CHEMICAL DIVERSITY AND BIOLOGICAL ACTIVITY OF SECONDARY METABOLITES IN EIGHT SPECIES OF *Curcuma*

UMMUL MARDIAH BINTI ELIAS

THESIS SUBMITTED IN FULFILLMENT FOR THE DEGREE OF MASTER OF SCIENCE

INSTITUTE FOR
TROPICAL BIOLOGY AND CONSERVATION
UNIVERSITI MALAYSIA SABAH

2015

UNIVERSITI MALAYSIA SABAH

BORANG PENGESAHAN STATUS TESIS

JUDUL : CHEMICAL DIVERSITY AND BIOLOGICAL ACTIVITY OF SECONDARY METABOLITES IN EIGHT SPECIES OF Curcuma

IJAZAH : SARJANA (ADVANCEMENT OF BIODIVERSITY)

Saya **Ummul Mardiah Binti Elias**, sesi pengajian **2011-2015**, mengaku membenarkan tesis Sarjana ini disimpan di Perpustakaan Universiti Malaysia Sabah dengan syarat-syarat kegunaan seperti berikut :-

1. Tesis ini adalah hak milik Universiti Malaysia Sabah
2. Perpustakaan Universiti Malaysia Sabah dibenarkan membuat salinan untuk tujuan pengajian sahaja
3. Perpustakaan dibenarkan membuat salinan tesis ini sebagai bahan pertukaran antara institusi pengajian tinggi
4. Sila tandakan (/)

☐ SULIT (Mengandungi maklumat yang berdarjah keselamatan atau kepentingan Malaysia seperti termaktub di dalam AKTA RAHSIA RASMI 1972)

☐ TERHAD (Mengandungi maklumat TERHAD yang telah ditentukan oleh organisasi/badan di mana penyelidikan dijalankan)

☑ TIDAK TERHAD

Disahkan oleh,

NURULAIN BINTI ISMAIL
LIBRARIAN
UNIVERSITI MALAYSIA SABAH

(Tandatangan Penulis)

Alamat: No 12 Jalan BP 11,
Taman Bukit Permata,
68100, Batu Caves,
Selangor

(Tandatangan Pustakawan)

(Prof. Dr. Charles S. Vairappan)
Penyelia

Tarikh : 22 August 2015

DECLARATION

I hereby declare that the materials in this thesis is my own except for quotations, excepts, equations, summaries and references, which have been duly acknowledged.

16th July 2015

Ummul Mardiah Binti Elias

PP20118047

CERTIFICATION

NAME : **UMMUL MARDIAH BINTI ELIAS**

MATRIC NO : **PP20118047**

TITLE : **CHEMICAL DIVERSITY AND BIOLOGICAL ACTIVITY OF SECONDARY METABOLITES IN EIGHT SPECIES OF *Curcuma***

DEGREE : **MASTER OF SCIENCE (ADVANCEMENT OF BIODIVERSITY)**

VIVA DATE : **10th JUNE 2015**

CERTIFIED BY

1. SUPERVISOR

Prof. Dr. Charles S. Vairappan

Signature

ACKNOWLEDGEMENT

Foremost, I would like to thank my family: my parents Elias Omar and Norsiah Darus, for giving birth to me at the first place and supporting me spiritually throughout my life.

Next, I would like to express my sincere gratitude to my advisor Prof. Charles S. Vairappan for the continuous support of my Master study and research, for his patience, motivation, enthusiasm, and immense knowledge. His guidance helped me in all the time of research and writing of this thesis. I could not have imagined having a better advisor and mentor for my Master study

My sincere thanks also go to ITBC communities for offering a very comfortable environment for me to go thru all hardship to finish up my study. I thank my fellow labmates in Marine Natural Product Laboratory (ITBS): Intan Irna, Thilahga, Kishneth, Tulasi, Marcus for the discussions, for the sleepless nights we were working together, and for all the fun we have had in the last three years. Also I thank my friends in ITBC: Rani, Que, Afif, Anati, Kevin. Thank you. 9 Ummul Mardiah Elias December 2014

Ummul Mardiah Binti Elias

July 2015

ABSTRAK

KEPELBAGAIAN KIMIA DAN AKTIVITI BIOLOGI UNTUK METABOLITE SEKUNDER DALAM LAPAN JENIS CURCUMA SP

*Curcuma (Zingiberacaea) telah didoumentasikan berasal daripada kawasan Indo-Malayan dan diketahui mempunyai sumbe metabolit sekunder dengan ciri-ciri farmalogikal yang menarik. Terdapat lebih kurang lapan spesis daripada genus ini yang digunakan oleh komuniti melayu. Akan tetapi, tidak banyak maklumat komposisi kimia mahupun aktiviti biologikal mengenai spesis ini. Di dalam kajian ini, minyak pati meruap dan metabolit sekunder telah di ekstrak, dipencilkan dan dikenalpasti melalui sistem kromatografi. Minyak pati diperolehi menggunakan penyulingan air dan di analisis menggunakan GCMC. Terdapat 40 komponen di dalam C. aeruginosa (0.17 %), 46 komponen di dalam C. caesia (0.16%), 65 komponen di dalam C. heyneana (0.23%), 25 komponen di dalam C. longa (0.33%), 10 komponen di dalam C. mangga (0.19%), 15 komponen di dalam C. rotunda (0.16%), 22 komponen di dalam C. xanthorrhiza (0.36%) and 20 komponen di dalam C. zedoaria (0.31%), dan ianya boleh dikategorikan ke dalam empat kumpulan. Kumpulan (1) terdiri daripada C. aeruginosa, C. caesia, C. longa and C. xanthorrhiza, yang mempunyai kandungan sesquiterpen oksida yang tinggi, manakala kumpulan (2), terdiri daripada C. rotunda danC. zedoaria mengandungi monoterpen oksida yang tinggi. Oleh kerana kandungan seskuiterpen terhidrogenasi dan monoterpen terhidrogenasi tinggi, C. heyneana dan C. mangga ditempatkan ke dalam kumpulan (3) dan (4), masing-masing. Selain daripada itu, ekstrak rhizom telah diperolehi daripada soxhlet dan dianalisis melalui PTLC dan NMR, memperembahkan kandungan 8 komponen di dalam C. aeruginosa (5.81%) and C. caesia (7.56%), 7 komponen di dalam C. heyneana (3.32%), 6 komponen di dalam C. longa (3.11%), 2 komponen di dalam C. mangga (1.92%), 5 komponen di dalam C. rotunda (2.07%), 6 komponen di dalam C. xanthorrhiza (3.23%) and 6 komponen di dalam C. zedoaria (3.72%). Analisis berdasarkan jenis komponen menunjukkan C. aeruginosa dan C. caesia di dalam kumpulan 1 (germacrane, carabrane, guaiane dan elemene), C. zedoaria di dalam kumpulan 2 (germacrane dan elemene), C. heyneana, C. mangga, C. longa, dan C. xanthorrhiza di dalam kumpulan 3 (diphenylheptanoid) dan C. rotunda di dalam kumpulan 4 (monoterpenoids). Tambahan lagi, minyak pati Curcuma sp. dievaluasi untuk aktiviti biosidal mereka terhadap risiko bakteri yang berasal dari makanan. Minyak pati dari C. xanthorrhiza menunjukkan zon perencatan yang baik terhadap Vibrio parahaemolyticus. Melalui kaedah ujian MIC dan MBA menunjukkan minyak pati Curcuma sp. mempunyai ciri-ciri berikut; i)agen bakteriostatik-C. mangga, C. rotunda dan C. zedoaria dan ii)agen baktericidal- C. heyneana, C. longa and C. xanthorrhiza, terhadap Staphylococcus - aureus. Manakala, minyak pati Curcuma sp. mempunyai ciri-ciri; i) agen bakteriostatik C. heyneana, C. mangga, C. rotunda dan C. zedoaria ii)agen baktericidal- C. longa dan C. xanthorrhiza terhadap MRSA. Selain itu, antikanser yang sederhana daripada komponen yang dipencilkan dari Curcuma dikesan ;komponen **9** dan **10** terhadap MCF-7 sel, dan komponen **7, 10, 11** dan **12** terhadap HeLa sel.*

