PHENOLIC COMPOUNDS FROM THE ROOT OF *GARCINIA MANGOSTANA* L. AND THE STEM BARK OF *GARCINIA XANTHOCHYMUS*

A DISSERTATION

BY

ORAPIN KOMUTIBAN

Presented in Partial Fulfillment of the Requirements for the

Doctor of Philosophy Degree in Applied Chemistry

at Srinakharinwirot University

May 2011

PHENOLIC COMPOUNDS FROM THE ROOT OF *GARCINIA MANGOSTANA* L. AND THE STEM BARK OF *GARCINIA XANTHOCHYMUS*

A DISSERTATION

BY

ORAPIN KOMUTIBAN

Presented in Partial Fulfillment of the Requirements for the

Doctor of Philosophy Degree in Applied Chemistry

at Srinakharinwirot University

May 2011

Copyright 2011 by Srinakharinwirot University

PHENOLIC COMPOUNDS FROM THE ROOT OF *GARCINIA MANGOSTANA* L. AND THE STEM BARK OF *GARCINIA XANTHOCHYMUS*

AN ABSTRACT

BY

ORAPIN KOMUTIBAN

Presented in Partial Fulfillment of the Requirements for the

Doctor of Philosophy Degree in Applied Chemistry

at Srinakharinwirot University

May 2011

Orapin komutiban. (2011). *Phenolic compounds from the root of Garcinia mangostana L. and the stem bark of Garcinia xanthochymus*. Dissertation, Ph.D. (Applied Chemistry). Bangkok: Graduate School, Srinakharinwirot University. Advisor Committee: Assoc. Prof. Dr. Sunit Suksamrarn, Dr. Prasert Pattanaprateeb, Asst. Prof. Dr. Maneekarn Chinworrungsee.

New xanthone as 3,6-dihydroxy-8-(3-hydroxy-3-methylbutyl)-7-methoxy-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone, along with eight known xanthones, including α-mangostin, β-mangostin, 1,3,7-trihydroxyxanthone or gentisein, gracinone D, norathyriol, cratoxylone, pruniflorone C and 9-hydroxycalabaxanthone. In addition, a benzophenone as maclurin and a phenolic glucoside as tachioside were isolated from *G. mangostana* root. Among these compounds, gentisein, cratoxylone, pruniflorone C and tachioside have not been reported from this plant.

Investigation of the phytochemicals from the EtOAc extract of the *G. xanthochymus* stem bark, led to the isolation of five xanthones, 6-deoxyisojacareubin, 1,6-dihydroxy-4,5-dimethoxyxanthone, 12b-hydroxy-des-*D*-garcigerrin A, 2,5-dihydroxy-1-methoxyxanthone and 2,6-dihydroxy-1,5-dimethoxyxanthone. This is the first of 2,5-dihydroxy-1-methoxyxanthone and 2,6-dihydroxy-1,5-dimethoxyxanthone isolated from this plant.

Their structures were elucidated by spectroscopic method, especially 1D and 2D NMR techniques, and by comparison of the data with the reported value.

สารประกอบฟีนอลิกจากรากมังคุดและเปลือกต้นมะดะหลวง

บทคัดย่อ

ของ

อรพิณ โกมุติบาล

เสนอต่อบัณฑิตวิทยาลัย มหาวิทยาลัยศรีนครินทรวิโรฒ เพื่อเป็นส่วนหนึ่งของการศึกษา

ตามหลักสูตรปริญญาปรัชญาดุษฎีบัณฑิต สาขาวิชาเคมีประยุกต์

พฤษภาคม 2554

อรพิณ โกมุติบาล. (2554). *สารประกอบฟีนอลิกจากรากมังคุดและเปลือกต้นมะดะหลวง*. ปริญญานิพนธ์ ปร.ด.(เคมีประยุกต์). กรุงเทพฯ: บัณฑิตวิทยาลัย มหาวิทยาลัยศรีนครินทรวิโรฒ. คณะกรรมการควบคุม: รองศาสตราจารย์ ดร.สุนิตย์ สุขสำราญ, ดร.ประเสริฐ พัฒนาประทีป ผู้ช่วยศาสตราจารย์ ดร. มณีกานต์ ชินวรรังสี.

จากการศึกษาองค์ประกอบทางเคมีจากรากมังคุดสามารถแยกสารประกอบแซนโทนชนิดใหม่ได้ 1 ชนิด คือ 3,6-dihydroxy-8-(3-hydroxy-3-methylbutyl)-7-methoxy-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone รวมทั้งสารประกอบสารประกอบแซนโทนอีก 8 ชนิด ได้แก่ α-mangostin, β-mangostin, 1,3,7-trihydroxyxanthone หรือ gentisein, gracinone D, norathyriol, cratoxylone, pruniflorone C และ 9-hydroxycalabaxanthone นอกจากนี้ยังพบสารประกอบเบนโซฟิโนน 1 ชนิด คือ maclurin และสารประกอบฟีนอลิก กลูโคไซด์ 1 ชนิดคือ tachioside โดยที่สารประกอบแซนโทนและฟีนอลิกกลูโคไซด์ ได้แก่ gentisein, gracinone D, cratoxylone, pruniflorone C และ tachioside เป็นสารประกอบฟีนอลิกที่ยังไม่เคยมีผู้รายงานการพบในพืชชนิดนี้

จากการศึกษาองค์ประกอบทางเคมีจากเปลือกต้นมะดะหลวง สามารถแยกสารประกอบแซนโทนได้ 5 ชนิด คือ 6-deoxyjacareubin และ 12b-hydroxy-des-*D*-garcigerrin A, 1,6-dihydroxy-4,5-dimethoxy xanthone, 2,5-dihydroxy-1-methoxyxanthone และ 2,5-dihydroxy-1,6-dimethoxyxanthone โดยที่สารประกอบ 2,5-dihydroxy-1-methoxyxanthone และ 2,5-dihydroxy-1,6-dimethoxyxanthone เป็นสารประกอบแซนโทนที่ยังไม่เคยมีผู้รายงานการพบในพืชชนิดนี้

การพิสูจน์โครงสร้างของสารบริสุทธิ์ใช้เทคนิคทางสเปกโทรสโคปี และใช้วิธีเปรียบเทียบข้อมูลทางสเปกโทรสโคปีของสารกับข้อมูลที่มีผู้รายงานไว้แล้ว

The dissertation titled

"Phenolic compounds from the root of *Garcinia mangostana* L.

and the stem bark of *Garcinia xanthochymus*"

by

Orapin Komutiban

has been approved by the Graduate School as partial fulfillment of the requirements for the

Doctor of Philosophy Degree in Applied Chemistry of Srinakharinwirot University.

..... Dean of Graduate School

(Assoc. Prof. Dr. Somchai Santiwattanakul)

May , 2011

Dissertation Committee

..... Major advisor
(Assoc. Prof. Dr. Sunit Suksamrarn)

..... Co-advisor
(Dr. Prasert Pattanaprateeb)

..... Co-advisor
(Asst. Prof. Dr. Maneekarn Chinworrungsee)

Oral Defense Committee

..... Chair
(Asst. Prof. Dr. Teerayuth Liwporncharoenvong)

..... Committee
(Assoc. Prof. Dr. Sunit Suksamrarn)

..... Committee
(Dr. Prasert Pattanaprateeb)

..... Committee
(Asst. Prof. Dr. Maneekarn Chinworrungsee)

..... Committee
(Assoc. Prof. Dr. Thanattkhun Mongkolaussavaratana)

Acknowledgements

I would like to express my sincere gratitude to my supervisor, Associate Professor Dr. Sunit Suksamrarn, for her kind and helpful supervision and her hearty encouragement throughout this work.

I am grateful to Dr. Prasert Pattanaprateeb and Asst. Prof. Dr. Maneekarn Chinworrungsee, my co-advisors, for their endless kindness, thoughtful advice, valuable time, patient reading and warm encouragement. In addition, I feel grateful to Assoc. Prof. Dr. Thanattkhun Mongkolaussavaratana, Chulabhorn Graduate Institute, and Asst. Prof. Dr. Teerayuth Liwporncharoenvong for their useful comments and encouragement.

I am grateful for partially supported by XANGO LLC, The Strategic Basic Research Grant of the Thailand Research Fund, The Center of Excellence for Innovation in Chemistry (PERCH-CIC) and Suan Dusit Rajabhat University. I wish to thank Mr. James F. Maxwell, Department of Biology, Faculty of Science, Chiang Mai University, for plant collection and identification. I am indebted to Mrs. Pontip Wongnapa for collection of the plant material.

I am grateful to Mr. Pichit Sudta and Mr. Payung Jiarawapi, Department of Chemistry, Faculty of Science, Srinakharinwirot University for recording the nuclear magnetic resonance spectra, Mr. Nitirat Chimnoi, Chulabhorn Research Institute for recording the HRMS, and to Asst. Prof. Dr. Boon-Ek Yingyongnarongkul, Mr. Widchaya Radchatawedchakoon and Miss Ratchanaporn Chikchaisiri, Department of Chemistry, Faculty of Science, Ramkhamhaeng University for recording the ESMS and optical rotations.

Many special thanks also go to my teachers, friends, colleagues and staff of the Department of Chemistry, Faculty of Science, Srinakharinwirot University for their friendship, kind support and encouragement.

Finally, this work was eventually successful with understanding, great love, supports and encouragement from my mathoer and family.

Orapin Komutiban

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

TABLE OF CONTENTS (continued)

LIST OF TABLES

LIST OF TABLES (continued)

LIST OF FIGURES

LIST OF FIGURES (continued)

LIST OF FIGURES (continued)

LIST OF SCHEMES

CHAPTER 1

INTRODUCTION

Background

The family Clusiaceae mainly confined to the tropics-the major exception being the genus *Garcinia* (Bennett; & Lee. 1989: 967-998). The genus *Garcinia* includes 50-300 species of evergreen trees and shrubs native to Asia, Australia, tropical and southern Africa and Polynesia. Many of the species bear edible fruits including *G. mangostana* (Obolskiy; et al., 2009: 1047-1065). According to Smitinand 2001, the genus *Garcinia* plants are found in Thailand (Smitinand. 2001: 246-248) as follows:

1. *G. acuminata* Planch. & Triana (Rong Thong: Nakhon Si Thammarat)
2. *G. atroviridis* Griff. Ex T. Anderson (Cha muang chang, Ma kham Khaek, Som ma won: Peninsular; Som khaek, Som Khwai: Trang; Som pha ngun: Pattani; A-sa-ka-lu-ko: Malay-Yala)
3. *G. bancana* (Miq.) Miq. (Cha muang pa, Cha muang ka: Narathiwat; Ka-ni-hu-tae: Malay-Narathiwat)
4. *G. cambogia* Desr. (Som khaek: Bangkok; Gamboge)
5. *G. costata* Hemsl. ex King (Ma phueng: Lampang; Mang Khut pa: satun)
6. *G. cowa* Roxb. ex DC. (Ka muang: Peninsular; Cha muang: central; Muang som: Nakhon Si Thammarat; Mak mok: Udon Thani; Ka-ni: Malay-Narathiwat)
7. *G. dulcis* (Roxb.) Kurz (Ma phut: Pattani)
8. *G. forbesii* King (Phawa pa: Narathiwat)
9. *G. fusca* Pierre (Madan pa: Maha Sarakham; Mak mong: Kamphaeng Phet)
10. *G. gracillis* Pierre (Bong nang: Sakon Nakhon; Mak paem: Nong Khai)
11. *G hanburyi* Hook. f. (Rong, Rong thong: Chanthaburi, Trat; Gum cambodge tree)
12. *G. hombroniana* Pierre (Wa: Yala)
13. *G. lanessanii* Pierre (Som kung yai: Khon Kaen)
14. *G. mangostana* L. (Mang khut: General; Mangosteen)
15. *G. mckeaniana* Craib (Mada: Phrae)
16. *G. merguensis* Wight (Nuan: Northern)

17. *G. nervosa* Miq. (Ma phut pa: Pattani)
18. *G. nigrolineata* Planch. ex T.Anderson (Cha muang: Trat)
19. *G. parvifolia* (Miq.) (Cha muang lek: Narathiwat)
20. *G. rostrata* (Hassk.) Miq. (Muang lai: Surat thani)
21. *G. schomburgkiana* Pierre (Madan: General)
22. *G. speciosa* Wall (Phawa: Surat thani)
23. *G. succifolia* Kurz (Ma pong ton: Northern)
24. *G. thorelii* Pierre T (Mada khi non: Chiang Rai)
25. *G. vilersiana* Pierre (Pha wa bai yai: Chanthaburi, Chonburi)
26. *G. xanthochymus* Hook. f. ex T.Anderson (Mada luang: Chiang mai; Egg tree)

G. mangostana or Mangosteen is a tropical fruit tree of cultivated in Southeast Asian countries (Tongdee; & Suwanagul. 1989: 151-155). In Thailand, the fruit of this plant is very popular and has been known as the "Queen of fruits". The main sources for growing mangosteen in Thailand are located in the eastern and southern parts of the country. (Pothitirat; & Gritsanapan. 2008: 161-166)

Mangosteen is an erect slow-growing tree that has a pyramidal crown. It attains 6-25 m in height and has dark-brown or nearly black bark. The inner bark contains yellow, gummy and bitter latex. Leaves are opposite, short-stalked. Shape is ovate-oblong or elliptic. The leaves have a cuneate base, acute apex, entire margin; contain numerous veins that are joined together by a vein running parallel to a midrib. The leaves are thick, dark green and glossy above and yellowish-green beneath, 9-25 cm long and 4.5-11 cm wide. The petiole is 1.2-2.5 cm long. The flowers are 4-5 cm in wide and may be male or hermaphrodite on the same tree. They form clusters of 3-9 at the branch tips. There are four sepals and four ovate, thick, fleshy petals. The petals' color is green with red spots on the outside, yellowish-green inside. The flowers carry a lot of stamens although they bear no pollen as they have no anthers. Hermaphrodite flowers are situated singly or in pairs at the tips of young branchlets. Their petals are usually yellowish-green edged with red or mostly red and are quickly shed. The fruit is capped by the prominent calyx at the stem end and with 4-8 triangular remnants of the stigma in a shape of a rosette at the apex. The fruit is round, smooth externally, 3.4-7.5 cm in diameter. The color is usually from dark-purple to red-purple. The rind is 6-10 cm thick, red in cross-section. Purplish-white on the inside. The rind contains bitter yellow latex and a purple,

staining juice. The fruit may be seedless or have 1-5 fully developed seeds with ovoid-oblong shape. The seeds are usually flattened, 2.5 cm long and 1.6 cm wide. The arils of the seeds are represented as 4-8 triangular segments of white, juicy and soft flesh. The flesh is slightly or distinctly acid in flavour and is claimed as very luscious (Farnsworth; & Bunyapraphatsana. 1992: 160-162); (Ramage; et al. 2004: 1-10); (Wieble; & Downton. 1992: 132-137); (Morton. 1987: 301-304); (Obolskiy; et al. 2009: 1047-1065).

G. xanthochymus is a medium sized bushy ever-green tree found widely distributed in the lower hill forests of Eastern Himalayas and in the southern parts of India. The fruits has a juicy pulp with a pleasant acid odour (Rao Rama; Venkatswamy; & Yemul. 1980: 627-633).

Ethnopharmacological Uses

Different parts of *G. mangostana*, mostly fruit hull, bark and root, have been used for hundreds of years in Southeast Asia as a medicine for a great variety of medical conditions. In India, Thailand, China and other parts of Asia, dried and powdered fruit hull is used as antimicrobial and antiparasitic agents (Nakatani; et al. 2002b: 73-79); (Moongkarndi; et al. 2004b: 375-377); (Saralamp; Temsiririrkkul; & Clayton. 1996); (Obolskiy; et al. 2009; 1047-1065) as well as externally for healing wounds, suppurations and chronic ulcers (Farnsworth; & Bunyapraphatsana. 1992: 160-162). Mangosteen leaves and bark are recognized to have strong anti-inflammatory properties and therefore an ointment derived from them is used for treating eczema, hyperkeratosis and other skin disorders such as psoriasis (Matsumato; et al. 2003: 1124-1127); (Sakagami; et al. 2005: 203-208); (Sato; et al. 2004: 33-40). The rind decoction is administered to relieve diarrhea, cystitis, gonorrhea and gleet. The decoction can additionally be applied externally as an astringent lotion (Farnsworth; & Bunyapraphatsana. 1992: 160-162); (Moongkarndi; et al. 2004a: 161-166); (Sato; et al. 2004: 33-40). The astringent qualities of mangosteen are also used for preventing dehydration and the loss of essential nutrients from the gastrointestinal tract in case of diarrhea. In Thai folk medicine, the fruit hull of *G. mangostana* has been used for the treatment of skin infections, wounds and for the relief of diarrhea (Jung; et al. 2006: 2077-2082); (Suksamrarn; et al. 2002: 761-763; 2003: 857-859), etc. (see in table 1).

In Philippines and Malaya, a tea made from the rind and decoction of the leaves and barks is used as a febrifuge as well as in the treatment of diarrhea, dysentery and different

urinary disorders. A root decoction is administered by women with menstrual disorders. Moreover, a bark extract called “amibiasine” has been used for the treatment of amoebic dysentery (Moongkarndi; et al. 2004b: 375-377); (Nakatani; et al. 2002a: 1137-1141).

G. mangostana has also found medical use in Caribbean and Latin America. A tea made from mangosteen fruits is used widely as a tonic for fatigue and low energy states. Brazilians use similar tea as a digestive aid. In Venezuela, parasitic skin infections are treated with poultices of the fruit rind (Chairungsrilerd; et al. 1996a: 351-356); (Gopalakrishnan; et al. 1997: 519-524).

Table 1 Traditional medicinal properties of *G. mangostana* (Chaverri; et al. 2008: 3227-3239)

Illness	**References**
Dysentery	(Morton. 1987: 301-304); (Yates; & Stout. 1958: 1691-1700)
Diarrhea and chronic diarrhea	(Morton. 1987: 301-304); (Wan. 1973: 297-300)
Wounds[a]	(Mahabusarakam; et al. 1986: 239-242; 1987: 474-478); (Wan. 1973: 297-300)
Skin infections	(Mahabusarakam; et al. 1986: 239-242; 1987: 474-478); (Jinsart; et al. 1992: 3711-3713)
Tuberculosis	(Harbone; Baxter; & Moss. 1993: 590); (Suksamrarn; et al. 2006: 301-305)
Inflammation	(Saralamp; Temsiririrkkul; & Clayton. 1996); (Chairungsrilerd; et al. 1996a: 351-356; 1996b: 471-472); (Harbone; Baxter; & Moss. 1993: 590)
Ulcers	(Harbone; Baxter; & Moss. 1993: 590); (Hasegawa; et al. 1996)
Micosis	(Saralamp; Temsiririrkkul; & Clayton. 1996); (Harbone; Baxter; & Moss. 1993: 590)
Gonorrhea, cystitis and urethra suppuration	(Morton. 1987: 301-304); (Moongkarndi; et al. 2004a: 161-166)

Table 1 (continued)

Illness	**References**
Fever	(Yates; & Stout. 1958: 1691-1700); (Morton. 1987: 301-304)
Amoebic dysentery	(Morton. 1987: 301-304)
Ecxema[b]	(Morton. 1987: 301-304)
Acne[c]	(Saralamp; Temsiririrkkul; & Clayton. 1996); (Chomnawang; et al. 2005: 330-333)
Abdominal pain	(Moongkarndi; et al. 2004a: 161-166)
Suppuration	(Moongkarndi; et al. 2004a: 161-166)
Leucorrhoea	(Moongkarndi; et al. 2004a: 161-166)
Cholera	(Sen; et al. 1980a: 1008)

[a] fruit hull poultice.

[b] Local use as an ointment.

[c] Cosmetic cream.

From the biological activities point of view of *Garcinia* species, it is interesting to study the chemical constituents of *Garcinia* plants. Most phytochemicals studies have been obtained from different parts of *G. mangostana*, mainly from the fruit hull and only two reports on the root so far and. In additional there are few studies obtained from *G. xanthochymus*. Thus, the root of *G. mangostana* and the stem bark of *G. xanthochymus* have been selected for this study to search for new chemical constituents.

Objectives of the Study

1. To isolate and purify components from the root of *G. mangostana* and the stem bark of *G. xanthochymus*.
2. To determine the chemical structure of the isolated compounds.

CHAPTER 2

REVIEW OF THE LITERATURE

1. Chemical constituents of *G. mangostana*

The major bioactive secondary metabolites of *G. mangostana* are xanthone derivatives (Jung; et al. 2006: 2077-2082); (Peres; Nagem; & Oliveira. 2000: 683-710). Xanthone is a yellow coloring matter and can be obtained from almost every part of the plant. Pharmacological activities of xanthones have aroused great interest to this class of substances. In addition, *G. mangostana* also produces benzophenones, flavonoids, anthocyanins and triterpenes.

1.1 Xanthones from *G. mangostana*

Xanthones is a class of polyphenolic compounds with a skeleton of a xanthene-9-one (Figure 1). It is a distinctive chemical structure component that is represented as the tricyclic aromatic ring system. The majority of xanthones present in mangosteen have a ring system that is substituted with a variety of isoprene, phenolic and methoxy groups that give a large variety of possible structures. Natural xanthones can be subdivided based on the nature of substituents, into simple oxygenated xanthones, glycosylated xanthones, prenylated xanthones and their derivatives, xanthone dimers, xanthonolignoids and miscellaneous (Pinto; Sousa; & Nascimento. 2005: 2517-2538).

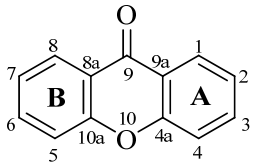
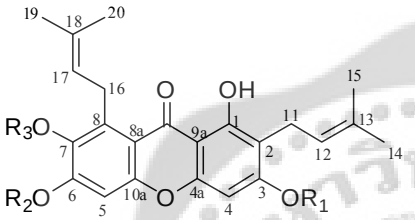


Figure 1 Skeleton of xanthene-9-one

More than fifty xanthones have been isolated from the mangosteen fruit hull. The first of them was named α-mangostin (**1**) which was obtained from the benzene extract of fruit

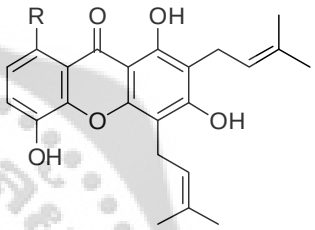
hull, bark and dried latex of *Garcinia mangostana* (Yates & Stout, 1958: 1691-1700). Later, the same group purified and identified β-mangostin (**2**) from the dried latex (Yates; & Bhat. 1968: 3770-3772). Jefferson's group (Jefferson; Scheinmann; & Sim. 1970: 2539-2543) and Govindachari's group (Govindachari; Kalyanaraman; & Muthukumaraswamy. 1971a: 3919-3926; 1971b: 505-506) also isolated α- and β-mangostins, along with γ-mangotin (**3**), gartanin (**4**) and 8-desoxygartanin (**5**) from the hexane extract of very ripe fruit, however, the partially ripe fruit contained only α- and γ-mangostins (Govindachari; Kalyanaraman; & Muthukumaraswamy. 1971a: 3919-3926; 1971b: 505-506).



α-mangostin; **1** $R_1 = R_2 = H$, $R_3 = CH_3$

β-mangostin; **2** $R_1 = R_3 = CH_3$, $R_2 = H$

γ-mangostin; **3** $R_1 = R_2 = R_3 = H$



gartanin; **4** R = OH

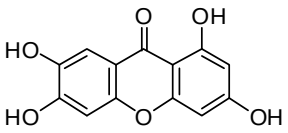
8-desoxygartanin; **5** R = H

Figure 2 Structures of compounds **1**-**5**

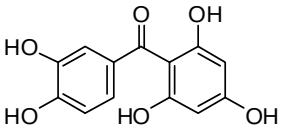
1,3,6,7-tetrahydroxyxanthone (**6**), its *O*-glucoside and pentahydroxy benzophenone or maclurin (**7**) were isolated from the hot $CHCl_3$ extract of the twig and branch of *G. mangostana*. Due to the absent of isoprenylated group was then postulated that compounds **6** and **7** could be the precursors of isoprenylated xanthones (Holloway; & Scheinmann. 1975: 2517-2518).

In 1980, Sen; et al. isolated and characterized a new polyoxygenated xanthone of the 1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-dimethylpyrano(2′,3′:3,2)xanthone (**8**) from the petrol extract of the dried and powdered fruit hull (Sen; et al. 1980b: 2223-2225). Later, they isolated two new 1,3,5- and 1,3,7-trioxygenated xanthones of 1,5-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**9**) and 1,7-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**10**), which possibly were the biogenetic precursors of 1,3,6,7- and 1,3,5,8-tetrahydroxygenated xanthones from the fruit hull of the same species (Sen; et al. 1981: 183-185).

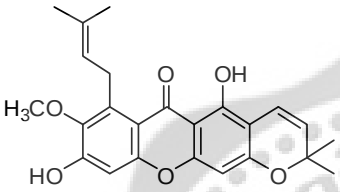
Garcinones A (**11**), B (**12**) and C (**13**) were isolated from the $CHCl_3$ extract of the fruit-hull (Sen; et al. 1980a: 1008; 1982: 1745-1750). Four years later, the same group isolated garcinone D (**14**) from the $CHCl_3$ extract of the dried and powdered well-ripe fruit hull. It was a minor xanthone having the 3-hydroxy-3-methylbutyl side chain (Sen; et al. 1986: 1157-1158).



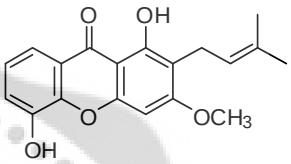
1,3,6,7 tetrahydroxyxanthone (**6**)



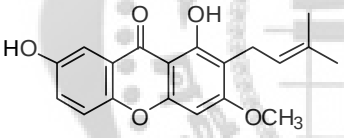
maclurin (**7**)



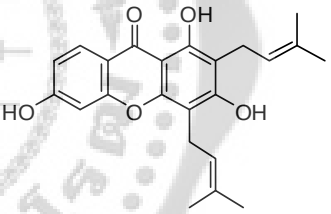
1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-dimethylpyrano(2′,3′:3,2)xanthone **(8)**



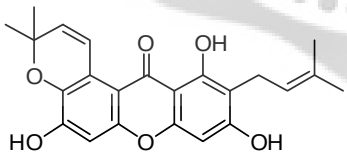
1,5-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone **(9)**



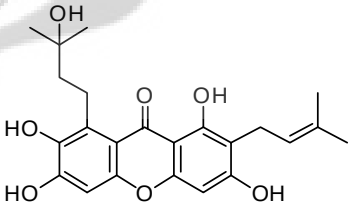
1,7-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**10**)



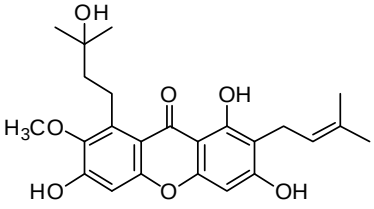
garcinone A



garcinone B (**12**)



garcinone C (**13**)



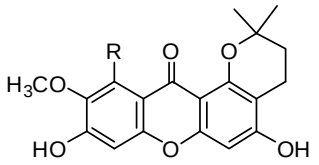
garcinone D (**14**)

Figure 3 Structures of compounds **6**-**14**

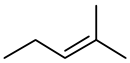
Eight new xanthones were isolated from the fruit hull and aril of mangosteen-fruit in 1987: 1-isomangostin (**15**), 1-isomangostin hydrate (**16**), 3-isomangostin (**17**) and 3-isomangostin hydrate (**18**) in addition to, α-, β- and γ-mangostins (**1**-**3**), gartanin (**4**). On the other hand, demethylcalabaxanthone (**19**), calabaxanthone (**20**), 1,3,7-trihydroxy-2,8-di-(3-methyl but-2-enyl)xanthone (**21**) and 1,7-dihydroxy-3-methoxy-2,8-di-(3-methylbut-2-enyl)xanthone (**22**) were isolated from the aril (Mahabusarakam; Wiriyachitha; & Taylor. 1987: 474-478). Antimicrobial activities of α- and γ-mangostins (**1**, **3**), gartanin (**4**), 1-isomangostin (**15**) and 3-isomangostin (**17**) isolated from *G. mangostana* were investigated against *Staphylococcus aureus*, both normal and penicillin-resistant strains. The order of the efficacy determined by the MIC (μg/mL) was found to be methicillin (3.9) > α-mangostin (15.6) > γ-mangostin (31.2) > 1-isomangostin (62.5) > 3-isomangostin (125) > gartanin (250) against normal strain, and for penicillin-resistant strains α-mangostin (1.56–12.5), methicillin (1.56–12.5) > 1-isomangostin (125) > 3-isomangostin (250), γ-mangostin (250) and gartanin (250). In addition, the activities of α-mangostin, gartanin and γ-mangostin against *Candida albicans*, *Cryptococcus neoformans, Tricophyton mentagrophytes* and *Microsporum gypseum* were tested. All of the components showed moderate activities against *T. mentagrophytes* and *M. gypseum* but exhibited no activity against *C. albicans* and *C. neoformans* (Mahabusarakam; Wiriyachitha; & Phongpaichit. 1986: 239-242).

A new isoprenylated xanthone as 1,5,8-trihydroxy-3-methoxy-2-(3-methylbut-2-enyl) xanthone (**23**) was isolated from ethyl acetate extract of the leaves of *G. mangostana* (Perveen; & Khan. 1987: 418). On the other hand, 1,6-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**24**) a new xanthone, and gartanin (**4**) were isolated from benzene extract of the dried and powdered leaves of *G. mangostana* (Parveen; & Khan. 1988: 3694-3696).

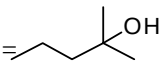
In 1988, Balasubramanian and Rajagopalan found BR-xanthone A (**25**) and BR-xanthone B (**26**) from the benzene and acetone extracts respectively of the powdered fruit hull (Balasubramanian; & Rajagopalan. 1988: 1552-1554).

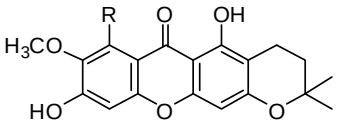


1-isomangostin; **15** R =

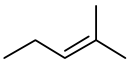


1-isomangostin hydrate; **16** R =

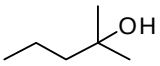


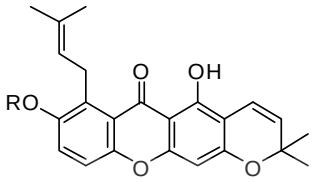


3-isomangostin; **17** R =



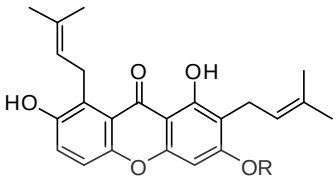
3-isomangostin hydrate; **18** R =





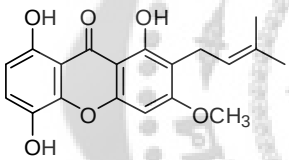
demethylcalabaxanthone; **19** R = H

calabaxanthone; **20** R = CH_3

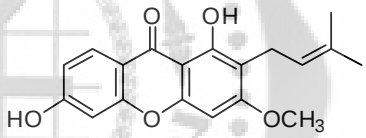


1,3,7-trihydroxy-2,8-di-(3-methylbut-2-enyl)xanthone; **21** R = H

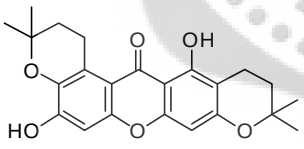
1,7-dihydroxy-3-methoxy-2,8-di-(3-methylbut-2-enyl)xanthone; **22** R = CH_3



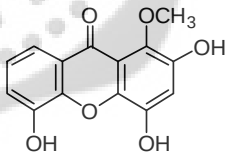
1,5,8-trihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**23**)



1,6-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**24**)



BR-xanthone A (**25**)



BR-xanthone B (**26**)

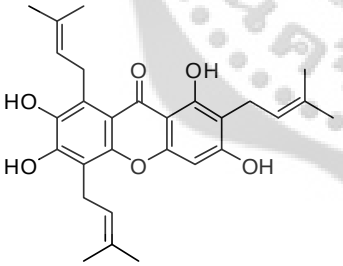
Figure 4 Structures of compounds **15**-**26**

Sakai; et al. found garcinone E (**27**) and eight known xanthones, including α-, β- and γ-mangostins (**1**-**3**), gartanin (**4**), 8-desoxygartanin (**5**), garcinone B (**12**), 1,3,7-trihydroxy-2, 8-di-(3-methylbut-2-enyl)xanthone (**21**), 1,5,8-trihydroxy-3-methoxy-2-(3-methyl-but-2-enyl)xanthone (**23**), from the fruit hull of *G. mangostana* collected in Thailand. The structure of garcinone E was elucidated as 1,3,6,7-tetrahydroxy-2,5,8-tri-(3-methylbut-2-enyl)xanthone (Sakai; et al.

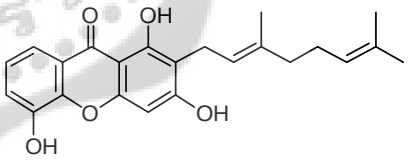
1993: 958-960). Later, Asai; et al. isolated a new xanthone with a geranyl group, mangostinone (**28**) from benzene extract of fruit hull of *G. mangostana* collected in Indonesia, in addition to, eight known xanthones α-, β- and γ-mangostins (**1**-**3**), gartanin (**4**), 8-desoxygartanin (**5**), 1,5-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**9**), 1,7-dihydroxy-3-methoxy-2-(3-methylbut -2-enyl)xanthone (**10**) and garcinone E (**27**) (Asai; et al. 1995: 943-944).

Furthermore, Krajewski's group isolated 2-ethyl-3-methylmalaeimide-2,3,4,6-tetraacetyl-*N*-β-*D*-glucopyranoside (**29**) from the methanol extract of leaves of *G. mangostana* (Krajeaski; Toth; & Schreier. 1996: 141-143).

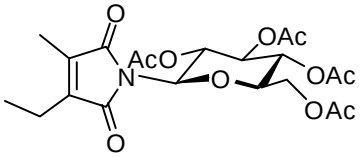
A new polyoxygenated xanthone, mangostanol (**30**) was isolated from methanol extract of the fruit hull, along with known xanthones including α- and γ-mangostins (**1**, **3**), gartanin (**4**), 8-desoxygartanin (**5**), 1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-di methylpyrano(2′,3′:3,2)xanthone (**8**), 1,3,7-trihydroxy-2,8-di-(3-methylbut-2-enyl)xanthone (**21**), garcinone E (**27**) and epicatechin were also isolated. Mangostanol, α- and γ-mangostins showed modulate inhibitory effects on cAMP phosphodiesterase with an IC_{50} less than 47, 24 and 50 μM, respectively (Chairungsrilerd; et al. 1996c: 1099-1102). Moreover, 1,3,8-trihydroxy-4-methyl-2,7-di-(3-methylbut-2-enyl)xanthone (**31**) and 7-carboxy-1,3-dihydroxy-2,8-di-(3-methylbut-2-enyl) xanthone (**32**) were isolated from methanol extract of fruit hull of *G. mangostana* (Gopalakrishnan; & Balaganesan. 2000: 607-609).



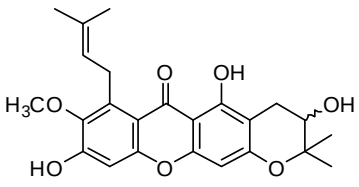
garcinone E (**27**)



mangostinone (**28**)

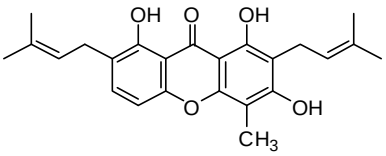


2-ethyl-3-methylmalaeimide-2,3,4,6-tetraacetyl-*N*-β-*D*-glucopyranoside (**29**)

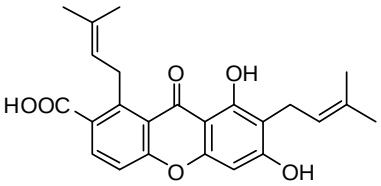


mangostanol (**30**)

Figure 5 Structures of compounds **27**-**30**



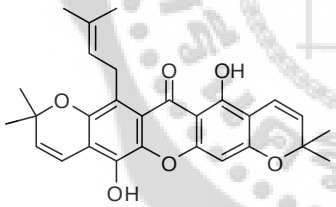
1,3,8-trihydroxy-4-methyl-2,7-di-(3-methylbut-2-enyl)xanthone (**31**)



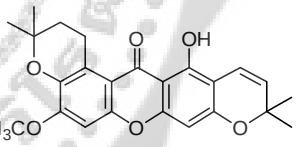
7-carboxy-1,3-dihydroxy-2,8-di-(3-methylbut-2-enyl)xanthone (**32**)

Figure 6 Structures of compounds **31**-**32**

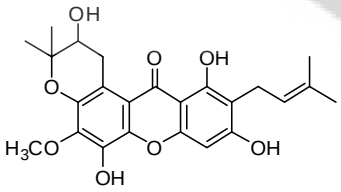
Garcimangosones A (**33**), B (**34**), C (**35**) and a benzophenone glucoside were isolated from ethanol extract of the dried fruit hull along with known xanthones, β- and γ-mangostins (**2**, **3**), gartanin (**4**), 8-desoxygartanin (**5**), 1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-dimethylpyrano(2′,3′:3,2)xanthone (**8**), 1,5-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl) xanthone (**9**), 1,7-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**10**), garcinone B (**12**), garcinone D (**14**), 1-isomangostin (**15**), 3-isomangostin (**17**), garcinone E (**27**), mangostanol (**30**), tovophyllin A (**36**), tovophyllin B (**37**) and 1,3,6,7-tetrahydroxy-8-(3-methylbut-2-enyl)xanthone (**38**) (Huang; et al. 2001: 903-906).



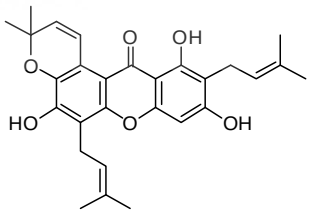
garcimangosone A (**33**)



garcimangosone B (**34**)

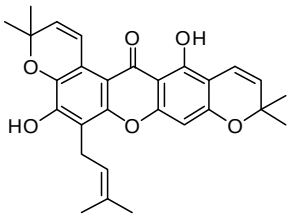


garcimangosone C (**35**)

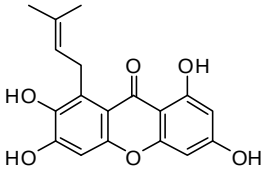


tovophyllin A (**36**)

Figure 7 Structures of compounds **33**-**36**



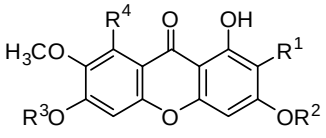
tovophyllin B (**37**)



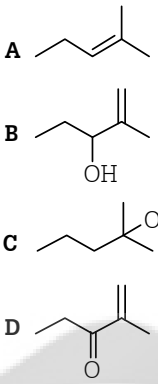
1,3,6,7-tetrahydroxy-8-(3-methylbut-2-enyl)xanthone (**38**)

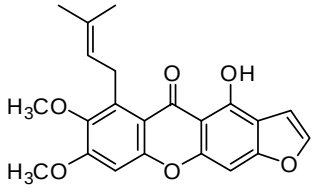
Figure 8 Structures of compounds **37**-**38**

The first novel compound, garciniafuran (**39**) was isolated from the hexane extract of the heartwood collected from Myanmar, in addition to 11 new xanthones: 1-hydroxy-8-(2-hydroxy-3-methylbut-3-enyl)-3,6,7-trimethoxy-2-(3-methylbut-2-enyl)xanthone (**40**), 1,6-dihydroxy-8-(2-hydroxy-3-methylbut-3-enyl)-3,7-dimethoxy-2-(3-methylbut-2-enyl)xanthone (**41**), 1,6-dihydroxy-2-(2-hydroxy-3-methylbut-3-enyl)-3,7-dimethoxy-8-(3-methylbut-2-enyl)xanthone (**42**), 1-hydroxy-2-(2-hydroxy-3-methylbut-3-enyl)-3,6,7-trimethoxy-8-(3-methylbut-2-enyl)xanthone (**43**), 1,3-dihydroxy-2-(2-hydroxy-3-methylbut-3-enyl)-6,7-dimethoxy-8-(3-methylbut-2-enyl)xanthone (**44**), (16E)-1,6-dihydroxy-8-(3-hydroxy-3-methylbut-1-enyl)-3,7-dimethoxy-2-(3-methylbut-2-enyl)xanthone (**45**), (16E)-1-hydroxy-8-(3-hydroxy-3-methylbut-1-enyl)-3,6,7-trimethoxy-2-(3-methylbut-2-enyl)xanthone (**46**), mangostanin (**47**), 6-*O*-methylmangostanin (**48**), 1,6-dihydroxy-3,7-dimethoxy-2-(3-methylbut-2-enyl)xanthone (**49**) and 1,6-dihydroxy-3,7-dimethoxy-2-(3-methylbut-2-enyl)-8-(2-oxo-3-methylbut-3-enyl)xanthone (**50**), along with 3 known xanthones, α-, β- and γ-mangostins (**1**-**3**) (Nilar; & Harrison. 2002: 541-548). Three years later, they isolated a new xanthone, mangoxanthone (**51**) from the acetone extract of the heartwood as well as the known xanthones, dulxanthone D (**52**), 1,3,7-trihydroxy-2-methoxyxanthone (**53**) and 1,3,5-trihydroxy-13,13-dimethyl-2H-pyran[7,6-b]xanthone-9-one (**54**) (Nilar; et al. 2005: 1718-1723).

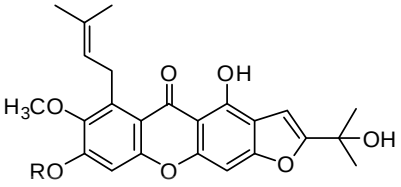


40 R^1 = A, R^2 = R^3 = CH_3, R^4 = B
41 R^1 = A, R^2 = CH_3, R^3 = H, R^4 = B
42 R^1 = B, R^2 = CH_3, R^3 = H, R^4 = A
43 R^1 = B, R^2 = R^3 = CH_3, R^4 = A
44 R^1 = B, R^2 = H, R^3 = CH_3, R^4 = A
45 R^1 = A, R^2 = CH_3, R^3 = H, R^4 = C
46 R^1 = A, R^2 = R^3 = CH_3, R^4 = C
49 R^1 = A, R^2 = CH_3, R^3 = R^4 = H
50 R^1 = A, R^2 = CH_3, R^3 = H, R^4 = D

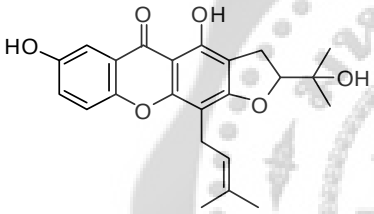




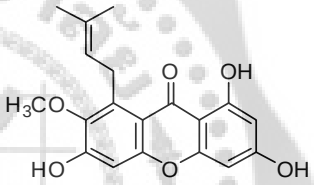
garciniafuran (**39**)



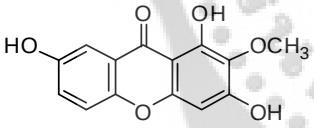
mangostanin; **47** R = H
6-*O*-methylmangostanin; **48** R = CH_3



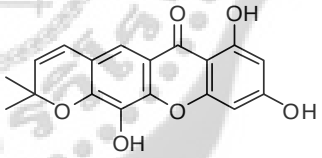
mangoxanthone (**51**)



dulxanthone D (**52**)



1,3,7-trihydroxy-2-methoxy xanthone (**53**)



1,3,5-trihydroxy-13,13-dimethyl-2H-pyran [7,6-b]xanthone-9-one (**54**)

Figure 9 Structures of compounds **39**-**54**

Mangostenol (**55**), mangostenone A (**56**) and mangostenone B (**57**) were isolated and elucidated from the methanol extract of green fruit hull of *G. mangostana*, along with known xanthones, trapezifolixanthone (**58**), α-, β-mangostins (**1**, **2**), garcinone B (**12**), mangostinone (**28**), mangostanol (**30**), (-)-epicatechin and tovophyllin B (**37**) (Suksamrarn; et al. 2002: 761-763). The antituberculosis potential of prenylated xanthones obtained from mangosteen fruit hull was evaluated. Among them, α-, β-mangostins (**1**, **2**) and garcinone B (**12**)

exhibited the most potent inhibitory effect against *Mycobacterium tuberculosis*, with an MIC of 6.25 μg/mL; whereas demethylcalabaxanthone (**19**) and trapezifolixanthone (**58**) had an MIC value of 12.5 μg/mL and γ-mangostin (**3**), garcinone D (**14**), tovophyllin B (**37**), mangostanin (**47**) and mangostenone A (**56**) had MIC values of 25 μg/mL. The xanthones with low antituberculosis potential were mangostanol (**30**) and mangostenol (**55**) with MIC values of 100 and 200 μg/mL, respectively (Suksamrarn; et al. 2003: 857-859).

In 2006, Suksamrarn; et al. isolated mangostenones C (**59**), D (**60**) and E (**61**) from the methanol extract of young fruit of *G. mangostana*, in addition to, α-, β- and γ-mangostins (**1**-**3**), gartanin (**4**), 8-desoxygartanin (**5**), 1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-dimethylpyrano(2′,3′:3,2)xanthone (**8**), garcinone B (**12**), garcinone C (**13**), garcinone D (**14**), demethylcalabaxanthone (**19**), garcinone E (**27**), mangostinone (**28**), mangostanol (**30**), mangostanin (**47**), thwaitesixanthone (**62**) and 11-hydroxy-1-isomangostin (**63**). The cytotoxic activities of these xanthones were determined against three different human cancer cell lines: epidermoid carcinoma of mouth (KB), breast cancer (BC-1), and small cell lung cancer (NCI-H187). Mangostenone C exhibited a cytotoxic effect against the three cell lines proved, with IC_{50} values of 2.8, 3.53, and 3.72 μg/mL, respectively. Among the isolates, α-mangostin exhibited the most potent effect against BC-1 cells with an IC_{50} value of 0.92 μg/mL, an activity that was greater than the standard drug ellipticine (IC_{50} = 1.46 μg/mL); α-mangostin also had a cytotoxic effect against KB cells (IC_{50} = 2.08 μg/mL); and gartanin was able to inhibit the NCI-H187 growth (IC_{50} = 1.08 μg/mL) (Suksamrarn; et al. 2006: 301-305).

In 2006, Jung; et al. isolated new xanthones, 8-hydroxycudraxanthone G (**64**) and mangostingone (**65**) or [1,3,6-trihydroxy-7-methoxy-2-(3-methyl-2-butenyl)-8-(2-oxo-3-methylbut-3-enyl)xanthone] from the methanol extract of fruit hull of *G. mangostana*, along with known xanthones, α- and γ-mangostins (**1**, **3**), gartanin (**4**), 8-desoxygartanin (**5**), garcinone B (**12**), garcinone D (**14**), 1-isomangostin (**15**), mangostinone (**28**), garcimangosone B (**34**), tovophyllin A (**36**), cudraxanthone G (**66**) and smeathxanthone A (**67**). Compound **67** was previously isolated from *Garcinia smeathmannii* (Komguem; et al., 2005: 1713-1717). The peroxynitrite ($ONOO^-$) scavenging capacities of 13 xanthones were measured by monitoring the oxidation of dihydrorhodamine 123 (DHR-123). $ONOO^-$ is the oxidant specie produced by the reaction between nitric oxide ($NO^{\bullet}$) and superoxide anion (O_2^-). The IC_{50} (μM) value for $ONOO^-$ scavenging was determined for several compounds. Xanthones with the highest capacity to

scavenge $ONOO^-$ were smeathxanthone A (**67**), 8-hydroxycudraxanthone G (**64**), γ-mangostin (**3**), gartanin (**4**), α-mangostin (**1**), garcinone E (**27**), garcimangosone B (**34**), 1-isomangostin (**15**) and garcinone D (**14**) with IC_{50} values of 2.2, 4.6, 8.0, 9.1, 12.2, 14.1, 15.9, 19.2 and 26.0 μM, respectively. They also studied the $ONOO^-$ scavenging capacity of cudraxanthone G, 8-deoxygartanin, mangostinone and tovophyllin A, but the activity was lower (IC_{50} > 30 μM). DL-penicillamine was used as a positive control (IC_{50} 3.1 μM). α-mangostin also inhibited DMBA-induced preneoplastic lesions with an IC_{50} of 1.0 μg/mL (2.44 μM) (Jung; et al. 2006: 2077-2082).

