they are thin walled but may not be dehiscent.

Internally, the seeds of Zingiberaceae possess perisperm (nucellus) which, in all cases investigated, is white and starchy, with endosperm round the embryo. At the base of a seed there is a plug with which the radicle of the embryo is in contact; when germination takes place this plug is pushed out by the growing radicle^{6,7,10}.

1.3 CLASSIFICATION OF TRIBES

The hard and tedious work carried out by various scientists, especially the botanists, in the classification of Zingiberaceae is notable. Some of the well-known botanists include Koenig, Roxburgh, Wallich, Roscoe, Gray, Ridley and Holttum. The process of classification of Zingiberaceae has to be done in discreet ways, thus may give rise to several variants. There are certain methods which may be considered to be unstable, or even unreliable, as in Schumann's arrangement which is based mainly on unstable flower characters. The sub-division of tribes by Holttum *et. al.* is based almost entirely on characters of the inflorescence and bracts. Scheme 1.1 and table 1.1 illustrate the summarised classification accomplished by Holttum⁷.

SCHEME 1.1 CLASSIFICATION OF ZINGIBERACEAE



**TABLE 1.1 GENERA OF ZINGIBERACEAE IN THE MALAYSIAN
FOREST**

Tribe 1 : Globbeae	Tribe 2 : Hedychieae	Tribe 3 : Alpineae
<i>Globba</i>	<i>Zingiber</i> <i>Curcuma</i> <i>Hedychium</i> <i>Camptandra</i> <i>Scaphochlamys</i> <i>Boesenbergia</i> <i>Kaempferia</i> <i>Haniffia</i>	<i>Cenolophon</i> <i>Alpinia</i> <i>Catimbium</i> <i>Languas</i> <i>Plagiostachys</i> <i>Hornstedtia</i> <i>Phaeomeria</i> <i>Achasma</i> <i>Amomum</i> <i>Elettariopsis</i> <i>Geocharis</i> <i>Geostachys</i> <i>Elettaria</i>

1.4 THE TRIBE : HEDYCHIEAE

Hedychium is the most primitive genus in this division of the Zingiberaceae family. The classification of the sub-division of this tribe is based on the structure of the inflorescence, which provides really distinctive characters. The main characteristics of the tribe are the development of the staminodes into petaloid structures and the ellipsoid seed with a deeply lacerate aril. Table 1.2 shows the distribution of species in genera of Hedychieae.

1.5 THE GENUS : KAEMPFERIA

Kaempferia plants are usually short plants with fleshy rhizome, each bearing one to a few leaves with a terminal inflorescence, or in a few cases, leaves and flowers on separate shoots. Table 1.3 illustrates the 4 species of *Kaempferia* and their distribution.

1.6 MEDICINAL SIGNIFICANCE AND KNOWN BIOLOGICAL IMPORTANCE OF ZINGIBERACEAE

The Zingiberaceae family (also known as the ginger family) is one of the largest families in the order of Zingiberales, distributed mainly in the tropical and subtropical regions. There are about 30 - 40 species of the Zingiberaceae which have long been utilized in traditional medicine. Approximately 40% of these species are used as medications for post-partum, 19 - 30% are used as tonics or cures for stomachache, rheumatism, fever and eradicating worms. Other species are used for

**TABLE 1.2 DISTRIBUTION OF SPECIES IN GENERA OF THE
TRIBE HEDYCHIEAE**

Name of genera	Number of species
<i>Zingiber</i>	13 + 3 var.
<i>Curcuma</i>	9
<i>Hedychium</i>	7
<i>Camptandra</i>	3
<i>Scaphochlamys</i>	20 + 4
<i>Boesenbergia</i>	8 + 1 var.
<i>Kaempferia</i>	4
<i>Haniffia</i>	1
Total	65 + 8 var.

**TABLE 1.3 DIFFERENT SPECIES OF THE GENUS *KAEMPFERIA*
AND THEIR DISTRIBUTION**

Species	Distribution
<i>K. rotunda</i>	South-eastern Asia, particularly in Indo-China, Malaysia, Indonesia and Singapore.
<i>K. galanga</i>	India, China, South-eastern Asia, particularly Malaysia and Singapore
<i>K. pulchra</i>	Malaysia (Langkawi, Penang) and Singapore
<i>K. elegans</i>	Malaysia (Langkawi and Kedah)

treatment against diseases such as skin disease, syphilis and asthma. Generally, most of the Zingiberaceae species are used for problems and diseases of women¹². The plants are used individually or in association with other plants.