ABSTRACT

Curcuma (Zingiberacae) are documented to originate from Indo-Malayan region and known to be a rich source of secondary metabolites with interesting pharmaceutical properties. There are at least eight species of this genus known to be utilized in the Malay community. However, not much information is available pertaining to its chemical composition nor of its biological potential. In this investigation, the volatile essential oil and its secondary metabolites were extracted, isolated and determined via chromatographic means. The essential oils were obtained by hydrodistillation and analyzed using GCMS. There were 49 compounds in *C. aeruginosa* (0.17%), 46 compounds in *C. caesia* (0.16%), 65 compounds in *C. heyneana* (0.23%), 25 compounds in *C. longa* (0.33%), 10 compounds in *C. mangga* (0.19%), 15 compounds in *C. rotunda* (0.16%), 22 compounds in *C. xanthorrhiza* (0.36%) and 20 compounds in *C. zedoaria* (0.31%), which then be categorize into four group. Belonging to group one, *C. aeruginosa, C. caesia, C. longa* and *C. xanthorrhiza,* contains high composition of oxygenated sesquiterpenes while in group (2), *C. rotunda* and *C. zedoaria* have high content of oxygenated monoterpenes. By having high content of hydrogenated sesquiterpenes and hydrogenated monoterpenes., *C. heyneana* and *C. mangga* were placed in group 3 and 4, respectively. On the other hand, rhizome extract derived via soxhlet and analyzed through PTLC and NMR, revealed presence of 8 compounds in *C. aeruginosa* (5.81%) and *C. caesia* (7.56%), 7 compounds in *C. heyneana* (3.32%), 6 compounds in *C. longa* (3.11%), 2 compounds in *C. mangga* (1.92%), 5 compounds in *C. rotunda* (2.07%), 6 compounds in *C. xanthorrhiza* (3.23%) and 6 compounds in *C. zedoaria* (3.72%). Analysis on type of compouds showed that C. aeruginosa and C. caesia belong to group 1 (germacrane, carabrane, guaiane and elemene), *C. zedoaria* in group 2 (germacrane and elemene), *C. heyneana, C. mangga, C. longa,* and *C. xanthorrhiza* in group 3 (diphenylheptanoid) and *C. rotunda* in group 4 (monoterpenoids). In addition, cude extract and essential oil of *Curcuma* sp. (1mg/ml) were evaluated for their biocidal activity againts food-borne bacteria. Essential oil of *C. xanthorrhiza* showed good inhibition zone againts *Vibrio parahaemolyticus.* Furthermore, via MIC and MBA testing, essential oil of *Curcuma* exhibit ; *i) bakteriostatic agent-C. mangga, C. rotunda and C. zedoaria,* ii) Bactericidal agent- *C. heyneana, C. longa* and *C. xanthorrhiza* against *Staphylococcus aureus.* While, essential oil of *Curcuma* exhibit; i) Bakteriostatic agent-*C. heyneana, C. mangga, C. rotunda* and *C. zedoaria,* ii) Bactericidal agent -*C. longa dan C. xanthorrhiza* againts *MRSA.* Moreover, it was also found moderate anticancer activity from compounds isolated from *Curcuma* sp.; compound **9** and **10** against MCF-7 cell, and compound **7, 10, 11** and **12** against HeLa cell lines.

CONTENT

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

1.1 Traditional Knowledge

Traditional knowledge can be interpreted as the understanding to comprise of aesthetic, useful elements, literary, artistic or scientific creations of a particular ethnic. This knowledge is transferred from a older generation to a younger generation with the intention to sustain information within community, which then becomes a part of cultural and spiritual identity of the ethnic. These are usually portrait in the form of music, dances, songs, handicrafts, designs, stories and artwork in the language of the particular ethnic. Traditional knowledge could also be categorized into three parts; traditional agricultural knowledge (TAK), traditional ecological knowledge (TEK) and traditional medicinal knowledge (TMK) (Overwalle, 2005).

Traditional Medicinal Knowledge (TMK) is reported to be useful, where up to 80 % of people worldwide are using this information and traditional knowledge as the primary medical health care in their community. This is mainly due to the unavailability of modern facilities and availability of cheap sources, withless side effects compared to synthetic drugs. Most of home-based remedies, including herbs and spices are used and marketed as high economic value medicinal plants. This phenomenon is gaining popularity and recognition worldwide, including in the developed and industrialized countries due to the promotion of TMK via health programs that are adapted local socioeconomic situations (Ghimire and Bastakoti, 2009; Bhat *et al.*, 2012).

In Malaysia, research on TMK from plant sources were reported by Ong and Norzalina (1999), Ong and Nordiana (1999), Kulip (2003), Lin (2005), Samuel *et al.* (2010) and Ong *et al.* (2011). Studies showed that local people use more than 100 species of plants as the principal component of their medicinal practices. Different

states or regions in Malaysia show different ways to utilize medicinal plants in the treatment of various diseases. Among the most common herbal plants are the members of *Curcuma,* which is one of the more common rhizomatous herbs (Zingiberaceae) that have been used as ethnomedicinal plants. *Curcuma* plants are being used in the treatment of pimples, sores, athlete's foot, abrasions and post-partum. They are also reported to have been consumed as supplement in the traditionally prepared tonics known as jamu (Habsah *et al.*, 2000), the oldest system of medicine in India called ayurveda (Policegoudra *et al.*, 2007), and traditional Chinese herb (Madhu *et al.*, 2010).

1.2 *Curcuma* sp.

Since ancient times, terrestrial plants have given benefit to human being as they become economics resources and play an important part in traditional medicinal practices of the local communities (Stern *et al.*, 2008). *Curcuma* is one of genus under Zingiberaceae family, which originated from Indo-Malayan region and now could be found throughout the tropics of Asia, Africa and Australia (Policegoudra *et al.*, 2007). *Curcuma* genus consists of over 70 species with rhizomatous characteristics where some of these species can be found in Malaysia; *Curcuma aeruginosa* Roxb., *Curcuma caesia* Roxb., *Curcuma heyneana* Val. and Zijp., *Curcuma manga* Roxb., *Curcuma longa* L./*C. domestica* Vel , *Curcuma rotunda* L., *Curcuma xanthorrhiza* Roxb. and *Curcuma zedoaria* (Christin.) Roscoe (Figure 1.1). Rhizomes of *Curcuma* are fleshy, aromatic, and remain dormant during winter. Their leaves are basal with blade broadly lanceolate or oblong and rarely narrowly linear while their inflorenscence is a terminal spike on pseudostems or on separate shoots arising from rhizomes, usually appearing before the leaves. The plants grow up to 1 m tall and widely cultivated in Asian countries (Lin & Larsen, 2000, Al-Reza *et al.*, 2010).

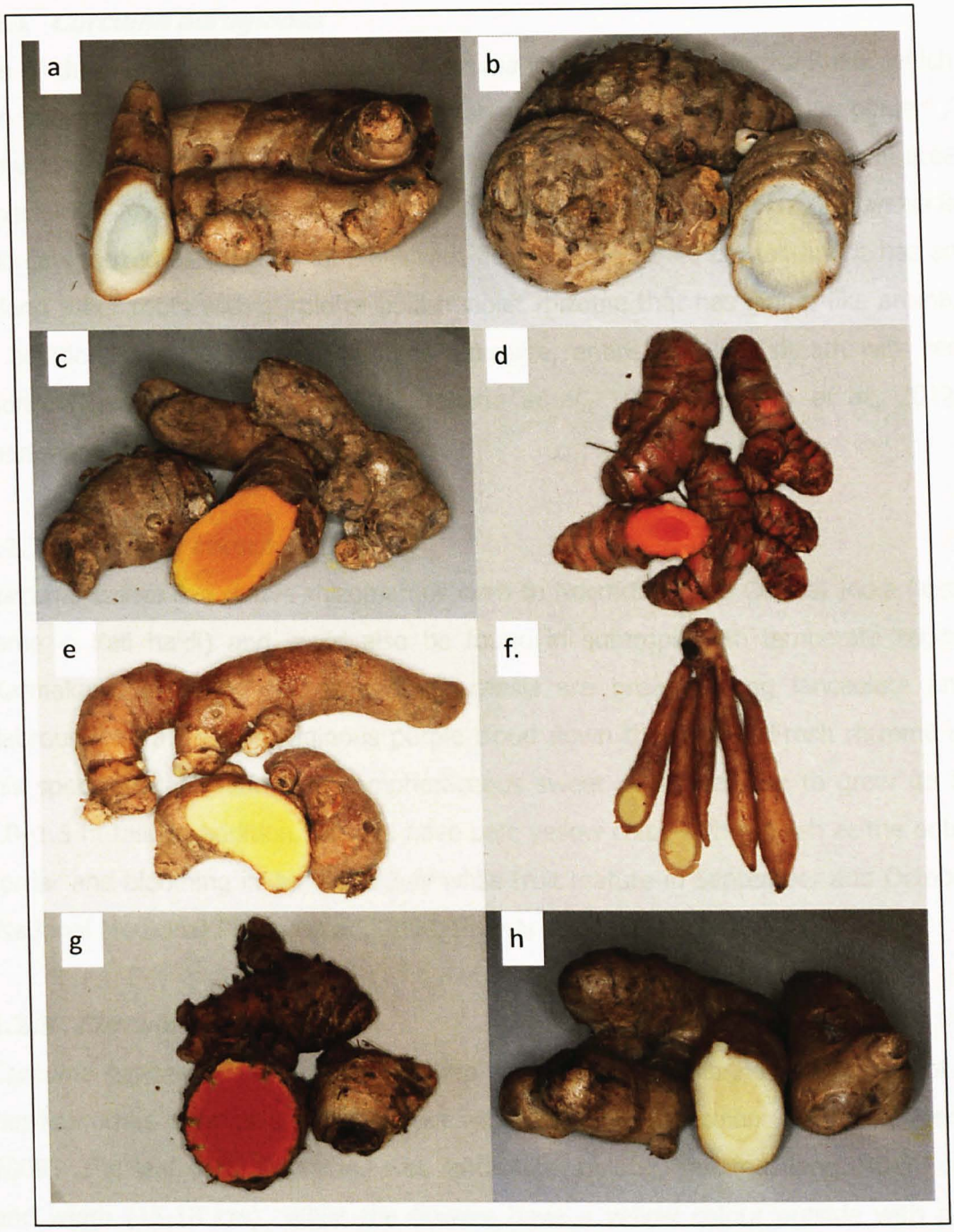

Figure 1.1 **Rhizome of common *Curcuma* species in Malaysia;**
a= *C. aeruginosa*; b= *C. caesia*; c= *C. heyneana*;
d= *C. longa*; e= *C. manga*; f= *C. rotunda*;
g= *C. xanthorrhiza* h= *C. zedoria*

1.2.1 *Curcuma aeruginosa*

One of the more common species of *Curcuma* is *Curcuma aeruginosa* Roxb. which also known as 'Gajutsu' in Japan, 'Wan mahamek' in Thai, 'pink and blue ginger' ,' arrowroot' or 'East Indian arrowroot' in English. It is a native plant in tropical area especially in Myanmar, Indonesia, Malaysia and south India. *Curcuma aeruginosa* is also categorized as a perennial plant with height up to 30-40 cm tall and it has an oblong tuber roots with purple or bullish violet rhizome that has ginger-like aroma. In addition, this *Curcuma* species has alternate, entire, red leaf sheath with red midrib. (Ranjini and Vijayan, 2005; Takano *et al.*, 1995, Suphrom *et al.*, 2012, Thanphong *et al.*, 2010)

1.2.2 *Curcuma caesia*

Curcuma caesia is a native rhizomatous herb to North-East and Central India (local name ~ Kali haldi) and could also be found in subtropical to temperate region (Karmakar*et al.*, 2011). Leaves of *C. caesia* are broad oblong lanceolate and glabrous with a deep ferruginous purple cloud down the middle. Fresh rhizome of this species is aromatic with camphoraceous sweet odor and able to grow up to 1.0–1.5 m tall. In addition, flowers have pale yellow color with reddish at the outer border and blooming in June and July while fruit mature in September and October (National Medicinal Plants Board, 2008, Paliwal *et al..*, 2011).