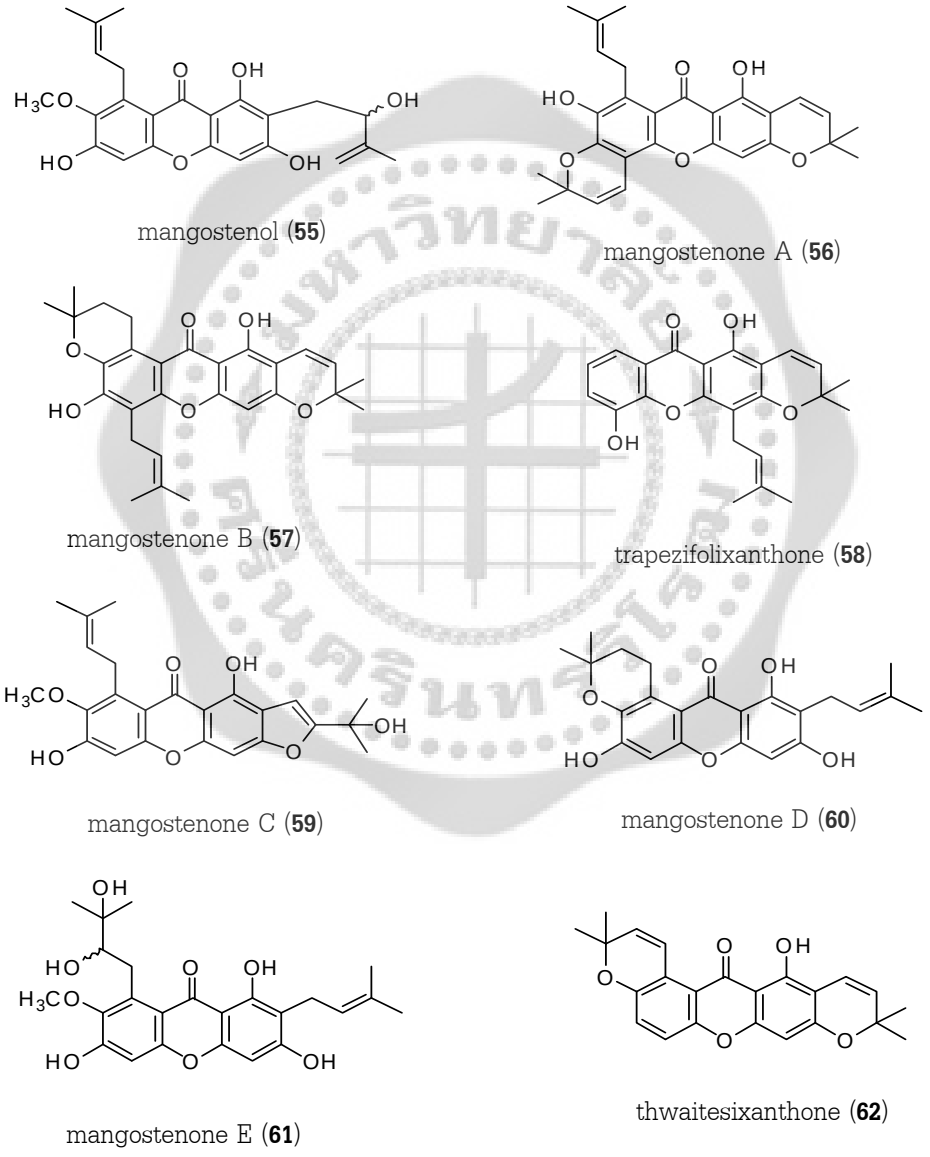
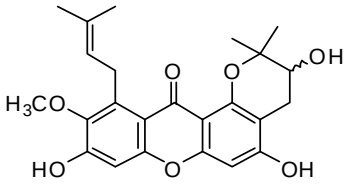
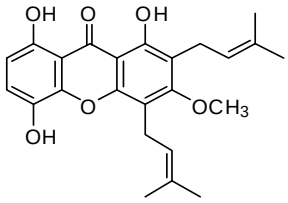


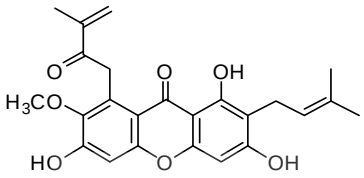
Figure 10 Structures of compounds **55**-**62**



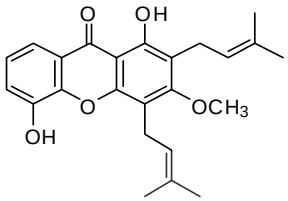
11-hydroxy-1-isomangostin (**63**)



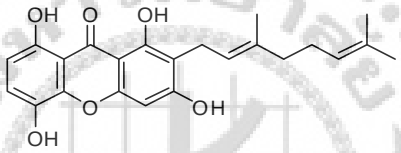
8-hydroxycudraxanthone G (**64**)



mangostingone (**65**)



cudraxanthone G (**66**)



smeathxanthone A (**67**)

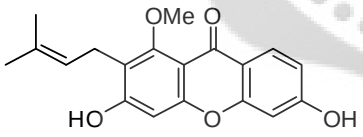
Figure 11 Structures of compounds **63**-**67**

Mangosharin (**68**) or 2,6-dihydroxy-8-methoxy-5-(3-methylbut-2-enyl)xanthone was isolated from the bark of *G. mangostana*, along with known xanthones, included α- and β-mangostins (**1**, **2**), 1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-dimethylpyrano(2′,3′:3,2) xanthone (**8**), garcinone D (**14**), mangostanol (**30**) and 1,6-dihydroxy-3,7-dimethoxy-2-(3-methyl but-2-enyl)xanthone (**49**) (Ee; et al., 2006: 1067-1073).

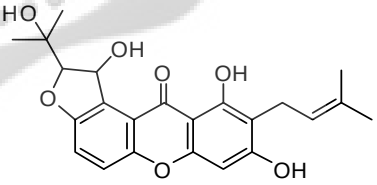
Chin; et al. isolated and identified five compounds, including two new xanthones, 1,2-dihydro-1,8,10-trihydroxy-2-(2-hydroxypropan-2-yl)-9-(3-methylbut-2-enyl)-furo[3,2-a]xanthone-11-one (**69**) and 6-desoxy-7-demethylmangostanin (**70**) from the CH_2Cl_2 extract of freeze-dried powder of the fruits of *G. mangostana*, collected in China and Southeast Asia, along with three known compounds, α-mangostin (**1**), 1,3,7-trihydroxy-2,8-di-(3-methylbut-2-enyl)xanthone (**21**) and mangostanin (**47**). The HO^--scavenging activity of 16 xanthones were determined only γ-mangostin (**3**) showed HO^--scavenging activity (IC_{50} = 0.2 μg/mL). In addition, the same xanthones were tested for the induction of quinone reductase (QR, phase II drug-metabolizing

enzyme), using murine hepatoma cells (Hepa1c1c7) in vivo. All the xanthones, with the exception of α-mangostin, were found to induce QR activity. The concentration required to double QR induction activity values of compounds were 1.3, 2.2, 0.68 and 0.95 μg/mL for compounds **69**, **70**, **21** and mangostanin (**47**), respectively. In addition, α-mangostin (pericarp isolated), mangosteen extract and commercial mangosteen juice, were able to scavenge directly ROS and prevent neurotoxicity and ROS production induced by 3-nitropropionic acid in cultured neurons (Chin, et al. 2008: 754-758). A new xanthone, 2,8-dihydroxy-6-methoxy-5-(3-methylbut-2-enyl)xanthone (**71**) was isolated from the ethanol extract of the stem bark of *G. mangostana*. Meanwhile, the hexane and chloroform extracts of the root bark of *G. mangostana* furnished six known prenylated xanthones, namely α-, β- and γ-mangostins (**1**-**3**), gartanin (**4**), garcinone D (**14**) and mangostanol (**30**) (Ee; et al. 2008: 481-485).

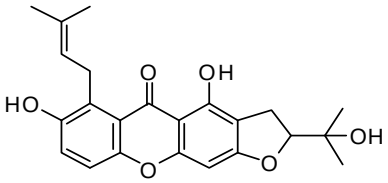
Recently, Han; et al. isolated a new xanthone, 11-hydroxy-3-*O*-methyl-1-isomangostin (**72**) from the chloroform-soluble extract of the stem bark of *G. mangostana*, in addition, ten known compounds included, α- and β-mangostins (**1**, **2**), gartanin (**4**), 8-deoxygartanin (**5**), 1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-dimethylpyrano(2′,3′:3,2) xanthone (**8**), 1,5-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**9**), garcinone D (**14**), 3-isomangostin (**17**), mangostanin (**47**), 11-hydroxy-1-isomangostin (**63**) and a bixanthone, cratoxyxanthone (**73**). The structure of this compound was elucidated by spectroscopic data analysis (Han; et al. 2008: 2187-2192).



mangosharin (**68**)

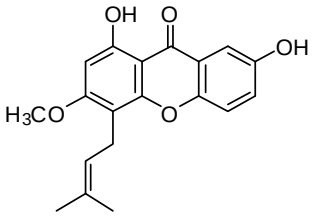


1,2-dihydro-1,8,10-trihydroxy-2-(2-hydroxy propan-2-yl)-9-(3-methylbut-2-enyl)-furo[3,2-a]xanthone-11-one **(69)**

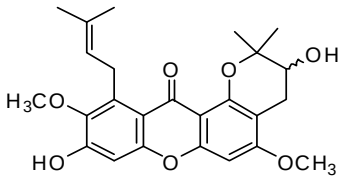


6-desoxy-7-demethylmangostanin (**70**)

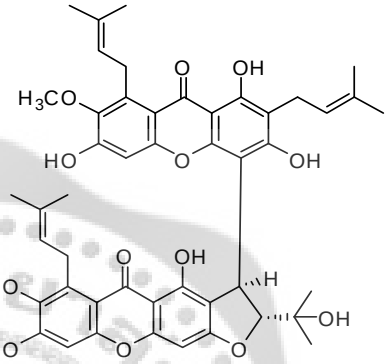
Figure 12 Structures of compounds **68**-**70**



2,8-dihydroxy-6-methoxy-5-(3-methylbut-2-enyl)xanthone (**71**)



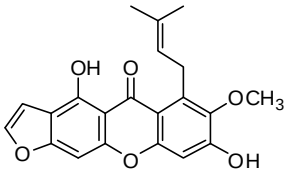
11-hydroxy-3-*O*-methyl-1-isomangostin (**72**)



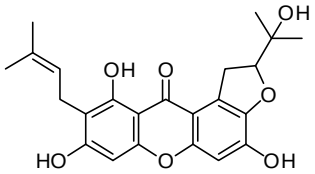
cratoxyxanthone (**73**)

Figure 13 Structures of compounds **71**-**73**

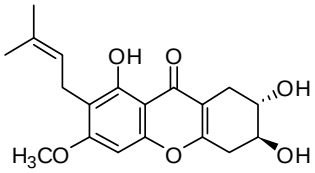
In this year, Mohd Ghazali, et al. studied the phytochemicals on the roots of *Garcinia mangostana* and resulted in the isolation of six xanthones, α-, β- and γ-mangostins (**1**-**3**), gartanin (**4**), garcinone D (**14**) and mangostanol (**30**) (Mohd Ghazali; et al. 2010: 134-142). Recently, Zhang and co-worker isolated two new prenylated xanthones and a new prenylated tetrahydroxanthone, garcimangosxanthone A-C (**74**-**76**), along with fourteen known xanthones were isolated from the pericarp of *Garcinia mangostana*, α- and γ-mangostins (**1**, **3**), gartanin (**4**), 8-desoxygartanin (**5**), 9-hydroxycalabaxanthone (**8**), 1,5-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**9**), 1,7-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**10**), garcinone B (**12**), garcinone C (**13**), garcinone D (**14**), tovophyllin A (**36**), dulxanthone D (**52**) trapezifolixanthone (**58**), and 1,3,7-trihydroxy-2-(3-methylbut-2-enyl)xanthone. The cytotoxicity of three new compounds was evaluated against human lung cancer (A549), human pulmonary carcinoma (LAC) and human hepatoma (A375) cell lines using the MTT colorimetric assay. Garcimangosxanthone A (**74**) and B (**75**) exhibited cytotoxicity against all the tested cell lines with IC_{50} value ranging from 5.7 μM to 24.9 μM, which were comparable with those of Doxorubicine (IC_{50} = 12.9-20.5 μM). Tetrahydroxanthone (**76**) showed evident activity against LAC but less than the positive control (Zhang; et al. 2010: 595-599).



garcimangosxanthone A (**74**)



garcimangosxanthone B (**75**)

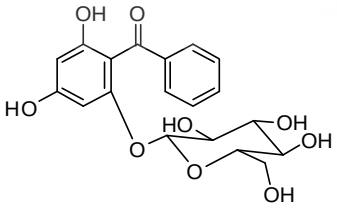


garcimangosxanthone C (**76**)

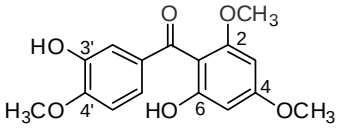
Figure 14 Structures of compound **74**-**76**

1.2 Benzophenones from *G. mangostana*

A benzophenone glucoside, garcimangosone D (**77**), was isolated from the ethanol extract of the dried fruit hull (Huang; et al. 2001: 903-906). In 2005, Nilar; et al. isolated a new benzophenone, 3′,6-dihydroxy-2,4,4′-trimethoxybenzophenone (**78**), from the acetone extract of the heartwood collected from Myanmar, as well as the known xanthones, mangoxanthone (**51**), dulxanthone D (**52**), 1,3,7-trihydroxy-2-methoxyxanthone (**53**) and 1,3,5-trihydroxy-13,13-dimethyl-2H-pyran[7,6-b]xanthone-9-one (**54**) (Nilar; et al. 2005: 1718-1723).



garcimangosone D (**77**)



3′,6-dihydroxy-2,4,4′-trimethoxybenzophenone (**78**)

Figure 15 Structures of compounds **77**-**78**

1.3 Flavonoids and anthocyanins from *G. mangostana*

In 1977, Du and Francis. isolated the major pigment cyanidin-3-sophoroside (**79**) and cyanidin-3-glucoside (**80**) from the fruit hull (Du; & Francis. 1977: 1667-1668).

A flavonoid, epicatechin (**81**) was isolated from the methanol extract of fruit hull (Chairungsrilerd; et al. 1996c: 1099-1102; Huang; et al. 2001: 903-906). In addition, Huang and coworkers isolated and identified anthocyanins, including proanthocyanidin A_1 (**82**), proanthocyanidin A_2 (**83**), procyanidin B_2 (**84**) and procyanidin B_5 (**85**) were isolated from the ethanol extract of the dried fruit hulls (Huang; et al. 2001: 903-906).

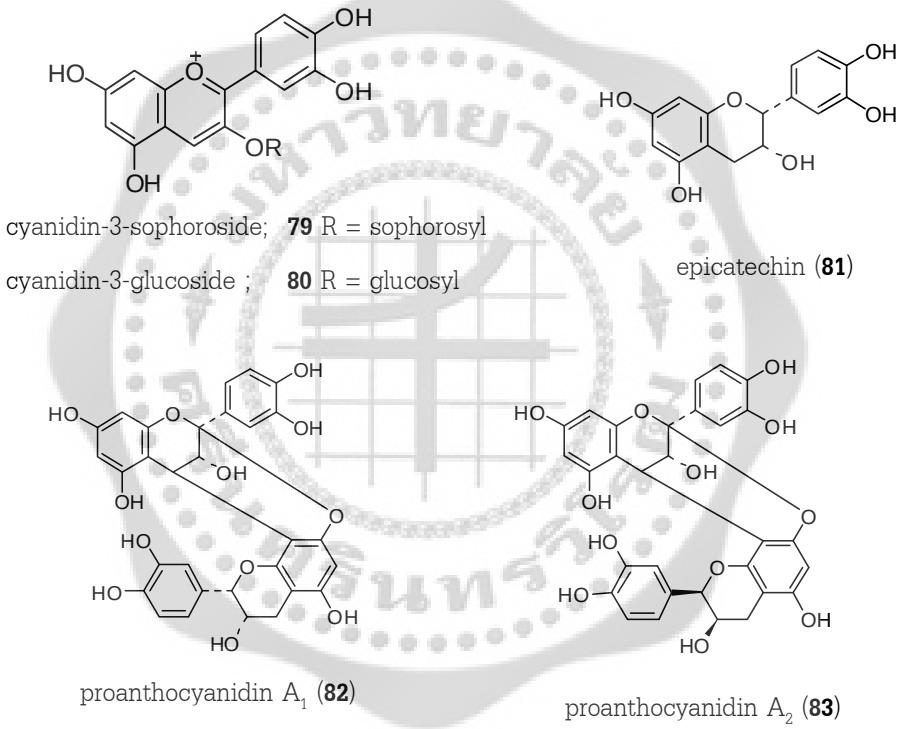
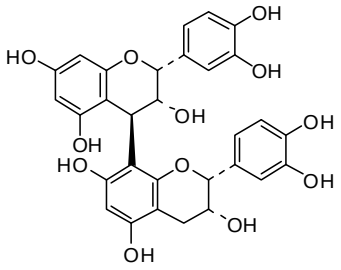
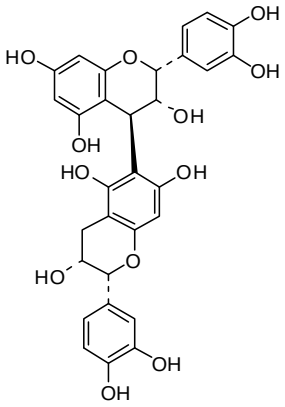


Figure 16 Structures of compounds **79**-**83**



procyanidin B_2 (**84**)



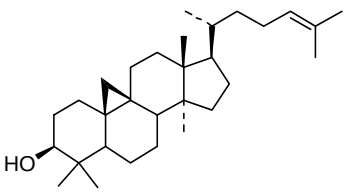
procyanidin B_5 (**85**)

Figure 17 Structures of compounds **84**-**85**

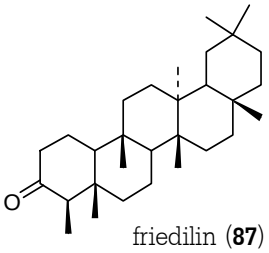
1.4 Triterpenes from *G. mangostana*

In 1982, Macleod and Pieris, identified components of the aroma volatiles of mangosteen by GC/MS and CIMS. The most impotents aroma components were hexyl acetate, cis-hex-3-enyl acetate and cis-hex-3-en-1-ol (Macleod; & Pieris. 1982: 117-119).

Triterpenes including cycloartenol (**86**), friedelin (**87**), β-sitosterol (**88**), 9,19-cyclolanost-25-en-3β,24-diol (**89**), betulin (**90**), mangiferadiol (**91**) and mangiferolic acid (**92**) were isolated from the extract of leaves (Parveen; et al. 1990: 86-87). Later, they isolated 3β-hydroxy-26-*nor*-9,19-cyclolanost-23-en-25-one (**93**) from the ethanol extract of leaves of *G. mangostana* (Parveen; et al. 1991: 361-362).



cycloartenol (**86**)



friedilin (**87**)

Figure 18 Structures of compounds **86**-**87**

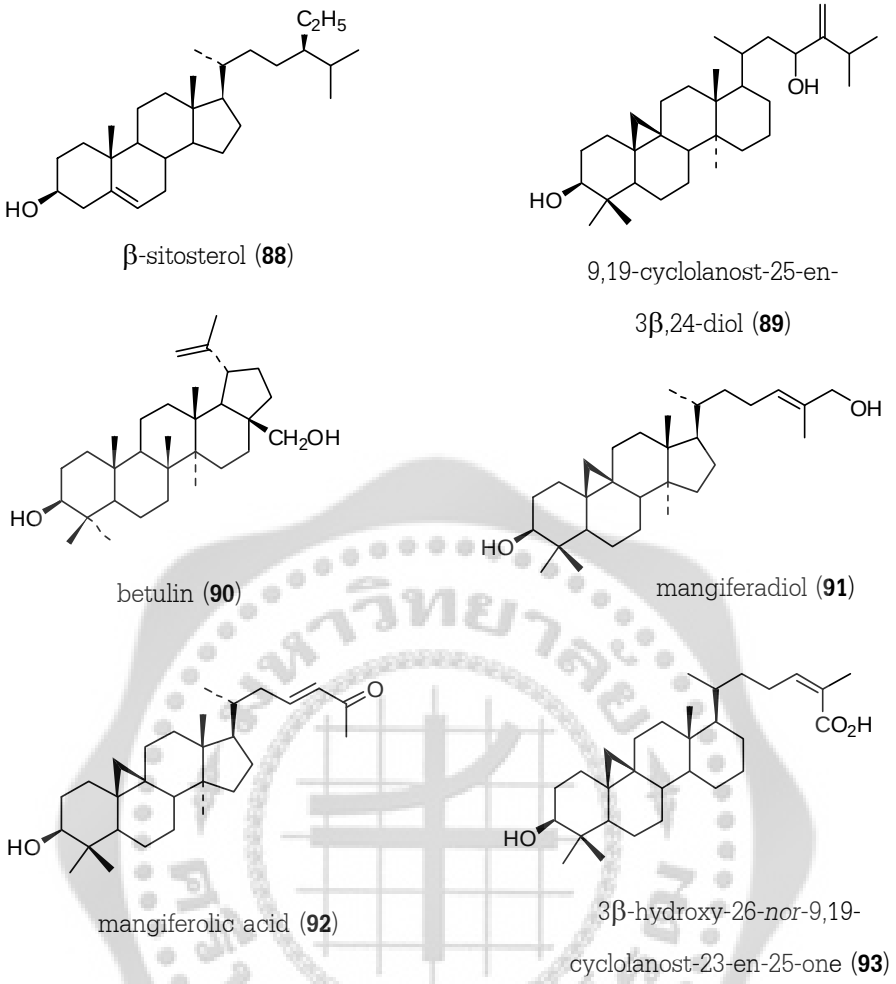


Figure 19 Structures of compounds **88**-**93**

2. Biological activities of *G. mangostana*

Extracts and pure compounds mainly xanthones derived from *G. mangostana*, were reported to have a great variety of pharmacological activities including antioxidant, antifungal, antibacterial, cytotoxic, anti-inflammation, antihistamine, anti-HIV and other activities.

2.1 Antioxidant properties

The antioxidant activity of extracts and xanthones isolated from *G. mangostana* were evaluated by using the following methods: 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity (Chomnawang; et al. 2007: 401-408), the ferric thiocyanate method (Fan; &

Su. 1997: 540-551) and the 2,20-azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid (ABTS) assay (Leong; & Shui, 2002: 69-75); (Haruenkit; et al. 2007: 5842-5849).

Fan and Su, found that the methanolic extract of *G. mangostana* hull showed DPPH radical scavenging activity. α- and γ-Mangostins (**1**, **3**) showed antioxidant activity by using the ferric thiocyanate method (Fan; & Su. 1997: 540-551).

Williams; et al. found that α-mangostin (**1**) decreases the human low density lipoproteins (LDL) oxidation induced by copper or peroxyl radical in a dose dependents manner over 5-50 μM (Williams; et al. 1995: 175-184).

Mahabusarakam; et al. found that α-mangostin (**1**) and their synthetic derivatives prevent the decrease of the α-tocopherol consumption induced by LDL oxidation. These authors found that the structural modifications of α-mangostin modified the antioxidant activity. For example, substitution of C-3 and C-6 with aminoethyl derivatives in **1** enhanced the activity; whereas substitution with methyl, acetate, propanediol or nitrile reduced the antioxidant activity (Mahabusarakam; et al. 2000: 643-659).

Weecharangsan; et al. studied the antioxidant and neuroprotective properties of the four extracts obtained from mangosteen fruit pericarp (water, 50% ethanol, 95% ethanol and ethyl acetate). The antioxidant capacity was evaluated by the DPPH method using 1, 10, 50 and 100 μg/mL of each extract. Water and 50% ethanolic extracts showed high antioxidant capacity with IC_{50} value of 34.98 ± 2.24 and 30.76 ± 1.66 μg/mL, respectively. The antioxidant capacity of these extracts was tested on a neuroblastoma cell line (NG108-15) exposed to hydrogen peroxide; both water and 50% ethanolic extracts exhibited neuroprotective activity when was the concentration of 50 μg/mL used. (Weecharangsan; et al. 2006: 281-287).

Leong and Shui, compared the total antioxidant capacity of twenty-seven fruits available in the Singapore market, including mangosteen, using the ABTS and DPPH assays. According to the AEAC (L-ascorbic acid equivalent antioxidant capacity) value of extract solution of fruits in ABTS model, mangosteen showed high antioxidant capacity with 2.7% AA contribution to AEAC (Leong; & Shui, 2002: 69-75).

Moongkarndi; et al. showed that a *G. mangostana* extract significantly diminished intracellular ROS production, which was measured using 2,7-dichlorofluorescein diacetate (DCFH-DA) in SKBR3 cell line (Moongkarndi; et al. 2004a:161-166; 2004b: 375-377).

Garcia; et al. studied the antioxidant capacity of several fruits and vegetables from the Philippines by measurement of lipoperoxidation (linoleic acid system) and hydroxyl radical

($HO^{\bullet}$) scavenging (deoxyribose method). They found that the extract obtained from the mangosteen-fruit pericarp showed one of the highest antioxidant activities (Garcia; et al. 2005: 78-83).

Chomnawang; et al. showed that *G. mangostana* the ethanolic extract possesses a significant antioxidant activity, as measured by the inhibition of the formation of DPPH radicals by 50%. This extract displayed an IC_{50} of 6.13 μg/mL in comparison with the ethanolic extracts of *Houttuynia cordata*, *Eupatorium odoratum* and *Senna alata* (IC_{50} of 32.53, 67.55 and 112.46 μg/mL, respectively). In addition, the extract of *G. mangostana* significantly reduced the reactive oxygen species (ROS) production of polymorphonuclear leucocytes (PML) with 77.8% of superoxide anion ($O_2^{\bullet-}$) inhibition ratio (62.6%, 44.9% and 35.18% for *H. cordata*, *E. odoratum*, and *S. alata*, respectively) (Chomnawang; et al. 2005: 330-333).

Jung; et al. measured the peroxynitrite ($ONOO^-$) scavenging capacity of 13 xanthones by monitoring the oxidation of dihydrorhodamine 123 (DHR-123) (see detail in page 16) (Jung; et al. 2006: 2077-2082).

Sampath and Vijayaraghavan evaluated the effect of α-mangostin (**1**) on the antioxidant defense system and on lipid peroxidation during isoproterenol-induced myocardial infarction in rats. α-Mangostin (**1**) preserves the myocaridiol membrane integrity and extenuates anomalous TNF-α and COX-2 expressions by mitigating ISO-induced oxidative stress and cellular damage effectively. This xanthone showed a protective effect against lipid peroxidation and antioxidant defense system during injury-induced myocardial infarction in rats (Sampath; & Vijayaraghavan. 2007: 357-364).

Haruenkit; et al. showed the antioxidant activity of mangosteen measured with DPPH and ABTS assays. They found that the values of 79.1 and 1268.6 μM trolox equivalents/100 g of fresh weight for DPPH and ABTS assays, respectively. In addition, in rats, fed with basal diet supplemented with 1% of cholesterol plus 5% of mangosteen, the increase in plasma lipids and decrease in antioxidant activity seen with cholesterol alone was prevented (Haruenkit; et al. 2007: 5842-5849).

Yu; et al. studied the antioxidant activities of phenolics from fruit pericarp of *Garcinia mangostana*. Three major phenolics were purified and identified as α-, γ-mangostins (**1**, **3**) and epicatechin (**78**). The antioxidant activities were evaluated using different tests, including the free radical scavenging capability and total antioxidant activity in a linoleic acid peroxidation. These three phenolic compounds exhibited different antioxidant activities in these

antioxidant tests. The hydroxyl radical and 1,1-diphenyl-2-picryldrazyl (DPPH) radical scavenging capabilities and the activity against linoleic acid peroxidation of γ-mangostin (85.1 % and 84.1 %, respectively) were greater than those of α-mangostin (49.4 % and 53.5 %, respectively) and epicatechin (55.9 % and 70.4 %, respectively), while the superoxide anion radical scavenging activity of epicatechin (73.7 %) was greater than that of γ-mangostin (51.8 %), but was close to that of α-mangostin (72.9 %) or α-tocopherol (73.0 %) (Yu; et al. 2007: 176-181).

Chin; et al. studied the HO^{-}-scavenging activity and tested the induction of quinone reductase (QR, phase II drug-metabolizing enzyme), using murine hepatoma cells (Hepa1c1c7) *in vivo* of xanthones were isolated from the fruit powder of *G. mangostana* (see detail in page 18) (Chin; et al. 2008: 754-758).

Zarena and Udaya Sankar, isolated the xanthones from mangosteen (*Garcinia mangostana*) pericarp. The Xanthones in the acetone, ethyl acetate and hexane extracts, was investigated by means of high performance liquid chromatography electrospray ionisation/mass spectrometry (HPLC.ESI/MS) technique. Chromatography of the xanthones on a RP-C-18 HPLC column followed by MS detection using ESI negative mode showed the presence of seven major known xanthones: α-mangostin (**1**), β-mangostin (**2**), gartanin (**4**), 8-desoxygartanin (**5**), 3-isomangostin (**17**), garcinone E (**27**) and 9-hydroxycalabaxanthone (**8**). The antioxidative properties of mangosteen fruit hull extracts which were the mixture of these xanthones obtained by different solvents were investigated for reactive oxygen species scavenging, like cytochrome C assay, molybdenum activity and lipid peroxidation inhibition assay. Of the solvent extracts acetone and ethyl acetate extracts, reduced oxidized cytochrome C to an OD of 0.455 and 0.321 at 400 μg; each of the extract reduced Mo (VI) to Mo (V) at 100 μg to 7967 ± 47.1 and 6803 ± 42.1 μmole/g of ascorbic acid equivalent. The IC_{50} value for lipid peroxidation was 9.2 ±3.8 and 10.0 ± 1.7 μg/mL, which was higher than standard BHA, respectively. Hexane extract showed less antioxidant activity in the above test because of the poor solubility of the xanthones (Zarena; & Udaya Sankar, 2009: 23-30).

2.2 Antitumor and anti-cancer properties

Several studies have been designed to examine the anticancer activities of xanthones isolated from mangosteen fruit hull. Hepatocellular carcinoma (Ho; et al. 2002: 975-979), SKBR3 human breast cancer (Moongkarndi; et al. 2004a: 161-166) and human leukemia (Matsumoto; et al. 2003: 1124-1127) cell lines have been used.

Ho; et al. found that garcinone E (**27**) has a potent cytotoxic effect on hepatocellular carcinoma cell lines. They studied the cytotoxic effect of 6 xanthones isolated from mangosteen fruit hull and found that garcinone E was the most toxic. Therefore, garcinone E was tested against HCC36, TONG, HA22T, Hep3B, HEpG2 and SK-Hep-1 hepatocellular carcinoma cell lines; NCIHut125, CH27 LC-1, H2891 and Calu-1 lung carcinoma cell lines; and AZ521, NUGC-3, KATO-III and AGS gastric carcinoma cell lines. Garcinone E exhibited a very broad spectrum of dose- and time-dependent cytotoxic effects against various cancer cell lines; with the exception of lung carcinoma cell line CH27 LC-1. All cell lines tested were killed. The values for garcinone E lethal dose 50% (LD_{50}) against the cell lines were used between 0.1 and 5.4 μM. Garcinone E had an antitumoral effect in the following order: SK-Hep-1 > HA22T > HEpG2 > Hep3B > HCC36 (Ho; et al. 2002: 975-979).

Suksamrarn; et al. determined the cytotoxic activities of xanthones isolated from the methanol extract of young fruit of *G. mangostana* on against three different human cancer cell lines (see detail in page 15) (Suksamrarn; et al. 2006: 301-305).

Matsumoto; et al. studied the effect of 6 xanthones α-, β- and γ-mangostins (**1**-**3**), 1,7-dihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthone (**10**), garcinone E (**27**) and mangostinone (**28**) isolated from mangosteen fruit hull on the cell growth inhibition of human leukemia cell line HL60. They examined cytotoxic effects 72 h after cell incubation with xanthone at 5 or 40 μM. All xanthones showed a significant inhibition effect, but α-, β- and γ-mangostins were particularly effective from 10 μM. The most abundant compound in the extract was α-mangostin (**1**), and it showed the highest inhibitory activity (IC_{50} 10 μM). In addition, the α-mangostin effect was shown in other leukemia cell lines: K562, NB4 and U937. Cell growth of all these leukemia cell lines was inhibited by α-mangostin at 5–10 μM (Matsumoto; et al. 2003: 1124-1127). Later, they studied the mechanism of cell death induced by α-mangostin treatment in human leukemia cell line HL60. They found that the xanthone induced apoptosis in HL60 cells, which was mediated by mitochondrial dysfunctions in the early phase. They found that α-mangostin induced capiases 9 and 3 activation, loss of mitochondrial membrane potential, and, release of ROS and cytochrome C. They also showed that neither bcl-2 family proteins nor activation of mitogen-activated protein kinases were involved in α-mangostin induced cell death. These results indicated that mitochondria played a pivotal role in induction of apoptosis by α-mangostin (Matsumoto; et al. 2004: 5799-5806).

Moongkarndi; et al. tested the antiproliferative activity of 9 Thai medicinal plants against SKBR3 human breast adenocarcinoma cell line. The extract obtained from *G. mangostana* had the most potent activity with an IC_{50} value of 15.45 ± 0.5 μg/mL (Moongkarndi; et al. 2004b). The antiproliferation, apoptosis and antioxidant activity of crude methanolic extract from mangosteen fruit hull was evaluated using SKBR3 human breast cancer cell line as a model. This methanolic extract had a significant antiproliferation activity (ED_{50} = 9.25 ± 0.64 μg/mL) by inducing apoptotic cell death. Also, the methanolic extract showed antioxidant activity by inhibiting the intracellular ROS production (Moongkarndi; et al. 2004a: 161-166).

Nabandith; et al. investigated whether the administration of α-mangostin (**1**) in the diet had short-term chemopreventive effects on putative preneoplastic lesions involved in rat colon carcinogenesis, induced by a subcutaneous injection of 1,2-dimethylhydrazine, DMH (40 mg/kg body weight once a week for 2 weeks). They found that dietary administration of α-mangostin significantly inhibited the occurrence of biomarkers for short-term colon carcinogenesis (aberrant crypt foci, dysplastic foci and β-catenin accumulated crypt) induced by DMH (Nabandith; et al. 2004: 433-438).

Matsumoto; et al. studied the antiproliferative effect of 4 prenylated xanthones (α-, β- and γ-mangostins (**1**-**3**) and methoxy-β-mangostin in human colon cancer DLD-1 cells. Except for methoxy-β-mangostin, the other three xanthones strongly inhibited cell growth at 20 μM at 72 h and their antitumor efficacy was correlated with the number of hydroxyl groups. Apoptosis was associated with antiproliferative effect of α- and γ-mangostins, but not of β-mangostin (Matsumoto; et al. 2005: 6064-6069). The expression affected of cyclins cdc2 and p27 shown that cell-cycle arrest was related with the antiproliferative effect of α-, β- (G1 arrest) and γ -mangostins (S arrest) (Akao; et al. 2008: 355-370).

Laphookhieo; et al. found that α- and γ-mangostins (**1**, **3**) have a cytotoxic effect against NCI-H187 (Laphookhieo; et al. 2006: 745-747).

Jung; et al. determined antitumoral properties in preneoplastic lesions induced by 7,12-dimethylbenz[a]anthracene (DMBA) in a mouse mammary organ culture of xanthones isolated from mangosteen fruit hull of *G. mangostana* (see detail in page 16) (Jung; et al. 2006: 2077-2082).

Nakagawa; et al. evaluated α-mangostin (**1**) for in vitro cytotoxicity against DLD-1 cells. They demonstrated that the number of viable cells was decreased by the treatment with α-mangostin 20 μM. They also showed the synergistic growth suppression in the cells by the

combination treatment with 2.5 μM of α-mangostin and 2.5 μM of 5-fluorouracil (5-FU), a chemotherapeutic agent for colorectal adenocarcinoma (Nakagawa; et al. 2007: 5620-5628).

Balunas; et al. studied aromatase inhibitory activities of xanthones from the botanical dietary supplement mangosteen (the fruit hull of *G. mangostana*) were screened using a noncellular, enzyme-based microsomal aromatase inhibition assay. The methanolic and chloroform-soluble extracts of *G. mangostana* were both found to be strongly inhibitory against aromatase in the microsomal assay. Twelve xanthones isolated from *G. mangostana*, were tested for aromatase inhibition in microsomes. Active compounds were then subjected to IC_{50} testing to determine if they acted in a dose-dependent manner. Of these compounds, γ-mangostin (**3**) (4.7 PCA, IC_{50} 6.9 μM) and garcinone D (**14**) (10.0 PCA, IC_{50} 5.2 μM) were found to be strongly active in microsomes. Two other xanthones, α-mangostin (**1**) (22.2 PCA, IC_{50} 20.7 μM) and garcinone E (**27**) (23.9 PCA, IC_{50} 25.1 μM), were found to be moderately active in microsomal assay. In a follow up cell-based assay using SK-BR-3 breast cancer cells that express high levels of aromatase, the most potent of these four xanthones was γ-mangostin (Balunas; et al. 2008: 1161-1166).

Yu; et al. studied immunomodulatory and anticancer activities of phenolics from fruit hull of *G. mangostana*. Three major phenolics were purified and identified as α- and γ-mangostins (**1, 3**), and epicatechin (**78**). *In vitro* cell proliferation trials indicated that γ-mangostin and epicatechin exhibited good immunomodulatory activities when 7.5 μg/mL was used. Furthermore, γ-mangostin and epicatechin showed good cytotoxicities against human breast cancer cells (MCF-7) and human colon cancer cells (LOVO). γ-Mangostin exhibited the maximal cytotoxicity of 73.06% against MCF-7 cells and of 46.27% against LOVO cells when 62.5 μg/mL was used. The cytotoxicities of α- and γ-mangostins, epicatechin and paclitaxel against normal embryonic lung fibroblast cells (HELF) were in a decreasing order: paclitaxel > epicatechin > γ-mangostin > α-mangostin (Yu; et al. 2009: 969-973).

2.3 Anti-inflammatory and anti-allergy activities

There is an evidence about anti-allergy and anti-inflammatory properties of *G. mangostana* in differerent in vitro models, such as RBL-2H3 cells (Nakatani; et al. 2002a: 1137-1141) and C6 rat glioma cells (Nakatani; et al. 2002b: 73-79; 2004: 667-674); (Yamakuni; et al. 2006: 206-210), rabbit thoracic aorta and guinea-pig trachea (Chairungsrilerd; et al. 1996a: 351-356) and several models *in vivo* in rats (Nakatani; et al. 2004: 667-674).

Gopalakrishnan; et al. showed that α-mangostin (**1**) isolated from the fruit hull of the mangosteen inhibited systemic anaphylaxis, immunecytoadherence in guinea pigs and rats, and inhibited the primary and secondary responses of adjuvant-induced arthritis in rats (Gopalakrishnan; et al. 1980: 843-846).

Chairungsrilerd; et al. demonstrated that the methanolic extract of mangosteen-fruit hull inhibited the contractions of isolated thoracic rabbit aorta induced by histamine and serotonin. They suggested that α- and γ-mangostins (**1**, **3**) are histaminergic and serotonergic receptor blocking agents, respectively. This same research group studied the effect of α-mangostin (**1**) on histamine-induced contractions in rabbit thoracic aorta and guinea-pig trachea. α-Mangostin inhibited histamine-induced contractions in a dose-dependent manner with or without cimetidine, an antagonist of the H2-histamine receptor. Also, α-mangostin inhibited contractions mediated by the histamine H1 receptor. Furthermore, α-mangostin competitively inhibited [3H] mepyramine (specific antagonist of histamine H1 receptor) binding to rat aortic smooth muscle cells. (Chairungsrilerd; et al. 1996a: 351-356; 1996b: 471-472) Two years later, the same group showed that 0.03–5 μM of γ-mangostin (**3**) purified from the *G. mangostana* caused a parallel rightwards shift of the concentration/ response curve for the contraction elicited by 0.5 mM of 5-hydroxytryptamine (5-HT) in the rabbit aorta without affecting the contractile responses to 30 mM of KCl, 3 μM of phenylephrine or histamine. The perfusion pressure response of rat coronary artery to 5-HT2A was reduced concentration dependently by γ-mangostin (IC_{50} = 0.32 μM). 5-HT amplified, ADP-induced aggregation of rabbit platelets was inhibited by γ-mangostin (IC_{50} = 0.29 μM). This xanthone (5 μM) also affected 5-HT-induced contraction of the guinea-pig ileum (3 μM of 5-HT3) in the presence of 5-HT1, 5-HT2 and 5-HT4 receptor antagonists and inhibited [3H] spiperone binding to cultured rat aortic myocytes (IC_{50} = 3.5 nM). In addition, γ-mangostin (10–40 nmol/mouse) inhibited 5-fluoro-α-methyltryptamine (5-FMT, 45 mg/kg i.p.) induced head-twitch response in mice by blocking $5\text{-}HT_{2A}$ receptors, not by blocking the release of 5-HT from the central neurone. γ-Mangostin is a promising 5-HT2A receptor antagonist in vascular smooth muscle, platelets and the central nervous system (Chairungsrilerd; et al. 1998: 855-862).

Nakatani; et al. studied the effect of extracts from mangosteen fruit (water and ethanol 40%, 70% and 100%) on histamine release and prostaglandin-E_2 (PGE_2) synthesis. They found that 40% ethanol extract (100 and 300 μg/mL) inhibited the histamine release induced by IgE in RBL-2H3 cells. This effect was higher than aqueous extract of *Rubus suavissimus*, which

has been used in Japan as antiallergic drug; whereas 70% and 100% extracts showed only weak inhibition. A 40% ethanol extract of *G. mangostana* extracts (3, 10, 30 and 100 μg/mL) potently inhibited A23187 (a calcium ionophore)-induced PGE_2 release in C6 rat glioma cells, while the water extract of *R. suavissimus* had no effect. In addition, passive cutaneous anaphylaxis reactions in rats were significantly inhibited by this ethanol extract. This same group examined the effect of γ-mangostin (**3**) isolated from mangosteen-fruit pericarp on arachidonic acid cascade in C6 rat glioma cells. They found that γ-mangostin has a potent inhibitory activity on A23187-induced PGE_2 release. This inhibition was concentration-dependent, with an IC_{50} of about 5 μM. Conversion of arachidonic acid to PGE_2 was inhibited by γ-mangostin, which also inhibited the activities of both constitutive cyclooxygenase-1 and inducible cyclooxygenase-2 (COX-1 and COX-2, respectively) in a concentration-dependent manner (IC_{50} of about 0.8 and 2 μM, respectively) (Nakatani; et al. 2002a: 1137-1141; 2002b: 73-79). The effect of γ-mangostin on spontaneous released of prostaglandin E_2 and COX-2 gene expression by using C6 rat glioma cells. After 18 h of γ-mangostin treatment, spontaneous release of PGE_2 was inhibited in a concentration-dependent manner (IC_{50} of about 2 μM). Furthermore, γ-mangostin prevents (in a concentration-dependent manner) the lipopolysaccharide-induced expression of COX-2 protein and its mRNA, but not those of constitutive COX-1. In this work, the effect of γ-mangostin on nuclear factor κB activation was also examined. It was found that γ-mangostin suppressed the inhibitor κB kinase activity to inhibit lipopolysaccharide-induced nuclear factor κB activation and thereby decreases COX-2 induction (Nakatani; et al. 2004: 667-674).

Yamakuni; et al. found that garcinone B (**12**) at 10 μM reduced by 30% the increase of PGE_2 release induced by A23187 in C6 rat glioma cells. Garcinone B at 20 μM also diminished approximately 30% of lipopolysaccharide-induced nuclear factor κB activation. These results suggested that garcinone B may be a pharmacological tool to investigate intracellular signaling pathways involved in inflammation (Yamakuni; et al. 2006: 206-210).

Deschamps; et al. demonstrated that α-mangostin (**1**) inhibited 12-human lipoxygenase (12-LOX) with an IC_{50} of 0.58 μM. The IgE receptor activated intracellular signal transductions resulting in the release of inflammatory signal mediators such as histamine and this was the primary event in several allergic responses (Deschamps; et al. 2007: 6900-6908).

Chen; et al. studied anti-inflammatory activity of mangostins α- and γ-mangostins (**1**, **3**) significantly inhibited lipopolysaccharide (LPS)-stimulated $NO^{\bullet}$ production and cytotoxicity to RAW 264.7 cells. The amount of $NO^{\bullet}$ production at 3 to 25 μM was continously measured,

and the IC_{50} values were 12.4 and 10.1 μM for α- and γ-mangostins. The α- and γ-mangostins also significantly reduced PGE_2 production in lipopolysaccharide -activated RAW 264.7 cells with IC_{50} values of 11.08 and 4.5 μM, respectively. The effects of these xanthones were probed by measuring the induction of inducible nitric oxide synthase (iNOS) and COX enzyme expressions. The two xanthones concentration-dependently reduced the induction of iNOS. The RAW 264.7 cells were activated with lipopolysaccharide (1 μg/mL) for 12 h and the treatment with α- or γ-mangostins (5 μg/mL) for 24 h weakly inhibited iNOS activity in activated RAW 264.7 macrophages. The anti-inflammatory effects of α- and γ-mangostins were evaluated by carrageenan-induced paw edema in mice. The α-mangostin and sulindac (reference compound) treatment showed a potent inhibition of paw edema at 3 h and 5 h, respectively. The action of α-mangostin was more rapid than that of sulindac. However, γ-mangostin did not significant inhibit the paw oedema in mice. This demonstrated that *in vivo* α-mangostin has more anti-inflammatory activity than γ-mangostin (Chen; et al. 2008: 688-693).

Itoh; et al. demonstrated that α-, β- and γ-mangostins (**1**-**3**) suppressed the degranulation in Ag-mediated activation of Ig E receptors in rat basophilic leukemia RBL-2H3 cells. These authors suggested that the inhibitory mechanism of degranulation by xanthones was mainly due to suppression of the SYK/PLCcs/PKC pathway. All the data above indicated that xanthones isolated from mangosteen could be a novel target of anti-inflammatory and antiallergic compounds (Itoh; et al. 2008: 4500-4508).

Tewtrakul; et al. studied of the extract of *G. mangostana* together with α- and γ-mangostins (**1**, **3**) which were tested for anti-inflammatory effect against lipopolysaccharide (LPS)-induced nitric oxide (NO), prostaglandin E_2 (PGE_2), tumor necrosis factor alpha (TNF-α) and interleukin-4 (IL-4) releases as well as their mechanisms in transcriptional levels using RAW264.7 macrophage cells. Mangosteen extract possessed potent NO inhibitory effect with an IC_{50} value of 1.0 μg/mL. The isolated compounds from the extract including α- and γ-mangostins, possessed marked inhibitory effect against NO release with IC_{50} values of 3.1 and 6.0 μM, respectively. The extract exhibited potent inhibitory effect on PGE_2 release (IC_{50} = 6.0 μg/mL), whereas those of α- and γ-mangostins were 13.9 and 13.5 μM, respectively. However, α-mangostin possessed only moderate effects towards TNF-α and IL-4 releases with IC_{50} values ranging from 31.8 to 64.8 μM. Both extracts and α-mangostin suppressed transcription of gene encoding inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) in dose-

dependent manners, whereas γ-mangostin had only an inhibitory effect on transcription of iNOS (Tewtrakul; et al. 2009: 379-382).

2.4 Antimicrobial, antibacterial, antifungal and antiviral activities

Several studies have demonstrated antibacterial, antifungal and antiviral properties of xanthones and extracts obtained from *G. mangostana*.

Sundaram; et al. studied the antibacterial and antifungal properties of α-mangostin (**1**) and its four derivatives. They found that bacteria *S. aureus, P. aeruginosa*, *Salmonella typhimurium* and *Bacillus subtilis* were highly susceptible to xanthones, whereas *Proteus* sp., *Klebsiella* sp. and *Escherichia coli* were only moderately susceptible to them. About fungi, *Epidermophyton floccosum, Alternaria solani, Mucor* sp., *Rhizupus* sp. and *Unninghamella echinulata* were also highly susceptible to xanthones, whereas *Trichophyton mentagrophytes*, *Microsporum canis, Aspergillus niger, Aspergillus flavus*, *Penicillium* sp., *Fusarium roseum* and *Curvularia lunata* were only moderately susceptible to them. The minimum inhibitory concentration (MIC, the lowest concentration of an antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation) of α-mangostin was between 12.5 and 50 μg/mL for bacteria and between 1 and 5 μg/mL for fungi. The order of the antibacterial and antifungal efficiency was as follows: α-mangostin (**1**) > γ-mangostin (**3**) > 3-*O*-methyl mangostin > 3,6-di-*O*-methyl mangostin. Mangostin triacetate had no activity (Sundaram; et al. 1983: 59-60).

Mahabusarakam; et al. investigated the antimicrobial activities of α- and γ-mangostin (**1**, **3**), gartanin (**4**), 1-isomangostin (**15**) and 3-isomangostin (**17**) isolated from *G. mangostana* against *S. aureus*, both normal and penicillin-resistant strains (see detail in page 9) (Mahabusarakam; et al. 1986: 239-242).

Phongpaichit; et al. studied the antibacterial activity of α- and γ-mangostins (**1**, **3**) and a mangostin mixture on 49 strains of MRSA isolated from patients in Songklanagarin Hospital. They also studied the antibacterial activity of α-mangostin (**1**) on 50 strains of MRSA and 13 strains of *Enterococcus* sp. isolated from patients in Maharaj Nakorn Chiang Mai Hospital. Mangostin mixture had the most potent effect against MRSA, with an MIC value of 1.48 μg/mL, which was the same value as vancomycin, an antimicrobial agent used as a positive control. Penicillin G was also used as control and its MIC was >50 μg/mL. Furthermore, α- and γ-mangostins also had an effect against MRSA, with MIC values of 3.12 and 2.26 μg/mL,

respectively. The MIC value of α-mangostin against MRSA was 8 μg/mL. Mangostin inhibited the growth of all *Enterococcus* sp. with an MIC value of 1 μg/mL (Phongpaichit; et al. 1994 399-405).

Chen; et al. showed that ethanolic extract of *G. mangostana* effectively inhibited HIV-1 protease. Two xanthones, α- and γ-mangostins (**1**, **3**), exhibited an IC_{50} value of 5.12 ± 0.41 and 4.81 ± 0.32 μM respectively, pepstatin A (IC_{50} = 76 ± 5.5 nM) was used as positive control (Chen; et al. 1996: 381-382).

Iinuma; et al. studied the inhibitory effect of several xanthones, isolated from mangosteen fruit hull, against the growth of methicillin-resistant *S. aureus* (MRSA). α-Mangostin (**1**) exhibited high efficacy, with MIC values of 1.57–12.5 μg/mL (Iinuma; et al. 1996: 861-865).

Chanarat; et al. found that polysaccharides obtained from mangosteen fruit hull can stimulate activity of polymorphonuclear phagocytic cells against *Salmonella enteritidis* (Chanarat; et al. 1997: S149-S154).

Gopalakrishnan; et al. demonstrated the antifungal activity of several xanthones isolated from mangosteen fruit hull and some α-mangostin derivatives against three *phytopathogenic* fungi (*Fusarium oxysporum vasinfectum, Alternaria tenuis and Dreschlera oryzae*). α- and γ-Mangostins (**1**, **3**), gartanin (**4**), garcinone D (**14**), BR-xanthone A (**25**) and euxanthone were incorporated into the medium in aseptic conditions to have concentrations of 1, 10, 100 and 1000 ppm in the culture medium. These xanthones showed high inhibitory activity against the three fungi; they used substitution in A and C rings of xanthone nucleus have been shown to modify the bioactivities of the compounds (Gopalakrishnan; et al. 1997: 519-524).

Suksamrarn; et al. studied the antituberculosis potential of prenylated xanthones obtained from mangosteen fruit hull (see detail in page 15) (Suksamrarn; et al. 2003: 857-859).

Chomnawang; et al. evaluated the antibacterial activity of 19 medicinal plants from Thailand against *Staphylococcus epidermidis* and *Propionibacterium acnes*, which have been recognized as forming bacteria triggering an inflammation in acne. Only 13 Thai medicinal plants were able to inhibit the growth of both bacteria. Among these, *G. mangostana* exhibited the most potent inhibitory effect, with an MIC value of 0.039 μg/mL for both bacteria. Furthermore, the *G. mangostana* minimal bactericidal concentration, that is the lowest concentration to kill bacteria, was 0.039 and 0.156 μg/mL against *P. acnes* and *S. epidermidis*,

respectively (Chomnawang; et al. 2005: 330-333). In addition, the same author showed that *G. mangostana* ethanolic extract could significantly reduce TNF-α production generated from peripheral blood mononuclear cells by stimulating with *P. acnes* (Chomnawang; et al. 2007: 401-408).

Sakagami; et al. found that α-mangostin (**1**) had inhibitory activity against vancomycin resistant *Enterococci* (VRE) and MRSA with MIC values of 6.25 and 12.5 μg/mL, respectively. Synergy between α-mangostin and gentamicin against VRE; and α-mangostin and vancomycin hydrochloride against MRSA was shown. Furthermore, partial synergy between α-mangostin and ampicillin or minocycline was also shown (Sakagami; et al. 2005: 203-208).