Extensive usage of plants from this family, especially as concoctions in native medicines and as food flavours, had long brought out the interests in scientists to collect and study 'recipes' from these folk remedies then isolate and identify the active components and other compounds that may be of some interest to their knowledge.

In Malaysia and Indonesia, *Kaempferia galanga* Linn. is used to make a gargle, the leaves and rhizomes are chewed to treat coughs, or pounded and used in poultices or lotions applied to relieve many ailments; the juice of the rhizome is expectorant and carminative, and is a part of children's medicine and tonics. The rhizome is also used to treat abdominal pain, also as an embrocation or sudorific to treat swelling and muscular rheumatism¹³. In China, it is used as a remedy for toothache; to remove dandruff or scabs on the head; as stimulant; as carminative to treat cholera, contusions, chest pains, headache and constipation. Table 1.4 lists several of the treatments which make use of the medicinal benefits of some Zingiberaceae plants^{12,14,15}.

In Malaysia, "jamu" is widely used amongst women. "Jamu" is a herbal medicinal mixture consisting of several species of plants, blended together and prepared into powder form. "Jamu" is eaten for various purposes, such as a general cure against ailments, to enhance body endurance, as beauty care and tonics.

**TABLE 1.4 LIST OF SOME OF THE ZINGIBERACEOUS PLANTS
USED IN TRADITIONAL TREATMENTS OF SEVERAL
AILMENTS^{12,14,15}**

Ailments	Zingiberaceous plants that can be used for treatments
Stomachache diarrhoea dysentery	<i>Alpinia galanga</i> , <i>A. japonica</i> , <i>A. mutica</i> , <i>A. officinarum</i> , <i>Amomum uliginosum</i> , <i>Curcuma domestica</i> , <i>Elettaria cardamomum</i> , <i>Globba pendula</i> , <i>Kaempferia galanga</i> , <i>K. rotunda</i> , <i>Hedychium coronarium</i> , <i>Zingiber officinale</i> and <i>Z. zerumbet</i> .
Asthma	<i>Curcuma aeruginosa</i> , <i>Kaempferia galanga</i> and <i>Costus speciosus</i> .
Rheumatism	<i>Alpinia conchigera</i> , <i>Boesenbergia rotunda</i> , <i>Curcuma domestica</i> , <i>C. xanthorrhiza</i> , <i>Globba pendula</i> , <i>Kaempferia galanga</i> , <i>Zingiber cassumunar</i> and <i>Z. officinale</i> .
Gonorrhoea	<i>Globba pendula</i> and <i>Zingiber cassumunar</i> .
Medications for post-partum	<i>Alpinia conchigera</i> , <i>A. galanga</i> , <i>A. melanocarpa</i> , <i>Boesenbergia rotunda</i> , <i>Curcuma domestica</i> , <i>C. zedoaria</i> , <i>Globba patens</i> , <i>G. pendula</i> , <i>G. variabilis</i> , <i>Kaempferia galanga</i> , <i>Zingiber cassumunar</i> , <i>Z. officinale</i> , <i>Z. officinale</i> var. <i>rubrum</i> , <i>Z. ottensii</i> and <i>Z. zerumbet</i> .
Coughs	<i>Costus speciosus</i> , <i>Curcuma aeruginosa</i> , <i>C. domestica</i> and <i>Kaempferia galanga</i> .
High blood pressure	<i>Globba patens</i> , <i>Hedychium chrysroleucum</i> and <i>Kaempferia galanga</i> .
Swellings	<i>Kaempferia galanga</i> , <i>Zingiber cassumunar</i> , <i>Z. spectabile</i> and <i>Z. zerumbet</i> .
Vermifuge / worms	<i>Amomum uliginosum</i> , <i>Globba pendula</i> , <i>Hedychium longicornutum</i> and <i>Zingiber zerumbet</i> .

Kaempferia galanga is a common ingredient used for the preparation of “jamu”. Table 1.5 shows the ingredients of two examples of “jamu” preparation¹⁶.

