CHEMICAL CONSTITUENTS FROM *Crotalaria pallida*, *Morinda citrifolia* AND *Chlorophyllum molybdites*

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FACULTY OF SCIENCE
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[CHEMICAL CONSTITUENTS FROM *CROTALARIA PALLIDA*, *MORINDA CITRIFOLIA* AND *CHLOROPHYLLUM MOLYBDITES*]

ABSTRACT

The present dissertation work focused on the phytochemical studies of three Malaysian plants, *Crotalaria pallida*, *Morinda citrifolia* and *Chlorophyllum molybdites. C. pallida*, from the family of Fabaceae, a herbaceous legume and used traditionally for treatment of several types of illness. This plant is also known to produce the toxic pyrrolizidine alkaloids and flavonoids. *M. citrifolia*, from the family of Rubiaceae, is a small evergreen shrub tree. It is known to produce anthraquinone compounds, which possess various therapeutic properties including antiviral, antibacterial, antioxidant, anticancer, antitumor, and anti-inflammatory. *C. molybdites* from the family of Agaricaceae is a poisonous mushroom often involved in poisoning cases throughout the world. This fungi is known to produce the toxic components such as a toxic protein, molybdophyllysin. In the present study, one new cyclopentylidene, crotolidene (**CP1**), and seven known compounds, *i.e.* hydroxydihydrobovolide (**CP2**), octacosane (**CP3**), trans-phytyl palmitate (**CP4**), linoleic acid (**CP5**), methyl oleate (**CP6**), ethyl palmitate (**CP7**), and palmitic acid (**CP8**) were isolated from the hexane extract of *C.pallida*. A total of five known anthraquinones were isolated from the chloroform extract of *M. citrifolia* which included damnacanthal (**MC1**), nordamnacanthal (**MC2**), rubiadin (**MC3**), 1,6-dihydroxy-2-methyl-anthraquinone (**MC4**), 1-hydroxy-3-methoxyanthraquinone (**MC5**), and 1-methoxy-2-hydroxyanthraquinone (**MC6**). Ethyl acetate extracts of *C. molybdites* gave four known compounds which are α-D-glucose (**CM1**), ethyl-β-D-glucopyranoside (**CM2**), 2,5-anhydro-D-hexitol (**CM3**), and

linoleic acid (**CP5**). All the compounds were isolated and characterized using extensive chromatographic and spectroscopic methods.

Keywords: Phytochemical studies, *Crotalaria pallida*, *Morinda citrifolia*, *Chlorophyllum molybdites*, spectroscopic analysis.

[JUZUK KIMIA DALAM *CROTALARIA PALLIDA*, *MORINDA CITRIFOLIA* DAN *CHLOROPHYLLUM MOLYBDITES*]

ABSTRAK

Disertasi ini memfokuskan kajian fitokimia ke atas tiga tumbuhan Malaysia, *Crotalaria pallida*, *Morinda citrifolia* dan *Chlorophyllum molybdites*. *C. pallida*, dari keluarga Fabaceae, adalah legum herba dan digunakan secara tradisional untuk rawatan beberapa jenis penyakit. Tumbuhan ini juga dikenali dalam menghasilkan toksik alkaloid pyrrolizidine dan flavonoid. *M. citrifolia*, dari keluarga Rubiaceae, adalah sejenis pokok malar hijau renek yang kecil. Ia dikenali dalam menghasilkan sebatian antrakuinon yang mana ianya mempunyai pelbagai ciri terapeutik termasuk antivirus, anti bakteria, antioksida, antikanser, antitumor, dan anti-radang. *C. molybdites*, dari keluarga Agaricaceaea adalah sejenis cendawan beracun yang seringkali terlibat dalam kes-kes keracunan di serata dunia. Kulat ini dikenali dalam menghasilkan komponen toksik seperti protin beracun, molybdophyllysin. Di dalam kajian ini, Satu siklopentilidena baru, crotolidine (**CP1**) dan tujuh sebatian lain, iaitu hidroksidihidrobovolide (**CP2**), octacosana (**CP3**), trans-phytil palmitat (**CP4**), asid linoleik (**CP5**), metil oleat (**CP6**), etil palmitat (**CP7**), dan asid palmitik (**CP8**) telah diasingkan dari ekstrak heksana *C. pallida.* Sejumlah lima sebatian antrakuinon yang telah dikenali telah diasingkan dari ekstrak klorofom termasuklah damnakantal (**MC1**), nordamnakantal (**MC2**), rubiadin (**MC3**), 1,6-dihidroksi-2-metilantrakuinon (**MC4**), 1-hidroksi-3-metoksiantrakuinon (**MC5**), dan 1-metoksi-2-hidroksiantrakuinon (**MC6**). Ekstrak etil asitat daripada *C. molybdites* telah menghasilkan pengasingan sebanyak empat sebatian yang telah dikenali iaitu α-D-glukosa (**CM1**), etil-β-D-glukopiranosida (**CM2**), 2,5-anhidro-D-heksitol (**CM3**), dan asid linoleik (**CP5**). Kesemua sebatian ini

telah diasingkan dan dikenalpasti dengan menggunakan pelbagai kaedah kromatografi dan spektroskopi.

Kata kunci: Kajian fitokimia, *Crotalaria pallida*, *Morinda citrifolia*, *Chlorophyllum molybdites*, analisis spektroskopi.

DEDICATION

The thesis work is dedicated to my late mother, Siti Alauwiah binti Haji Kabeb and my lovely father, Fadzil bin Mahmood, who has been a constant support in my academic journey. This work is also dedicated to my understanding husband, Mohd Asrul Effandi bin Nasir and my precious son, Rayyan Abqari bin Mohd Asrul Effandi, who has been my "big why' to keep going and finished all my research work. Last but not least, I dedicate this work to my younger brother, Mohammad Dzull Faqaar bin Fadzil. To all these five names that I have mentioned above, I am truly blessed to have all of you in my life.

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LIST OF ABBREVIATION

AD	:	Anno Domini
ADHD	:	Attention-Deficit Hyperactivity Disorder
BC	:	Before Christ
CC	:	Column Chromatography
COSY	:	Correlation Spectroscopy
CTLC	:	Centrifugal Thin Layer Chromatography
DEPT	:	Distortionless Enhancement by Polarization Transfer
DNA	:	Deoxyribonucleic Acid
EGF	:	Epidermal Growth Factor
ESI	:	Electrospray Ionization
EtOH	:	Ethanol
FRAP	:	Ferric Reducing Antioxidant Power
HIV	:	Human Immunodeficiency Virus
HMBC	:	Heteronuclear Multiple Bond Correlation
HPLC	:	High Performance Liquid Chromatography
HRESIMS	:	High Resolution Electrospray Ionization Mass Spectrometry
HSQC	:	Heteronuclear Single Quantum Coherence
IR	:	Infrared Spectroscopy
ITSrDNA	:	Internal Transcribed Space Ribosomal Deoxyribonucleic Acid
LCMS	:	Liquid Chromatography Mass Spectrometry
MAA	:	Marketing Authorization Application
MEPs	:	Metalloendopeptidase
MS	:	Mass Spectrometry
NaCl	:	Natrium chloride
NFE	:	Nitrogen Free Extract

NMR	:	Nuclear Magnetic Resonance
NPs	:	Natural Products
ORAC	:	Oxygen Radical Absorbance Capacity
PAs	:	Pyrolizidine Alkaloid
PTLC	:	Preparative Thin Layer Chromatography
Q-TOF	:	Quadrapole Time-of-Flight
RBCs	:	Red Blood Cells
TCM	:	Traditional Chinese Medicine
TLC	:	Thin Layer Chromatography
UV	:	Ultraviolet Spectroscopy
Vpr	:	Viral Protein R
WHO	:	World Health Organization

LIST OF SYMBOLS

α	:	Alpha
β	:	Beta
J	:	Coupling Constant
δ	:	Chemical shift
ε	:	Epsilon
g	:	Gram
Hz	:	Hertz
Kg	:	Kilogram
λ	:	Lambda
MHz	:	Megahertz
nm	:	Nanometer
%	:	Percentage
R_f	:	Retention Factor

CHAPTER 1: INTRODUCTION

1.1 Natural products: modern drugs from natural sources

Throughout the ages, humans have relied on nature for their basic needs, especially the medicines that has been used for treatment of many diseases. Natural products have been a source of medicines to cure diseases since early human history. Before the "Synthetic Era" around the early 1900s, 80% of all medicines were obtained from plants either from roots, bark, or leaves. In more recent time, natural products have continued to be significant sources of drugs and drug-leads. Over 80% of the drugs developed for treatment of diseases were reported from or inspired by natural product compounds (Cragg & Newman, 2013; Harvey, 2008; McChessney et al., 2007).

The early records of natural products were written on clay tablets in cuneiform from the Mesopotamia (2,600 BC). The best known record of the Egyptian medicine the "Ebers Papyrus" (1,500 BC) while the best documentation of Indian Ayurvedic system is perhaps the most ancient of all medicinal traditions which dates before 1,000 BC. The Chinese Materia Medica (1,100 BC), with the first record from Wu Shi Er Bing Fang reported 52 prescriptions, Shennong Herbal (~ 100 BC) reported 365 drugs, and the Tang Herbal (659 AD) reported 850 drugs. In the ancient Western world, the Greeks contributed significantly by the work of the philosopher and natural scientist Theophratus (~ 33 BC) and physician Dioscorides (100 AD) who authored *History of plants* and *De Materia Medica* respectively (Atanasov et al., 2015; Cragg & Newman, 2013; Dias et al., 2012; Gumani et al., 2014; Gurib-Fakim, 2006).

Natural sources can be divided into a group of four, *i. e.* plant, marine, animal and microbial resources. In 1985, William Withering published his treatment for heart patients using diatonic foxglove extract that is also known as digitalis. This treatment has led to the discovery of digoxin, which has been used for the treatment of arrhythmia and congestive heart failure. At the end of the 18th century, Felix Hoffmann has synthesized aspirin from salicylic acid obtained from willow bark (*Salix alba*). This is an example of a synthetic drug that had been isolated from a plant. In early 19th century, Freidrich Serturner isolated morphine from opium poppy, *Papaver somniferum*. The finding of morphine has led to the discovery of dose-controlled medicine for pain. In 1820, the French pharmacists, Caventou and Pelletier isolated the antimalarial drug, quinine from the bark of *Cinchona* species (Balunas & Kinghom, 2005; Cragg & Newman, 2013; Rishton, 2008).

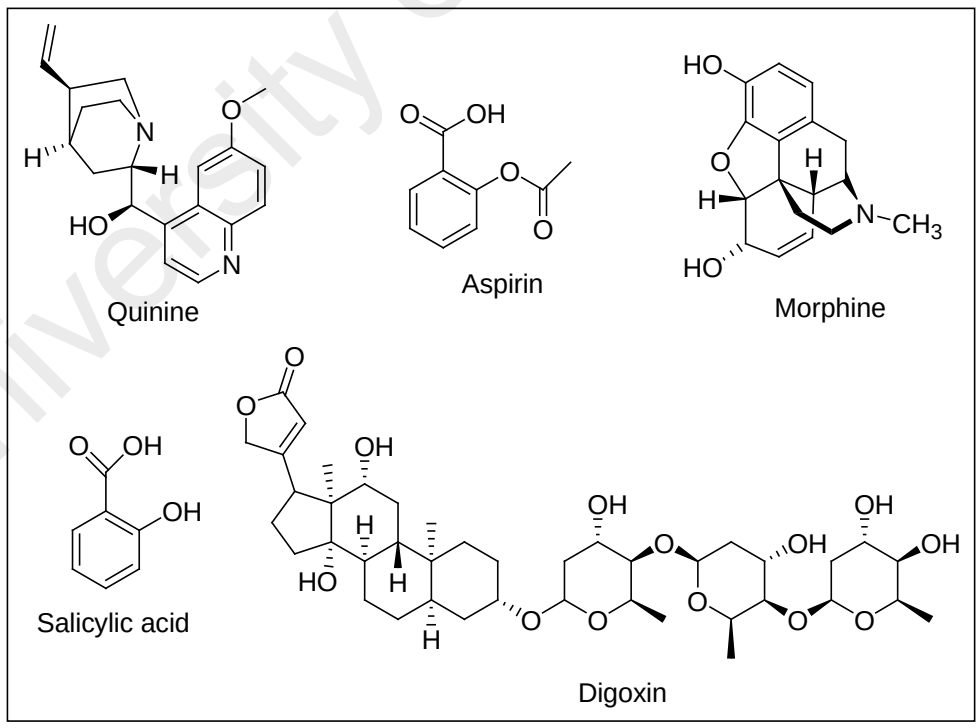


Figure 1.1: Structure of compounds isolated from plants.

The studies of microorganism as sources of drugs started when Professor Alexander Fleming published his findings on an active agent named penicillin from *Penicillium notatum* in the British Journal of Experimental Pathology in June 1929. Penicillin was isolated in a yellow powder form and used as a potent antibacterial compound during World War II. The huge success of penicillin encouraged a worldwide effort to assemble a large collection of microorganism for research purpose to discover new drugs and it finally lead to the discovery of antibacterial agents (cephalosporins), antidiabetic agents (acarbose), and anticancer agents (epirubicin) (Demain & Sanchez, 2009). Other than penicilin, there are many other example of drugs from microorganism sources. For example, the isolation of lovastatin from *Pleurotus ostreatus* which is capable not only to help in reducing blood cholesterol, but it also has an anti-fungal property and anti-carcinogenic effects (Lakshmanan & Radha, 2012). Also the discovery of Cyclosporin A (CyA) from *Tolypocladium inflatum* as a promising drug was attributed to its immunosuppressive and its antifungal activities (Survase et al., 2009).

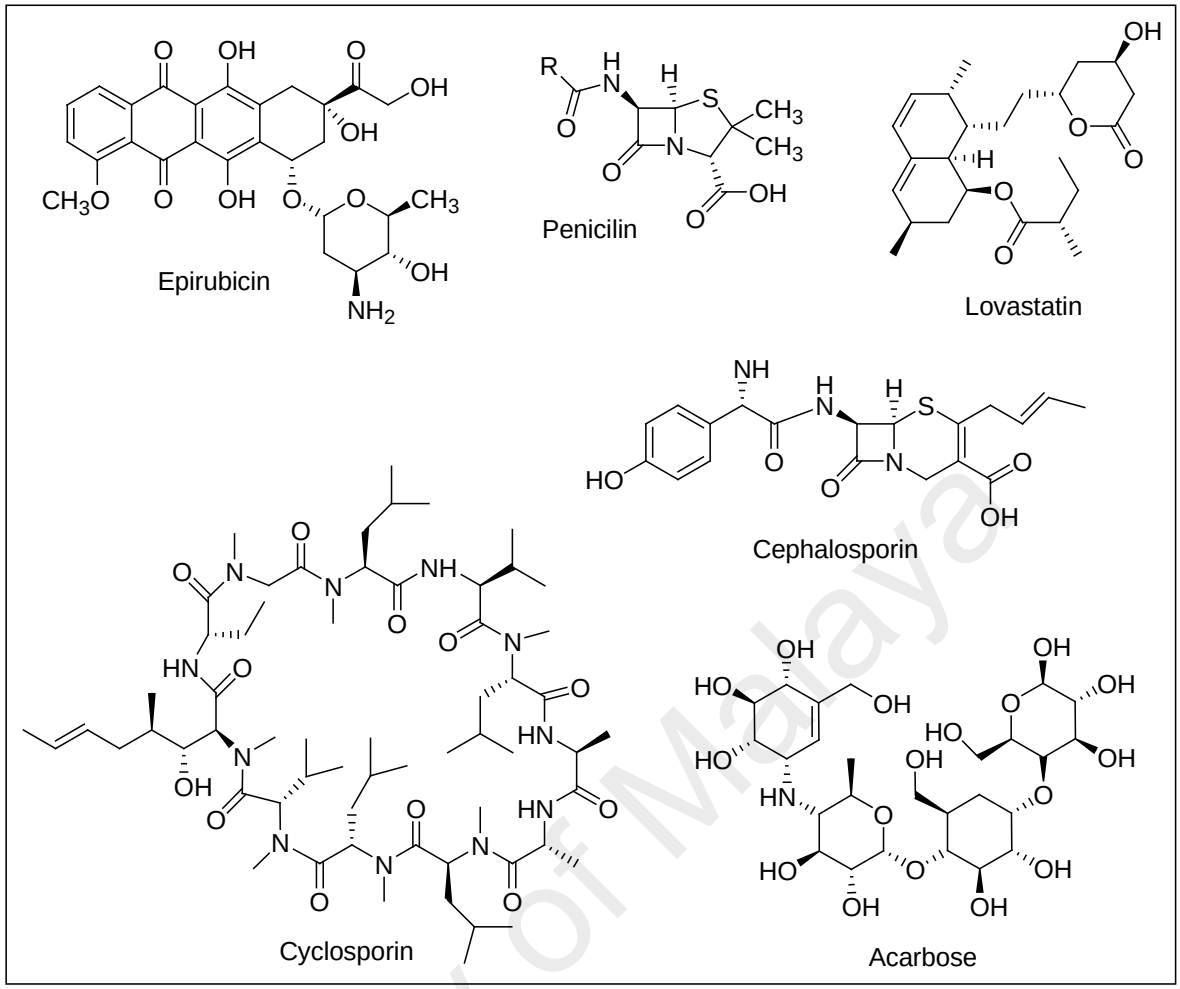


Figure 1.2: Structure of compounds isolated from microorganisms.

Animals are also one of the sources in the drug discovery research and development. The treatment of human diseases by using therapeutics based on medicines obtained from animals is known as zootherapy. In the current modern culture, zootherapy was found to be an important alternative treatment among many other known therapies practiced worldwide. By-products (e.g., hooves, skins, bones, feathers, tusks) of wild animals formed the important ingredients in the preparation of this alternative medicine. In Traditional Chinese Medicine (TCM), more than 1500 animals-derived medicines have been recorded while in Bahia State, over 180 animal-derived medicines have been recorded. In India, nearly 15–20% of the Ayurvedic medicines are based on animal-derived substances (Alves & Rosa, 2005). The example

of animal-derived natural products includes epibatidine, derived from the skin of an Ecuadorian poison frog. Epibatidine was reported to be ten times more potent than morphine (Dias et al., 2012; Omprakash, 2013). Other example including teprotide from a Brazilian pit viper *Bothrops jararaca* which has led to the development of antihypertensive agent cilazapril and captopril, and echistatin, a disintegrin from the venom of saw-scaled viper *Echis carinatus* which then lead to the development of the antiplatelet drug tirofiban (Patlak, 2003; Pedrosa et al., 2013).

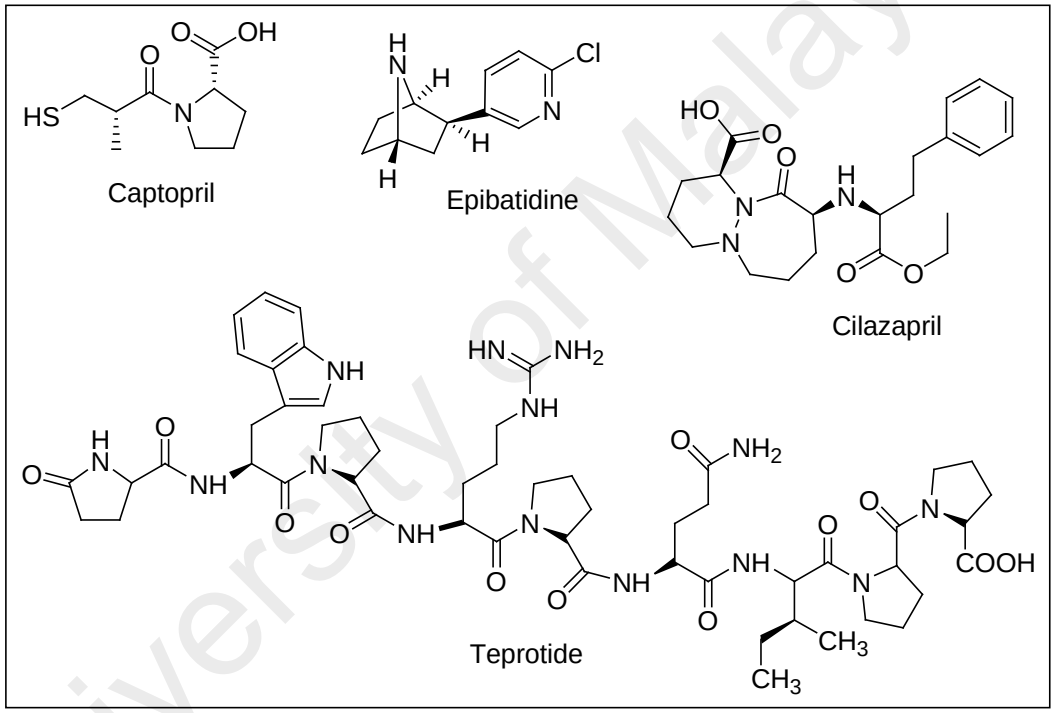


Figure 1.3: Structure of compounds isolated from animal sources.

In contrast with other sources of natural products, marine organisms never have a significant history of usage in traditional medicines. The organised research of marine environments only began in earnest in the mid-1970s. During the decade (1977–1987), about 2,500 new metabolites were reported from a variety of marine organisms (Cragg & Newman, 2013). In the early 1950s, the first notable discovery is the isolation of C-nucleosides, spongouridine or uridine and spongothymidine from the Caribbean

sponge, *Cryptotheca crypta*. The synthesis of structural analogues of the compounds have led to the discovery of cytosine arabinoside (Ara-C) as a clinical anticancer agent, and (Ara-A) as an antiviral agent. In the other hand, isolation from the mediterranean tunicate *Aplidium albicans* has resulted to the discovery of a depsipeptide named plitidepsin (Aplidin®,PharmaMa). Plitidepsin is effective in treating various cancers, including small cell and nonsmall cell lung, melanoma, bladder as well as non-hodgkin lymphoma and acute lymphoblastic leukemia (Omprakash, 2013; Schwartsmann et al., 2001).

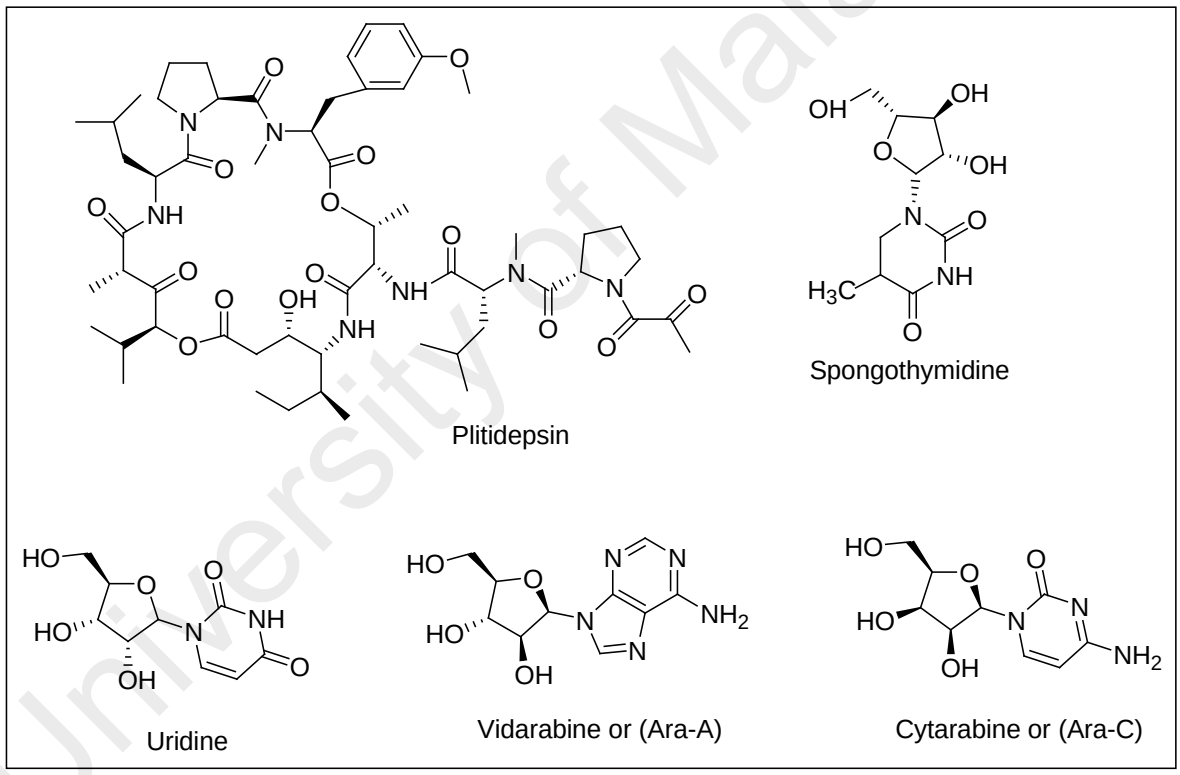


Figure 1.4: Structure of compounds isolated from marine sources.

Natural product compounds that have undergone the clinical evaluation for marketing purpose can be classified into three groups which is; natural products (NPs), semi-synthetic NPs, and NP-derived compounds. The NPs group compounds are derived from natural sources such as plant, animals and microorganism as discussed

above, which have biological activities. While the semi-synthetic NPs group compounds are derived from NP template but using semi-synthetic, and the compounds that synthetically derived from NP template are grouped into NP-derived compounds. Between the years of 2005 to 2010, a total 19 NP based drugs were approved for marketing worldwide from Marketing Authorization Application (MAA) in Europe. Among that, seven are classified as NPs, 10 as semi-synthetic NPs, and two as NP-derived drugs (Mishra & Tiwari, 2011).

Sativex ®, a mixture of dronabinol and cannabinol was derived from the cannabis plant is an example of NPs drug. It is the first pharmaceutical prescription medicine in the world. Sativex ® was launched in Canada on April 2005 for neuropathic pain relief in multiple sclerosis. In 2007, Health Canada approved Sativex ® as an adjunctive analgesis for severe pain in advanced cancer patients, reducing the depending of opioid medications (Nurmikko et al., 2007; Wade et al., 2003). Other NPs drug includes Fumagilin (Flisint ®), which was isolated from *Aspergillus fumigatus.* It is an antimicrobial that capable on inhibiting the proliferation of endothelial cells. In 2005, fumagilin was approved for used against intestinal microsporidiosis, a disease from *Enterocytozoon bieneusi* parasite that is causing chronic diarrhea (McCowen et al., 1951). Exenatide (Byetta ®) was isolated from the oral secretions of the poisonous lizard *Heloderma suspectum* (Gila monster). Exenatide was approved as an adjunctive therapy in type 2 diabetis mellitus in 2006 (Cvetković & Plosker, 2007).

In 2007, the marine alkaloid named trabectedin (Yondelis®), isolated from the ascidian *Ecteinascidia turbinate* became the first marine anticancer drug to be approved in the European Union. It was approved for used against ovarian cancer and soft tissue

sarcomas. In present, trabectedin is in trials against breast cancer, pediatric sarcomas and prostate cancers (Montaser & Luesch, 2011; Soares et al., 2007).

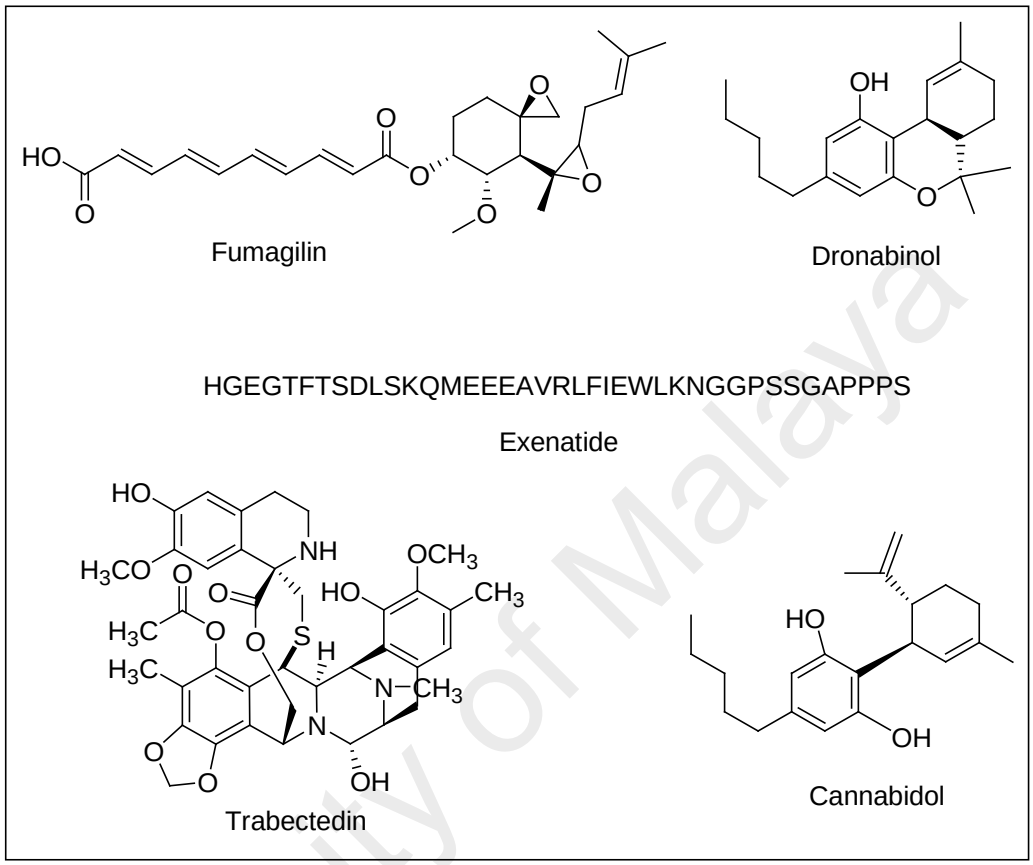


Figure 1.5: Structure of new approved drugs based on Natural products (NPs).

Ixabepilone (Ixempra ®) is a semi-synthetic derivative of epothilone B produced by *Somngium cellulosum* and it was developed as anticancer drug. It also has a unique antibacterial and antifungal activities. In the preclinical study, it is shown that natural epothilones A and B have potent antineoplastic activity against a wide range of tumor cell (Lee et al., 2008). Tigecycline (Tygacil ®) is an antibiotic structurally similar to tetracycline. Its capability to inhibit protein translation is by blocking the entry of amino-acyl molecules into the ribosome. In 2005, tigecycline was approved for the treatment of complicated skin and skin structure infections, and intra-abdominal infections (Nishamin, 2006). Anidulafungin (Eraxis ™ in US, Ecalta ™ in Europe) is a

semi-synthetic derivative of the fungal metabolite named echinocandin B. It was used against invasive and oesophageal candidiasis and candidemia (Debono et al., 1995). Telavancin (Vibativ ™) is a semi-synthetic analogue of vancomycin. It is capable to inhibit the growth of bacterial for the treatment of nosocomial pneumonia (Judice & Pace, 2003; Laohavaleeson & Nicolau, 2007).

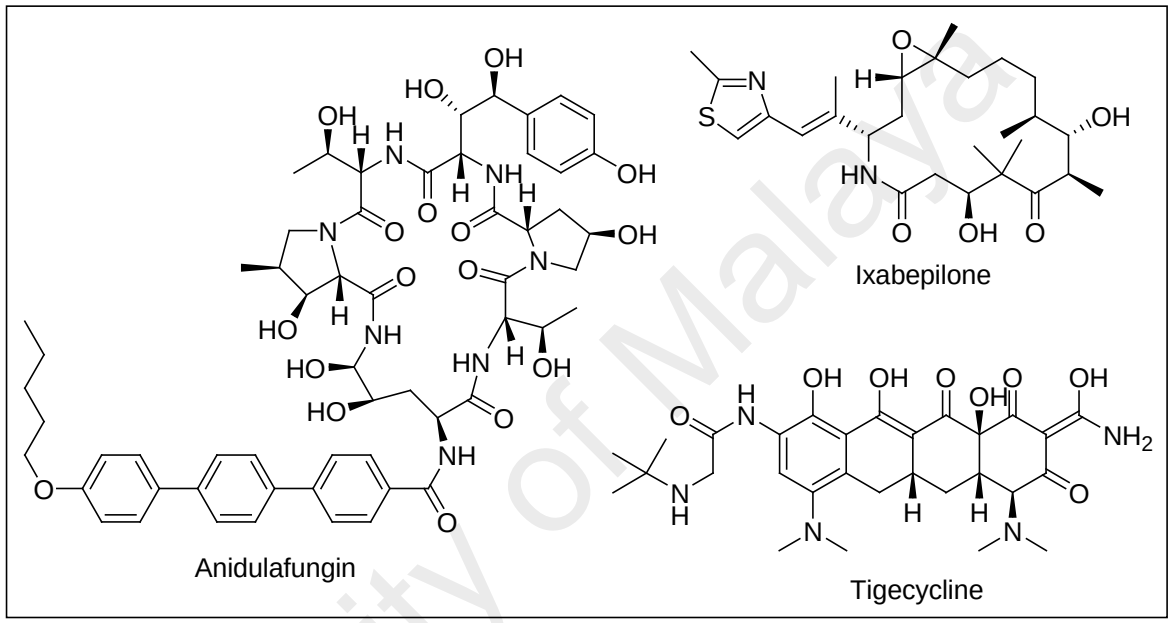


Figure 1.6: Structure of new approved drugs based on semi-synthetic NPs.

Presently, there are nine β-lactams (one penem, two cephalosporins, and six carbapenems) in clinical trials undergoing the drug registration. Among them, doripenem is one of the ultra-broad spectrum injectable antibiotics. Doripenem (Finibax ®) was launched in 2005. It showing a wide-range of antibacterial spectrum and getting the approval for use in intra-abdominal and urinary tract infections (Keam, 2008; Mishra & Tiwari, 2011).

Attention-Deficit Hyperactivity Disorder (ADHD), is a neuro-developmental disorder. For many years, methylphenidate and amphetamines have been used for ADHD management. But due to abuse potential, both drugs are being controlled and limited. Lisdexamfetamine (Vyvanse ™) consist of dextroamphetamine. It was designed to help ADHD patients when combined with essential amino acid (Biljana et al., 2009; Blick & Keating, 2007).