Voravuthikunchai and Kitpipit, studied aqueous and ethanolic extracts obtained from 10 traditional Thai medicinal plants for their ability to inhibit MRSA from 35 hospitals. Nine Thai plants had activity against these bacteria. Ethanolic extracts from *G. mangostana*, *Punica granatum* and *Quercus infectoria* were highly efficient at inhibiting bacterial growth, with MIC values of 0.05, 0.2 to 0.4 and 0.1 to 1.6 μg/mL, respectively (Voravuthikunchai; & Kitpipit. 2005: 510-512).

Boonnak; et al. studied antibacterial activity against both gram-positive (*Bacillus substilis* and *Stephylococcus aureus*) and gram-negative (*Streptococcus faecalis*, *Salmonella typhi*, *Shigella sonei* and *Pseudomonas aeruginosa*) bacteria. Cytotoxicity against MCF-7 (breast adenocarcinoma), HeLa (Human cervical cancer), HT-29 (colon cancer) and KB (human oral cancer) cell lines was also evaluated. α-Mangostin (**1**) showed potent antibacterial activity against *B. substilis*, *S. aureus* and *S. faecalis* at MIC value less than 1.1 μg/mL. whereas pruniflorone C exhibited strong activity against *B. substilis* and *S. aureus* at MIC value less than 1.1 μg/mL. β-Mangostin (**2**) was highly active specifically against *S. aureus* at MIC value less than 1.1 μg/mL. In addition, antibacterial activity α- and β-mangostins showed less cytotoxicity all cancer cell lines (Boonnak; et al. 2006: 8850-8859).

2.5 Antimalarial activity

Several xanthones isolated from *G. mangostana* have shown antimalarial activity *in vitro* against *Plasmodium falciparum*. α- and β-Mangostins (**1**-**2**) exhibited α comparable IC_{50} value (5.1 and 7 μM, respectively), whereas mangiferin, a xanthone-glucoside, exhibited an IC_{50} value higher than 50 μM (Riscoe; et al. 2005: 2539-2549).

Mahabusarakam; et al. found that α-mangostin (**1**) and its alkylamine exhibited an IC_{50} value of 17 μM against *P. falciparum* (Mahabusarakam; et al. 2006: 912-916).

2.6 Other activities

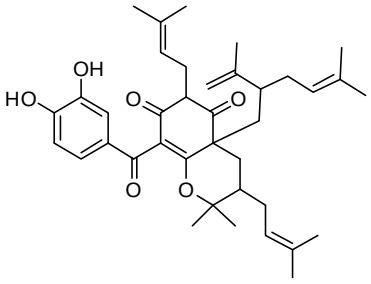
Jinsart; et al. studied the inhibition of wheat embryo calcium-dependent protein kinase and other kinases by α- and γ-mangostins (**1**, **3**). α- and γ-Mangostins were isolated from the fruit hull *G. mangostana*. Both xanthones are potent inhibitors of rat liver cAK assayed with IC_{50} value of 13 and 2 μM, respectively, but are relatively poor inhibitors of avian Ca^{2+}-calmodulin-dependent myosin light chain kinase (MLCK) an IC_{50} value of 120 and 110 μM, respectively. (Jinsart; et al. 1992: 3711-3713).

Kikuchi, et al. studied a luciferase assay of natural products that enhance death receptor 5 (DR5) expression and bioassay-guided fractionation of two organisms, the pericarp of *G. mangostana* (mangosteen) and actinomycete CKK609 strain, led to the isolation of eight xanthones and teleocidin A-2. Among them, eight xanthones including α-, β- and γ-mangostins (**1**-**3**), gartanin (**4**), 8-deoxygartanin (**5**), 1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-dimethylpyrano(2′,3′:3,2)xanthone (**8**), garcinone D (**14**) and 1,5,8-trihydroxy-3-methoxy-2-(3-methyl-2-butenyl)xanthone (**23**) were isolated from *G. mangostana* and teleocidin A-2 was isolated from the actinomycete showed potent DR5 promoter activity. Furthermore, their revealed that combined treatment with gartanin (**4**) and tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL) showed a potentiating effect in sensitizing TRAIL-resistant human gastric adenocarcinoma (AGS) cells (Kikuchi; et al. 2010: 452-455).

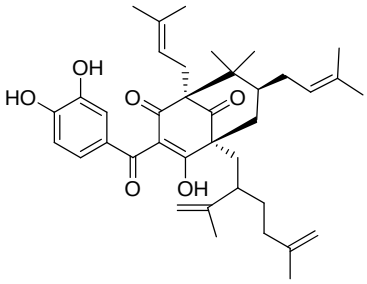
3. Chemical constituents of *G. xanthochymus*

3.1 Benzophenones from *G. xanthochymus*

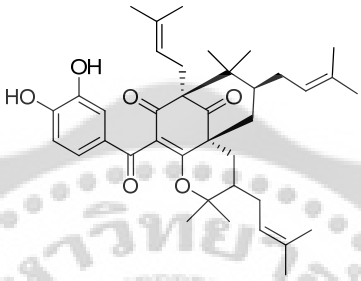
Xanthochymol and isoxanthochymol (**96**) were isolated from *G. xanthochymus* fruits. The structures were assigned from spectral and chemical data, and an x-ray crystallographic analysis of **96** bis-(*p*-bromobenzenesulfonate) (Karanjgoakar; et al. 1973: 4977-4980). In 1976 Blount and Williams had revised structure of xanthochymol (**95**) (Blount and Williams. 1976).



xanthochymol



xanthochymol (**95**)



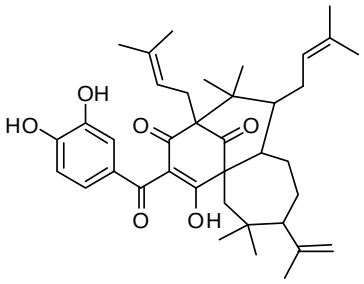
isoxanthochymol (**96**)

Figure 20 Structures of compounds **95**-**96**

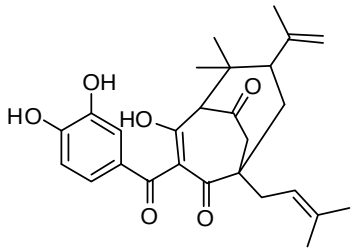
(+)-Xanthochymol (**95**) and (+)-isoxanthochymol (**96**), optically polyprenylated benzophenones having the same molecular formula, $C_{38}H_{50}O_6$, and many other common features, were isolated from the fruits of *G. xanthochymus*. Xanthochymol has a free enolic OH group which forms a part of the chroman ring in isoxanthochymol. Chemical and spectral evidence clearly indicated that both of these compounds were derived from maclurin (**7**) in which the acetate-derived phloroglucinol ring becomes the target of attack by five "active isoprene" groups. (+)-Xanthochymol was smoothly converted to (+)-isoxanthochymol by acid-catalyzed reactions (Rao Rama; et al. 1980: 627-633).

Guttiferone H (**97**) and gambogenone (**98**) were isolated from the MeOH extract of *G. xanthochymus* fruits. Compound **97** contains a seven-membered ring attached to the bicyclo[3.3.1]nonane system position 7 and 8 and displayed cytotoxicity in the SW-480 colon cancer cells at IC_{50} value 12 μM. Compound **98** has a novel benzophenone bicyclo[3.3.2]decane system and displayed in the SW-480 colon cancer cells (IC_{50} = 188 μM). Both **97** and **98** induced apoptosis in SW-480 colon cancer cells and showed antioxidant activity in the 1,1-diphenyl-2-picryhydrazyl (DPPH) assay at IC_{50} value 64 and 38.7 μM, respectively. Along with known

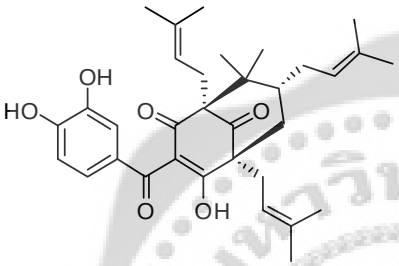
compounds, included aristophenone A (**99**), gutiferone E (**100**) and cycloxanthochymol (**101**) (Baggett; et al. 2005: 354-360).



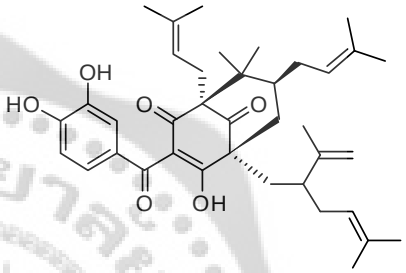
guttiferone H (**97**)



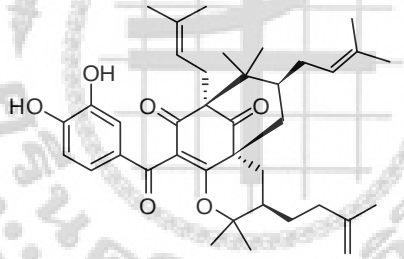
gambogenone (**98**)



aristophenone A (**99**)



guttiferone E (**100**)



cycloxanthochymol (**101**)

Figure 21 Structures of compounds **97**-**101**

3.2 Flavonoids and biflavonoids from *G. xanthochymus*

Volkensiflavone (**102**), morelloflavone (**103**), 5,7,4',3",5",7",4"'-heptahydroxy-(3-8")-biflavanone or GB-1 (**104**), 5,7,4',5",7",4"'-hexahydroxy-(3-8")-biflavanone or GB-1a (**105**), xanthones, xanthochymol (**95**), isoxanthochymol (**96**) and maclurin (**7**) were isolated from C_6H_6 and petroleum ether extracts of air-dired fruits of *G. xanthochymus* (Baslas and Kumer. 1979: 814-815; Baslas; & Kumer. 1981: 31-34).

In 1994, Parveen; et al. isolated agathisflavone (**106**), 7-*O*-methylamentoflavone (**107**) and vitexin (**108**) from leaves of *G. xanthochymus* (Parveen; et al. 1994: 89-90).

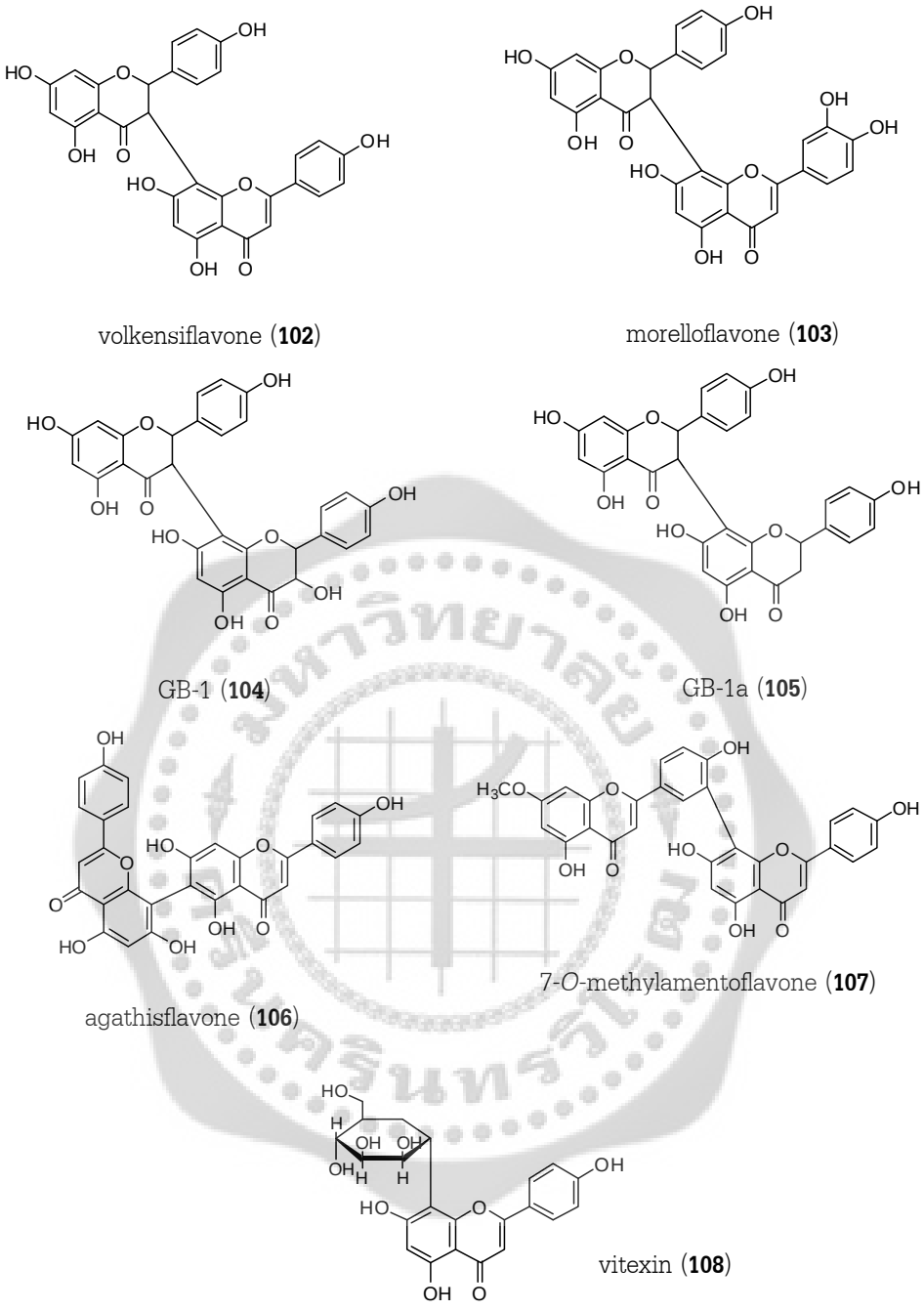
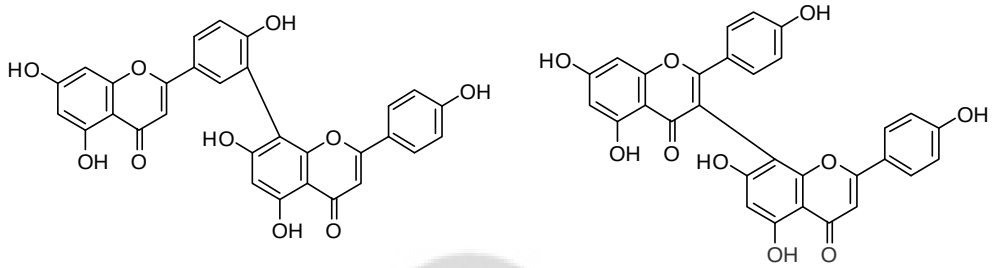


Figure 22 Structures of compounds **102**-**108**

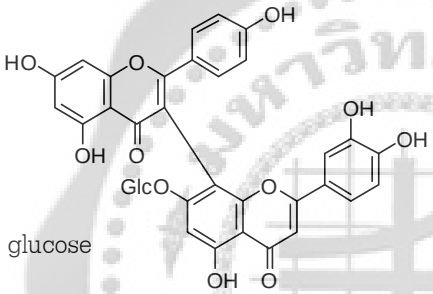
In 2005, Baggett; et al. isolated amentoflavone (**109**), 3,8"-biapigenin (**110**), (±)-fukugeside (**111**), (±)-volkensiflavone (**102**) and (±)-fukugetin or (±)-morelloflavone (**103**). This was the first report on isolation of compounds **109**, **110** and **111** from *G. xanthochymus* fruits (Baggett; et al. 2005: 354-360).

Prenylated flavonoid, 6-prenylapigenenin (**112**) was isolated from the $CHCl_3$ fraction of the twig bark of *G. xanthochymus*. This compound showed moderate cytotoxicities against breast cancer (MDA-MB-435S) cell line and lung adenocarcinoma (A549) cell lines at IC_{50} value 10.10 and 12.93 μg/mL, respectively (Han; et al. 2007: 940-946).



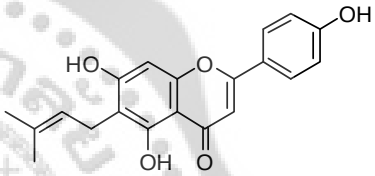
amentoflavone (**109**)

3,8"-biapigenin (**110**)



Glc = glucose

(±)-fukugeside (**111**)

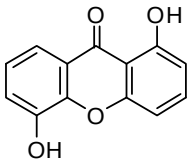


6-prenylapigenin (**112**)

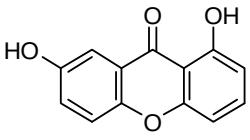
Figure 23 Structures of compounds **109**-**112**

3.3 Xanthones from *G. xanthochymus*

1,5-Dihydroxyxanthone (**113**) and 1,7-dihydroxyxanthone (**114**) were isolated from extracts of fruit of *G. xanthochymus* (Baslas; & Kumer. 1979: 814-815; 1981: 31-34).



1,5-dihydroxyxanthone (**113**)

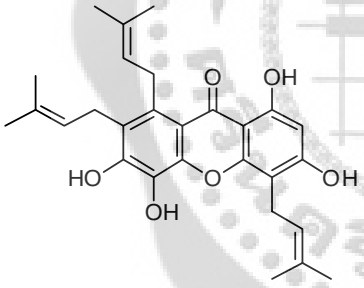


1,7-dihydroxyxanthone (**114**)

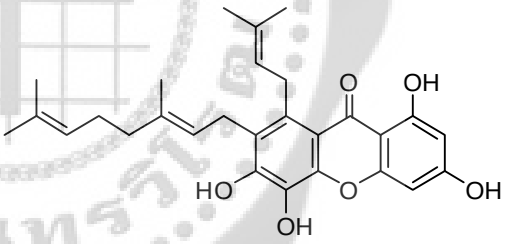
Figure 24 Structures of compounds **113**-**114**

A new prenylated xanthone, 1,3,5,6-tetrahydro-4,7,8-tri-(3-methylbut-2-enyl)xanthone (**115**), was isolated from the wood of *G. xanthochymus* together with a known xanthone, garciniaxanthone E (**116**). Compounds **115** (3 μM) and **116** (10 μM) elicited marked enhancement of nerve growth factor-mediated neurite outgrowth in PC 12D cells (Chanmahasathien; et al. 2003a: 1332-1334). Moreover, they isolated two new xanthones, 1,4,5,6-tetrahydroxy-7,8-di-(3-methylbut-2-enyl)xanthone (**117**) and 1,2,6-trihydroxy-5-methoxy-7-(3-methylbut-2-enyl)xanthone (**118**) along with a known xanthones, 12b-hydroxy-des-*D*-garcigerrin A (**119**). Their structures were elucidated by spectroscopic analysis. Compounds **117** (10 μM), **118** (10-30 μM) and **119** (10 μM) showed a markedly enchancing of nerve growth factor (NGF)-mediated neurite outgrowth on PC 12D cells (Chanmahasathien; et al. 2003b: 981-986).

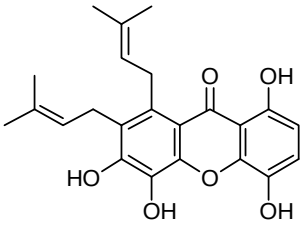
In 2005, Baggett; et al. isolated alloathyriol (**120**) from *G. xanthochymus* fruits together with known compounds, including aristophenone A (**99**), gutiferone E (**100**), cycloxanthochymol (**101**), amentoflavone (**109**), 3,8"-biapigenin (**110**), (±)-fukugeside (**111**), (±)-volkensiflavone (**102**) and (±)-fukugetin or (±)-morelloflavone (**103**), were also obtained (Baggett; et al. 2005: 354-360).



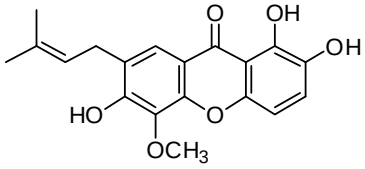
1,3,5,6-tetrahydro-4,7,8-tri-(3-methylbut-2-enyl)xanthone (**115**)



garciniaxanthone E (**116**)

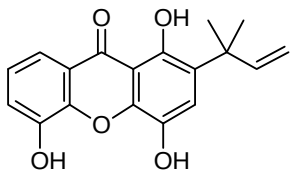


1,4,5,6-tetrahydroxy-7,8-di-(3-methylbut-2-enyl)xanthone (**117**)

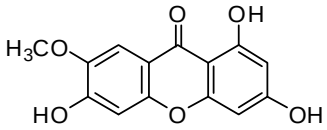


1,2,6-trihydroxy-5-methoxy-7-(3-methylbut-2-enyl)xanthone (**118**)

Figure 25 Structures of compounds **115**-**118**



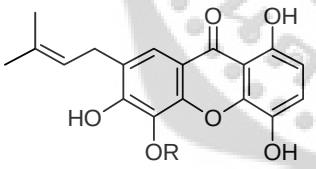
12b-hydroxy-des-*D*-garcigerrin A (**119**)



alloathyriol (**120**)

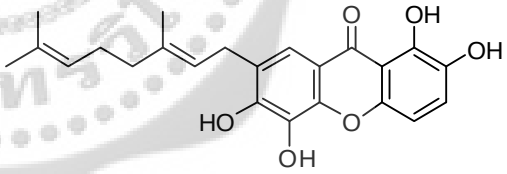
Figure 26 Structures of compounds **119**-**120**

Three new hydroxylated xanthoes with prenyl and geranyl substituents, 1,4,6-trihydroxy-5-methoxy-7-(3-methylbut-2-enyl)xanthone (**121**), 1,4,5,6-tetrahydroxy-7-(3-methylbut-2-enyl)xanthone (**122**) and 1,2,5,6-tetrahydroxy-7-geranyl-xanthone (**123**), were isolated from the twig bark of *G. xanthochymus*, along with known xanthones 1,3,5,6-tetrahydro-4,7,8-tri-(3-methylbut-2-enyl)xanthone (**115**), garciniaxanthone E (**116**), 1,4,5,6-tetrahydroxy-7,8-di-(3-methylbut-2-enyl)xanthone (**117**). All compounds showed moderate cytotoxicities against breast cancer (MDA-MB-435S) and lung adenocarcinoma (A549) cell lines, but lacked antifungal activity against *Candida albicans* (Han; et al. 2007: 940-946).



1,4,6-trihydroxy-5-methoxy-7-(3-methylbut-2-enyl)xanthone; **121** R = Me

1,4,5,6-tetrahydroxy-7-(3-methylbut-2-enyl) xanthone; **122** R = H

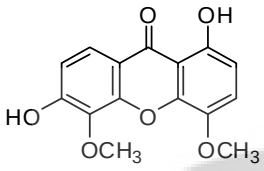


1,2,5,6-tetrahydroxy-7-geranyl-xanthone (**123**)

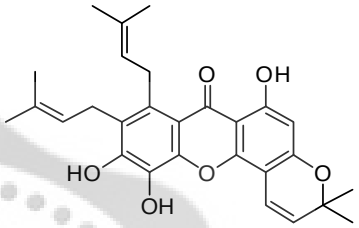
Figure 27 Structures of compounds **121**-**123**

In 2007, Zhong; et al isolated two new xanthones, 1,6-dihydroxy-4,5-dimethoxy xanthone (**124**) and 1,5,6-trihydroxy-7-8-di-(3-methylbut-2-enyl)-6',6'-dimethylpyrano(2',3':3,4)xanthone (**125**) from the bark of *G. xanthochymus* collected from Yunnan province, PR China (Zhong, et al. 2007: 849-851). A new bisxanthone, bigarcinenone A (**126**) which is the first

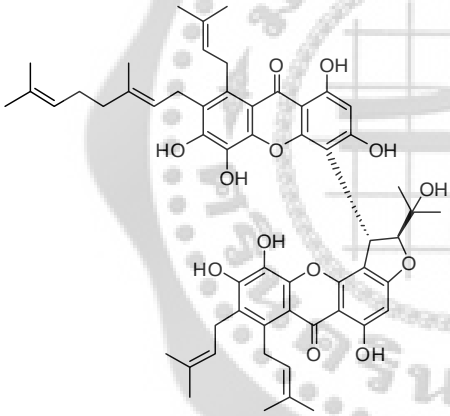
example of a bis-xanthone with the xanthone-xanthone linkage between an aromatic C-atom and a C_5 side chain from a Clusiaseae plant, a new phloroglucinol derivative, garcinenone F (**127**), together with seven known xanthones were isolated from the bark. Bigarcinenone A (**126**) exhibited potent antioxidant activity in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging test with a IC_{50} value of 9.2 μM, compared to the positive control, the well-known antioxidant butylated hydroxytolulene (BHT) with a IC_{50} of 20 μM (Zhong; Chen; & Yang. 2008: 1695-1703).



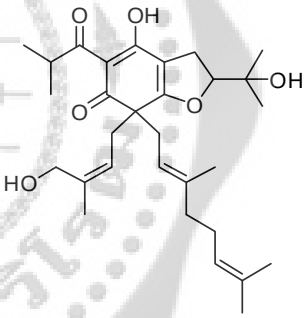
1,6-dihydroxy-4,5-dimethoxyxanthone (**124**)



1,5,6-trihydroxy-7-8-di-(3-methylbut-2-enyl)-6',6'-dimethylpyrano(2',3':3,4)xanthone (**125**)



bigarcinenone A (**126**)



garcinenone F (**127**)

Figure 28 Structures of compounds **124**-**127**

Garcinexanthones A-E (**128**-**132**), were isolated from the bark of *G. xanthochymus*. Their structures were elucidated by spectral analysis, primarily NMR, MS, and UV (Chen; et al. 2008: 1180-1184). In 2009, Zhong; et al. isolated five new xanthones, garcinenone A (**133**), B (**134**), C (**135**), D (**136**) and E (**137**), along with seven known compounds, jacareubin (**138**), subeliptenone B (**139**), symphoxanthone (**140**), 1,3,5,6-tetrahydro-4,7,8-tri-(3-methylbut-2-enyl)xanthone (**115**), garciniaxanthone E (**116**), 12b-hydroxy-des-*D*-garcigerrin A (**119**) and 1,4,6-trihydroxy-5-methoxy-7-(3-methylbut-2-enyl)xanthone (**121**) from the EtOAc-soluble extract of the

bark. The isolated compounds exhibited potent antioxidant activity in the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging test with a IC_{50} value in the 6.0-23.2 μM. These results suggested that *G. xanthochymus* could be a promising rich source of natural antioxidant (Zhong; et al. 2009: 74-80).

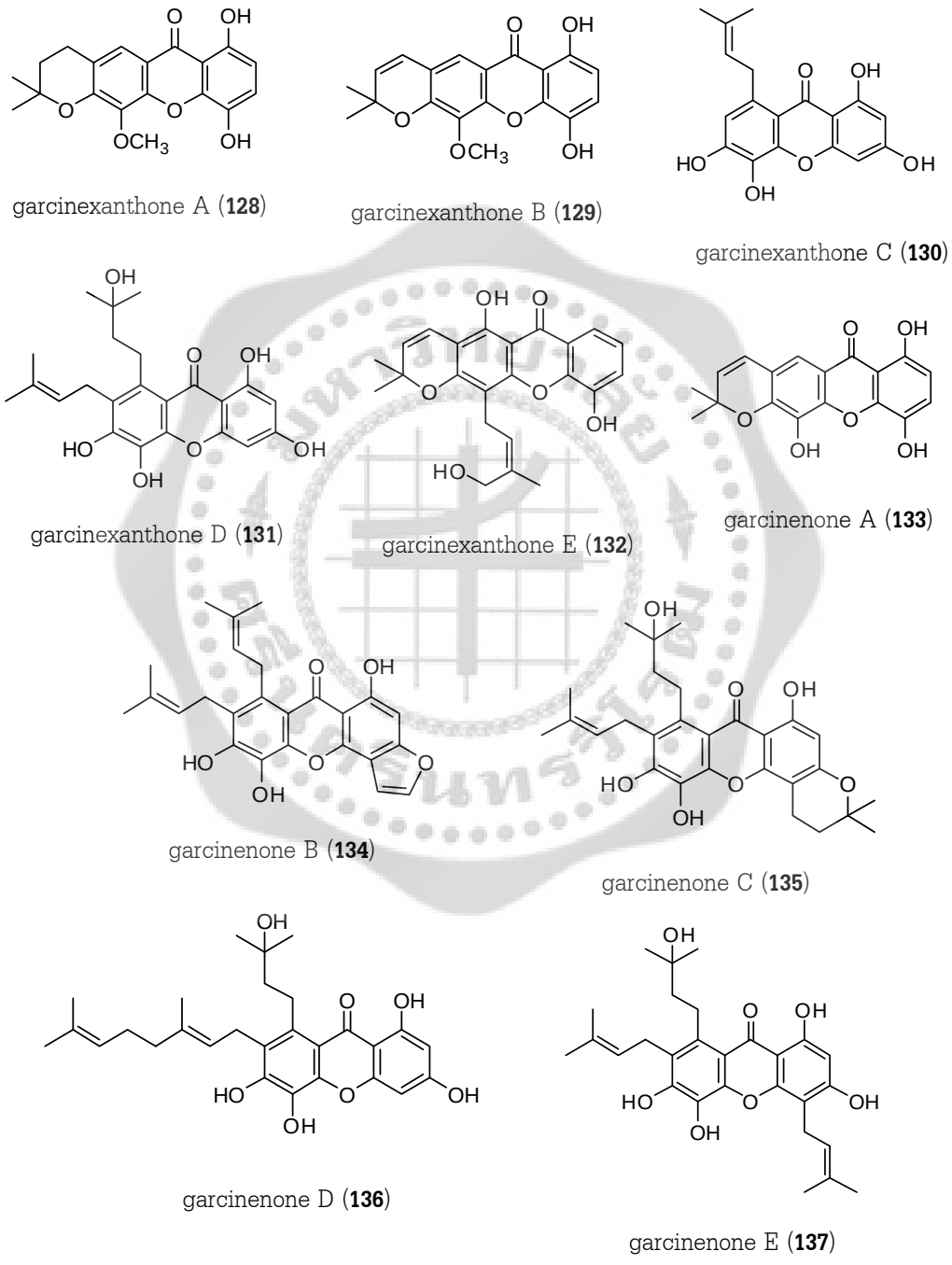
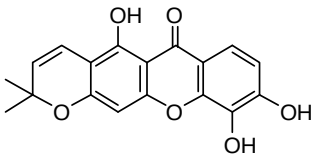
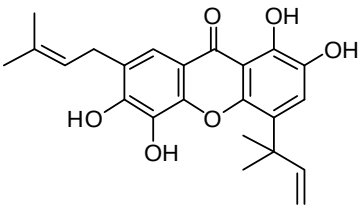


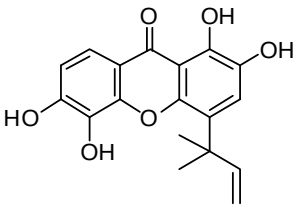
Figure 29 Structures of compounds **128**-**137**



jacareubin (**138**)



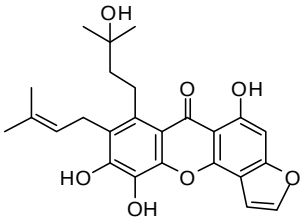
subeliptenone B (**139**)



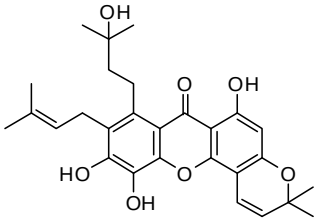
symphoxanthone (**140**)

Figure 30 Structures of compounds **138**-**140**

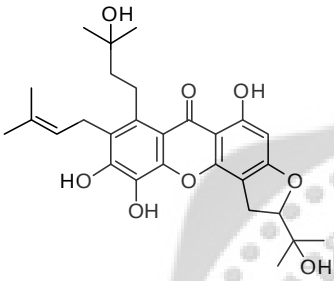
In 2010, Chen and coworkers isolated six new xanthones, including 1,5,6-tri hydroxy-7-(3-methylbut-2-enyl)-8-(3-hydroxy-3-methylbutyl)-furano(2',3':3,4)xanthone (**141**), 1,5,6-tri hydroxy-7-(3-methylbut-2-enyl)-8-(3-hydroxy-3-methylbutyl)-6',6'-dimethylpyrano(2',3':3,4)xanthone (**142**), 1,5,6-trihydroxy-7-(3-methylbut-2-enyl)-8-(3-hydroxy-3-methylbutyl)-5'-(1-hydroxy-1-methyl-ethyl)-4',5'-dihydrofurano(2',3':3,4)xanthone (**143**), 1,2,5,4'-tetrahydroxy-4-(1,1-dimethylallyl)-5'-(2-hydropropan-2-yl)-4',5'-dihydrofurano(2',3':6,7)xanthone (**144**), 1,3,5,6-tetrahydroxy-7-geranyl-xanthone (**145**) and 1,4-dihydroxy-6',6'-dimethylpyrano(2',3':5,6)xanthone (**146**) from the EtOAc extract of *G. xanthochymus* bark. Free-radical-scavenging activities of the isolated compounds were elucidated through DPPH method. Most of the isolated compounds showed considerable free radical scavenging activity on DPPH assay. Compound **141** exhibited effective antioxidant scavenging activity against DPPH radical with IC_{50} value of 19.64 μM, and compound **146** showed the lowest activity among all the tested molecules, with an IC_{50} value of 66.88 μM (Chen, et al. 2010: 7438-7449). Recently, 1,3,5,6-tetrahydroxy-4-(3-hyroxy-3-methylbutyl)-7,8-di-(3-methylbut-2-enyl)xanthone (**147**) and 3,4-dihydro-3,6,7,11-tetrahydroxy-8,9-di-(3-methylbut-2-enyl)-2,2-dimethylpyrano[2,3-c]xanthone (**148**), together with twelve known xanthones, subelliptenone H (**149**), ananixanthone (**150**), pyranojacareubin (**151**), rheediaxanthone A (**152**), toxyloxanthone (**153**), 6-deoxyisojacareubin (**154**), atroviridin (**155**), 6-deoxyjacareubin (**156**), 1-*O*-methylsymproxanthone (**157**), 1-*O*-methylglobuxanthone (**158**), globuxanthone (**159**) and garciniaxanthone H (**160**) from the EtOAc fraction of the ethanolic extract of *G. xanthochymus* gathered in Yunnan province of China. Compounds **147** and **148** were evaluated for their antimicrobial activities in broth microdilution bioassay. Compounds **148** displayed moderate activity against *Candida tropicalis* with MICs 8.13 μM using nystatin as a positive control (MICs 0.53 μM). Compound **147** was inactive against tested fungi (Chen; et al. 2010: 3418-3420).



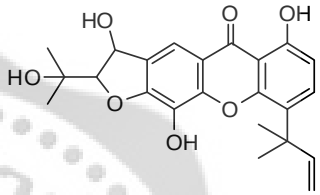
1,5,6-trihydroxy-7-(3-methylbut-2-enyl)-8-(3-hydroxy-3-methylbutyl)-furano(2',3':3,4) xanthone (**141**)



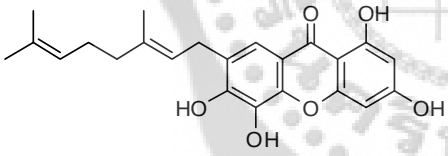
1,5,6-trihydroxy-7-(3-methylbut-2-enyl)-8-(3-hydroxy-3-methylbutyl)-6',6'-dimethylpyrano (2',3':3,4) xanthone (**142**)



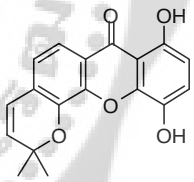
1,5,6-trihydroxy-7-(3-methylbut-2-enyl)-8-(3-hydroxy-3-methylbutyl)-5'-(1-hydroxy-1-methyl-ethyl)-4',5'-dihydrofurano(2',3':3,4) xanthone (**143**)



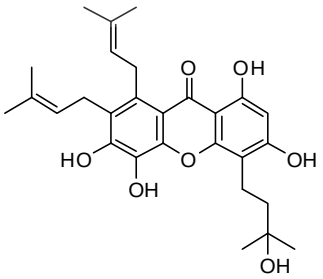
1,2,5,4'-tetrahydroxy-4-(1,1-dimethylallyl)-5'-(2-hydropropan-2-yl)-4',5'-dihydrofurano (2',3':6,7)xanthone (**144**)



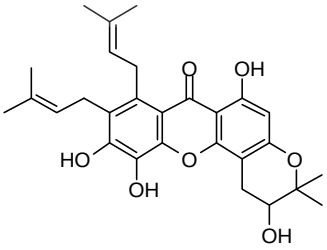
1,3,5,6-tetrahydroxy-7-geranylxanthone (**145**)



1,4-dihydroxy-6',6'-dimethylpyrano (2',3':5,6) xanthone (**146**)



1,3,5,6-tetrahydroxy-4-(3-hyroxy-3-methyl butyl)-7,8-di-(3-methylbut-2-enyl) xanthone (**147**)



3,4-dihydro-3,6,7,11-tetrahydroxy-8,9-di-(3-methylbut-2-enyl)-2,2-dimethylpyrano [2,3-c]xanthone (**148**)

Figure 31 Structures of compounds **141**-**148**

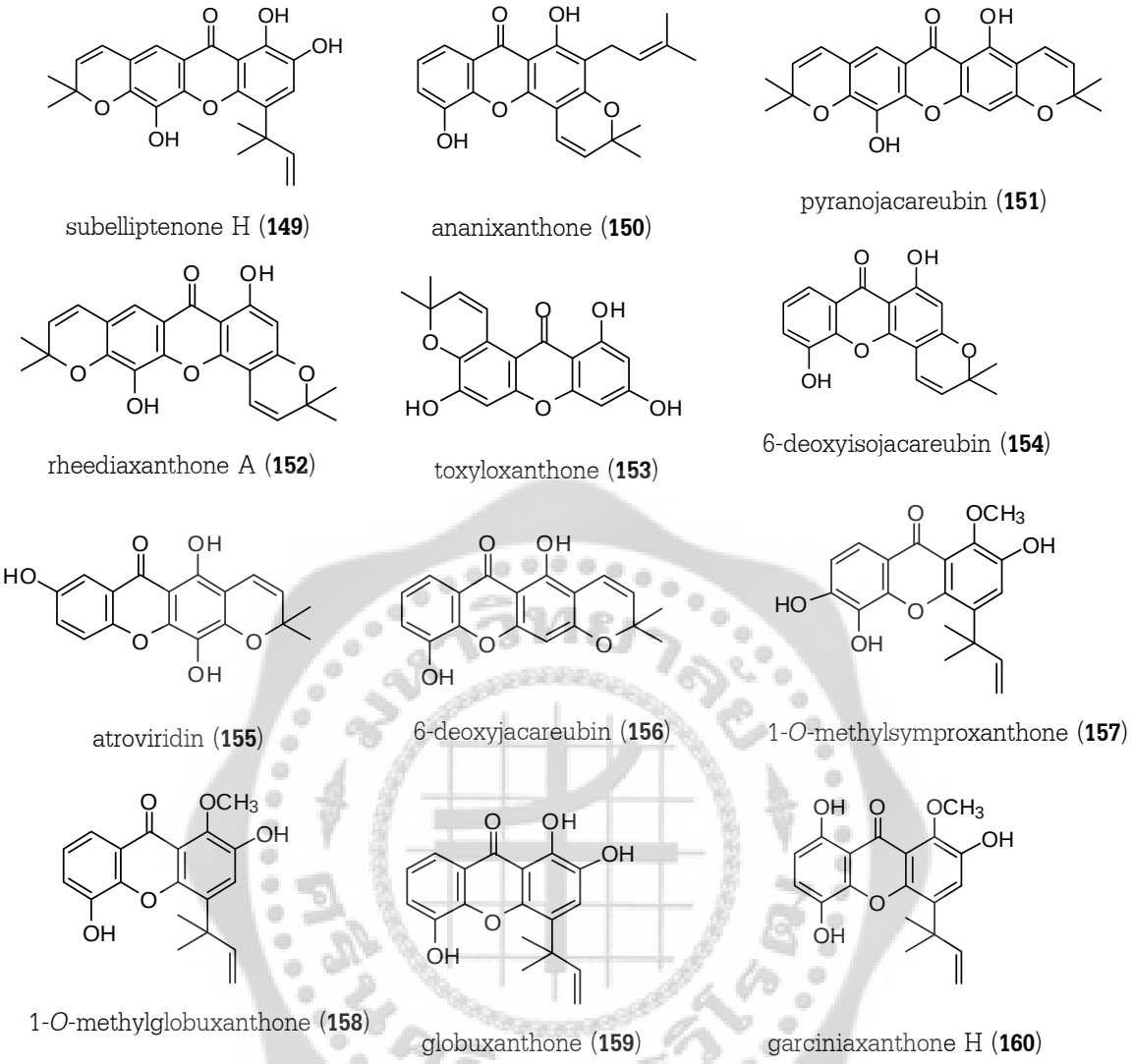
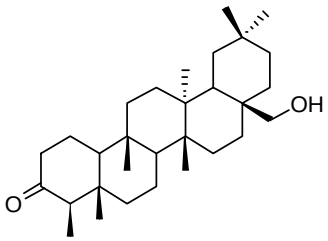


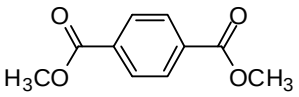
Figure 32 Structures of compounds **149**-**160**

3.4 Triterpenes from *G. xanthochymus*

In 1991, Singh; et al. isolated canophyllol (**161**), dimethyl terephthalate (**162**), friedelin (**87**), β-sitosterol (**88**) and betulin (**90**) from the dried leaves of *G. xanthochymus* (Singh; et al. 1991: 286).



canophyllol (**161**)



dimethyl terephthalate (**162**)

Figure 33 Structures of compounds **161**-**162**

CHAPTER 3

EXPERIMENTAL

Plant materials

The dried roots of *G. mangostana* were collected from Kombang sub-district, Mueang District, Chanthaburi Province, Thailand, in March 2003. A voucher specimen (Pontip Wongnapa No. 002) was been deposited at the Faculty of Science, Srinakharinwirot University.

The stem bark of *G. xanthochymus* was collected from the northern part of Thailand in May 2003. Identified and collected by Mr. James F. Maxwell, Department of Biology, Faculty of Science, Chiang Mai University.

General techniques

1. Thin-layer chromatography (TLC)

Techniques : One dimension, ascending.

Adsorbent : Silica gel 60 F_{254} pre-coated on aluminium plate (Merck 1.05554)

Layer thickness : 1.25 mm

Plate size : 1 x 5 cm and 2 x 5 cm

Detection : 1. Spots on TLC were visualized under ultraviolet light at wavelengths of 254 and 365 nm.

2. Developing reagent: anisaldehyde-sulphuric reagent (0.5% anisaldehyde in methanolic solution containing 4.5% sulphuric acid and 10% glacial acetic acid). After heating of TLC plate at 100-110 $^{\circ}$C for 2-3 minutes, the spots of organic compounds gave specific colors with this reagent.

2. Column chromatography (CC)

2.1 Liquid column chromatography

Adsorbent : 1. Silica gel 60, particle size finer than 0.063 mm (Merck 1.07729)

2. Silica gel 60, particle size 0.063-0.0200 mm (Merck 1.07734)

Packing method : Slurry packing method

Sample loading : The sample was dissolved in a small volume of suitable organic solvent. The solution was mixed with silica gel (particle size 0.063-0.0200 mm, Merck 1.07734). The sample was evaporated under reduced pressure and added onto the top of column.

Elution : After loading of sample onto the column, an appropriate solvent system was used as a mobile phase in the isocratic or gradient systems.

2.2 Quick column chromatography

Adsorbent : Silica gel 60 GF_{254} for thin-layer chromatography (Merck 1.07730)

Packing method : Dry vacuum packing method

Sample loading : The sample was dissolved in a small volume of an appropriate solvents. The solution was mixed with Merck silica gel 60 GF_{254}. The sample was evaporated under reduced pressure and added onto the top of column.

Elution : After loading of sample onto the column, an appropriate solvent system was used as a mobile phase in the gradient systems.

2.3 Size-Exclusion gel column chromatography

Adsorbent : Sephadex-LH 20

Packing method : Slurry packing method

Sample loading : The sample was dissolved in a small volume of MeOH and added onto the top of column.

Elution : The column was eluted with MeOH.

Physical properties

1. Optical rotations

Optical rotations were recorded in MeOH on a JASCO-1020 digital polarimeter (Department of Chemistry, Faculty of Science, Ramkhamhaeng University).

2. Melting points

Melting points were measured on a Griffin melting point apparatus in degree Celsius of temperature.

Spectroscopy

1. Infrared (IR) absorption spectra

IR spectra were recorded on a Perkin Elmer FT-IR Spectrum BX spectrophotometer by using potassium bromide (KBr) disc.

2. Ultraviolet (UV) absorption spectra

UV spectra were obtained on a Shimadzu UV-2450 PC spectrophotometer.

3. Mass spectra

Electrospray ionization mass spectra (ESMS), EIMS and HRTOFMS (APCI) were measured on a Finnigan LC-Q (Department of Chemistry, Faculty of Science, Ramkhamhaeng University) and a Bruker MicroTOF mass spectrometers (the Chulaborn Research Institute).

4. Nuclear Magnetic Resonance (NMR) spectra

1H-NMR (300 MHz) and 13C-NMR (75 MHz) spectra were acquired on a Bruker AVANCE 300 FT-NMR spectrometer.

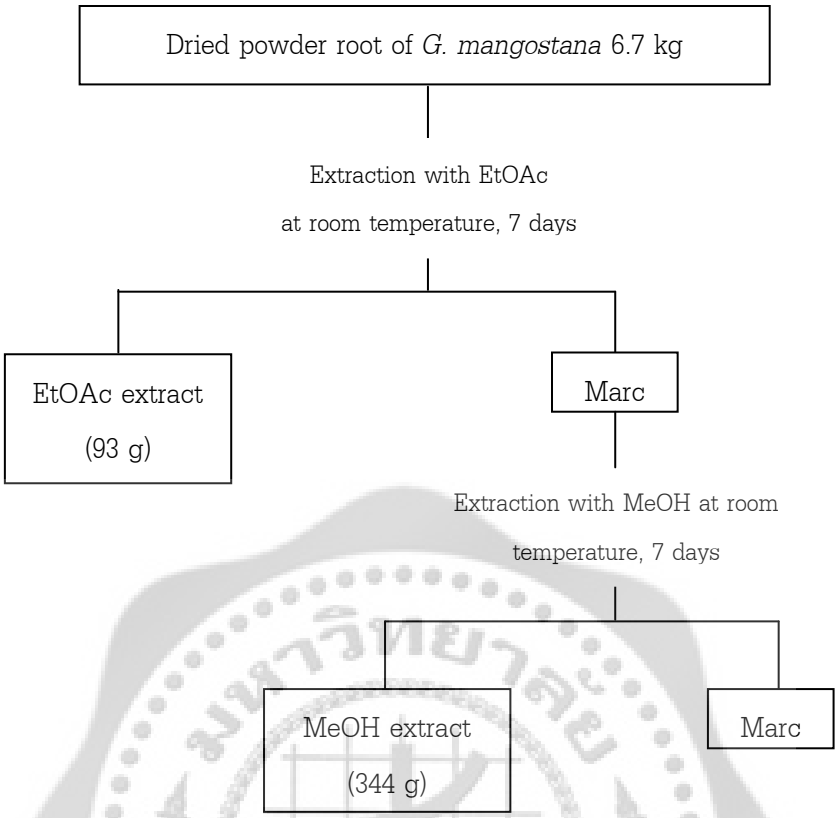
Data analysis

The structures of compounds were determined using spectroscopic techniques such as Nuclear Magnetic Resonance (NMR), Mass (MS), Infrared (IR) and Ultraviolet (UV).

Extraction, isolation and purification

1. Extraction of the root of *G. mangostana*

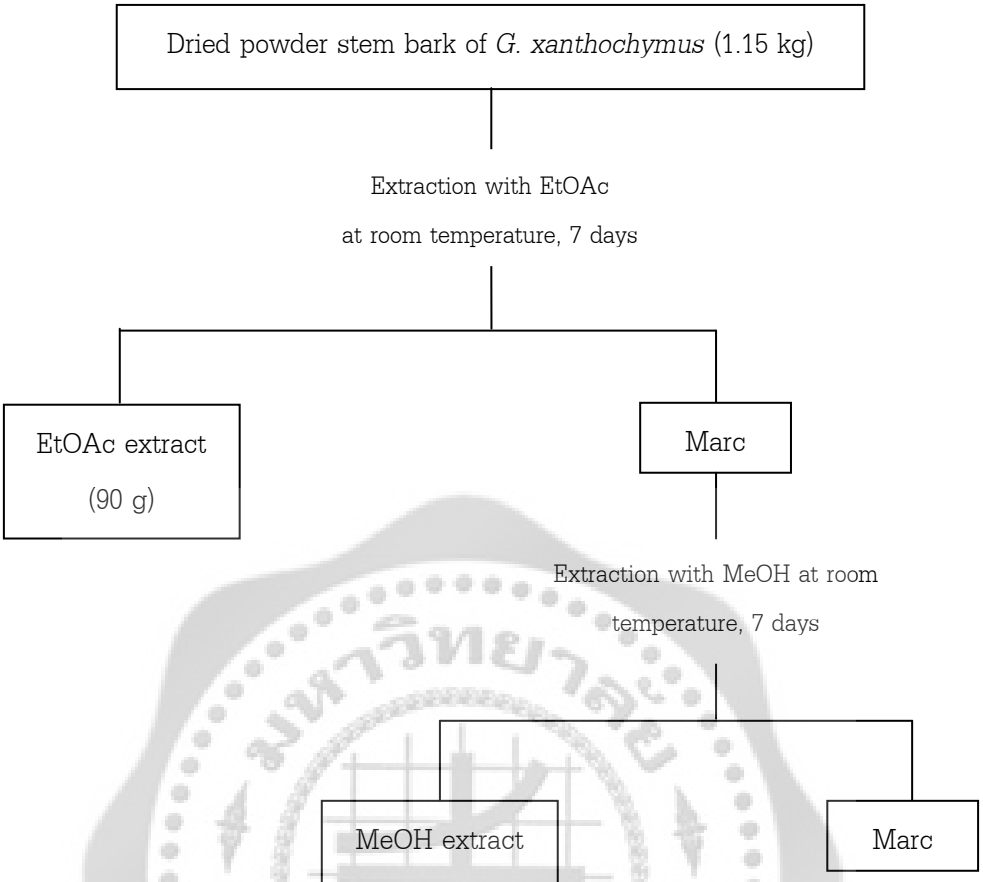
The dried root of *G. mangostana* (6.7 kg) was extracted with ethyl acetate (EtOAc) by exhaustive maceration (3 x 10 L) at room temperature for each 7 days and then with methanol (MeOH) (3 x 10 L). Each extract was evaporated under reduced pressure at 40 $^{\circ}$C using a rotary vacuum evaporator. The EtOAc and MeOH extracts were obtained in 93 g and 344 g of each residue, respectively. The extraction procedure is shown in Scheme 1.