1.2.3 *Curcuma heyneana*

Curcuma heyneana is an indigenous plant to Java Island, Indonesia. Rhizome of *C. heyneana* has a sweet-aromatic odour with pale yellow in colour (Sirat and Meng, 2009). The leaf of *C. heyneana* was lanceolate, oblong, sheated, long (40-50 cm) and width (15-18 cm). While the flowers have a yellow colour outside with pale yellow inside. The bract of flowers usually has a light green colour at below part with pinkcolour at the upper side. Moreover, this plan, also known as 'Temugiring', and was classified as an annual plants which can grow up to 1 m (Napitupilu *et al.,* 2008).

1.2.4 *Curcuma longa*

Another important species under genus *Curcuma* is *Curcuma longa*, also known as Tumeric and Haldi in Hindi. *Curcuma longa* is indigenous to tropical climates and widely found in India, China, Bangladesh and other Asian countries. This perennial herb was identified by having short stem, large, ovate and oblong leaves, pyriform or oblong rhizome with brownish-yellow colour and can grow up to 2 feet tall. (Khan *et al.,* 2008; Chattopadhyay*et al.*, 2004).

1.2.5 *Curcuma mangga*

Curcuma mangga originated from Indo-Malayan region and widely founds in tropics region including Asia, Africa and Australia. This plant is known as mango-ginger due to its mango-like aroma when the fresh rhizome being crush or cut. They can grow up to 1m tall with lanceolate, oblong, sheated, long, radical and petiolare leaves and their rhizomes are in bluff-coloured, fleshy, the diameter is 2-5 cm, with 5-10 cm long, branched and have pungent taste (Policegoudra *et al.*, 2011).

1.2.6 *Curcuma rotunda*

*Curcuma rotunda*has eight different botanical names; *Boesenbergia cochinchinensis, Boesenbergia pandurata, Gastrochilus panduratus, Gastrochilus rotundus, Kaempferia cochinchinensis, Kaempferia ovate, Kaempferia pandurata* and *Boesenbergia rotunda.* This plant is also known as temu kunci, finger root, Chinese-keys, krachai or krachai-dang (Chong *et al.*, 2012) and has been consumed as food and traditional medicine. Asian communities are known to use this rhirome to treat aphthous ulcer, dry mouth, stomach discomfort, leukorrhea, and dysentery (Cheenpracha *et al.*, 2005).

1.2.7 *Curcuma xanthorrhiza*

Curcuma xanthorrhiza is also known as temu lawa, false turmeric, was widely found in Asian region including Malaysia, Indonesia and Thailand. This plant can grow up to 2 m tall with branched orange-red inner-part colour of rhizome. Leaves of *C. xanthorrhiza* were blade, oblong, glaborous with green and purple mid vein colour while the flower came out from rhizome in separate shoots with mixture of purple, green and white colour (Lin and Larsen, 2000).

1.2.8 *Curcuma zedoaria*

Curcuma zedoaria, also known as 'temu putih', zedorary, krachura, gandamatsi and sutha , is a perennial rhizomatheous herbs that is native to Bangladesh, Sri Lanka and India. It is now widely cultivated in other Asian countries. This species can grow up to 1.8 tall with upright pseudostem and having a fleshy underground branches or rhizome. The white inner-part of rhizome having ginger-like taste and the large, oblong, deeply veined leaves having a bitter taste. Furthermore, *C. zedoaria* also can be identified through the whitish or pale-yellow with bright reddish-green bracts flower which uprising from the rhizome. Usually, flowering was happened during May-June and the ovoid capsule fruits were rarely to occur. (National Meditional Plants Board, 2008 ; Das and Rahman, 2012).

1.3 Justification

Over the centuries rhizomes of *Curcuma* have been consumed and used in traditional medicinal practices widely (Ong and Norzalina, 1999; Ong and Nordiana, 1999; Kulip, 2003; Lin, 2005; Samuel *et al.*, 2010; Ong *et al.*, 2011). However, only few reports are available on the secondary metabolites profiles of *Curcuma* from Malaysia (Sirat *et al.*, 1994; Ruslay*et al.*, 2007; Zaibunnisa *et al.*, 2008; Ishii *et al.*, 2011; Jantan *et al.*, 2012; Kamazeri *et al.*, 2012; Vairappan *et al.*, 2013). There is also a lack of information of the chemical profiles of their essential oils. In addition, even less is available on their biological properties and their medicinal importance to justify their use in traditional practices in the Asian communities. Hence, further research is warranted to better understand the chemical composition, their importance as chemo-taxonomical markers and their bioactive potentials. Information obtained from this research will enhance our understanding on the use of *Curcuma* in traditional medicinal practices in Malaysia.

1.4 Research Objectives

The eight *Curcuma* species identified for research are recognized as the most common *Curcuma* in Malaysia. This study will investigate the chemical composition in eight species of *Curcuma* based on their essential oil composition and secondary metabolites. Isolated chemicals will also be subjected to bioassay to evaluate their antibacterial and anticancer potentials. Therefore, the objectives of this study are:

1. To quantify the essential oil yield and composition
2. To quantify and profile the crude extracts
3. To isolate and elucidate the chemical structures of secondary metabolites
4. To identify antibacterial properties from extract
5. To evaluate anticancer properties from secondary metabolites

CHAPTER 2

LITERATURE REVIEW

2.1 Family Zingiberaceae

One of the largest family in the Plantae Kingdom is Zingiberaceae, and it consists of 53 genera and over 1200 species. Members of this family are distributed mostly in tropical and subtropical region especially in Malesian region that consists of Indonesia, Malaysia, Singapore, Brunei, Philippines and Papua New Guinea (Sirigusa, 1998). This family has been differentiated from other family in Plantae Kingdom based on their specific characteristic such as perennial, terrestrial, rarely epiphytic, presence of tuberous and non-tuberous rhizomes, short stem and other specific features (Sirigusa, 1998, Lin and Larsen, 2000).

Members of this family have been widely used as food, spices, medicines, dyes and also as traditional medicine by local people. Medicinal applications often involve consumption or applied as paste upon being homogenized, boiled in water and mixed with other herbs. In addition, species such as *Curcuma aromatica, Elettaria cardomomum, Zingiber montanum* are used as anti-venom to cure snake bites, *Kaempferia rotunda, Heychium spicatum, Zingiber cassumunar* are used to cure stomach ache and indigestion while *Zingiber zerumbet, Alpinia barcteata* are applied for tooth decay (Tushar *et al.*, 2010, Usia *et al.*, 2006).

Zingiberaceae has also become a major source of secondary metabolites and volatile hydrocarbons important in the production of new remedies. To date, diversity of chemicals with interesting skeleton type has been isolated from Zingiberaceae. These comprises the skeleton types of labdane diterpenoids (Sob *et al.*, 2007), flavonoids, chalcone flavonoids, cyclohexane diepoxide, bisabolane sesquiterpenes, diphenylheptanoid, cadalene (Jantan *et al.*, 2008), oxygenated bisabolane , oxygenated menthane (Sy and Brown, 1997) polyoxygenated

cyclohexane derivatives, acylated derivatives, triacylated derivative and cyclohexane diepoxide (Stevenson *et al.*, 2007).

Other than that, based on previous study, essential oil and crude sample of Zingiberaceae have shown great result in various biological assays. Species under this family have shown interesting biological properties including fumigant toxicity (Suthisut *et al.*, 2011), antimicrobial, antioxidant (Habsah *et al.*, 2000) antiallergic (Tewtrakul and Subhadhirasakul, 2006) antiinflamantory (Tewtrakul *et al.*, 2009) and tyrosinase inhibition properties (Chan *et al.*, 2008).