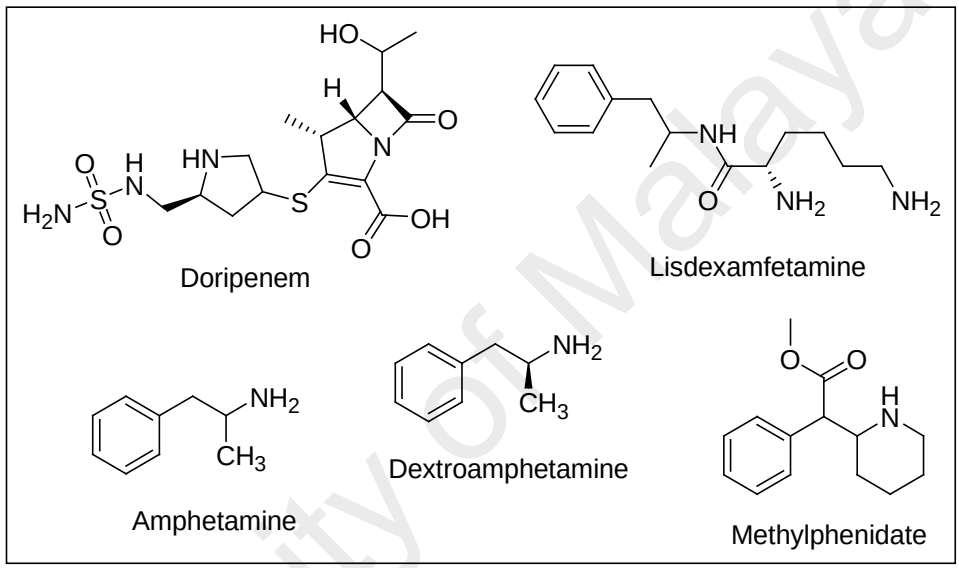


Figure 1.7: Structure of new approved drugs based on NP-derived compounds.

Despite from all the successes from natural products history, many large pharmaceutical companies have limited usage of natural products in the drug discovery screening processes. The main factors that cause this problem are the difficulties in access and supply, also the complexities of natural product chemistry itself. So, as a natural product chemist, we need to improve the access to natural products and make it look interesting to be exploring (Harvey, 2008).

1.2 Objectives

This work aimed on the study of chemical constituents from three Malayan plant species, *i.e. Crotalaria pallida*, *Morinda citrifolia* and *Chlorophyllum molybdite*. The objectives of this study were to isolate and characterize new compounds from the above mentioned plants by using extensive chromatographic and spectroscopic methods.

CHAPTER 2: LITERATURE REVIEW

2.1 *Crotalaria pallida* Aiton

2.1.1 General

The genus *Crotalaria* L. (Leguminosae, Papilionoideae, and Crotalarieae) comprising about 600 species is widely distributed throughout tropical, neutropical and subtropical regions. The centres of diversity are on eastern and southern tropical Africa and India, and two other new centres found in Mexico and Brazil (Flores et al., 2009). The genus *Crotalaria* is commonly known as devil-bean, shake shake, rattlebox or rattlepod. It gets the name from the sound made when their pod-like fruit is shaken and the seeds will "rattle" around inside (Wunderlin & Hansen, 2008). Although *Crotalaria* species is a part of human diet, many species are known to be toxic to man and livestock (Culvenor & Smith, 1962). It is also reported to be poisonous and is a death cause (crotalism) in grazing cattle, horses, sheep or livestock fed with grains containing seeds from this plant (Fletcher et al., 2009).

According to the International Legume DATABASE & Information Service, *Crotalaria Pallida* Aiton are now considered as one single species together with the other ten, which are *Crotalaria Brownei, Crotalaria falcate, Crotalaria fertilis, Crotalaria Hookeri, Crotalaria mucronata*, *Crotalaria pallida* Klotzsch, *Crotalaria pisiformis, Crotalaria striata*, *Crotalaria striata* var. *acutifolia*, *Crotalaria tinctoria*, and *Crotalaria zuccarininana Crotalaria pallida* (White, 2017). *C. pallida*, from Fabaceae family, popularly known as "rattle" or "rattlesnake" is a perennial herb or sub-shrub, with multi-branched stems ascending or erect, 1-2 m tall (Morad, 2017). In Malaysia, *C. pallida* is known as *kiri-kiri*, *tirik-irik*, *giring-giring*, or *kacang kayu*

(Abdullah, 1990; Morad, 2017). *C. pallida* is a species native to Africa and usually grows in warm, open areas and in arid and semiarid regions (Fonseca et al., 2006).

Various parts of *C. pallida* are used in folk medicines to treat several type of illness such as urinary problems and fever. The leaves of *C. pallida* were used as vermifuge (Jain & Borthakur, 1980). The Karbi people mentioned as Mikir, are one of the major ethnic groups in Northest India that live in the hill areas of Assam take the extract of *C. pallida* leave to kill intestinal worms (Sharma & Kumar, 2013). The leave powder and root bark of *C. pallida* added with the leaf of *Wrightia tinctoria* and *Tragia involucrata* has been used for treatment of skin disease (Ayyuanar & Ignacimuthu, 2005). In the other hand, the roots of *C. pallida* are used as poultice and applied to swelling of joints (Jain & Borthakur, 1980). Chakma tribe also known as Daingnet people used the roots and leaves of *C. pallida* to treat stomach pain and urination problem (Roy et al., 2008).

Many researchers have reported their findings on *C. pallida*. It possesses various therapeutic properties including antidiabetic, antibacterial, antimicrobial, anti-inflammatory, anthelmintic, and antioxidant. Ethanol extract from leaves *C. pallida* showed highest antimicrobial activity than other solvent extracts towards bacterial strains *X. axanopodis* pv. *malvacearum*, *Vibrio cholere*, *Shigella flexneri*, *Shigella dysenteriae*, *E. coli* and *C. michiganensis* sub spp. *michiganensis*. Antifungal activity also shows the ethanol extract was more active against all bacterial strains followed by petroleum ether, ethyl acetate, water and chloroform extracts. Phytochemical screening showed that the ethanol extract yielded strongly the presence of combined reducing sugar, glycosides, alkaloids, flavonoids, terpenoids, saponins, phenols, steroid and tannins. Strong occurrence of all these polyphenolic compounds confirmed the

antioxidant and anti-inflammatory activity in *C. pallida* extract while the presence of flavonoid compounds confirmed the antibacterial activity. The ethanol extract also showed a maximum inhibition of heat induced hemolysis of red blood cells (RBCs) and have highest membrane stabilization activity. In addition, it is also showed anti-lipoxygenase activity and anthelmintic activity (Alam et al., 2014; Govindappa et al., 2011). Anthelmintic activity was done on adult worm *Paramhistoma cervi* (trematoda) and the extract showed dose dependent decrease in paralysis and death time. This result suggests the possible used of *C. pallida* extract as a vermifuge previously (Alam et al., 2014).

Diabetes mellitus is the most common endocrine disorder with more than 150 million people suffering worldwide. It is predicted to increase to 300 million people by the year 2025. Thus, the World Health Organization (WHO) has recommended the use of traditional plant as alternative method of treatment due to their perceived effectiveness with minimal side effects in clinical experiments. In 2005, Panda and his colleagues respond to this problem with their studies on screening the antidiabetic activity of leaf extract of *C. pallida* in alloxan induced diabetic rats. They reported that ethanol extract of *C. pallida* leaves showed most potent antidiabetic activity and this effect are comparable with the standard drug (Glibenclamide). However, further studies are required to examine the mechanism of antidiabetic activity and to isolate the active compound responsible for this pharmacological activity (Panda et al., 2005). Other studies has shown ethanol extract of *C. pallida* leaves is more significant in wound healing process in excision and incision wound models. This is due to the presence of the phytoconstituent compounds that may exhibit the synergistic effect towards healing of wounds. With all the results from that study, it supports the traditional use of the leaves from *C. pallida* by folks previously (Panda et al., 2015).

On the other hand, a novel antimicrobial peptide named Cp-AMP has been isolated and characterized from the seed of *C. pallida* which showed promising bioactivity against the gram-negative bacterium *Proteus* sp. as well as a potent phytopathogenic fungi *Fusarium osysporum* (Pelegrini et al., 2009). A proteinaceous trypsin inhibitor named CpaTI was purified from the seed of *C. pallida* and its deleterious effects against insect pests *Callosobruchus maculatus* (cowpea weevil) and *Ceratitis capitata* (fruit fly) were examined. *In vitro* and *in vivo* susceptibility of *C. maculatus* and *C. capitata* enzymes to CpaTI shows a strong susceptibility for both insect larvae but when CpaTI was added to artificial diets, *C. maculatus* still shows its susceptibility while *C. capitata* shows disagreement towards CpaTI. The occurrence of a high inhibition of CpaTI in vitro activity indicated a possibility to use CpaTI as an insecticidal agent in insect control strategies (Gomes et al., 2005).

Seeds of *Crotalaria* sp. also contain lectin. Lectins are carbohydrate-binding proteins in many plants, animals and also other organism. A lectin from the seed of *C. pallida* dubbed (CPL) showed hemagglutination activity specific to types A and B of human erythrocytes which inhibited by raffinose and galactose (Rego et al., 2002). Other than that, flower extracts from *C. pallida* which is rich in coumarins shows *in vitro* anti-HIV properties on phytochemical screening (Govindappa et al., 2013). The genus *Crotalaria* is a well-known plant that contains the toxic pyrrolizidine alkaloid (PAs), and non-proteic aminoacids, mainly in the seeds. Monocrotaline is a pyrrolizidine alkaloid that commonly found in the seed of many *Crotalaria* sp. (Pilbeam & Joyce, 1983). Monocrotaline is proven to be a neurotoxin by inducing cytotoxicity in the central nervous system and also cause genotoxic effects (Pitanga et al., 2011; Silva-Neto et al., 2010). In the other hand, some of the pyrrolizidine alkaloids

such as madurensine and doronecine show anticancer properties on cancerous U-937 cells (Roux et al., 2011).

2.1.2 Compounds isolated from the genus *Crotalaria*

Table 2.1 lists the compounds isolated from the *Crotalaria* sp. and Figure 2.1 shows the structures of compounds previously isolated from *Crotalaria* sp.

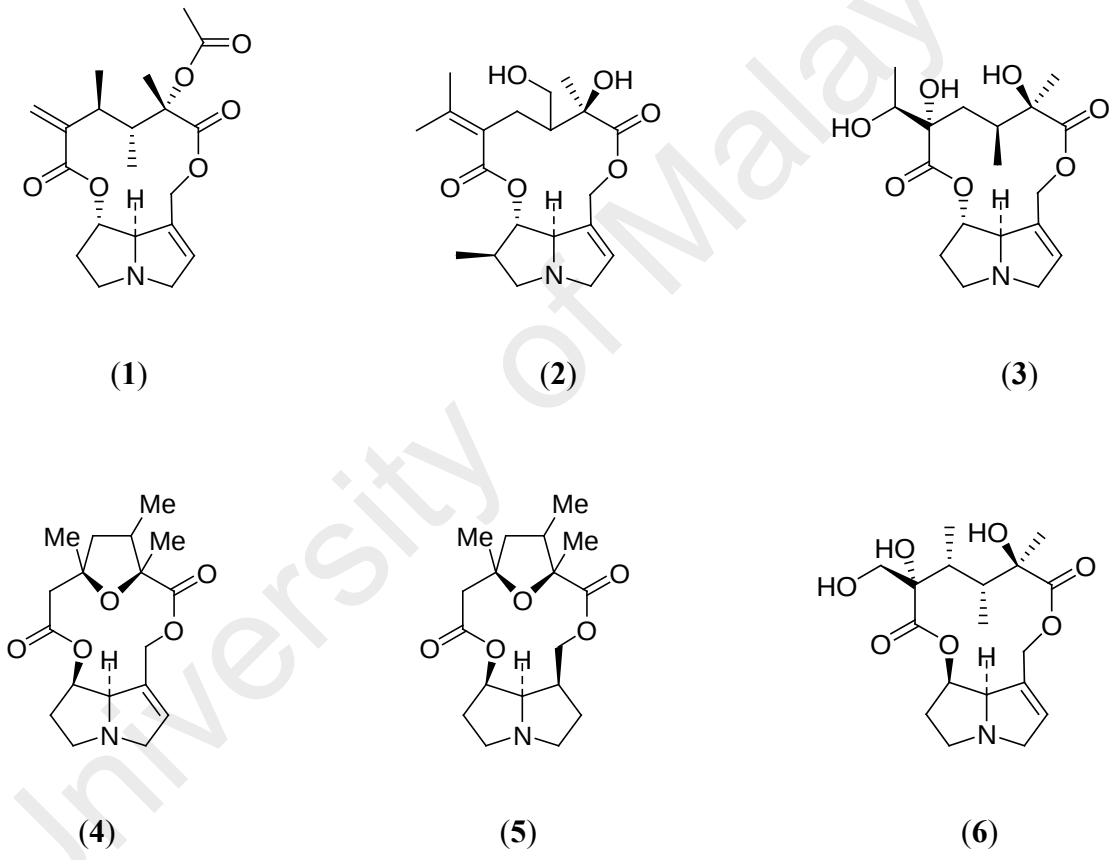
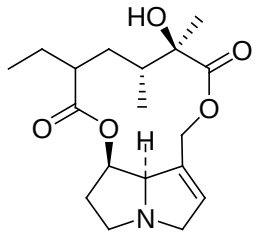


Figure 2.2: Structure of compounds isolated from the genus *Crotalaria*



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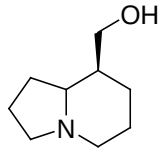

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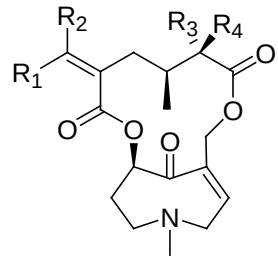
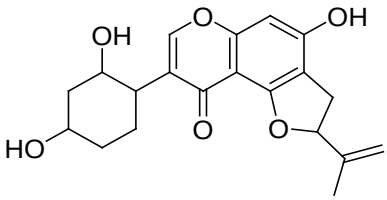


(**9**) R_1 = Me R_2 = H, R_3 = CH_2OH, R_4 = OH
(**10**) R_1 = Me R_2 = H, R_3 = Me, R_4 = OH
(**11**) R_1 = H, R_2 = Me, R_3 = OH, R_4 = Me
(**12**) R_1 = H, R_2 = Me, R_3 = OAc, R_4 = Me



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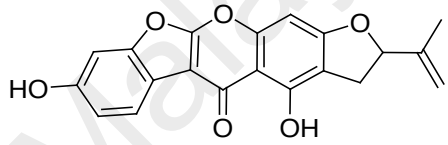
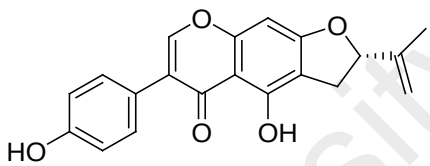


(**14**)



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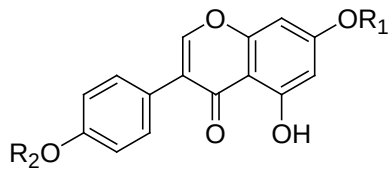
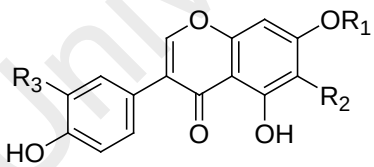
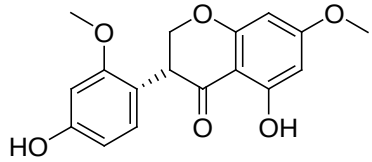


(**16**) R_1 = Me, R_2 = H

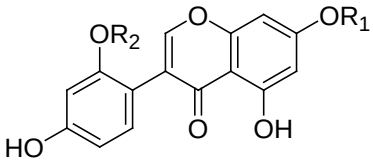


(**17**) R_1 = H, R_2 = H, R_3 = OMe
(**18**) R_1 = Me, R_2 = OMe, R_3 = H

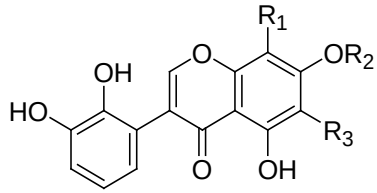


(**19**) R_1 = H, R_2 = Me

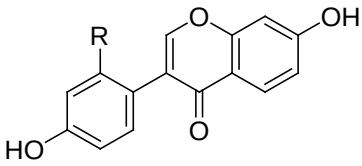
Figure 2.1, continued



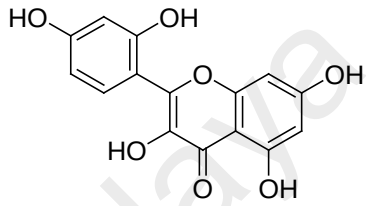
(**20**) R_1 = Me, R_2 = H
(**21**) R_1 = H, R_2 = H
(**22**) R_1 = H, R_2 = Me



(**23**) R_1 = H, R_2 = α-L-Rham, R_3 = H
(**24**) R_1 = Glc, R_2 = H, R_3 = H
(**25**) R_1 = H, R_2 = H, R_3 = Glc
(**26**) R_1 = H, R_2 = β-D-glucosyl, R_3 = H



(**27**) R = H
(**28**) R = OH



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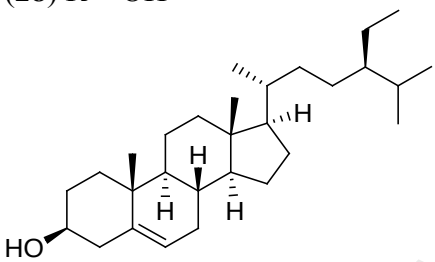

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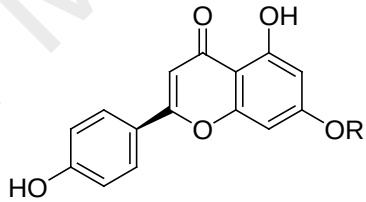
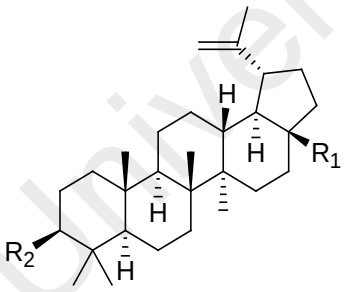
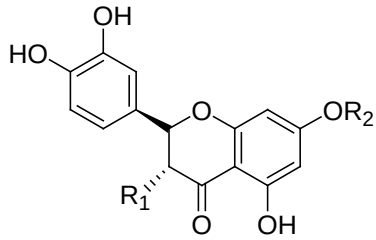


(**31**) R = H
(**32**) R = β-D-glucosyl

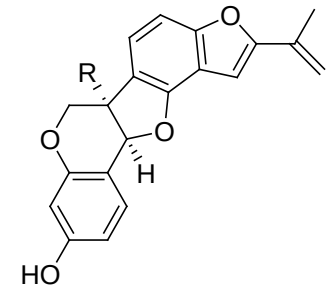


(**33**) R_1 = H, R_2 = OH
(**34**) R_1 = H, R_2 = Ac
(**35**) R_1 = COOH, R_2 = OH

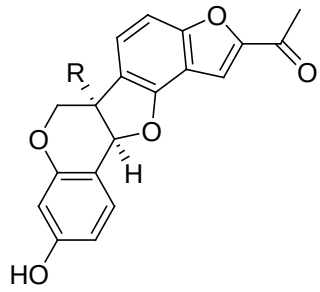


(**36**) R_1 = OH, R_2 = H
(**37**) R_1 = H, R_2 = β-D-glucosyl

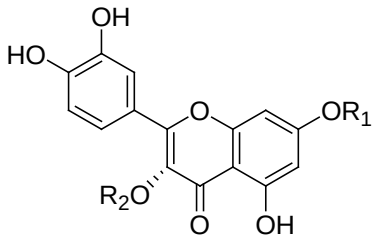
Figure 2.1, continued



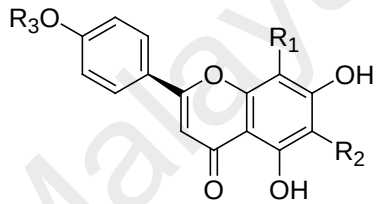
(**38**) R = H
(**39**) R = OH



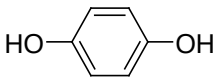
(**40**) R = H
(**41**) R = OH



(**42**) R_1 = *β*-D-glucosyl, R_2 = H
(**43**) R_1 = H, R_2 = H
(**44**) R_1 = H, R_2 = Gal



(**45**) R_1 = Glc, R_2 = H, R_3 = H
(**46**) R_1 = H, R_2 = Glc, R_3 = H
(**47**) R_1 = Glc, R_2 = H, R_3 = Xyl



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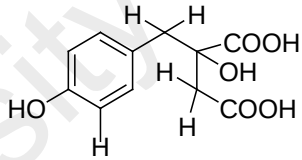

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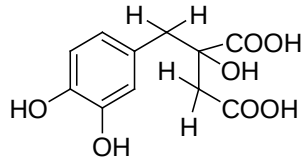

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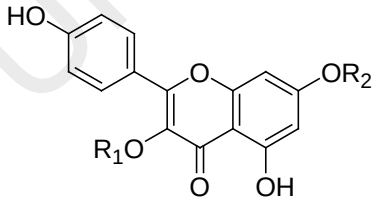
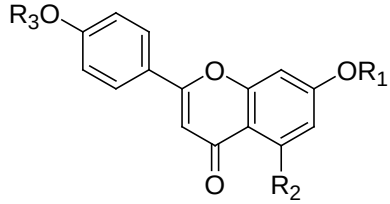
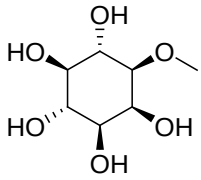


(**51**) R_1 = H, R_2 = H
(**52**) R_1 = Me, R_2 = H
(**53**) R_1 = Xyl, R_2 = Rham
(**54**) R_1 = Rham, R_2 = Rham
(**55**) R_1 = Gal-Rham, R_2 = Rham



(**56**) R_1 = H, R_2 = OH, R_3 = H
(**57**) R_1 = Glu-apiosyl, R_2 = OH, R_3 = H
(**58**) R_1 = Glu-apiosyl, R_2 = OH, R_3 = Me
(**59**) R_1 = Me, R_2 = H, R_3 = H

Figure 2.1, continued



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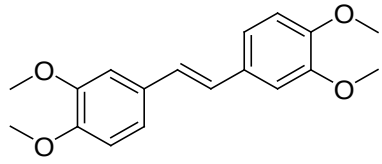

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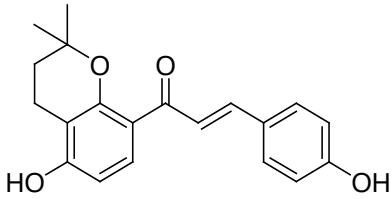

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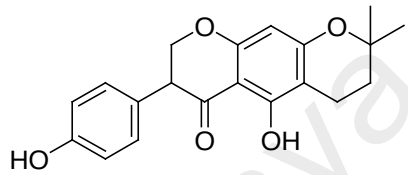

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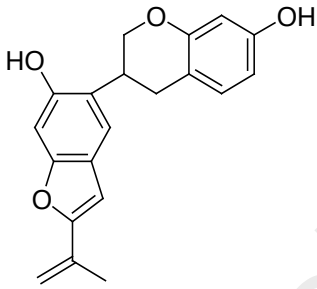

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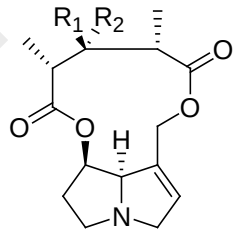
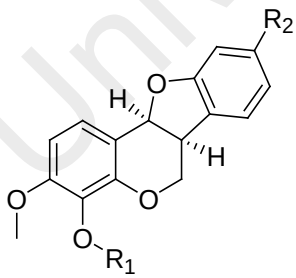
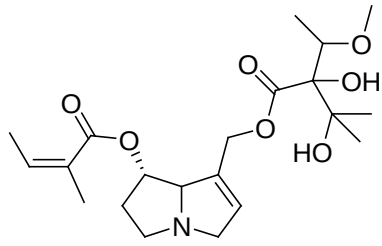


(**65**) R_1 = OH, R_2 = H
(**66**) R_1 = H, R_2 = OH

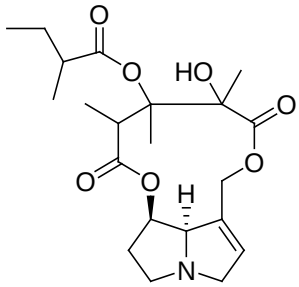


(**67**) R_1 = *O*-*β*-D-glucopyranoside, R_2 = H
(**68**) R_1 = H, R_2 = *O*-*β*-D-glucopyranoside



(**69**)

Figure 2.1, continued



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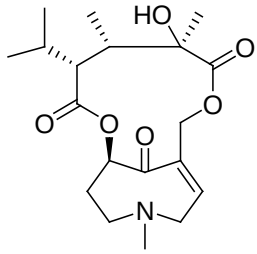

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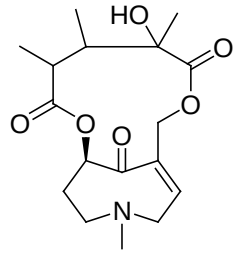

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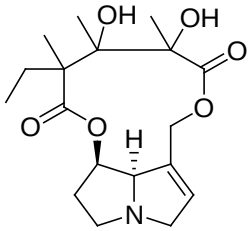

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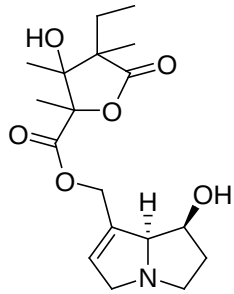

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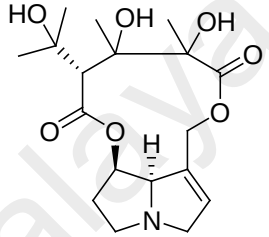

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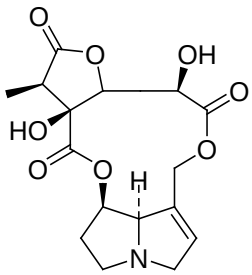

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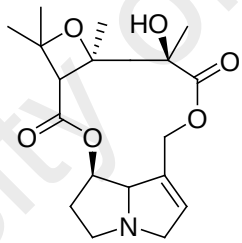

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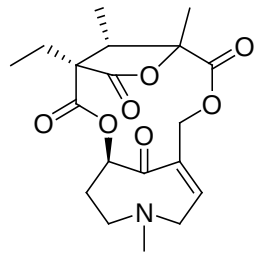
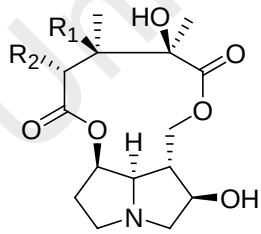
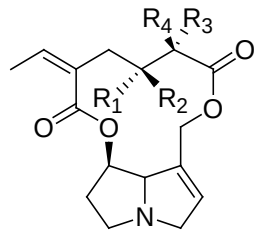


(**78**)

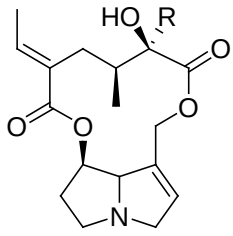


(**79**) R_1 = H, R_2 = Me
(**80**) R_1 = OH, R_2 = i-Pr

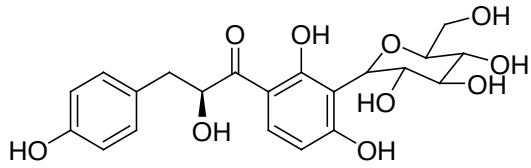


(**81**) R_1 = Me, R_2 = H, R_3 = Me, R_4 = OH
(**82**) R_1 = Me, R_2 = H, R_3 = CH_2OH, R_4 = OH
(**83**) R_1 = Me, R_2 = H, R_3 = H, R_4= AcO
(**84**) R_1 = H, R_2 = Me, R_3 = CH_2OH, R_4 = OH
(**85**) R_1 = Me, R_2 = H, R_3 = H, R_4 = OH

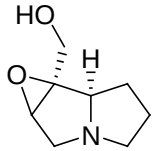
Figure 2.1, continued



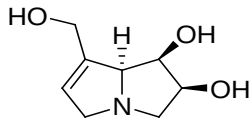
(**86**) R = Me
(**87**) R = CH_2OH



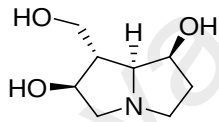
(**88**)



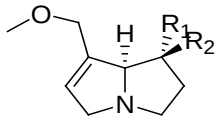
(**89**)



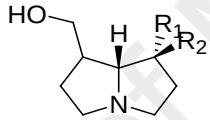
(**90**)



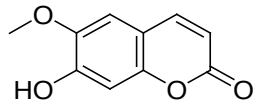
(**91**)



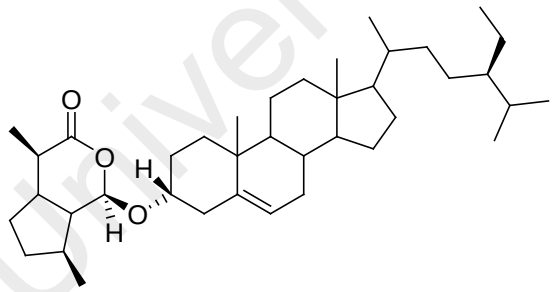
(**92**) R_1 = H, R_2 = OAc
(**93**) R_1 = OH, R_2 = H
(**94**) R_1 = H, R_2 = H



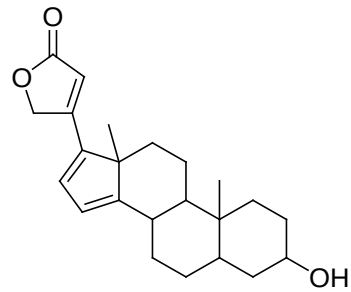
(**95**) R_1 = H, R_2 = OH
(**96**) R_1 = OH, R_2 = H



(**97**)

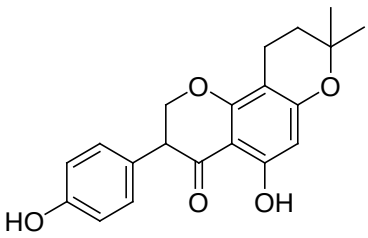


(**98**)

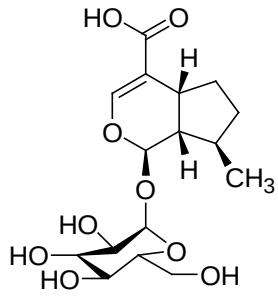


(**99**)

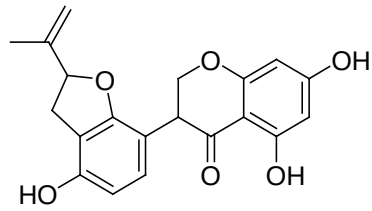
Figure 2.1, continued



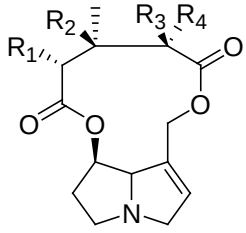
(**100**)

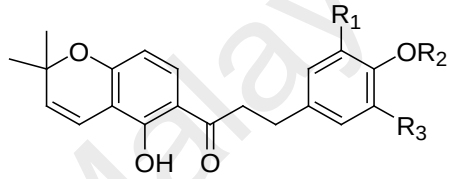


(**101**)



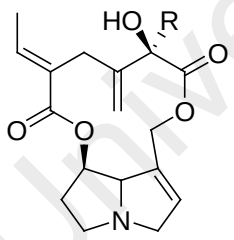
(**102**)

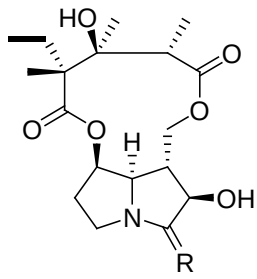


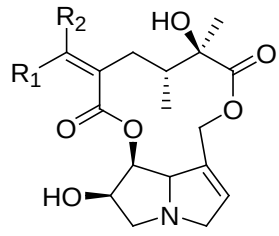


(**103**) R_1 = H, R_2 = OH, R_3 = H, R_4 = H
(**104**) R_1 = H, R_2 = OAc, R_3 = H, R_4 = H
(**105**) R_1 = Me, R_2 = OH, R_3 = Me, R_4 = H
(**106**) R_1 = Me, R_2 = OAc, R_3 = OH, R_4 = Me
(**107**) R_1 = Me, R_2 = OH, R_3 = OH, R_4 = Me
(**108**) R_1 = i-Pr, R_2 = OH, R_3 = OH, R_4 = Me
(**109**) R_1 = i-Pr, R_2 = OH, R_3 = OH, R_4 = CH_2OH

(**110**) R_1 = H, R_2 = H, R_3 = H
(**111**) R_1 = H, R_2 = Me, R_3 = H
(**112**) R_1 = H, R_2 = H, R_3 = OH
(**113**) R_1 = OMe, R_2 = Me, R_3 = OMe





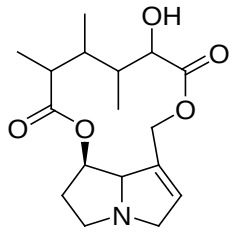


(**114**) R = Me
(**115**) R = CH_2OH

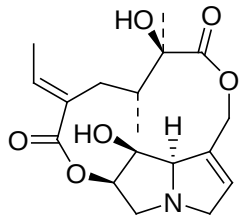
(**1**) R = O
(**2**) R = CH_2

(**118**) R_1 = Me, R_2 = H
(**119**) R_1 = H, R_2 = Me

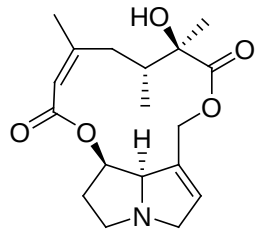
Figure 2.1, continued



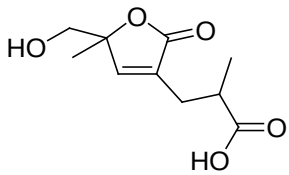
(**120**)



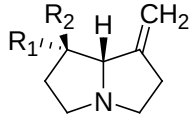
(**121**)