Scheme 1 Extraction procedure of the root of *G. mangostana*

2. Extraction of the stem bark of *G. xanthochymus*

The dried stem bark of *G. xanthochymus* (1.15 kg) was extracted with EtOAc by exhaustive maceration (5 x 10 L) at room temperature for each 7 days and then with MeOH (5 x 10 L). Each extract was evaporated under reduced pressure at 40 °C using a rotary vacuum evaporator to yield 90 g and 111 g of the EtOAc and MeOH extracts, respectively. The extraction procedure is shown in Scheme 2.



Scheme 2 Extraction procedure of the stem brak of *G. xanthochymus*

3. Isolation and Purification of pure compounds from crude EtOAc and MeOH extracts of *G. mangostana*. The isolation and purification procedure is shown in Scheme 3 and 4.

3.1 Forty grams of EtOAc extract was fractionated by quick column chromatography (Merck silica gel 60 GF_{254}, 150 g), eluted with n-hexane, n-hexane-CH_2Cl_2, CH_2Cl_2, CH_2Cl_2-EtOAc, EtOAc, EtOAc-MeOH and MeOH with increasing amounts of the more polar solvent. Fractions were collected and checked by TLC on silica gel (Merck), fractions showing similar profiles were combined. Column chromatography gave 9 fractions (Fr.1-9) were obtained.

3.1.1 Fraction 2 (12.2 g, eluted with CH_2Cl_2-EtOAc (90:10)) was further purified by CC on silica gel (Silica gel 60, particle size finer than 0.063 mm and 0.063-0.0200 mm, Merck)

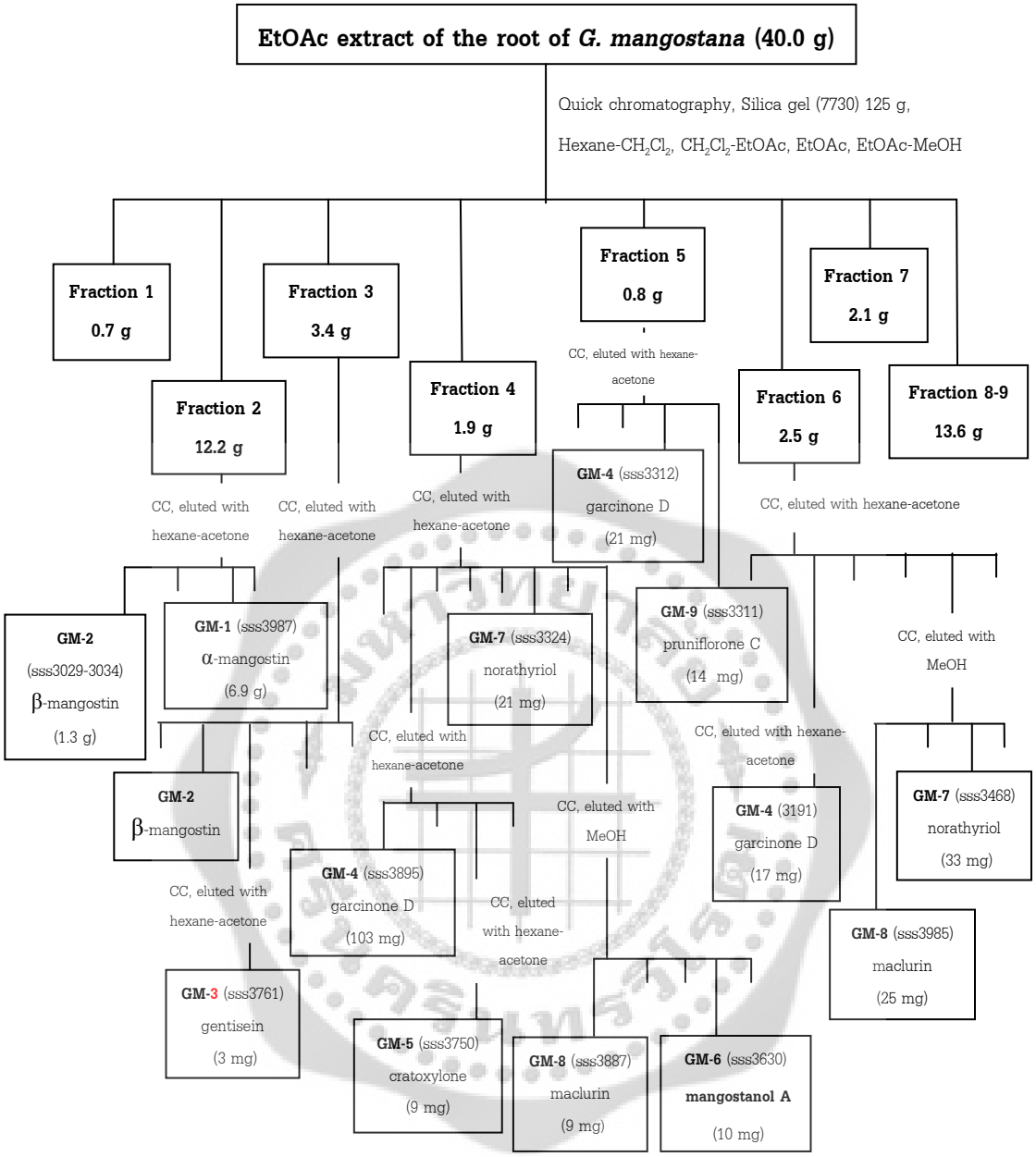
and eluted with a gradient of hexane-acetone to give compound **GM-2** (β-mangostin, sss3029-3034, 1.287 g, eluted with hexane-acetone (95:5)) and compound **GM-1** (α-mangostin, sss3987, 6.98 g, eluted with hexane-acetone (93:7)).

3.1.2 Fraction 3 (3.47 g, eluted with CH_2Cl_2-EtOAc (70:30)) was further separated by CC over silica gel to give 8 sub-fractions. The sixth sub-fraction (2.2 g, eluted with CH_2Cl_2-EtOAc (80:20-50:50)) was purified by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to give 9 fractions. The eighth fraction (1.31g, eluted with hexane-acetone (90:10)) was applied to twice silica gel column eluted with hexane-acetone in a polarity-gradient manner gave compound **GM-3** (gentisein, sss 3761, 3.1 mg, eluted with hexane-acetone (85:15))

3.1.3 Fraction 4 (1.97 g, eluted with CH_2Cl_2-EtOAc (40:60)) was applied to a silica gel column eluted with hexane-acetone in a polarity-gradient manner to yielded 19 sub-fractions. The eighth to twelfth sub-fractions (333.2 mg, eluted with hexane-acetone (80:20-75:25)) were combined and purified by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to give 9 fractions. The fifth fraction (113.5 mg, eluted with hexane-acetone (80:20-78:22)) was purified by recrystallization from hexane-acetone to give compound **GM-4** (garcinone D, sss3895, 103.4 mg, eluted with hexane-acetone (80:20)). The fourth fraction (62.5 mg, eluted with hexane-acetone (80:20)) was subjected to twice of silica gel CC with a gradient of hexane-acetone to afford compound **GM-5** (cratoxylone, sss 3750, 9 mg, eluted with hexane-acetone (85:15)). The thirteenth and fourteenth sub-fractions (258.8 mg, eluted with hexane-acetone (70:30)) were combined and purified by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to give 10 fractions. The fourth and fifth fractions (36.4 mg, eluted with hexane-acetone (97:3)) were combined and applied on Sephadex LH-20 column (2.0 x 130 cm, 70 g) with MeOH to give compound **GM-6** (**sss 3630,** 10 mg). The eighth fraction (106.3 mg, eluted with hexane-acetone (94:6)) was further purified on Sephadex LH-20 column (2.0 x 130 cm, 70 g) with MeOH to afford compound **GM-7** (norathyriol, sss3324, 21.3 mg). The fifteenth and sixteenth sub-fractions (442.5 mg, eluted with hexane-acetone (70:30)) were combined and purified by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to yield 8 fractions. The third to fifth fractions (260.3 mg, eluted with hexane-acetone (97:7-95:5)) was further purified by CC on silica gel to afford 5 fractions. The second fraction (93.6 mg, eluted with hexane-acetone (70:30-65:35)) was purified on Sephadex LH-20 column with MeOH gave compound **GM-8** (maclurin, sss 3887, 9.9 mg).

3.1.4 Fraction 5 (0.79 g, eluted with CH_2Cl_2-EtOAc (30:70)) was further separated by CC over silica gel to yield 12 sub-fractions. The seventh (29.9 mg, eluted with hexane-acetone (82:18)) and ninth sub-fractions (146.6 mg, eluted with hexane-acetone (80:20-78:22)) were combined and purified by recrystallization from hexane-acetone to afford compound **GM-9** (pruniflorone C, sss 3311, 14.5 mg) and compound **GM-4** (garcinone D, sss3312, 21.0 mg), respectively.

3.1.5 Fraction 6 (2.59 g, eluted with CH_2Cl_2-EtOAc (20:80)) was applied by silica gel CC with solvent mixture of CH_2Cl_2-MeOH in a polarity-gradient manner to yield 12 sub-fractions. The fifth to tenth sub-fractions (1.18 g, eluted with CH_2Cl_2-MeOH (96:4-90:10)) were combined and separated by CC over silica gel to yield 8 fractions. The second fraction (47.6 mg, eluted with hexane-acetone (94:6-89:11)) was recrystallized from hexane-acetone to give compound **GM-4** (garcinone D, sss3191, 17.2 mg). The fifth fraction (57.2 mg, eluted with hexane-acetone (88:12)) and sixth fraction (92.1 mg, eluted with hexane-acetone (88:12)) were combined and separated on Sephadex LH-20 column with MeOH to give compound **GM-7** (norathyriol, sss3468, 33.6 mg) and **GM-8** (maclurin, sss 3985, 25.0 mg).



Scheme 3 Isolation of compounds from the EtOAc extract of the root of *G. mangostana*

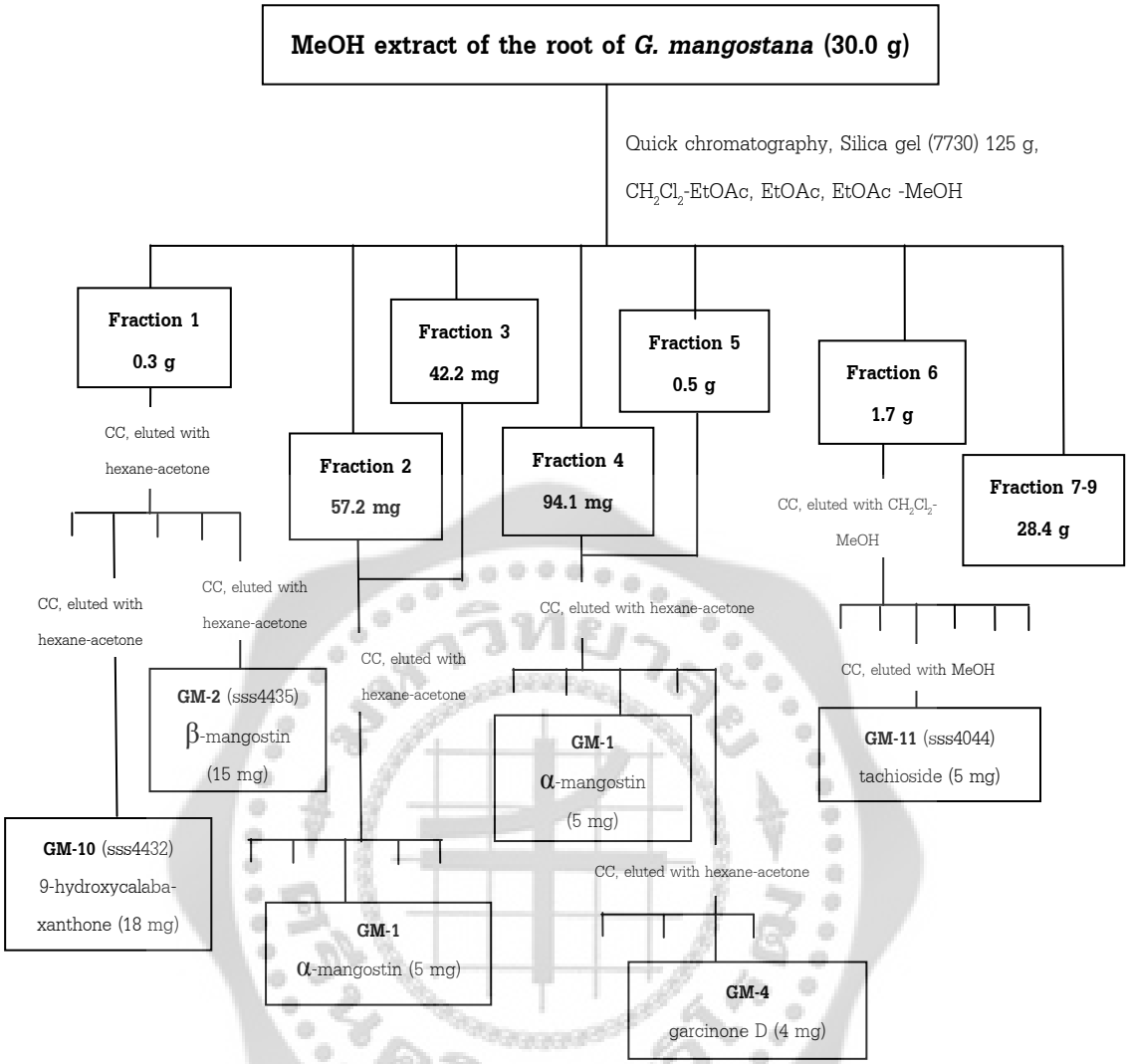
3.2 Thirty grams of MeOH extract was separated by quick column chromatography (Merck silica gel 60 GF_{254}, 150 g), eluted with CH_2Cl_2, CH_2Cl_2-EtOAc, EtOAc, EtOAc-MeOH and MeOH with increasing amounts of the more polar solvent. Fractions were collected and checked by TLC on silica gel (Merck), fractions showing similar profiles were combined column chromatography to yield 9 fractions (Fr.1-9).

3.2.1 Fraction 1 (327.3 mg, eluted with CH_2Cl_2) was subjected by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to yield 9 sub-fractions. The second sub-fraction (9.4 mg, eluted with hexane-acetone (98:2)), fourth sub-fraction (34.7 mg, eluted with hexane-acetone (96:4)) and the sixth sub-fraction (27.8 mg, eluted with hexane-acetone (95:5)) were loaded on a silica gel column with solvent mixture of hexane-acetone in a polarity-gradient to give compound **GM-10** (9-hydroxycalaba- xanthone, sss 4432, 18.3 mg) and compound **GM-2** (β-mangostin, sss4435, 15.2 mg), respectively.

3.2.2 Fractions 2 and 3 (604.1 mg, eluted with CH_2Cl_2-EtOAc (50:50)) were combined and purified by silica gel CC to yield 8 sub-fractions. The second to fourth sub-fraction (148.1 mg, eluted with hexane-acetone (92:8-84:16)) were subjected to column chromatography over silica gel with solvent mixture of hexane-acetone in a polarity-gradient to afford compound **GM-1** (α-mangostin, 5.2 mg, eluted with hexane-acetone (88:12)).

3.2.3 Fractions 4 and 5 (604.1 mg, eluted with CH_2Cl_2-EtOAc (50:50)) were combined and purified by silica gel CC to yield 8 sub-fractions. The second to fourth sub-fractions (148.1 mg, eluted with hexane-acetone (92:8-84:16)) were combined and subjected to column chromatography over silica gel with solvent mixture of hexane-acetone in a polarity-gradient to afford compound **GM-1** (α-mangostin, 5.2 mg, eluted with hexane-acetone (88:12)). The fifth to seventh sub-fractions (205.7 mg, eluted with hexane-acetone (82:18-74:26)) were combined and applied by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to yield 8 fractions. The second fraction (16.0 mg, eluted with hexane-acetone (84:16)) was recrystallized from hexane-acetone to give compound **GM-4** (garcinone D, 4.2 mg).

3.2.4 Fraction 6 (1.6949 g, eluted with CH_2Cl_2-EtOAc (50:50)) was applied by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to yield 8 sub-fractions. The sixth sub-fraction (106.2 mg, eluted with hexane-acetone (80:20)) was purified by silica gel CC to yield 6 fractions. The second fraction (32.4 mg, eluted with hexane-acetone (80:20-75:25)) was loaded on a Sephadex LH-20 column with MeOH to give compound **GM-11** (tachioside, sss 4044, 5.4 mg).



Scheme 4 Isolation of compounds from the MeOH extract of the root of *G. mangostana*

4. Isolation and Purification of pure compounds from crude EtOAc extract of *G. xanthochymus*. The isolation and purification procedure is shown in Scheme 5.

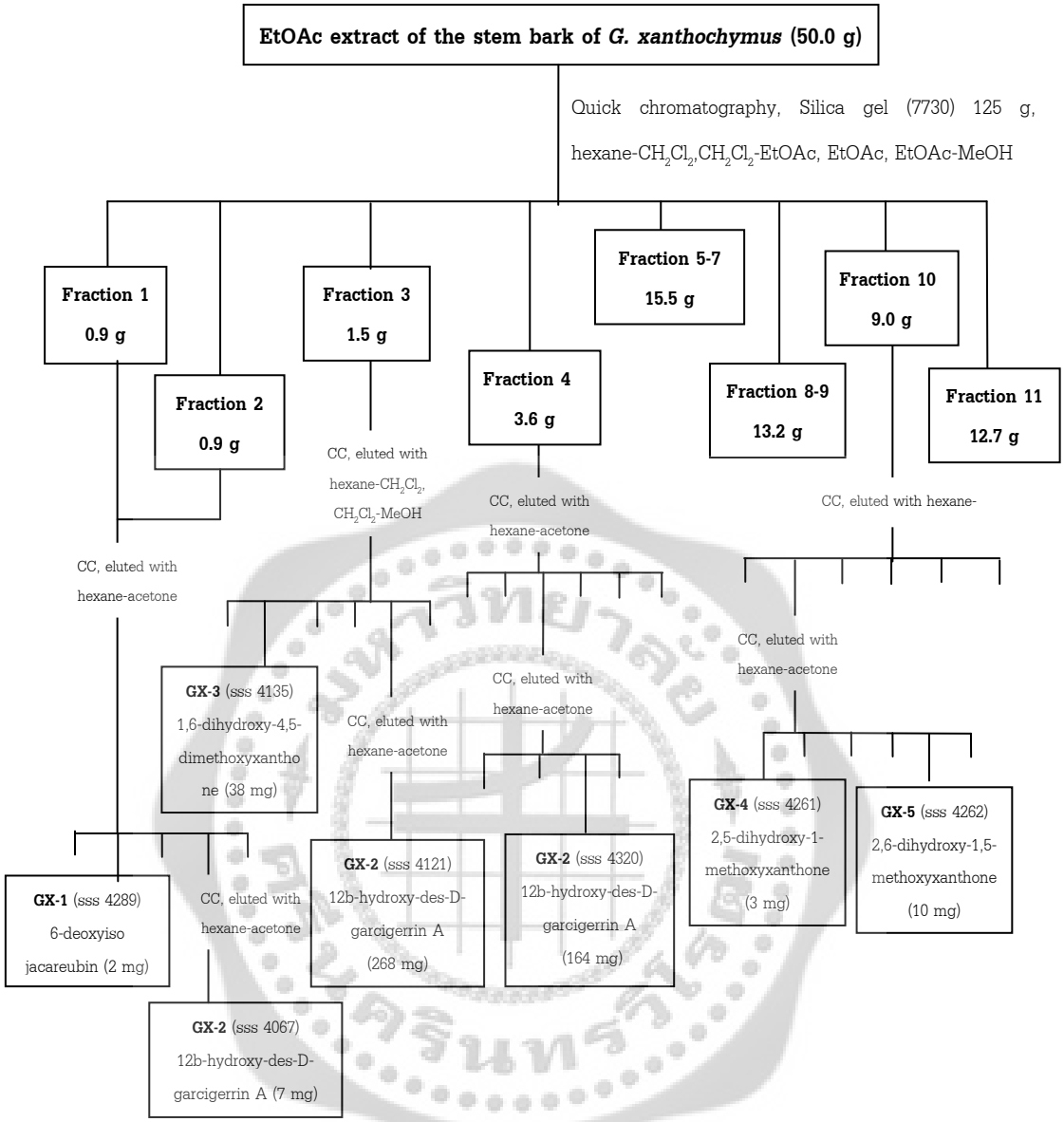
4.1 Fifty grams of EtOAc extract was fractionated by quick column chromatography (Merck silica gel 60 GF_{254}, 150 g), eluted with n-hexane, n-hexane-CH_2Cl_2, CH_2Cl_2, CH_2Cl_2-EtOAc, EtOAc, EtOAc-MeOH and MeOH with increasing amounts of the more polar solvent. Fractions were collected and checked by TLC on silica gel (Merck), fractions showing similar profiles were combined. Column chromatography gave 11 fractions (Fr.1-11) were obtained.

4.1.1 Fractions 1-2 (1.95 g, eluted with hexane-CH_2Cl_2 (50:50)-(20:80) were further purified by CC on silica gel (Silica gel 60, particle size finer than 0.063 mm and 0.063-0.0200 mm, Merck) and eluted with a gradient of hexane-acetone to give 7 fractions. The second sub-fraction (263.2 mg, eluted with hexane-acetone (93:7)) was recrystallized from hexane-acetone to give compound **GX-1** (6-deoxyisojacareubin, sss4289, 2.6 mg) and fifth sub-fraction (139.5 mg, eluted with hexane-acetone (99:1)-(90:10)) was applied by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to give compound **GX-2** (12b-hydroxy-des-D-garcigerrin A, sss4067, 7.1 mg, eluted with hexane-acetone (93:7)).

4.1.2 Fraction 3 (1.53 g, eluted with hexane-CH_2Cl_2 (20:80) to CH_2Cl_2-EtOAc (90:10)) was applied by CC on silica gel (Silica gel 60, particle size finer than 0.063 mm and 0.063-0.0200 mm, Merck) and eluted with a gradient of hexane-CH_2Cl_2 and CH_2Cl_2-MeOH to give 11 fractions. The four to nine sub-fractions (289.6 mg, eluted with hexane-CH_2Cl_2 (50:50) to (0: 100)] were combined and applied by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to give compound **GX-3** (2,6-dihydroxy-4,5-dimethoxyxanthone, sss4135, 38.5 mg, eluted with hexane-acetone (93:7)). The eleven sub-fraction [(828.9 g, eluted with CH_2Cl_2-MeOH (90:5)-(90:100]] was subjected to column chromatography over silica gel with solvent mixture of hexane-acetone in a polarity-gradient to afford compound **GX-2** (12b-hydroxy-des-D-garcigerrin A, sss4121, 268.1 mg, eluted with hexane-acetone (93:7)).

4.1.3 Fraction 4 (3.61 g, eluted with hexane-CH_2Cl_2 (20:80) to CH_2Cl_2-EtOAc (90:10)) was subjected by CC on silica gel (Silica gel 60, particle size 0.063-0.0200 mm, Merck) and eluted with a gradient of hexane-acetone to give 10 fractions. The third sub-fraction [(193.4 mg, eluted with hexane-acetone (90:10)] was applied by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to give compound **GX-2** (12b-hydroxy-des-D-garcigerrin A, sss4320, 164.8 mg, eluted with hexane-acetone (93:7)).

4.1.4 Fraction 10 [(9.09 g, eluted with CH_2Cl_2-EtOAc (85:15)-(65:35)] was applied by CC on silica gel (Silica gel 60, particle size 0.063-0.0200 mm, Merck) and eluted with a gradient of hexane-acetone to give 9 fractions. The second sub-fraction [(91.6 mg, eluted with hexane-acetone (70:30)-(55:45)] was applied by silica gel CC with solvent mixture of hexane-acetone in a polarity-gradient manner to give compound **GX-4** (2,5-dihydroxy-1-methoxyxanthone,sss4261, 3.2 mg, eluted with hexane-acetone (95:5)) and compound **GX-5** (2,6-dihydroxy-1,5-dimethoxyxanthone, sss4262, 10.4 mg, eluted with hexane-acetone (95:5)).



Scheme 5 Isolation of compounds from the EtOAc extract of the stem bark of *G. xanthochymus*

Physical and spectral data of the isolated compounds from the EtOAc and MeOH extracts of *G. mangostana*

Compound GM-1 (α-mangostin, sss 3987)

Yellow needles 6.98 g, soluble in acetone and MeOH

mp : 174-175 °C [lit. 177-178 °C (Orapin Komutiban. 2007: 37); 180-182 °C (Yates; & Stout. 1958: 1691-1700)]

R_f : 0.38 (30% acetone-hexane), a yellow green coloration with anisaldehyde-H_2SO_4 reagent

UV MeOH; λ_{max} (log ε) : 243 (4.53), 257 (4.42), 314 (4.36), 361 (3.82)

IR KBr; ν_{max} (cm^{-1}) : 3442, 2927, 1642, 1609, 1578, 1460, 1385, 1291, 1281, 1195, 1158, 1093, 1046, 1017

^{1}H-NMR ($CDCl_3$, 300 MHz): (Table 6)

Compound GM-2 (β-mangostin, sss 3029-3034)

Pale yellow needles 1.29 g, soluble in CH_2Cl_2, acetone and MeOH

mp : 166-167 °C [lit. 173-175 °C (Narisara Suwannapoch. 2002: 30)]

R_f : 0.3 (20% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

UV MeOH ; λ_{max} (log ε) : 244 (4.65), 256 (4.58), 314 (4.45), 357 (4.01)

IR KBr; ν_{max} (cm^{-1}) : 3405, 2927, 1645, 1601, 1460, 1429, 1385, 1282, 1207, 1154, 1171, 1113, 1053

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C-NMR (acetone-d_6, 75 MHz) : (Table 7)

Compound GM-3 (gentisein, sss 3761)

Pale yellow amorphous 3.1 mg, soluble in acetone and MeOH

mp : 260 °C [lit. not recorded (Wang; et al. 2007: 793-798), 316-318 °C (Atkinson; Gupta; & Lewis. 1969: 1507-1511)]

R_f : 0.26 (30% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

ES-MS m/z (% rel. Intensity) : 245 $[M+H]^+$ (100)

UV MeOH ; λ_{max} (log ε) : 234 (4.46), 258 (4.49), 309 (4.08), 373 (3.83)

IR KBr; ν_{max} (cm^{-1}) : 3421, 3282, 1645, 1620, 1584, 1481, 1450, 1353, 1299, 1259, 1212, 1165, 1149, 1078, 1020

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C-NMR (acetone-d_6, 75 MHz) : (Table 9)

Compound GM-4 (garcinone D, sss 3191, 3202, 3312)

Pale yellow needles 145.8 mg, soluble in acetone and MeOH

mp : 198-199 °C [lit. 210-211 °C (Orapin Komutiban. 2007: 37); 202-204 °C (Sen; et al. 1986: 1157-1158)]

R_f : 0.41 (40% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 429 $[M+H]^+$ (34), 266 (21); m/z: 427 $[M-H]^-$ (47)

UV MeOH; λ_{max} (log ε) : 243 (4.57), 258 (4.46), 316 (4.38), 353 (4.02)

IR KBr; ν_{max} (cm^{-1}) : 3416, 3260, 2968, 1645, 1608, 1566, 1461, 1384, 1342, 1302, 1278, 1230, 1200, 1093, 1078, 1056, 1010

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C-NMR (acetone-d_6, 75 MHz) : (Table 11)

Compound GM-5 (cratoxylone, sss 3750)

Yellow solid 9.0 mg, soluble in CH_2Cl_2, acetone and MeOH

mp : 230-231 °C [lit. gum (Bennett; et al. 1993: 1245-1251)]

R_f : 0.38 (40% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 429 $[M+H]^+$ (100)

UV MeOH ; λ_{max} (log ε) : 243 (4.62), 257 (4.52), 317 (4.42), 351 (4.12)

IR KBr; ν_{max} (cm^{-1}) : 3418, 3188, 2971, 1645, 1606, 1577, 1559, 1466, 1385, 1299, 1281, 1215, 1197, 1158, 1096, 1078, 1053, 1020

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C-NMR (acetone-d_6, 75 MHz) : (Table 13)

Compound GM-6 (sss 3597, 3630)

Pale yellow solid 10 mg, soluble in acetone and MeOH

mp : 192-193 °C

R_f : 0.16 (50% acetone-hexane), a blue green orange coloration with anisaldehyde-H_2SO_4 reagent

HR-TOFMS; m/z: 443.1714 calc 443.1711 for $[C_{24}H_{28}O_8-H]^-$

$[\alpha]_D^{28.9}$: 4.36 (c = 0.25, CH_3OH)

UV MeOH ; λ_{max} (log ε) : 207(4.59), 243(4.67), 251(4.60)sh, 305(4.43), 332(4.17)

IR KBr; ν_{max} (cm^{-1}) : 3443, 2971, 1613, 1598, 1577, 1461, 1439, 1407, 1383, 1279, 1199, 1134, 1084, 1002

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C-NMR (acetone-d_6, 75 MHz) : (Table 15)

Compound GM-7 (norathyriol, sss 3324, 3468)

Pale yellow amorphous 54.9 mg, soluble in acetone and MeOH

mp : 255 °C [lit. not recorded (Wang; et al. 2007: 793-798), 290 °C (Holloway; & Scheinmann. 1975: 2517-2518), 300 °C (Yates; & Stout. 1958: 1691-1700)]

R_f : 0.39 (50% acetone-hexane), a yellow orange coloration with anisaldehyde-H_2SO_4 reagent

HR-TOFMS; m/z: 259.0245 calc 259.0248 for $[C_{13}H_8O_6\text{-}H]^-$

ES-MS: m/z (% rel. Intensity) : 261 $[M+H]^+$ (95)

UV MeOH; λ_{max} (log ε) : 237 (4.56), 254 (4.61), 270 (4.21, sh), 312 (4.28), 364 (4.29)

IR KBr; ν_{max} (cm^{-1}) : 3385, 3231, 1653, 1635, 1610, 1570, 1475, 1447, 1418, 1385, 1297, 1178, 1125, 1078

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C-NMR (acetone-d_6, 75 MHz) : (Table 17)

Compound GM-8 (maclurin, sss 3887, 3985)

Yellow solid 34.9 mg, soluble in acetone and MeOH

mp : 211-213 °C [lit, 221-222 °C (Locksley; Moore; & Scheinmann. 1967: 2229-2234.)]

R_f : 0.38 (30% acetone-hexane), a yellow orange coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 261 $[M-H]^-$ (100); 263 $[M+H]^+$ (8)

UV MeOH: λ_{max} (log ε) : 233 (3.98), 253 (3.88), 314 (3.83), 364 (3.65)

IR KBr; ν_{max} (cm^{-1}) : 3442, 3202, 1618, 1476, 1403, 1291, 1168, 1111, 1060

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C-NMR (acetone-d_6, 75 MHz) : (Table 19)

Compound GM-9 (pruniflorone C, sss 3311, 4022)

Pale yellow solid 14.5 mg, soluble in acetone and MeOH

mp : 168-170 °C [lit, 134-136 °C (Boonnak; et al. 2006: 8850-8859)]

R_f : 0.39 (40% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 442 $[M^+]$ (63); 441 $[M-H]^-$ (100)

UV MeOH ; λ_{max} (log ε) : 243 (4.21), 255 (4.13), 314 (3.77), 352 (3.59)

IR KBr; ν_{max} (cm^{-1}) : 3447, 2968, 1645, 1599, 1577, 1458, 1425, 1385, 1284, 1208, 1172, 1114, 1053, 1010

^{1}H-NMR ($CDCl_3$, 300 MHz) and ^{13}C-NMR ($CDCl_3$, 75 MHz) : (Table 21)

Compound GM-10 (9-hydroxycalabaxanthone, sss 4332)

Yellow paste 18.3 mg, soluble in CH_2Cl_2, acetone and MeOH

R_f : 0.38 (30% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 407 $[M-H]^-$ (100)

UV MeOH ; λ_{max} (log ε) : 218 (4.36, sh), 242 (4.28), 277 (4.51, sh), 289 (4.58), 329 (4.24), 365 (3.80), 416 (3.36), 446 (3.21)

IR KBr; ν_{max} (cm^{-1}) : 3405, 2975, 2927, 1650, 1601, 1530, 1462, 1389, 1286, 1176, 1158, 1123, 1089, 1042

^{1}H-NMR ($CDCl_3$/CD_3OD, 300 MHz) : (Table 23)

Compound GM-11 (tachioside, sss 4044)

Brown solid 5.4 mg, soluble in MeOH

mp : 191-193 °C [colorless needles lit. 211-213 °C (Inoshiri; et al. 1987: 2811-2814)]

R_f : 0.3 (20% MeOH-CH_2Cl_2), a pink coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 604 $[2M]^+$ (67), 602 $[2M-2H]^-$ (100), 325 (64), 301 (44), 304 $[M+2H]^+$ (100), 302 $[M]^+$ (35)

$[\alpha]_D^{29.1}$: -28.8 (c = 0.25, CH_3OH) [lit. $[\alpha]_D$ -55.4 (c = 0.21, CH_3OH) (Inoshiri; et al. 1987: 2811-2814)]

UV MeOH ; λ_{max} (log ε) : 225 (4.14), 285 (3.80)

IR KBr; ν_{max} (cm^{-1}) : 3405, 2920, 1616, 1513, 1450, 1407, 1384, 1299, 1223, 1197, 1168, 1083, 1046

^{1}H-NMR (CD_3OD, 300 MHz) and ^{13}C-NMR (CD_3OD, 75 MHz) : (Table 24)

Physical and spectral data of the isolated compounds from the EtOAc extract of *G. xanthochymus*

Compound GX-1 (6-deoxyisojacareubin, sss 4289, 4369)

Yellow solid 2.6 mg, soluble in acetone and MeOH

mp : 233-234 °C [lit. 235-236 °C (Helesbeux; et al. 2004: 2293-2300)]

R_f : 0.45 (30% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 619 $[2M-H]^-$ (100), 345 (35)

UV MeOH ; λ_{max} (log ε) : 222 (3.1), 232 (3.2), 250 (3.5), 267 (3.4), 308 (2.9), 329 (3.00), 378 (2.4)

IR KBr; ν_{max} (cm^{-1}) : 3556, 3481, 3415, 1639, 1617, 1158, 1116, 1022

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C-NMR (acetone-d_6, 75 MHz) : (Table 28)

Compound GX-2 (12b-hydroxy-des-D-garcigerrin A, sss 4121, 4320)

Orange solid 640 mg, soluble in acetone and MeOH

mp : 229-230 °C [lit. not recored (Linuma; et al. 1995: 279-284)]

R_f : 0.30 (30% acetone-hexane), a blue green coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 623 $[2M-H]^-$ (100), 311 (24)

UV MeOH ; λ_{max} (log ε) : 238 (3.28), 249 (3.30), 264 (3.55), 317 (2.83), 409 (2.47)

IR KBr; ν_{max} (cm^{-1}) : 3548, 3481, 3414, 1637, 1617, 1586, 1500, 1458, 1402, 1287, 1237, 1176, 1015

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C NMR (acetone-d_6, 75 MHz) : (Table 30)

Compound GX-3 (1,6-dihydroxy-4,5-dimethoxyxanthone, sss 4135)

Yellow solid 38.5 mg, soluble in acetone and MeOH

mp : 220-221 °C [lit. not recored (Zhong; et al. 2007: 849-851.)]

R_f : 0.40 (30% acetone-hexane), a dark blue coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 287 $[M-H]^-$ (100)

UV MeOH ; λ_{max} (log ε) : 242 (3.5), 280 (3.1), 298 (3.0, sh), 314 (3.0), 374 (2.8)

IR KBr; ν_{max} (cm^{-1}) : 3474, 1654, 1609, 1584, 1496, 1458, 1361, 1254, 1195, 1094, 1068

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C NMR (acetone-d_6, 75 MHz) : (Table 32)

Compound GX-4 (2,5-dihydroxy-1-methoxyxanthone, sss 4261)

Yellow solid 3.2 mg, soluble in acetone and MeOH

mp : 200-201 °C [lit. 214-218 °C (Minami; et al. 1996: 629-633)]

R_f : 0.35 (40% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 257 $[M-H]^-$ (32), 273 (100)

UV MeOH ; λ_{max} (log ε) : 241 (3.6), 257 (3.7, sh), 288 (2.8), 309 (2.6), 377 (2.8)

IR KBr; ν_{max} (cm^{-1}) : 3548, 3481, 3415, 1623, 1593, 1497, 1436, 1373, 1290, 1226, 1203, 1165, 1079, 1056

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C NMR (acetone-d_6, 75 MHz) ; (Table 34)

Compound GX-5 (2,6-dihydroxy-1,5-dimethoxyxanthone, sss 4198, 4262)

Pale yellow solid 10.4 mg, soluble in acetone and MeOH

mp : 240-241 °C [lit. 206-209 °C (Minami; et al. 1994: 501-506)]

R_f : 0.3 (40% acetone-hexane), a yellow coloration with anisaldehyde-H_2SO_4 reagent

ES-MS: m/z (% rel. Intensity) : 452 $[2M+H]^+$ (46), 289 (27); m/z: 287 $[M-H]^-$ (79)

UV MeOH ; λ_{max} (log ε) : 241 (3.4), 249 (3.4, sh), 282 (2.8), 310 (3.0), 360 (2.6)

IR KBr; ν_{max} (cm^{-1}) : 3414, 1654, 1618, 1597, 1508, 1467, 1430, 1355, 1310, 1368, 1205, 1174, 1062

^{1}H-NMR (acetone-d_6, 300 MHz) and ^{13}C NMR (acetone-d_6, 75 MHz) : (Table 36)

CHAPTER 4

RESULTS AND DISCUSSION

1. Extraction and purification of compounds from *G. mangostana* root

A portion of the ethyl acetate extract (40 g) of the dried *G. mangostana* root was investigated by extensive column chromatographic methods (scheme 3, p. 56) to give a new xanthone as 3,6-dihydroxy-8-(3-hydroxy-3-methylbutyl)-7-methoxy-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone, along with seven known xanthones, including α- and β-mangostins (**1** and **2**), gentisein, gracinone D (**14**), norathyriol (**6**), cartoxylone, puniflorone C and known benzophenones, maclurin (**7**). In a likewise manner, a portion of the methanol extract (30 g) of the dried root of *G. mangostana* was isolated by column chromatographic methods (scheme 4, p. 58) to yield four xanthones, including α- and β-mangostins (**1** and **2**), 9-hydroxycalabaxanthone (**8**), gracinone D (**14**) and a phenol glycoside, tachioside. Their structures were established based on their UV, IR, MS and NMR data and by comparison their spectroscopic data with the literature values.

Table 2 All compounds obtained from *G. mangostana* root

	Compound	NMR code	isolable yield (based on 40 g of EtOAc extract)	isolable yield (based on 30 g of MeOH extract)
GM-1	α-mangostin (**1**)	3987	6.9 g	5 mg
GM-2	β-mangostin (**2**)	3029-3034	1.3 g	15 mg
GM-3	gentisein	3761	3.1 mg	-
GM-4	garcinone D (**14**)	3312, 3191	141 mg	4 mg
GM-5	cratoxylone	3750	9 mg	-
GM-6		3597,3630	10 mg	-
GM-7	norathyriol (**6**)	3324, 3468	54 mg	-
GM-8	maclurin (**7**)	3887, 3985	34 mg	-
GM-9	puniflorone C	3311, 4022	14 mg	-
GM-10	9-hydroxycalabaxanthone (**8**)	4432	-	18 mg
GM-11	tachinoside	4044	-	5 mg

Table 3 Phenolic compounds obtained from *G. mangostana*

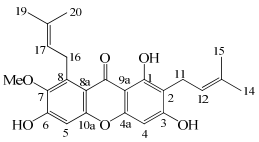
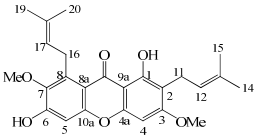
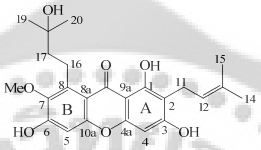
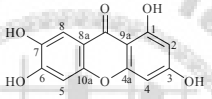
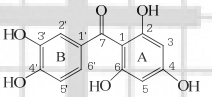
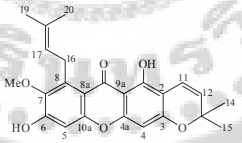
	Compound	Structure	Reference
GM-1	α-mangostin (**1**)		Yates; & Stout. 1958: 1691-1700 Suksamrarn; et al. 2003: 857-9
GM-2	β-mangostin (**2**)		Yates; & Bhat. 1968: 3770-3772 Suksamrarn; et al. 2003: 857-9
GM-4	garcinone D (**14**)		Bennett; et al. 1993: 1245-51 Suksamrarn; et al. 2003: 857-9 Orapin Komutiban; 2005: 94-95
GM-7	norathyriol (**6**)		Wang; et al. 2007: 793-798
GM-8	maclurin (**7**)		Kitanov; & Nedialkov. 2001: 1237-1243 Locksley; Moore; & Scheinmann. 1967: 2229-2234 Chiang; et al. 2003: 1070-1073
GM-10	9-hydroxy calabaxanthone (**8**)		Sen; et al. 1981: 183-185 Suksamrarn; et al. 2003: 857-9

Table 4 Phenolic compounds obtained from the different plants

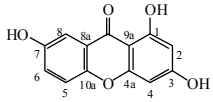
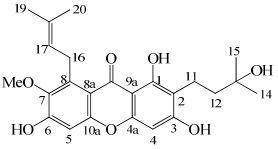
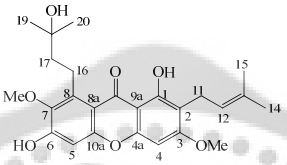
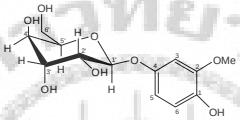
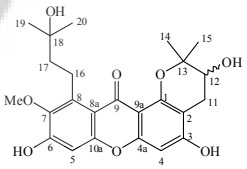
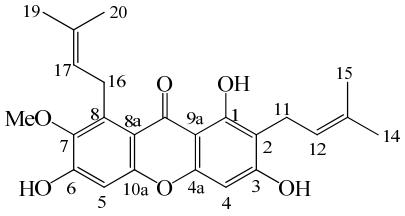
Compound		Structure	Reference
GM-3	gentisein		Kitanov; & Nedialkov. 2001: 1237-1243 Wang; et al. 2007: 793-798
GM-5	cratoxylone		Bennett; et al. 1993: 1245-51
GM-9	pruniflorone C		Boonnak; et al. 2006: 8850-8859
GM-11	tachinoside		Inoshiri; et al. 1987: 2811-2814

Table 5 New phenolic compounds obtained from the *G. mangostana*

	Compound	Structure
GM-6	3,6-dihydroxy-8-(3-hydroxy-3-methylbutyl)-7-methoxy-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano (2',3':1,2)xanthone	

1.1 Structures determination of compounds isolated from the ethyl acetate extract of *G. mangostana*

1.1.1 Structure determination of compound GM-1 (α-mangostin, sss 3987)



Compound **GM-1** was obtained as yellow needles with the R_f value of 0.38 (30% acetone-hexane) and gave a yellow green coloration with anisaldehyde-H_2SO_4 reagent. Its UV spectrum showed λ_{max} at 207, 243, 257, 314 and 361 nm and the IR absorption spectrum displayed ν_{max} at 3442 (OH stretching), 1642 (C=O stretching), 1609 and 1460 (C=C aromatic ring) cm^{-1}. The UV and IR spectra are in agreement with a xanthone nucleus (Roberts. 1961: 591-605, Scheinmann. 1962: 853-858).

The ^{1}H-NMR spectrum (Table 6) showed one chelated phenolic hydroxyl group [δ_H 13.74 (1-OH, *s*)], two signals of prenyl unit [δ_H 5.26 (1H, *brt*, *J* = 7.1 Hz), δ_H 3.41 (2H, *d*, *J* = 7.1 Hz), δ_H 1.66 (3H, *s*), δ_H 1.75 (3H, *s*) and δ_H 5.26 (1H, *brt*, *J* = 6.1 Hz), δ_H 4.06 (2H, *d*, *J* = 6.1 Hz), δ_H 1.81 (6H, *s*)], two aromatic singlets [δ_H 6.26 and 6.78] and a methoxyl group [δ_H 3.77 (*s*)].

The comparison of ^{1}H-NMR data of compound **GM-1** with known α-mangostin (**1**) isolated by our group (Suksamrarn; et al. 2003: 857-9) (Figure 49), compound **GM-1** was thus identified as 1,3,6-trihydroxy-7-methoxy-2,8-di-(3-methylbut-2-enyl)xanthone or α-mangostin (**1**).

α-Mangostin is the yellow coloring matter and always obtained as the major xanthones from various parts of the mangosteen tree. Mangosteen is by far the rich source, yielding 30-50% of mangostin (Yates; & Stout. 1958: 1691-1700).

Table 6 Comparison of NMR data of α-mangostin (**1**) with compound **GM-1**

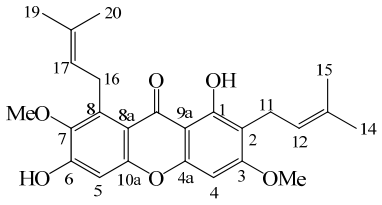
position	**α-mangostin** (CD_3OD)				**GM-1** (acetone-d_6)
	δ_H [a]	δ_C [c]	δ_H [b]	δ_C [b]	δ_H
1-OH	13.80 (1H, *s*)	159.8	13.74 (1H, *s*)	160.1	13.74 (1H, *s*)
2		109.8		109.9	
3		162.2		161.7	
4	6.28 (1H, *s*)	92.2	6.27 (1H, *s*)	92.2	6.26 (1H, *s*)
4a		154.1		154.7	
5	6.82 (1H, *s*)	101.7	6.72 (1H, *s*)	101.6	6.78 (1H, *s*)
6		156.8		155.6	
7		143.3		142.9	
7-OMe	3.81 (3H, *s*)	60.1	3.79 (3H, *s*)	60.9	3.77 (3H, *s*)
8		136.3		137.2	
8a		110.9		111.4	
9		181.2		181.8	
9a		101.9		103.0	
10a		154.5		155.3	
11	3.45 (2H, *d*, *J* = 7.0 Hz)	20.9	3.36 (2H, *d*, *J* = 7.0 Hz)	21.2	3.41 (2H, *d*, *J* = 7.1 Hz)
12	5.28 (2H, *t*)	122.5	5.27 (2H, *m*)	122.2	5.26 (1H, *brt*, *J* = 7.1 Hz)
13		130.2		131.4	
14	1.82 (3H, *s*)	17.8	1.81 (3H, *s*)	17.5	1.75 (3H, *s*)
15	1.70 (3H, *s*)	25.4	1.69 (3H, *s*)	25.5	1.66 (3H, *s*)
16	4.11 (2H, *d*, *J* = 7.0 Hz)	25.7	4.11 (2H, *d*, *J* = 6.3 Hz)	26.1	4.06 (2H, *d*, *J* = 6.1 Hz)
17	5.28 (2H, *t*)	123.7	5.27 (2H, *m*)	123.3	5.26 (1H, *brt*, *J* = 6.1 Hz)
18		130.3		131.8	
19	1.85 (3H, *s*)	17.9	1.83 (3H, *s*)	17.9	1.81 (3H, *s*)
20	1.78 (3H, *s*)	25.5	1.69 (3H, *s*)	25.6	1.81 (3H, *s*)

[a] Mahabusarakam; Wiriyachitha; & Taylor. 1987: 474-478.

[b] Measured in $CD_3OD/CDCl_3$ (Narisara Suwannapoch. 2002: 34-35.)

[c] Chen; Wan; & Loh. 1996: 381-382.

1.1.2 Structure determination of compound GM-2 (β-mangostin, sss 3030)



Compound **GM-2** was obtained as pale yellow needles with the R_f value of 0.3 (20% acetone-hexane) and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent. The UV spectrum showed λ_{max} at 244, 256, 314 and 357 nm. The IR absorption spectrum displayed ν_{max} at 3405 (OH stretching), 1645 (C=O stretching), 1601 and 1460 (C=C aromatic ring) cm^{-1}. The UV and IR data were characteristic of an oxygenated xanthone.

The ^{1}H-NMR spectrum (Table 7) showed chelated hydroxyl group [δ_H 13.40 (1-OH, *s*)], two signals of prenyl unit [δ_H 5.24 (1H, *brt*, *J* = 6.7 Hz), δ_H 3.33 (2H, *d*, *J* = 6.7 Hz), δ_H 1.66 (3H, *s*), δ_H 1.77 (3H, *s*) and δ_H 5.24 (1H, *brt*, *J* = 5.4 Hz), δ_H 4.07 (2H, *d*, *J* = 5.4 Hz), δ_H 1.67 (3H, *s*), δ_H 1.81 (3H, *s*)], two aromatic singlets [δ_H 6.32 (*s*) and 6.80 (*s*)] and two methoxyl groups [δ_H 3.79 (*s*) and δ_H 3.88 (*s*)]. The ^{13}C-NMR and DEPT spectrum (Table 7) showed 25 signals due to four methyls, two methylenes, two methoxyls, four methines, twelve quaternary carbons and a carbonyl carbon.

The comparison of ^{1}H-NMR data of **GM-2** with compound **GM-1** (Figure 50) showed the similar ^{1}H-NMR pattern, except for the presence of additional methoxyl group at δ_H 3.88 (s). The location of the methoxyl group was established at C-3 by the HMBC (Table 8, Figure 34) which showed correlation from the methoxyl group at δ_H 3.88 with C-3 (δ_C 55.8). The HMBC correlations from chelated hydroxyl group at δ_H 13.40 (1-OH) to C-1 (δ_C 159.7), C-2 (δ_C 111.5) and C-9a (δ_C 103.8), the prenyl proton H-11 at δ_H 3.33 showed correlations with C-1 (δ_C 159.7), C-2 (δ_C 111.5), C-3 (δ_C 163.5), C-12 (δ_C 122.3) and C-13 (δ_C 131.6) and correlations between H-16 at δ_H 4.07 with C-7 (δ_C 142.5), C-8 (δ_C 137.0), C-8a (δ_C 112.4), C-17 (δ_C 123.1) and C-18 (δ_C 132.0) were observed. These confirmed the position of the two prenyl and hydroxyl moieties in compound **GM-2** at C-2, C-8 and C-1, respectively.

From the comparison of ^{1}H- and ^{13}C-NMR spectra with the known β-mangostin (**2**) isolated by our group (Suksamrarn; et al. 2003: 857-9), compound **GM-2** was thus identified as 1,6-dihydroxy-3,7-dimethoxy-2,8-di-(3-methylbut-2-enyl)xanthone or β-mangostin (**2**).