2.2 Chemical constituents of essential oil in *Curcuma*

Essential oil, also known as volatile or ethereal oils, is aromatic oily liquids obtain from plants parts such as flowers, leaves, bud, seeds, twigs, bark, wood, fruits or roots (Burt, 2004). Extracted under low boiling points and atmospheric pressure, essential oils obtained are often rich with a diversity of volatile chemical constituents. Compositions of essential oils in *Curcuma* sp. has been widely study and consist of terpene, aromatics and cinnamic acids group (Baser and Buchbauer, 2010). The understanding of their structure is important to develop these oils into concoctions with pharmaceutical potential. Essential oil compositions are also been used as chemotaxonomy markers in species differentiation in this family in addition to the conventional approach based on their structure, ecological process and their potential biological activity (Mandi and Sharma, 1994). The common chemical skeletons often found in Curcuma species are described in the following subchapters:

2.2.1 Monoterpenes: Cineole Type

Secondary metabolites of the chemical skeleton monoterpene are widely distributed in genus *Curcuma*, common representative is known as 1,8-cineole (**1**). This compound was found in *C. aeruginosa* (Jirovetz *et al.*, 2000), *C. amada, C. aromatica, C. longa* (Singh *et al.*, 2002), *C. caesia* (Pandey and Chowdhury, 2003), *C. cochinchinensis* (Grayson, 1998), *C. zedoaria* (Mau *et al.*, 2003). Moreover, •-3-carene (**2**) was also classified under cineole derivatives and recorded in *C. aromatic* and *C. zedoaria* (Singh *et al.*, 2002). Figure 1.2 shows chemical structure of **1** and **2**.

REFERENCES

Abas, F., Lajis, N.H., Shaari, K., Israf, D.A., Stanslas, J., Yusuf, U.K. & Raof, S.M. 2005. A labdane diterpene glucoside from the rhizomes of *Curcuma mangga*. *Journal of Natural Product*. **68**; 1090-1093.

Ahmad, S., Ali. M., Ansari, S.H. & Ahmed, F. 2010. Phytoconstituents from the rhizomes of Curcuma aromatica Salisb. Journal of Saudi Chemical Society. **15**: 287-290.

Almeida, P.L., Cherubino, A.P.F., Alves, R.J., Dufosse, L. & Floria, M.B.A. 2005. Separation and determination of the physico-chemical charactheristics of curcumin, demethoxycurcumin and bisdeethoxycurcumin. *Food Research International*. **38**: 1039-1044.

Al-Reza, S.M., Rahman, A., Sattar, M.A., Rahman, M.O. & Fida, H.M. 2010. Essential oil composition and antioxidant activities of Curcuma aromatica Salisb. *Food and Chemical Toxicology*. **48**: 1757–1760.

Bajpai, V.K., Rahman, A. & Kang, S.C. 2008. Chemical compoition and inhibitory parameters of essential oil and extract of *Nandina domestica* Thunb. to control food borne pathogenic and spoilage bacteria. *International Journal of Food Microbiology*. **125**; 117-122.

Balunas, M.J. & Kinghorn, A.D. 2005. Drug Discovery from Medicinal Plants. *Life Sciences*. **78**; 431-441.

Baser, K.H.C. & Buchbauer, G. 2010. *Handbook of Essentil Oils: Science, Technology and Applications*. CRC Press, Taylor and Francis Group. Boca Raton, Florida.

Bernardi, M.D., Vidari, G. & Finzi, P.V. 1976. Dehydrozingerone from *Aframomum giganteum*. *Phytochemistry*. **15**; 1785-1786.

Bhamarapravati, S., Juthapruth, S., Mahachai, W. & Mahady, G. 2005. Antibacterial activity of *Boesenbergia rotunda* (L.) Mansf. and Myristica frangrans Houtt. against *Helicobacter pylori*. *Songklanakarin. Journal of Science and Technology*. **28**: 157-163.

Bhat, P., Hedge, G. & Hegde, G.R. 2012. Ethnomedicinal practices in different communities of Uttara Kannada district of Karnataka for treatment of wounds. *Journal of Ethnopharmacology*. **143** : 501-514.

Burt, S. 2004.Essential oils: their antibacterial properties and potential applications in foods-a review. *International Journal of Food* Microbiology. **94**: 223-253.

Caldentey, K.M.O. & Inze, D. 2004. Plant cell factories in the post-genomic era: new ways to produce designer secondary metabolites. *Trends in Plant Science*. **9**: 433-440.

Chan, E.W.C., Lim, Y.Y., Wong, L.F., Lianto, F.S., Wong, S.K., Lim, K.K., Joe, C.E. & Lim, T.Y. 2008. Antioxidant and tyrosinase inhibition properties of leaves and rhizomes of ginger species. *Food Chemistry*. **109**:477–483.

Chattopadhyay, I., Biswas, K., Bandyopadhyay, U. & Banerjee. R.K. 2004. Turmeric and curcumin: Biological actions and medicinal applications. *Current science.* **87.**

Cheah, S.C., Appleton, D.R., Lee, S.T., Lam, M.L., Hadi, A.H.A. & Mustafa, M.R. 2011. Panduratin A inhibits the growth of A549 cells through induction of apoptosis and inhibition of NF-KappaB Translocation. *Molecules.* **16**; 2583-2598.

Cheenpracha, S., Karalai, C., Ponglimanont, C., Subhadhirasakul, S. & Tewtrakul, S. 2005. Anti-HIV-1 protease activity of compounds from *Boesenbergia pandurata. Bioorganic & Medicinal Chemistry.* **14**:1710–1714.

Chen, X., Pei, L., Zhong, Z., Guo, J., Zhang, Q., Wang, Y. 2011. Anti-tumor potential of ethanol extract of *Curcuma phaeocaulis* Valeton against breast cancer cells. *Phytomedicine.* **18**; 1238-1243.

Chin, Y.W., Balunas, M.J., Chai, H.B. & Kinghorn, A.D. 2006. Drug Discovery from Natural Sources. *The AAPS Journal.* **8**; 239-253.

Chong, T.E., Kee, L.Y., Fei, C.C., Han, H.C., Ming, W.S., Ping, C.T.L., Teck, F.G., Khalid, N., Rahman, N.A., Karsani, S.A., Othman, S., Othman, R. & Yusof, R. 2012. Review Article *Boesenbergia rotunda* : From Ethnomedicine to Drug Discovery. *Evidence-Based Complementary and Alternative Medicine.* **2012**: 25.

Chorawala, M.R., Oza, P.M. & Shah, G.B. 2012. Mechanisms of anticancer drugs resistance: An overview. International *Journal of Pharmaceutical Sciences and Drug Research.* **4**: 01-09.

Chowdhury, J.U., Nandi, N.C., Bhuiyan, M.N.I. & Mobarok, M.H. 2008. Essential Oil Constituents of the Rhiomes of Two Types of *Curcuma longa* of Bangladesh. *Bangladesh Journal of Scientific and Industrial Research.* **43**: 259-266

Chowdhury, Z., Islam, M.S., Hoque, M.R., Chowdhury, A.M.M.A., Bhuiyan, R.H., Alauddin, M. 2010. Antibacterial and Antifungal Activity of Ethanol Extract of *Curcuma caesia. J.B. Sci.* **5**; 149-154.

CLSI. 1999. *Methods fro determining bactericidal activity of antimicrobial agents; approved guideline.* In Approved Guideline Document M26-A, Wayne Pennsylvania Clinical and Laboratory Standards Institute, pp: 1-29.

Crombie, L., King, R.W. & Whiting, D.A. 1975. Carbon-13 magnetic resonance spectra. Synthetic presqualene esters related cyclopropanes and isoprenoids. *J. Chem. Soc., Perkin Trans. 1*, **0**;913-915

Daley, R.F. & Daley, S.J. 2005. Organic Chemistry: Chapter 3 Molecular Conformations. 122-167.

Das, K. & Rahman, M.A. 2012. Analgesic and Antimicrobial Activites of *Curcuma zedoaria. International Journal of Pharmacy and Pharmaceutical Sciences.* **4**: 322-328.

Du, Z.T., Zheng, S., Chen, G. & Lv, D. 2011. A short synthesis of Bisabolane sesquiterpens. *Molecules.* **16**; 8053-8061.

Edris, A.E. 2007. Pharaceutical and therapeutic potentials of essential oils and their individual volatile constituents: A review. *Phytother Res.* **21**: 308-23.

Etoh, H., Kondoh, T., Yoshioka, N., Sugiyama, K., Ishikawa, H. & Tanaka, H. 2003. 9-Oxo-neoprocurcumenol from *Curcuma aromatica* (Zingiberaccae) as an attachment inhibitor against the Blue Mussel,*Mytilus edulis galloprovincialis. Biosci Biotech Biochem.* **67**:911-913.

Eun, S., Choi, I. & Shim, S.H. 2010. A new sesquiterenoid from the rhizome of *Curcuma zedoaria. Bulletin Korean Chemical Society.* **31**; 1387-1388.

Firman, K., Kinoshita, T., Itai, A. & Sankawa, U. 1988. Terpenoids from *Curcuma heyneana.Phytochemistry.* **27**. 3887-3891.

Fukushima, S., Kuroyanagi, M., Ueno, A., Akahori, Y. & Saiki, Y. 1970. Structure af Cuzerenone, a new sesquiterpene from *Curcuma zedoaria. Yakugaku Zasshi.* **90**; 863-869.

Gao, J.F, Xie, J.H., Iitaka, Y. & Inayama, S. 1989. The stereostructure of wenjine and related (1*S*,10*S*),(4*S*,5*S*)-germacrone-1(10),4-diepoxide isolated from *Curcuma wenyujin. Chem Pharm Bull .* **37**: 233-236.

Ghimire, K. & Bastakoti, R.R. 2009. Ethnomedicinal Knowledge and Healtcare Practices Among the Tharus of Nawalparasi district in central Nepal. *Forest Ecology and Management.* **257**: 2066-2072.