There have been many scientific reports on bioactivities, mostly *in vitro*, of crude extracts and compounds isolated from plants of the Zingiberaceae family. These reports further support the medicinal properties of these plants as claimed by traditional medicine practitioners. For example, Itokawa *et. al.* reported the isolation of 1'-acetoxychavicol acetate **1** and 1'-acetoxyeugenol acetate **2** from *Alpinia galanga* Wild. as antitumour principles against Sarcoma 180 ascites in mice¹⁷. Denyer *et. al.* reported the isolation of β -sesquiphellandrene **3** from *Zingiber officinale* and showed *in vitro* activity against the rhinovirus IB (one of the viruses causing the common cold) with IC_{50} of 0.44 μM ¹⁸. Endo *et. al.* reported the isolation of gingerone A **4** from the rhizomes of *Zingiber officinale* which exhibited moderate anticoccidium activity *in vitro* and strong antifungal effect to *Pyricularia oryzae*¹⁹. Apisariyakul *et. al.* reported the antifungal activity of turmeric oil extracted from *Curcuma longa* against *Tricophyton*-induced dermatophytosis²⁰.

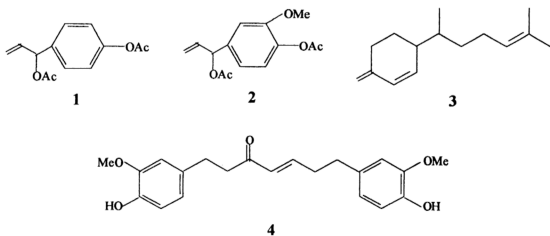


TABLE 1.5 : THE INGREDIENTS OF JAMU USED FOR BODY
ENDURANCE AND PROTECTION¹⁶

INGREDIENTS					
	FAMILY	SCIENTIFIC NAME	VERNACULAR NAME	PART OF PLANT USED	TREATMENT
Jamu awet ayu (jamu for beauty care)	Zingiberaceae	<i>Curcuma heyneana</i> Val. & v. Zijp.	Temu giring	fresh rhizomes	To protect body balances and stabilities and for women
	Zingiberaceae	<i>Curcuma phaeocaulis</i> Val.	Temu ireng	fresh rhizomes	
	Lamiaceae	<i>Orthosiphon aristatus</i>	Kumis kucing	fresh leaves	
	Euphorbiaceae	<i>Phyllanthus niruri</i> L.	Meniran	fresh leaves	
	Acanthaceae	<i>Pluchea indica</i> L.	Beluntas	fresh leaves	
	Rutaceae	<i>Murraya paniculata</i> (L.)	Kemuning	fresh leaves	
	Zingiberaceae	<i>Curcuma xanthorrhiza</i> Roxb.	Temu lawak	fresh rhizomes	
	Zingiberaceae	<i>Curcuma domestica</i> Val.	Kunyit	fresh rhizomes	
	Zingiberaceae	<i>Zingiber officinale</i> Roxb.	Jahe	fresh rhizomes	
Jamu sihat wanita (for woman's health)	Zingiberaceae	<i>Kaempferia galanga</i> L.	Kencur	fresh rhizomes	To repair and stimulate female hormones
	Arecaceae	<i>Arenga pinnate</i> (Wurm.) Merr	Gula aren	sap of	
	Usnaceae	<i>Usnea dasypoda</i> Frien.	Kayu angin	dried herb	
	Fabaceae	<i>Caesalpinia sappan</i> L.	Secang	dried wood	
	Loganiaceae	<i>Strychnos ligustrina</i> Bl.	Kayu pahit	dried wood	
	Apiaceae	<i>Centella asiatica</i> (L.) Urb.	Pegagan	fresh herb	
	Caricaceae	<i>Carica papaya</i> L.	Papaya	fresh leaves	
	Fabaceae	<i>Abrus precatorius</i> L.	Saga	fresh leaves	
	Lauraceae	<i>Cinnamomum burmanii</i> Ness ex Bl.	Kayu manis	dried bark	
	Zingiberaceae	<i>Ammomum compactum</i> Soland. ex Maton	Kapulaga	dried seeds	
	Zingiberaceae	<i>Curcuma domestica</i> Val.	Kunyit	fresh rhizomes	
	Zingiberaceae	<i>Curcuma xanthorrhiza</i> Roxb.	Temu lawak	fresh rhizomes	
	Zingiberaceae	<i>Curcuma phaeocaulis</i> Val.	Temu ireng	fresh rhizomes	
	Zingiberaceae	<i>Kaempferia galanga</i> L.	Kencur	fresh rhizomes	
	Arecaceae	<i>Arenga pinnata</i> (Wurm.) Merr.	Gula aren	sap of	