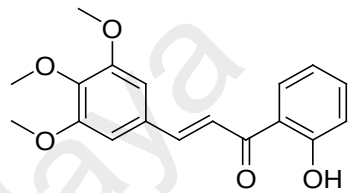
(**122**)



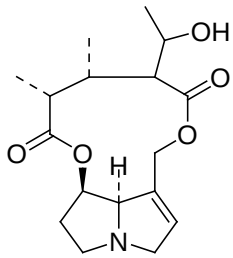
(**123**)



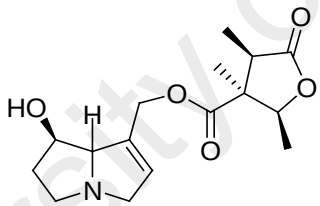
(**124**) R_1 = OH, R_2 = H
(**125**) R_1 = H, R_2 = OH



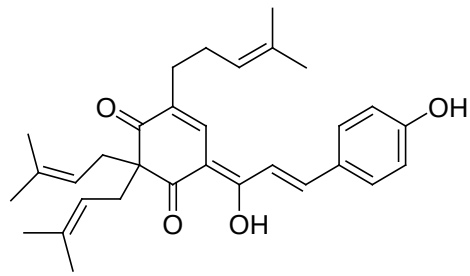
(**126**)



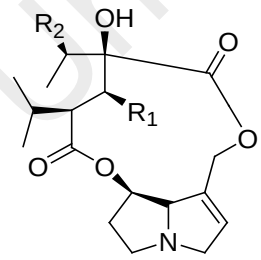
(**127**)



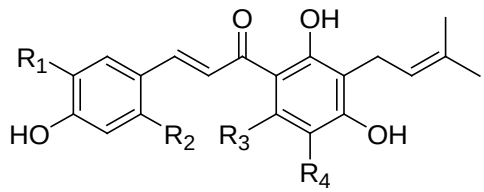
(**128**)



(**129**)

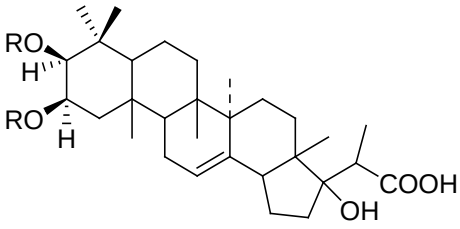


(**130**) R_1 = OH, R_2 = H
(**131**) R_1 = OH, R_2 = OH
(**132**) R_1 = H, R_2 = OH

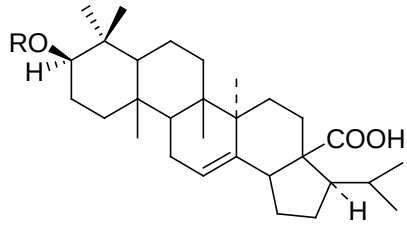


(**133**) R_1 = OH, R_2 = OH, R_3 = H, R_4 = H
(**134**) R_1 = OMe, R_2 = H, R_3 = H, R_4 = H
(**135**) R_1 = H, R_2 = H, R_3 = H, R_4 = Prenyl
(**136**) R_1 = H, R_2 = H, R_3 = OH, R_4 = Prenyl

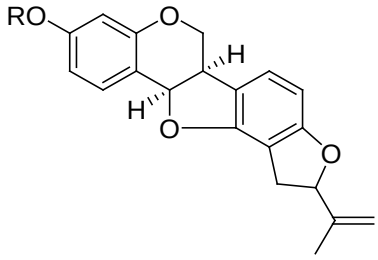
Figure 2.1, continued



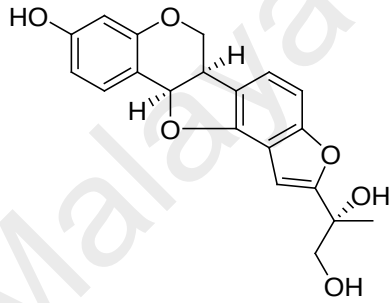
(**137**) R = H
(**138**) R = Ac



(**339**) R = H
(**140**) R = Ac

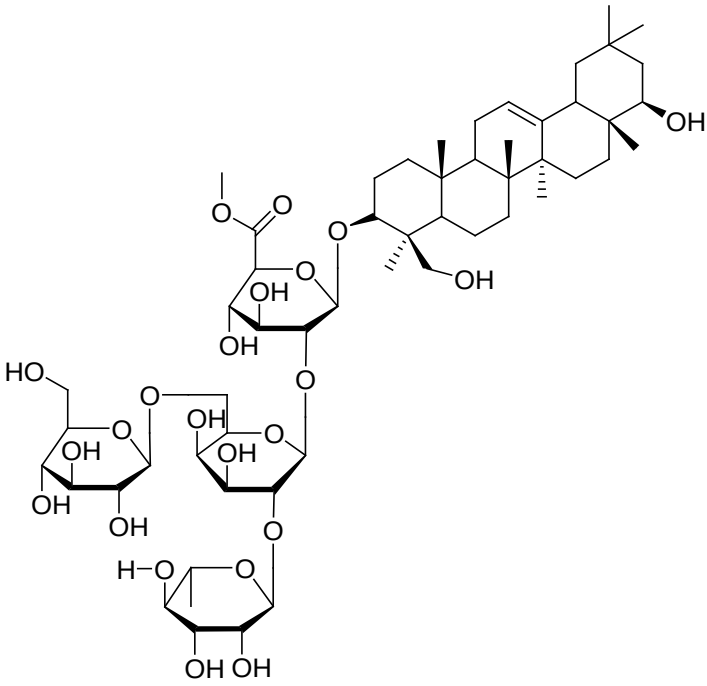


(**141**) R = H
(**142**) R = Ac

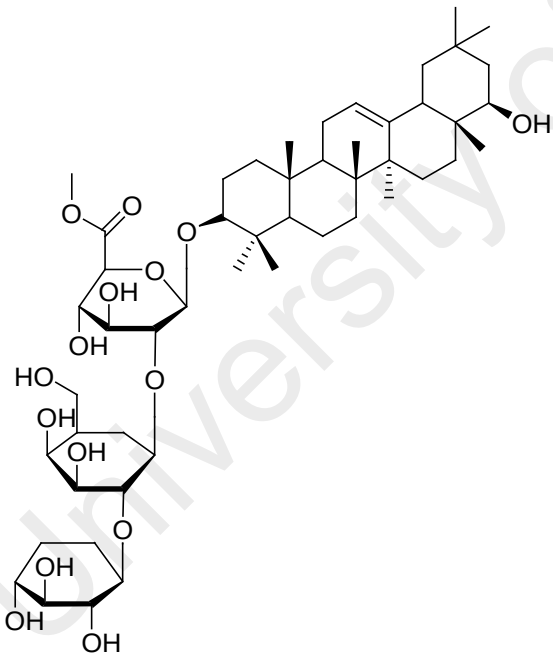


(**143**)

Figure 2.1, continued



(**144**)



(145)

Table 2.1: Name of compounds isolated from different *Crotalaria* sp.

No.	Compound name	Source	Ref.
1	Acetylsenecivernine	*C. gillettii*	(Asres et al., 2004)
2	Gynuramine	*C. gillettii*	(Asres et al., 2004)
3	Jacoline	*C. fascicularis*	(Asres et al., 2004)
4	Retroisosenine	*C. gillettii*	(Asres et al., 2004)
5	Nemorensine	*C. incana* subsp. *purpurascens*	(Asres et al., 2004)
6	Scleratine	*C. fascicularis*	(Asres et al., 2004)
7	Dihydrosenecionine	*C. incana* subsp. *purpurascens*	(Asres et al., 2004)
8	Tashiromine	*C. emarginella* *C. philipsiae*	(Asres et al., 2004)
9	Senkirkine	*C. laburnifolia* *C. phillipsiae*	(Asres et al., 2004)
10	Hydroxysenkirkine	*C. laburnifolia*	(Asres et al., 2004)
11	Crotaverrine	*C. verrucosa* Linn	(Suri et al., 1976)
12	O12-Acetylcrotaverrine	*C. verrucosa* Linn	(Suri et al., 1976)
13	Lachnoisoflavone A	*C. lachnophora*	(Awouafack et al., 2011)
14	Lachnoisoflavone B	*C. lachnophora*	(Awouafack et al., 2011)
15	Licoagroisoflavone	*C. lachnophora*	(Awouafack et al., 2011)
16	Prunetin	*C. lachnophora*	(Awouafack et al., 2011)
17	3'-*O*-methylorobol	*C. lachnophora*	(Awouafack et al., 2011)
18	7-*O*-methyltectorigenin	*C. lachnophora*	(Awouafack et al., 2011)
19	Cajanol	*C. lachnophora*	(Awouafack et al., 2011)
20	Cajanin	*C. lachnophora*	(Awouafack et al., 2011)

Table 2.1, continued

No.	Compound name	Source	Ref.
21	2'-hydroxygenistein	*C. pallida* (bark)	(Ko et al., 2004)
22	5,7,4'-trihydroxy-2'-methoxyisoflavanone	*C. pallida* (bark)	(Ko et al., 2004)
23	Luteolin-7-*O*-*α*-L-rhamnoside	*C. lachnophora*	(Awouafack et al., 2011)
24	Orientin	*C. sessiliflora*	(Mun'im et al., 2003)
25	Isoorientin	*C. sessiliflora*	(Mun'im et al., 2003)
26	Luteolin-7-glucoside	*C. verrucosa* Linn	(Naidu et al., 1998)
27	Daidzein	*C. pallida* (bark)	(Ko et al., 2004)
28	2'-hydroxydaidzein	*C. pallida* (bark)	(Ko et al., 2004)
29	Morin	*C. pallida* (bark)	(Ko et al., 2004)
30	Naringenin	*C. assamica* (seed)	(Ko et al., 2004)
31	Naringenin-7-*O*-*β*-D-glucopyranoside	*C. assamica* (seed)	(Ko et al., 2004)
32	*β*-sitosterol	*C. pallida* (bark)	(Ko et al., 2004)
33	Lupeol	*C. pallida* (bark)	(Ko et al., 2004)
34	Lupeol acetate	*C. pallida* (bark)	(Ko et al., 2004)
35	Betulinic acid	*C. trifoliastrum* Willd. (root)	(Rao et al., 1999)
36	Taxifolin	C. assamica (seed)	(Ko et al., 2004)
37	Eriodictyol-7-*O*-*β*-D-glucopyranoside	*C. sessiliflora*	(Mun'im et al., 2003)
38	Crotafuran A	*C. pallida*	(Ko et al., 2004)
39	Crotafuran C	*C. pallida*	(Weng et al., 2002)
40	Crotafuran B	*C. pallida* (bark)	(Ko et al., 2004)
41	Crotafuran D	*C. pallida* (bark)	(Weng et al, 2002)
42	Quercetin-7-O-β-D-glucopyranoside	*C. pallida*	(Ko et al., 2004)
43	Quercetin	C. verrucosa Linn	(Naidu et al., 1998)
44	Quercetin-3-galactoside	*C. paniculata* Willd. (flower)	(Subramaniam & Nagarajan, 1970)

Table 2.1, continued

No.	Compound name	Source	Ref.
45	Vitexin	*C. sessiliflora*	(Mun'im et al., 2003)
46	Isovitexin	*C. sessiliflora*	(Yoo et al., 2004)
47	Vitexin-4'-*O*-xyloside	*C. striata* DC	(Subramaniam & Nagarajan, 1970)
48	Hydroquinone	*C. sessiliflora*	(Mun'im et al., 2003)
49	Eucomic acid	*C. sessiliflora*	(Mun'im et al., 2003)
50	Hydroxyeucomic acid	*C. sessiliflora*	(Mun'im et al., 2003)
51	Kaempferol	*C. verrucosa* Linn	(Naidu et al., 1998)
52	4',5,7-trihydroxy-3-methoxyflavone	*C. madurensis*	(Bhakuni & Chaturvedi, (1984)
53	Lepidoside	*C. semperflorens* Vent.	(Dhasmana & Garg, 1991)
54	Kaempferitin	*C. semperflorens* Vent.	(Dhasmana & Garg, 1991)
55	Robinin	*C. zanziriba* (*C. usaramoensis*)	(Shitamoto et al., 2010)
56	Apigenin	*C. pallida* (bark)	(Subramaniam & Nagarajan, 1970)
57	Apigenin-7-*O*-*β*-D-apiofuranosyl-(1→6)-glucopyranoside	*C. podocarpa*	(Wanjala & Majinda, 1999)
58	Acacetin-7- *O*-*β*-D-apiofuranosyl-(1→6)-glucopyranoside	*C. podocarpa*	(Wanjala & Majinda, 1999)
59	4',7-dihydroxyflavone	*C. sessiliflora*	(Yoo et al., 2004)
60	1-*O*-methyl-myo-inositol	*C. trifoliastrum* (root)	(Rao et al., 1999)
61	Methoxystilbene	*C. madurensis*	(Bhakuni & Chaturvedi, (1984)
62	Crotmadine	*C. madurensis*	(Bhakuni & Chaturvedi, (1984)
63	Dihydroxyalpinumisoflavone	C. madurensis	(Bhakuni & Chaturvedi, (1984)
64	Crotmarine	*C. madurensis*	(Bhakuni & Chaturvedi, (1984)

Table 2.1, continued

No.	Compound name	Source	Ref.
65	Fulvine	*C. fulva* *C. crispate* *C. madurensis*	(Willette & Cammarato, 1972) (Culvenor & Smith, 1962) (Bhakuni & Chaturvedi, (1984)
66	Crispatine/crotaleschenine	*C. crispate* *C. leschenaultia*	(Culvenor & Smith, 1962) (Smith et al, 1988)
67	Melilocarpan 8-*O*-*β*-D-glucopyranoside	*C. zanzibarica* (*C. usaramoensis*)	(Shitamoto et al., 2010)
68	Melilocarpan 4'-*O*-*β*-D-glucopyranoside	*C. zanzibarica* (*C. usaramoensis*)	(Shitamoto et al., 2010)
69	Lasiocarpine	*C. grahamiana*	(Atal et al., 1969)
70	Grahamine	*C. grahamiana*	(Atal et al., 1969)
71	Crosemperine	*C. semperflorens* *C. Burhia* Buch-Ham *C. aegyptiaca*	(Sharma & Hebborn, 1968) (Ahmad & Fatima, 1986) (Roeder et al., 1993)
72	Croaegyptine	*C. aegyptiaca*	(Roeder et al., 1993)
73	Crotalarine	*C. aegyptiaca* *C. burhia*	(Roeder et al., 1993) (Rao et al., 1975)
74	Crotalarine lactone	*C. aegyptiaca*	(Roeder et al., 1993)
75	Globiferine	*C. globifera*	(Brown et al., 1984)
76	Gratianine	*C. grantiana* *C. virgulata* subsp. *grantiana* *C. globifera*	(Adams & Gianturco, 1956) (Smith & Culvenor, 1984) (Brown et al., 1984)
77	Grantaline	*C. virgulata* subsp. *grantiana* *C. globifera*	(Smith & Culvenor, 1984) (Brown et al., 1984)
78	Retusamine	*C. retusa*	(Culvenor & Smith, 1957)

Table 2.1, continued

No.	Compound name	Source	Ref.
79	Retusine	*C. retusa*	(Culvenor & Smith, 1957)
80	Croalbidine	*C. albida*	(Sawhney & Atal, 1973)
81	Integerrimine	*C. incana* Linn (seed) *C. tetragona* *C. narahutensis*	(Sawhney & Atal, 1970) (Puri et al., 1974) (Mattocks & Nwude, 1988)
82	Usaramine	*C. mucronata* Desv. *C. usaramoensis* E. G. Baker *C. incana* Linn *C naragutensis*	(Atal & Sawhney, 1968) (Culvenor & Smith, 1966) (Sawhney & Atal, 1970) (Mattocks & Nwude, 1988)
83	Crotastriatine	*C. striata*	(Gandhi et al., 1968)
84	Mucronatinine	*C. mucronata*	(Bhacca & Sharma, 1968)
85	Nilgrine	*C. mucronata*	(Atal & Sawhney, 1968)
86	Senecionine	*C. usaramoensis*	(Culvenor & Smith, 1966)
87	Retrorsine	*C. usaramoensis*	(Culvenor & Smith, 1966)
88	Coatline A isomer (*α-S*-hydroxyl)	*C. zanzibarica* (*C. usaramoensis*)	(Shitamoto et al., 2010)
89	1*β*,2*β*-epoxy-1*α*-hydroxymethyl-8*α*-pyrrolizidine	*C. trifoliastrum*	(Culvenor et al., 1967)
90	Crotanecine	*Crotalaria* sp.	(Atal & Kapur, 1966)
91	Croalbinecine	*C. albida* Heyne ex Roth.	(Sawhney et al., 1974)
92	7*β*-acetoxyy-1-methoxymethyl-1,2-dehydro-8*α*-pyrrolizidine	*C. aridicola*	(Culvenor et al., 1967)

Table 2.1, continued

No.	Compound name	Source	Ref.
93	7*α*-hydroxy-1-methoxymethyl-1,2-dehydro-8*α*-pyrrolizidine	*C. madicagenia* *C. aridicola* *C. trifoliastrum* Willd.	(Sawhney et al., 1970) (Culvenor & Smith, 1962)
94	1-methoxymethyl-1,2-dehydro-8*α*-pyrrolizidine	*C. madicagenia* *C. aridicola*	(Sawhney et al., 1970) (Culvenor & Smith, 1962)
95	Retronecine	*C. goreensis*	(Culvenor, 1965)
96	Heliotridine	*C. goreensis*	(Culvenor, 1965)
97	Scopoletin	*C. mysorensis* Roth.	(Sawhney & Atal, 1968)
98	Crotasteroiridocin	*C. emarginella*	(Ahmed et al., 2006)
99	Cardiogenin 3-*O*-*β*-D-xylopyranoside	*C. juncea* (seeds)	(Yadav & V., 1994)
100	*Bis*-desoxy-dihydromonotropein	*C. emarginella*	(Ahmed et al., 2006)
101	Crotalarin	*C. madurensis*	(Yadav & V., 1994)
102	Crotarin	*C. madurensis*	(Chaturvedi et al., 1987)
103	Dicrotaline	*C. lachnosema*	(Mattocks & Nwude, 1988)
104	Acetyldicrotaline	*C. lachnosema*	(Mattocks & Nwude, 1988)
105	Cromadurine	*C. madurensis*	(Rao et al., 1975)
106	Spectabiline	*C. grahamiana*	(Atal et al., 1969)
107	Monocrotaline	*C. aegyptiaca* *C. recta* Steud. ex A. Rich. *C. grahamiana* *C. sagittalis* L. Fruit *C. leioloba* Bartl. (seeds)	(Roeder et al., 1993) (Crout, 1969) (Atal et al., 1969) (Willette & Cammarato, 1972) (Puri et al., 1974)

Table 2.1, continued

No.	Compound name	Source	Ref.
108	Trichodesmine	*C. rubiginosa* Willd. *C. recta* Steud. ex A. Rich. *C. tetragona* Roxb. *C. globifera*	(Atal et al., 1966) (Crout, 1969) (Puri et al., 1974) (Brown et al., 1984)
109	Junceine	*C. juncea* (seed) *C. rubiginosa* Willd.	(Adams & Gianturco, 1956) (Atal et al., 1966)
110	Crotaramosmin	*C. ramosissima*	(Kumar et al., 1999)
111	Crotaramin	*C. ramosissima*	(Kumar et al., 1999)
112	Crotin	*C. ramosissima*	(Kumar et al., 1999)
113	Trimethoxychalcone	*C. ramosissima*	(Rao & Narukulla, 2007)
114	Seneciphylline	*C. juncea*	(Adams & Gianturco, 1956)
115	Ridelliine	*C. juncea*	(Adams & Gianturco, 1956)
116	Neocroalbidinone	*C. albida*	(Sun et al., 2013)
117	Neocroalbidine	*C. albida*	(Sun et al., 2013)
118	Anacrotine (crotalaburnine)	*C. incana* *C. laburnifolia* (seeds)	(Mattocks, 1968) (Sawhney & Atal, 1971)
119	Trans-anacrotine	*C. capensis*	(Verdon & van Wyk, 1992)
120	Crotananine	*C. nana*	(Siddiqi et al., 1978)
121	Madurensine	*C. agatiflora* subsp. *agatiflora* Schweinf	(Roux et al., 2011)
122	Doronenine	*C. agatiflora* subsp. *agatiflora* Schweinf	(Roux et al., 2011)

Table 2.1, continued

No.	Compound name	Source	Ref.
123	2-methyl-3-(2-oxo-[5H]-5-hydroxymethyl-5-methylfuran-3-yl)-propanoic acid	*C. verrucosa*	(Suri et al., 1989)
124	7*β*-hydroxy-1-methylene-8*α*-pyrrolizidine	*C. goreensis*	(Culvenor & Smith, 1961)
125	7*β*-hydroxy-1-methylene-8*β*-pyrrolizidine	*C. goreensis* *C. maypurensis* H. B. & K.	(Culvenor & Smith, 1961) (Culvenor et al., 1968)
126	Crotaoprostrin	*C. prostrate*	(Krohn et al., 2002)
127	Cronaburmine	*C. nana*	(Siddiqi et al., 1978)
128	Assamicadine	*C. assamica*	(Cheng et al., 1989)
129	Munchiwarin	*C. medicagenia*	(Narender et al., 2005)
130	Axillaridine	*C. scassellatii* (Seed)	(Wiedenfeld et al., 1985)
131	Axillarine	*C. scassellatii* (Seed)	(Wiedenfeld et al., 1985)
132	Desoxyaxillarine	*C. scassellatii* (Seed)	(Wiedenfeld et al., 1985)
133	Ramosismin	*C. ramosissima*	(Khalilullah et al., 1993)
134	Crotaorixin	*C. orixensis* (aerial)	(Narender et al., 2005)
135	Medicagenin	*C. medicagenia* DC (root)	(Narender et al., 2005)
136	3',5'-di-*C*-prenyl-2,4',4-trihydroxy chalcone	*C. medicagenia* (root)	(Rao et al., 1987)
137	Emarginellic acid	*C. emarginella*	(Ahmed et al., 2006)
138	Emarginellic acetate	*C. emarginella*	(Ahmed et al., 2006)
139	Crotalic acid	*C. emarginella*	(Ahmed et al., 2006)
140	Crotalic acetate	*C. emarginella*	(Ahmed et al., 2006)
141	Barbacarpan	*C. barbata* (aerial)	(Babu et al., 1998)
142	Barbacarpan acetate	*C. barbata* (aerial)	(Babu et al., 1998)

Table 2.1, continued

No.	Compound name	Source	Ref.
143	Crotafuran E	*C. pallida* (bark)	(Weng et al., 2003)
144	3-*O*-*α*-L-rhamnopyranosyl(1→2)[*β*-D-glucopyranosyl(1→6)]-*β*-D-galactopyranosyl(1→2)-6-*O*-methyl-*β*-D-glucuronopyranosyl soyasapogenol B	*C. albida*	(Ding et al., 1991)
145	3-*O*-*β*-D-xylopyranosyl(1→2)-*β*-D-galactopyranosyl(1→2)-6-*O*-methyl-*β*-D-glucuronopyranosyl sophoradiol	*C. albida*	(Ding et al., 1991)

2.2 *Morinda citrifolia* L.

2.2.1 General

The name of *Morinda citrifolia* is originated from two Latin words; morus (mulberry) and indicus (Indian). *Morinda citrifolia* L. (Noni) belongs to the Rubiaceae family and the genus consists of 80 species (Nelson & Elevitch, 2006). *M. citrifolia* is believed to have originated in Southeast Asia, widely spread across the tropics to Australia, Carribean and the Pasific areas (Chunhieng et al., 2005; Kinghorn et al., 2011). It has different names in different geographical locations. It is called ba ji tian in China, cheesefruit in Australia, noni in Hawaii, nono in Tahiti, Indian Mulberry in India, nonu in Samoa and Tonga, ura in Rotuma, nhau in Vietnam, Mengkudu in Brunei and Malaysia, Bengkudo in Indonesia, monkey dumpling and forbidden fruit in Barbados, painkiller bush in Carribean, and yaw weed in Guyana (Braun & Cohen, 2015; Seaforth, 2005; Wang & Su, 2001).

M. citrifolia trees are small evergreen shrubs with 3-10 m tall with an abundant wide elliptical leaves (5-17 cm length, 10-40 cm width), small tubular white flowers and oval in shape with an embossed appearance fruits (3-10 cm length, 3-6 cm width). The unripe fruit is light green and it turning whitish yellow and almost white at the time of picking. The fruit is slightly wrinkly and has lumpy surface with strong butyric acid-like rancid smell. The root of *M. citrifolia* is a deep taproot and grows vertically downward (Chunhieng et al., 2005; Dixon et al., 1999; Swanholm et al., 1959).

M. citrifolia has been used in folk remedies during the last couple of decades. Many studies discovered that all parts of this plant include leaves, roots, fruits, flowers, bark and stem contain medicinally active components that possess various therapeutic

properties (Chan-Blanco et al., 2006; Zin & Abdul-Hamid, 2002). *M. citrifolia* is also popular as a source of red, yellow, and purple dyes (Singh, 2012). In mid-1950s, *M. citrifolia* is more popular as a dye. In Polynesia, they get the yellow dye from the trunk bark, while a red dye was made by mixing the root of *M. citrifolia* with lime that derived from coral. Javanese people employed the root of *M. citrifolia* for dyeing batik, Australian Aborigines for dyeing cotton and wool, Indians for dyeing yarn, carpets and turban, and Polynesians for dyeing *kapa* (bark cloth) (Chan-Blanco et al., 2006).

Various publications have shown that *M. citrifolia* can be consumed to treat, relieve and as an alternative medicines for different kind of illnesses. These include hiccough, hoarseness, gingivitis, gastric ulcers, sprains, headaches, atheroselerosis, blood vessel problems, heartburn, arthritis, antiemetic, diarrhea, infertility, postpartum haemorrhage, cancer, vaginal bleeding, menorrhagia, mental depression, poor digestion, secondary amenorrhoea, high blood pressure, menstrual difficulties, muscle ache and pain, uterine haemorrhage, coryza, neuralgia, oedema, carcinomas, induration, pain of breast, heart trouble, ostcodynia and many other ailments (Bushnell, 1993; Dittmar, 1993; Dixon et al., 1999).

In India, the leaves of this plant is make into juice and applied externally for gout, and used internally as a tonic and to treat fever. The leaves are also used to apply wounds and ulcers for treatment purpose. For the throat and gum complaints, dysentery and leucorrhoea, they used the fruits of *M. citrifolia* as treatment (Jain & DeFilipps, 1991; Kamboj, 1988; Moorthy & Reddy, 1970; Morton, 1992; Ross, 2001). While the root of *M. citrifolia* is used for cathartic and febrifuge (Hu, 2005; Li, 2002).

In New Guinea the leaves are used to relieve headaches, treat sores of leprosy and sometimes it was taken internally for stomach ache (Cambie & Brewis, 1997; Weiner, 1976). They also used the root of *M. citrifolia* to make a juice and consume internally for fevers and skin disorders (Hu, 2005; Li, 2002). People in Guyana macerated the leaves of *M. citrifolia* alone or mixed with *Pothomorphe peltata*, in coconut oil for an external rub to relieve rheumatic pains and arthritic, also chewed the fruits to heal mouth ulceration (DeFilipps et al., 2004).

In Hawaii, leaves and bark are pounded, cooked, strained and used as a tonic, take orally as abortifacient. The fruits are taken orally for asthma, insecticide for hair, and used as a poultice to heal broken bones and deep cuts and bruises. The immature fruit juice are taken internally to treat diabetes, menstrual cramp, hypertension, digestive disorders, and as a general tonic. While the mash green fruit is used for skin condition, and the rotten-ripe fruit is used for lassitude of old age (Degener, 1973; Tabrah & Eveleth, 1966; Wagner et al., 1990).

In West Indies, the leaves are used as a poultice to wrap around the rheumatic joints and treatment for pain while the fruits are heated to treat sores of inflammation (Ayensu, 1981). While in Fiji, the leaves were consumed with leaves of *Epipremnum pinnatum* to relieve pregnancy pains or with *Psychotria* sp. to heal haemorrhoids. People in Australia used the roots of *M. citrifolia* to relieve fever, toothache, inflammation, malaria, skin disorder, jaundice, sore throat, diarrhea and dysentery. The root was grated to use as treatment to heal the stings from insects and stonefish. The roots of *M. citrifolia* are also used with *Euodia hortensis* and *Geniostoma vitiense* to treat malnutrition (Pawlus & Kinghorn, 2007). In China, the roots of *M. citrifolia* are believed to be able to treat cancer, beri-beri, cholecystitis, lumbago, stimulate the

endocrine system and increase the leucocyte count. The whole plant extract is taken to relieve aching bones (Hu, 2005; Li, 2002).

The main group of active compounds in this plant is the anthraquinones, which possess various therapeutic properties including antiviral, antibacterial, antioxidant, anticancer, antitumor, anti-tubercular effects, and anti-inflammatory (Singh, 2012). Damnacanthal (**287**), a component from *M. citrifolia* fruit was identified as an inhibitor of Viral protein R (Vpr) induced cell death. But the mechanism of damnachantal inhibits Vpr induced apoptosis is still under the research. Damnacanthal (**287**) was also reported as a unique anthraquinones with anti-cancer and anti-HIV activity (Hiramitsu et al., 1993). In the other hand, 1-methoxy-2-formyl-3-hydroxy anthraquinone obtained from the roots suppressed the cytopathic effect of HIV infected MT-4 cells, without inhibiting cell growth (Umezawa, 1992).

The presence of phenolic compounds such as L-asperuloside (**203**), acubin (**309**) and alizarin (**301**) in *M. citrifolia* fruits, and the anthraquinones in the roots, are accounted for the antimicrobial activities in this plant. All these compounds have been shown to have activity against infectious bacteria strains such as *Pseudomonas aeruginosa*, *Shigela sp., Staphylococcus aureus*, *Escherichia coli*, *Proteus morgaii*, *Bacillus subtilis*, and *Salmonella sp.* These antibacterial compounds are effective for skin infection treatment, fever, colds, and other bacterial-caused health problems (Atkinson, 1956). The acetonitrile extracts of the dried fruits inhibited the growth of *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Streptococcus pyrogene* (Locher et al., 1995). It is also helps in stomach ulcer through inhibition of the bacteria, *H. pylori* (Duncan et al., 1998). Lee and colleagues reported the methanol and aqueous crude of fruits extract inhibited the growth of *Vibrio harveyi, Vibrio*

alginolyticus, Streptoccus sp. and *E. coli*. They also found that hexane and ethanol extract of the fruits are able to provide protection against *Mycobacterium tuberculosiss* (Lee at al., 2008). In another studies, Murray et. al reported that the antibacterial effect of this plant is greater when the fruit is ripe.

Ethyl acetate extract of the fruits from this plant has been reported to exhibit higher antioxidative activity and this lead to the isolation of three antioxidant phenolic compounds; aesculetin (**308**), 3, 3',4',5, 7-pentahydroxyflavone or (quercetin) (**271**) and isoscopoletin (**307**) by Chang and his colleagues (Chang-hong et al., 2007). Other researchers have been reporting that the seed extract from this plant exhibit significant antioxidant activity in the Ferric Reducing Antioxidant Power (FRAP) and Oxygen Radical Absorbance Capacity (ORAC) (Brett et al., 2011).

The methanol extract of fruits were reported to exhibit cytotoxic activity against neuroblastoma (LAN5) cell lines and breast cancer (MCF7) in 3-(4,5-dimethythiazol-. 2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay (Arpornsuwan & Punjanon, 2006). The ethanol precipitate of *M. citrifolia* juice possess antitumor and immunomodulatory activity against Sarcoma 180 ascites tumor in mice (Furusawa et al., 2003). In 1993, Hiramitsu and his colleagues found that damnacanthal (**287**) is a new inhibitor of *ras* function and thus suppress *ras*-expressing tumors (Hiramitsu et al., 1993). This anthraquinone also showed potent inhibitory activity towards tyrosine kinase such as Src, Lyn, Lck and EGF receptor (Bowie & Cooke, 1962). Other studies has reported two novel glycosides; 6-*O*-(β-D-glucopyranosyl)-1-*O*-octanoyl-β-D-glucopyranose (**167**) and asperulosidic acid (**305**) that obtained from isolation of the fruits extract showed effectiveness in suppressing 12-*O*-tedtradecanoylphorbol-13-acetate (TPA) or epidermal growth factor (EGF), thereby inducing the cell

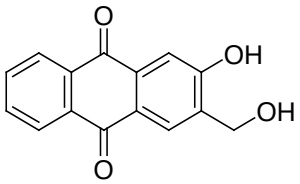
transformation and associated AP-1 activity (Guangming et al., 2001). Moon and colleagues have reported that scopoletin (**242**) has a regulatory effect in the inflammatory reactions mediated by the human mast cell line HMC-1. Scopoletin (**242**) is a phenolic coumarin that is medicinally active and showed positive potential as antitumor against skin cancer, antihyperlipidemic, antiulcer, antiviral and antimicrobial (Moon et al., 2007; Nam & Kim, 2015).

Researchers from Philippines reported that *M. citrifolia* has been found to kill *Mycobacterium tuberculosis*. It was also found that the extract of *M. citrifolia* leaves have an antitubercular effect which inhibits the growth of bacteria in a test tube. Ralph Heinicke state that the fruits of M. citirfolia contain a natural precursor for Xeronine, named Proxeroninase (Heinicke, 1985). Proxeronine is converted to the alkaloid in the body by enzymes, Proxeroninase. He claims that Xeronine has a capasity to modify the molecular structure of protein. Thus, Xeronine has a wide range of biological activities especially for a problem in the cell due to protein structural (Heinicke, 2001).

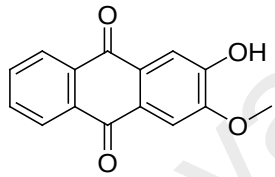
Approximately 200 phytochemicals have been isolated and identified from different parts of *M. citrifolia* and different location all over the world. Anthraquinones are the major phenolic compounds that have been isolated from this plant (Bowie & Cooke, 1962).