Giang, P.M. & Son, P.T. 2004. Phytochemical investigation of *Aplinia globosa* (Lour). Horaninov, Zingiberaceae. *Journal of Chemistry.* **42**; 376-378.

Gottesman, M.M. 2002. Mechanisms of Cancer Drug Resistance. *Annual Reviews Medical.* **53**; 615- 627.

Gounder, D.K. & Lingamallu, J. 2012. Comparison of chemical composition and antioxidant potential of volatile oil from fresh, dried and cured turmeric (*Curcuma longa*) rhizomes. *Industrial Crops and Products.* **38**: 124-131.

Grayson, D.H. 1998. Monoterpenoids. *Natural Product Reports.* **15;** 439-475.

Habsah, M., Amran, M., Mackeen, M.M., Lajis, N.H., Kikuzaki, H., Nakatani, N., Rahman, A.A., Ghafar & Ali, A.M. 2000. Screening of Zingiberaceae extracts for antimicrobial and antioxidant activities. *Journal of Ethnopharmacology.* **72**: 403–410.

He, X.G., Lin, L.Z., Lian, L.Z. & Lindenmaier, M. 1998. Liquid Chromatography-electrospray mass spectrometric analysis of curcuminoids and sesquiterpenoids in turmeric *(Curcuma longa). Journal of Chromatography A.* **818**: 127-132.

Hikino, H., Agatsuma, K., Konno, C. & Takemoto, T. 1970. Structure of Furanodiene and Isofuranogermacrane (Curzerene). *Chem Pharm Bull.* **18**: 752-755.

Hikino, H., Konno, C., Agatsuma, K. & Takemoto, T., Horibe, I., Tori, K., Ueyama, M. & Takeda, K. 1975. Sesquiterpenoids. Part XLVII. Structure, Configuration, Conformation and Thermal Rearrangement of Furanodienone, Isofuranodienone, Curzerenone, Epicurzerenone and Pyrocurzerenone,

Sesquiterpenoid of *Curcuma zedoaria*. *Journal of Chemical Society, Perkin Transactions 1*. **5**; 478–484.

Hikino, H., Konno, C., Nagashima, T., Kohama, T. & Takemoto, T. 1971. Stereoselective epoxidation of germacrane by *Cunninghamella blakesleeana*. *Tetrahedron letters*. **4**; 337-340.

Hikino, H., Meguro, K., Sakurai, Y., & Takemoto, T. 1965. Structure of curcumol. *Chem Pharm Bull* . **13**:1484-1485.

Hikino, H., Sakurai, Y., Numabe, S., & Takemoto, T. 1968. Structure of curcumenol. *Chem Pharm Bull*. **16**: 39-42.

Hiroshi, H., Sakurai, Y. & Takemoto, T. 1968. Structure and absolute configuration of Curcolone. *Chem Pharm Bull*. **16** : 827-831.

Husein, S., Parhusip, A. & Romasi, E. F. 2009. Study on Antibacterial Activity from 'Temulawak' (*Curcuma xanthorrhiza* Roxb.) Rhizomes against Panthogenics Microbes Cell Destruction. *Journal of Applied and Insudtrial Biotechnology in Tropical Region*. **2** : 1-4.

Hwang, J. K., Shim, J. S. & Pyun, Y. R. 2000. Antibacterial activity of xanthorrhizol from *Curcuma xanthorrhiza* against oral pathogens. *Fitoterapia*. **71**: 321-323.

Isa, N.M., Abdul, A.B., Abdelwahab, S.I., Abdullah, R., Sukari, M.A., Kamalidehghan, B., Hadi, A.H.A., Mohan, S. 2012. Boesenbergin A, a chalcone from *Boesenbergia rotunda* induces apoptosis via mitochondrial dysregulation and cyctochrome c release in A549 cells in votri: Involvement of HSP70 and Bcl2/Bax signaling pathways. *Journal of Functional Foods*. **5**; 87-97.

Ishii, T., Matsuura, H., Kaya, K. & Vairappan, C.S. 2011. A new bisabolane-type sesquiterpenoid from *Curcuma domestica*. *Biochemical Systematic and Ecology*. **39** : 864-867.

Itokawa, H., Hiarayama, F., Funakoshi, K. & Takeya, K. 1985. Studies on the antitumor bisabolan sesquitepenoids isolated from *Curcuma xanthorrhiza*. *Chem Pharm Bull*. **33**; 3488-3492.

Jamal, M.A.H.M., Rahman, S., Islam, M.A., Karim, M.R., Alam, M.S. & Rahman, M.Z. 2012. Minimum Inhibitoy Concentration Analysis of *Nerium oleander* against Bacterial Pathogens. *Asian Pacific Journal of Tropical Biomedicine*. **2012**; 1664-1666.

Jang, M.K., Lee, H.J., Kim, J.S. & Ryu, J.H. 2004. A curcuminoid and two sesquiterpenoids from Curcuma zedoaria as inhibitors of nitric oxide synthesis in activated macrophages. *Arch Pharm Res*. **27**: 1220-1225.

Jantan, I., Raweh, S.M., Sirat, H.M., Jamil, S., Mohd Yasin, Y.H., Jalil, J. & Jamal, J.A. 2008. Inhibitory effect of compounds from Zingiberaceae species on human platelet aggregation. *Phytomedicine*. **15**: 306–309.

Jantan, I., Saputri, F.C., Qaisar, M.N. & Buang, F. 2012. Correlation between Chemical Composition of *Curcuma domestica* and *Curcuma xanthorrhiza* and Their Antioxidant Effect on Human Low-Density Lipoprotein oxidation. *Evidence-Based Complementary and Alternative Medicine*. **2012**: 1-10.

Jantan, I.B., Basni, I., Ahmad, A.S., Ali, N.A.M., Ahmad, A.R. & Ibrahim, H. 2001. Constituents of the rhizome oils of *Boesenbergia pandurata* (Roxb.) Schlecht from Malaysia, Indonesia and Thailan. *Flavour and Fragrance Journal.* **16**; 110-112.

Jarikasem, S., Thubthimthed, S., Chawananoraseth, K., Suntornanasat, T. Brophy, J.J. 2005. Essential oil from three Curcuma species collected in Thailand. *ISHS Acta Horticulturae 677.* **3**: 37-40

Jiang, T., Wang, L., Zhang, S., Sun, P.C., Ding, C.F., Chu, Y.Q. & Zhou, P. 2011. Interaction of Curcumin with Al (III) and its complex structures based on experiments and theoretical calculations. *Journal of Molecular Structure.* **1004**: 163-173.

Jing, L. J., Mohamed, M., Rahmat, A. & Abu Bakar, M. F. 2010. Phytochemicals, antioxidant properties and anticancer investigations of the different parts of several gingers species (*Boesenbergia rotunda, Boesenbergia pulchella* var *attenuate* and *Boesenbergia armeniaca*). *Journal of Medicinal Plants Research.* **4** : 27-32.

Jirovetz, L., Buchbauer, G., Puschmann, C., Shafi, M.P. & Nambiar, M.K.G. 2000. Essential oil analysis of Curcuma aeruginosa Roxb. leaves from South India. *J Essential Oil Res* .**12**: 47-49.

Jitoe, A., Masuda, T. & Nakatani, N. 1993. Phenylbutenoid dimers from the rhizomes of *Zingiber cassumunar. Phytochemistry.* **32**; 357-363.

Joshi, J., Ghaisas, S., Vaidya, A., Vaidya, R., Kamat, D.V., Bhagwat, A.N., Bhide, S. 2003. Early Human Safety Study of Tumeric Oil (Curcuma longa oil) administered orally in healthy volunteers. *Journal of Association of India.* **51** : 1055-1060.

Kamarezi, T.S.A., Samah, O.A., Taher, M., Susanti, D., Qaralleh, H. 2012. Antimicrobial activity and essential oils of *Curcuma aeruginosa, Curcuma mangga* and *Zingiber cassumunar* from Malaysia. *Asian Pacific Journal of Tropical Medicine.* **5**; 202-209.

Karmakar, I., Dolai, N., Bala, A. & Haldar, P.K. 2011. Anxiolytic and CNS depressant activities of methanol extracts of *Curcuma caesia* rhizome. *Pharmacologyonline.* **2**: 738-747.

Khan, M.G.U., Nahar, K., Rahman, M.S., Hasan, C.M. & Rashid, M.A. 2008. Phytochemical and Biological Investigation of *Curcuma longa. Dhaka Univ. J. Pharm. Sci.* **8**: 39-45.

Kim, S.H., Hong, K.O., Hwang, J.K. & Park, K.K. 2005. Xanthorrhizol has a potential to attenuate the high dose cisplation-induced nephrotoxicity in mice. *Food and Chemical Toxicology.* **43**; 117-122.

Kimura, Y., Takido, M., Nakano, K. & Takishita, M. 1966. Studies on the constituents of *Alpinia.* X. o the constituents of the rhizomata of *Alpinia speciosa* K. Schumann

and *A. kumatake* Makino (*A. formosana* K. Schumann). *Yakugaku Zasshi.* **86**; 1184-1187.

Kiso, Y., Suzuki, Y., Oshima, Y. & Hikino, H. 1983. Stereostructure of curlone, a sesquterpenoid of *Curcuma longa* rhizomes. *Phytochemistry.* **22**; 596-597.

Kiuchi, F., Goto, Y., Sugimoto, N., Akao, N., Kondo, K. & Tsuda, Y. 1993. Nematocidal activity of turmeric: synergistic action of curcuminoids. *Chem Pharm Bull.* **41**: 1640-1643.