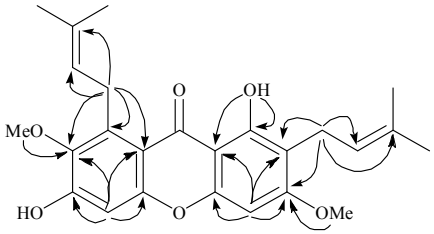


Figure 34 Selected HMBC correlations of compound **GM-2**

Table 7 Comparison of NMR data of β-mangostin (**2**) with compound **GM-2** in $CDCl_3$

position	β-mangostin			GM-2			
	δ_H [a]	δ_H [b]	δ_C [b]	δ_H	δ_C	DEPT 90	DEPT 135
1-OH	13.42 (1H, *s*)	13.39 (1H, *s*)	159.8	13.40 (1H, *s*)	159.7		
2			111.7		111.5		
3			163.5		163.5		
3-OMe	3.87 (3H, *s*)	3.88 (3H, *s*)	56.1	3.88 (3H, *s*)	55.8		55.8
4	6.34 (1H, *s*)	6.32 (1H, *s*)	89.0	6.32 (1H, *s*)	88.8	88.8	88.8
4a			155.7		155.7		
5	6.83 (1H, *s*)	6.81 (1H, *s*)	101.6	6.80 (1H, *s*)	101.4	101.4	101.4
6			155.3		155.2		
7			142.6		142.5		
7-OMe	3.81 (3H, *s*)	3.79 (3H, *s*)	62.3	3.79 (3H, *s*)	62.0		62.0
8			137.1		137.0		
8a			112.6		112.4		
9			181.9		181.9		
9a			104.0		103.8		
10a			154.4		154.3		
11	3.35 (2H, *d*, *J* = 7.1 Hz)	3.33 (2H, *d*, *J* = 7.0 Hz)	21.7	3.33 (2H, *d*, *J* = 6.7 Hz)	21.3		21.3
12	5.25 (1H, *m*)	5.21 (1H, *d*, *J* = 7.0 Hz)	122.4	5.24 (1H, *brt*, *J* = 6.7 Hz)	122.3	122.3	122.3
13			131.7		131.6		
14	1.80 (3H, *s*)	1.78 (3H, *s*)	18.1	1.77 (3H, *s*)	18.2		18.2
15	1.69 (3H, *s*)	1.67 (3H, *s*)	18.1	1.66 (3H, *s*)	25.8		25.8
16	4.09 (2H, *d*, *J* = 6.2 Hz)	4.08 (2H, *d*, *J* = 6.4 Hz)	26.9	4.07 (2H, *d*, *J* = 5.4 Hz)	26.5		26.5
17	5.25 (1H, *m*)	5.24 (1H, *d*, *J* = 6.4 Hz)	123.3	5.24 (1H, *brt*, *J* = 5.4 Hz)	123.1	123.1	123.1
18			132.1		132.0		
19	1.83 (3H, *s*)	1.81 (3H, *s*)	18.6	1.81 (3H, *s*)	17.7		17.7
20	1.69 (3H, *s*)	1.67 (3H, *s*)	26.1	1.67 (3H, *s*)	25.8		25.8
6-OH	6.32 (1H, *br s*)	6.30 (1H, *s*)					

[a] Likhitwitayawuid; Phadungcharoen; & Krungkrai. 1998: 70-72.

[b] Narisara Suwannapoch. 2002: 36-38.

Table 8 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-2**

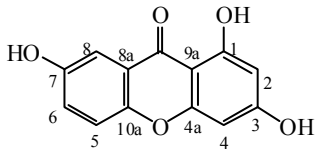
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1-OH	13.40 (1H, *s*)			C-1, C-2, C-9a
4	6.32 (1H, *s*)		C-4	C-2, C-3, C-4a, C-9, C-9a
5	6.80 (1H, *s*)		C-5	C-6, C-7, C-8a, C-10a
11	3.33 (2H, *d*, *J* = 6.7 Hz)	H-12	C-11	C-1, C-2, C-3, C-12, C-13
12	5.24 (1H, *brt*, *J* = 6.7 Hz)	H-11, H-14, H-15	C-12	C-11,C-14, C-15
14	1.77 (3H, *s*)	H-12	C-14	C-12, C-13, C-15
15	1.66 (3H, *s*)	H-12	C-15	C-12, C-13, C-14
16	4.07 (2H, *d*, *J* = 5.4 Hz)	H-17	C-16	C-7, C-8, C-8a, C-17, C-18
17	5.24 (1H, *brt*, *J* = 5.4 Hz)	H-16, H-19, H-20	C-17	C-19, C-20
19	1.81 (3H, *s*)	H-17	C-19	C-17, C-18, C-20
20	1.67 (3H, *s*)	H-17	C-20	C-17, C-18, C-19
3-OMe	3.88 (3H, *s*)			C-3
7-OMe	3.79 (3H, *s*)			C-7

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

1.1.3 Structure determination of compound GM-3 (gentisein or 1,3,7-trihydroxy xanthone, sss 3761)



Compound **GM-3** yielded in a very small amount (1.8 mg) as pale yellow solid with polarity [R_f value of 0.26 (30% acetone-hexane)] and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent. **GM-3** showed a molecular ion peak at *m/z* 245 $[M+H]^+$ in the ES-MS, corresponding to a molecular formula of $C_{13}H_8O_5$. The UV spectrum showed λ_{max} at 234, 258, 309 and 373 nm. The IR absorption spectrum displayed ν_{max} at 3421 (OH stretching), 1645 (C=O stretching), 1620 and 1481 (C=C aromatic ring) cm^{-1}. The UV and IR data indicated the **GM-3** to be a simple oxygenated xanthone structure.

The ^{1}H-NMR spectra of compound **GM-3** (Table 9, Figure 51) showed one chelated hydroxyl group [δ_H 12.97 (1-OH, *s*)], two signals of *meta*-coupled aromatic protons at δ_H 6.24 (1H, *d, J* = 2.0 Hz) and δ_H 6.39 (1H, *d*, *J* = 2.0 Hz), signals of ABX system aromatic protons at δ_H 7.44 (1H, *d*, *J* = 9.2 Hz), δ_H 7.35 (1H, *dd*, *J* = 9.2, 2.8 Hz) and δ_H 7.55 (1H, *d*, *J* = 2.8 Hz). The ^{13}C-NMR and DEPT spectra showed 13 carbon signals including five methines, seven quaternary carbons and a carbonyl carbon (Table 9).

HMBC spectrum (Table 10, Figure 35) of **GM-3** displayed a long-range correlations from *meta*-coupled aromatic proton at δ_H 6.24 (H-2) to C-1 (δ_C 164.6), C-3 (δ_C 166.3), C-4 (δ_C 94.5) and C-9a (δ_C 104.6), the HMBC correlations of an aromatic proton H-8 (δ_H 7.55) with C-6 (δ_C 125.1) and C-7 (δ_C 151.8). The chelated hydroxyl group (1-OH) at δ_H 12.97 exhibited HMBC cross-peaks with C-1 (δ_C 164.6), C-2 (δ_C 98.7) and C-9a (δ_C 104.6). Their observations together with the comparisons of the ^{1}H- and ^{13}C-NMR data of **GM-3** with 1,3,7-trihydroxyxanthone (Wang; et al. 2007: 793-798), led to the identification of **GM-3** to be 1,3,7-trihydroxyxanthone or gentisein which has been isolated from the methanol extract of the herb of *Hypericum annulatum* (Kitanov; & Nedialkov. 2001: 1237-1243

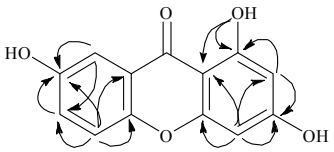


Figure 35 Selected HMBC correlations of compound **GM-3**

Table 9 Comparison of ^{1}H and ^{13}C NMR data of gentisein (in DMSO-d_6) with compound **GM-3** in acetone-d_6

Position	Gentisein		GM-3			
	δ_H [a]	δ_C [a]	δ_H	δ_C	DEPT 90	DEPT 135
1		162.5	12.97 (1H, *s*)	164.6		
2	6.20 (1H, *d*, *J* = 1.7 Hz)	97.8	6.24 (1H, *d*, *J* = 2.0 Hz)	98.7	98.7	98.7
3		165.5		166.3		
4	6.38 (1H, *d*, *J* = 1.7 Hz)	93.4	6.39 (1H, *d*, *J* = 2.0 Hz)	94.5	94.5	94.5
4a		157.6		158.9		
5	7.48 (1H, *d*, *J* = 9.0 Hz)	119.1	7.4 (1H, *d*, *J* = 9.2 Hz)	119.7	119.7	119.7
6	7.29 (1H, *dd*, *J* = 2.8, 9.0 Hz)	124.5	7.35 (1H, *dd*, *J* = 9.2, 2.8 Hz)	125.1	125.1	125.1
7		153.8		151.8		
8	7.42 (1H, *d*, *J* = 2.8 Hz)	108.0	7.55 (1H, *d*, *J* = 2.8 Hz)	109.3	109.3	109.3
8a		120.5		121.8		
9		179.9		180.0		
9a		102.0		104.6		
10a		149.1		151.8		

[a] Wang; et al. 2007: 793-798.

Table 10 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-3**

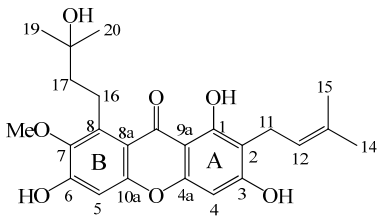
Position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1	12.97 (1H, *s*)			C-1, C-2, C-9a
2	6.24 (1H, *d*, *J* = 2.0 Hz)	H-4	C-2	C-1, C-3, C-4, C-9a
4	6.39 (1H, *d*, *J* = 2.0 Hz)	H-2	C-4	C-2, C-3, C-4a, C-9a
5	7.4 (1H, *d*, *J* = 9.2 Hz)	H-6	C-5	C-7, C-8a, C-10a
6	7.35 (1H, *dd*, *J* = 9.2, 2.8 Hz)	H-5, H-8	C-6	C-7, C-8
8	7.55 (1H, *d*, *J* = 2.8 Hz)	H-6	C-8	C-6, C-7

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

1.1.4 Structure determination of compound GM-4 (garcinone D, sss 3312)



Compound **GM-4** yielded as pale yellow needles with higher polarity [R_f value of 0.41 (40% acetone-hexane)] than α-mangostin (**1**) and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent as α-mangostin which indicated of a phenylated xanthone. The UV spectrum showed λ_{max} at 243, 258, 316 and 353 nm. The IR absorption spectrum displayed ν_{max} at 3416 (OH stretching), 1645 (C=O stretching), 1608 and 1461 (C=C aromatic ring) cm^{-1}. The UV and IR data were characteristic of a xanthone skeleton same as α-mangostin. It gave a molecular ion peak at *m/z* 429 $[M+H]^+$ in the ES-MS, corresponding to a molecular formula of $C_{24}H_{28}O_7$.

The ^{1}H-NMR spectrum (Table 11) showed the presence of a A_2B_2 system [δ_H 3.45 (2H, *brt*, *J* = 8.3 Hz), δ_C 23.2; δ_H 1.75 (2H, *brt*, *J* = 8.3 Hz), δ_C 45.6], a methyl singlet [δ_H 1.30 (6H, *s*), δ_C 29.5], a prenyl unit [δ_H 5.27 (1H, *brt*, *J* = 7.2 Hz), δ_C 123.4; δ_H 3.33 (2H, *d*, *J* = 7.2 Hz), δ_C 21.9; δ_H 1.77 (3H, *s*), δ_C 25.9 and δ_H 1.63 (3H, *s*), δ_C 17.9], a chelated hydroxyl [δ_H 13.82 (1-OH, *s*), δ_C 161.7], two aromatic singlets [δ_H 6.39 (*s*), δ_C 93.1 and 6.81 (*s*), δ_C 102.5] and a methoxyl group [δ_H 3.84 (*s*), δ_C 61.6]. The ^{13}C-NMR and DEPT spectrum (Table 11) showed 24 signals due to four methyls, three methylenes, a methoxyl, three methines, twelve quaternary carbons and a carbonyl carbon.

The ^{1}H-NMR spectra of compound **GM-4** (Table 11) was similar to those of compound **GM-1** (Figure 52), except for the presence of a 3-hydroxyl-3-methylbutyl group, instead of the prenyl group in ring B present in compound **GM-1**. In HMBC spectrum (Table 12, Figure 36) of **GM-4** displayed a long-range correlations from the A_2B_2 proton at δ_H 4.07 (H-16) to C-7 (δ_C 144.4), C-8 (δ_C 140.1), C-8a (δ_C 111.0), C-17 (δ_C 45.6) and C-18 (δ_C 70.5) confirming the placement of the 3-hyroxy-3-methylbutyl at C-8. The prenyl proton at δ_H 3.33 (H-11) showed correlations with C-2 (δ_C 112.0), C-3 (δ_C 163.0), C-12 (δ_C 123.4) and C-13 (δ_C 131.4), a methoxyl group at δ_H 3.84 showed correlation with C-7 (δ_C 144.4). This confirmed the position of the prenyl and methoxyl moieties in compound **GM-4** at C-2 and C-7, respectively.

From the comparison of ^{1}H-NMR spectra with the known garcinone D (**14**) (Table 11) isolated from the young fruit of *G. mangostana* of my M.S. Thesis report (Orapin Komutiban; 2005: 94-95), the structure of compound **GM-4** was deduced as 1,3,6-trihydroxy-2-(3-methylbut-2-enyl)-7-methoxy-8-(3-hydroxy-3-methylbutyl)xanthone or garcinone D.

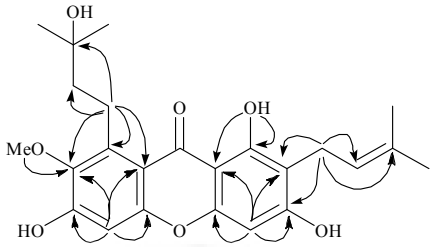


Figure 36 Selected HMBC correlations of compound **GM-4**

Table 11 Comparison of NMR data of garcinone D (**14**) with compound **GM-4** in acetone-d_6

Position	garcinone D[a]		GM-4			
	δ_H	δ_C	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1-OH	13.48 (1H, *s*)	161.7	13.82 (1H, *s*)	161.7		
2		111.8		112.0		
3		163.1		163.0		
4	6.40 (1H, *s*)	43.1	6.39 (1H, *s*)	93.1	93.1	93.1
4a		156.3		156.3		
5	6.82 (1H, *s*)	102.5	6.81 (1H, *s*)	102.5	102.5	102.5
6		157.7		157.4		
7		144.5		144.4		
7-OMe	3.86 (3H, *s*)	61.5	3.84 (3H, *s*)	61.6		61.6
8		140.0		140.1		
8a		111.0		111.0		
9		182.8		182.8		
9a		103.6		103.5		
10a		155.7		155.7		
11	3.32 (2H, *d*, *J* = 7.2 Hz)	22.0	3.33 (2H, *d*, *J* = 7.2 Hz)	21.9		21.9
12	5.28 (1H, *brt*, *J* = 7.2 Hz)	123.5	5.27 (1H, *brt*, *J* = 7.2 Hz)	123.4	123.4	123.4
13		131.3		131.4		
14	1.79 (3H, *br s*)	25.9	1.77 (3H, *s*)	25.9		25.9
15	1.65 (3H, *br s*)	17.9	1.63 (3H, *s*)	17.9		17.9
16	3.47 (2H, *m*)	23.2	3.45 (2H, *brt*, *J* = 8.3 Hz)	23.2		23.2
17	1.75 (2H, *m*)	45.7	1.75 (2H, *brt*, *J* = 8.3 Hz)	45.6		45.6
18		70.5		70.5		
19, 20	1.34 (6H, *s*)		1.30 (6H, *s*)	29.5		29.5

[a] Bennett; et al. (1993): 1245-51.

Table 12 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-4**

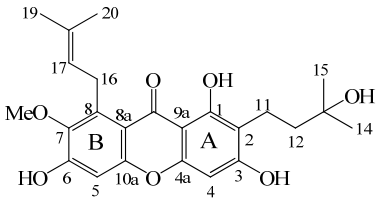
Position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1-OH	13.82 (1H, *s*)		C-1	C-1, C-2, C-9a
4	6.39 (1H, *s*)		C-4	C-2, C-3, C-4a, C-9, C-9a
5	6.81 (1H, *s*)		C-5	C-6, C-7, C-8a
11	3.33 (2H, *d, J* = 7.2 Hz)	H-12	C-11	C-2, C-3, C-12, C-13
12	5.27 (1H, *brt*, *J* = 7.2 Hz)	H-11, H-14, H-15	C-12	C-11, C-13, C-14, C-15
14	1.77 (3H, *s*)	H-12	C-14	C-12, C-13, C-15
15	1.63 (3H, *s*)	H-12	C-15	C-12, C-13, C-14
16	3.45 (2H, *brt*, *J* = 8.3 Hz)	H-17	C-16	C-7, C-8, C-8a, C-17
17	1.75 (2H, *brt*, *J* = 8.3 Hz)	H-16	C-17	C-16, C-18, C-19, C-20
19, 20	1.30 (6H, *s*)	H-16, H-17	C-19	C-17, C-18
7-OMe	3.84 (3H, *s*)			C-7

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

1.1.5 Structure determination of compound GM-5 (cratoxylone, sss 3750)



Compound **GM-5** was isolated in a small amount (9.0 mg) as a yellow solid, which showed a molecular ion peak at *m/z* 429 $[M+H]^+$ in the ESMS, corresponding to a molecular formula of $C_{24}H_{28}O_7$. The UV [λ_{max} at 243, 257, 317 and 351 nm] and IR [ν_{max} at 3418 (OH stretching), 1645 (C=O stretching), 1606 and 1466 (C=C aromatic ring) cm^{-1}] spectra of **GM-5** exhibited the same pattern as those of **GM-4**. The polarity of **GM-5** [R_f value of 0.38 (40% acetone-hexane)] and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent same as **GM-4**.

Extensive 1D and 2D NMR analysis of **GM-5** reveal that this xanthone has the same substituents as **GM-4** for a 3-hydroxyl-3-methylbutyl, a prenyl, one chelated hydroxyl, two aromatic protons and one methoxyl (Table 13). However, the ^{1}H- (Figure 53) and ^{13}C-NMR (Figure 54) spectral data of **GM-4** and **GM-5** exhibited different chemical shifts for the 3-hydroxyl-3-methylbutyl and prenyl moieties.

From HMBC spectral data (Table 14, Figure 37) the methylene proton at δ_H 2.74 (H-11) of a 3-hydroxyl-3-methylbutyl showed correlations with δ_C 161.6 (C-1) and δ_C 112.3 (C-2). It was therefore apparent there that the 3-hydroxyl-3-methylbutyl group was located at C-2 in ring A. In addition, the signal for downfield shift methylene proton at δ_H 4.10 (H-16) of a prenyl unit in compound **GM-5** showed correlations with δ_C 144.4 (C-7), δ_C 138.0 (C-8) and δ_C 112.0 (C-8a) and the methoxyl group at δ_H 3.78 showed correlation with δ_C 144.4 (C-7). It confirmed the position of the prenyl and methoxyl moieties in compound **GM-5** at C-8 and C-7, respectively.

From the spectroscopic evidence, the structure of compound **GM-5** was concluded to be 1,3,6-trihydroxy-2-(3-hydroxy-3-methylbutyl)-7-methoxy-8-(3-methylbut-2-enyl) xanthone or cratoxylone. Cratoxylone has been isolated from bark of *Cratoxylum cochinchinense* (Bennett; et al. 1993: 1245-51).

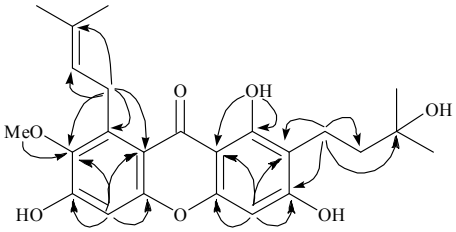


Figure 37 Selected HMBC correlations of compound **GM-5**

Table 13 Comparison of NMR data of cratoxylone with compound **GM-5**

position	**cratoxylone**[a] ($CDCl_3$)		**GM-5** (acetone-d_6)			
	δ_H	δ_C	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1-OH	13.83 (1H, *s*)	161.6	13.78 (1H, *s*)	161.6		
2		111.8		112.3		
3		163.3		163.2		
4	6.38 (1H, *s*)	93.3	6.36 (1H, *s*)	93.3	93.3	93.3
4a		155.6		156.1		
5	6.83 (1H, *s*)	102.7	6.81 (1H, *s*)	102.6	102.6	102.6
6		157.6		157.4		
7		144.5		144.4		
7-OMe	3.80 (3H, *s*)	61.2	3.78 (3H, *s*)	61.2		61.2
8		138.0		138.0		
8a		112.3		112.0		
9		182.8		182.8		
9a		103.5		103.5		
10a		156.2		155.6		
11	2.72 (2H, *m*)	17.8	2.74 (2H, *brt*, *J* = 8.0 Hz)	17.8		17.8
12	1.70 (2H, *m*)	43.2	1.69 (2H, *brt*, *J* = 8.0 Hz)	43.1		43.1
13		70.6		70.6		
14, 15	1.26 (6H, *s*)	29.1	1.24 (6H, *s*)	29.5		29.5
16	4.13 (2H, *d*, *J* = 6.5 Hz)	26.8	4.10 (2H, *d*, *J* = 6.6 Hz)	26.8		26.8
17	5.28 (1H, *brt*, *J* = 6.6 Hz)	124.8	5.26 (1H, *brt*, *J* = 6.6 Hz)	124.7	124.7	124.7
18		131.3		131.3		
19	1.83 (3H, *br s*)	25.9	1.81 (3H, *s*)	25.9		25.9
20	1.66 (3H, *br s*)	18.3	1.64 (3H, *s*)	18.2		18.2

[a] Bennett; et al. 1993: 1245-51

Table 14 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-5**

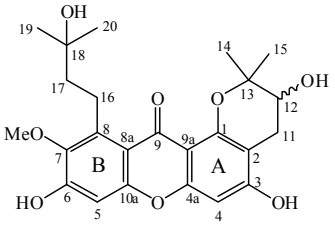
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1-OH	13.78 (1H, *s*)			C-1, C-2, C-9, C-9a
4	6.36 (1H, *s*)		C-4	C-2, C-3, C-4a, C-9, C-9a
5	6.81 (1H, *s*)		C-5	C-6, C-7, C-8, C-8a, C-9, C-10a
11	2.74 (2H, *brt*, *J* = 8.0 Hz)	H-12	C-11	C-1, C-2, C-3, C-12, C-13
12	1.69 (2H, *brt*, *J* = 8.1 Hz)	H-11	C-12	C-2, C-11, C-13
14, 15	1.24 (3H, *s*)		C-14, C-15	C-11, C-12, C-13, C-14, C-15
16	4.10 (2H, *d*, *J* = 6.6 Hz)	H-17	C-16	C-7, C-8, C-8a, C-17, C-18
17	5.26 (1H, *brt*, *J* = 6.6 Hz)	H-16	C-17	
19	1.81 (3H, *s*)		C-19	C-17, C-18, C-20
20	1.64 (3H, *s*)		C-20	C-17, C-18, C-19
7-OMe	3.78 (3H, *s*)			C-7

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

1.1.6 Structure determination of new compound GM-6 (sss 3630)



Compound **GM-6** was obtained as a yellow solid, mp 192-193 °C, the higher polarity of **GM-6** with the R_f value of 0.16 (50% acetone-hexane) than α-mangostin (**1**) and gave a blue-green coloration with anisaldehyde-H_2SO_4 reagent. A pseudo molecular ion at *m/z* 443.1714 in the negative-ion HR-TOF-MS established the molecular formula of $C_{24}H_{28}O_8$. The UV showed λ_{max} at 243 (4.67), 251 (4.60 sh), 305 (4.43), 332 (4.17) nm and IR spectrum displayed ν_{max} at 3443 (OH stretching), 1613 (C =O stretching), 1598 and 1461 (C=C aromatic ring) cm^{-1}. Its UV and IR data suggested that **GM-6** also possesses a xanthone skeleton.

The ^{1}H-NMR spectrum (Table 15) displayed signals for a 1,3,6,7-tetraoxygenated xanthone, which included two aromatic singlets at δ_H 6.37 and 6.69, a methoxyl group at δ_H 3.78, a 3-hydroxy-3-methylbutyl unit [δ_H 3.75 (2H, *brt*, *J* = 8.2 Hz), 1.72 (2H, *brt*, *J* = 8.2 Hz), 1.24 (6H, *s*)], a carbinol proton [δ_H 3.81 (1H, *brt, J* = 5.6, 7.7 Hz)], methylene proton of dimethylchroman ring showed signal at δ_H 2.53 (1H, *dd*, *J* = 7.7, 16.9 Hz) and 2.90 (1H, *dd*, *J* = 5.6, 16.9 Hz) and singlet of two tertiary methyl groups at δ_H 1.40 and 1.27, established a 3-hydroxy-2,2-dimethylchromane ring. Neither hydroxyl was present in the position since the ^{1}H-NMR spectrum (Table 15) lacked resonances for a chelated hydroxyl.

The ^{1}H- and ^{13}C-NMR spectral data of **GM-6** (Figure 55 and 56) closely resembled those of 11-hydroxy-1-isomangostin (**63**) (Sia; et al. 1995: 1521-1528) and garcinone D (**14**) (Bennett; et al. 1993: 1245-51) except for the presence in **GM-6** of a 3-hydroxy-3-methylbutyl moiety instead of a prenyl group. The ^{13}C-NMR and DEPT spectrum (Table 15) revealed 24 carbon signals including one methoxyl (δ_C 61.5), four methyls, three methylenes, three methines (δ_C 68.8, 93.9 and 101.8), twelve quaternary carbons and a carbonyl carbon at δ_C 176.4.

The structural assignments were substantiated by 2D NMR techniques (HMQC and HMBC) and NOE experiments. HMBC spectrum (Table 16, Figure 38) of **GM-6** displayed the methylene protons at δ_H 2.53 and 2.90 (H-11) showed a long-range heteronuclear connectivities with C-1 (δ_C 157.5), C-2 (δ_C 104.8) and C-3 (δ_C 160.7) as well as with C-12 (δ_C 68.8) and C-13 (δ_C 78.5), whereas H-12 (δ_C 3.81) was coupled with C-2 (δ_C 104.8), C-11 (δ_C 27.0), C-13

(δ_C 78.5), C-14 (δ_C 26.0) and C-15 (δ_C 20.5). The H-16 protons, resonating at δ_H 3.75, exhibited HMBC interactions with C-7 (δ_C 143.9), C-8 (δ_C 139.5), C-8a (δ_C 115.0), C-17 (δ_C 45.4) and C-18 (δ_C 70.2). The methoxyl signal at δ_H 3.78 showed a cross-peak with a quaternary aromatic carbon at δ_C 143.9. In an NOE enhancement, irradiation of H-16 (δ_H 3.75) gave rise to the enhancement of the methoxyl signal at δ_H 3.78. Similarly, irradiation of H-12 also results in NOE enhancement of the H-11, H-14 and H-15 resonances. Thus, the observed NMR signals are characteristic of a 1,3,6,7-tetraoxygenated xanthone with methoxyl, 3-hydroxy-3-methylbutyl, and 3-hydroxy-2,2-dimethylchromane ring moiety at C-7, C-8 and C-2, respectively.

Therefore, **GM-6** could be assigned as 3,6-dihydroxy-8-(3-hydroxy-3-methylbutyl)-7-methoxy-6',6'-dimethyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone. However, the data obtained did not permit the assignment of absolute configuration at C-12 for this compound.

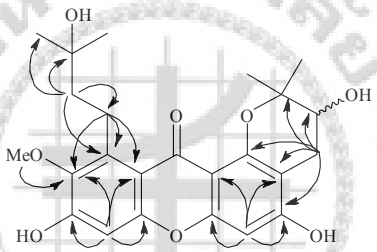


Figure 38 Selected HMBC correlations of compound **GM-6**

Table 15 Comparison of NMR data of garcinone D (**14**) and 11-hydroxy-1-isomangostin (**63**) with compound **GM-6** in acetone-d_6

position	garcinone D[a]		11-hydroxy-1-isomangostin[b]		GM-6			
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	DEPT 90	DEPT 135
1	13.48 (1H, *s*)	161.7		155.9		157.5		
2		111.8		105.0		104.8		
3		163.1		161.0		160.7		
4	6.40 (1H, *s*)	43.1	6.40 (1H, *s*)	94.2	6.37 (1H, *s*)	93.9	93.9	93.9
4a		156.3		157.6		155.4		
5	6.82 (1H, *s*)	102.5	6.72 (1H, *s*)	102.1	6.69 (1H, *s*)	101.8	101.8	101.8
6		157.7		155.8		156.0		
7		144.5		144.3		143.9		
7-OMe	3.86 (3H, *s*)	61.5	3.77 (3H, *s*)	61.0	3.78 (3H, *s*)	61.5		61.5
8		140.0		137.6		139.5		
8a		111.0		115.1		115.0		
9		182.8		176.3		176.4		
9a		103.6		107.7		107.6		
10a		155.7		154.9		155.0		
11	3.32 (2H, *d*, *J* = 7.2 Hz)	22.0	a 2.56 (1H, *dd*, *J* = 7.8, 16.8 Hz) b 2.94 (1H, *dd*, *J* = 5.7, 16.8 Hz)	27.1	a 2.53 (1H, *dd*, *J* = 7.7, 16.9 Hz) b 2.90 (1H, *dd*, *J* = 5.6, 16.9 Hz)	27.0		27.0
12	5.28 (2H, *brt*, *J* = 7.2 Hz)	123.5	3.82 (1H, *dd*, *J* = 5.7, 7.8 Hz)	69.0	3.81 (1H, *brt*, *J* = 5.6, 7.7 Hz)	68.8	68.8	68.8
13		131.3		78.5		78.5		
14	1.79 (3H, *br s*)	25.9	1.40 (3H, *s*)	20.6	1.40 (3H, *s*)	26.0		26.0
15	1.65 (3H, *br s*)	17.9	1.30 (3H, *s*)	26.0	1.27 (3H, *s*)	20.5		20.5
16	3.47 (2H, *m*)	23.2	4.05 (2H, *d*, *J* = 6.8 Hz)	26.6	3.75 (2H, *brt*, *J* = 8.2 Hz)	22.5		22.5
17	1.75 (2H, *m*)	45.7	5.31 (1H, *brt*, *J* = 6.8 Hz)	125.8	1.72 (2H, *brt*, *J* = 8.2 Hz)	45.4		45.4
18		70.5		130.5		70.2		
19, 20	1.34 (6H, *s*)		1.64 (3H, *s*) 1.81 (3H, *s*)	18.3 26.1	1.24 (6H, *s*)	29.5		29.5

[a] Bennett; et al. 1993: 1245-1251

[b] Sia; et al. 1995. 2521-2528

Table 16 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-6**

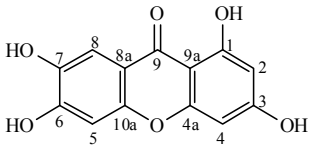
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
4	6.37 (1H, s)		C-4	C-1, C-2, C-3, C-9, C-9a
5	6.69 (1H, s)		C-5	C-6, C-7, C-8, C-8a, C-9, C-10a
11	a 2.53 (1H, *dd*, *J* = 7.7, 16.9 Hz)	H-12	C-11	C-1, C-2, C-3, C-12, C-13
	b 2.90 (1H, *dd*, *J* = 5.6, 16.9 Hz)			
12	3.81 (1H, *brt*, *J* = 5.6, 7.7 Hz)	H-11	C-12	C-2
14	1.40 (3H, *s*)		C-14	C-12, C-13, C-15
15	1.27 (3H, *s*)		C-15	C-12, C-13, C-14
16	3.75 (2H, *brt*, *J* = 8.2 Hz)	H-17	C-16	C-7, C-8, C-8a, C-17, C-18
17	1.72 (2H, *brt*, *J* = 8.2 Hz)	H-16	C-17	C-8, C-16, C-18, C-19, C-20
19, 20	1.24 (6H, *s*)		C-19, 20	C-17, C-18, C-19, C-20
7-OMe	3.78 (3H, *s*)			C-7

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

1.1.7 Structure determination of compound GM-7 (1,3,6,7-tetrahydroxyxanthone or norathyriol, sss 3324)



Compound **GM-7** yielded as pale yellow solid with polarity [R_f value of 0.39 (50% acetone-hexane)] and gave a yellow-orange coloration with anisaldehyde-H_2SO_4 reagent. It showed a molecular ion peak at *m/z* 261 $[M+H]^+$ in the ES-MS, corresponding to a molecular formula of $C_{13}H_8O_6$. The UV spectrum showed λ_{max} at 237, 254, 312 and 364 nm indicated the **GM-7** to be a simple oxygenated xanthone structure. The IR absorption spectrum displayed ν_{max} at 3385 (OH stretching), 1653 (C=O stretching), 1610 and 1475 (C=C aromatic ring) cm^{-1}.

The ^{1}H-NMR spectra of compound **GM-7** (Table 17) showed one singlet of chelated phenolic hydroxyl group [δ_H 13.19 (1-OH)], two aromatic singlets [δ_H 6.88 and 7.49] and the *meta*-coupled aromatic proton signals [δ_H 6.18 (1H, *d*, *J* = 1.6 Hz) and 6.32 (1H, *d*, *J* = 1.6 Hz)]. The ^{13}C-NMR and DEPT spectrum showed 13 carbon signals including four methines, eight quaternary carbons and a carbonyl carbon (Table 17).

HMBC spectrum (Table 18, Figure 39) of **GM-7** displayed a long-range correlations from *meta*-coupled aromatic proton at δ_H 6.18 (H-2) to C-1 (δ_C 163.5), C-3 (δ_C 164.6), C-4 (δ_C 93.5) and C-9a (δ_C 157.5), the aromatic proton signal at δ_H 7.49 (H-8) showed correlations with C-6 (δ_C 153.8), C-7 (δ_C 143.4), C-8a (δ_C 112.7) and C-9 (δ_C 179.5) and correlations between δ_H 6.88 (H-5) with C-6 (δ_C 153.8), C-7 (δ_C 143.4), C-8a (δ_C 112.7), C-9 (δ_C 179.5) and C-10a (δ_C 151.7) were observed. These observations together with the comparisons of the ^{1}H- and ^{13}C-NMR data of **GM-7** with norathyriol (**6**) (Wang; et al. 2007: 793-798), led to the identification of **GM-7** to be 1,3,6,7-tetrahydroxyxanthone or norathyriol (**6**). This compound was previously isolated from the heart wood of *G. mangostana* (Holloway; & Scheinmann. 1975: 2517-2518), from the aerial part of *Hypericum umbellatum* (Nediakov; et al. 2007: 118-120) and from the metabolites of mangiferin in rat urine (Wang; et al. 2007: 793-798)

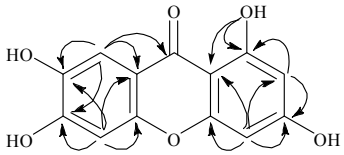


Figure 39 Selected HMBC correlations of compound **GM-7**

Table 17 Comparison of NMR data of norathyriol (**6**) in DMSO-d_6 with compound **GM-7** in acetone-d_6

position	norathyriol		GM-7			
	δ_H [a]	δ_C [a]	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1-OH		162.3	13.19 (1H, *s*)	163.5		
2	6.15 (1H, *d*, *J* = 1.6 Hz)	97.6	6.18 (1H, *d*, *J* = 1.6 Hz)	97.6	97.6	97.6
3		164.4		164.6		
4	6.33 (1H, *d*, *J* = 1.8 Hz)	93.6	6.32 (1H, *d*, *J* = 1.6 Hz)	93.5	93.5	93.5
4a		157.4		157.9		
5	6.83 (1H, *s*)	102.5	6.88 (1H, *s*)	102.5	102.5	102.5
6		154.1		153.8		
7		143.8		143.4		
8	7.36 (1H, *s*)	107.8	7.49 (1H, *s*)	108.1	108.1	108.1
8a		111.8		112.7		
9		178.8		179.5		
9a		101.6		102.2		
10a		151.2		151.7		

[a] Wang; et al. 2007: 793-798.

Table 18 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-7**

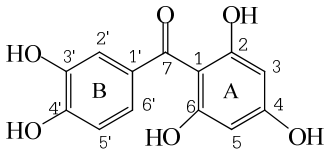
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1-OH	13.19 (1H, *s*)			C-1, C-2, C-9a
2	6.18 (1H, *d*, *J* = 1.6 Hz)	H-4	C-2	C-1, C-3, C-4, C-9a
4	6.32 (1H, *d*, *J* = 1.6 Hz)	H-2	C-4	C-2, C-3, C-4a, C-9a
5	6.88 (1H, *s*)		C-5	C-6, C-7, C-8a, C-9, C-10a
8	7.49 (1H, *s*)		C-8	C-6, C-7, C-8a, C-9, C-10a

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

1.1.8 Structure determination of compound GM-8 (maclurin, sss 3887)



Compound **GM-8** was obtained as yellow solid with the R_f value of 0.38 (30% acetone-hexane) and gave a yellow-orange coloration with anisaldehyde-H_2SO_4 reagent. It showed a molecular ion peak at *m/z* 263 $[M+H]^+$ in the ES-MS, corresponding to a molecular formula of $C_{13}H_{10}O_6$. The UV spectrum showed λ_{max} at 243, 255, 314 and 352 nm. The IR absorption spectrum displayed ν_{max} at 3442 (OH stretching), 1645 (C=O stretching), 1599 and 1458 (C=C aromatic ring) cm^{-1}.

The ^{1}H-NMR spectral data (Table 19, Figure 57) showed the presence of broad signals for the two chelated hydroxyl protons at δ_H 9.98 (2H). The presence of five substituents of aromatic rings of **GM-8** was confirmed by DEPT experiment (Table 19). The signals at δ_H 5.84 indicated a symmetrical tri-substituted benzene ring A, which was confirmed by the presence of the overlapping signals in ^{13}C-NMR at δ_C 164.4 (C-2 and C-6) and δ_C 95.8 (C-3 and C-5), the signals of ABX system of three aromatic protons from ring B, at δ_H 7.20 (1H, *d*, *J* = 2.0 Hz, H-2'); δ_C 116.8, δ_H 6.83 (1H, *d*, *J* = 8.3 Hz, H-5'); δ_C 115.0 and δ_H 7.06 (1H, *dd*, *J* = 8.3, 2.0 Hz, H-6'); δ_C 123.2. This fact pointed to the *ortho*- and *meta*-positions of the protons and an asymmetrical structure of this ring.

The ^{13}C-NMR (Figure 58) and DEPT spectrum (Table 19) which showed 13 carbon signals including five methines (δ_C 95.8 x 2, 115.0, 117.1 and 123.3), two quaternary carbons (δ_C 105.7 and 133.7), five oxygen-bearing quaternary carbons (δ_C, 145.0, 149.9, 162.7 and 164.4 x 2) and a carbonyl carbon at δ_C 197.9 was characteristic of a benzophenone derivative.

HMBC spectrum (Table 20, Figure 40) of **GM-8** displayed a long-range correlations from *meta*-coupled aromatic proton at δ_H 5.84 (H-3, H-5) to C-1 (δ_C 105.7), C-2 (δ_C 164.4), C-3 (δ_C 95.8), C-4 (δ_C 162.7), C-5 (δ_C 95.8) and C-7 (δ_C 197.9), the aromatic proton signals at δ_H 7.10 (H-2') and δ_H 6.71 (H-5') correlated to C-1' (δ_C 133.7), C-3' (δ_C 145.0), C-4' (δ_C 149.9), C-6' (δ_C 123.3) and C-7 (δ_C 197.9) were also observed. The ^{1}H- and ^{13}C-NMR spectra were similar to those of 3',4,4',6-tetrahydroxy-2-methoxybenzophenone. The only difference between their structures was that **GM-8** had a hydroxyl group attached to C-2, instead of a methoxyl group existing in 3',4,4',6-tetrahydroxy-2-methoxybenzophenone. These spectral data disclosed that

GM-8 was a benzophenone comprising 1,2,4,6-tetrasubstituted (ring A), and 1,3,4-trisubstituted (ring B) benzene rings. Ring A was assigned as 2,4,6-trihydroxyphenyl and Ring B was shown to be 3,4-dihydroxyphenyl by analysis of HMBC (Figure 40). Their observations together with the comparisons of the ^{1}H-NMR data of **GM-8** with 2,4,6,3'4'-pentahydroxy benzophenone or maclurin (**7**) (Locksley; Moore; & Scheinmann. 1967: 2229-2234), Chiang; et al. 2003: 1070-1073), led to the identification of **GM-8** to be 2,4,6,3'4'-pentahydroxy benzophenone or maclurin (**7**).

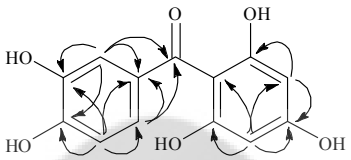
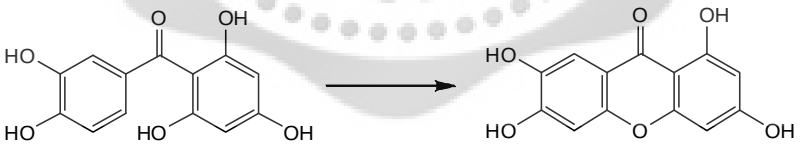


Figure 40 Selected HMBC correlations of compound **GM-8**

In our case, in the *G. mangostana* we found the co-occurrence of benzophenone (**GM-8**) together with 1,3,6,7-tetrahydroxyxanthone (**GM-7**). The benzophenone **GM-8** was easily transformed into **GM-7** by acid or enzymatic hydrolysis. This fact supports the evidence that **GM-8** is a precursor of **GM-7** (Figure 40). The transformation is realized by dehydration involving hydroxyls from phloroglucinol ring A, located *ortho* to the carbonyl group. These results pointed to the fact that one of the biosynthesis pathways of xanthone formation in plants (Kitanov; & Nedialkov. 2001: 1237-1243).



benzophenone **(GM-8)** 1,3,6,7-tetrahydroxyxanthone (**GM-7**)

Figure 41 Transformation of benzophenone (**GM-8**) into 1,3,6,7-tetrahydroxyxanthone (**GM-7**)

Table 19 Comparison of NMR data of 4,6,3'4'-tetrahydroxy-2-methoxybenzophenone, maclurin (**7**) with compound **GM-8**

position	**4,6,3'4'-tetrahydroxy-2-methoxybenzophenone** (CD_3OD)		**maclurin (7)** (DMSO-d_6)	**GM-8** (acetone-d_6)			
	δ_H [a]	δ_C [a]	δ_H [b]	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1		107.8			105.7		
2		157.9		9.98 (1H, *br s*, OH)	164.4		
2-OMe	3.54 (3H, *s*)	54.7					
3	5.95 (1H, *d*, *J* = 1.8 Hz)	90.2	6.21 (1H, *d*, *J* = 2.0 Hz)	5.84 (1H, *br s*)	95.8	95.8	95.8
4		158.9		8.53 (1H, *br s*, OH)	162.7		
5	5.98 (1H, *d*, *J* = 1.8 Hz)	94.8	6.21 (1H, *d*, *J* = 2.0 Hz)	5.84 (1H, *br s*)	95.8	95.8	95.8
6		155.7		9.98 (1H, *br s*, OH)	164.4		
7		192.7			197.9		
1'		129.9			133.7		
2'	7.14 (1H, *d*, *J* = 1.8 Hz)	115.6	7.62 (1H, *d*, *J* = 1.7 Hz)	7.10 (1H, *d*, *J* = 2.0 Hz)	117.1	117.1	117.1
3'		144.3		8.53 (1H, *br s*, OH)	145.0		
4'		149.8			149.9		
5'	6.74 (1H, *d*, *J* = 8.2 Hz)	114.4	6.91 (1H, *d*, *J* = 8.4 Hz)	6.71 (1H, *d*, *J* = 8.2 Hz)	115.0	115.0	115.0
6'	7.04 (1H, *dd*, *J* = 8.2, 1.8 Hz)	121.6	7.52 (1H, *dd*, *J* = 8.4, 1.7 Hz)	7.02 (1H, *dd*, *J* = 8.2, 2.0 Hz)	123.3	123.3	123.3

[a] Chiang; et al. 2003: 1070-1073

[b] www. nmrdb.org

Table 20 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-8**

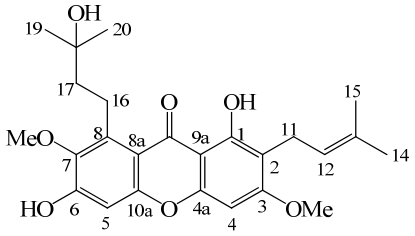
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
2	9.98 (1H, *br s*, OH)			
3	5.84 (1H, *br s*)	H-5	C-3	C-1, C-2, C-4, C-5
4	8.53 (1H, *br s*, OH)			
5	5.84 (1H, *br s*)	H-3	C-5	C-1, C-3, C-4, C-6, C-7
6	9.98 (1H, *br s*, OH)			
2'	7.10 (1H, *d*, *J* = 2.0 Hz)	,H-6'	C-2'	C-1′, C-3′, C-4′, C-6′, C-7
5'	6.71 (1H, *d*, *J* = 8.2 Hz)	H-6'	C-5'	C-1′, C-2′, C-3′, C-4′, C-6′
6'	7.02 (1H, *dd*, *J* = 8.2, 2.0 Hz)	H-2',H-5'	C-6'	C-2′, C-3′, C-4′, C-5′, C-7

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

1.1.9 Structure determination of compound GM-9 (pruniflorone C, sss 3311)



Compound **GM-9** was obtained as yellow solid with the R_f value of 0.39 (40% acetone-hexane) and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent. It showed a molecular ion peak at *m/z* 441 $[M-H]^-$ in the ES-MS, corresponding to a molecular formula of $C_{25}H_{30}O_7$. The UV spectrum showed λ_{max} at 243, 255, 314 and 352 nm. The IR absorption spectrum displayed ν_{max} at 3447 (OH stretching), 1645 (C=O stretching), 1599 and 1458 (C=C aromatic ring) cm^{-1}. The UV and IR spectra are in agreement with a xanthone nucleus.

The ^{1}H-NMR spectral data (Table 21) showed signals characteristic of a chelated phenolic hydroxyl [δ_H 13.68 (1-OH, *s*); δ_C 160.5], a prenyl unit at δ_H 5.19 (1H, *brt*, *J* = 7.1 Hz, H-12); δ_C 123.2, δ_H 3.33 (2H, *d*, *J* = 7.1 Hz, H-11); δ_C 20.5, δ_H 1.74 (3H, *s*, H-14); δ_C 25.8, δ_H 1.62 (3H, *s*, H-15); δ_C 17.8, signals for a 3-hydroxyl-3-methylbutyl group at δ_H 3.45 (2H, *brt*, *J* = 8.4 Hz, H-16); δ_C 23.2, δ_H 1.74 (2H, *brt*, *J* = 8.5 Hz, H-17); δ_C 45.6 and δ_H 1.27 (6H, *s*, H-19,20); δ_C 29.5, two aromatic singlets [δ_H 6.50 (*s*, H-4); δ_C 89.8 and 6.84 (*s*, H-5); δ_C 102.4] and two methoxyl groups [δ_H 3.96 (*s*); δ_C 56.5 and δ_H 3.84 (*s*); δ_C 61.6]. The ^{13}C-NMR and DEPT spectrum (Table 21) showed 25 signals due to four methyls, three methylenes, two methoxyls, three methines, twelve quaternary carbons and a carbonyl carbon.

The comparison of ^{1}H-NMR data of compound **GM-9** (Figure 59) showed the similar ^{1}H-NMR pattern as garcinone D (**14**), except for the presence of two singlet signals for methoxyl group at δ_H 3.79 and δ_H 3.88. The locations of the methoxyl groups were established to be at C-3 and C-7 by the HMBC experiment (Table 22, Figure 42) which showed correlations of the methoxyl group at δ_H 3.96 and δ_H 3.84 with C-3 (δ_C 164.5) and C-7 (δ_C 144.5), respectively. The chelated hydroxyl group (1-OH) at δ_H 13.68 exhibited HMBC cross-peaks with C-1 (δ_C 160.5), C-2 (δ_C 112.1) and C-9a (δ_C 104.1), the prenyl proton H-11 at δ_H 3.33 showed correlations with C-1 (δ_C 160.5), C-2 (δ_C 112.1), C-3 (δ_C 164.5), C-12 (δ_C 123.2), C-13 (δ_C 131.5), C-14 (δ_C 17.8) and C-15 (δ_C 25.8) and correlation between H-16 at δ_H 3.45 with C-7 (δ_C 144.5), C-8 (δ_C 140.1), C-8a (δ_C 111.7), C-17 (δ_C 45.6), C-18 (δ_C 70.4), C-19 and C-20 (δ_C 29.5). This confirmed the

position of the prenyl moietie at C-2 and a 3-hydroxyl-3-methylbutyl at C-8, respectively, in compound **GM-9**. Moreover, an NOE enhancement was observed from the 3-OMe to H-4 in NOESY spectrum also confirmed the placement of 3-OMe.

Comparison of the above NMR data with known Pruniflorone C (Boonnak; et al. 2006: 8850-8859), compound **GM-9** was thus identified as 1,6-dihydroxy-8-(3-hydroxy-3-methyl butyl)-3,7-dimethoxy-2-(3-methylbut-2-enyl)xanthone or pruniflorone C which has been isolated from the root and bark of *Cratoxylum formosum* sp. *pruniflorum*.