2.2.2 Compounds isolated from *Morinda citrifolia*

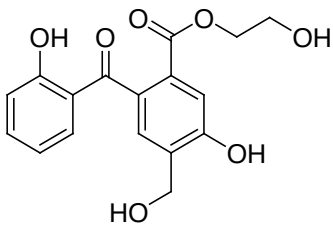
Figure 2.2 shows the structures of compounds previously isolated from *M. citrifolia.* Table 2.2 lists the compounds in Figure 2.2, which were separated from different parts of the plant.



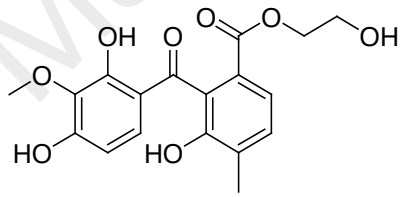
(**146**)



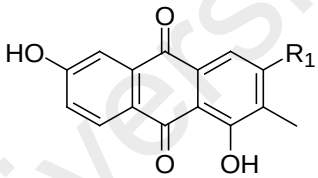
(**147**)



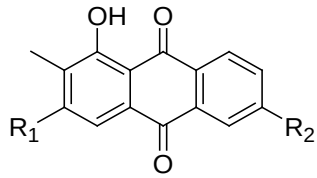
(**148**)



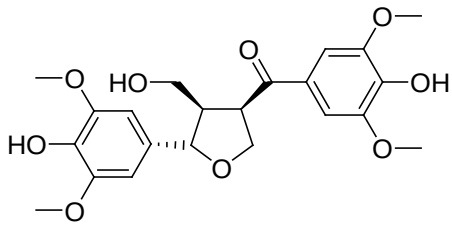
(**149**)



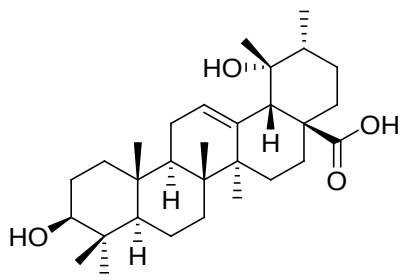
(**150**) R_1 = OH
(**MC4**) R_1 = H



(**152**) R_1 = OH, R_2 = OH
(**153**) R_1 = H, R_2 = H

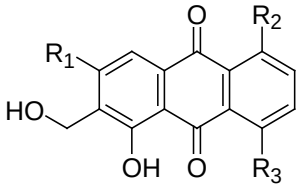


(**154**)

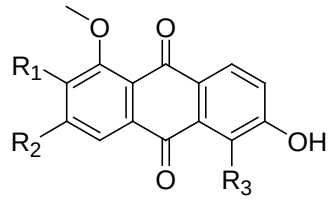


(**155**)

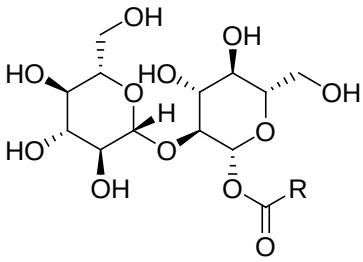
Figure 2.2: Structure of compounds isolated from *Morinda citrifolia*



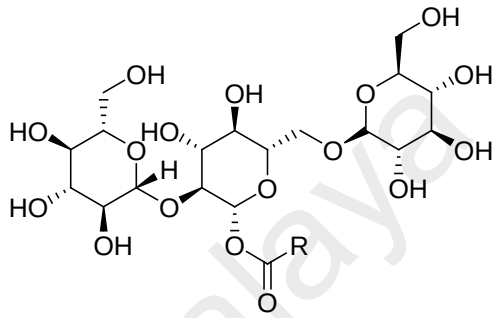
(**156**) R_1 = H, R_2 = OCH_3, R_3 = OH
(**157**) R_1 = OCH_3, R_2 = H, R_3 = H



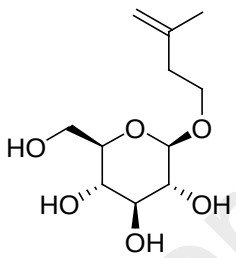
(**158**) R_1 = CH_3, R_2 = O, R_3 = H
(**159**) R_1 = CH_2OCH_3, R_2 = H, R_3 = OCH_3



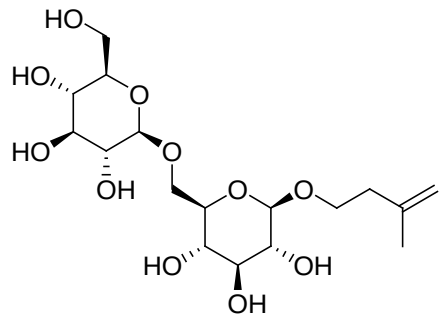
(**160**) R = C_5H_{11}
(**161**) R = C_7H_{15}



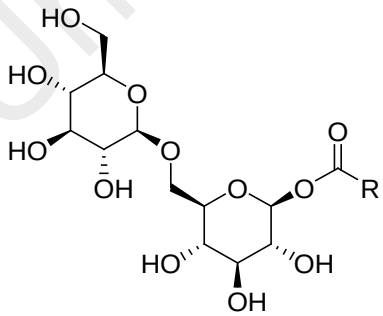
(**162**) R = C_5H_{11}
(**163**) R = C_7H_{15}



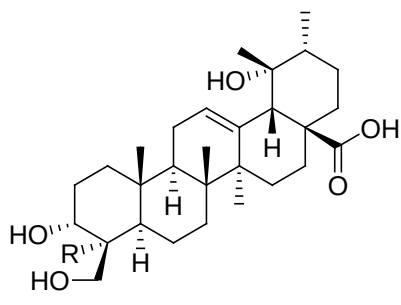
(**164**)



(**165**)

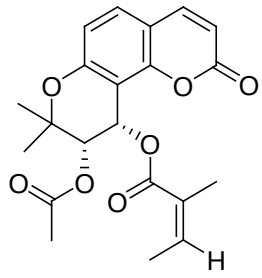


(**166**) R = C_5H_{11}
(**167**) R = C_7H_{15}

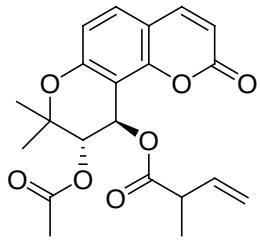


(**168**) R = CH_3
(**169**) R = CH_2OH

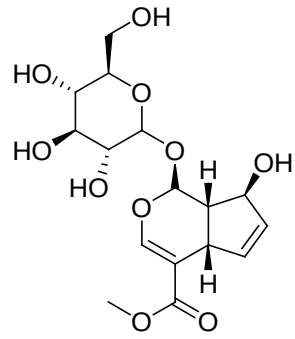
Figure 2.2, continued



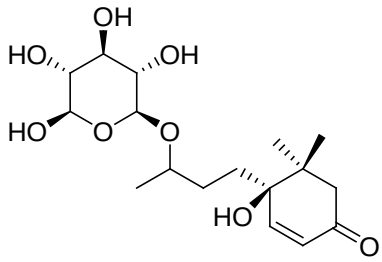
(**170**)



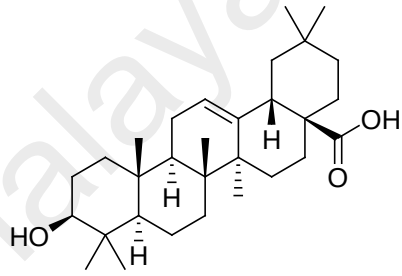
(**171**)



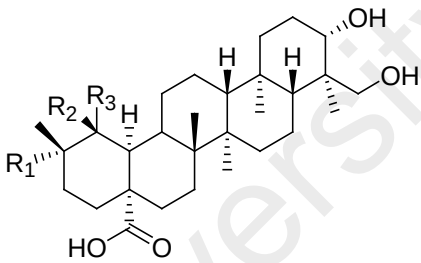
(**172**)



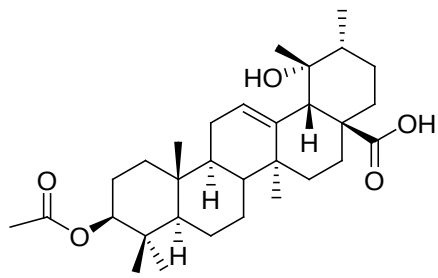
(**173**)



(**174**)

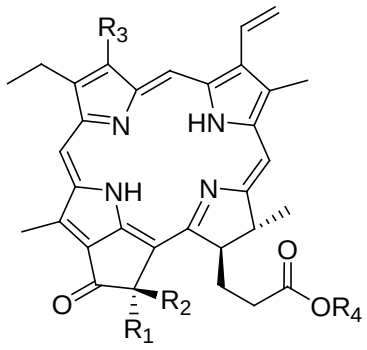


(**175**) $R_1 = CH_3$, $R_2 = H$, $R_3 = H$
(**176**) $R_1 = H$, $R_2 = OH$, $R_3 = CH_3$

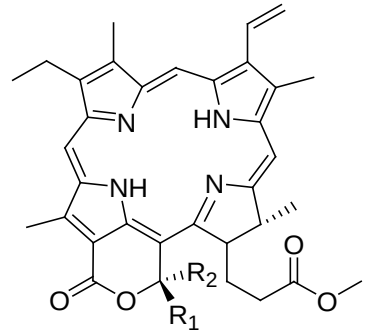


(**177**)

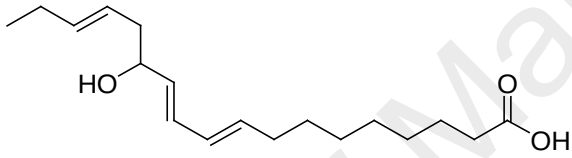
Figure 2.2, continued



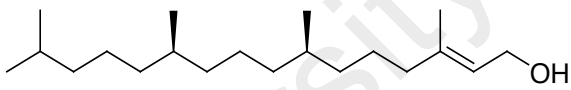
(**178**) R_1 = $COOCH_3$, R_2 = OH, R_3 = CH_3, R_4 = CH_3
(**179**) R_1 = OH, R_2 = $COOCH_3$, R_3 = CH_3, R_4 = CH_3
(**180**) R_1 = $COOCH_3$, R_2 = H, R_3 = CH_3, R_4 = CH_3
(**181**) R_1 = $COOCH_3$, R_2 = H, R_3 = CHO, R_4 = CH_3
(**182**) R_1 = $COOCH_3$, R_2 = H, R_3 = CH_3, R_4 = H
(**183**) R_1 = H, R_2 = $COOCH_3$, R_3 = CH_3, R_4 = CH_3



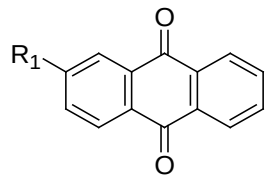
(**184**) R_1 = $COOCH_3$, R_2 = OH
(**185**) R_1 = OH, R_2 = $COOCH_3$



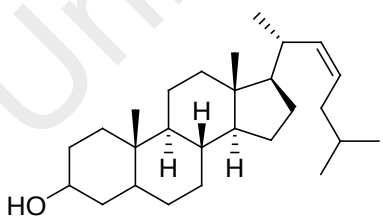
(**186**)



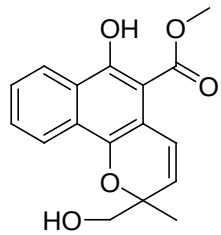
(**187**)



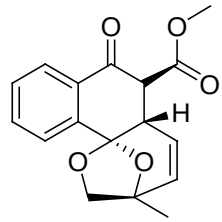
(**188**) R_1 = CH_3
(**189**) R_1 = CHO



(**190**)

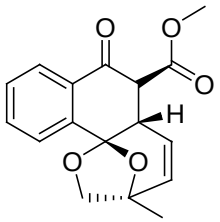


(**191**)

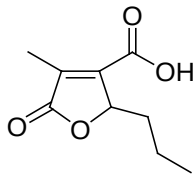


(**192**)

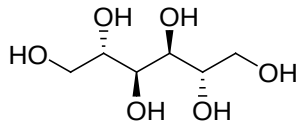
Figure 2.2, continued



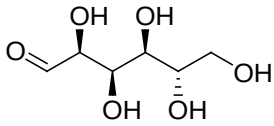
(**193**)



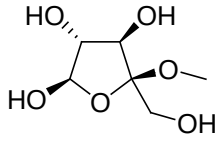
(**194**)



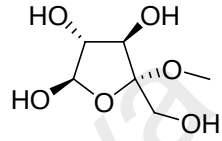
(**195**)



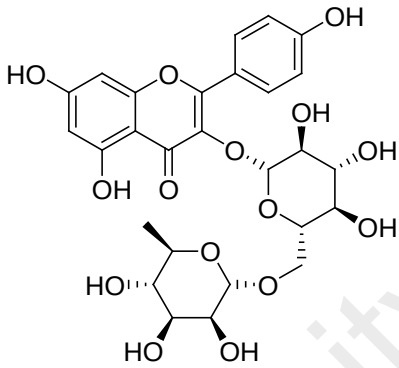
(**196**)



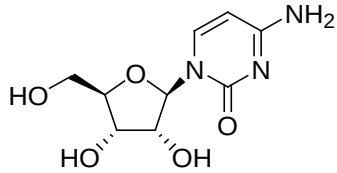
(**197**)



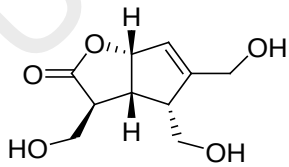
(**198**)



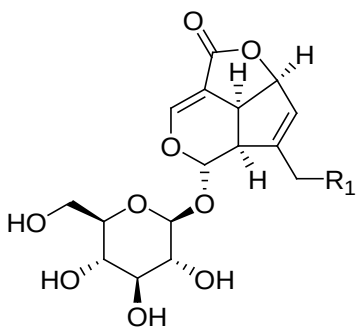
(**199**)



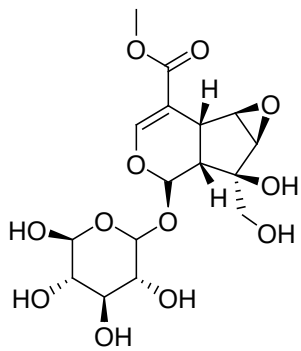
(**200**)



(**201**)

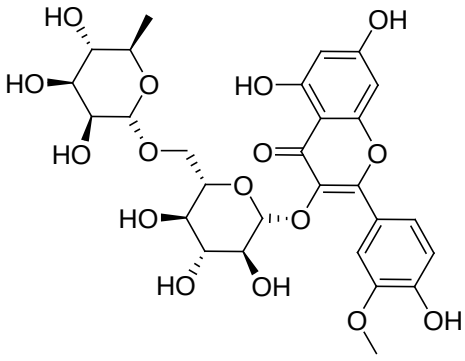


(**202**) R_1 = OH
(**203**) R_1 = $COOCH_3$

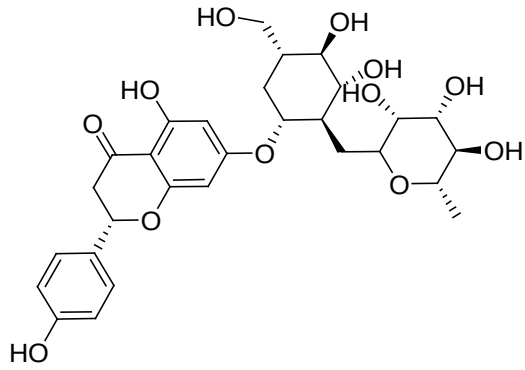


(**204**)

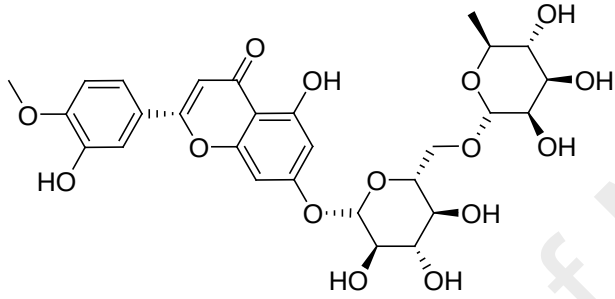
Figure 2.2, continued



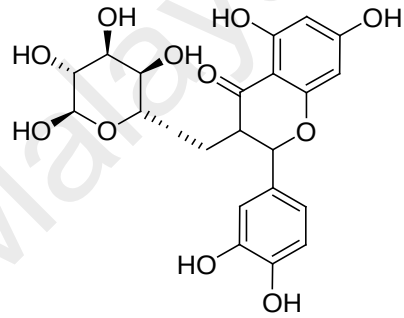
(**205**)



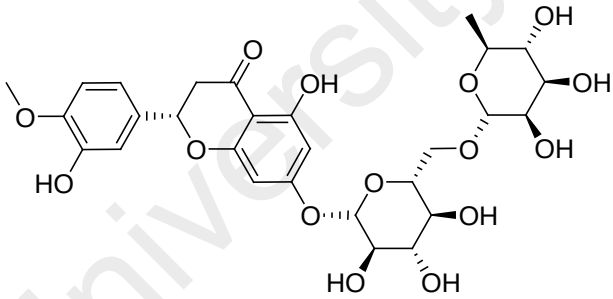
(**206**)



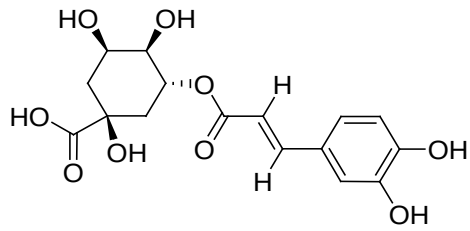
(**207**)



(**208**)

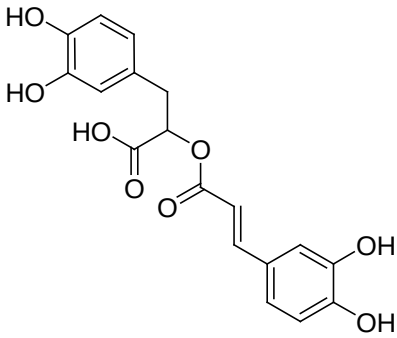


(**209**)

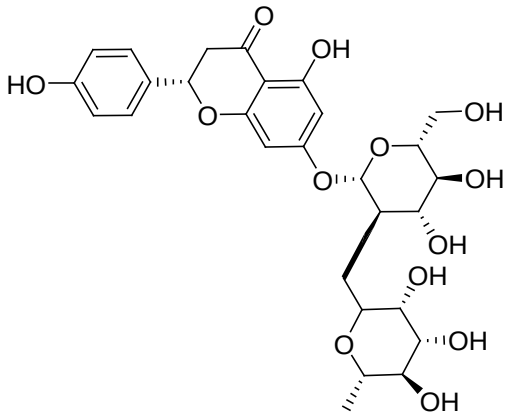


(**210**)

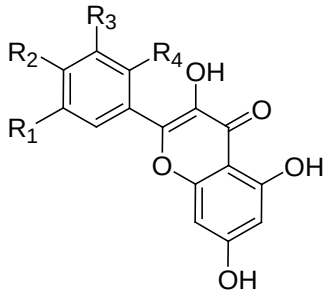
Figure 2.2, continued



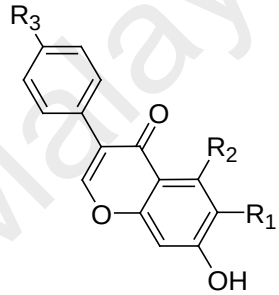
(**211**)



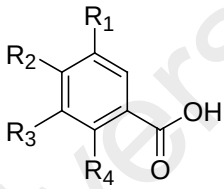
(**212**)



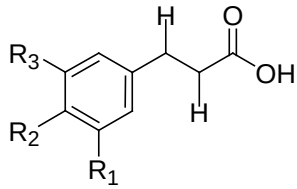
(**213**) R_1 = OH, R_2 = OH, R_3 = OH, R_4 = H
(**214**) R_1 = H, R_2 = OH, R_3 = H, R_4 = OH
(**215**) R_1 = OCH_3, R_2 = OH, R_3 = H, R_4 = H



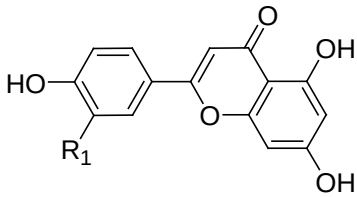
(**216**) R_1 = H, R_2 = H, R_3 = OH
(**217**) R_1 = OCH_3, R_2 = H, R_3 = OH
(**218**) R_1 = H, R_2 = OH, R_3 = OH



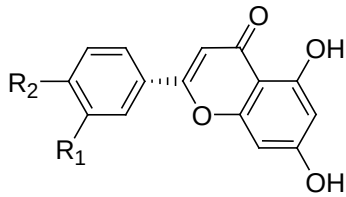
(**219**) R_1 = OH, R_2 = OH, R_3 = OH, R_4 = H
(**220**) R_1 = OH, R_2 = H, R_3 = H, R_4 = OH
(**221**) R_1 = H, R_2 = OH, R_3 = OCH_3, R_4 = H



(**222**) R_1 = H, R_2 = OH, R_3 = H
(**223**) R_1 = H, R_2 = OH, R_3 = OCH_3
(**224**) R_1 = OCH_3, R_2 = OH, R_3 = OCH_3

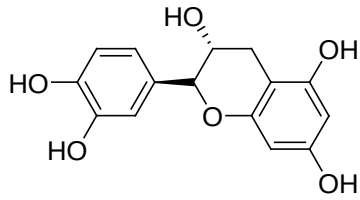


(**225**) R_1 = H
(**226**) R_1 = OH

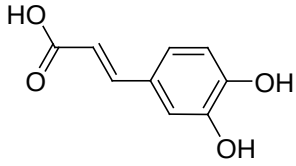


(**227**) R_1 = OH, R_2 = OH
(**228**) R_1 = OH, R_2 = OCH_3

Figure 2.2, continued



(**229**)



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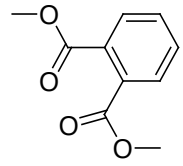

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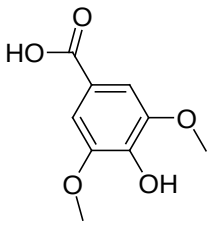
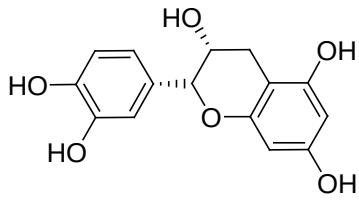


(**232**)



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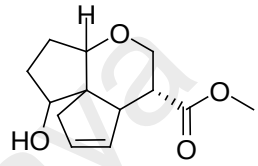

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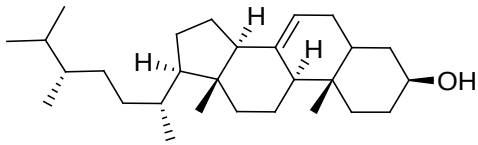
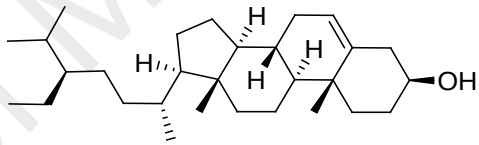
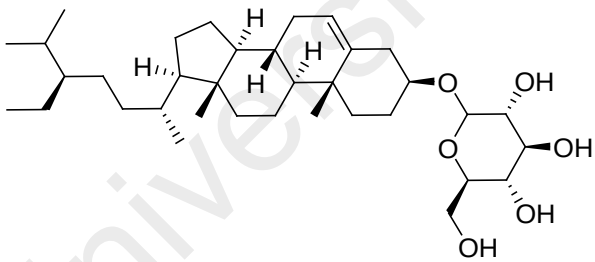


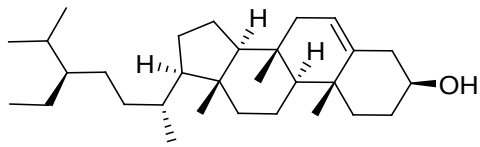
(**235**)



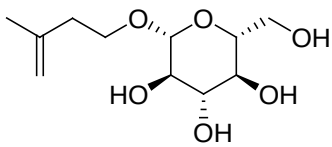
(**236**)



(**237**)



(**238**)



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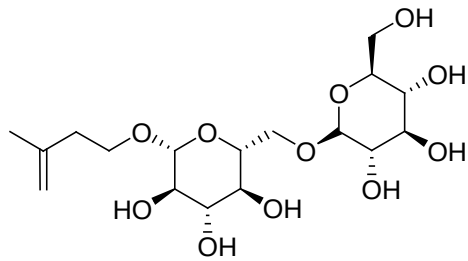
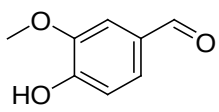
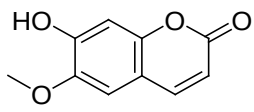


(**240**)

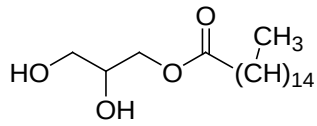
Figure 2.2, continued



(**241**)



(**242**)



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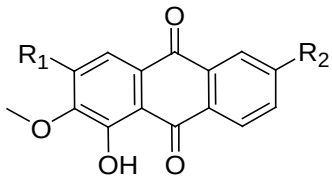
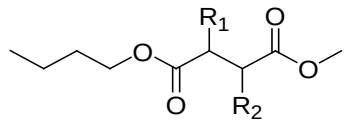
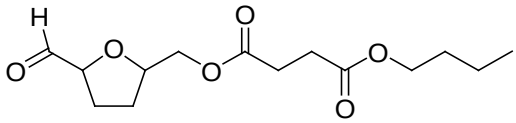


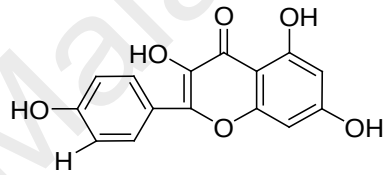
(**244**) R_1 = OH, R_2 = OH
(**245**) R_1 = H, R_2 = H



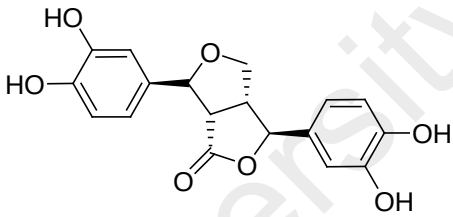
(**246**) R_1 = OH, R_2 = H
(**247**) R_1 = H, R_2 = OH



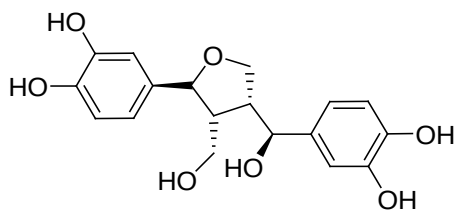
(**248**)



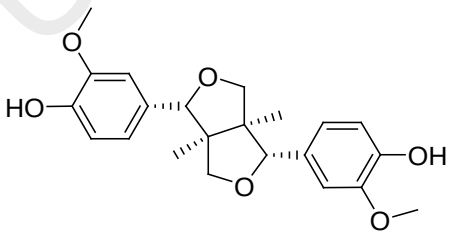
(**249**)



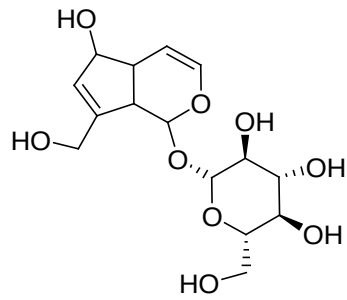
(**250**)



(**251**)

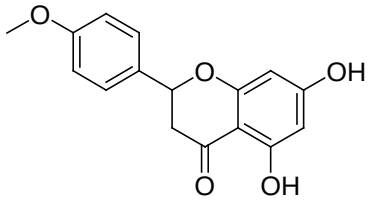


(**252**)

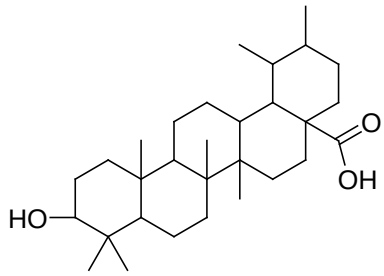


(**253**)

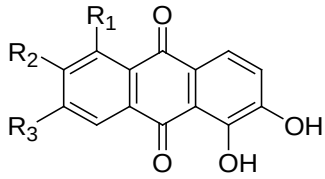
Figure 2.2, continued



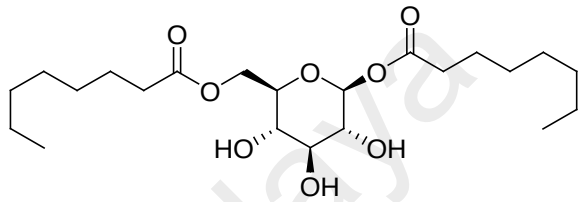
(**254**)



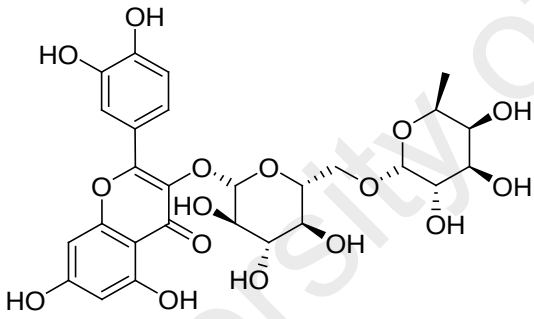
(**255**)



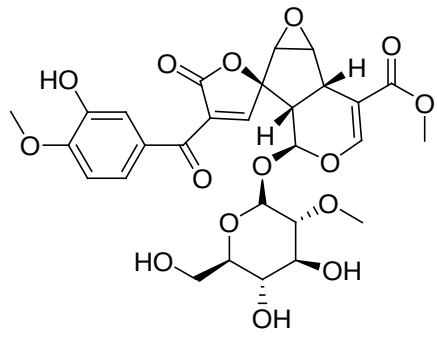
(**256**) R_1 = OH, R_2 = CH_2OH, R_3 = OH
(**257**) R_1 = OH, R_2 = CH_3, R_3 = OH
(**258**) R_1 = H, R_2 = CH_3, R_3 = OH



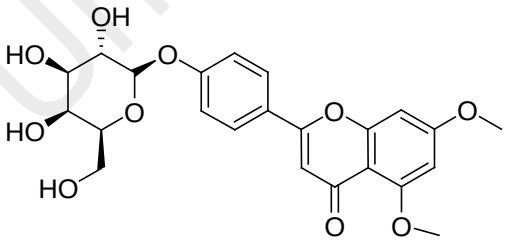
(**259**)



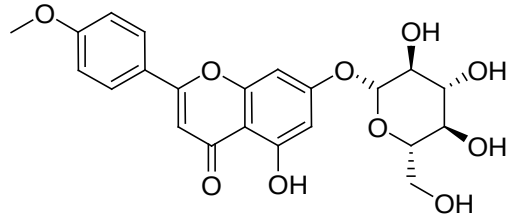
(**260**)



(**261**)

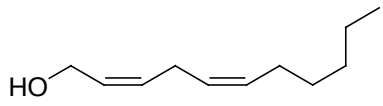


(**262**)

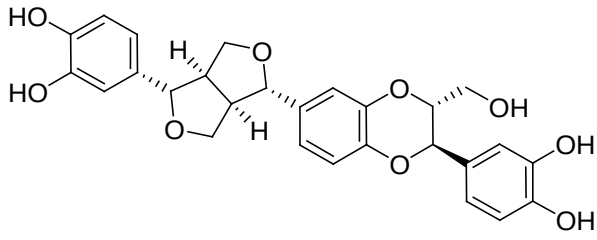


(**263**)

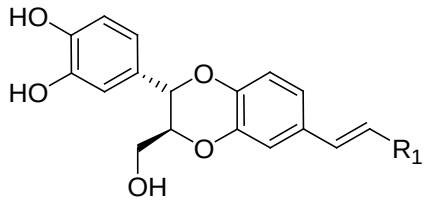
Figure 2.2, continued



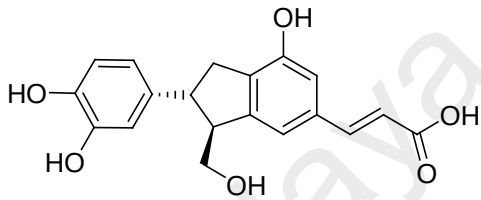
(**264**)



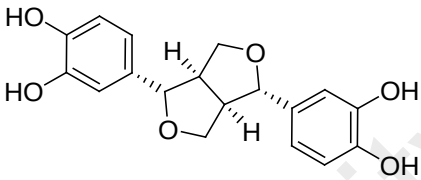
(**265**)



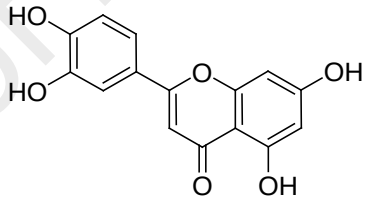
(**266**) $R_1 = CH_2OH$
(**267**) $R_1 = CHO$
(**268**) $R_1 = COOH$



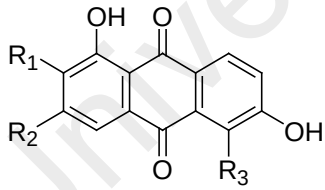
(**269**)



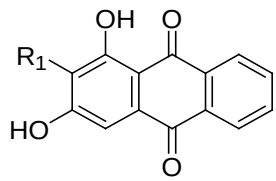
(**270**)



(**271**)

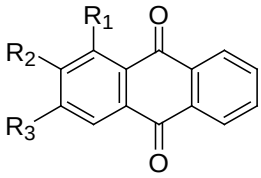


(**272**) $R_1 = H$, $R_2 = CH_3$, $R_3 = OCH_3$
(**273**) $R_1 = CH_3$, $R_2 = H$, $R_3 = H$
(**274**) $R_1 = CH_3$, $R_2 = H$, $R_3 = OH$
(**275**) $R_1 = CH_3$, $R_2 = H$, $R_3 = OCH_3$
(**276**) $R_1 = CH_2OCH_3$, $R_2 = H$, $R_3 = OCH_3$

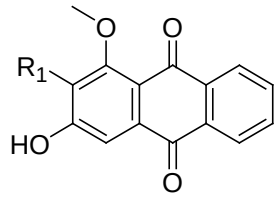


(**MC2**) $R_1 = CHO$
(**MC3**) $R_1 = CH_3$
(**279**) $R_1 = CH_2OCH_2CH_3$
(**280**) $R_1 = CH_2OH$
(**281**) $R_1 = CH_2OCH_3$
(**282**) $R_1 = OCH_3$