Kojima, H., Yanai, T., & Toyota, A. 1998. Essential oil constituents from Japanese and Indian *Curcuma aromatica* rhizomes. *Planta Medica.* **64**: 380-381.

Krishnaraj, M., Rao, K.M. & Mathivanan, N. 2008. Antibacterial Activity of Crude Rhizome Extract of *Curcuma caesia* Roxb. *Proc. A.P.Akademi of Sciences, Hyderabad.* **12**; 280-282.

Kulip, J. 2003. An ethnobotanical survey of medicinal and other useful plants of Muruts in Sabah, Malaysia. *Telopea.* **10** : 81-98.

Kuroyanagi, M. & Natori, S. 1970. Cucuminoids from Zingerberaceae plants. *Yakugaku Zasshi.* **90**: 1467-1470.

Kuroyanagi, M. & Natori, S. 1970. Some observation on curcuminoids from Zingiberaceae plants. *Yakugaku Zasshi.* **90**; 1467-1470.

Kuroyanagi, M., Fukushima, S., Yoshihira, K., Natori, S., Dechatiwongse, T., Mihashi, K., Nishi, M. & Hara, S. 1980. Further Characterization of the constituents of a Thai medicinal pant, *Zingiber cassumnunar* Roxb. *Chem Pharm Bull.* **28**; 2948-2959.

Kuroyanagi, M., Ueno, A., Koyama, K. & Natori, S. 1990. Structures of sesquiterpenes of *Curcuma aromatica* Salisb. studies on minor sesquiterpenes. *Chem Pharm Bull.* **38**: 55-58.

Kuroyanagi, M., Ueno, A., Ujiie, K. & Sato, S. 1987. Structures of sesquiterpenes from *Curcuma aromatica* Salisb. *Chem Pharm Bull.* **35**: 53-59.

Lakshmi, S., Padmaja, G. & Remani, P. 2011. Antitumor effect of isocurcumenol isolated from *Curcuma zedoaria* rhizomes on human and murine cancer cells. *International Journal of Medicinal Chemistry.* **2011**; 1-13.

Lawhavinit, O., Kongkathip, N. & Kongkathip, B. 2010. Antimicrobial Activity of Curcuminoids of *Curcuma longa* L. on Panthogenic Bacteria of Shrimp and Chicken. *Kasetsart Journal (Natural Science).* **44**; 364-371.

Levinson, M.E.2004. Pharmacodynamics of antimicrobial drugs. *Infectious Disease Clinics of North America.* **162**; 1141-1153.

Li, S., Yuan, W., Deng, G., Wang, P., Yang, P. & Aggarwal, B.B. 2011. Chemical composition and product quality control of turmeric (Curcuma longa L.). *Pharmaceutical Crops.* **2**:28-54.

Lin, K.W. 2005. Ethnobotanical Study of Medicinal Plants used by the ah Hut Peoples in Malaysia. *Indian Journal of Medical Sciences.* **59** : 156-161.

Lin, W.T. & Larsen, K. 2000. Zingiberaceae. *Flora of China.* **24**: 322–377.

Linscott, A.J. 2011. Food Borne Illness. *Clinical Microbiology Newsletter.***33**;41-45.

Liu, Y. & Nair, M.G. 2010. Labdane diterpenes in Curcuma mangga rhizomes inhibit lipid peroxidation, cyclooxygenase enzymes and human tumor cell proliferation. *Food Chemistry.* **124**: 527-532.

Liu, Y., Roy, S. S., Nebie, R. H. C., Zhang, Y. & Nair, M. G. 2013. Functional food quality of *Curcuma caesia, Curcuma zedoaria* and *Curcuma aeruginosa* Endemic to Northeastern India. *Plant Foods Human Nutritional.* **68**: 72-77.

Liu, Z.L., Zhao, N.N., Liu, C.M., Zhou, L. & Du, S.S. 2012. Identification of insecticidal constituents of the essential oil of *Curcuma wenyujin* rhizomes active against *Liposcelis bostrychopila* Badonnel. *Molecules.* **17**: 12049-12060.

Lorimer, S.D. & Weavers, R.T. 1987. Foliage sesquiterpenes and diterpenes of *Podocarpus spicatus. Phytochemistry.* **26**; 3207-3215.

Madhu, S.K., Shaukath, A.K. & Vijay, V.A. 2010. Efficacy of bioactive compounds from *Curcuma aromatica* against mosquito larvae. *Acta Tropica.* **113**: 7–11.

Maggi, F., Maggi, F., Barboni, L., Papa, F., Caprioli, G., Ricciutelli, M., Sagratini, G. & Vittori, S. 2012. A forgotten vegetable (*Smyrnium olusatrum* L., Apiaceae) as a rich source of isofuranodiene. *Food Chemistry.* **135**; 2852-2862.

Makabe, H., Maru, N., Kuwabara, A., Kamo, T. & Hirota, M. 2006. Anti inflammatory sesquiterpenes from *Curcuma zedoaria. Natural Product Research.* **20**; 680-685.

Malek, S.N.A., Lee, G.S., Hong, S.L., Yaacob, H., Wahab, N.A., Webe, J.F.F. & Shah, S.A.A. 2011. Phytochemical and Cytotoxic Investigation of *Curcuma mangga* rhizomes. *Molecules.* **16**; 4539-4548.

Mandi, K.K. & Sharma, A.K. 1994. Chemical constituents of Zingiberaceae as taxonomic markers: A review. *The Nucleus.* **37**: 123-1 31

Mangunwardoyo, W., Deasywaty & Usia, T. 2012. Antimicrobial and identification of active compound *Curcuma xanthorrhiza* Roxb. *International Journal of Basic & Applied Sciences.* **12**: 69-78.

Mary Helen, P.A., Susheela Gomathy, K., Jayasree, S., Nizzy, A.M., Rajagopal, B. & Jeeva, S. 2012. Phytochemical characterization and antimicrobial activity of *Curcuma xanthorrhiza* Roxb. *Asian Pacific Journal of Tropical Biomedicine.* **2012**: 637-640.

Masuda, T., J. Isobe, A. Jitoe and N. Nakatani. 1992. Antioxidative curcuminoids from rhizomes of *Curcuma xanthorrhiza. Phytochemistry.* **31**: 3645-3647.

Masuda, T., Jitoe, A. & Nakatani, N. 1991. Structure of Aerugidiol, a New Bridge-head Oxygenated Guaiane Sesquiterpene. *Chemistry Letters.* 1625-1628

Masuda, T., Jitoe, A., Isobe, J., Nakatani, N. & Yonemori, S. 1993. Anti oxidative and anti inflammatory curcumin related phenolics from rhizomes of *Curcuma domestica. Phytochemistry.* **32**: 1557-1560.

Masuda, T., Jitoe, A., Nakatani, N. 1991. Structure of aerugidiol, a new bridge-head oxygenated guaiane sesquiterpene. *Chem Letts* . **9**:1625-1628.

Matsuda, H., Morikawa, T., Ninomiya, K. & Yoshikawa, M. 2001. Absolute stereostructure of carabrane-type sesquiterpene and vasorelaxant-active sesquiterpenes from Zedoariae Rhizoma. *Tetrahedron.* **57**: 8443-8453.

Matsuda, H., Morikawa, T., Toguchida, I., Ninomiya, K. & Yoshikawa, M. 2001. Medicinal Foodstuffs. XXVIII.1) Inhibitors of nitric oxide production and new sesquiterpenes, Zedoarofuran, 4-Epicurcumenol, Neocurcumenol, Gajutsulactones A and B, and Zedoarolides A and B, from Zedoariae Rhizoma. *Chem. Pharm. Bull.* **49**:1558—1566.

Matsuda, H., Tewtrakul, S., Morikawa, T., Nakamura, A. & Yoshikawa, M. 2004. Anti-allergic principles from Thai zedoary: structural requirements of curcuminoids for inhibition of degranulation and effect on the release of TNF-a and IL-4 in RBL-2H3 cells. *Bioorganic & Medicinal Chemistry.* **12**: 5891-5898

Mau, J.L., Lai, E.Y.C., Wang, N.P., Chen, C.C., Chang, C.H. & Chya, C.C. 2003. Composition and antioxidant activity of the essential oil from *Curcuma zedoaria*. *Food Chemistry.* **82**: 583–591

Mendez, M., Rodriguez, R., Ruiz, J., Adame, D.M., Castillo, F., Castillo, F.D.H., Aguilar, C.N. 2012. Antibacterial activity of plant extracts obtained with Iternative organics solvents against food-borne panthogen bacteria. *Industrial Crops and Products*. **37**; 445-450.

Miksusanti, Jenie, B.S.L., Priosoeryanto, B.P., Syarief, R. & Trimulyadirekso, G. 2008. Mode of action Tu Kuci (*Kaempferia pandurata*) essential oil *E. coli* K1.1 cell determined by leakage of material cell and salt tolerance assays. *Journal of Biosciences*. **15**: 56-60.

Nahar, L., Sarker, S., 2007. Tumeric: Phytochemistry of the Genus *Curcuma* .*Taylor & Francis Group*. pg: 71.

Nakayama, R., Tamura, Y., Yamakana, H., Kikuzaki, H. & Nakatani, N. 1993. Two curcuminoid pigments from Curcuma domestica. *Phytochemistry*. **22**: 501-502.