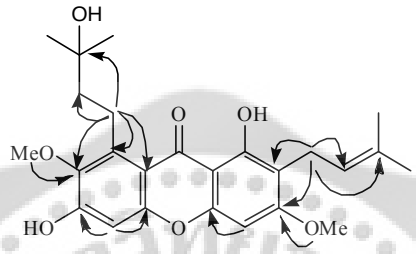


Figure 42 Selected HMBC correlations of compound **GM-9**

Table 21 Comparison of NMR data of pruniflorone C with compound **GM-9**

position	pruniflorone C		GM-9[b]			
	δ_H [a]	δ_C [a]	δ_H	δ_C	DEPT 90	DEPT 135
1-OH		159.1	13.68 (1H, *s*)	160.5		
2		111.3[a]		112.1		
3		163.3		164.5		
3-OMe	3.90 (3H, *s*)	55.3	3.96 (3H, *s*)	56.5		56.5
4	6.32 (1H, *s*)	88.7	6.50 (1H, *s*)	89.8	89.8	89.8
4a		155.1		156.3		
5	6.75 (1H, *s*)	101.7	6.84 (1H, *s*)	102.4	102.4	102.4
6		156.0		157.5		
7		143.1		144.5		
7-OMe	3.84 (3H, *s*)	61.2	3.84 (3H, *s*)	61.6		61.6
8		138.4		140.1		
8a		111.2[a]		111.7		
9		181.8		182.9		
9a		103.5		104.1		
10a		155.6		156.1		
11	3.33 (2H, *d*, *J* = 7.2 Hz)	21.1	3.33 (2H, *d*, *J* = 7.1 Hz)	20.5		20.5
12	5.21 (1H, *brt*, *J* = 7.2 Hz)	122.1	5.19 (1H, *brt*, *J* = 7.1 Hz)	123.2	123.2	123.2
13		131.6		131.5		
14	1.79 (3H, *s*)	17.5	1.74 (3H, *s*)	25.8		25.8
15	1.68 (3H, *s*)	25.6	1.62 (3H, *s*)	17.8		17.8
16	3.39 (2H, *m*)	21.8	3.45 (2H, *brt*, *J* = 8.4 Hz)	23.2		23.2
17	1.77 (2H, *m*)	44.0	1.74 (2H, *brt*, *J* = 8.5 Hz)	45.6	45.6	45.6
18		70.8		70.4		
19, 20	1.32 (6H, *s*)	28.7	1.27 (6H, *s*)	29.5		29.5

[a] Measured in $CD_3OD/CDCl_3$ (Boonnak; et al. 2006: 8850-8859)

[b] Measured in $CDCl_3$

Table 22 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-9**

position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1-OH	13.68 (1H, *s*)			C-1, C-2, C-9a
4	6.50 (1H, *s*)		C-4	C-2, C-3, C-4a, C-9, C-9a
5	6.84 (1H, *s*)		C-5	C-6, C-7, C-8, C-8a, C-9
11	3.33 (2H, *d*, *J* = 7.1 Hz)	H-12	C-11	C-1, C-2, C-3, C-12, C-13
12	5.19 (1H, *brt*, *J* = 7.1 Hz)	H-11	C-12	C-11
14	1.74 (3H, *s*)	H-12	C-14	C-12, C-13, C-15
15	1.62 (3H, *s*)	H-12	C-15	C-12, C-13, C-14
16	3.45 (2H, *brt*, *J* = 8.4 Hz)	H-17	C-16	C-7, C-8, C-8a, C-17, C-18
17	1.74 (2H, *brt*, *J* = 8.5 Hz)	H-16	C-17	C-8, C-16, C-18, C-19, C-20
19, 20	1.27 (6H, *s*)	H-19, H-20	C-19, C-20	C-17, C-18, C-19, C-20
3-OMe	3.96 (3H, *s*)			C-3
7-OMe	3.84 (3H, *s*)			C-7

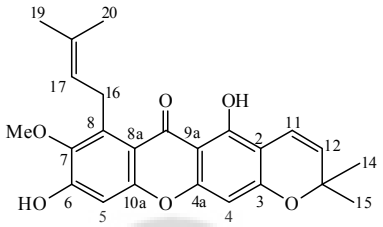
[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

1.2 Structures determination of compounds isolated from the methanol extract of *G. mangostana*

1.2.1 Structure determination of compound GM-10 (9-hydroxycalabaxanthone, sss 4332)



Compound **GM-10** was isolated as a yellow paste with lower polarity [R_f value of 0.37 (20% acetone-hexane)] than α-mangostin (**1**) and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent as α-mangostin which indicated of a phenylated xanthone. Which showed a molecular ion peak at *m/z* 407 $[M-H]^-$ in the ES-MS, corresponding to a molecular formula of $C_{24}H_{24}O_6$. The UV spectrum showed λ_{max} at 203, 218 sh, 242, 277 sh, 289, 329, 365, 416, 446 nm. The IR absorption spectrum displayed ν_{max} at 3405 (OH stretching), 1650 (C=O stretching), 1601 and 1462 (C=C aromatic ring) cm^{-1}. The UV and IR data were characteristic of a xanthone skeleton.

The ^{1}H-NMR spectrum (Table 23) showed signals of prenyl unit [δ_H 4.09 (2H, *d*, *J* = 6.2 Hz), δ_H 5.24 (1H, *brt*, *J* = 6.2 Hz), δ_H 1.69 (3H, s) and δ_H 1.73 (3H, s)], one 2,2-dimethylchromene ring [δ_H 6.72 (1H, *d*, *J* = 10 Hz), δ_H 5.57 (1H, *d*, *J* = 10 Hz) and δ_H 1.46 (6H, *s*)], one chelated hydroxyl group [δ_H 13.84 (*s*)], two aromatic singlets [δ_H 6.23 (*s*) and 6.76 (*s*)] and one methoxyl group [δ_H 3.79 (*s*)]. The comparison of ^{1}H-NMR data with compound **GM-1** showed the similar ^{1}H-NMR pattern, except the one prenyl unit of **GM-1** was instanced with 2,2-dimethylchromene ring. From the literature search, compound **GM-10** showed the same ^{1}H-NMR data as 9-hydroxycalabaxanthone (Sen; et al. 1981: 183-185). Therefore, compound **GM-10** was identified as 1,6-dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-6′,6′-dimethylpyrano-(2′,3′:3,2) xanthone or 9-hydroxycalabaxanthone (**8**).

Table 23 Comparison of NMR data of 9-hydroxycalabaxanthone (**8**) with compound **GM-10**

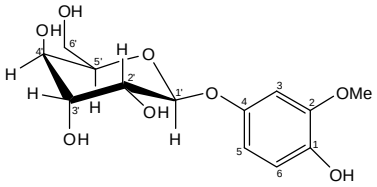
position	9-hydroxycalabaxanthone			GM-10[c]
	δ_H [a]	δ_C [a]	δ_H [b]	δ_H
1-OH	13.55 (1H, *s*)	157.8	13.72 (1H, *s*)	13.84 (1H, *s*)
2		104.4		
3		159.8		
4	6.15 (1H, *s*)	94.0	6.31 (1H, *s*)	6.23 (1H, *s*)
4a		156.1		
5	6.27 (1H, *s*)	101.6	6.82 (1H, *s*)	6.76 (1H, *s*)
6-OH		154.5		
7		142.7		
7-OMe	3.73 (3H, *s*)	61.8	3.82 (3H, *s*)	3.79 (3H, *s*)
8		136.9		
8a		112.1		
9		181.8		
9a		103.6		
10a		155.6		
11	6.64 (1H, *d*, *J* = 10.0 Hz)	115.6	6.73 (1H, *d*, *J* = 10.0 Hz)	6.72 (2H, *d*, *J* = 10 Hz)
12	5.47 (1H, *d*, *J* = 10.0 Hz)	126.9	5.55 (1H, *d*, *J* = 10.0 Hz)	5.57 (1H, *d*, *J* = 10 Hz)
13		77.8		
14, 15	1.40 (2x3H, 2x*s*)	28.3	1.49 (2x3H, 2x*s*)	1.46 (6H, *s*)
16	4.01 (2H, *d*, *J* = 6.5 Hz)	26.5	4.09 (2H, *d*, *J* = 6.0 Hz)	4.09 (2H, *d*, *J* = 6.2 Hz)
17	5.18 (1H, *t*, *J* = 6.5 Hz)	123.1	5.29 (1H, *t*, *J* = 6.0 Hz)	5.24 (1H, *brt*, *J* = 6.2 Hz)
18		131.8		
19	1.76 (3H, *s*)	18.1	1.85 (3H, *s*)	1.73 (3H, *s*)
20	1.62 (3H, *s*)	25.6	1.72 (3H, *s*)	1.69 (3H, *s*)

[a] Measured in $CDCl_3$ (Sen; et al. 1981: 183-185)

[b] Measured in $CDCl_3$ (Orapin Komutiban. 2004: 44-47)

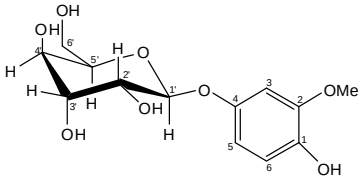
[c] Measured in $CDCl_3$/ 5drps CD_3OD

1.2.2 Structure determination of compound GM-11 (tachioside, sss 4044)

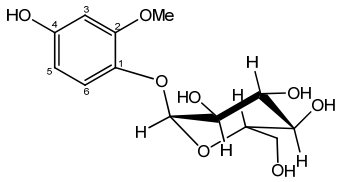


Compound **GM-11** was obtained as a brown solid with high polarity [R_f value of 0.30 (20% MeOH-CH_2Cl_2)], **GM-11** gave a pink coloration with anisaldehyde-H_2SO_4 reagent which indicated that it was not a xanthone. It showed a molecular ion peak at *m/z* 301 $[M-H]^-$ in its negative ion ES-MS, which corresponding to a molecular formula of $C_{13}H_{18}O_8$. The UV spectrum showed λ_{max} at 225, 285 nm. The IR absorption spectrum suggested for the presence of ν_{max} at 3405 (OH stretching), 1513 (C-O stretching), 1616 and 1450 (C=C aromatic ring) cm^{-1}.

The ^{1}H-NMR spectrum (Table 24, Figure 60) showed the presence of a singlet methoxyl group [δ_H 3.70; δ_C 56.3)], an ABX system of aromatic protons [δ_H 6.79 (1H, *d*, *J* = 2.6 Hz); δ_C 103.7), δ_H 6.57 (1H, *dd*, *J* = 8.6, 2.6 Hz); δ_C 110.0 and δ_H 6.67 (1H, *d*, *J* = 8.6 Hz); δ_C 116.0] which is typical of 1,2,4-trisubstituted aromatic ring, and a glucose unit with a glucosyl anomeric porton [δ_H 4.73 (1H, *d*, *J* = 7.2 Hz); δ_C 103.7], [δ_H 3.35 (1H, *br d*, *J* = 7.2 Hz), δ_C 75.0; H-2'], [δ_H 3.38 (2H, *m*), δ_C 78.1 and 71.5; H-3',4'], [δ_H 3.40 (1H, *m*), δ_C 78.0; H-5'] and [δ_H 3.89 (1H, *dd*, *J* = 12, 1.9 Hz; H-6'a) and δ_H 3.69 (1H, *dd*, *J* = 12, 5.4 Hz; H-6'b) δ_C 62.6]. The ^{13}C-NMR (Figure 61) and DEPT spectrum showed 13 carbon signals including eight methines, one methylene, three quaternary carbons and a methoxyl carbon (Table 24). **GM-11** could be a phenolic glucoside with a methoxyl group. The structure of **GM-11** was apparent to be tachioside (**a**) or isotachioside (**b**) (Inoshiri; et al. 1987: 2811-2814).



a



b

The ^{1}H -^{13}C long range correlation spectrum (Table 25, Figure 43) showed correlation of the glucosyl carbon at δ_C 103.7 (C-1') with aromatic protons at δ_H 6.79 (H-3) and δ_H 6.57 (H-5) and methoxyl group at δ_H 3.70 showed correlation with C-2 (δ_C 142.9). Thus, the

glucosyl anomeric proton must be attached to the phenolic hydroxyl at C-4 and methoxyl group attached at C-2.

The ^{1}H- and ^{13}C-NMR data of **GM-11** was similar to that of tachioside and isotachioside. Thus the structure of compound **GM-11** is assigned to be methoxyhydroquinone-4-*O*-β-D-glucopyranoside or tachioside. Tachioside has been isolated from the stems of *Berchemia racemosa* (Inoshiri; et al. 1987: 2811-2814).

A comparison of NMR data (Table 25) of **GM-11** with a phenolic glucoside of methoxyhydroquinone-4-*O*-β-D-apiosyl-(1→6)-*O*-β-D-glucopyranoside (Sugiyama; et al. 1991: 3147-3149) under the source NMR solvent (CD_3OD) showed that both compounds are in very similar.

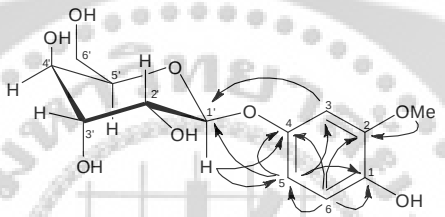


Figure 43 Selected HMBC correlations of compound **GM-11**

Table 24 Comparison of NMR data of tachioside and isotachioside with compound **GM-11**

position	tachioside[a] (C_5D_5N)		isotachioside[a] (C_5D_5N)		GM-11[b] (CD_3OD)			
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1	8.55 (1-OH, *s*)	141.2	9.08 (1-OH, *s*)	139.3		142.9		
2		147.7		149.8		149.2		
2-OMe	3.71 (3H, *s*)	55.4	3.70 (3H, *s*)	55.5	3.70 (3H, *s*)	56.3		56.3
3	7.16 (1H, *d*, *J* = 2.5 Hz)	102.4	6.92 (1H, *d*, *J* = 3 Hz)	100.8	6.79 (1H, *d*, *J* = 2.6 Hz)	103.7	103.7	103.7
4		150.6		152.6		152.8		
5	7.05 (1H, *dd*, *J* = 2.5, 8 Hz)	107.9	6.71 (1H, *dd*, *J* = 3, 8 Hz)	105.9	6.57 (1H, *dd*, *J* = 8.6,2.6 Hz)	110.0	110.0	110.0
6	7.15 (1H, *d*, *J* = 8 Hz)	115.1	7..55 (1H, *d*, *J* = 9 Hz)	117.2	6.67 (1H, *d*, *J* = 8.6 Hz)	116.0	116.0	116.0
1'	5.55 (1H, *d*, *J* = 7 Hz)	101.6	5.56 (1H, *d*, *J* = 7 Hz)	101.4	4.73 (1H, *d*, *J* = 7.2 Hz)	103.7	103.7	103.7
2'	4.45-4.29 (1H, *m*)	73.2	4.48-4.27 (1H, *m*)	73.2	3.35 (1H, *br d*, *J* = 7.2 Hz)	75.0	75.0	75.0
3'	4.45-4.29 (1H, *m*)	76.9	4.48-4.27 (1H, *m*)	76.8	3.38 (1H, *m*)	78.0	78.0	78.1
4'	4.45-4.29 (1H, *m*)	69.9	4.48-4.27 (1H, *m*)	69.7	3.38 (1H, *m*)	71.5	71.5	71.5
5'	4.12 (1H, *br s*)	76.6	4.07 (1H, *br s*)	76.7	3.40 (1H, *m*)	78.1	78.1	78.0
6'	4.59 (1H, *br d*, *J* = 10 Hz) 4.40 (1H, *dd*, *J* = 5, 10 Hz)	60.8	4.54 (1H, *br d*, *J* = 10 Hz) 4.42 (1H, *dd*, *J* = 5, 10 Hz)	60.7	3.89 (1H, *dd*, *J* = 12, 1.9 Hz) 3.69 (1H, *dd*, *J* = 12, 5.4 Hz)	62.6		62.6

[a] Inoshiri; et al. 1987: 2811-2814

Table 25 Comparison of NMR data of methoxyhydroquinone-4-*O*-*β*-D-apiosyl-(1→6)-*O*-*β*-D-glucopyranoside and tachioside with compound **GM-11**

position	**methoxyhydroquinone-4-*O*-*β*-D-apiosyl-(1→6)-*O*-*β*-D-glucopyranoside** [a] (CD_3OD)		**tachioside** [b] (C_5D_5N)		**GM-11** (CD_3OD)	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1		143.1	8.55 (1-OH)	141.2		142.9
2		149.3		147.7		149.2
2-OMe	3.83 (3H, *s*)	56.5	3.71 (3H, *s*)	55.4	3.70 (3H, *s*)	56.3
3	6.76 (1H, *d*, *J* = 2.6 Hz)	104.0	7.16 (1H, *d*, *J* = 2.5 Hz)	102.4	6.79 (1H, *d*,*J* = 2.6 Hz)	103.7
4		152.8		150.6		152.8
5	6.59 (1H, *dd*, *J* = 8.8, 2.6 Hz)	110.1	7.05 (1H, *dd*, *J* = 2.5, 8 Hz)	107.9	6.57 (1H, *dd*, *J* = 8.6, 2.6 Hz)	110.0
6	6.70 (1H, *d*, *J* = 8.8 Hz)	116.1	7.15 (1H, *d*, *J* = 8 Hz)	115.1	6.67 (1H, *d*, *J* = 8.6 Hz)	116.0
1'	4.71 (1H, *d*, *J* = 7.3 Hz)	103.8	5.55 (1H, *d*, *J* = 7 Hz)	101.6	4.73 (1H, *d*, *J* = 7.2 Hz)	103.7
2'		75.0	4.45-4.29 (1H, *m*)	73.2	3.35 (1H, *br d*, *J* = 7.2 Hz)	75.0
3'		78.1	4.45-4.29 (1H, *m*)	76.9	3.38 (1H, *m*)	78.1
4'		71.7	4.45-4.29 (1H, *m*)	69.9	3.38 (1H, *m*)	71.5
5'		77.0	4.12 (1H, *br s*)	76.6	3.40 (1H, *m*)	78.0
6'		68.8	4.59 (1H, *br d*, *J* = 10 Hz) 4.40 (1H, *dd*, *J* = 5, 10 Hz)	60.8	3.89 (1H, *dd*, *J* = 12, 1.9 Hz) 3.69 (1H, *dd*, *J* = 12, 5.4 Hz)	62.6
1"	4.98 (1H, *d*, *J* = 2.6 Hz)	111.0				
2"		78.0				
3"		80.6				
4"		75.0				
5"		65.6				

[a]Sugiyama; et al. 1991: 3149-3151

[b]Inoshiri; et al. 1987: 2811-2814

Table 26 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GM-11**

position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
3	6.79 (1H, *d*, *J* = 2.6 Hz)	H-5	C-3	C-1, C-2, C-4, C-5, C-1'
5	6.57 (1H, *dd*, *J* = 8.6,2.6 Hz)	H-3, H-6	C-5	C-1, C-3, C-4, C-1'
6	6.67 (1H, *d*, *J* = 8.6 Hz)	H-5	C-6	C-1, C-2, C-4, C-5
1'	4.73 (1H, *d*, *J* = 7.2 Hz)	H-2'	C-1'	C-4
2'	3.35 (1H, *br d*, *J* = 7.2 Hz)	H-1', H-3'	C-2'	C-3′
3'	3.38 (1H, *m*)	H-2', H-4'	C-3'	C-2′, C-4′
4'	3.38 (1H, *m*)	H-3', H-5'	C-4'	C-3′, C-5′
5'	3.40 (1H, *m*)	H-4', H-6'	C-5'	C-4′
6'	3.89 (1H, *dd*, *J* = 12, 1.9 Hz)	H-5'	C-6'	
	3.67 (1H, *dd*, *J* = 12, 5.4 Hz)			
2-OMe	3.70 (3H, *s*)			C-2

[a] proton-proton correlation

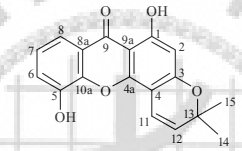
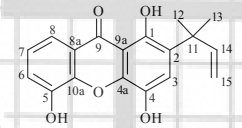
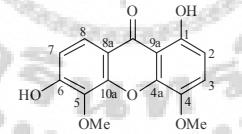
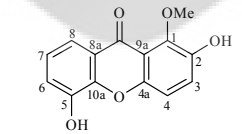
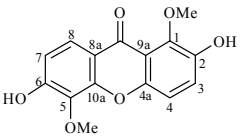
[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

2. Extraction and purification of compounds from *G. xanthochymus* stem bark

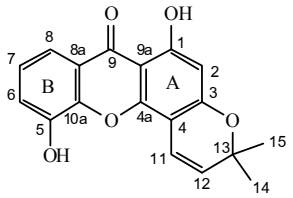
A portion of the ethyl acetate extract (50 g) of the dried *G. xanthochymus* stem bark was investigated by extensive column chromatographic methods (scheme 5, p. 60) to give five xanthones, 6-deoxyisojacareubin (**154**), 12b-hydroxy-des-*D*-garcigerrin A (**119**), 1,6-dihydroxy-4,5-dimethoxyxanthone (**124**), 2,5-dihydroxy-1-methoxyxanthone and 2,6-dihydroxy-1,5-dimethoxy-xanthone. Their structures were elucidated by spectroscopic method, especially 1D and 2D NMR techniques, and by comparison of the data with the reported value.

Table 27 Phenolic compounds obtained from the *G. xanthochymus* stem bark

	Compound	Structure	Reference
GX-1	6-deoxyjacareubin		Helesbeux; et al. 2004: 2293-2300
GX-2	12b-hydroxy-des-*D*-garcigerrin A		Iinuma; et al. 1995: 279-284
GX-3	1,6-dihydroxy-4,5-dimethoxyxanthone		Zhong; et al. 2007: 849-851
GX-4	2,5-dihydroxy-1-methoxyxanthone		Minami; et al. 1996: 629-633
GX-5	2,6-dihydroxy-1,5-dimethoxyxanthone		Minami; et al. 1994: 501-506

2.1 Structures determination of compounds isolated from the EtOAc extract of *G. xanthochymus*

2.1.1 Structure determination of compound GX-1 (6-deoxyisojacareubin, sss 4289)



Compound **GX-1** yielded in very small amount (2.6 mg) as a yellow solid with the R_f value of 0.45 (30% acetone-hexane), and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent. It showed a molecular ion peak at *m/z* 619 $[2M-H]^-$ in its negative ion ES-MS, which corresponding to a molecular formula of $C_{18}H_{14}O_5$. The UV spectrum showed λ_{max} at 222, 232, 250, 267, 308, 329 and 378 nm. The IR absorption spectrum displayed ν_{max} at 3481 (OH stretching), 1639 (C=O stretching). The UV and IR data were characteristic of xanthone skeleton (Roberts. 1961: 591-605, Scheinmann. 1962: 853-858).

The ^{1}H-NMR spectrum (Table 28, Figure 62) showed a chelated hydroxyl group at δ_H 13.40 (1-OH, *s*) and another broad hydroxyl group at δ_H 9.17. In the aliphatic region two methyl group signals at δ_H 1.48 (6H, *s*), and two doublets (J = 10 Hz) each due to olefinic protons at δ_H 5.74 and 7.05 as characteristic of the 2,2-dimethylpyran part of a chromen ring system. The signals of ABM system of three aromatic protons [δ_H 7.67 (1H, *d*, J = 7.8 Hz, H-8), δ_H 7.37 (1H, *d*, J = 7.8, 1.7 Hz, H-6) and δ_H 7.29 (1H, *t*, J = 7.8 Hz, H-7), a singlet an aromatic proton at δ_H 6.19. Consideration of the 2,2-dimethylpyran ring and the chelated hydroxyl group led us to postulate that the aromatic proton at δ_H 6.19 should be located at C-2 (δ_C 99.6) and C-4 (δ_C 102.2) in ring A. Comparison of suitable reference compound (Table 23) indicates that the other hydroxyl group is in the 5-position. Thus, signal of the lowest field aromatic proton at C-8 appear as a doublet at δ_H 7.67, owing to *ortho*- and *meta*-splitting (J = 7.8 Hz) with proton at C-7 and C-6, which give rise to the signals at δ_H 7.29 and δ_H 7.37, respectively. The ^{13}C-NMR and DEPT spectrum (Table 28) showed 18 carbon signals that consist of two methyls, two methylenes, four methines, nine quaternary carbons and a carbonyl carbon.

The location of 2,2-dimethylpyran ring was confirmed by HMBC spectrum (Table 29, Figure 44) which showed correlations from the methine proton H-11 (δ_H 7.03) to C-3

(δ_C 157.1), C-4 (δ_C 102.2), C-4a (δ_C 155.0) and C-13 (δ_C 79.1), an aromatic proton at δ_H 6.19 (H-2) exhibited HMBC cross-peaks with C-1 (δ_C 161.7), C-3 (δ_C 157.1) and C-4 (δ_C 102.2). This confirmed the position of attachment of the 2,2-dimethylpyran ring at C-4. Thus, the structure of compound **GX-1** was assigned as 6-deoxyisojacareubin (**154**) (Helesbeux; et al. 2004: 2293-2300).

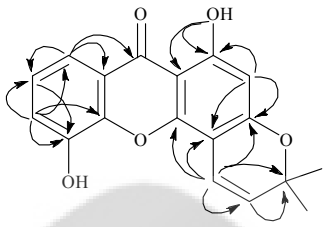


Figure 44 Selected HMBC correlations of compound **GX-1**

Table 28 Comparison of NMR data of 6-deoxyisojacareubin (**154**) with compound **GX-1** in acetone-d_6

position	6-deoxyisojacareubin[a]		GX-1			
	δ_H	δ_C	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1-OH	13.10 (1H, *s*)	161.7	13.0 (1H, *s*)	161.7		
2	6.20 (1H, *s*)	99.6	6.19 (1H, *s*)	99.6	99.6	99.6
3		164.1		164.1		
4		102.1		102.2		
4a		156.1		157.1		
5		146.9		146.9		
6	7.39 (1H, *dd*, *J* = 8, 1.5 Hz)	122.0	7.37 (1H, *d*, *J* = 7.8 Hz)	122.0	122.0	122.0
7	7.30 (1H, *d*, *J* = 8, 7.5 Hz)	125.1	7.29 (1H, *t*, *J* = 7.8 Hz)	125.1	125.1	125.1
8	7.68 (1H, *dd*, *J* = 8, 1.5 Hz)	115.7	7.67 (1H, *d*, *J* = 7.8 Hz)	115.7	115.7	115.7
8a		122.2		120.5		
9		181.8		182.0		
9a		104.1		104.0		
10a		146.0		145.2		
11	7.05 (1H, *d*, *J* = 10 Hz)	116.5	7.03 (1H, *d*, *J* = 10 Hz)	116.5	116.5	116.5
12	5.77 (1H, *d*, *J* = 10 Hz)	128.1	5.74 (1H, *d*, *J* = 10 Hz)	128.1	128.1	128.1
13		79.1		79.1		
14	1.48 (3H, *s*)	28.4	1.48 (3H, *s*)	28.4		28.4
15	1.48 (3H, *s*)	28.4	1.48 (3H, *s*)	28.4		28.4

[a] Helesbeux; et al. 2004: 2293-2300.

Table 29 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GX-1**

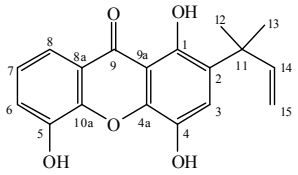
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1-OH	13.0 (1H, *s*)			C-1, C-2, C-9a
2	6.19 (1H, *s*)		C-2	C-1, C-3, C-4
6	7.37 (1H, *d*, *J* = 7.8 Hz)	H-7, H-8	C-6	C-5, C-8
7	7.29 (1H, *t*, *J* = 7.8 Hz)	H-6, H-8	C-7	C-5, C-6, C-8, C-8a
8	7.67 (1H, *d*, *J* = 7.8 Hz)	H-6, H-7	C-8	C-6, C-7, C-8a, C-9
11	7.03 (1H, *d*, *J* = 10 Hz)	H-12	C-11	C-3, C-4, C-4a, C-12, C-13
12	5.74 (1H, *d*, *J* = 10 Hz)	H-11	C-12	C-11, C-13, C-14, C-15
14, 15	1.48 (6H, *s*)		C-14, C-15	C-12, C-13, C-14, C-15

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

2.1.2 Structure determination of compound GX-2 (12b-hydroxy-des-*D*-garcigerrin A, sss 4320)



Compound **GX-2** was obtained as an orange solid with the R_f value of 0.32 (30% acetone-hexane), and gave a blue-green coloration with anisaldehyde-H_2SO_4 reagent. Its molecular formula $C_{18}H_{16}O_5$ was revealed by the molecular ion peak at *m/z* 311 $[M-H]^-$ in ES-MS. The UV spectrum showed λ_{max} at 238, 249, 264, 317 and 409 nm. The IR absorption spectrum displayed ν_{max} at 3481 (OH stretching), 1637 (C=O stretching), 1582 and 1458 (C=C aromatic ring) cm^{-1}. The UV and IR data were characteristic of xanthone nucleus.

The ^{1}H-NMR spectrum (Table 30, Figure 63) showed the presence of chelated hydroxyl group [δ_H 12.88 (1H, *s*)], an ABM system attributable to a 1,2,3-trisubstituted benzene ring [δ_H 7.28 (1H, *d*, *J* = 7.8 Hz, H-7), δ_H 7.37 (1H, *dd*, *J* = 7.8, 1.8 Hz, H-6) and δ_H 7.69 (1H, *dd*, *J* = 7.6, 1.8 Hz, H-8)], a singlet of an aromatic proton at δ_H 7.35 and an olefinic ABX system [δ_H 4.98 (1H, *d*, *J* = 10.7 Hz, H-15Z), δ_H 5.02 (1H, *d*, *J* = 17.5 Hz, H-15E) and δ_H 6.28 (1H, *dd*, *J* = 10.7, 17.5 Hz, H-14)], two allylic methyl groups [1.52 (2x3H, *s*, H-12,13)] were typical of 1,1-dimethylallyl moiety. The ^{13}C-NMR and DEPT spectra (Table 30) displayed signals attributable to the pentasubstituted benzene ring, 18 signals that consist of two methyls, one methylene carbon, five methines, nine quaternary carbons and a carbonyl carbon.

The HMBC spectrum (Table 31, Figure 45) which showed a long-range correlations from the aromatic proton at δ_H 7.35 (H-3) to C-1 (δ_C 153.2), C-2 (δ_C 129.5), C-4 (δ_C 136.8) and correlation between H-3 with C-11 (δ_C 40.9) of 1,1-dimethylallyl group. The HMBC correlations of the methine proton H-8 (δ_H 7.69) with C-6 (δ_C 121.8), C-7 (δ_C 125.1), C-8a (δ_C 123.2) and C-9 (δ_C 183.8) and two methyl groups at δ_H 1.52 (H-12, 13) of 1,1-dimethylallyl group showed a C-H long-range correlations with C-2 (δ_C 129.5), C-11 (δ_C 40.9), C-14 (δ_C 147.8) and C-15 (δ_C 111.0), which was connected to C-2 position. Comparisons of their ^{1}H- and ^{13}C-NMR data with the reported values, led to the identification of compound **GX-2** to be 12b-hydroxy-des-*D*-garcigerrin A (**119**) (Iinuma; et al. 1995: 279-284).

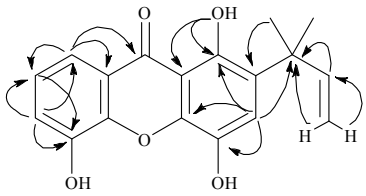


Figure 45 Selected HMBC correlations of compound **GX-2**

Table 30 Comparison of NMR data of 12b-hydroxy-des-D-garcigerrin A (**119**) with compound **GX-2** in acetone-d_6

position	12b-hydroxy-des-*D*-garcigerrin A [a]		GX-2			
	δ_H	δ_C	δ_H	δ_C	DEPT 90	DEPT 135
1-OH	12.85 (1H, *s*)	153.5	12.88 (1H, *s*)	153.2		
2		129.8		129.5		
3	7.34 (1H, *s*)	123.4	7.35 (1H, *s*)	123.2	123.2	123.2
4		137.0		136.8		
4a		142.2		142.0		
5		147.0		147.0		
6	7.35 (1H, *d*, *J* = 8, 2 Hz)	122.0	7.37 (1H, *dd*, *J* = 7.8, 1.8 Hz)	121.8	121.8	121.8
7	7.30 (1H, *t*, *J* = 8 Hz)	125.2	7.28 (1H, *t*, *J* = 7.9 Hz)	125.1	125.1	125.1
8	7.71 (1H, *d*, *J* = 8, 2 Hz)	116.8	7.69 (1H, *dd*, *J* = 7.6, 1.8 Hz)	116.5	116.5	116.5
8a		121.9		123.2		
9		183.9		183.8		
9a		109.4		109.3		
10a		145.8		145.6		
11		41.1		40.9		
12	1.54 (3H, *s*)	29.3	1.52 (3H, *s*)	26.8		26.8
13	1.54 (3H, *s*)	29.3	1.52 (3H, *s*)	26.8		26.8
14	6.31 (1H, *dd*, *J* = 11, 18 Hz)	148.1	6.28 (1H, *dd*, *J* = 10.7, 17.5 Hz)	147.8	147.8	147.8
15	5.00 (1H, *dd*, *J* = 18, 1 Hz, H15E) 5.01 (1H, *dd*, *J* = 11, 1 Hz, H15Z)	111.5	5.02 (1H, *d*, *J* = 17.5 Hz, H15E) 4.98 (1H, *d*, *J* = 10.7 Hz, H15Z)	111.0	111.0	111.0

[a] Iinuma; et al. 1995: 279-284.

Table 31 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GX-2**

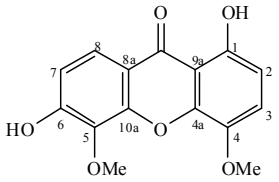
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1-OH	12.88 (1H, *s*)			C-1, C-2, C-9, C-9a
3	7.35 (1H, *s*)		C-3	C-1, C-4, C-4a, C-9a, C-11
6	7.37 (1H, *dd*, *J* = 7.8, 1.8 Hz)	H-7, H-8	C-6	C-5, C-8, C-10a
7	7.28 (1H, *t*, *J* = 7.9 Hz)	H-6, H-8	C-7	C-5, C-6, C-8, C-8a
8	7.69 (1H, *dd*, *J* = 7.6, 1.8 Hz)	H-6, H-7	C-8	C-5, C-6, C-8, C-8a, C-9, C-10a
12	1.52 (3H, *s*)		C-12	C-2, C-11, C-13, C-14, C-15
13	1.52 (3H, *s*)		C-13	C-2, C-11, C-12, C-14, C-15
14	6.28 (1H, *dd*, *J* = 10.7, 17.5 Hz)	H-15	C-14	C-2, C-11, C-12, C-13, C-15
15	5.02 (1H, *d*, *J* = 17.5 Hz, H15E)	H-14	C-15	C-11, C-12, C-13, C-14
	4.98 (1H, *d*, *J* = 10.7 Hz, H15Z)			

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

2.1.3 Structure determination of compound GX-3 (1,6-dihydroxy-4,5-dimethoxy xanthone, sss 4135)



Compound **GX-3** was obtained as a yellow solid with the R_f value of 0.40 (30% acetone-hexane), and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent. Its molecular formula $C_{15}H_{12}O_6$ was revealed by the molecular ion peak at *m/z* 287 $[M-H]^-$ in negative ion ES-MS. The UV spectrum showed λ_{max} at 242, 280, 298, 314 and 374 nm. The IR absorption spectrum displayed ν_{max} at 3374 (OH stretching), 1654 (C=O stretching), 1584 and 1496 (C=C aromatic ring) cm^{-1}. The UV and IR data were characteristic of a simple oxygenated xanthone structure.

The ^{1}H-NMR spectrum (Table 32, Figure 64) displayed two sets of *ortho*-coupled protons at δ_H 6.69, 7.04, 7.43 and 7.87 (each *d*, 1H, *J* = 8.9 Hz), a chelated hydroxy phenolic group at δ_H 12.21 (1H, *s*), a free hydroxy group at δ_H 9.52 (*br s*) and two methoxyl group at δ_H 3.97 and 4.05. The presence of only one low field aromatic proton (δ_H 7.87), therefore, indicated that either C-1 or C-8 of the xanthone moiety is free. This was confirmed by a chelated hydroxyl group in the xanthone as shown by its ^{1}H-NMR spectrum. Two methoxyl groups [δ_H 3.97 and 4.05] and free hydroxyl groups at δ_H 9.52 suggesting the xanthone to be tetraoxygenated. The ^{13}C-NMR and DEPT spectrum (Table 32) showed 15 carbon signals due to two methoxyls, four methines, eight quaternary carbons and a carbonyl carbon.

The HMBC spectrum (Table 33, Figure 46) which showed a long-range correlations of the *ortho*-coupled proton at δ_H 6.69 (H-2) with C-1 (δ_C 155.6), C-3 (δ_C 122.0), C-4 (δ_C 141.2) and C-9a (δ_C 108.3), and correlation between δ_H 7.43 (H-3) with C-2 (δ_C 109.5) C-4 (δ_C 141.2) and C-4a (δ_C 145.2). The HMBC correlations of the methine proton H-8 (δ_H 7.87) with C-6 (δ_C 158.0), C-7 (δ_C 114.8), C-8a (δ_C 114.0) and C-9 (δ_C 179.7) and two methoxyl groups at δ_H 3.97 and 4.05 exhibited HMBC cross-peaks with C-4 (δ_C 141.2) and C-5 (δ_C 138.7), respectively. It confirmed the position of attachment of the two methoxyl group at C-4 and C-5. Comparisons of their ^{1}H- and ^{13}C-NMR data with the reported values, led to the identification of compound **GX-3** as 1,6-dihydroxy-4,5-dimethoxyxanthone (**124**) (Zhong; et al. 2007: 849-851).

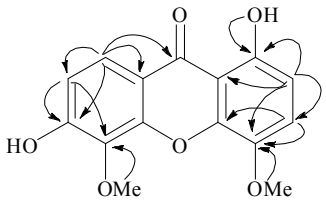


Figure 46 Selected HMBC correlations of compound **GX-3**

Table 32 Comparison of NMR data of 1,6-dihydroxy-4,5-dimethoxyxanthone (**124**) with compound **GX-3**

position	**1,6-dihydroxy-4,5-dimethoxyxanthone**[a](DMSO-d_6)		**GX-3** (acetone-d_6)			
	δ_H	δ_C	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1-OH	12.15 (1H, *s*)	154.3	12.21 (1H, *s*)	155.6		
2	6.69 (1H, *d*, *J* = 9 Hz)	109.3	6.69 (1H, *d*, *J* = 8.9 Hz)	109.5	109.5	109.5
3	7.44 (1H, *d*, *J* = 9 Hz)	121.7	7.43 (1H, *d*, *J* = 8.9 Hz)	122.0	122.0	122.0
4		140.5		141.2		
4a		145.7		145.2		
5		135.3		138.7		
6		157.8		158.0		
7	7.01 (1H, *d*, *J* = 9 Hz)	115.2	7.04 (1H, *d*, *J* = 8.9 Hz)	114.8	114.8	114.8
8	7.78 (1H, *d*, *J* = 9 Hz)	121.4	7.87 (1H, *d*, *J* = 8.9 Hz)	121.7	121.7	121.7
8a		114.0		114.0		
9		181.5		179.7		
9a		108.9		108.3		
10a		151.3		152.3		
4-OMe	3.89 (1H, *s*)	57.9	3.97 (1H, *s*)	57.9		57.9
5-OMe	3.92 (1H, *s*)	61.4	4.05 (1H, *s*)	61.7		61.7
6-OH	10.92 (1H, *br s*)		9.52 (1H, *br s*)			

[a] Zhong; et al. 2007: 849-851

Table 33 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GX-3**

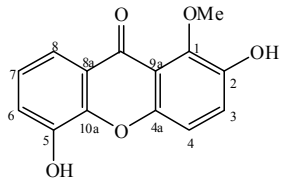
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
1-OH	12.21 (1H, *s*)			C-1, C-2
2	6.69 (1H, *d*, *J* = 8.9 Hz)	H-3	C-2	C-1, C-3, C-4, C-9a
3	7.43 (1H, *d*, *J* = 8.9 Hz)	H-2	C-3	C-1, C-2, C-4, C-4a
7	7.04 (1H, *d*, *J* = 8.9 Hz)	H-8	C-7	C-5, C-6, C-8, C-8a
8	7.87 (1H, *d*, *J* = 8.9 Hz)	H-7	C-8	C-6, C-7, C-8a, C-9, C-10a
4-OMe	3.97 (1H, *s*)			C-4
5-OMe	4.05 (1H, *s*)			C-5

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

2.1.4 Structure determination of compound GX-4 (2,5-dihydroxy-1-methoxy xanthone, sss 4261)



Compound **GX-4** was obtained in very small amount (3.2 mg) as yellow solid with the R_f value of 0.35 (40% acetone-hexane), and gave a blue-gray coloration with anisaldehyde-H_2SO_4 reagent and its molecular formula was determined to be $C_{14}H_{10}O_5$ by ESMS at *m/z* 257 $[M-H]^-$. The UV spectrum showed λ_{max} at 241, 257, 288, 309 and 377 nm. The IR spectrum showed ν_{max} at 3481 (OH stretching), 1623 (C=O stretching), 1593 and 1497 (C=C aromatic ring) cm^{-1}. The UV and IR data were indicated that **GX-4** to be a simple oxygenated xanthone structure.

The ^{1}H-NMR spectrum of **GX-4** (Table 34) showed a pair of *ortho*-coupled aromatic proton signals at δ_H 7.27 (1H, *d*, *J* = 9.0 Hz) and 7.38 (1H, *d*, *J* = 9.0 Hz), a singlet methoxyl signal at δ_H 3.91 as well as the presence of an ABM system signals at δ_H 7.20 (1H, *t*, *J* = 7.8 Hz), 7.27 (1H, *dd*, *J* = 7.8, 1.7 Hz) and 7.66 (1H, *dd*, *J* = 7.8, 1.7 Hz) attributable to a 1,2,3-trisubstituted benzene ring. In its ^{13}C-NMR and DEPT spectra, 14 carbon signals, including one methoxyl carbon, five methines, seven quaternary carbons and a carbonyl carbon (Table 34).

HMBC spectrum (Table 35, Figure 47) of **GX-4** displayed a long-range correlations of the methoxyl group at δ_H 3.91 with C-1 (δ_C 146.1) confirming the placement of the methoxyl group at C-1. The exhibited HMBC cross-peaks from the *ortho*-coupled aromatic proton at δ_H 7.38 (H-3) to C-2 (δ_C 146.9) and C-4 (δ_C 114.6), the aromatic proton signal H-8 (δ_H 7.66) showed correlations with C-7 (δ_C 124.1) and C-9 (δ_C 176.2) and H-6 (δ_H 7.27) displayed a long-range correlations with C-5 (δ_C 147.4) and C-7 (δ_C 124.1). These observations together with the comparisons of the ^{1}H- and ^{13}C-NMR data of **GX-4** with 2,5-dihydroxy-1-methoxyxanthone, led to the identification of **GX-4** to be 2,5-dihydroxy-1-methoxyxanthone (Minami; et al. 1996: 629-633). 2,5-Dihydroxy-1-methoxyxanthone has been isolated from the wood of *Garcinia subelliptica* (Minami; et al. 1996: 629-633).

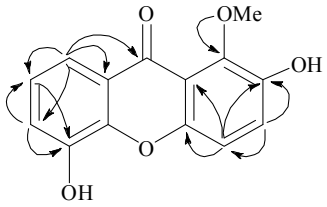


Figure 47 Selected HMBC correlations of compound **GX-4**

Table 34 Comparison of NMR data of 2,5-dihydroxy-1-methoxyxanthone with compound **GX-4**

position	**2,5-dihydroxy-1-methoxyxanthone**[a] (DMSO-d_6)		**GX-4** (acetone-d_6)			
	δ_H	δ_C	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1-OH		145.1		146.1		
2	9.48 (1H, *s*, OH)	146.6	8.33 (1H, *s*, OH)	146.9		
3	7.38 (1H, *d*, *J* = 9.3 Hz)	124.4	7.38 (1H, *d*, *J* = 9.0 Hz)	123.9	123.9	123.9
4	7.29 (1H, *d*, *J* = 9.3 Hz)	113.7	7.30 (1H, *d*, *J* = 9.0 Hz)	114.6	114.6	114.6
4a		149.5		151.1		
5	10.31 (1H, *s*, OH)	146.2	9.21 (1H, *s*, OH)	147.4		
6	7.24 (1H, *dd*, *J* = 7.8, 1.5 Hz)	119.3	7.27 (1H, *dd*, *J* = 7.8, 1.7 Hz)	120.1	120.1	120.1
7	7.19 (1H, *t*, *J* = 7.8 Hz)	123.4	7.20 (1H, *t*, *J* = 7.8 Hz)	124.1	124.1	124.1
8	7.53 (1H, *dd*, *J* = 7.8, 1.5 Hz)	115.2	7.66 (1H, *dd*, *J* = 7.8, 1.7 Hz)	116.8	116.8	116.8
8a		122.6		123.8		
9		175.4		176.2		
9a		116.1		117.1		
10a		144.4		145.5		
1-OMe	3.80 (3H, *s*)	61.0	3.91 (3H, *s*)	62.1		62.1

[a] Minami; et al. 1996: 629-633

Table 35 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GX-4**

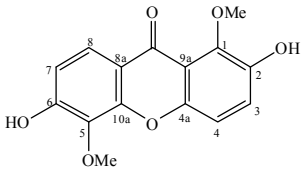
position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
2	8.33 (1H, *s*, OH)			
3	7.38 (1H, *d*, *J* = 9.0 Hz)	H-4	C-3	C-2, C-4, C-9a
4	7.30 (1H, *d*, *J* = 9.0 Hz)	H-3	C-4	C-2, C-3, C-4a, C-9, C-9a
5	9.21 (1H, *s*, OH)			
6	7.27 (1H, *dd*, *J* = 7.8, 1.7 Hz)	H-7, H-8	C-6	C-5, C-7, C-8
7	7.20 (1H, *t*, *J* = 7.8 Hz)	H-6, H-8	C-7	C-5, C-6, C-8, C-8a
8	7.66 (1H, *dd*, *J* = 7.8, 1.7 Hz)	H-6, H-7	C-8	C-6, C-7, C-8a, C-9
1-OMe	4.05 (1H, *s*)			C-1

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

2.1.5 Structure determination of compound GX-5 (2,6-dihydroxy-1,5-dimethoxy xanthone, sss 4262)



Compound **GX-5** yielded in a small amount (10.4 mg) as pale yellow solid with the R_f value of 0.3 (40% acetone-hexane, and gave a yellow coloration with anisaldehyde-H_2SO_4 reagent and its molecular formula was determined to be $C_{15}H_{12}O_6$ by ESMS at *m/z* 287 $[M-H]^-$. The UV spectrum showed λ_{max} at 241, 249, 282, 310 and 360 nm. The IR absorption spectrum displayed ν_{max} at 3414 (OH stretching), 1654 (C=O stretching), 1597 and 1467 (C=C aromatic ring) cm^{-1}. The UV and IR spectrum indicated that **GX-5** had characteristic xanthone skeleton.

The ^{13}C-NMR, DEPT, HMQC and COSY (Table 36) provided 15 carbon signals including two methoxyl carbon, four methines, eight quaternary carbons and a carbonyl carbon. The ^{1}H-NMR spectrum of **GX-5** (Table 36) showed two sets of *ortho*-coupled protons at δ_H 6.95 and 7.83 (each *d*, *J* = 8.9 Hz), and δ_H 7.28 and 7.33 (each *d*, *J* = 9.1 Hz). The presence of only one low field aromatic proton (δ_H 7.83), therefore, indicated that either C-1 or C-8 of the xanthone moiety is free. This was confirmed by the absence of a chelated hydroxyl group in the xanthone as shown by its ^{1}H-NMR spectrum. Two hydroxyl groups [δ_H 8.24 and 9.22] and two methoxyl groups at δ_H 3.90 and 3.99 suggesting the xanthone to be tetraoxygenated. The presence of two pairs of *ortho*-coupled protons in two different aromatic rings is evident from the above ^{1}H-NMR data. Comparisons of their ^{1}H- and ^{13}C-NMR data with the reported values, led to the identification of this compound could be 2,6-dihydroxy-1,5-dimethoxyxanthone (Minami; et al. 1994: 501-506).

In HMBC spectrum (Table 37, Figure 48) which showed correlations from two methoxyl group signals at δ_H 3.90 and 3.99 to C-1 (δ_C 156.0) and C-5 (δ_C 135.5), respectively. The HMBC correlations of *ortho*-coupled aromatic proton H-8 (δ_H 7.83) with C-7 (δ_C 113.8) and C-9 (δ_C 176.3). The aforementioned spectral effect showed that there were two methoxyl and two hydroxyl groups at C-1, C-5 and C-2, C-6 on the xanthone ring, respectively. The structure of **GX-5** was deduced as 2,6-dihydroxy-1,5-dimethoxyxanthone which has been isolated from the wood of *Garcinia subelliptica* (Minami; et al. 1994: 501-506).

.

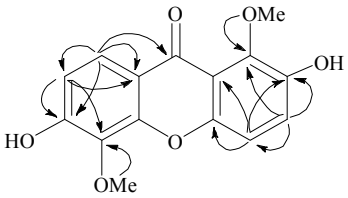


Figure 48 Selected HMBC correlations of compound **GX-5**

Table 36 Comparison of NMR data of 2,6-dihydroxy-1,5-dimethoxyxanthone with compound **GX-5**

position	**2,6-dihydroxy-1,5-dimethoxyxanthone**[a] (DMSO-d_6)		**GX-5** (acetone-d_6)			
	δ_H	δ_C	δ_H	δ_C	**DEPT 90**	**DEPT 135**
1-OH		155.4		156.0		
2	10.56 (1H, *s*, OH)	146.7	8.24 (1H, *s*, OH)	146.2		
3	7.33 (1H, *d*, *J* = 9.3 Hz)	123.2	7.33 (1H, *d*, *J* = 9.1 Hz)	123.2	123.2	123.2
4	7.28 (1H, *d*, *J* = 9.3 Hz)	121.3	7.28 (1H, *d*, *J* = 9.1 Hz)	114.5	114.5	114.5
4a		149.8		150.9		
5		134.0		135.5		
6	9.42 (1H, *s*, OH)	145.3	9.22 (1H, *s*, OH)	147.5	147.5	147.5
7	6.92 (1H, *d*, *J* = 9.3 Hz)	115.9	6.95 (1H, *d*, *J* = 8.9 Hz)	113.8	113.8	113.8
8	7.72 (1H, *d*, *J* = 9.3 Hz)	113.4	7.83 (1H, *d*, *J* = 8.9 Hz)	122.6	122.6	122.6
8a		115.3		117.1		
9		174.3		175.3		
9a		113.4		117.1		
10a		149.4		151.2		
1-OMe	3.78 (3H, *s*)	60.7	3.90 (3H, *s*)	61.6		61.6
5-OMe	3.88 (3H, *s*)	60.9	3.99 (3H, *s*)	62.1		62.1

[a]Minami; et al. 1994: 501-506

Table 37 ^{1}H-NMR, COSY, HMQC and HMBC data of compound **GX-5**

position	^{1}H-NMR	COSY[a]	HMQC[b]	HMBC[c]
2	8.24 (1H, *s*, OH)			
3	7.33 (1H, *d*, *J* = 9.1 Hz)	H-4	C-3	C-1, C-2, C-4, C-4a
4	7.28 (1H, *d*, *J* = 9.1 Hz)	H-3	C-4	C-2, C-3, C-4a, C-9a
6	9.22 (1H, *s*, OH)			
7	6.95 (1H, *d*, *J* = 8.9 Hz)	H-8	C-7	C-5, C-6, C-8, C-8a
8	7.83 (1H, *d*, *J* = 8.9 Hz)	H-7	C-8	C-6, C-7, C-8a, C-9
1-OMe	3.90 (3H, *s*)			C-1
5-OMe	3.99 (3H, *s*)			C-5

[a] proton-proton correlation

[b] 1-bond heteronuclear ^{1}H-^{13}C correlation

[c] long range heteronuclear ^{1}H-^{13}C correlation

CHAPTER 5

CONCLUSION

Investigation of the chemical constituents of the root of *G. mangostana* led to the isolation of a new xanthone as 3,6-dihydroxy-8-(3-hydroxy-3-methylbutyl)-7-methoxy-6',6'-di methyl-5'-hydroxy-4',5'-dihydropyrano(2',3':1,2)xanthone, together with eight known xanthones, including α-mangostin, β-mangostin, 1,3,7-trihydroxyxanthone or gentisein, gracinone D, norathyriol, cratoxylone, pruniflorone C and 9-hydroxycalabaxanthone. In addition, a benzophenone as maclurin and a phenolic glucoside as tachioside. Among these compounds, gentisein, cratoxylone, pruniflorone C and tachioside have not been reported before from this plant. The structures of all isolated compounds were elucidated by spectroscopic techniques and by comparisons of spectroscopic data with those of reported values.