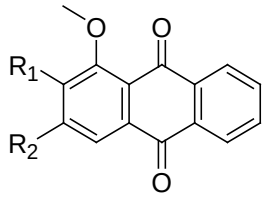
Figure 2.2, continued



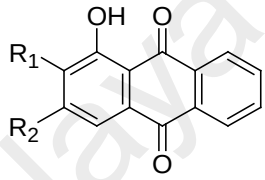
(**283**) $R_1 = OCH_3$, $R_2 = CH_2O$-primeverose, $R_3 = O^-$
(**284**) $R_1 = OH$, $R_2 = CH_2O$-primeverose, $R_3 = O^-$
(**285**) $R_1 = CH_3$, $R_2 = H$, $R_3 = OH$
(**286**) $R_1 = OCH_3$, $R_2 = CH_2OCH_3$, $R_3 = OCH_3$



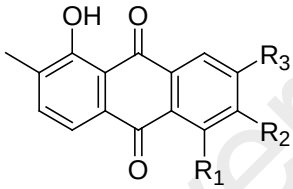
(**MC1**) $R_1 = CHO$
(**288**) $R_1 = CH_2$-primeverose
(**289**) $R_1 = CH_3$
(**290**) $R_1 = CH_2OH$
(**291**) $R_1 = CH_2OCH_3$



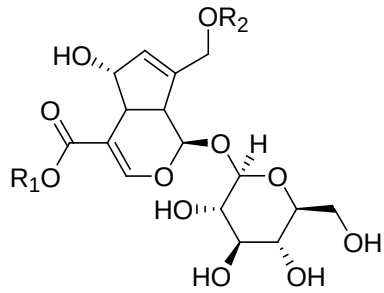
(**292**) $R_1 = CH_2OH$, $R_2 =$ O-primeverose
(**293**) $R_1 = CH_2O$-gentiobiose, $R_2 = H$
(**MC6**) $R_1 = OH$, $R_2 = OH$
(**295**) $R_1 = H$, $R_2 = OH$
(**296**) $R_1 = OH$, $R_2 = H$



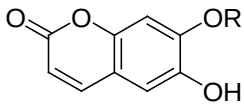
(**297**) $R_1 = CH_2OH$, $R_2 =$ O-primeverose
(**298**) $R_1 = CH_2O$-primeverose, $R_2 = H$
(**MC5**) $R_1 = H$, $R_2 = OCH_3$
(**300**) $R_1 = CHO$, $R_2 = H$
(**301**) $R_1 = OH$, $R_2 = H$



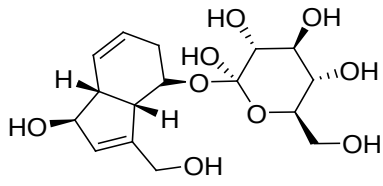
(**302**) $R_1 = OH$, $R_2 =$ O-primeverose, $R_3 = H$
(**303**) $R_1 = OCH_3$, $R_2 = OCH_3$, $R_3 =$ O-primeverose



(**304**) $R_1 = H$, $R_2 = H$
(**305**) $R_1 = H$, $R_2 = COCH_3$
(**306**) $R_1 = CH_3$, $R_2 = H$

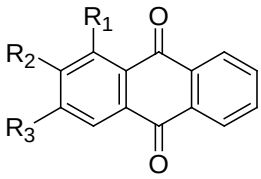


(**307**) $R = CH_3$
(**308**) $R = H$

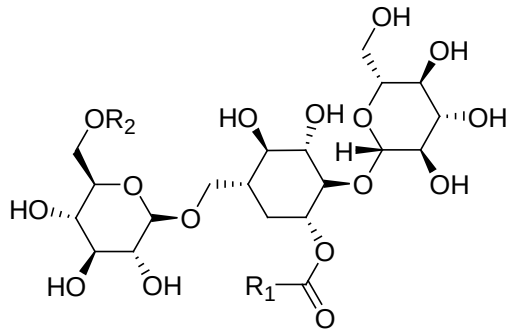


(**309**)

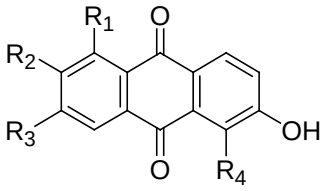
Figure 2.2, continued



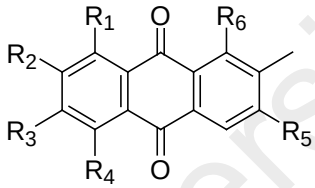
(**310**) $R_1 = OCH_3$, $R_2 = OCH_3$, $R_3 = OH$
(**311**) $R_1 = OCH_3$, $R_2 = OH$, $R_3 = OCH_3$
(**312**) $R_1 = OH$, $R_2 = OCH_3$, $R_3 = OCH_3$
(**313**) $R_1 = OH$, $R_2 = OCH_3$, $R_3 = OH$



(**314**) $R_1 = C_5H_{11}$, $R_2 = H$
(**315**) $R_1 = C_7H_{15}$, $R_2 = H$
(**316**) $R_1 = C_7H_{15}$, $R_2 = C_7H_{15}$
(**317**) $R_1 = C_7H_{15}$, $R_2 = C_5H_{11}$



(**318**) $R_1 = OH$, $R_2 = CH_2OCH_3$, $R_3 = H$, $R_4 = OCH_3$
(**319**) $R_1 = OCH_3$, $R_2 = OH$, $R_3 = OCH_3$, $R_4 = H$
(**320**) $R_1 = OH$, $R_2 = CH_3$, $R_3 = H$, $R_4 = OCH_3$



(**321**) $R_1 = OH$, $R_2 = OCH_3$, $R_3 = H$, $R_4 = OH$, $R_5 = H$, $R_6 = H$
(**322**) $R_1 = OCH_3$, $R_2 = OH$, $R_3 = H$, $R_4 = H$, $R_5 = H$, $R_6 = H$
(**323**) $R_1 = OCH_3$, $R_2 = H$, $R_3 = OCH_3$, $R_4 = H$, $R_5 = OH$, $R_6 = H$
(**324**) $R_1 = OH$, $R_2 = OCH_3$, $R_3 = H$, $R_4 = H$, $R_5 = H$, $R_6 = OH$

Table 2.2: Name of compounds isolated from *Morinda citrifolia*

No.	Compound name	Source	Ref.
146	2-hydroxy-3-(hydroxymethyl)anthraquinone	Roots	(Deng et al., 2007)
147	2-hydroxy-3-methoxyanthraquinone	Roots	(Deng et al., 2007)
148	Morintrifolin A	Roots	(Deng et al., 2007)
149	Morintrifolin B	Roots	(Deng et al., 2007)
150	1,3,6-trihydroxy-2-methylanthraquinone	Roots	(Deng et al., 2007)
MC4	1,6-dihydroxy-2-methylanthraquinone	Roots	(Deng et al., 2007)
152	1,3,6-trihydroxy-2-methylanthraquinone	Roots	(Deng et al., 2007)
153	1,6-dihydroxy-2-methylanthraquinone	Roots	(Deng et al., 2007)
154	Ciwujiatone	Roots	(Deng et al., 2007)
155	Pomolic acid	Roots	(Deng et al., 2007)
156	1,8-dihydroxy-2-hydroxymethyl-5-methoxyanthraquinone or hydyotanthraquinone	Roots	(Deng et al., 2007)
157	1-hydroxy-2-(hydroxymethyl)-3-methoxyanthraquinone	Roots	(Deng et al., 2007)
158	6-hydroxy-1-methoxy-2-methylanthraquinone	Roots	(Deng et al., 2007)
159	1,5,15-tri-*O*-methylmorindol	Fruits	(Akihisa et al., 2007)
160	2-*O*-(*β*-D-glucopyranosyl)-1-*O*-hexanoyl-*β*-D-gluropyranose	Fruits	(Akihisa et al., 2007)
161	2-*O*-(*β*-D-glucopyranosyl)-1-*O*-octanoyl-*β*-D-gluropyranose	Fruits	(Akihisa et al., 2007)
162	2,6-*O*-(*β*-D-glucopyranosyl)-1-*O*-hexanoyl-*β*-D-gluropyranose	Fruits	(Akihisa et al., 2007)
163	2,6-*O*-(*β*-D-glucopyranosyl)-1-*O*-octanoyl-*β*-D-gluropyranose or Nonioside B	Fruits	(Akihisa et al., 2007)
164	3-methylbut-3-enyl-*β*-D-glucopyranose	Fruits	(Akihisa et al., 2007)
165	3-methylbut-3-enyl-6-*O*-*β*-D-glucopyranosyl-*β*-D-glucopyranose	Fruits	(Akihisa et al., 2007)
166	6-*O*-(*β*-D-glucopyranosyl)-1-*O*-hexanoyl-*β*-D-gluropyranose or Nonioside D	Fruits	(Akihisa et al., 2007)

Table 2.2, continued

No.	Compound name	Source	Ref.
167	6-*O*-(*β*-D-glucopyranosyl)-1-*O*-octanoyl-*β*-D-gluropyranose or Nonioside C	Fruits	(Akihisa et al., 2007)
168	Barbinervic acid	Leaves	(Takashima et al., 2007)
169	Clethric acid	Leaves	(Takashima et al., 2007)
170	Pteryxin	Leaves	(Takashima et al., 2007)
171	Peucedanocoumarin III	Leaves	(Takashima et al., 2007)
172	Citrifoside	Leaves	(Takashima et al., 2007)
173	Roseoside II	Leaves	(Takashima et al., 2007)
174	Oleanolic acid	Leaves	(Takashima et al., 2007)
175	Hederagenin	Leaves	(Takashima et al., 2007)
176	Rotungenic acid	Leaves	(Takashima et al., 2007)
177	3-*O*-acetylpomolic acid	Leaves	(Takashima et al., 2007)
178	13^2(*R*)-hydroxypheophorbide a methyl ester	Leaves	(Takashima et al., 2007)
179	13^2(*S*)-hydroxypheophorbide a methyl ester	Leaves	(Takashima et al., 2007)
180	Methyl pheophorbide a	Leaves	(Takashima et al., 2007)
181	Methyl pheophorbide b	Leaves	(Takashima et al., 2007)
182	Pheophorbide a	Leaves	(Takashima et al., 2007)

Table 2.2, continued

No.	Compound name	Source	Ref.
183	13-*epi*-phaeophorbide a methyl ester	Leaves	(Takashima et al., 2007)
184	15^1(*R*)-hydroxypurpurin-7 lactone dimethyl ester	Leaves	(Takashima et al., 2007)
185	15^1(*S*)-hydroxypurpurin-7 lactone dimethyl ester	Leaves	(Takashima et al., 2007)
186	13-hydroxy-9,11,15-octadecatrienoic acid	Leaves	(Takashima et al., 2007)
187	Phytol	Leaves	(Takashima et al., 2007)
188	2-methylanthraquinone or tectoquine	Roots	(Lv et al., 2011)
189	2-formylanthraquinone	Roots	(Lv et al., 2011)
190	Cholest-22-en-3-ol	Roots	(Lv et al., 2011)
191	Nonin A	Roots	(Lv et al., 2011)
192	Nonin B	Roots	(Lv et al., 2011)
193	Nonin C	Roots	(Lv et al., 2011)
194	Decumbic acid	Roots	(Lv et al., 2011)
195	D-mannitol	Fruits	(Su et al., 2005)
196	D-glucose	Fruits	(Su et al., 2005)
197	Methyl *β*-D-fructanoside	Fruits	(Su et al., 2005)
198	Methyl *α*-D-fructanoside	Fruits	(Su et al., 2005)
199	Nicotifloroside	Fruits	(Su et al., 2005)
200	Cytidine	Fruits	(Su et al., 2005)
201	Borreriagenin or morindacin	Fruits	(Su et al., 2005) (Tang et al., 2009)
202	Deacetylasperuloside	Fruits	(Su et al., 2005) (Tang et al., 2009)
203	Asperuloside	Leaves Fruits	(Sang et al., 2001) (Tang et al., 2009)
204	6*β*,7*β*-epoxy-8-*epi*-splendoside	Fruits	(Su et al., 2005)
205	Narcissoside	Fruits	(Su et al., 2005)
206	Naringin	Fruits	(Lin et al., 2013)
207	Diosmine	Fruits	(Lin et al., 2013)
208	Quercitrin	Fruits	(Lin et al., 2013)

Table 2.2, continued

No.	Compound name	Source	Ref.
209	Hesperidin	Fruits	(Lin et al., 2013)
210	Chlorogenic acid	Fruits	(Lin et al., 2013)
211	Rosmarinic acid	Fruits	(Lin et al., 2013)
212	Neohesperidin	Fruits	(Lin et al., 2013)
213	Myricetin	Fruits	(Lin et al., 2013)
214	Morin	Fruits	(Lin et al., 2013)
215	Isorhamnetin	Fruits	(Lin et al., 2013)
216	Daidzein	Fruits	(Lin et al., 2013)
217	Glycitein	Fruits	(Lin et al., 2013)
218	Genistein	Fruits	(Lin et al., 2013)
219	Gallic acid	Fruits	(Lin et al., 2013)
220	Gentisic acid	Fruits	(Lin et al., 2013)
221	Vanilic acid	Fruits	(Lin et al., 2013)
222	*p*-coumaric acid or 4-coumaric acid	Fruits	(Lin et al., 2013)
223	Ferulic acid	Fruits	(Lin et al., 2013)
224	Sinapic acid	Fruits	(Lin et al., 2013)
225	Apigenin	Fruits	(Lin et al., 2013)
226	Luteolin	Fruits	(Lin et al., 2013)
227	Eriodictyol	Fruits	(Lin et al., 2013)
228	Hesperetin	Fruits	(Lin et al., 2013)
229	Catechin	Fruits	(Lin et al., 2013)
230	Caffeic acid	Fruits	(Lin et al., 2013)
231	Dimethyl phthalate	Fruits	(He at al., 2012)
232	Syringic acid	Fruits	(Lin et al., 2013)
233	Epicatechin	Fruits	(Lin et al., 2013)
234	4-*epi*-dunnisinin	Fruis	(Tang et al., 2009) (He at al., 2012)
235	19-hydroxyl-ursolic acid	Fruits	(He at al., 2012)
236	(24*S*)-ergost-7-en-3*β*-ol	Fruits	(He at al., 2012)
237	Daucosterol	Fruits	(He at al., 2012)
238	*β*-sitosterol	Fruits	(He at al., 2012)
239	1-*O*-(3'-methylbut-3'-enyl)-*β*-D-glucopyranose	Fruits	(He at al., 2012)
240	3-methylbut-3-enyl-6-*O*-*β*-D-glucopyranosyl-*β*-D-glucopyranoside or Nonioside A	Fruits	(Wang et al., 2000) (He at al., 2012)

Table 2.2, continued

No.	Compound name	Source	Ref.
241	Vanilin	Fruits	(He at al., 2012)
242	Scopoletin	Fruits	(He at al., 2012)
243	1-monopalmitin	Fruits	(Pawlus et al., 2005)
244	2-methoxy-1,3,6-trihydroxyanthraquinone	Fruits	(Pawlus et al., 2005)
245	1-hydroxy-2-methoxyanthraquinone	Roots	(Pawlus et al., 2005)
246	1-*n*-butyl-4-methyl-2-hydroxysuccinate	Fruits	(Samoylenko et al., 2006)
247	1-*n*-butyl-4-methyl-3-hydroxysuccinate	Fruits	(Samoylenko et al., 2006)
248	1-*n*-butyl-4-(5'-formyl-2'-furanyl)methyl succinate	Fruits	(Samoylenko et al., 2006)
249	Kaempferol	Fruits	(Lin et al., 2013) (Deng et al., 2007)
250	(+)-3,4,3',4'-tetrahydroxy-9-7'α-epoxylignano-7α,9-lactone	Fruits	(Deng et al., 2007)
251	(+)-3,3'-bisdemethyltanegool	Fruits	(Deng et al., 2007)
252	(-)-pinoresinol	Fruits	(Deng et al., 2007)
253	Aucubin	Fruits	(Chan-Blanco et al., 2006)
254	Aracetin	Fruits	(Chan-Blanco et al., 2006)
255	Ursolic acid	Fruits	(Chan-Blanco et al., 2006)
256	5,6-dihydroxylucidin	Fruits	(Chan-Blanco et al., 2006)
257	3-hydroxymorindone	Fruits	(Chan-Blanco et al., 2006)
258	2-methyl-3,5,6-trihydroxyanthraquinone	Fruits	(Chan-Blanco et al., 2006)
259	1,6-di-*O*-octanoyl-β-D-glucopyranose	Fruits	(Kim et al., 2010)
260	Rutin	Fruits	(Akihisa et al., 2007) (Lin et al., 2013)
261	Citrifolinoside or yopaaoside A	Leave	(Sang et al., 2001)
262	5,7-dimethylapigenin 4'-*O*-β-D-galactopyranoside	Flower	(Singh & Tiwari, 1976)

Table 2.2, continued

No.	Compound name	Source	Ref.
263	Acacetin 7-*O*-*β*-D-glucopyranoside	Flower	(Singh & Tiwari, 1976)
264	(*Z*,*Z*)-2,5-Undecadien-1-ol	Fruits	(Farine et al., 1996)
265	Isoprincepin	Fruits	(Kamiya et al., 2004)
266	Americanol A	Fruits	(Kamiya et al., 2004)
267	Americanin A	Fruits	(Kamiya et al., 2004)
268	Americanoic acid A	Fruits	(Kamiya et al., 2004)
269	Morindolin	Fruits	(Kamiya et al., 2004)
270	3,3'-bisdemethylpinoresinol	Fruits	(Deng et al., 2007) (Kamiya et al., 2004)
271	3,3',4',5,7-pentahydroxyflavone or quercetin	Fruits	(Deng et al., 2007) (Liu et al., 2007) (Lin et al., 2013)
272	1,7-dihydroxy-8-methoxy-2-methylanthraquinone or morindone-5-methylether	Roots	(Lv et al., 2011)
273	Soranjidiol	Roots	(Kamiya et al., 2010)
274	Morindone	Roots	(Kamiya et al., 2010)
275	1,6-dihydroxy-5-methoxy-2-methylanthraquinone	Fruits	(Pawlus et al., 2005)
276	5,15-di-*O*-methylmorindol	Fruits	(Akihisa et al., 2007) (Takashima et al., 2007)
MC2	1,3-dihydroxy-2-formylanthraquinone or nordamnacanthal	Roots	(Lv et al., 2011) (Kamiya et al., 2010)
MC3	1,3-dihydroxy-2-methylanthraquinone or rubiadin	Roots	(Lv et al., 2011)
279	Ibericin	Roots	(Kamiya et al., 2010)
280	Lucidin	Roots	(Kamiya et al., 2010)
281	1,3-dihydroxy-2-methoxymethylanthraquinone	Roots	(Kamiya et al., 2010)
282	1,3-dihydroxy-2-methoxyanthraquinone	Roots	(Pawlus et al., 2005)
283	1-methoxy-2-primeverosyloxymethyl-anthraquinone-3-olate	Roots	(Kamiya et al., 2009)
284	1-hydroxy-2-primeverosyloxymethyl-anthraquinone-3-olate	Roots	(Kamiya et al., 2009)

Table 2.2, continued

No.	Compound name	Source	Ref.
285	1-methyl-3-hydroxyanthraquinone	Roots	(Lv et al., 2011)
286	1,3-dimethoxy-2-methoxymethylanthraquinone	Roots	(Lv et al., 2011)
MC1	1-methoxy-3-hydroxy-2-formylanthraquinone or damnacanthal	Roots	(Lv et al., 2011) (Kamiya et al., 2010)
288	Damnacanthol-11-*O*-*β*-primeveroside	Roots	(Kamiya et al., 2009)
289	Rubiadin 1-methylether or rubiadin monomethyl ether	Roots	(Kamiya et al., 2010)
290	3-hydroxy-2-(hydroxymethyl)-1-methoxyanthraquinone or damnacanthol	Roots	(Kamiya et al., 2010)
291	3-hydroxy-1-methoxy-2-methoxymethylanthraquinone	Roots	(Kamiya et al., 2010)
292	Damnacanthol-3-*O*-*β*-D-primeveroside	Roots	(Kamiya et al., 2008)
293	Digiferruginol-1-methylether-11-*O*-*β*-gentibiose	Roots	(Kamiya et al., 2009)
MC6	1-methoxy-2-hydroxyanthraquinone or alizarin 1-methyl ether	Roots	(Lv et al., 2011)
295	1-methoxy-3-hydroxynthraquinone	Roots	(Lv et al., 2011)
296	2-hydroxy-1-methoxyanthraquinone	Fruits	(Pawlus et al., 2005)
297	Lucidin-3-*O*-*β*-D-primeveroside	Roots	(Kamiya et al., 2008)
298	Digiferruginol-11-*O*-*β*-primeveroside	Roots	(Kamiya et al., 2009)
MC5	1-hydroxy-3-methoxyanthraquinone	Roots	(Lv et al., 2011)
300	2-formyl-1-hydroxyanthraquinone	Roots	(Iwao & Kuraishi, 1987)
301	1,2-dihydroxyanthraquinone or alizarin	Roots Fruits	(Deng et al., 2007) (Wang et al., 2002)
302	Morindone-6-*O*-*β*-D-primeveroside	Roots	(Kamiya et al., 2008)
303	1-hydroxy-5,6-dimethoxy-2-methyl-7-primeverosyloxyanthraquinone	Roots	(Kamiya et al., 2009)
304	Deacetylasperulosidic acid	Roots Fruits	(Kamiya et al., 2008) (Samoylenko et al., 2006)
305	Asperulosidic acid	Roots Leaves Fruits	(Kamiya et al., 2008) (Akihisa et al., 2007) (Su et al., 2005) (Tang et al., 2009)

Table 2.2, continued

No.	Compound name	Source	Ref.
306	6*α*-hydroxyadoxoside	Fruits	(Su et al., 2005)
307	Isoscopoletin	Fruits	(Deng et al., 2007) (Liu et al., 2007)
308	Aesculetin	Fruits	(Liu et al., 2007)
309	Acubin	Fruits	(Leach et al., 1998)
310	Anthragallol 1,2-di-*O*-methyl ether	Roots	(Dalsgaard et al., 2006)
311	Anthragallol 1,3-di-*O*-methyl ether	Fruits	(Kamiya et al., 2005)
312	Anthragallol 2,3-di-*O*-methyl ether	Heartwood	(Dalsgaard et al., 2006)
313	Anthragallol 2-*O*-methyl ether	Fruits	(Kamiya et al., 2005)
314	Nonioside E	Fruits	(Kim et al., 2005)
315	Nonioside F	Fruits	(Kim et al., 2005)
316	Nonioside G	Fruits	(Kim et al., 2005)
317	Nonioside H	Fruits	(Kim et al., 2005)
318	5,15-dimethylmorindol	Fruits	(Takashima et al., 2007)
319	6-hydroxy-anthragallol-1,3-dimethylether	Fruits	(Kamiya et al., 2005)
320	Morindone-5-methylether	Fruits	(Kamiya et al., 2005)
321	1,4-dihydroxy-2-methoxy-7-methylanthraquinone or austrocortinin	Fruits	(Pawlus & Kinghorn, 2007)
322	2-hydroxy-1-methoxy-7-methylanthraquinone	Roots	(Sang & Ho, 2009)
323	Morenone-1	Roots	(Jain & Srivastava, 1992)
324	Morenone-2	Roots	(Jain & Srivastava, 1992)

2.3 *Chlorophyllum molybdites*

2.3.1 General

Mushrooms belong to the class of basidomycetes which consist of fruits bodies and mycelium. Generally, the edible species are called mushrooms while the poisonous species called toadstool (Adedayo, 2011). The terms toadstool comes from the German word *todestuhl* meaning death's stool and has been used when referring to the poisonous mushroom. There are about 5000 mushrooms species was reported in the world and approximately only 50-100 are known to be poisonous to human (Barbato, 1993; Bryson, 1996).

Mycotoxins refer to any toxic substance by a fungus that capable to poison other organisms (Bennett, 1987). The toxic components of poisonous mushrooms have been identified as amatoxins, phallatoxins, gyromitrin, orellanine, muscarine, tricholomic acid, ibotenic acid, muscinol, psilocybin, psilocin, and tetraethyl thiuram disulphate (Benedict, 2013; Buku et al., 1980; Fasidi & Kadiri, 1995; Saupe, 1981). In clinical practice, only amatoxins are topic of interest for chemical study because it is thermostable and cannot be removed or destroyed by cooking. Amatoxins can be analyzed in urine, blood and various organs and it is extremely powerful poisons that can cause fatality (Faulstich et al., 1980; Faulstich et al., 1982; Vellinga, 2006).

Chlorophyllum species are characterized by their spores. The spore can be green, or without any colour. Based on parsimony analysis of ITS rDNA (Internal Transcribed Space Ribosomal DNA) sequences from European collections, four *Chlorophyllum* species that is *Chlorophyllum rachodes, Chlorophyllum brunneum, Chlorophyllum olivieri* and *Chlorophyllum molybdites* has been carried out (Vellinga, 2006). While in China, they have discovered other species of this genus which is

Chlorophyllum agaricoides, Chlorophyllum hortense, and *Chlorophyllum sphaerosporum* (Ge & Yang, 2006).

Chlorophyllum molybdites (Meyer: Fr) Massee previously known as Lepiota Morgani or the 'green parasol' mushroom (Blayney et al., 2006). It is also known by a variety of common names such as *Lepiota esculenta*, *Lepiota molybdites*, *Morgan's Lepiota*, False parasol, and Green-Lined Parasol. It has a green spores which are a bit wider than those of the other species, but the rest are looks very much like *Chlorophyllum rachodes* and it has very similar appearance to *Amanitas* except for the gills (Berger & Guss, 2005; Watling, 1991). The Mushroom Poisoning Case Registry of North American Mycological Association's Toxicology Committee lists *C. molybdites* as the most common mushroom poisoning reported because of the misidentification (Augenstein, 1994). *C. molybdites* can be found either alone or in partial or fairy rings (up to 16 feet in diameter) on grasslands, gardens, lawns, and occasionally in open woods during the wet periods of spring, summer and fall (Augenstein, 1994; Berger & Guss, 2005; Vellinga, 2006).

C. molybdites is a common species that is widely distributed in the eastern states of North America, and also has been found in Hawaii, Tahiti, the Philippines, New Guinea, Australia, India, east and central Africa, the West Indies, China and much of South America including Brazil and Argentina, and with continuing high summer temperatures it might well spread northwards in Europe (Arora, 1986; Bessey, 1939; Ge & Yang, 2006; Vellinga, 2006). *C. molybdites* are often involved in poisonings throughout the world. The consumption and ingestion of this *C. molybdites* is almost never resulting any fatality. But, it can causes discomfort situation to the consumer such as intoxication, dizziness, diarrhea, nausea was followed by profuse

continuous vomiting, convulsion, intestinal pain, and also griping stomach pain (Blayney et al., 1980; Fasidi & Kadiri, 1995; Gosh et al., 1977; Gray, 1973; Lehmann & Khazan, 1992; Wieland, 1968).

Many researchers have reported their findings on this species either on clinical studies or in the other fields. In 1996, Floch and his colleagues reported a series of *in vivo* and *in vitro* experiments using extracts from *C. molybdites*. In the experiment, it is found that the extract was innocuous when administered orally in mice, but when injected intraperitoneally it resulted in fatality. The results also indicated that the extract will lost its effectiveness over the time (Floch et al., 1966).

In 1974, Eilers and Nelson published a report on the toxicity of *C. molybdites,* in mice, chicks and dogs. The force feeding and administration via subcutaneous routes produced a little toxicity, while intraperitoneal injection produced significant toxicity for both mice and chicks. In the other hand, intravenous injections of toxin extracts was given to the dogs and it result in a decrease in mean blood pressure. The report also stated that the toxins in *C. molybdites* was found in all parts of the mushrooms but the most concentrated part is in the cap followed by the stripe, gills and spores, in mature or immature specimens of the species (Eilers & Nelson, 1974).

The study on chemical composition and toxic trace element composition in *C. molybdites* indicated the presence of higher tannin and trypsin contents in this species (Falade et al., 2008). Tannins are known to retard growth through reduced digestion and/or absorption (Laurena et al., 1984). While the results obtain for all of the trace elements (Lead, Cadmium, Nickel, Arsenic Chromium and Mercury) shows that mercury has the lowest while lead has the highest. Lead has been reported to cause

irreversible damage to the central nervous system and permanent mental retardation, while Mercury poison was reported to cause fetal malformation, kidney and liver damage (Chisolm, 1965; Falade et al., 2008; Weiss & Landrigan, 2000; Yilmaz et al., 2003).

Pharmacological and toxicological studies have shown the reduction severity of toxic signs in mice poisoned with the lyophilized extract of *C. molybdites* when tested with Penicilin G although it doesn't completely eliminate the toxins. Penicilin G in this case is used as a drug that block the transport system responsible for the amatoxin uptake by the hepatocytes. Administration of penicillin G was shown to have significant prophylactic and therapeutic effect to reduce the severity in mice dose but it did not confer significant protection from injury induced by the mushroom toxins on tissue and organs in the mice (Ambali et al., 2008; Rumack & Spoerke, 1994).

The studies on proximate, mineral and phytate composition of this mushrooms have indicates that the crude of *C. molybdites* have very low content in that three variables. It had a lowest content of crude fat, protein, sodium, potassium, phosphorus, zinc, copper, and the chloride content. But in the other hand, the mushroom has the highest Nitrogen free extract (NFE) content (Ndamitso & Abulude, 2013).

Previous studies on mushroom toxins suggested the presence of a cholinergic compound in this species. However, Eilers and Nelson reported that the toxic component in this fungus is a polymeric protein. In a later study, Yamada and colleagues isolated a toxic metalloendopeptidase (MEPs) named molybdophyllysin from *C. molybdites*. Molybdophyllysin was found as a relatively small protein with proteolytic activity and this shows a contrast finding from Eilers and Nelson. It was

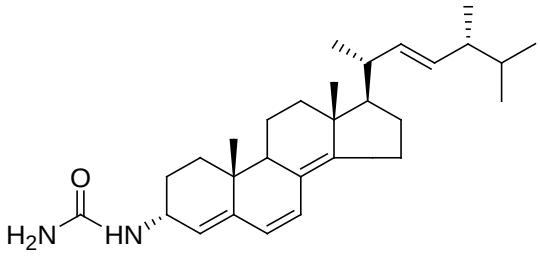
reported that molybdophyllysin is a member of the deuterolysin family of MEPs that contain aspzincin zinc-binding motif (Yamada et al., 2012).

In a subsequent study, Kobayashi and his colleagues isolated the new lectin from *C. molybdites* known as *Chlorophyllum molybdites* lectin (CML). In this research, it was discovered that CML exhibited *N*-glycolylneuraminic acid (NeuGc) binding specificity and showed strong hemagglutination of Pronase-treated porcine erythrocytes. NeuGc is a common sialic acid found in most mammals and lectins that can recognize sialic acids have been used as a medical and biological probe for sugar or sugar chain detector. NeuGc-specific lectins are rare and difficult to get commercially (Kobayashi et al., 2004).

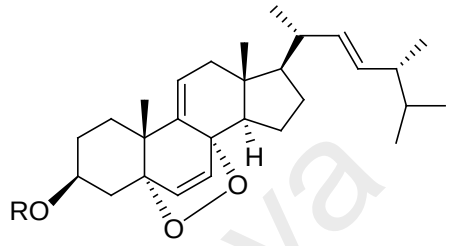
In 2001, Yoshikawa and his colleagues isolated two new steroidal derivatives from this fungus. Both (22*E*,24*R*)-3α-ureido-ergosta-4,6,8(14),22-tetraene (**325**) and (22*E*,24*R*)-5α,8α-epidioxyergosta-6,22-diene-3β-ol-3-*O*-β-$_{D}$-glucopyranoside (**326**) have indicated the moderate cytotoxicity against the human stomach cancer cell Kato-III (Yoshikawa et al., 2001).