Napitupulu, R., Wisaksono, L.S., Efizal, S.M., Mooduto, L., Herawaty, T., Novianti, A., Wahyu, S. & Tumino. 2008. *Taksonomi Koleksi Tanaman Obat Kebun Tanaman Obat Citeureup*. Jakarta: Global Express.

Narang, A. S. & Desai, D. S. 2009. Anticancer drug development, unique aspects of pharmaceutical development. *Pharmaceutical Perceptives of Cancer Therapeutics*. 49-92.

Nasar-Abbas, S.M. & Halkman, A.K. 2004. Antimicrobial effect of water extract of sumac (*Rhus coriaria* L.) on the growth of some food borne bacteria including pathogens. *International Journal of Food Microbiology*. **97**; 63-69.

National Medicinal Plants Board. 2008.The Energy and Resources Institute Press. New Delhi.

Newell, D.G., Koopmans, M., Vehoef, L., Duizer, E., Kane, A.A., Sprong, H., Opsteegh, M., Langelaar, M., Threfall, J., Scheutz, F., Giessen, J. & Kruse, H. 2010. Food-

borne diseases- The challenges of 20 years ago still persisit while new ones continue to emerge. *Intenational Journal of Food Microbiology*. **139**; 3-15.

Norajit, K., Laohakunjit, N. & Kerdchoechuen, O. 2007. Antibacterial Effect of Five Zingiberaceae Essential Oils. *Molecules*. **12**: 2047-2060.

Ohshiro, M., Kuroyanagi, M. & Ueno, A. 1990. Structures of sesquitepenes from *Curcuma longa*. *Phytochemistry*. **29**; 2201-2205.

Ong, H.C. & Nordiana, M. 1999. Malay ethno-medico botany in aching, Kelantan, Malaysia. *Fitoterapia*. **70** : 502-513.

Ong, H.C. & Norzalina, J. 1999. Malay herbal medicine in Gemencheh, Negri Sembilan, Malaysia. *Fitoterapia*. **70** : 10-14.

Ong, H.C., Zuki, R.M. & Milow, P. 2011. Traditional Knowledge of Medicinal Plants among the Malay Villagers in Kampung Mak Kemas, Terangganu, Malaysia. *Ethno Medicinal*. **5**: 175-185.

Overwalle, G.V. 2005. Protecting and sharing biodiversity and traditional knowledge: holder and user tools. *Ecological Economics*. **53**: 585-607.

Paliwal, P., Pancholi, S.S., Patel, R.K. 2011. Pharmacognostic parameters for evaluation of the rhizomes of *Curcuma caesia*. *Journal of Advanced Pharmaceutical Technology and Research*. **2**, 56.

Pande, B.S., Krishnappa, S., Bisaraya, S.C. & Dev, S. 1971. Studies in sesquiterpenes-XLVII; Cis and Trans-atlantones from *Cedrus deodara* Loud. *Tetrahedron*. **27**; 841-844.

Pandey, A. K. & Chowdhury, A. R. 2003. Volatile constituents of the rhizome oil of *Curcuma caesia* Roxb. from central India. *Flavour and Fragrance Journal* . **18**; 463-465.

Pandji, C., Grimm, C., Wray, V., Witte, L. & Proksch, P. 1993. Insecticidal constituents from four species of the zingiberaceae. *Phytochemistry*. **34**; 415-419.

Pankey, G.A. & Sabath, L. D. 2004. Clinical relevance of bacteriostatic versus bacteriacidal mechanisms of action in the treatment of Gram positive bacterial infections. *Clinical Infectious Diseases*. **38**; 864-870.

Park, S.Y. & Kim, D.S.H.L. 2002. Discovery of natural products from Curcuma longa that protect cells from beta-amyloid insult: A drug discovery effort against Alzheimer's disease. *J Nat Prod*. **65**: 1227-1231.

Parry, E.J. 1922. The chemistry of essential oils and artificial perfumes (Volume II). Scott, Greenwood and Son. London.

Policegoudra, R.S., Abiraj, K., Gowdab, D. C., Aradhya, S.M. 2007. Isolation and characterization of antioxidant and antibacterial compound from mango ginger (*Curcuma amada* Roxb.) rhizome. *Journal of Chromatography B*. **852**:40–48.

Policegoudra, R.S., Aradhya, S.M. & Singh, L. 2011. Mango ginger (*Curcuma amada* Roxb.)- A promising spice for phytochemicals and biological activities. *Journal of Bioscience*. **36**: 739-748.

Qu, Y., Xu, F., Nakamura, S., Matsuda, H., Poongpiriyadacha, Y., Wu, L. & Yoshikawa, M. 2009. Sesquiterpene of Curcuma comosa. *Journal of Nat. Med.* **62**: 102-104.

Ramsewak, R. S., DeWitt, D. L. & Nair, M. G. 2000. Cytotocity, antioxidant and anti-inflammatory activities of Curcumin I-III from *Curcuma longa.Phytomedicine.* **7** : 303-308.

Ranjini, C.E. & Vijayan, K.K. 2005, Structural characterization of a glucan from the tubers of *Curcuma aeruginosa. Indian Journal of Chemistry.* **44**: 643-647.

Rao, S.R. & Ravishankar, G.A. 2002. Plant cell cutures: Chemical factories of secondary metabolites. *Biotechnology Advances.* **20**; 101- 153.

Rimpler, H., Hansel, R. & Kochendoerfer, L. 1970. Xanthorrhizol, a new sesquiterpene from *Curcuma xanthorrhiza. Z Naturforsch B.* **25**: 995-998.

Roth, G.N., Chandra, A. & Nair, M.G. 1998. Novel bioactivities of Curcuma longa constituents. *J Nat Prod.* **61**: 542-545.

Rucker, G. 1971. Die strutur des isofuranodiens aus *Steocylax michelii* (Myrtaceae). *Phytochemistry.* **40**; 221-224.

Ruslay, S., Abas, F., Shaari, K., Zainal, Z., Maulidiani, Sirat, H., Israf, D.A. & Lajis, N.H. 2007. Characterization of the components present in the active fractions of health gingers (*Curcuma xanthorrhiza* and *Zingiber zerumbet*) by HPLC-DAD-ESIMS. *Food Chemistry.* **104** : 1183-1191.

Saifudin, A., Tanaka, K., Kadota, S. & Tezuka, Y. 2013. Sesquiterpenes from the rhizomes of *Curcuma heyneana. Journal of Natural Product.* **76**; 223-229.

Samuel, A.J.S.J., Kalusalingam, A., Chellappan, D.K., Gopinath, R., Radhamani, S., Husain, A., Muruganandham, V. & Promwichit, P. 2010. Ethnomedical survey of plants used by the Orang Asli in Kampung Bawong, Perak, West Malaysia. *Journal of Ethnobioloy and Ethnomedicine.* **6**: 1-5.

Schramm, A., Ebrahimi, S.N., Raith, M., Zaugg, J., Rueda, D.C., Hering, S. & Hamburger, M. 2013. Phytochemiccal profiling of *Curcuma kwangsiensis* rhizome extract and identification of labdane diterpenoids as positive GABA receptor modulator. *Phytochemistry.* **96**: 318-329.

Shiobara, Y., Asakawa, Y., Kodama, M. & Takemoto, T. 1986. Zedoarol, 13-hydroxygermacrone and curzeone,3 sesquiterpenoids from *Curcuma zedoaria. Phytochemistry.* **25**: 1351-1353.

Shiobara, Y., Asakawa, Y., Kodama, M., Yasuda, K. & Takemoto, T. 1985. Curcumenone, curcumanolide-A and curcumanolide-B, 3 sesquiterpenoids from *Curcuma zedoaria. Phytochemistry* .**24**: 2629-2633.

Shiobara, Y., Asakawa, Y., Kodama, M., Yasuda, K. & Takemoto, T. 1985. Curcumenone, Curcumanolide A and Curcumanolide B, three sesquterpenoids form *Curcuma zedoaria. Phytochemistry.* **24**; 2629-2633.

Singh, G., Kapoor, I.P.S., Singh, P., Heluani, C.S.D., Lampasona, M.P.D. & Catalan, C.A.N. 2010. Comparative study of chemical composition and antioxidant

activity of fresh and dry rhizomes of turmeric (*Curcuma longa* Linn.). *Food and Chemical Toxicology.* **48**:1026–1031.

Singh, G., Singh, O.P. & Maurya, S. 2002. Chemical and biocidal investigation on essential oils of some indian *curcuma* species. *Progress in crystal growth and characterization of materials.* **45**:75-81

Singh, T.K. 2012. Microbial extracellular polymeric substances: production, isolation and applicatins. *IOSR Journal of Pharmacy.* **2**; 271-281

Sirat, H.M. & Meng, L.L. 2009. Chemical Components of the Rhizome Oil of *Curcuma heyneana* Val. *Malaysian Journal of Science.* **28**: 323 – 328.

Sirat, H.M., Hong, N.M. & Jauri, M.H. 2007. Chemistry of xanthorrhizol: synthesis of several bisabolane sesquterpenoids from xanthorrhizol. *Tetrahedron Letters.* **48**; 457-460.

Sirat, H.M., Masri, D. & Rahman, A.A. 1994. The Distribution of Labdane Diterpenes in the Zingiberaceae of Malaysia. *Phytochemistry.* **36**: 699-701.

Sirigusa, P. 1998. Thai Zingiberaceae: Species Diversity and Their Uses. *Pure Appl. Chem.* **70**: 11.

Smith, J.M.B. 2007. *Laboratory evaluation of antimicrobial agents. In Hugo and Russell's Pharmaseutical Microbiology (7th Edi).* Denyer SP, Hodges NA, and Gorman SP (eds). Oxford United Kingdom, Blackwell Publishing pp: 187-201.