Investigation of the phytochemicals from the EtOAc extract of the *G. xanthochymus* stem bark, collected from the northern part of Thailand, led to the isolation of five xanthones, 6-deoxyisojacareubin, 12b-hydroxy-des-*D*-garcigerrin A, 1,6-dihydroxy-4,5-dimethoxyxanthone, 2,5-dihydroxy-1-methoxyxanthone and 2,6-dihydroxy-1,5-dimethoxyxanthone. This is the first report of 2,5-dihydroxy-1-methoxyxanthone and 2,6-dihydroxy-1,5-dimethoxyxanthone isolated from this plant. Their structures were elucidated by spectroscopic method, especially 1D and 2D NMR techniques, and by comparison of the data with the reported value.

BIBLIOGRAPHY

BIBLIOGRAPHY

Akao Y, Nakagawa Y, Iinuma M, Nozawa Y. (2008). Anti-cancer effects of xanthones from pericarps of mangosteen. *Int. J. Mol. Sci.* 9: 355-370.

Amornmart Jaratrungtawee. (2007). Phytochemicals from the very young fruit of *Garcinia mangostana* L. Master Thesis, M.Sc. (chemistry). p. 50-51.

Ampofo SA, Waterman PG. (1986). Xanthone and neoflavonoids from two Asian species of *Calophyllum*. *Phytochemistry*. 25: 2617-2620.

Asai F, Iinuma M, Tanaka T, Tosa H. (1995). A xanthone from *Garcinia mangostana*. *Phytochemistry*. 39: 943-944.

Atkinson JE, Gupta P, Lewis JR. (1969). Some phenolic constituents of *Gentiana lutea*. *Phytochemistry*. 24: 1507-1511.

Azebaze AGB, Meyer M, Valentin A, Nguemfo EL, Fomum ZT, Nkengfack AE. (2006). Prenylated xanthone derivatives with antiplasmodial activity from *Allanblackia monticala*. *Chem. Pharm. Bull*. 54: 111-113.

Baggett S, Protiva P, Mazzola EP, Yang H, Ressler ET, Basile MJ, et al. (2005). Bioactive benzophenones from *Garcinia xanthochymus* fruits. *J. Nat. Prod*. 68: 354-360.

Balasubramanian K, Rajagopapan K. (1988). Novel xanthones from *Garcinia mangostana*, structure of BR-xanthone A and BR-xanthone B. *Phytochemistry*. 27: 1552-1554.

Balunas MJ, Su B, Brueggemeier RW, Kinghorn AD. (2008). Xanthones from the botanical dietary supplement mangosteen (*Garcinia mangostana*) with aromatase inhibitory activity. *J. Nat. Prod*. 71: 1161-1166.

Baslas RK, Kumar P. (1979). Chemical examination of the fruits of *Garcinia xanthochymus*. *Curr. Sci*. 48(18): 814-815. [abstract] from SciFinder. CAN 91:189827.

Baslas RK, Kumar P. (1981). Isolation and characterization of biflavanone and xanthones in the fruits of *Garcinia xanthochymus*. *Acta Ciencia Indica Chem*. 7(1-4): 31-4. [abstract] from SciFinder. CAN 97:36104.

Bennett GJ, Harrison LJ, Sia GL, Sim KY. (1993). Triterpenoids, tocotrienols and xanthones from the bark of *Cratoxylum cochinchinense*. *Phytochemistry*. 32(5): 1245-51.

Bennett GJ, Lee H-H. (1989). Xanthones from Guttiferae. *Phytochemistry*. 8(4): 967-998.

Blount JF, Williams TH. (1976). Revised structure of xanthochymol. *Tetrahedron Lett*. 34: 2921-2924.

Boonnak N, Karalai C, Chantrapromma S, Ponglimanont C, Fun H-K, Kanjana-Opas A, Laphookhieo S. (2006). Bioactive prenylated xanthones and anthraquinones from *Cratoxylum formosum* ssp. *pruniflorum*. *Tetrahedron*. 62: 8850-8859.

Bumrungpert A, Kalpravidh RW, Chitchumroonchokchai C, Chuang C-C, West T, Kennedy A, McIntosh M. (2009). Xanthones from mangosteen prevent lipopolysaccharide-mediated inflammation and insulin resistance in primary cultures of human adipocytes. *J. Nutr*. 139: 1185-1191.

Chairungsrilerd N, Furukawa KI, Ohta T, Nozoe S, Ohizumi T. (1996a). Pharmacological properties of α-mangostin, a novel histamine H1 receptor antagonist. *Eur. J. Pharmacol*. 314: 351-356.

Chairungsrilerd N, Furukawa KI, Ohta T, Nozoe S, Ohizumi T. (1996b). Histaminergic and serotonergic receptor blocking substances from the medicinal plant *Garcinia mangostana*. *Planta Med*. 62: 471-472.

Chairungsrilerd N, Furukawa KI, Tadano T, Kisara K, Ohizumi T. (1998). Effect of γ-mangostin through the inhibition of 5-hydroxy-tryptamine 2A receptors in 5-fluoro-alpha-methyltryptamine-induced head-twitch responses of mice. *Br. J. Pharmacol*. 123: 855-862.

Chairungsrilerd N, Takeuchi K, Ohizumi T, Nozoe S, Ohta T. (1996c). Mangostanol, a prenyl xanthone from *Garcinia mangostana*. *Phytochemistry*. 43: 1099-1102.

Chanarat P, Chanarat N, Fujihara M, Nagumo T. (1997). Immunopharmacological activity of polysaccharide from the pericarb of mangosteen *garcinia*: phagocytic intracellular killing activities. *J. Med. Assoc. Thai*. 80: S149-S154.

Chanmahasathien W, Li Y, Satake M, Oshima Y, Ishibashi M, Ruangrungsi N, et al. (2003a). Prenylated xanthones from *Garcinia xanthochymus*. *Chem. Pharm. Bull*. 51(11): 1332-1334.

Chanmahasathien W, Li Y, Satake M, Oshima Y, Ruangrungsi N, Ohizumi Y. (2003b). Prenylated xanthones with NGF-potentiating activity from *Garcinia xanthochymus*. *Phytochemistry*. 64: 981-986.

Chaverri JP, Fermin LMR, Amaya EGN, Ibarra MO, Camposa ONM, Cuahutencosa OG, Cruzb IR, Mata R. (2009). ROS scavenging capacity and neuroprotective effect of α-mangostin

against 3-nitropropionic acid in cerebellar granule neurons. *Exp. Toxicol. Pat*. 61: 491-501.

Chaverri JP, Rodriguez NC, Ibarra MO, Rojas JM. (2008). Medicinal properties of mangosteen (*Garcinia mangostana*). *Food. Chem. Toxicol*. 46: 3227-3239.

Chen LG, Yang LL, Wang CC. (2008). Anti-imflammatory activity of mangostins from *Garcinia mangostana*. *Food Chem. Toxicol*. 46: 688-693.

Chen S, Wan M, Loh BN. (1996). Active constituents against HIV-1 protease from *Garcinia mangostana*. *Planta Med*. 62: 381-382.

Chen Y, Fan H, Yang GZ, Jiang Y, Zhong FF, He HW. (2010). Prenylated xanthones from the bark of *Garcinia xanthochymus* and their 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging activities. *Molecules*. 15: 7438-7449.

Chen Y, Yang GZ, Zhong FF, He HW. (2010). Two new prenylated xanthones from the bark of *Garcinia xanthochymus*. *Bull. Korean Chem. Soc*. 31(11): 3418-3420.

Chen Y, Zhong FF, He HW, Hu Y, Zhu D, Yang GZ. (2008). Structure elucidation and NMR spectral assignment of five new xanthones from the bark of *Garcinia xanthochymus*. *Magn. Reson. Chem*. 46: 1180-1184.

Chiang YC, Kuo YH, Oota S, Fukuyama Y. (2003). Xanthones and benzophenones from the stems of *Garcinia multiflora*. *J. Nat. Prod*. 66: 1070-1073.

Chin YM, Jung HA, Chai H, Keller WJ, Kinghorn AD. (2008). Xanthones with quinine reductase-inducing activity from the fruits of *Garcinia mangostana* (Mangosteen). *Phytochemistry*. 69: 754-758.

Chomnawang MT, Surassmo S, Nukoolkorn VS, Gritsanapan W. (2005). Antimicrobial effects of Thai medicinal plants against acne-inducing bacteria. *J. Ethnopharmacol*. 101: 330-333.

Chomnawang MT, Surassmo S, Nukoolkorn VS, Gritsanapan W. (2007). Effect of *Garcinia mangostana* on inflammation caused by *Propionibacterium acnes*. *Fitoterapia*. 78: 401-408.

Chomnawang MT, Surassmo S, Wongsariya K, Bunyapraphatsara N. (2009). Antibacterial Activity of Thai Medicinal Plants against Methicillin-resistant *Staphylococcus aureus*. *Fitoterapia*. 80: 102-104.

Deschamps JD, Gautschi JT, Whitman S, Johnson TA, Gassner NC, Crews P, et al. (2007). Discovery of platelet-type 12-human lipoxygenase selective inhibitors by high-throughput screening of structurally diverse libraries. *Bioorg. Med. Chem*. 15: 6900-6908.

Du CT, Francis FJ. (1977). Anthocyanins of mangosteen, *Garcinia mangostana*. *J. Food Sci*. 42(6): 1667-1668.

Dutta P, Sem A, Sarkar K, Banerji N. (1987). Acid-catalysed cyclizations of xanthones: structure of a new xanthone from *Garcinia mangostana* Linn. *Indian J. Chem*. 26B: 281-282.

Ee GC, Daud S, Taufiq-Yap YH, Ismail NH, Rahmani M. (2006). Xanthones from *Garcinia mangostana* (Guttiferae). *Nat. Prod. Res*. 20: 1067-1073.

Ee GCL, Daud S, Izzaddin SA, Rahmani M. (2008). *Garcinia mangostana*: a source of potential anti-cancer lead compounds against CEM-SS cell line. *J. Asian Nat. Prod. Res*. 10(5): 481-485.

Fan C, Su J. (1997). Antioxidative mechanism of isolated components from methanol extract of fruit hulls of *G. mangostana* L. *J. Chin. Agr. Chem. Soc*. 35: 540-551.

Farnsworth RN, Bunyapraphatsara N. (1992). *Garcinia mangostana* Linn. In Thai medicinal plants. Prachachon Co., Ltd.: Bangkok, p. 160-162.

Garcia VV, Magpantay TO, Escobin LD. (2005). Antioxidant potential of selected Philippine vegetables and fruits. *Philipp. Agr. Sci*. 88: 78-83.

Gopalakrishnan C, Shankaranarayanan D, Kameswaran L, Nazimudeen SK. (1980). Effect of mangostin, a xanthone from *Garcinia mangostana* Linn. in immunopathological and inflammatory reactions. *Indian J. Exp. Biol*. 18: 843-846.

Gopalakrishnan G, Balaganesan B. (2000). Two novel xanthones from *Garcinia mangostana*. *Fitoterapia*. 71: 607-609.

Gopalakrishnan G, Banumathi B, Suresh G. (1997). Evaluation of the antifungal activity of natural xanthones from the fruits of *Garcinia mangostana* and their synthetic derivatives. *J. Nat. Prod*. 60: 519-524.

Govindachari TR, Kalyanaraman PS, Muthukumaraswamy N. (1971a). Xanthones of *Garcinia mangostana* Linn. *Tetrahedron*. 27: 3919-3926.

Govindachari TR, Kalyanaraman PS, Muthukumaraswamy N. (1971b) Isolation of three new xanthones from *Garcinia mangostana* Linn. *Indian J. Chem*. 9: 505-506.

Hamada M, Iikubo K, Ishikawa Y, Ikeda A, Umezawa K, Nishiyama S. (2003). Biological activities of α-mangostin derivatives against acidic sphingomyelinase. *Bioorg. Med. Chem. Lett*. 13: 3151-3153.

Han A-R, Kim J-A, Lantvit DD, Kardono LBS, Riswan S, Chai H, et al. (2009). Cytotoxic xanthone constituents of the stem bark of *Garcinia mangostana* (mangosteen). *J. Nat. Prod*. 72: 2028-2031.

Han QB, Qiao CF, Song JZ, Yang NY, Cao XW, Peng Y, et al. (2007). Cytotoxic prenylated phenolic compounds from the twig bark of *Grcinia xanthochymus*. *Chem. Biodiv*. 4(5): 940-946.

Han Q-B, Yang N-Y, Tian H-L, Qiao C-F, Song J-Z, Chang DC, et al. (2008). Xanthones with growth inhibition against HeLa cells from *Garcinia xipshuanbannaensis*. *Phytochemistry*. 69: 2187-2192.

Harbone J, Baxter H, Moss G. (1993). Phytochemical dictionary - a handbook of bioactive compounds from plant. Taylor & Francis. p. 590.

Haruenkit R, Poovarodom S, Leontowicz H, Leontowicz M, Sajewicz M, Kowalska T, et al. (2007). Comparative study of health properties and nutritional value of durian, mangosteen and sneke fruit: Experiments *in vitro* and *in vivo*. *J. Agr. Food Chem*. 55: 5842-5849.

Hasegawa H, Sasaki S, Almi N, Takayama H, Koyano T. (1996). *Helycobacter pylori* inhibitors containing xanthones from *Garcinia mangostana*. Japanese patent No. JP 08231396.

Helesbeux J-J, Duval O, Dartiguelongue C, Se´raphin D, Oger J-M, Richomme P. (2004). Synthesis of 2-hydroxy-3-methylbut-3-enyl substituted coumarins and xanthones as natural products. Application of the Schenck ene reaction of singlet oxygen with ortho-prenylphenol precursors. *Tetrahedron*. 60: 2293-2300.

Ho CK, Huang YL, Chen CC. (2002). Garcinone E, a xanthone derivative, has potent cytotoxic effect against the *hepatocellular* carcinoma cell lines. *Planta Med*. 68: 975-979.

Holloway DM, Scheinmann F. (1975). Phenolic conpounds from the heartwood of *Garcinia mangostana*. *Phytochemistry*. 14: 2517-2518.

Huang YL, Chen CC, Chen YJ, Huang RL, Shieh BJ. (2001). Three xanthones and a benzophenone from *Garcinia mangostana*. *J. Nat. Prod*. 64: 903-906.

Iikubo K, Ishikawa Y, Ando N, Umezawa K, Nishiyama S. (2002). The first direct synthesis of α-mangostin, a potent inhibitor of the acidic sphingomyelinase. *Tetrahedron Lett*. 43: 291-293.

Iinuma M, Tosa H, Tanaka T, Asai F, Kobayashi Y, Shimano R, et al. (1996). Antibacterial activity of xanthones from guttiferaeous plants against methicillin-resistant *Staphylococcus aureus*. *J. Pharm. Pharmacol*. 48: 861-865.

Iinuma M, Tosa H, Tanaka T, Asai F, Shimano R. (1995). Two new xanthones from the root bark of *Garcinia subelliptica*. *Heterocycles*. 40(1): 279-284.

Inoshiri S, Sasaki M, Kohda H, Otsuka H, Yamasaki K. (1987). Aromatic glycosides from *Berchemia racemosa*. *Phytochemistry*. 26(10): 2811-2814.

Itoh T, Ohguchi K, Inhuma M, Nozawa Y, Asao Y. (2008). Inhibitory effect of xanthones isolated from the pericarp of *Garcinia mangostana* L. on rat basophilic leukemia RBL-2H3 cell degranulation. *Bioorg. Med. Chem*. 16: 4500-4508.

Jefferson A, Scheinmann QF, Sim KY. (1970). Studies in the xanthone series. *Aust. J. Chem*. 23: 2539-2543.

Jinsart W, Ternai B, Buddhasukh D, Poly GM. (1992). Inhibition of wheat embryo calcium-dependent protein kinase and other kinases by mangostin and γ-mangostin. *Phytochemistry*. 31: 3711-3713.

Jung HA, Su BN, Keller WJ, Mehta RG, Kinghorn D. (2006). Antioxidant xanthones from pericarp of *Garcinia mangostana* (Mangosteen). *J. Agr. Food Chem*. 54: 2077-2082.

Karanjgoakar CG, Rao Rama AV, Venkataraman K, Yemul SS, Palmer KJ. (1973). Constitution of xanthochymol and isoxanthochymol. *Tetrahedron Lett*. 50: 4977-4980.

Kikuchi H, Ohtsuki T, Koyano T, Kowithayakorn T, Sakai T, Ishibashi M. (2010). Activity of mangosteen xanthones and teleocidin A-2 in death receptor expression enhancement and tumor necrosis factor related apoptosis-inducing ligand assays. *J. Nat. Prod*. 73: 452-455.

Kitanov GM, Nedialkov PT. (2001). Benzophenone *O*-glucoside, a biogenic precursor of 1,3,7-trioxygenated xanthones in *Hypericum annulatum*. *Phytochemistry*. 57: 1237-1243.

Komguem J, Meli AL, Manfouo RN, Lontsi D, Ngounou FN, Kuete V, et al. (2005). Xanthones from *Garcinia smeathmannii* (Oliver) and their antimicrobial activity. *Phytochemistry*. 66: 1713-1717.

Krajewski D, Toth G, Schreier P. (1996). 2-Ethyl-3-methylmaleimide *N*-β-*D*-glucopyranoside from the leave of mangosteen (*Garcinia mangostana*). *Phytochemistry*. 43(1): 141-143.

Laphookhieo S, Syers JK, Kiattansakul R, Chantrapromma K. (2006). Cytotoxic and antimalarial prenylated xanthones from *Cratoxylum cochinchinense*. *Chem. Pharm. Bull*. 54: 745-747.

Leong L, Shui G. (2002). An investigation of antioxidant capacity of fruits in Singapore markets. *Food Chem*. 76: 69-75.

Likhitwitayawuid; Phadungcharoen; & Krungkrai. (1998). Antimalarial xanthones from *Garcinia cowa*. *Planta Med*. 64: 70-72.

Locksley HD, Moore I, Scheinmann F. (1967). Extractives from Guttiferae-VI. The significance of maxlurin in xanthone biosynthesis. *Phytochemistry*. 23: 2229-2234**.**

Lu ZX, Hasmeda M, Mahabusarakam W, Ternai B, Ternai PC, Polya GM. (1998). Inhibition of eukaryote protein kinases and of a cyclic nucleotide-binding phosphatase by prenylated xanthones. *Chem. Bio. Interact*. 114: 121-140.

Macleod AJ, Pieris NM. (1982). Volatile flavour components of mangosteen, *Garcinia mangostana*. *Phytochemistry*. 21: 117-119.

Mahabusarakam W, Kuaha K, Wilairat P, Taylor WC. (2006). Prenylated xanthones as potential antiplasmodial substance. *Planta Med*. 72: 912-916

Mahabusarakam W, Proudfoot J, Taylor W, Croft K. (2000). Inhibition of lipoprotein oxidation by prenylated xanthones derived from mangostin. *Free Radic. Res*. 33: 643-659.

Mahabusarakam W, Wiriyachitha P, Phongpaichit S. (1986). Antimicrobial activities of chemical constituents from *G. mangostana* Linn. *J. Sci. Soc. Thailand*. 12: 239-242.

Mahabusarakam W, Wiriyachitha P, Taylor W. (1987). Chemical constituents of *Garcinia mangostana*. *J. Nat. Prod*. 50: 474-478.

Matsumato K, Akao Y, Kobayashi E, Ohguchi K, Ito T, Iinuma M, et al. (2003). Induction of apoptosis by xanthones from mangosteen in human leukemia cell lines. *J. Nat. Prod*. 66: 1124-1127.

Matsumato K, Akao Y, Ohguchi K, Ito T, Tanaka T, Iinuma M, et al. (2005). Xanthones induce cell-cycle arrest and apoptosis in human colon cancer DLD-1 cells. *Bioorg. Med. Chem*. 13: 6064-6069.

Matsumato K, Akao Y, Yi H, Ohguchi K, Ito T, Tanaka T, et al. (2004). Preferential target is mitochondria in α-mangostin induced apoptosis in human leukemia Hl60 cells. *Bioorg. Med. Chem*. 12: 5799-5806.

Menasria F, Azebaze AGB, Billard C, Faussat AM, Nkengfack AE, Meyer M, et al. (2008). Apoptotic effects on B-cell chronic lymphocytic leukemia (B-CLL) cells of heterocyclic compounds isolated from Guttiferaes. *Leukemia Res*. 32: 1914-1926.

Minami H, Kinoshita M, Fukuyama Y, Kodama M, Yoshizawa T, Sugiura M, et al. (1994). Antioxidant xanthones from *Garcinia subelliptica*. *Phytochemistry*. 36(2): 501-506.

Minami H, Takahashi E, Kodama M, Fukuyama Y. (1996). Three xanthones from *Garcinia subelliptica*. *Phytochemistry*. 41(2): 629-633.

Mohd Ghazali SAIS, Cheng Lian GE, Abd Ghani KD. (2010). Chemical constituent from roots of *Garcinia mangostana* Linn. *Int. J. Chem*. 2(1): 134-142.

Moongkarndi P, Kosem N, Kasluhga S, Luanratana O, Pongpan N, Neungton N. (2004a). Antiproliferation, antioxidation and induction of apoptosis by *Garcinia mangostana* (mangosteen) on SKBR3 human breast cancer cell line. *J. Ethnopharmacol*. 90: 161-166.

Moongkarndi P, Kosem N, Luanratana O, Jongsomboonkusol S, Pongpan N. (2004b). Antiproliferative activity of Thai medicinal plant extracts on human breast adenocarcinoma cell line. *Fitoterapia*. 75: 375-377.

Morton JF. (1987). Fruits of warm climates. Miami, FL: Creative Resource Systems, Inc. p. 301-304.

Nabandith V, Suzui M, Morioka T, Kaneshiro T, Kinjo T, Matsumato K, et al. (2004). Inhibitory effects of crude α-mangostin, a xanthone derivative, on two different categories of colon preneoplastic lesions induced by 1,2-dimethylhydrazine in the rat. *Asian Pac. J. Cancer. Prev*. 5: 433-438.

Nakagawa Y, Iinuma M, Naoe T, Nozawa Y, Akao Y. (2007). Characterized mechanism of α-mangostin-induced cell death: caspase-independent apoptosis with release of endonuclease-G from mitochondria and increased miRNA-143 expression in human colorectal cancer DLD-1 cells. *Bioorg. Med. Chem*. 15: 5620-5628.

Nakatani K, Atsumi M, Arakawa T, Oosawa K, Shimura S, Nakahata N, et al. (2002a). Inhibitions of histamine release and prostaglandin E_2 synthesis by mangosteen, a Thai medicinal plant. *Biol. Pharm. Bull*. 25: 1137-1141.

Nakatani K, Atsumi M, Arakawa T, Yasuda H, Ohizumi Y. (2002b). Inhibition of cyclooxygenase and prostaglandin E_2 synthesis by γ-mangostin, a xanthone derivative in mangosteen, in C6 rat glioma cells. *Biochem. Pharmacol*. 63: 73-79.

Nakatani K, Yamakuni T, Kondo N, Arakawa T, Oosawa K, Shimura S, et al. (2004). γ-Mangostin inhibits inhibitor-kappaB kinase activity and decreases lipopolysaccharide-induced cyclooxygenase-2 gene expression in C6 rat glioma cells. *Mol. Pharmacol*. 66: 667-674.

Narisara Suwannapoch. (2002). Xanthones from unriped pericarps of *Garcinia mangostana* Linn. Master Thesis, M.Sc. (biological chemistry). p. 36-38.

Nedialkov PT, Kitanov GM, Zheleva-Dimitrova DZ, Girreser U. (2007). Flavonoids and a xanthone from *Hypericum umbellatum* (Guttiferae). *Biochem. Sys. Ecol.* 35: 118-120.

Nilar, Harrison LJ. (2002). Xanthones from the heartwood of *Garcinia mangostana*. *Phytochemistry*. 60: 541-548.

Nilar, Nguyen LHD, Venkatraman G, Sim KY, Harrison LJ. (2005). Xanthones and benzophenones from *Garcinia griffithii* and *Garcinia mangostana*. *Phytochemistry*. 66: 1718-1723.

Obolskiy D, Pische, I, Siriwatanametanon N, Heinrich M. (2009). *Garcinia mangostana* L.: A Phytochemical and pharmacological review. *Phytotherapy Res*. 23: 1047-1065.

Orapin Komutiban. (2005). Study on xanthones from the young fruits of *Garcinia mangostana* Linn. Master Thesis, M.Sc. (chemistry). p. 94-95.

Parveen M, Khan NU. (1988). Two xanthones from *Garcinia mangostana*. *Phytochemistry*. 27: 3694-3696.

Parveen M, Khan NU-D, Achari B, Dutta PK. (1990). Triterpenoids from *Garcinia mangostana*. *Fitoterapia*. 61(1): 86-87. [Abstract]. CAN 113: 217918.

Parveen M, Khan NU-D, Achari B, Dutta PK. (1991). A triterpene from *Garcinia mangostana*. *Phytochemistry*. 30(1): 361-362.

Parveen N, Singh MP, Khan NU, Logani MK. (1994). Flavonoid constituents of *Garcinia xanthochymus* leaves. *Fitoterapia*. 65(1): 89-90. [abstract] from SciFinder. CAN 121:200863.

Peres V, Nagem T, Oliveira FF. (2000). Tetraoxygenated naturally occurring xanthones. *Phytochemistry*. 55: 683-710.

Peres V, Nagem TJ. (1997). Trioxygenated naturally occurring xanthones. *Phytochemistry*. 44(2): 191-214.

Perveen M, Khan NU-D. (1987). A new isoprenylated xanthone from *Garcinia mangostana* Linn. *Chem. Ind*. 15: 418.

Phongpaichit S, Ongsakul M, Nilrat L, Tharavichitkul P, Bunchoo S, Chuaprapaisilp T, et al. (1994). Antibacterial activities of extracts from *Garcinia mangostana* pericarps on methicillin-resistant *Staphylococcus aureus* and *Enterococcus* species. *Songklanakarin J. Sci. Technol*. 16: 399-405.

Pinto MM, Sousa ME, Nascimento MS. (2005). Xanthones derivatives: new insights in biological activities. *Curr. Med. Chem*. 12: 2517-2538.

Pothitirat W, Chomnawang MT, Supabphol R, Gritsanapan W. (2009). Comparison of bioactive compounds content, free radical scavenging and anti-acne inducing bacteria activities of extracts from the mangosteen fruit rind at two stages of maturity. *Fitoterapia*. 80: 442-447.

Pothitirat W, Gritsanapan W. (2008). Quantitative analysis of total mangostins in *Garcinia mangostana* fruit rind. *J. Health Res*. 22(4): 161-166.

Ramage CM, Sando L, Peace CP, Carroll BJ, Drew RA. (2004). Genetic diversity in the apomictic fruit species *Garcinia mangostana* L. (mangosteen). *Euphytica*. 136: 1-10.

Rao Rama AV, Venkatswamy G, Yemul SS. (1980). Xanthochymol & isoxanthochymol, two novel polyisoprenylated benzophenones from *Garcinia xanthochymus*. *Indian J. Chem*. 19B: 627-633.

Riscoe M, Kelly JX, Winte, R. (2005). Xanthones as antimalarial agents: discovery, mode of action, and optimization. *Curr. Med. Chem*. 12: 2539-2549.

Roberts JC. (1961). Naturally occurring xanthones. *Chem. Rev*. 61: 591-605.

Sakagami Y, Iinuma M, Piyasena KGNP, Dharmaratne HRW. (2005). Antibacterial activity of α-mangostin against vancomycin resistant *Enterococci* (VRE) and synergism with antibiotics. *Phytomedicine*. 12: 203-208.

Sakai S, Katsura M, Takayama H, Aimi N, Chokethaworn N, Suttajit M. (1993). The structure of garcinone E. *Chem. Pharm. Bull*. 41: 958-960.

Sampath PD, Vijayaragavan K. (2007). Ameliorative prospective of alpha-mangostin, a xanthone derivative from *Garcinia mangostana* against β-adrenergic cathecolamine-induced myocardial toxicity and anomalous cardiac TNF-α and COX-2 expressions in rats. *Exp. Toxicol. Pat*. 60: 357-364.

Saralamp P, Temsiririrkkul R, Clayton T. (1996). Medical Plants in Thailand: Amarin printing and publishing public Co., Ltd.: Bangkok, Thailand. p. 98.

Sato A, Fujiwara H, Oku H, Ishiguro K, Ohizumi Y. (2004). Alpha-mangostin induces Ca^{2+}-ATPase-dependent apoptosis via mitochondrial pathway in PC12 cells. *J. Pharmacol. Sci*. 95: 33-40.

Scheinmann F. (1962). Studies in the xanthone series-V infrared spectra of some substituted and extended xanthones. *Tetrahedron*. 18: 853-858.

Sen AK, Sarka KK, Majumder PC, Banerji N. (1981). Minor xanthones of *Garcinia mangostana*. *Phytochemistry*. 20: 183-185.

Sen AK, Sarkar KK, Mazumder PC, Banerji N. (1980a). Isolation of three new minor xanthones from *Garcinia mangostana* Linn. *Indian J. Chem*. 19B: 1008.

Sen AK, Sarkar KK, Mazumder PC, Banerji N. (1986). Garcinone-D, a new xanthone from *Garcinia mangostana*. *Indian J. Chem*. 25B: 1157-1158.

Sen AK, Uusvuori R, Hase TA, Banerji N, Sarkar KK, Mazumder PC. (1980b). A xanthone from *Garcinia mangostana*. *Phytochemistry*. 19: 2223-2225.

Sen AK, Uusvuori R, Hase TA, Banerji N, Sarkar KK, Mazumder PC. (1982). The structure of garcinones A, B and C: three new xanthones from *Garcinia mangostana*. *Phytochemistry*. 21: 1747-1750.

Sia GL, Benett GJ, Harrison LJ, Sim KY. (1995). Minor xanthones from the bark of *Cratoxylum cochinchinense*. *Phytochemistry*. 38: 1521-1528.

Singh MP, Parveen N, Khan NU, Achari B, Dutta PK. (1991). Constituents of *Garcinia xanthochymus*. *Fitoterapia*. 62(3): 286. [abstract] from SciFinder. CAN 116:148166.

Smitinand T. (2001). Thai plant names. rev. ed. Bangkok: The Forest Herbarium, Royal Forest Department. p. 246-248.

Sugiyama M, Kikuchi M. (1991). Phenolic glycosides from *Osmanthus asiaticus*. *Phytrochemistry*. 30(9): 3149-3151.

Suksamrarn S, Komutiban O, Ratananukul P, Chimnoi N, Lartpornmatulee N, Suksamrarn A. (2006). Cytotoxic prenylated xanthones from the young fruit of *Garcinia mangostana*. *Chem. Pharm. Bull*. 54: 301-305.

Suksamrarn S, Suwannapoch N, Phakhodee W, Thanuhiranlert J, Ratananukul P, Chimnoi N, et al. (2003). Antimycobacterial activity of prenylated xanthones from the fruits of *Garcinia mangostana*. *Chem. Pharm. Bull*. 51: 857-859.

Suksamrarn S, Suwannapoch N, Ratananukul P, Aroonlerk N, Suksamrarn A. (2002). Xanthones from the green fruit hulls of *Garcinia mangostana*. *J. Nat. Prod*. 65: 761-763.

Sundaram BM, Gopalakrishnan C, Subramanian S, Shankarayanan D, Kameswaran L. (1983). Antimicrobial activities of *Garcinia mangostana*. *Planta Med*. 48: 59-60.

Tewtrakul S, Wattanapiromsakul C, Mahabusarakam W. (2009). Effects of compounds from *Garcinia mangostana* on inflammatory mediators in RAW264.7 macrophage cells. *J. Ethnopharmacol*. 121: 379-382.

Tongdee SC, Suwanagul A. (1989). Postharvest mechanical damage in mangosteens. *Asean Food. J.* 4(4): 151-155.

Tosa H, Iinuma M, Tanaka T, Nozaki H, Ikeda S, Tsutsui K, et al. (1997). Inhibitory activity of xanthone derivatives isolated from some Guttiferaeous plants against DNA topoisomerases I and II. *Chem. Pharm. Bull.* 45(2): 418-420.

Voravuthikunchai SP, Kitpipit L. (2005). Activity of medicinal plant extracts against hospital isolates of methicillin-resistant *Staphylococcus aureus*. *Clin. Microbiol. Infect*. 11, 510-512.

Wan ASC. (1973). *Garcinia mangostana*. High resolution NMR studies of mangostin. *Planta Med*. 24: 297-300.

Wang H, Ye G, Ma C-H, Tang Y-H, Fan M-S, Li Z-X, et al. (2007). Identification and determination of four metabolites of mangiferin in rat urine. *J. Pharma. Biomed. Anal.* 45: 793-798.

Weecharangsan W, Opanasopit P, Sukma M, Ngawhirunpat T, Sotanaphun U, Siripong P. (2006). Antioxidative and neuroprotective activities of extracts from the fruit hull of mangosteen (*Garcinia mangostana* Linn.). *Med. Princ. Pract*. 5: 281-287.

Wieble JEKC, Downton WJS. (1992). Mangosteen (*Garcinia mangostana* L.)-Apotential crop for northern Australia. *Acta Hortic*. 321: 132-137.

Williams P, Ongsakul M, Proudfoot J, Croft K, Beilin L. (1995). Mangostin inhibits the oxidative modification of human low density lipoprotein. *Free Radic. Res*. 23: 175-184.

www. nmrdb.org

Yamakuni T, Aoki K, Nakatani K, Kondo N, Oku H, Ishiguro K, et al. (2006). Garcinone B reduce prostaglandin E_2 release and NF-κB-mediated transcription in C6 rat glioma cells. *Neurosci. Lett*. 394: 206-210.

Yates P, Bhat HB. (1968). Structure of β-mangostin. *Can. J. Chem*. 46: 3770-3772.

Yates P, Stout GH. (1958). The structure of mangostin. *J. Am. Chem. Soc*. 80: 1691-1700.

Yu L, Zhao M, Yang B, Bai W. (2009). Immunomodulatory and anticancer activities of phenolics from *Garcinia mangostana* fruit pericarp. *Food Chem*. 116: 969-973.

Yu L, Zhao M, Yang B, Zhao O, Jiang Y. (2007). Phenolics from hull of *Garcinia mangostana* fruit and their antioxidant activities. *Food Chem*. 104: 176-181.

Zarena AS, Udaya Sanka K. (2009). Screening of xanthone from mangosteen (*Garcinia mangostana* L.) peels and their effect on cytochrome C reductase and phosphomolybdenum activity. *J. Nat. Prod*. 2: 23-30.

Zhang Y, Song Z, Hao J, Qiu S, Xu Z. (2010). Two new prenylated xanthones and a new prenylated tetrahydroxanthone from the pericarp of *Garcinia mangostana*. *Fitoterapia*. 81: 595-599.

Zhong FF, Chen Y, Mei ZN, Yang GZ. (2007). Xanthones from the bark of *Garcinia xnathochymus*. *Chin. Chem. Lett*. 18: 849-851.

Zhong FF, Chen Y, Ping W, Huijin F, Yang GZ. (2009). Xanthones from the bark of *Garcinia xanthochymus* and their 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging activitiy. *Chin. J. Chem*. 27: 74-80.

Zhong FF, Chen Y, Yang GZ. (2008). Chemical constituents from the bark of *Garcinia xanthochymus* and their 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging activities. *Helv. Chim. Acta*. 91(9): 1695-1703.

APPENDIX

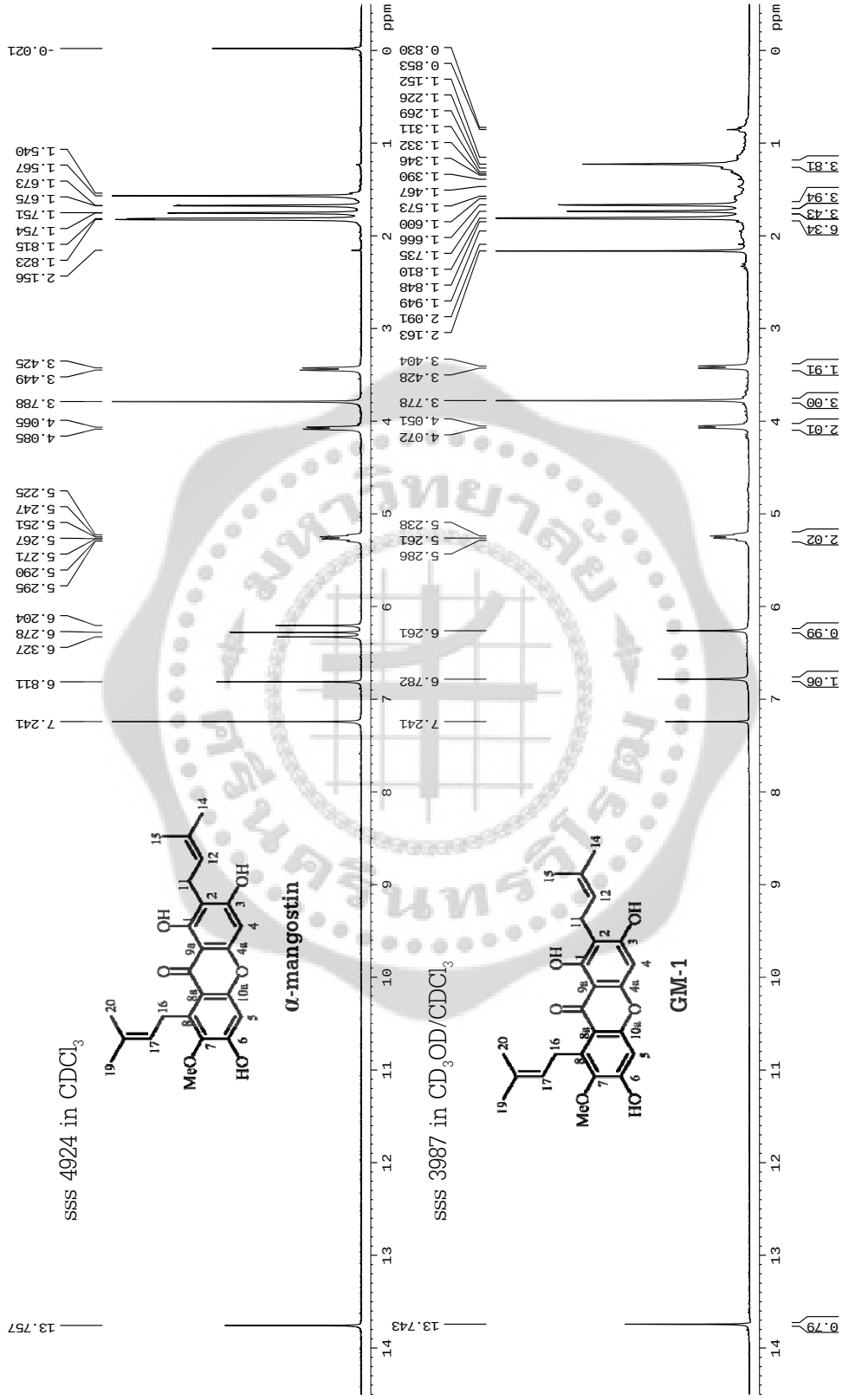


Figure 49 ^{1}H-NMR spectra of compounds **α**-mangostin and compound **GM-1** (sss 3987)

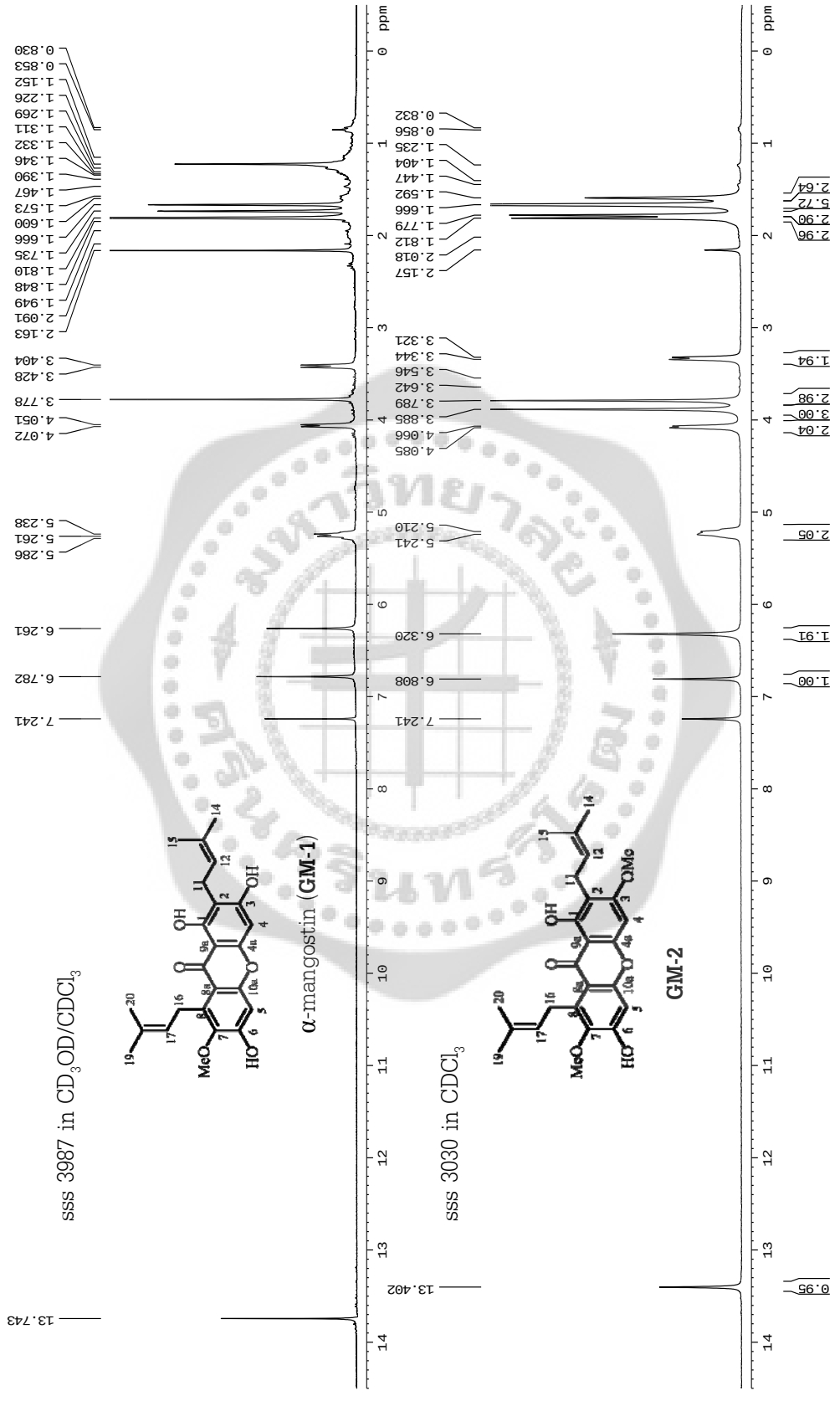


Figure 50 ^{1}H-NMR spectra of compounds α-mangostin (**GM-1**) and compound **GM-2** (sss 3030, β-mangostin)

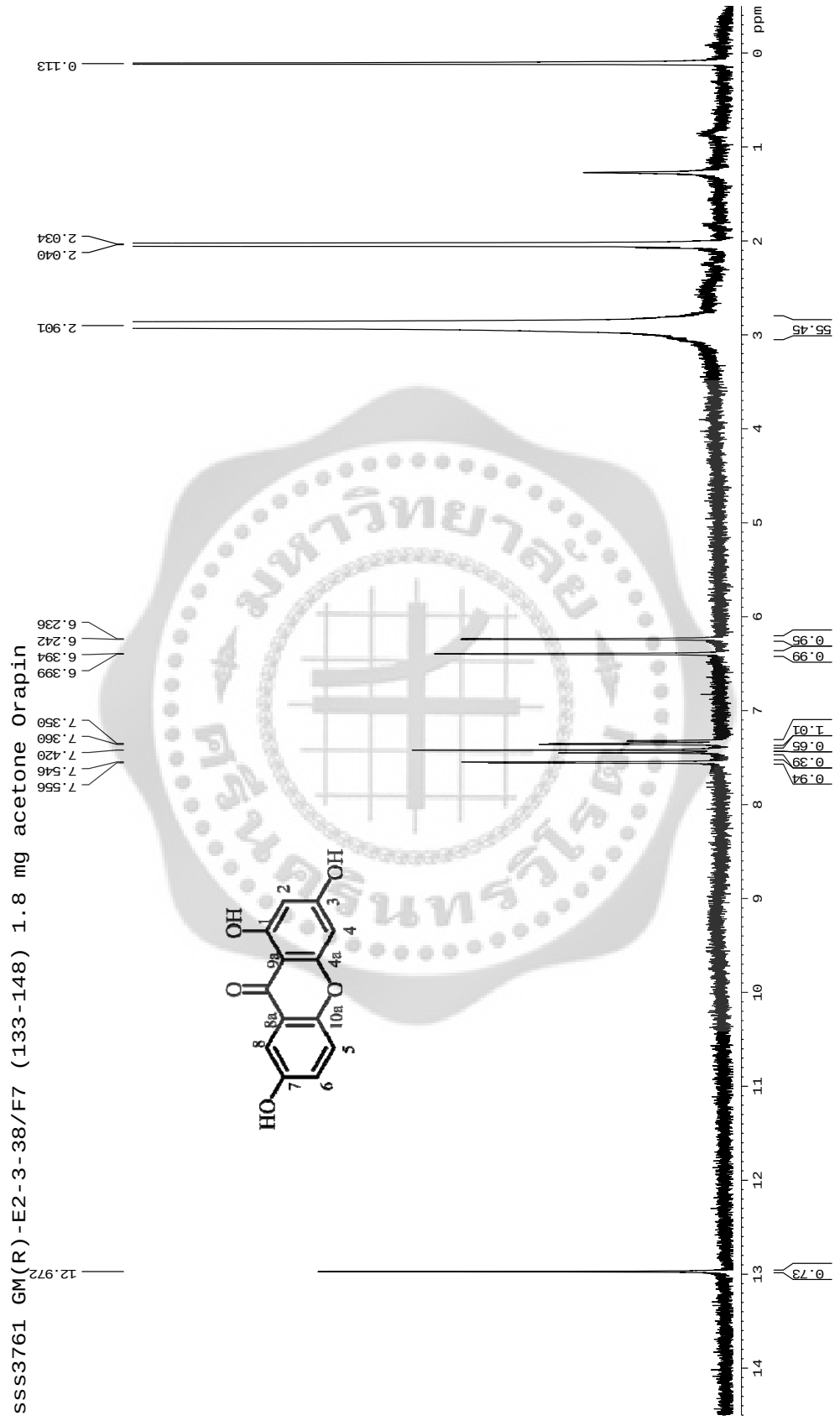


Figure 51 ^{1}H-NMR spectrum of compound **GM-3** (sss 3761, gentisein) in acetone-d_6

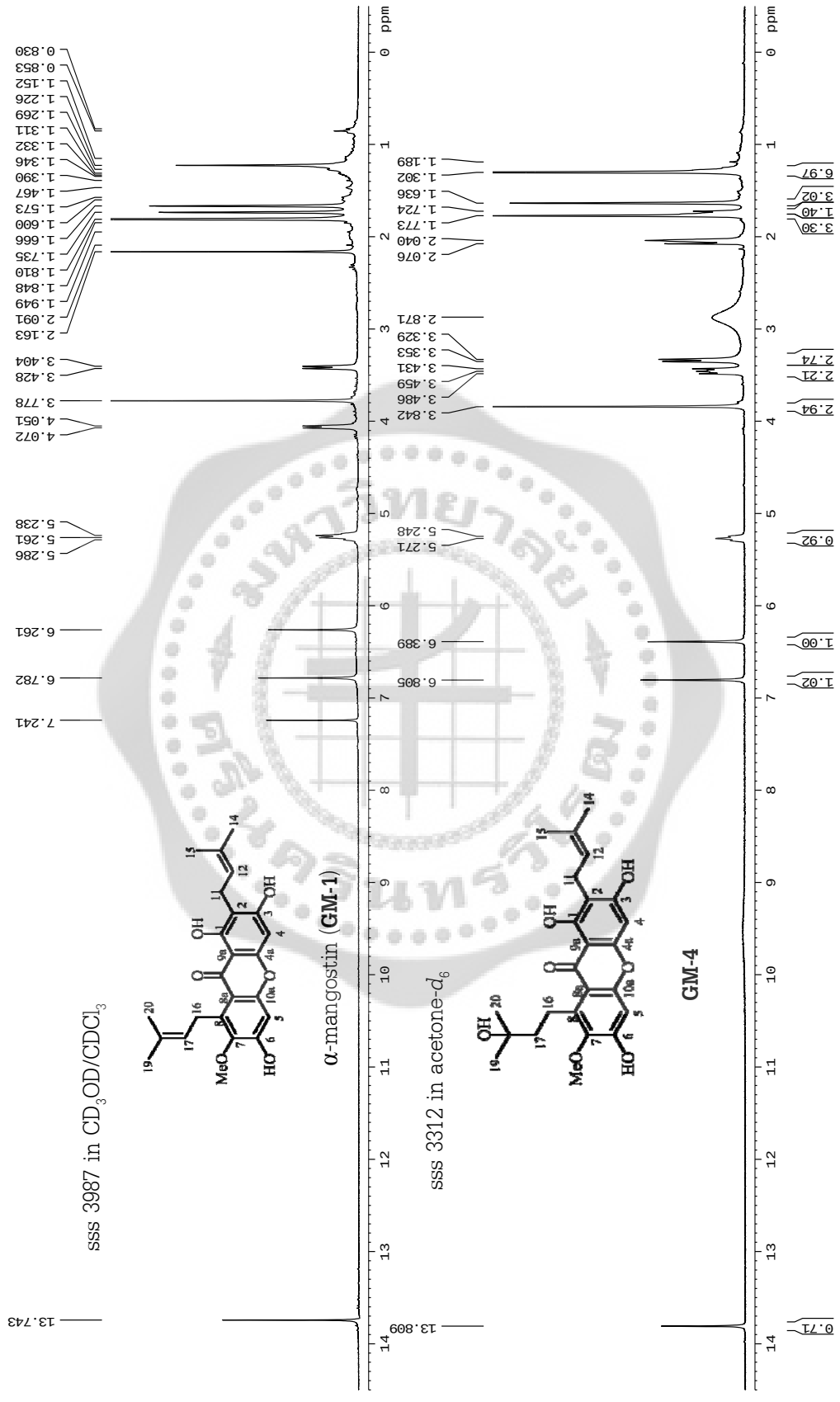


Figure 52 ^{1}H-NMR spectra of compounds α-mangostin (**GM-1**) and compound **GM-4** (sss 3312, garcinone D)