2.3.2 Compounds isolated from *Chlorophyllum molybdites*

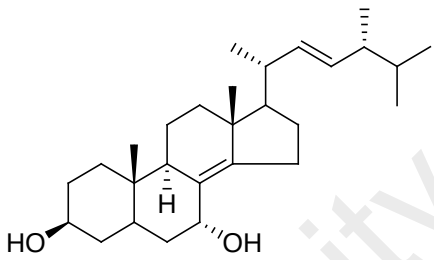
Table 2.3 lists the compounds isolated from the *C. molybdites* and Figure 2.3 shows the structures of compounds previously isolated from *C. molybdites.*



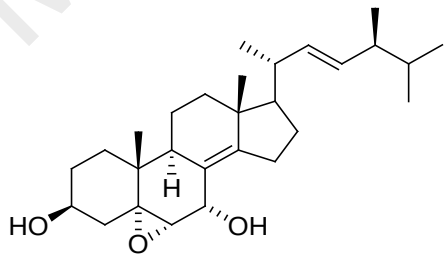
(**325**)



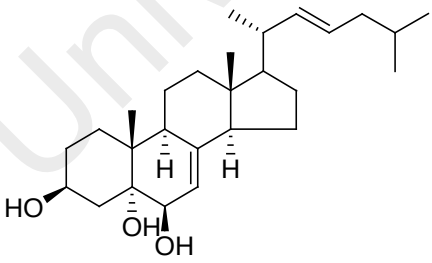
(**326**) R = β-D glucopyranosyl
(**327**) R = H
(**328**) R = Glc



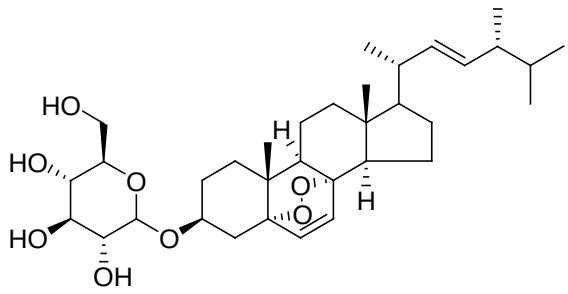
(**329**)



(**330**)

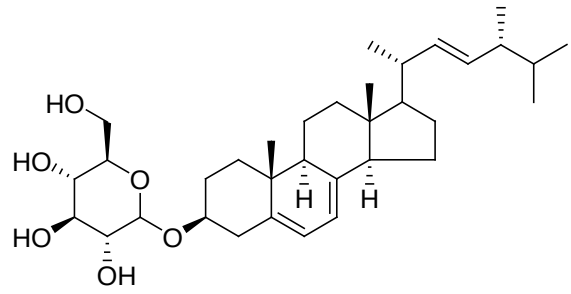


(**331**)

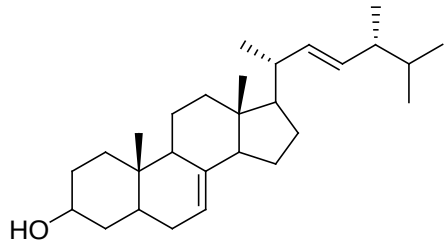


(**332**)

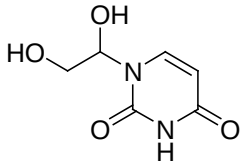
Figure 2.3: Structure of compounds isolated from *Chlorophyllum molybdites*



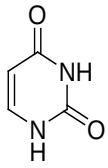
(**333**)



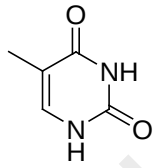
(**334**)



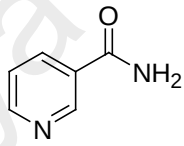
(**335**)



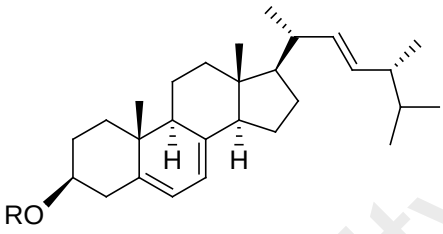
(**336**)



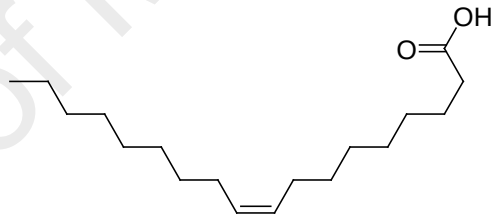
(**337**)



(**338**)

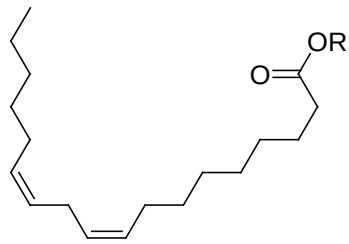


(**339**) R =H
(**340**) R = Glc



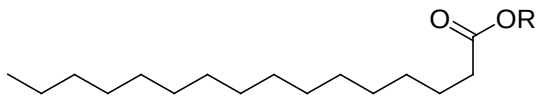
(**341**)

(**342**)

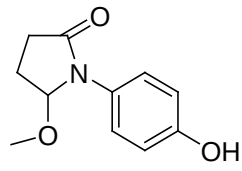


(**CP5**) 9Z, 12Z; R = H
(**344**) 9Z, 12Z; R = CH_2CH (OH) CH_2OH
(**345**) 9Z, 12Z; R = Glc

Figure 2.3, continued



(**346**) R = H
(**347**) R = Glc



(**348**)

Table 2.3: Name of compounds isolated from *Chlorophyllum molybdites*

No.	Compound name	Source	Country	Ref.
325	(22*E*,24*R*)-3*α*-ureido-ergosta-4,6,8(14),22-tetraene	Fruit body	Japan	(Yoshikawa et al., 2001)
326	(22*E*,24*R*)-5*α*,8*α*-epidioxyergosta-6,22-diene-3*β*-ol-3-*O*-*β*-$_D$-glucopyranoside	Fruit body	Japan	(Yoshikawa et al., 2001)
327	(22*E*, 24*R*)-5*α*,8*α*-epidioxyergosta-6,9,22-triene-3*β*-ol	Fruit body	Japan United States	(Yoshikawa et al., 2001) (Su et al., 2013)
328	(22*E*,24*R*)-5*α*,8*α*-epidioxyergosta-6,9,22-triene-3*β*-ol-3-*O*-*β*-$_D$-glucopyranoside	Fruit body	United States	(Su et al., 2013)
329	(22*E*, 24*R*)-ergosta-8(14),22-diene-3β,7α-diol	Fruit body	Japan	(Yoshikawa et al., 2001)
330	(22*E*,24*R*)-5*α*, 6*α*-epoxyergosta-8(14),22-diene-3*β*,7*α*-diol	Fruit body Mycelium	Japan China	(Yoshikawa et al., 2001) (Su et al., 2013)
331	(22*E*,24*R*)- ergosta-7,22-diene-3*β*,5*α*,6*β*-triol	Fruit body	Japan United States	(Yoshikawa et al., 2001) (Su et al., 2013)
332	(22*E*,24*R*)-5*α*,8*α*-epidioxyergosta-6,22-triene-3*β*-ol-3-*O*-*β*-$_D$-glucopyranoside	Fruit body	Japan	(Yoshikawa et al., 2001)
333	(22*E*,24*R*)-ergosta-5,7,22-triene-3*β*-ol 3-*O*-*β*-$_D$-glucopyranoside	Fruit body	Japan	(Yoshikawa et al., 2001)
334	(9*Z*,12*Z*)-1-(9,12-octadecadienoate)-*β*-$_D$-glucopyranose	Fruit body	United States	(Su et al., 2013)
335	(*S*)-glycoxyuracil	Fruit body	United States	(Su et al., 2013)
336	Uracil	Fruit body	United States	(Su et al., 2013)
337	Thymine	Fruit body	United States	(Su et al., 2013)

Table 2.3, continued

No.	Compound name	Source	Country	Ref.
338	Nicotinamide	Fruit body	United States	(Su et al., 2013)
339	Ergosterol	Fruit body	United States	(Su et al., 2013)
340	Ergosterol-3-*O*-*β*-$_{D}$-glucopyranoside	Fruit body	United States	(Su et al., 2013)
341	Oleic acid	Fruit body	United States	(Su et al., 2013)
342	Palmityl-1-*O*-*β*-$_{D}$-glucopyranoside	Fruit body	United States	(Su et al., 2013)
CP5	Linoleic acid	Fruit body	United States	(Su et al., 2013)
344	1-linoleylglycerol	Fruit body	United States	(Su et al., 2013)
345	(22*E*,24*R*)- ergosta-7,22-diene-3*β*-ol	Mycelium	China	(Gong et al., 2010)
346	Palmitoleic acid	Fruit body	United States	(Su et al., 2013)
347	Palmitic acid	Fruit body	United States	(Su et al., 2013)
348	Lepiotin B	Fruit body	Japan	(Ohta et al., 1998)

CHAPTER 3: METHODOLOGY

3.1 Source and authentication

3.1.1 *Crotalaria pallida*

The whole plants of *Crotalaria pallida* were collected from Cameron Highland, Perak, Malaysia on 2012. The plant was deposited in the Herbarium of University of Malaya with a voucher specimen number KLU 47957. This plant species has been authenticated by the botanist of University of Malaya, Dr Sugumaran. The whole plant of *C. pallida* was leave air-dried to remove the moisture content, and prior to extraction.

Figure 3.1: The whole plant of *C. pallida*

3.1.2 *Morinda citrifolia*

The roots (with root barks) of *Morinda citrifolia* were collected from Kuala Lipis, Pahang, Malaysia on June 2013. A voucher specimen is deposited at the Herbarium of Chemistry Department, University of Malaya. The roots were cut into smaller pieces, air-dried to remove the moisture content, and finally subjected to extraction.

Figure 3.2: The roots of *M. citrifolia*

3.1.3 *Chlorophyllum molybdites*

The fruit bodies of *Chlorophyllum molybdites* were collected in University of Malaya, Kuala Lumpur on January 2013. A voucher specimen is deposited at the Herbarium of Chemistry Department, University of Malaya. The mushroom was cleaned in the laboratory, leave air-dried to remove the moisture content, and prior to extraction.

Figure 3.3: The fruit bodies of *C. molybdites*

3.2 General

NMR spectral data were obtained using 600 MHz Bruker AVANCE III (Bruker, Fallanden, Switzerland) NMR spectrometers with chemical shifts (δ) expressed in ppm and TMS as an internal standard in $CDCl_3$ or CD_3OD. The coupling constants (*J*) are reported in Hz. The HRESIMS data were obtained from the Agilent 6530 Q-TOF (Agilent Technologies, Santa Clara, CA, USA) mass-spectrometer equipped with the Agilent 1200 series Rapid Resolution LC system. The ESI-MS data were obtained from the Agilent 6490 Triple Quad (Agilent Technologies, Santa Clara, CA, USA) mass-spectrometer equipped with Agilent 1290 Infinity u-HPLC system. The UV measurement was carried out using the Agilent Cary 60 UV Vis spectrophotometer (Agilent Technologies, Santa Clara, CA, USA). The IR measurement was carried out on the Perkin-Elmer RX1 FT-IR (Perkin Elmer, Waltham, MA, USA) spectrophotometer using NaCl cell.

3.3 Plant Extraction

3.3.1 *Crotalaria pallida*

1.8 kg whole plant of dried *C. pallida* were grounded and extracted with 95% ethanol to give 195 g of crude ethanolic extract. The ethanolic extract was further partitioned into n-hexane, chloroform and ethanol extract by sequential solvent-solvent extraction respectively, with each solvent extraction repeating for three times. 23 g of n-hexane, 50 g of chloroform and 118 g of ethanol crude were obtained from the evaporation of solvent using rotary-evaporator. Preliminary TLC screening indicated that the most promising extract is the n-hexane extract, and the chloroform and ethanol extracts do not

have as many spots as the n-hexane extract. The n-hexane crude extracts were later subjected to various chromatographic methods to isolate pure compounds.

3.3.2 *Morinda citrifolia*

0.85 kg of the dry *M. citrifolia* roots were extracted with chloroform and denatured ethanol consecutively, and each solvent extraction was repeated three times. 8.6 g of chloroform crude extract and 15.4 g of ethanol crude extract was yielded from evaporation of solvent using rotary-evaporator. Preliminary TLC screening indicated that the most promising extract is the chloroform extract and the ethanol extracts do not have as many spots as the chloroform extract. The chloroform crude extract was later subjected to various chromatographic methods for isolation of pure compounds.

3.3.3 *Chlorophyllum molybdites*

2.2 kg of the dry fruit bodies of *C. molybdites* were crushed and extracted with hexane, ethyl acetate and denatured ethanol consecutively, with each solvent extraction repeating for three times. The extracts were concentrated to dryness under reduced pressure which gives 1.1 g of hexane, 16.2 g of ethyl acetate and 67.9 g of ethanol crude extract consecutively. Preliminary TLC screening indicated that the most promising extract is the ethyl acetate extract and hexane and ethanol extracts do not have as many spots as the ethyl acetate extract. The ethyl acetate crude extract was later subjected to various chromatographic methods to isolate pure compounds.

3.4 Chromatographic methods

3.4.1 Thin Layer Chromatography (TLC)

TLC was extensively used in the isolation process of pure compounds. TLC were performed on pre-coated silica gel plates (Kieselgel 60 F24, Merck, Darmstadt, Germany), and spotted using a fine glass capillary tube, followed by development in a solvent saturated TLC tank with various solvents. The developed TLC plate was then viewed under short wave and/or long wave UV light, and stained with iodine and anisaldehyde staining reagents.

3.4.2 Column Chromatography (CC)

CC was carried out using silica gel 60 (0.063-0.200 and 0.040-0.063 mm, Merck, Darmstadt, Germany). The column was packed by preparing silica gel slurry in desired eluting solvent and then settling the gel into the column. The solvent systems used were hexane, ethyl acetate, acetone, chloroform and diethyl ether, in different mixing compositions and gradients. TLC was used to aid in monitoring the fractions.

CC was also carried out using Sephadex LH20 (silica gel 60, 0.040-0.063 mm, Merck, Darmstadt, Germany). The column was packed by firstly preparing Sephadex LH20 slurry in desired eluting solvent before settling the gel into the column. The solvent system used is methanol and water, in different mixing compositions and gradients. This material is designed to be used for organic solvents and water mixtures. TLC was used to aid in monitoring the fractions.

3.4.3 Centrifugal Thin Layer Chromatography (CTLC)

CTLC was carried out by using the Kieselgel 60 with gypsum silica gel (Merck, Darmstadt, Germany) prepared on a round glass plate of 24 cm in diameter. The silica gel slurry was prepared by using about 30 g of silica gel dissolved in 90 mL of distilled water (to prepare for 1 cm thickness on the plate). The glass plate was taped on the edge by using cellophane tape before pouring the silica gel slurry evenly on the glass plate. The slurry was air-dried before removing the cellophane tape and the plate was subsequently baked in an oven at 80 °C for 2 hours to remove any water remained. Then, the plate was allowed to cool at room temperature for 6 hours before scrapping the plate 5 mm from the edge and 30 mm from the centre. Chromatography was carried out by first wetting the spinning plate mounted on the machine with eluting solvent, and then the sample was loaded on the center to form a thin band before eluting with the desired solvent system. TLC was used to aid in monitoring the fractions obtained.

3.4.4 Preparative Thin Layer Chromatography (PTLC)

Prep TLC is a useful technique for the purification of the small quantities of sample because it allows rapid separation of a number of components in a reaction mixture. It was carried out using the TLC silica gel 60 F_{254} (Merck, Darmstadt, Germany). The TLC plate were gently marked roughly 1.5 cm from one side of the plate. This is the "origin" line. Using a fine glass capillary tube, a thin line of sample was deposited across the pencil line. After obtained the prep TLC chamber, pour in the eluent, approximately about 150 mL. Then, the plate was placed in and the top sealed with lid. A typical run takes about 1 hour to 2 hours. After that, the plate was removed and visualized under UV. The bands that appear were marked with pencil, cut into pieces by using a scissor and put it in a small

bottom flask, then soaked in a mixture of methanol, chloroform, and acetone. The sample then was concentrated to dryness by using the rotary evaporator or speed evaporator. To separate the sample with the silica gel, the sample was soaked with the solvent that the sample can dissolved in (e.g. chloroform and acetone). The supernatant was taken out and concentrated to dryness, and then it was subjected to ^{1}H NMR experiment.

3.4.5 High-Performance Liquid Chromatography (HPLC)

HPLC was carried out through an Agilent ZORBAX Eclipse XDB-C18 (9.4 x 250 mm; 5 micron) column, on Waters 600E series HPLC equipped with Waters UV detector. Reverse Phase HPLC (RP-HPLC) was carried out by using a general gradient solvent system of 95% water: 5% acetonitrile to 5% water: 95% acetonitrile. The solvents used were HPLC grade.

3.5 Staining reagents for TLC

3.5.1 Iodine staining reagent

A 100 mL wide mouth chamber (with cap) was assembled with a piece of filter paper and a few iodine crystals were added to saturate the chamber with iodine vapor. TLC plate was then placed in the chamber and incubated for a few minutes to allow reaction between the iodine vapor and the compounds on the TLC plate. When the entire TLC plate turned brownish, the TLC was removed to identify the dark brown spots on the brownish TLC plate. The spots were marked with a pencil. This reagent is normally used to detect unsaturated compounds.

3.5.2 Anisaldehyde staining reagent

A 100 mL anisaldehyde staining reagent was prepared by mixing 1 mL of anisaldehyde, 100 mL of denatured ethanol, and 2 mL of 98% sulphuric acid together. The staining was carried out by flooding the TLC plate with the stain solution and immediately heated using dryer until the TLC plate turned pink or the maximal visualization of the reacted compounds. The colour changes to violet, blue, red, grey or green according to functional groups namely lichen constituents, phenols, terpenes, sugars and steroids.

3.6 Isolation of compounds

3.6.1 Isolation of compounds from the hexane extract of *Crotalaria pallida*

The hexane extract that obtained from the whole plant of *C. pallida* (23 g) was subjected to extensive chromatographic separation as summarized in the flow diagram shown in Figure 3.4 to yield eight compounds.

3.6.2 Isolation of compounds from the chloroform extract of *Morinda citrifolia*

The chloroform extract that obtained from the roots of *M. citrifolia* (2.3 g) was subjected to extensive chromatographic separation as summarized in the flow diagram shown in Figure 3.5 to yield six compounds.

3.6.3 Isolation of compounds from the ethyl acetate extract of *Chlorophyllum molybdites*

The ethyl acetate extract that obtained from the fruit bodies of *C. molybdites* (16.2 g) was subjected to extensive chromatographic separation as summarized in the flow diagram shown in Figure 3.6 to yield four compounds.

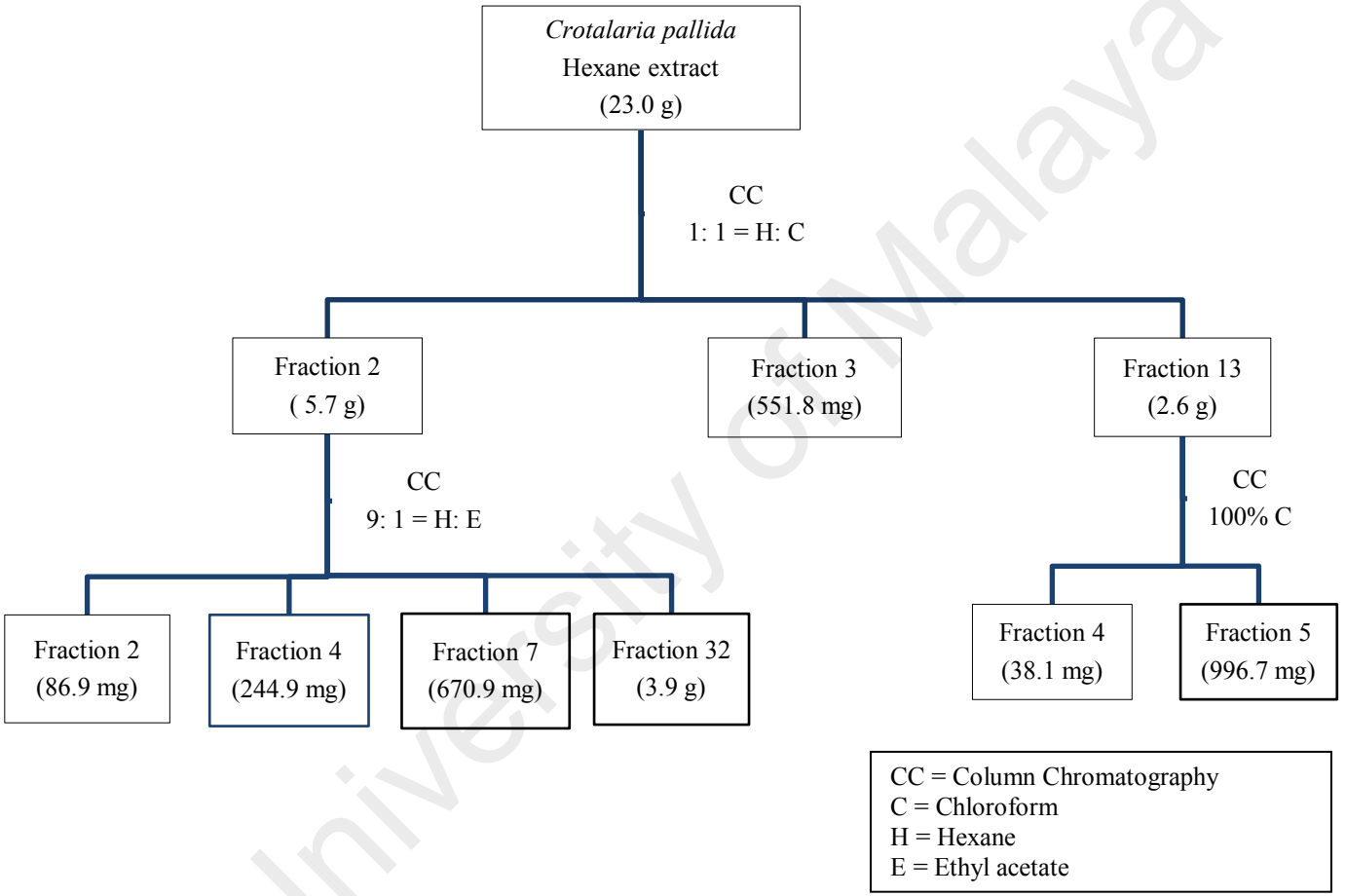


Figure 3.4: Isolation of compounds from the hexane extract of *Crotalaria pallida*

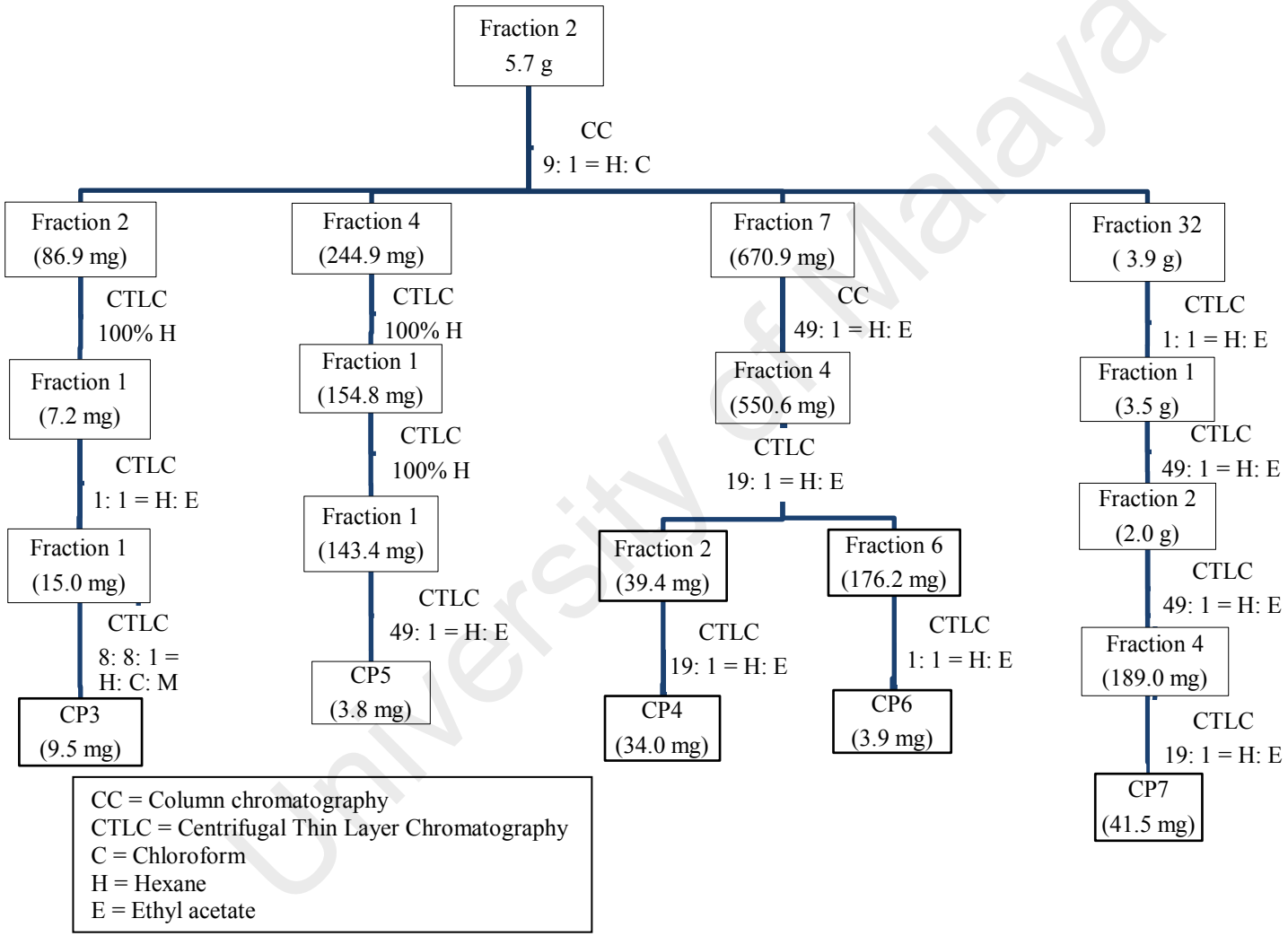


Figure 3.4, continued

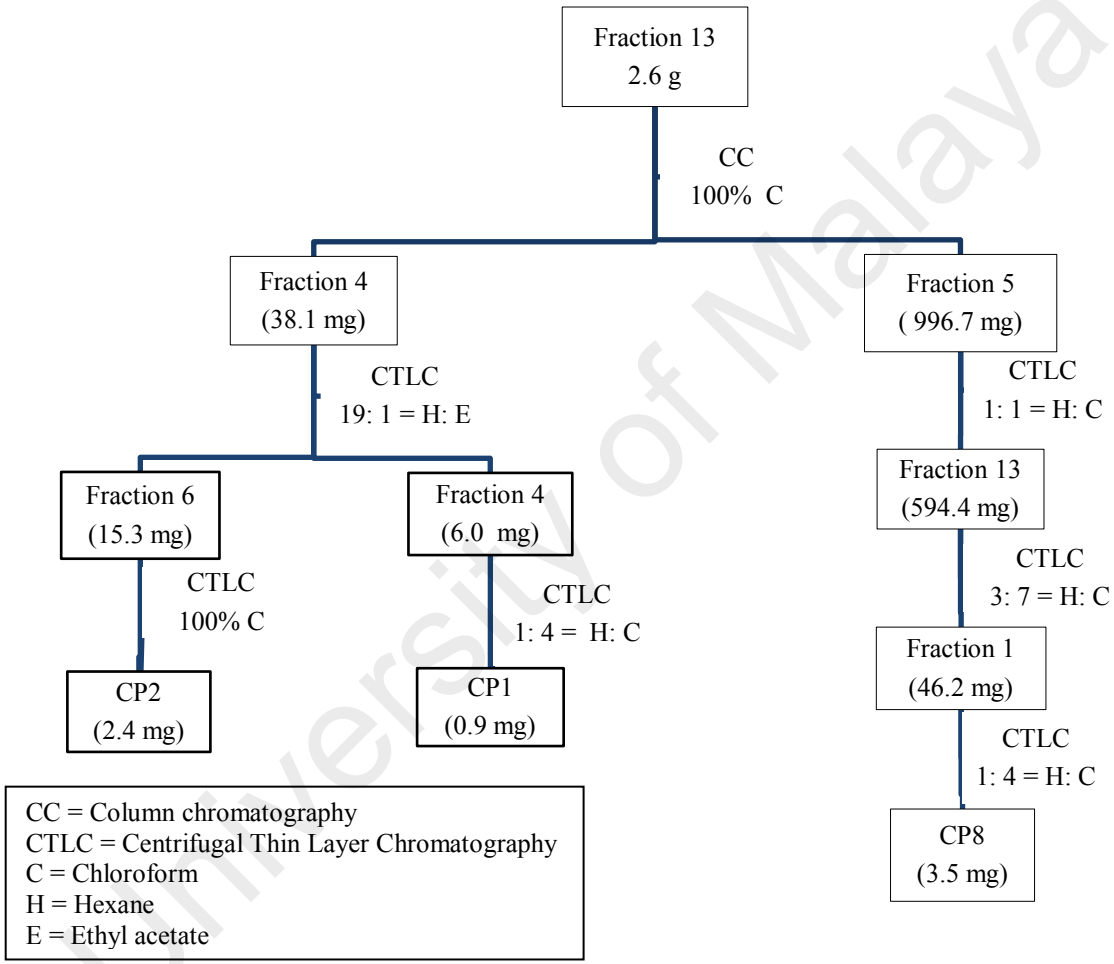


Figure 3.4, continued

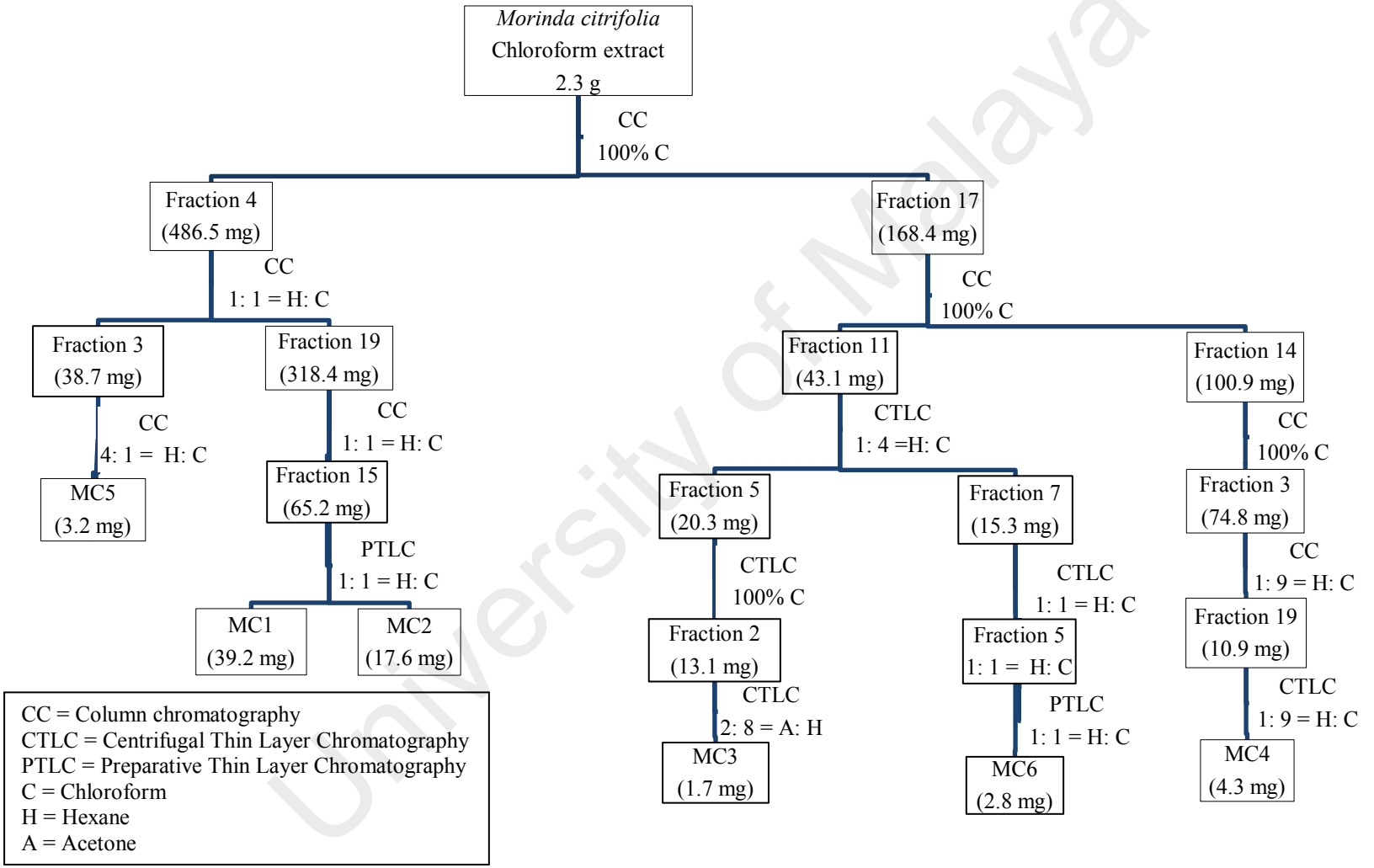


Figure 3.5: Isolation of compounds from the chloroform extract of *Morinda citrifolia*

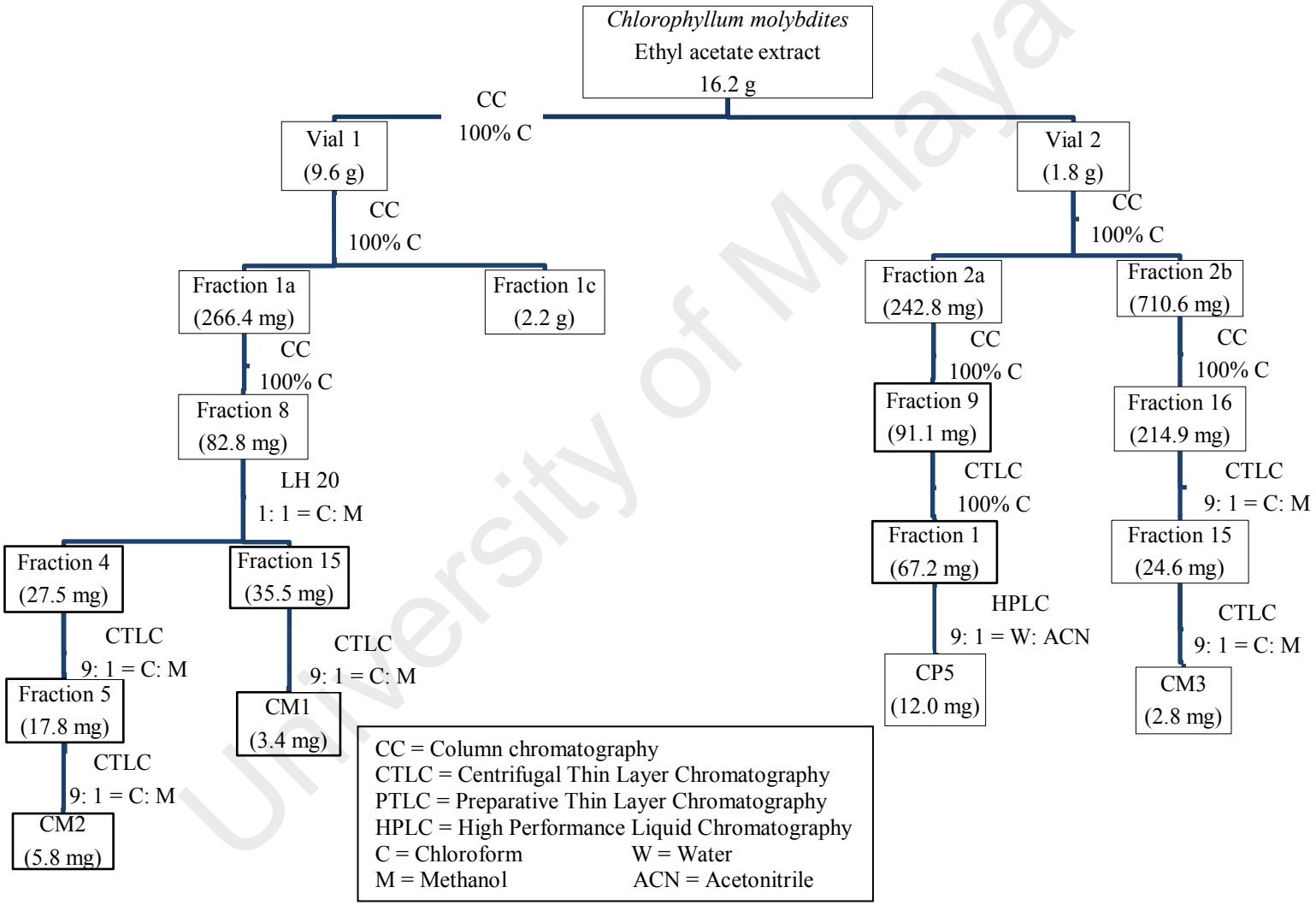


Figure 3.6: Isolation of compounds from the ethyl acetate extract of *Chlorophyllum molybdites*

3.7 Compound data

3.7.1 Compounds isolated from *Crotalaria pallida*

Crotolidene (CP1): Colourless oil; molecular formula $C_{14}H_{22}O_2$; $[\alpha]_D$ -66.7 (*c* 0.237, $CHCl_3$); UV (EtOH) λ_{max} (log ε) 205 (1.70), 276 (0.56) nm; IR (NaCl) ν_{max} 3250, 3010, 2959, 2937, 2870, 1674, 1653, 1608, 1457, 1363, 1259, 1175, 1049, 982, 803 and 771 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.19 (1H, d, *J* = 16 Hz, H-3), 6.09 (1H, d, *J* = 16 Hz, H-4), 3.99 (1H, m, H-8), 2.41 (1H, dd, *J* = 17 and 6 Hz, H-7a), 2.27 (3H, s, Me-1), 2.06 (1H, dd, *J* = 17 and 11 Hz, H-7b), 1.78 (1H, m, H-9a), 1.75 (3H, s, Me-11), 1.47 (1H, t, *J* = 12 Hz, H-9b), 1.10 (3H, s, Me-13), 1.09 (3H, s, Me-12). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 198.7 (C, C-2), 142.4 (CH, C-3), 135.9 (C, C-6), 132.6 (CH, C-4), 132.4 (C, C-5), 64.8 (CH, C-8), 48.6 (CH_2, C-9), 43.0 (CH_2, C-7), 37.1 (C, C-10), 30.3 (CH_3, C-12), 28.8 (CH_3, C-13), 27.5 (CH_3, C-1), 21.8 (CH_3, C-11). HMBC: ^2J C-2 to Me-1 and H-3; C-4 to H-3; C-5 to Me-11; C-8 to H-7b and H-9b; C-10 to H-9a and H-9b; C-12 to Me-13; C-13 to Me-12; ^3J C-3 to Me-1; C-4 to Me-11; C-5 to H-7a and H-7b; C-6 to H-4, Me-11, Me-12 and Me-13; C-7 to H-9a and H-9b; C-9 to Me-12 and Me-13; C-13 to H-9a and H-9b. HRESIMS *m/z* 223.1497 $[M+H]^+$ (calcd for $C_{14}H_{22}O_2$+H, 223.1698) and *m/z* 205.1316 $[M\text{-}OH]^-$ (calcd for $C_{14}H_{22}O_2$-OH, 205.1592).