Sob, S.V.T, Tane, P., Ngadjui, B.T., Connollyc, J.D & Ma, D. 2007. Trypanocidal labdane diterpenoids from the seeds of Aframomum aulacocarpos (Zingiberaceae). *Tetrahedron.* **63**: 8993–8998.

Solanki, R. 2010. Some Medicinal Plants with Antibacterial Activity. *International Journal of Coprehensive Pharmacy.* **4**; 1-4.

Stern, K.R., Bidlack, J.E. & Jansky, S.H. 2008. *Introductory Plant Biology.* McGraw-Hill, New York.

Stevenson, P.C., Veitch, N.C. & Simonds, M.S.J. 2007. Polyoxygenated cyclohexane derivatives and other constituents from Kaempferia rotunda L.. *Phytochemistry.* **68** : 1579–1586.

Su, H.C.F., Horvat, R. & Jilani, G. 1982. Isolation, purification, and characterization of insect repellents from *Curcuma longa* L. *J Agric Food Chem.* **30**: 290-292

Sukari, M.A., Mohd Sharif, N.W., Yap, A.L.C., Neoh, B.K., Rahmani, M., Ee, G.C.L., Taufiq-Yap, Y.H. & Yusof, U.K. 2008. Chemical constituents variations of essential oils from rhizomes of four Zingiberaceae species. *The Malaysian Journal of Analytical Sciences.* **12**; 638.644.

Suksararn, A., Eiamong, S., Piyachaturawat, P. & Byrne, L.T. 1997. A Phloracetophenone glucoside with choleretic activity from Curcuma comosa. *Phytochemistry.* **45**: 103-105.

Suphrom, N., Pumthong, G., Khorana, N., Waranuch, N., Lipeanchob, N. & Ingkaninan, K. 2012. Anti-androgenic effect of sesquiterpenes isolated from the rhizomes of *Curcuma aeruginosa* Roxb. *Fitoterapia*. **83**:864–871.

Suthisut, D., Fields, P.G. & Chandrapatya, A. 2011. Fumigant toxicity of essential oils from three Thai plants (Zingiberaceae) and their major compounds against Sitophilus zeamais, Tribolium castaneum and two parasitoids. *Journal of Stored Products Research*. **47**: 222-230.

Sy, L.K. & Brown, G.D. 1997. Oxygenated Bisabolanes from Alpinia Densibracteata, Pii: Soo31-9422(96)0086-L

Syamkumar, S. & Sasikumar, B. 2007. Molecular marker based genetic diversity analysis of *Curcuma* species from India. *Scientia Horticulture*. **112**; 235-241.

Takahashi, K., Shibata, S., Yano, S., Harada, M., Saito, H., Tamura, Y. & Kumagai, A. 1980. Labdane and bisnorlabdane type diterpenes from *Alpinia speciosa* K. Schum. *Chem Pharm Bull*. **28**; 3452-3454.

Takano, I., Yasuda, I., Takeya, K. & Itokawa, H. 1995. Guaiane Sesquiterpene Lactones from *Curcuma aeruginosa*. *Phytochemistry*. **40**: 1197-1200.

Taylor, P.W. & Sommer, A. P.2005. Towards rational treatment of bacterial infections during extended space travel. *International Journal of Antimicrobial Agents*. **26**;183-187.

Tenover, F. C. 2006. Mechanisms of antimicrobial resistance in bacteria. *The American Journal of Medicine*. **119**: 3-10.

Tewtrakul, S. & Subhadhirasakul, S. 2006. Anti-allergic activity of some selected plants in the Zingiberaceae family. *Journal of Ethnopharmacology*. **109**:535–538.

Tewtrakul, S., Subhadhirasakul, S.,Karalai, C., Ponglimanont, C. & Cheempracha, S. 2009. Anti-inflammatory effects of compounds from *Kaempferia parviflora* and *Boesenbergia pandurata*. *Food Chemistry*. **115**:534–538.

Tg Kamarezi, T.S.A., Abd Samah, O., Taher, M., Susanti, D. & Qaralleh, H. 2012. Antimicrobial activity and essential oils of *Curcuma aeruginosa, Curcuma mangga,* and *Zingiber cassumunar* from Malaysia. *Asian Pacific Journal of Tropical Medicine*. 202-209.

Theanphong, O., Songsak, T. & Kirdmanee, C. 2010. Effect of plant growth regulators on micropropagation of *Curcuma aeruginosa* Roxb. *Thai Journal of Botany 2 (Special Issue)*. 135-142.

Toume, K., Takahashi, M., Yamaguchi, K., Koyano, T., Kowithayakorn, T., Hayashi, M., Komiyama, K. & Ishibashi, M. 2004. Parviflorenes B–F, novel cytotoxic unsymmetrical sesquiterpene-dimers with three backbone skeletons from *Curcuma parviflora*. *Tetrahedron*. 60: 10817-10824.

Tushar, Basak, S., Sarma, G.C. & Rangan, L. 2010. Ethnomedical uses of Zingiberaceous plants of Northeast India. *Journal of Ethnopharmacology*. **132** : 286–296.

Uehara, S., Yasuda, I., Takeya, K. & Itokawa, H. 1989. New bisabolane sesquiterpenoids from the rhizomesof *Curcuma xanthorrhiza* (zingiberaceae). *Chem Pharm Bull* . **37**:237-240.

Uehara, S., Yasuda, I., Takeya, K. & Itokawa, H. 1992. Terpenoids and curcuminoids of the rhizome of *Curcuma xanthorrhiza* Roxb. *Yakugaku Zasshi.* **112**: 817-823.

Uehara, S., Yasuda, I., Takeya, K. & Itokawa, H. 1992. Terpenoids and curcuminoids of the rhizoma of *Curcuma xanthorrhiza* Roxb. *Yakugaku Zasshi.* **112**; 817-823.

Uehara, S., Yasuda, I., Takeya, K., Itokawa, H. & Iitaka, Y. 1990 New bisabolane sesquiterpenoids from therhizomes of *Curcuma xanthorrhiza* (Zingiberaceae) ii. *Chem Pharm Bull.* **38**: 261-263.

Usia, T., Iwata, H., Hiratsuka, A., Watabe, T., Kadota, S. & Tezuka, Y. 2006. CYP3A4 and CYP2D6 inhibitory activities of Indonesian medicinal plants. *Phytomedicine.* **13**: 67–73.

Vairappan, C.S., Elias, U.M., Ramachandram, T.R. & Kamada, T. 2013. Secondary metabolites from rhizome of *Curcuma caesia* Roxb. (Zingiberaceae). *Biochemical Systematic and Ecology.* **48** : 107-110.

Voravuthikunchai, S.P., Limsuwan, S., Supapol, O. & Subhadhirasakul, S. 2006. Antibacterial activity of extracts from family Zingiberaceae against foodborne pathogens. *Journal of Food Safety.* **26**: 325-334.

Wahab, I.R.A., Blagojevic, P.D., Radulovic, N.S. & Boylan, F. 2011. Volatiles of *Curcuma mangga* Val & Zijp (Zingiberaceae) from Malaysia. Chemistry & Biodiversity. **8**: 2005-2015.

Wright, G.D. 2005. Bacterial resistance to antibiotics: enzymatic degradation and modification. *Advanced Drug Delivery* Reviews. **57**; 1451-1470.

Yasni, S., Imaizumi, K., Sin, K., Sugano, M., Nonaka, G. & Sidik, S. 1994. Identification of an active principle in essential oils and hexane-soluble fractions of *Curcuma xanthorrhiza* Roxb. Showing triglyceride lowering action in rats. *Food and Chemical Toxicology.* **32***:* 273-278.

Yoshihara, M., Shibuya, H., Kitano, E., Yanagi, K. & Kitagawa, I. 1984. The absolute stereotructure of (4S,5S)-(+)-Germacrone 4,5-epoxide from zedoariae rhizoma cultivated in Yakushima island. *Chem Pharm Bull.* **32**; 2059-2062.

Yoshikawa, M., Murakami, T., Morikawa, T. & Matsuda, H. 1998. Absolute stereostructures of carabrane-type sesquiterpenes, curcumenone, 4S-dihydrocurcumenone, and curcarabranols A and B: Vasorelaxant activity of zedoary sesquiterpenes. *Chem Pharm Bull.* **46:** 1186-1188.

Zaeoung, S., Plubrukarn, A. & Keaepradub, N. 2005. Cytotoxic and free radical scavenging activities of Zingiberaceous rhizomes. *Songklanakarin Journal of Science and Technology.* **27**; 799-812.

Zaibunnisa, A.H., Norashikin, S., Mamot, S. & Osman, H. 2008. An experimental design approach for the extraction of volatile compounds from tumeric leaves (*Curcuma domestica*) using pressurized liquid extraction (PLE). *LWT-Food Science and Technology.* **42** : 233-238.

Zhang, P., Huang, W., Song, Z., Zhang, M., Cheng, L., Cheng, Y., Qu, H., Ma, Z. 2008. Cytotoxic diterpenes fro the radix of *Curcuma wenyujin*. *Phytochemistry Letters*. **1** :103-106.

Zhou, X., Li, Z., Lian, G., Wang, D. & Cai, Z. 2007. Analysis of Volatile Components of *Curcuma sichuanensis* X.X. Chen by gas chromatography-mass spectrometry. *Journal of Pharmaceutical and Biomedical Analysis*. **43**: 440-444.