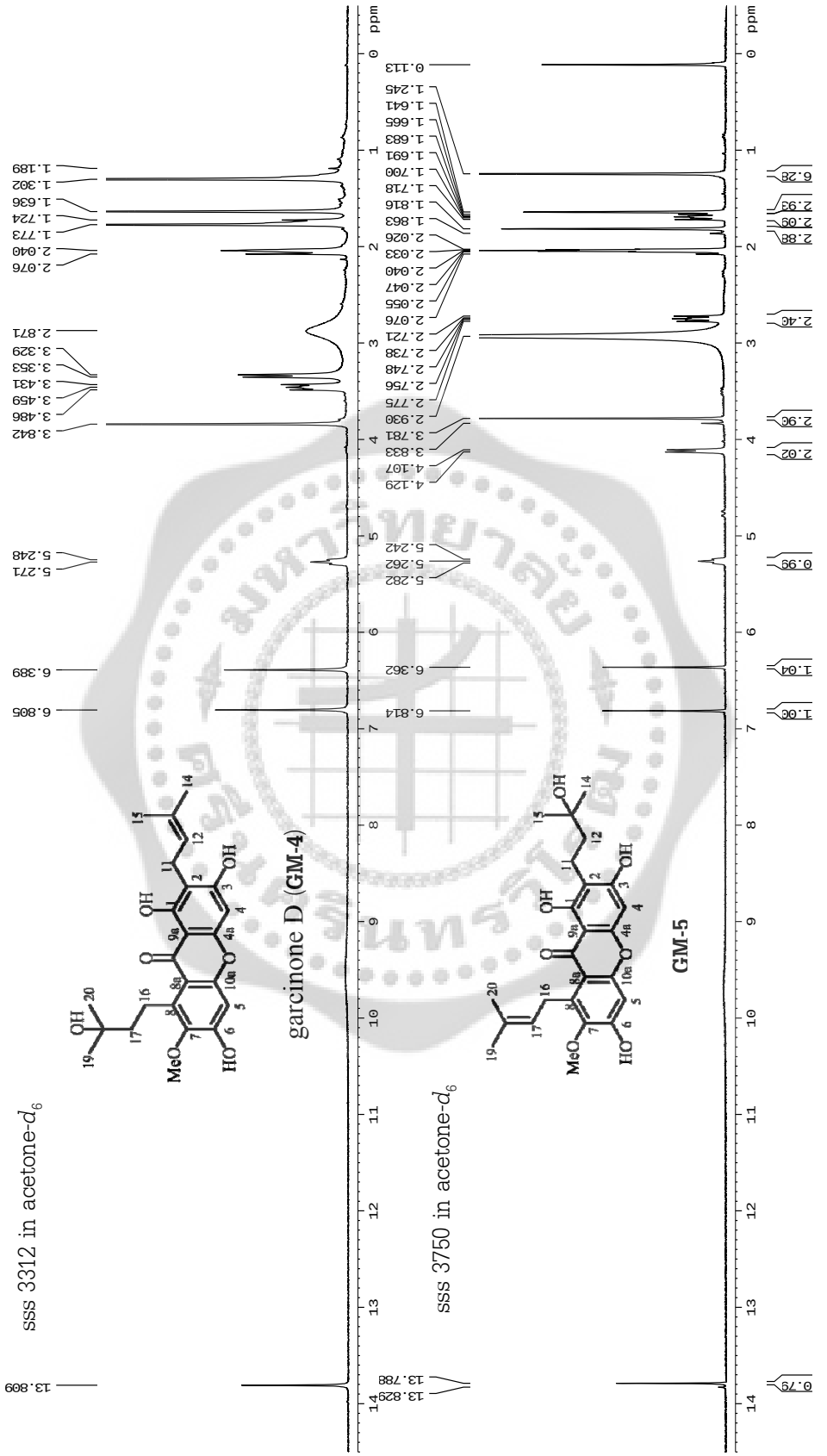


Figure 53 ^{1}H-NMR spectra of compounds garcinone D (**GM-4**) and compound **GM-5** (sss 3750, cratoxylone)

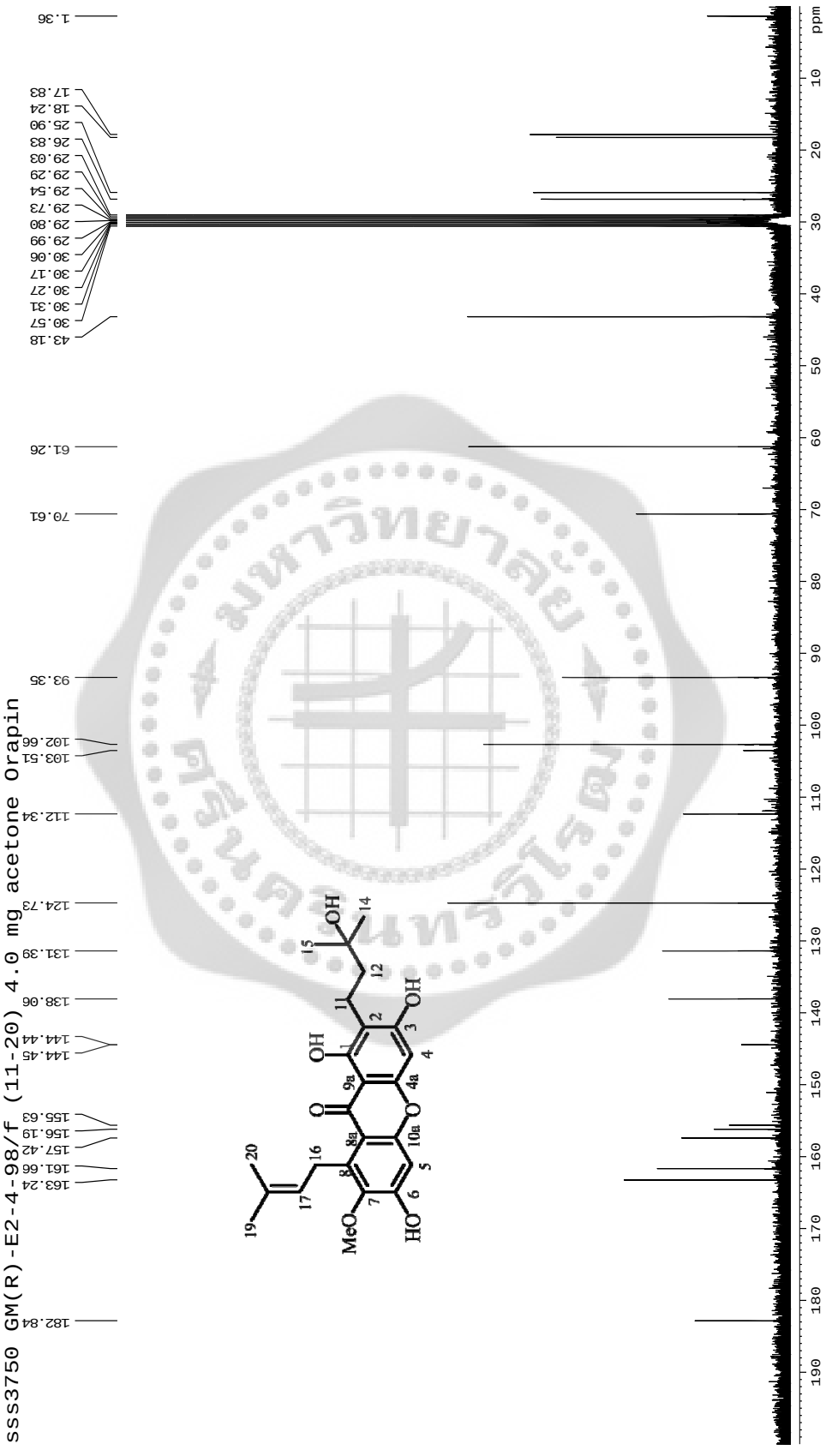


Figure 54 ^{13}C-NMR spectrum of compound **GM-5** (sss 3750, cratoxylone) in acetone-d_6

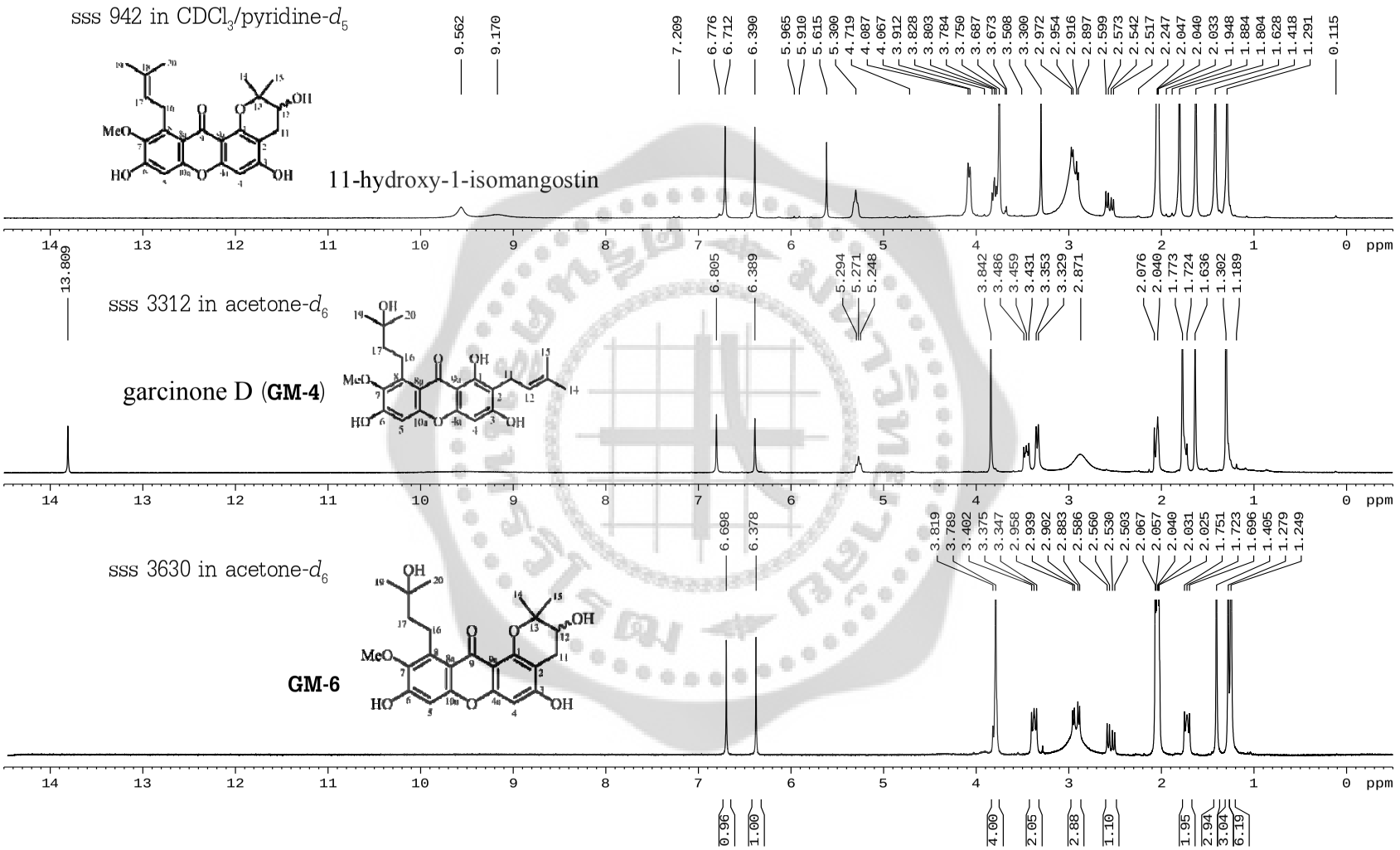


Figure 55 ^{1}H-NMR spectra of compounds 11-hydroxy-1-isomangostin, garcinone D (**GM-4**) and compound **GM-6** (sss 3630)

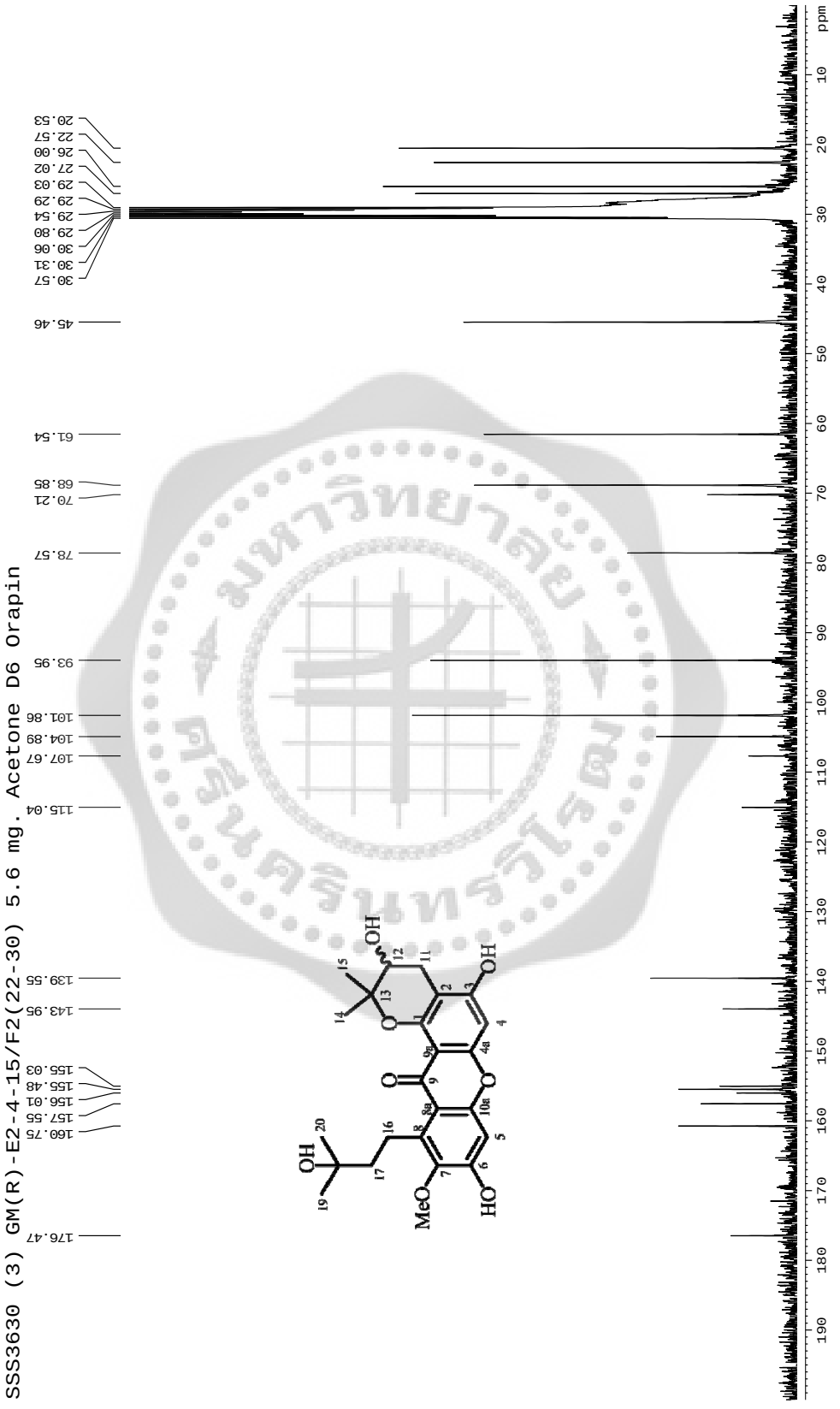


Figure 56 ^{13}C-NMR spectrum of compound **GM-6** (sss 3630) in acetone-d_6

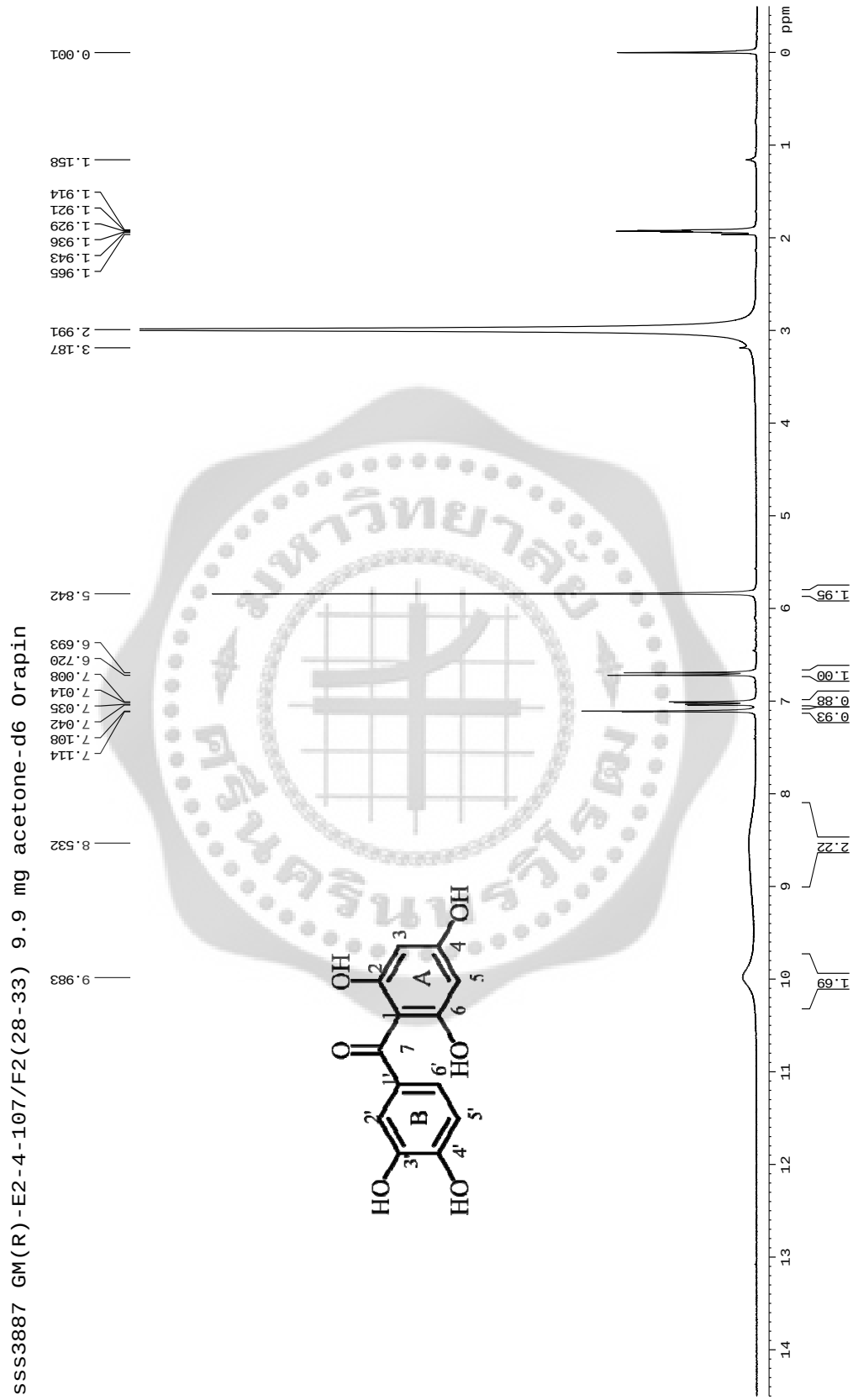


Figure 57 ^{1}H-NMR spectrum of compound **GM-8** (sss 3887, maclurin) in acetone-d_6

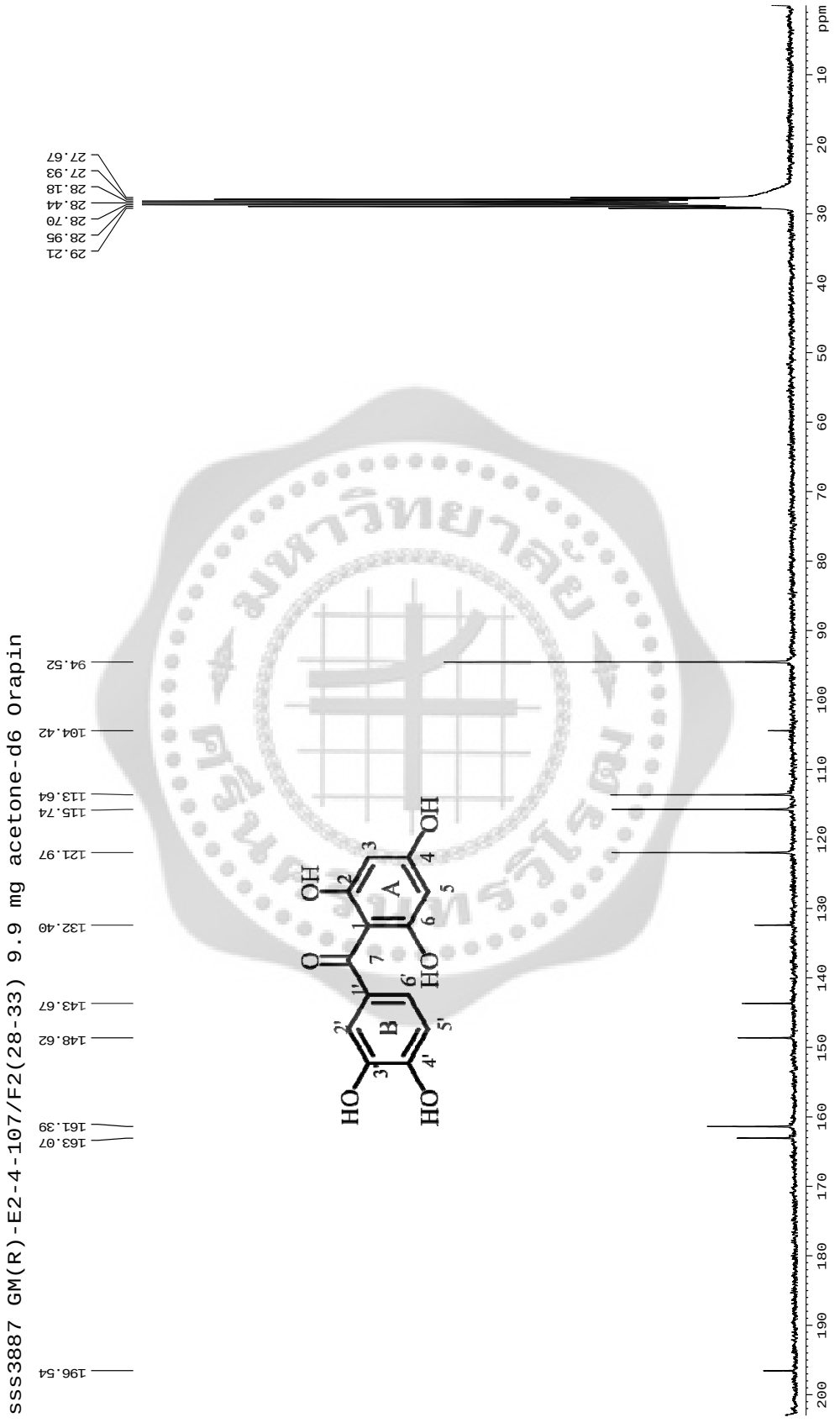


Figure 58 ^{13}C-NMR spectrum of compound **GM-8** (sss 3887, maclurin) in acetone-d_6

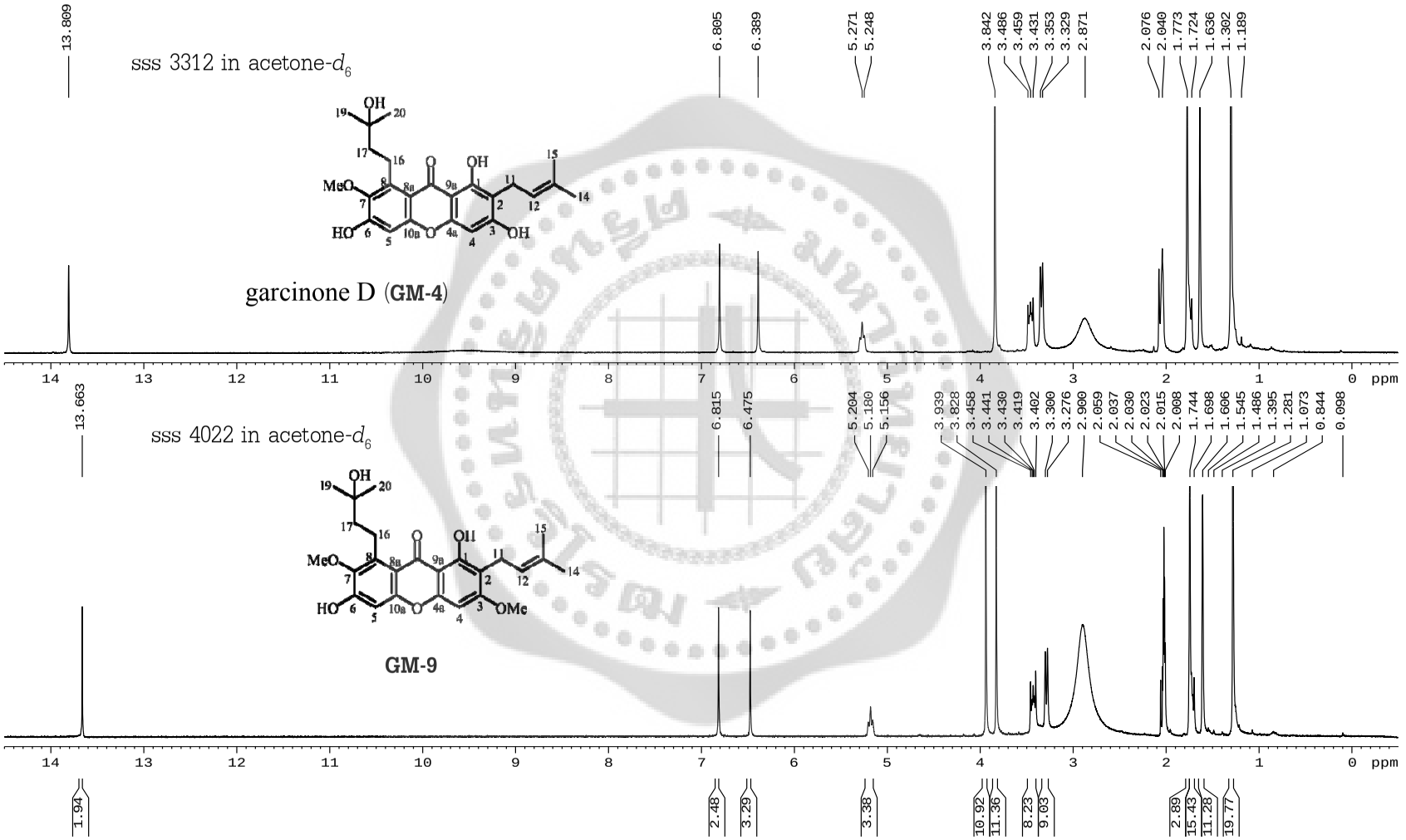


Figure 59 ^{1}H-NMR spectra of compounds garcinone D (**GM-4**) and compound **GM-9** (sss 4022, pruniflorone C)

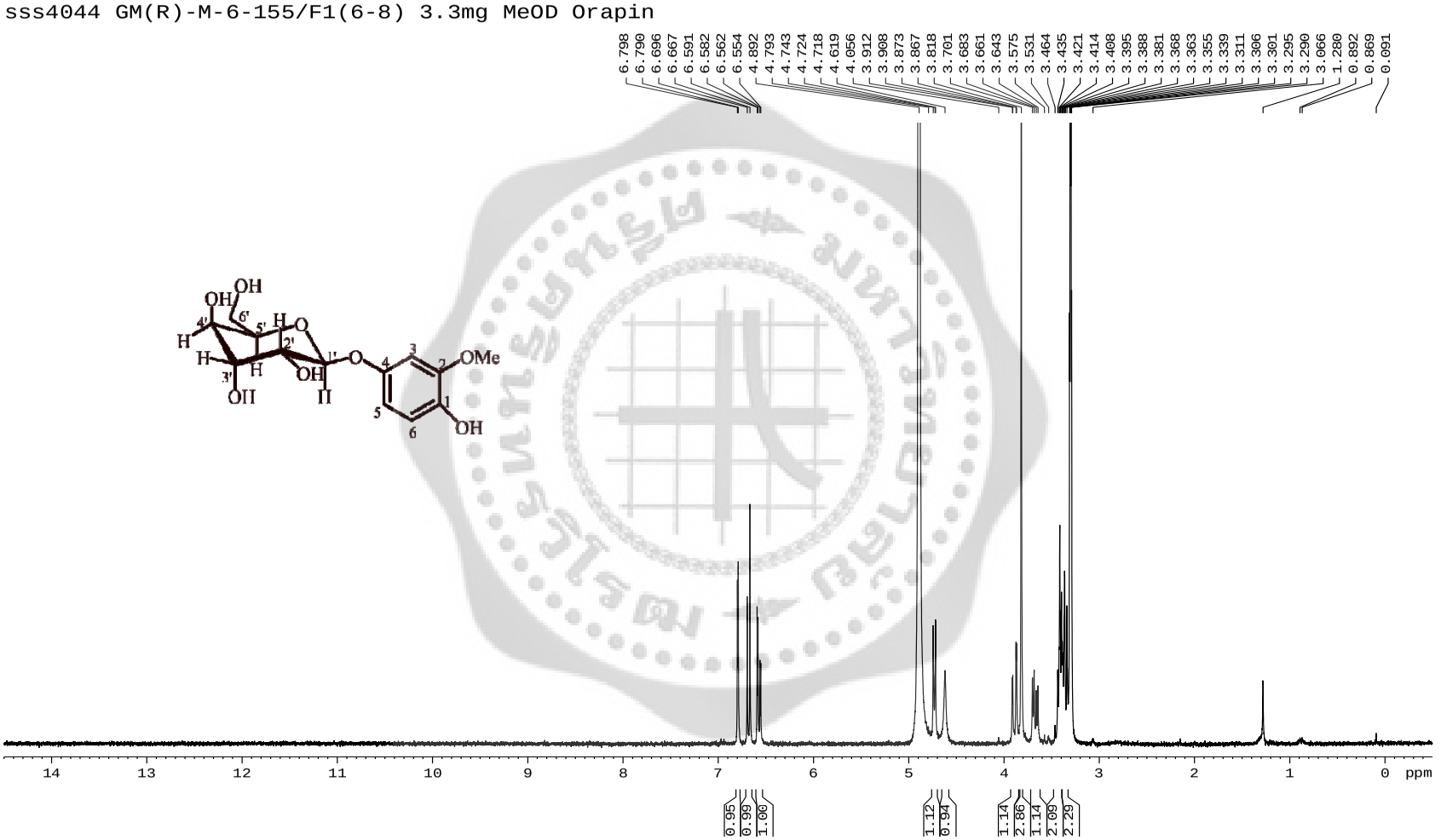


Figure 60 ^{1}H-NMR spectrum of compound **GM-11** (sss 4044, tachioside) in CD_3OD

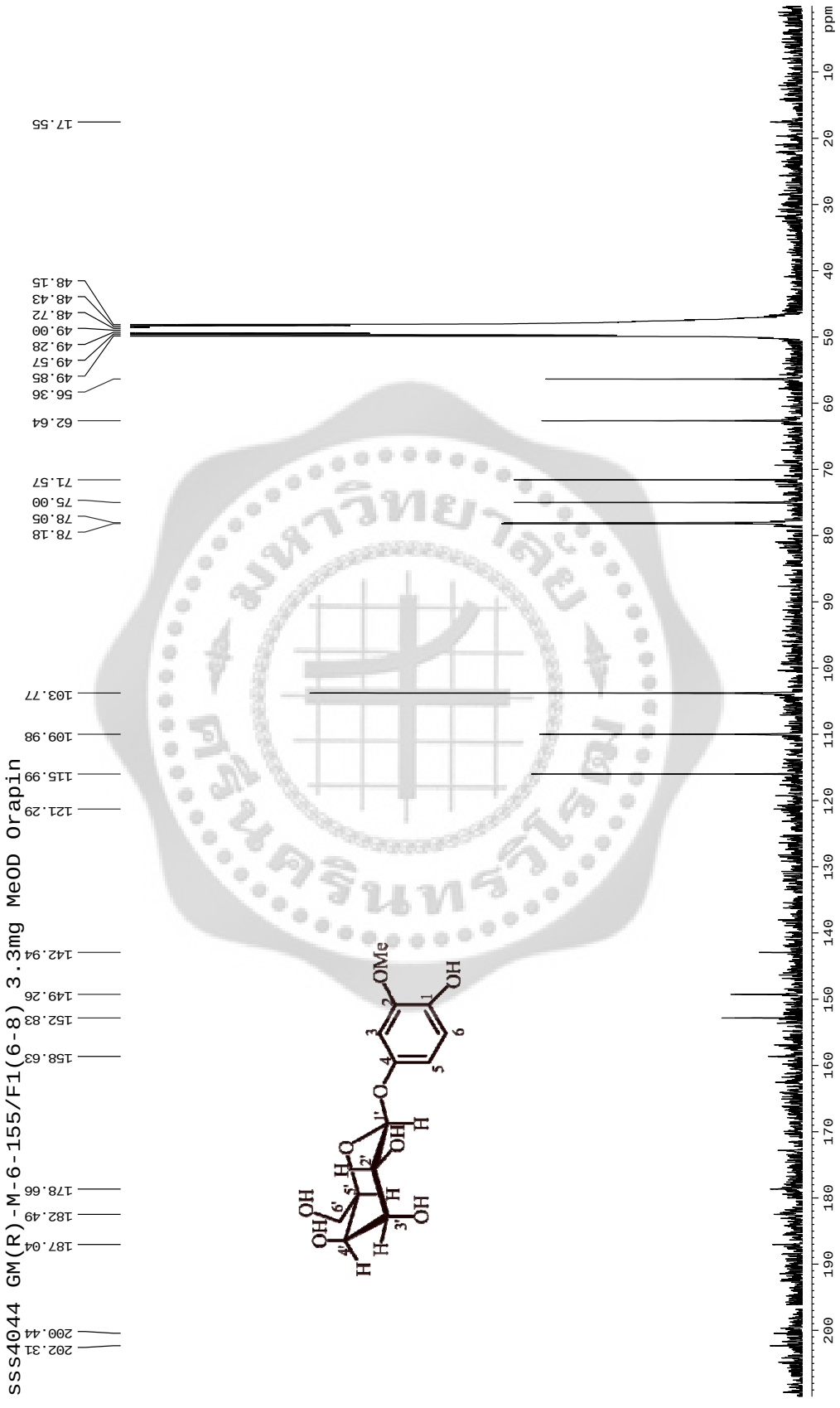


Figure 61 ^{13}C-NMR spectrum of compound **GM-11** (sss 4044, tachioside) in CD_3OD

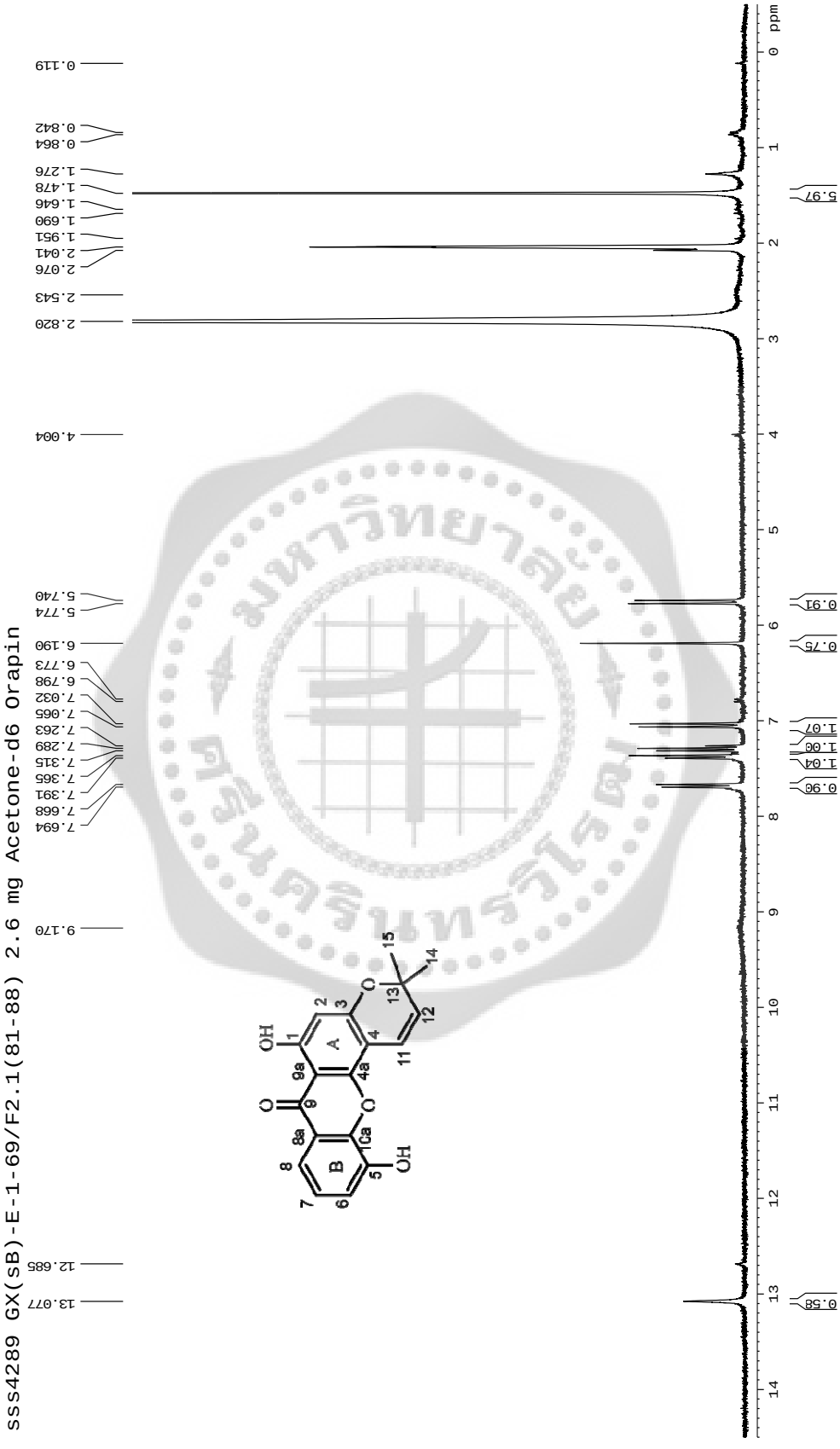


Figure 62 ^{1}H-NMR spectrum of compound **GX-1** (sss 4289, 6-deoxyisojacareubin) in acetone-d_6

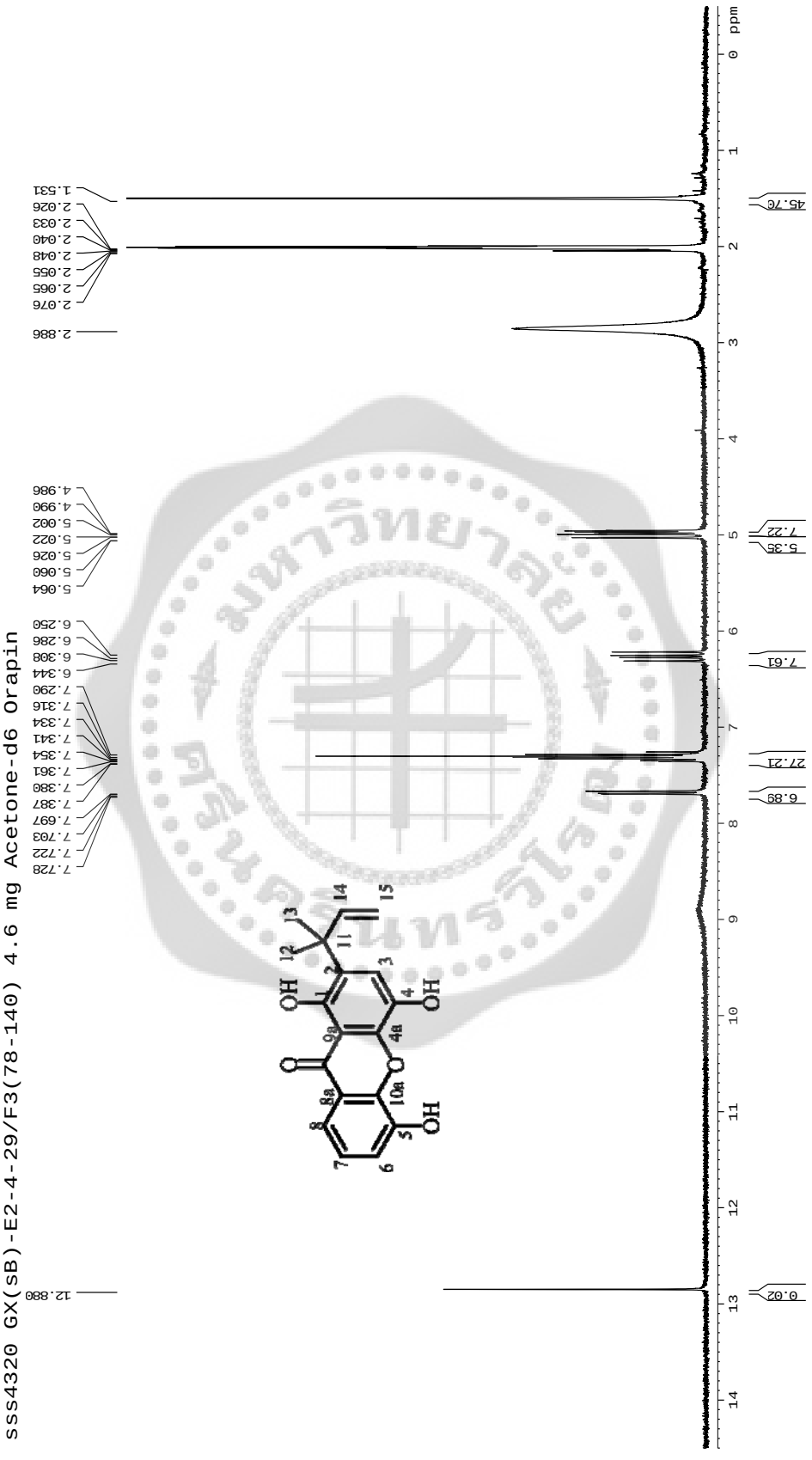


Figure 63 ^{1}H-NMR spectrum of compound **GX-2** (sss 4320, 12-hydroxy-des-D-garcigerrin A) in acetone-d_6

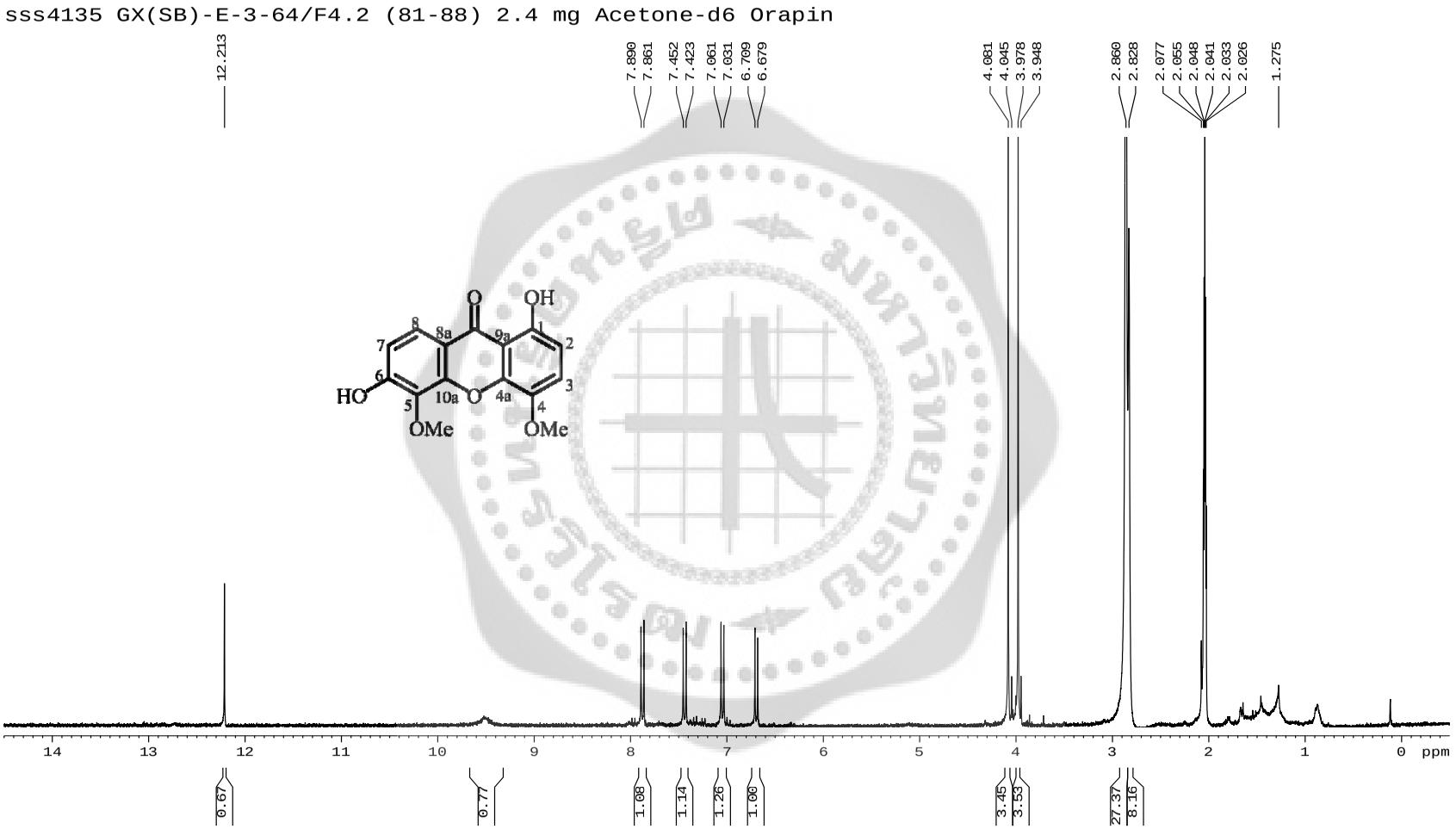


Figure 64 ^{1}H-NMR spectrum of compound **GX-3** (sss 4135, 1,6-dihydroxy-4,5-dimethoxyxanthone) in acetone-d_6

GLOSSARY

LIST OF ABBREVIATIONS AND SYMBOLS

acetone-d_6	=	Deuterated acetone
α	=	Alpha
$[\alpha]_D^{27.0}$	=	Specific rotation at 27.0° and sodium D line
β	=	Beta
br *d*	=	Broad doublet (for NMR data)
br *t*	=	Broad triplet (for NMR data)
br *s*	=	Broad singlet (for NMR data)
CC	=	Column Chromatography
$CDCl_3$	=	Deuterated chloroform
CD_3OD	=	Deuterated methanol
C_5D_5N	=	Deuterated pyridine
$CHCl_3$	=	Chloroform
CH_2Cl_2	=	Dichloromethane
°C	=	Degree Celsius
^{13}C NMR	=	Carbon-13 Nuclear Magnetic Resonance
c	=	Concentration
calcd	=	Calculated
cm	=	Centimeter
cm^{-1}	=	Reciprocal centimeter (unit of wave number)
d	=	Doublet (for NMR data)
dd	=	Doublet of doublets (for NMR data)
DEPT	=	Distortionless Enhancement by Polarization Transfer
δ	=	Chemical shift (for NMR data)
ESMS	=	Electrospray ionization Mass Spectrometry
EIMS	=	Electron-Ionization Mass Spectrometry
EtOAc	=	Ethyl acetate
g	=	Gram
h	=	Hour
^1H-^1H COSY	=	Homonuclear (Proton-Proton) Correlation Spectroscopy

LIST OF ABBREVIATIONS AND SYMBOLS (continued)

^{1}H NMR	=	Proton Nuclear Magnetic Resonance
HMBC	=	^{1}H-Detected Heteronuclear Multiple Bond Coherence
HMQC	=	^{1}H-Detected Heteronuclear Multiple Quantum Coherence
HRTOFMS	=	High Resolution Time of Flight Mass Spectrometry
Hz	=	Hertz
IC_{50}	=	50% Inhibitory Concentration
IR	=	Infrared Spectrum
J	=	Coupling constant
KBr	=	Potassium bromide
Kg	=	Kilogram
L	=	Liter
λ_{max}	=	Wavelength at maximal absorption
ε	=	Molar absorptivity
Me	=	Methyl
MeOH	=	Methanol
MIC	=	Minimum Inhibitory Concentration
$[M+H]^+$	=	Protonated molecular ion
m	=	Multiplet (for NMR data)
mg	=	Milligram
m/z	=	Mass to charge ratio
mL	=	Milliliter
μl	=	Microliter
μg	=	Microgram
NMR	=	Nuclear Magnetic Resonance Spectroscopy
NOESY	=	Nuclear Overhauser Effect Spectroscopy
nm	=	Nanometer
ν_{max}	=	Wave number at maximal absorption
s	=	Singlet (for NMR data)
sh	=	shoulder

LIST OF ABBREVIATIONS AND SYMBOLS (continued)

TLC	=	Thin Layer Chromatography
TMS	=	Tetramethylsilane
t	=	Triplet (for NMR data)

CURRICULUM VITAE

CURRICULUM VITAE

Name : Orapin Komutiban

Date of Birth : December 14, 1979

Place of Birth : Bangkok

Address : 1/1 Soi Prachautith 13, Prachautith Rd, Ratburana, Bangkok, 10140

Educational Background :

1997 Bachelor of Science in Chemistry
Suan Dusit Ratjabhat University, Bangkok, Thailand

2004 Master of Education in Chemistry
Srinakharinwirot University, Bangkok, Thailand

2011 Doctor of Philosophy Degree in Applied Chemistry
Srinakharinwirot University, Bangkok, Thailand

Publication :

1. Suksamrarn, S.; **Komutiban, O**.; Ratananukul, P.; Chimnoi, N.; Lartpornmatulee, N.; Suksamrarn, A. Cytotoxic prenylated xanthones from the young fruits of *Garcinia mangostana*. Chem. Pharm. Bull. 2006, 54(3), 301-305.