Hydroxydihydrobovolide (CP2): Colorless oil; molecular formula $C_{11}H_{18}O_3$; $[\alpha]_D$ -13.3 (*c* 0.015, $CHCl_3$); UV (EtOH) λ_{max} (log ε) 220 (3.49), 291 (0.23) nm; IR (NaCl) ν_{max} 3369, 2956, 2926, 2859, 1741, 1694, 1458, 1438, 1381, 1287, 1260, 1133, 1101, 1056, 974, 956, 903, 767 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.96 (1H, m, H-6a), 1.92 (3H, s, 4-Me), 1.80 (3H, s, 3-Me), 1.74 (1H, m, H-6b), 1.29 (2H, m, CH_2-9), 1.27 (2H, m, CH_2-8), 1.15 (2H, m, CH_2-7), 0.86 (3H, t, *J* = 7 Hz, CH_3-10). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.2 (C, C-2), 157.8 (C, C-3), 125.6 (C, C-4), 107.0 (C, C-5), 36.2 (CH_2, C-6), 31.7 (CH_2, C-8), 22.8 (CH_2, C-9), 22.6 (CH_2, C-7), 14.1 (CH_3, C-10), 10.9 (CH_3, 4-Me),

8.7 (CH_3, 3-Me); HRESIMS *m/z* 199.1335 $[M+H]^+$ (calcd for $C_{11}H_{18}O_3$+H, 199.1329) and *m/z* 181.1233 $[M+H - H_2O]^+$ (calcd for $C_{11}H_{18}O_3$-OH, 181.1223).

Octacosane (CP3): White amorphous solid; molecular formula $C_{28}H_{58}$; UV (Hex) λ_{max} (log ε) 207 (3.11) nm; IR (NaCl) ν_{max} 2926, 2854, 1459, 908, 734 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.26-1.24 (48H, m, CH_2-3 to CH_2-26), 1.11 (4H, m, CH_2-2 and CH_2-27), 0.88 (6H, t, J = 7 Hz, CH_3-1 and CH_3-28).^{13}C NMR ($CDCl_3$, 150 MHz) δ 32.3 (CH_2, C-3 and C-26), 30.0 (CH_2, C-5 to C-24), 29.6 (CH_2, C-4 and C-25), 23.0 (CH_2, C-2 and C-27), 14.4 (CH_3, C-1 and C-28).

***Trans*-phytyl palmitate (CP4):** White amorphous solid; molecular formula $C_{36}H_{70}O_2$; $[\alpha]_D$ -1.4 (*c* 0.237, $CHCl_3$); UV (Hex) λ_{max} (log ε) 210 (3.33) nm; IR (NaCl) ν_{max} 2916, 2849, 1738, 1732, 1641, 1462, 1456, 1372, 1236, 1165, 1114, 1046, 958, 756, 729, and 719 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 5.30 (1H, t, J = 7 Hz, H2'), 4.56 (2H, d, J = 7 Hz, CH_2-1'), 2.28 (2H, t, J = 8 Hz, CH_2-2), 1.97 (2H, t, J = 7 Hz, CH_2-4'), 1.68 (3H, s, 3'-Me), 1.58 (2H, m, CH_2-3), 1.50 (1H, m, H-15'), 1.38-1.25 (36H, m, CH_2-4 to CH_2-15, CH_2-5', CH_2-7', CH_2-9' and CH_2-11' to CH_2-13'), 1.13 (2H, m, CH_2-14'), 1.05 (6H, m, CH_2-6', CH_2-8' and CH_2-10'), 0.88 (3H, m, CH_3-16), 0.86 (6H, m, 15'-CH_3 and CH_3-16'), 0.84 (6H, m, 7'-CH_3 and 11'-CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 174.1 (C, C-1), 142.7 (C, C-3'), 118.5 (CH, C-2'), 61.4 (CH_2, C-1'), 40.1 (CH_2, C-4'), 39.6 (CH_2, C-14'), 37.5-37.3 (CH_2, C-6', C-8' and C-10'), 36.8 (CH_2, C-12'), 34.6 (CH_2, C-2), 33.0 (CH, C7' and C-11'), 32.2 (CH_2, C-14), 29.9-29.4 (CH_2, C-4 to C-13), 28.2 (CH, C-15'), 25.2-24.7 (CH_2, C-3, C-5', C-9' and C-13'), 22.9 (CH_2, C-15), 22.8 (CH_3, 15'-CH_3 and C-16'), 19.9 (CH_3, 7'-CH_3 and 9'-CH_3), 16.6 (CH_3, 3'-CH_3), 14.3 (CH_3, C-16); GCMS *m/z* 57 (79), 68 (100) $[C_5H_8]^+$, 71 (43), 82 (74), 95 (83), 123 (36), 137 (4).

Linoleic acid (CP5): Light yellowish amorphous solid; molecular formula $C_{18}H_{32}O_2$; UV (EtOH) λ_{max} (log ε) 224 (1.28), 272 (0.36) nm; IR (NaCl) ν_{max} 3436, 3024, 2984, 2918, 2850, 1741, 1710, 1648, 1465, 1374, 1243, 1047 and 758 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 5.32-5.36 (4H, m, H-9, H-10, H-12, and H-13), 2.79 (1H, t, J = 7, H-11a), 2.75 (1H, t, J = 7, H-11b), 2.32 (2H, t, J = 8 Hz, CH_2-2), 2.03 (4H, m, CH_2-8 and CH_2-14), 1.61 (2H, m, CH_2-3), 1.26 (14H, m, CH_2-4 to CH_2-7 and CH_2-15 to CH_2-17), 0.87 (3H, t, J = 7 Hz, CH_3-18). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 179.8 (C, C-1), 130.5 (CH, C-13), 130.3 (CH, C-9), 128.3 (CH, C-12), 128.1 (CH, C-10), 34.2 (CH_2, C-2), 31.8 (CH_2, C-16), 29.9-29.3 (CH_2, C-4 to C-7 and C-15), 27.4 (CH_2, C-8 and C-14), 25.9 (CH_2, C-11), 24.9 (CH_2, C-3), 22.8 (CH_2, C-17), 14.3 (CH_3, C-18); HRESIMS with *m/z* 279.2371 $[M-H]^-$ (calcd for $C_{18}H_{32}O_2$-H, *m/z* 279.2330).

Methyl oleate (CP6): Yellowish oil; molecular formula $C_{19}H_{36}O_2$; UV (Hex) λ_{max} (log ε) 202 (2.80), 222 (0.68), 277 (0.11) nm; IR (NaCl) ν_{max} 2926, 2855, 1744, 1458, 1437, 1376, 1364, 1245, 1196, 1171, 1018, 882 and 722 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 5.32 (2H, m, H-9 and H-10), 3.64 (3H, s, 1-OCH_3), 2.28 (2H, t, J = 8 Hz, CH_2-2), 1.98 (4H, m, CH_2-8 and CH_2-11), 1.59 (2H, m, CH_2-3), 1.28 (20H, m, CH_2-4 to CH_2-7 and CH_2-12 to CH_2-17), 0.86 (3H, t, J = 7 Hz, CH_3-18). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 174.6 (C, C-1), 130.2 (CH, C-10), 130.0 (CH, C-9), 52.7 (CH_3, 1-OCH_3), 34.3 (CH_2, C-2), 32.1 (CH_2, C-16), 30.0-29.3 (CH_2, C-4 to C-7 and C-12 to C-15), 27.4 (CH_2, C-8 and C-11), 25.2 (CH_2, C-3), 22.9 (CH_2, C-17), 14.3 (CH_3, C-18); GCMS 296 (3) $[M]^+$, 264 (14), 222 (10), 180 (8), 137 (9), 123 (17), 110 (27), 97 (52), 83 (61), 73 (60), 69 (74), 55 (100).

Ethyl palmitate (CP7): Yellowish oil; molecular formula $C_{18}H_{36}O_2$; UV (Hex) λ_{max} (log ε) 206 (3.10), 274 (0.11) nm; IR (NaCl) ν_{max} 2924, 2853, 1740, 1465, 1420, 1373,

1349, 1302, 1244, 1177, 1116, 1098, 1036, 859, 804, 721 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 4.08 (2H, q, J = 7 Hz, 1-O$\underline{CH_2}CH_3$), 2.38 (2H, t, J = 8 Hz, CH_2-2), 1.57 (2H, m, CH_2-3), 1.24 (24H, m, CH_2-4 to CH_2-15), 1.21 (3H, t, J = 7, 1-O$CH_2\underline{CH_3}$), 0.84 (3H, t, J = 7 Hz, CH_3-16). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.8 (C, C-1), 60.4 (CH_2, 1-O$\underline{CH_2}CH_3$), 34.6 (CH_2, C-2), 32.2 (CH_2, C-14), 30.0-29.4 (CH_2, C-4 to C-13), 25.3 (CH_2, C-3), 23.0 (CH_2, C-15), 14.5 (CH_3, 1-O$CH_2\underline{CH_3}$), 14.4 (CH_3, C-16); GCMS *m/z* 284 (4) $[M]^+$, 255 (2), 241 (6), 157 (11), 101 (53), 88 (100), 70 (26), 55 (27).

Palmitic acid (CP8): White amorphous solid; molecular formula $C_{16}H_{32}O_2$; UV (EtOH) λ_{max} (log ε) 208 (0.73), 268 (0.18) nm; IR (NaCl) ν_{max} 3409, 2917, 2850, 1707, 1464, 1411, 1297, 908, 735 and 650 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.33 (2H, t, J = 8 Hz, CH_2-2), 1.61 (2H, m, CH_2-3), 1.28 (24H, m, CH_2-4 to CH_2-15), 0.86 (3H, t, J = 7 Hz, CH_3-16). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 178.7 (C, C-1), 34.0 (CH_2, C-2), 32.1 (CH_2, C-14), 29.9-29.3 (CH_2, C-4 to C-13), 24.9 (CH_2, C-3), 22.9 (CH_2, C-15), 14.2 (CH_3, C-16); HRESIMS with *m/z* 255.2369 $[M-H]^-$ (calcd for $C_{16}H_{32}O_2$-H, *m/z* 255.2330).

3.7.2 Compounds isolated from *Morinda citrifolia*

Damnachantal (MC1): Yellow amorphous powder; molecular formula $C_{16}H_{10}O_5$; UV (EtOH) λ_{max} (log ε) 210 (2.58), 255 (3.60), 285 (4.21), 400 (0.33) nm; IR (NaCl) ν_{max} 3462, 2922, 1678, 1646, 1575, 1457, 1388, 1345, 1261, and 715 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 12.27 (1H, s, 3-OH), 10.46 (1H, s, 2-CHO), 8.29 (1H, dd, J = 8 and 1 Hz, H-8), 8.24 (1H, dd, J = 8 and 1 Hz, H-5), 7.82 (1H, td, J = 8 and 1 Hz, H-7), 7.77 (1H, td, J = 8 and 1 Hz, H-6), 7.67 (1H, s, H-4), 4.13 (1H, s, 1-OMe). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 195.5 (C, 2-CHO), 181.9 (C, C-10), 180.2 (C, C-9), 166.9 (C, C-1), 166.7 (C, C-3), 141.6 (C, C-4a), 134.9 (C, C-8a), 134.9 (CH, C-7), 133.7 (CH, C-6), 132.5 (C, C-10a), 127.4 (CH, C-5), 127.2 (CH, C-8), 118.1 (C, C-2), 117.7 (C, C-9a),

113.1 (CH, C-4), 64.8 (C, 1-OMe) ; HRESIMS with *m/z* 281.0 $[M-H]^-$ (calcd for $C_{16}H_{10}O_5$-H, 281.0).

Nordamnachantal (MC2): Yellow-orange needles; molecular formula $C_{15}H_8O_5$; UV (EtOH) λ_{max} (log ε) 210 (2.08), 265 (4.26), 290 (3.26), 430 (0.89) nm; IR (NaCl) ν_{max} 3075, 1674, 1593, 1574, 1269, 1191, and 714 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 14.05 (1H, s, 1-OH), 12.67 (1H, s, 3-OH), 10.50 (1H, s, 2-CHO), 8.31 (1H, dd, *J* = 8 and 1 Hz, H-8), 8.28 (1H, dd, *J* = 8 and 1 Hz, H-5), 7.83 (1H, m, H-7), 7.83 (1H, m, H-6), 7.33 (1H, s, H-4). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 194.1 (C, 2-CHO), 186.9 (C, C-9), 181.5 (C, C-10), 169.2 (C, C-1), 168.3 (C, C-3), 139.5 (C, C-4a), 134.8 (CH, C-7), 134.7 (CH, C-6), 133.3 (C, C-10a), 133.2 (C, C-8a), 127.8 (CH, C-5), 127.0 (CH, C-8), 112.2 (C, C-2), 109.4 (CH, C-4), 109.1 (C, C-9a) ; HRESIMS with *m/z* 267.0 $[M-H]^-$ (calcd for $C_{15}H_8O_5$-H, 267.0).

Rubiadin (MC3): Yellow amorphous powder; molecular formula $C_{15}H_{10}O_4$; UV (EtOH) λ_{max} (log ε) 210 (2.87), 245 (2.77), 280 (3.33), 425 (0.69) nm; IR (NaCl) ν_{max} 3391, 2923, 1629, 1593, 1336, 1121, and 710 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 13.07 (1H, s, 1-OH), 8.18 (1H, dd, *J* = 8 Hz, H-8), 8.11 (1H, dd, *J* = 5 Hz, H-5), 7.68 (1H, td, *J* = 8 Hz, H-7), 7.64 (1H, td, *J* = 8 Hz, H-6), 7.13 (1H, s, H-4), 2.11 (1H, s, 2-Me). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 186.8 (C, C-9), 183.7 (C, C-10), 163.3 (C, C-1), 162.7 (C, C-3), 134.4 (C, C-8a), 134.4 (CH, C-7), 134.0 (CH, C-6), 133.5 (C, C-10a), 132.1 (C, C-4a), 127.2 (CH, C-5), 126.9 (CH, C-8), 119.2 (C, C-9a), 109.9 (C, C-2), 107.8 (CH, C-4), 8.3 (C, 2-Me) ; ESI-MS *m/z* 253.0 $[M-H]^-$ (calcd for $C_{15}H_{10}O_4$-H, 253.1).

1,6-Dihydroxy-2-methylanthraquinone (MC4): Yellow-orange amorphous powder; molecular formula $C_{15}H_{10}O_4$; UV (EtOH) λ_{max} (log ε) 220 (4.51), 270 (5.50), 420 (1.30)

nm; IR (NaCl) ν_{max} 3419, 1641, 1596, 1451, 1361, 1282, 1259, and 1033 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 13.11 (1H, s, 1-OH), 8.13 (1H, d, J = 8, H-8), 7.63 (1H, d, J = 8, H-4), 7.49 (1H, s, H-5), 7.41 (1H, d, J = 8, H-8), 7.11 (1H, d, J = 8, H-7), 2.31 (1H, s, 2-Me). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 187.5 (C, C-9), 170.8 (C, C-6), 169.1 (C, C-1), 136.7 (C, C-10a), 136.6 (CH, C-3), 136.6 (C, C-2), 131.3 (C, C-4a), 130.0 (CH, C-8), 121.7 (C, C-7), 119.3 (CH, C-4), 118.5 (CH, C-9a), 113.2 (CH, C-5), 16.4 (C, 2-Me); HRESIMS *m/z* 253.0 $[M-H]^-$ (calcd for $C_{15}H_{10}O_4$-H, 253.1).

1-Hydroxy-3-methoxyanthraquinone (MC5): Yellow amorphous powder; molecular formula $C_{15}H_{10}O_4$; UV (EtOH) λ_{max} (log ε) 205 (2.37), 255 (2.43), 340 (0.21), 420 (0.45) nm; IR (NaCl) ν_{max} 3400, 2926, 2855, 1730, 1674, 1593, 1455, and 709 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 13.33 (1H, s, 1-OH), 8.33 (1H, m, H-5), 8.33 (1H, m, H-8), 7.85 (1H, m, H-6), 7.85 (1H, m, H-7), 7.53 (1H, s, H-4), 6.26 (1H, s, H-2), 3.42 (1H, s, 3-OMe). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 134.9 (CH, C-7), 134.9 (CH, C-6), 127.5 (CH, C-5), 127.5 (CH, C-8), 108.5 (CH, C-4); HRESIMS with *m/z* 253.0 $[M-H]^-$ (calcd for $C_{15}H_{10}O_4$-H, 253.1).

1-Methoxy-2-hydroxyanthraquinone (MC6): Yellow amorphous powder; molecular formula $C_{15}H_{10}O_4$; UV (EtOH) λ_{max} (log ε) 205 (2.82), 245 (3.67), 275 (3.93), 405 (0.75) nm; IR (NaCl) ν_{max} 3370, 2927, 1573, 1285, and 716 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 13.01 (1H, s, 2-OH), 8.24 (1H, m, H-5), 8.24 (1H, m, H-8), 8.12 (1H, d, J = 9, H-4), 7.75 (1H, m, H-6), 7.75 (1H, m, H-7), 7.34 (1H, d, J = 9, H-3), 4.01 (1H, s, 1-OMe). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 181.7 (C, C-10), 155.3 (C, C-2), 146.6 (C, C-1), 134.2 (CH, C-6), 134.1 (CH, C-7), 134.1 (CH, C-8a), 134.1 (C, C-10a), 127.2 (CH, C-4a), 127.4 (C, C-8), 126.9 (CH, C-5), 125.9 (CH, C-4), 125.9 (C, C-9a), 120.4 (CH, C-3), 62.6 (C, 1-OMe) ; HRESIMS with *m/z* 253.0 $[M-H]^-$ (calcd for $C_{15}H_{10}O_4$-H, 253.1).

3.7.3 Compounds isolated from *Chlorophyllum molybdites*

***α*-D-glucose (CM1):** White powder; molecular formula $C_6H_{12}O_6$; UV (EtOH) λ_{max} (log ε) 220 (2.49), 260 (1.19) nm; IR (NaCl) ν_{max} 3362, 2937, 1661, 1600, 1416, 1149, 1049, 993, 710 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 5.13 (1H, d, J = 4 Hz, H-1), 3.84 (2H, m, H-6b), 3.82 (1H, m, H-5), 3.80 (2H, m, H-6a), 3.70 (1H, dd, J = 11 and 5 Hz, H-3), 3.50 (1H, dd, J = 10 and 4 Hz, H-2), 3.32 (1H, m, H-4).^{13}C NMR ($CDCl_3$, 150 MHz) δ 93.6 (CH, C-1), 73.1 (CH, C-3), 72.3 (CH, C-2), 71.8 (CH, C-5), 70.5 (CH, C-4), 61.2 (CH_2, C-6); HRESIMS with m/z 197.1 [M-OH]+ (calcd for $C_6H_{12}O_6$+OH, 197.0).

Ethyl-*β*-D-glucopyranoside (CM2): White powder; molecular formula $C_8H_{16}O_6$; UV (EtOH) λ_{max} (log ε) 223 (1.26), 256 (0.92) nm; IR (NaCl) ν_{max} 3352, 2979, 2933, 1715, 1695, 1417, 1077, 900, 768 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 4.28 (1H, d, J = 8 Hz, H-1), 3.97 (2H, dd, J = 10 and 2 Hz, H-7a), 3.87 (1H, dd, J = 12 and 3 Hz, H-5a), 3.68 (1H, dd, J = 12 and 6 Hz, H-5b), 3.63 (2H, dd, J = 7 and 3 Hz, H-7b), 3.36 (1H, t, J = 9 Hz, H-3), 3.30 (2H, m, H-6), 3.28 (1H, m, H-4), 3.18 (1H, dd, J = 17 and 1 Hz, H-2), 1.25 (3H, t, J = 7 Hz, CH_3-7); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 102.78 (CH, C-1), 76.78 (CH, C-4), 76.59 (CH, C-3), 73.72 (CH, C-2), 70.27 (CH_2, C-6), 64.82 (CH_2, C-7), 61.38 (CH, C-5), 14.05 (CH_3, 7-Me); HRESIMS with m/z 225.2 [M-OH]+ (calcd for $C_8H_{16}O_6$+OH, 225.2).

2,5-Anhydro-D-hexitol (CM3): White powder; molecular formula $C_{16}H_{12}O_5$; UV (EtOH) λ_{max} (log ε) 220 (3.66), 262 (1.56) nm; IR (NaCl) ν_{max} 3334, 2939, 1602, 1360, 1081, 1042, cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 3.80 (2H, dd, J = 11 and 6 Hz, H-1 and H-6), 3.77 (1H, m, H-2 and H-5), 3.69 (1H, m, H-3 and H-4), 3.64 (2H, dd, J = 11 and 6 Hz, H-1 and H-6) ; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 71.6 (CH, C-2), 71.6 (CH, C-2), 69.9 (CH, C-3), 69.9 (CH, C-4), 63.7 (CH_2, C-1), 63.7 (CH_2, C-6).

3.8 Table of R_f Values

Table 3.1: The R_f values

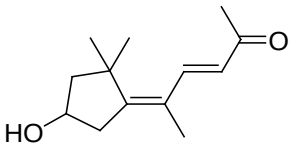
Compound ID	4:1 = H:C	1:1 = H:C	1:4 = H:C	1:9 = H:C	49:1 = H:E	19:1 = H:E	1:1 = H:E	100% C	8:8:1 = H:C:M	2:8 = A:H	9:1 = C:M
CP1	-	-	0.57	-	-	-	-	-	-	-	-
CP2	-	-	-	-	-	-	-	0.51	-	-	-
CP3	-	-	-	-	-	-	-	-	0.74	-	-
CP4	-	-	-	-	-	0.12	-	-	-	-	-
CP5	-	-	-	-	0.33	-	-	-	-	-	-
CP6	-	-	-	-	-	-	0.73	-	-	-	-
CP7	-	-	-	-	-	0.18	-	-	-	-	-
CP8	-	-	0.22	-	-	-	-	-	-	-	-
MC1	-	0.30	-	-	-	-	-	-	-	-	-
MC2	-	0.18	-	-	-	-	-	-	-	-	-
MC3	-	-	-	-	-	-	-	-	-	0.21	-
MC4	-	-	-	0.07	-	-	-	-	-	-	-
MC5	0.15	-	-	-	-	-	-	-	-	-	-
MC6	-	0.07	-	-	-	-	-	-	-	-	-
CM1	-	-	-	-	-	-	-	-	-	-	0.11
CM2	-	-	-	-	-	-	-	-	-	-	0.06
CM3	-	-	-	-	-	-	-	-	-	-	0.05

***** C = Chloroform, H = Hexane, A = Acetone, E = Ethyl acetate, M = Methanol.

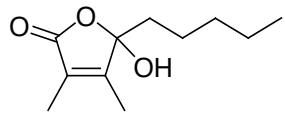
CHAPTER 4: RESULTS AND DISCUSSION

4.1 Compound isolated from *Crotalaria pallida*

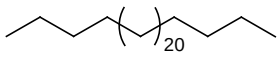
Eight compounds have been isolated from the hexane extract of the *C. pallida*. The isolated compounds are summarized below.



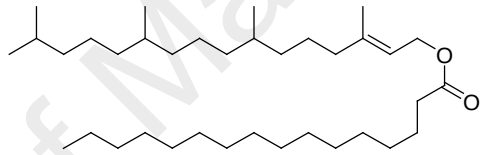
Crotolidene (**CP1**)



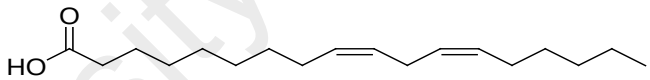
Hydroxydihydrobovolide (**CP2**)



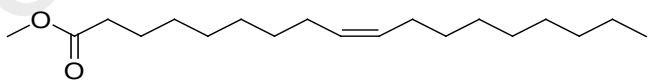
Octacosane (**CP3**)



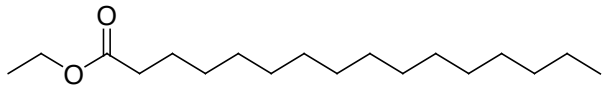
Trans-phytyl palmitate (**CP4**)



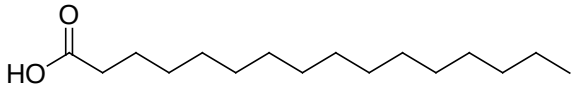
Linoleic acid (**CP5**)



Methyl oleate (**CP6**)

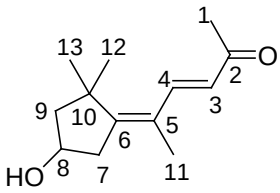


Ethyl palmitate (**CP7**)



Palmitic acid (**CP8**)

4.1.1 CP1: Crotolidene (New)



CP1 was isolated as colourless oil with molecular formula $C_{14}H_{22}O_2$, as determined by HRESIMS with *m/z* 223.1497 $[M+H]^+$ (calculated for $C_{14}H_{22}O_2$+H, 223.1698) and *m/z* 205.1316 $[M-OH]^-$ (calculated for $C_{14}H_{22}O_2$-OH, 205.1592). **CP1** showed an optical activity $[\alpha]_D$ -66.7 (*c* 0.237, $CHCl_3$). The UV spectrum showed absorption maxima at 205 and 276 nm. The IR absorptions indicated the presence of hydroxyl group (3250 cm^{-1}), aliphatic group (2959, 2937 and 2870 cm^{-1}), conjugated ketone (1674 cm^{-1}), and double bond (3010 cm^{-1}).

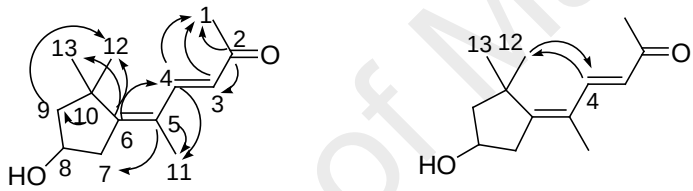
The ^1H NMR spectrum (Figure 4.2, Table 4.1) indicated the presence of four methyl singlets at δ_H 1.09 (Me-12), 1.10 (Me-13), 1.75 (Me-11) and 2.27 (Me-1); one sp^3 oxymethine at δ_H 3.99 (H-8), two sp^2 methines at δ_H 6.09 (H-4) and 7.19 (H-3), and two set of sp^3 methylenes at δ_H 2.41, 2.06 (H-7a and H-7b), and δ_H 1.47, 1.78 (H-9b and H-9a). The methyl signal at δ_H 2.27 (δ_C 27.5) is typical of the methyl ketone functionality.

The ^{13}C NMR spectrum (Figure 4.3, Table 4.1) showed the presence of 13 carbon signals which are attributed to four methyls, two methylenes, three methines and four quaternary carbons. The observations of the methine signal at δ_C 64.8 (δ_H 3.99) suggested an oxymethine functionality consistent with the IR results. The quaternary carbons signal at δ_C 198.7 (C-2) suggested the presence of a carbonyl functionality in agreement with the IR results.

The COSY spectrum gave two partial structures consisted of CH_2-CH(OH)-CH_2 and CH=CH, consistent with the IR, ^{13}C and ^{1}H NMR data as discussed above. The first partial structure CH_2-CH(OH)-CH_2 containing two methylenes and an oxymethine corresponds to C(7)-C(8)-C(9), while the second alkene-methine partial structure CH=CH is assigned to C(3)-C(4). The observed coupling constant of 16 Hz for the sp^2 methines suggested H-3 and H-4 are arranged in *trans*-configuration (3*E*).

The HMBC spectrum (Figure 4.1) showed J^2 correlations from carbonyl C-2 to Me-1, and H-3 and J^3 correlation from C-3 to Me-1 connecting the methyl ketone functionality to the CH=CH (*i.e.* C(3)-C(4)) partial structure providing the Me-CO-CH=CH- fragment. The J^2 HMBC correlations from C-5 to Me-11, and J^3 HMBC correlations from C-4 to Me-11 and C-6 to H-4 and Me-11, extended the conjugation of the fragment to Me-CO-CH=CH-C(Me)=C- (methyl-hexadienone) corresponding to C(1)-C(2)-C(3)-C(4)-C(5)C(11)-C(6)-. Hence, three of the four degrees of unsaturation indicated by the molecular formula of **CP1** can be attributed to the C(2) ketone, and C(3)-C(4) and C(5)-C(6) double bonds. The C-5 of the methyl-hexadienone fragment showed J^3 HMBC correlation to H-7, connecting the Me-CO-CH=CH-C(Me)=C- (methyl-hexadienone) to the CH_2-CH(OH)-CH_2 partial structures together. The *vice versa* J^3 HMBC correlation between Me-12 and Me-13 suggested both the methyls group are connected to the same carbon center (C-10). The observation of J^3 HMBC correlation from C-6 to Me-12 and Me-13 suggested C-6 is α positioned to the C-10 carbon center which is connecting to both Me-12 and Me-13. The final key HMBC J^2 correlation from C-10 to H-9 and J^3 correlations from C-9 to Me-12 and Me-13 formed the cyclopentyl ring of structure **CP1**. The cyclopentyl ring accounted for the last degree of unsaturation in the structure of **CP1**.

The configuration of the C-5 and C-6 alkene is assigned as *Z*. In the 5*Z* configuration, the Me-11 is located in further distance from other protons such as CH_2-7 and H-3. However, in the case of 5*E* configuration, the Me-11 is located in near proximity with Me-12 and Me-13. The NOESY experiments of **CP1** show no correlations between Me-11 and other protons suggested no proximate protons in the Me-11 vicinity supporting the 5*Z* configuration. Due to the minute amount of compound **CP1**, we were not able to assign the configuration of OH-8. The enantiomeric relationship of α-OH-8 and β-OH-8 structures was not resolvable in the NMR experiments. Hence, the structure of crotolidene (**CP1**) is (3*E*,5*Z*)-5-(4-hydroxy-2,2-dimethylcyclopentylidene)hex-3-en-2-one. This is the first report for **CP1**.



(a) (b)

Figure 4.3: Selected (a) HMBC (b) NOESY of **CP1** (Crotolidene)

Table 4.2: The NMR ($CDCl_3$, 600 MHz) data of **CP1** (Crotolidene)

Position	δ_H	δ_C	HMBC	NOESY
1	2.27 (s)	27.5	2, 3, 4	
2	-	198.7	3, 11	
3	7.19 (d, 16)	142.5	2, 4	1, 4, 11, 12
4	6.09 (d, 16)	132.6	3, 11	1, 3, 5, 11, 12
5	-	132.4	7, 11	
6	-	135.9	4, 11, 12, 13	
7	2.41 (dd, 6, 17)	43.0	5, 9	
	2.06 (dd, 11, 17)	43.0	5, 9	
8	3.99 (m)	64.8	7, 9	8, 10, 11, 12
9	1.78 (m)	48.6	7, 8, 10, 12, 13	
	1.47 (t, 12)	48.6	7, 8, 10, 12, 13	
10	-	37.1	9	
11	1.75 (s)	21.8	4, 5, 6	
12	1.09 (s)	30.3	6, 9, 13	
13	1.10 (s)	28.8	6, 9, 12	

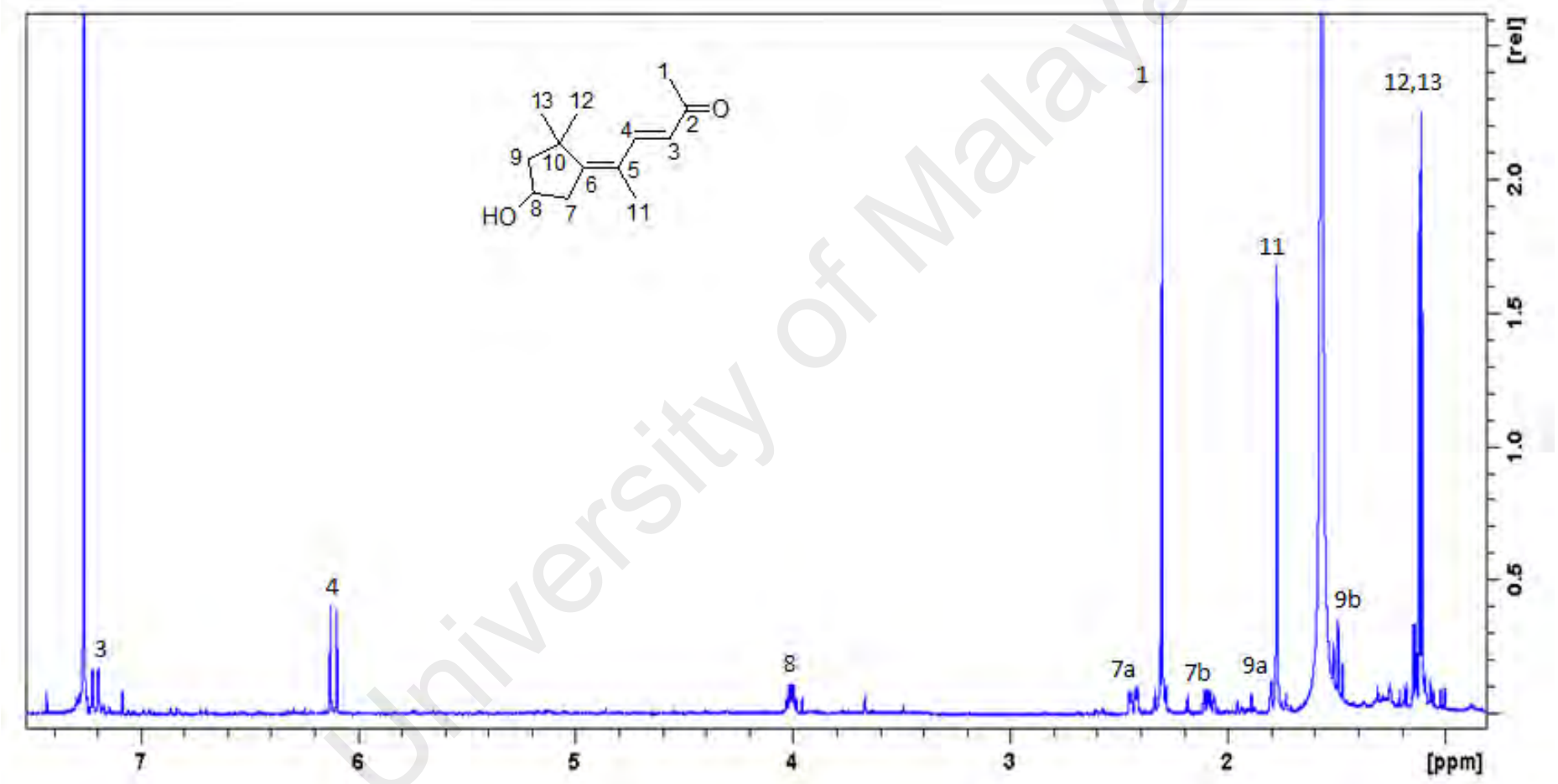


Figure 4.4: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CP1** (Crotolidene)

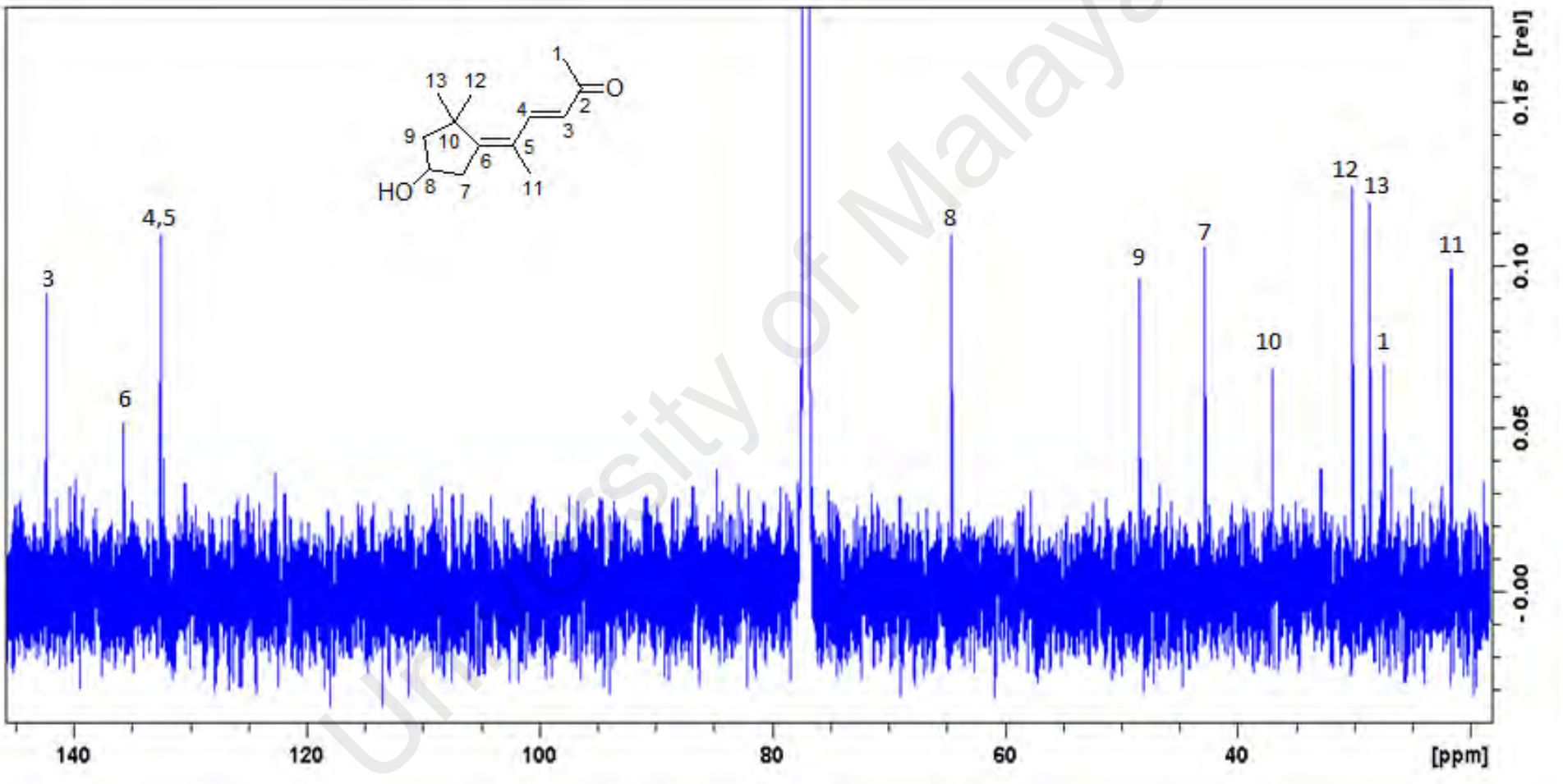
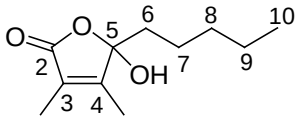


Figure 4.5: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **CP1** (Crotolidene)

4.1.2 CP2: Hydroxydihydrobovolide



CP2 was isolated as colourless oil with the molecular formula $C_{11}H_{18}O_3$, as determined by HRESIMS *m/z* 199.1335 $[M+H]^+$ (calculated for $C_{11}H_{18}O_3$ + H 199.1329) and *m/z* 181.1233 $[M+H-H_2O]^+$ (calculated for $C_{11}H_{18}O_3$ - OH 181.1223). **CP2** showed an optical activity $[\alpha]_D$ -13.3 (*c* 0.02, $CHCl_3$). The UV showed absorption maxima at 220 and 291 nm. The IR spectrum showed absorptions for hydroxyl group (3369 cm^{-1}), aliphatic group (2956, 2927 and 2859 cm^{-1}), conjugated ester (1741 cm^{-1}), and the conjugated alkene (1694 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.5, Table 4.2) showed the presence of three methyl signals at δ_H 1.92 (4-Me), 1.80 (3-Me) and 0.86 (CH_3-10), and three set of methylene signals. The ^{13}C NMR spectrum (Figure 4.6, Table 4.2) showed the presence of eleven carbon signals consisting of three methyls, four methylenes and four quaternary carbons. The carbon signals at δ_C 172.2 is typical of the carbonyl carbon (C-2) of the 2-furanone moiety, while the carbon signal at δ_C 107.0 (C-5) suggested that this carbon is flanked between two oxygen atoms.

The COSY spectrum showed only one partial structure, such as $CH_3CH_2CH_2CH_2$ corresponding to C(6)-C(7)-C(8)-C(9)-C(10) pentyl side chain. The HMBC (Figure 4.4) showed J^3 correlations from C-2 and C-4 to 3-Me, and C-3 and C-5 to 4-Me confirming the presence of the dimethyl-2-furanone moiety. The observation ^{13}C NMR chemical shift of C-5 at δ_C 107.0 suggested that the hydroxyl group is attached to this carbon. The pentyl side chain is connected to the hydroxyl-dimethyl-2-

furanone moiety at C-5, a deduction from the HMBC results with the observation of J^2 correlation from C-5 to H-6, hence completing the structure of **CP2** as 5-hydroxy-3,4-dimethyl-5-pentylfuran-2(5H)-one. **CP2** has been previously isolated from microorganism and named as hydroxydihydrobovolide and was reported to show mild antimicrobial activity. The experiment data were similar with those reported and this is the first isolation report of hydroxydihydrobovolide from a plant source (Koshino et al, 1989; Wu et al., 2011; Yuan et al., 2016).

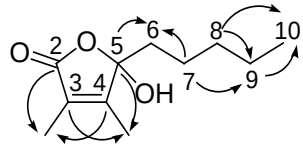


Figure 4.6: Selected HMBC of **CP2** (Hydroxydihydrobovolide)

Table 4.3: The NMR ($CDCl_3$, 600 MHz) data of **CP2** (Hydroxydihydrobovolide)

Position	δ_H	δ_C	HMBC
2	-	172.2	
3	-	157.8	
4	-	125.6	
5	-	107.0	
6	1.96 (m)	36.2	5, 7
	1.74 (m)	36.2	
7	1.15 (m)	22.6	
8	1.27 (m)	31.7	
9	1.29 (m)	22.8	7, 8, 10
10	0.86 (t, 7)	14.1	8, 9
3-Me	1.80 (s)	8.7	2, 3, 4
4-Me	1.92 (s)	10.9	2, 3, 4, 5
5-OH	1.61 (br s)	-	

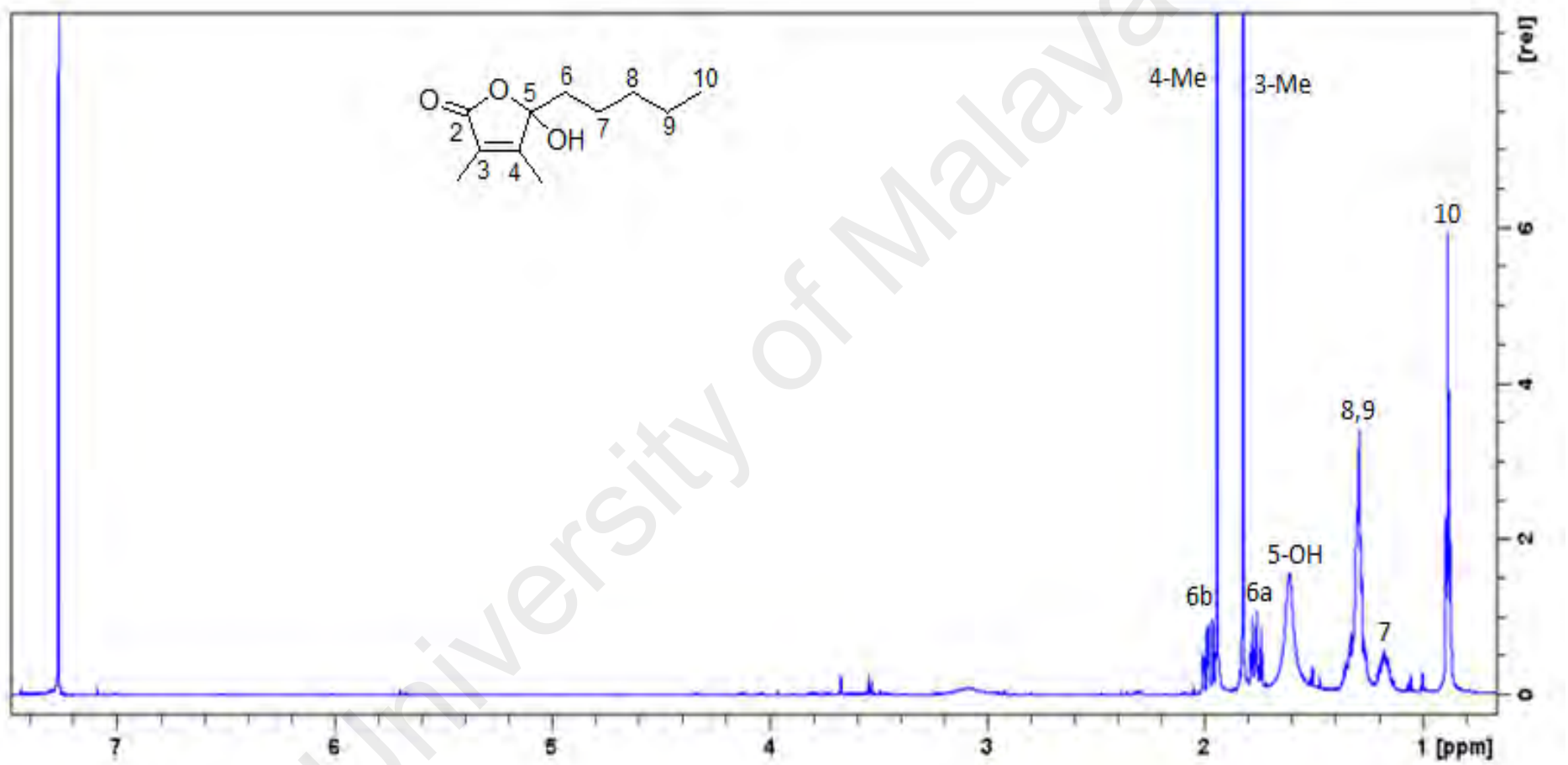


Figure 4.7: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CP2** (Hydroxydihydrobovolide)

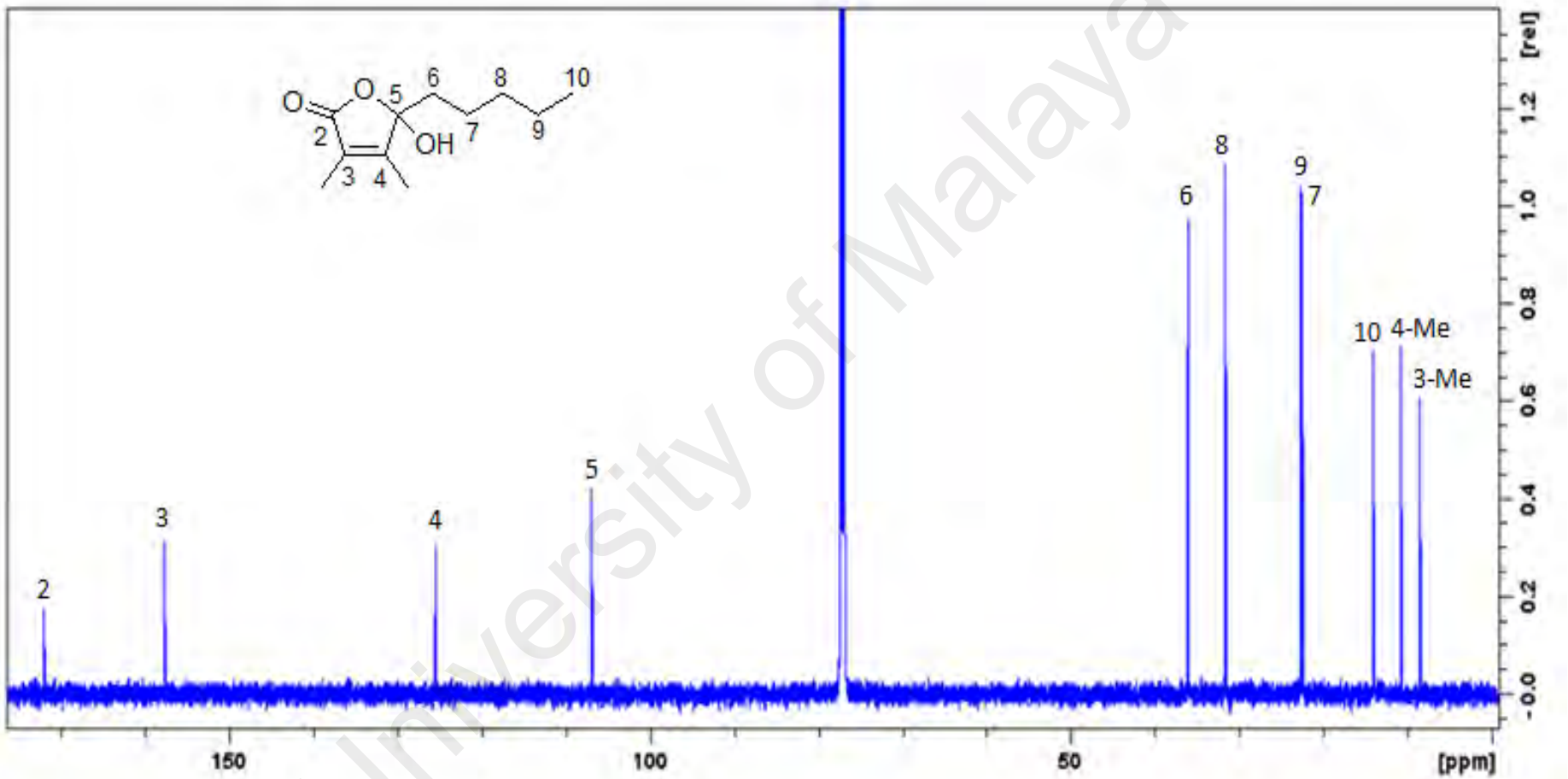
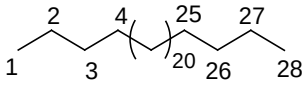


Figure 4.8: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **CP2** (Hydroxydihydrobovolide)

4.1.3 CP3: Octacosane



CP3 was isolated as a white amorphous solid with molecular formula $C_{28}H_{58}$. The IR spectrum showed absorptions for the aliphatic functionality at 2926, 2854, 908, 734, 668 and 651 cm^{-1}. The ^{1}H NMR spectrum (Figure 4.7, Table 4.3) reveal the presence of a methylene cluster signal at δ_H 1.11-1.26 integrated for 56 protons and assigned to [(CH_2-2) to (CH_2-27)]; and two methyl signal at δ_H 0.88 (Me-1 and Me-28).

The ^{13}C NMR spectrum (Figure 4.8, Table 4.3) showed the presence of five carbon signals attributed to twenty-eight carbons which include the terminal methyl signal at δ_C 14.4 (C-1 and C-28). The HMBC spectrum (Table 4.3) showed the terminal methyl (Me-1) correlated to CH_2-2 through J^2 correlation and CH_2-3 through J^3 correlation. While the terminal methyl (Me-28) correlate to CH_2-27 through J^2 correlation and CH_2-26 through J^3 correlation. The results indicated that the position of terminal methyl Me-1 and Me-28 is at C-1 and C-28 respectively. The experimental data of **CP3** is in agreement with the reported data (Speight et al., 2011).

Table 4.4: The NMR ($CDCl_3$, 400 MHz) of **CP3** (Octacosane)

Position	δ_H	δ_C	HMBC
1	0.88 (t,7)	14.4	2, 3
2	1.11 (m)	23.0	3, 4
3	1.24 (m)	32.2	2, 4
4	1.26 (m)	29.6	3, 5-24
5-24	1.26 (m)	30.0	3, 5-24
25	1.26 (m)	29.6	5-24, 26
26	1.24 (m)	32.2	25, 27
27	1.11 (m)	23.0	25, 26
28	0.88 (t, 7)	14.4	26, 27

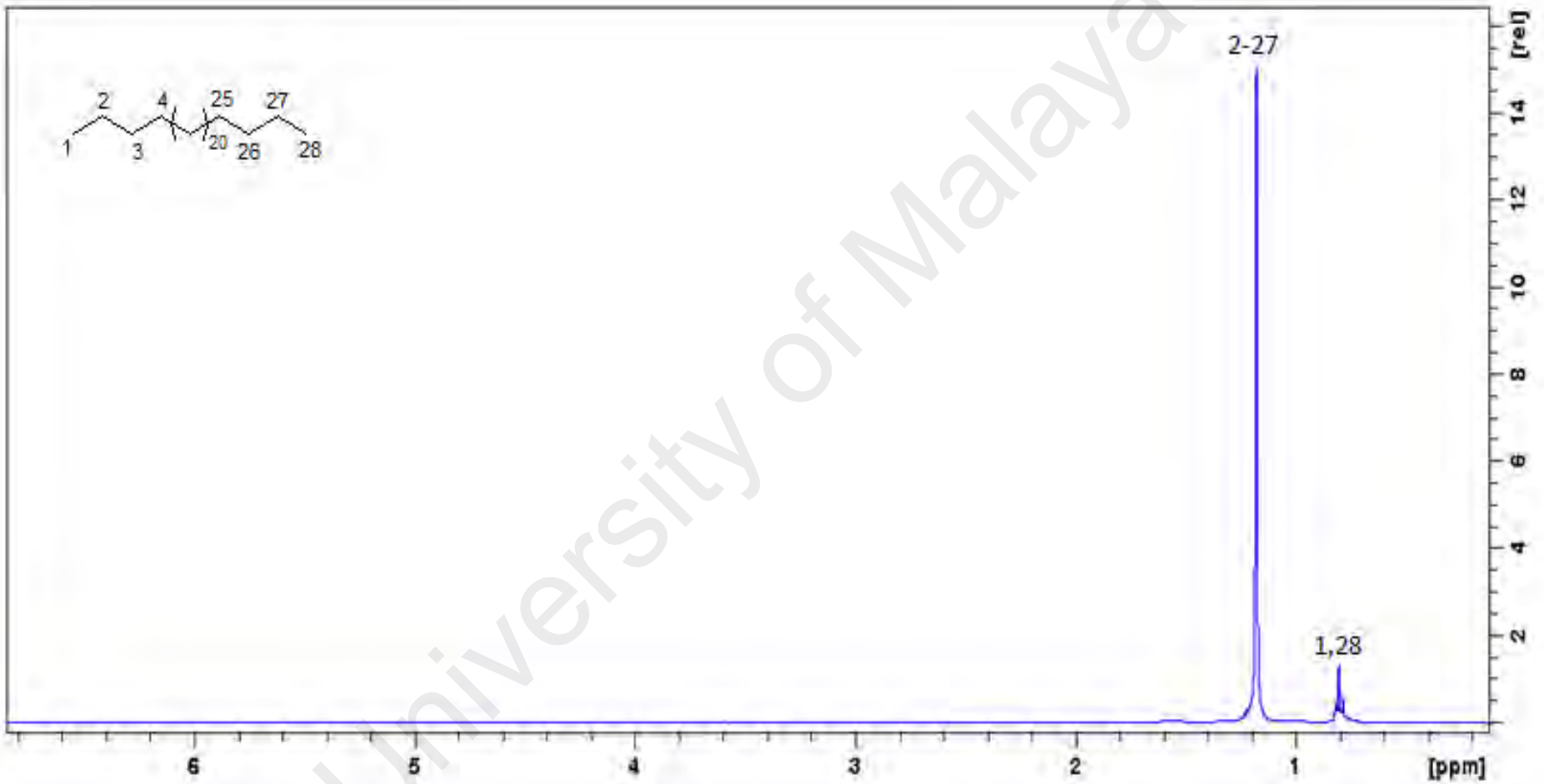


Figure 4.9: ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **CP3** (Octacosane)

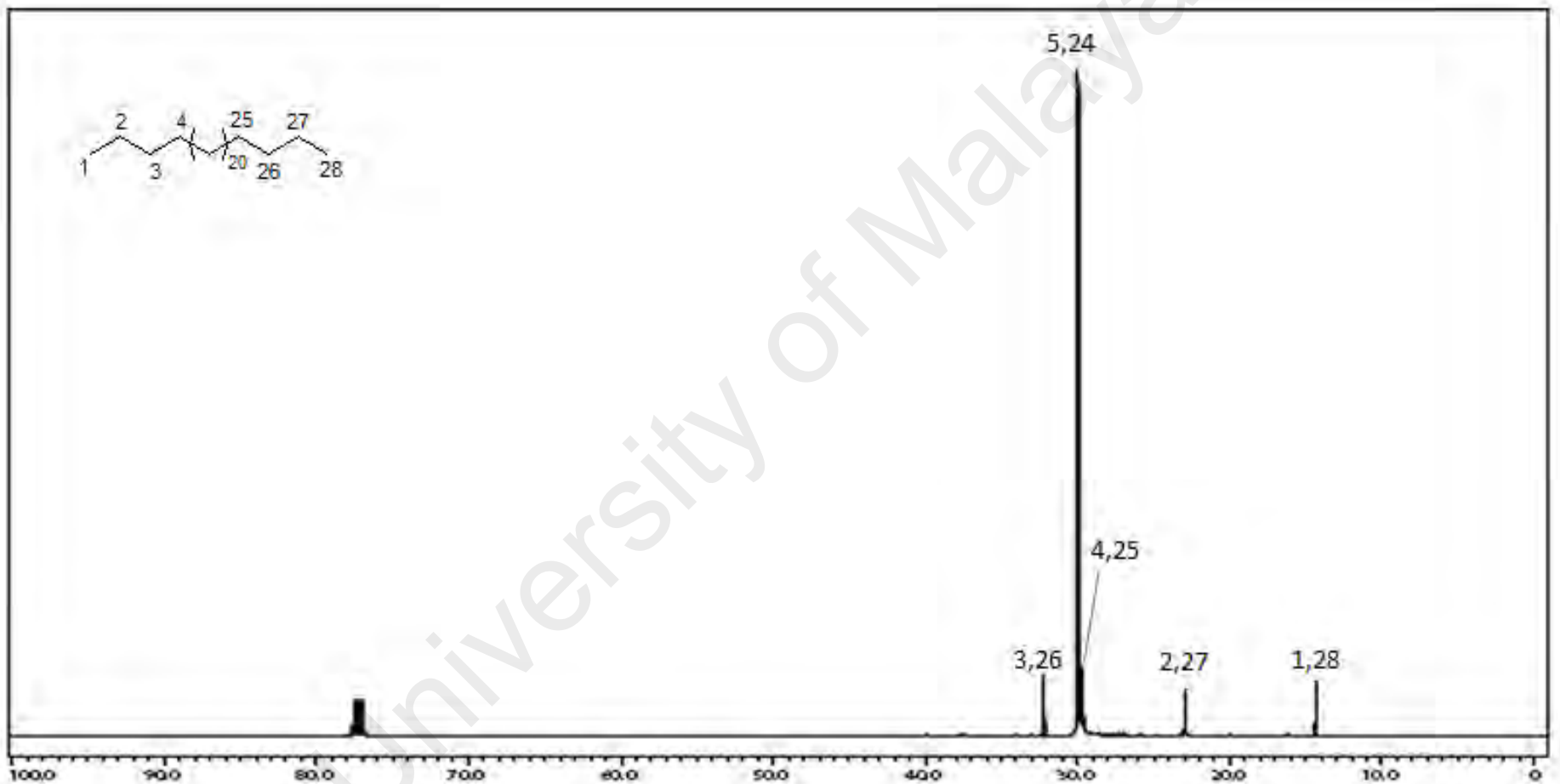
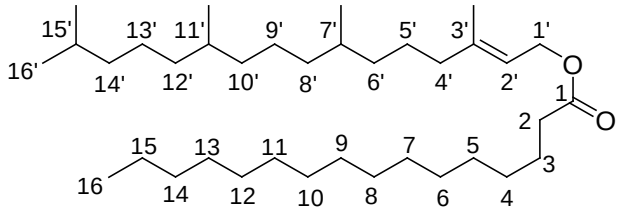


Figure 4.10: ^{13}C NR spectrum ($CDCl_3$, 100 MHz) of **CP3** (Octacosane)

4.1.4 CP4: *Trans*-phytyl palmitate



CP4 was isolated as white amorphous solid with molecular formula $C_{36}H_{70}O_2$ as determined by GCMS which give *m/z* 57 (79), 68 (100) $[C_5H_8]^+$, 71 (43), 82 (74), 95 (83), 123 (36), 137 (4). **CP4** showed an optical activity of $[\alpha]_D$ -1.4 (*c* 0.237, $CHCl_3$). The UV spectrum showed absorption maximum at 210 nm. The IR spectrum showed absorptions for aliphatic (2916 and 2849 cm^{-1}), carbonyl (1732 cm^{-1}) and vinyl (1641 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.10, Table 4.4) revealed the presence of an olefinic proton signal at δ_H 5.30 (H-2'), methine signals at δ_H 1.50 (H-15'), 1.35 (H-7' and H-11'); methylene signals at δ_H 4.56 (CH_2-1'), δ_H 2.28 (CH_2-2), 1.97 (CH_2-4'), 1.58 (CH_2-3), 1.38 (CH_2-5'), 1.25 [CH_2-(4-15), CH_2-9', CH_2-12' and CH_2-13'], 1.13 (CH_2-14') and 1.05 (CH_2-6', CH_2-8' and CH_2-10'); a methyl group attached to a quaternary carbon at δ_H 1.68 (3'-Me); a methyl group attached to a secondary carbon at δ_H 0.88 (Me-16); and four methyl groups attached to tertiary carbon at δ_H 0.84-0.86 (Me-16', 7'-Me, 11'-Me and 15'-Me). The methylene signal at δ_H 4.56 (CH_2-1') appeared at the most deshielded region due to its location which is adjacent to the ester oxygen. The ^{13}C NMR spectrum (Figure 4.11, Table 4.4) showed the presence of 36 carbon atoms which include a carbonyl carbon at δ_C 174.1 (C-1), and a quaternary olefinic carbon at δ_C 142.7 (C-3').

The HMBC spectrum (Figure 4.9, Table 4.4) showed J^3 correlation from C-1 to CH_2-1' indicated the connectivity between ester bond from the phytyl moiety to the fatty acid moiety. 3'-Me showed HMBC correlations to H-2' and CH_2-4'; 7'-Me showed HMBC correlations to CH_2-6', H-7'and CH_2-8'; 11'-Me showed HMBC correlation to H-11'; 15'-Me showed HMBC correlations to H-15' and Me-16'; and Me-16' showed HMBC correlations to H-15' and 15'-Me confirming the position of branched methyl of phytyl moiety are at C-3', C-7', C-11' and C-15' respectively. The HMBC correlations between C-2' with CH_2-1' and C-3' with CH_2-1' indicated the presence of a double bond at C(2')=C(3'). The J^3 HMBC correlations from C-16' to 15'-Me and vice versa indicated the position of terminal methyl from phytyl moiety is at C-16' (Asand et al., 1991).

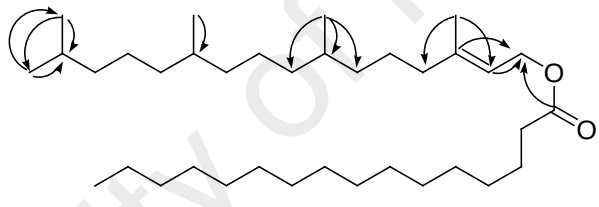


Figure 4.11: Selected HMBC of **CP4** (*Trans*-phytyl palmitate)

Table 4.5: The NMR ($CDCl_3$, 400 MHz) data of **CP4** (*Trans*-phytyl palmitate)

Position	δ_H	δ_C	HMBC
1	-	174.1	
2	2.28 (t, 8)	34.6	1, 3, 4,
3	1.58 (m)	25.2	1, 2, 4
4	1.25 (m)	29.4	
5	1.25 (m)	29.5	
6	1.25 (m)	29.7	
7-10	1.25 (m)	29.9	
11	1.25 (m)	29.8	
12	1.25 (m)	29.6	
13	1.25 (m)	29.6	
14	1.25 (m)	32.2	
15	1.25 (m)	22.9	14
16	0.88 (m)	14.3	
1’	4.56 (d, 7)	61.4	1, 2’, 3’
2’	5.30 (t, 7)	118.5	1’,3’-Me, 4’
3’	-	142.7	
4’	1.97 (t, 7)	40.1	2’, 3’, 3’-Me, 5’, 6’
5’	1.38 (m)	25.2	4’, 6’
6’	1.05 (m)	37.7	5’
7’	1.35 (m)	33.0	5’, 9’
8’	1.05 (m)	37.6	9’
9’	1.25 (m)	24.7	
10’	1.05 (m)	37.5	9’
11’	1.35 (m)	33.0	9’, 13’
12’	1.25 (m)	36.8	
13’	1.25 (m)	25.0	12’, 14’
14’	1.13 (m)	39.6	
15’	1.50 (m)	28.2	13’,15’-Me, 16’
16’	0.86 (m)	22.8	15’-Me
3’-Me	1.68 (s)	16.6	1’, 3’, 4’
7’-Me	0.84 (m)	19.9	6’, 7’, 8’
11’-Me	0.84 (m)	19.9	11’
15’-Me	0.86 (m)	22.8	16’

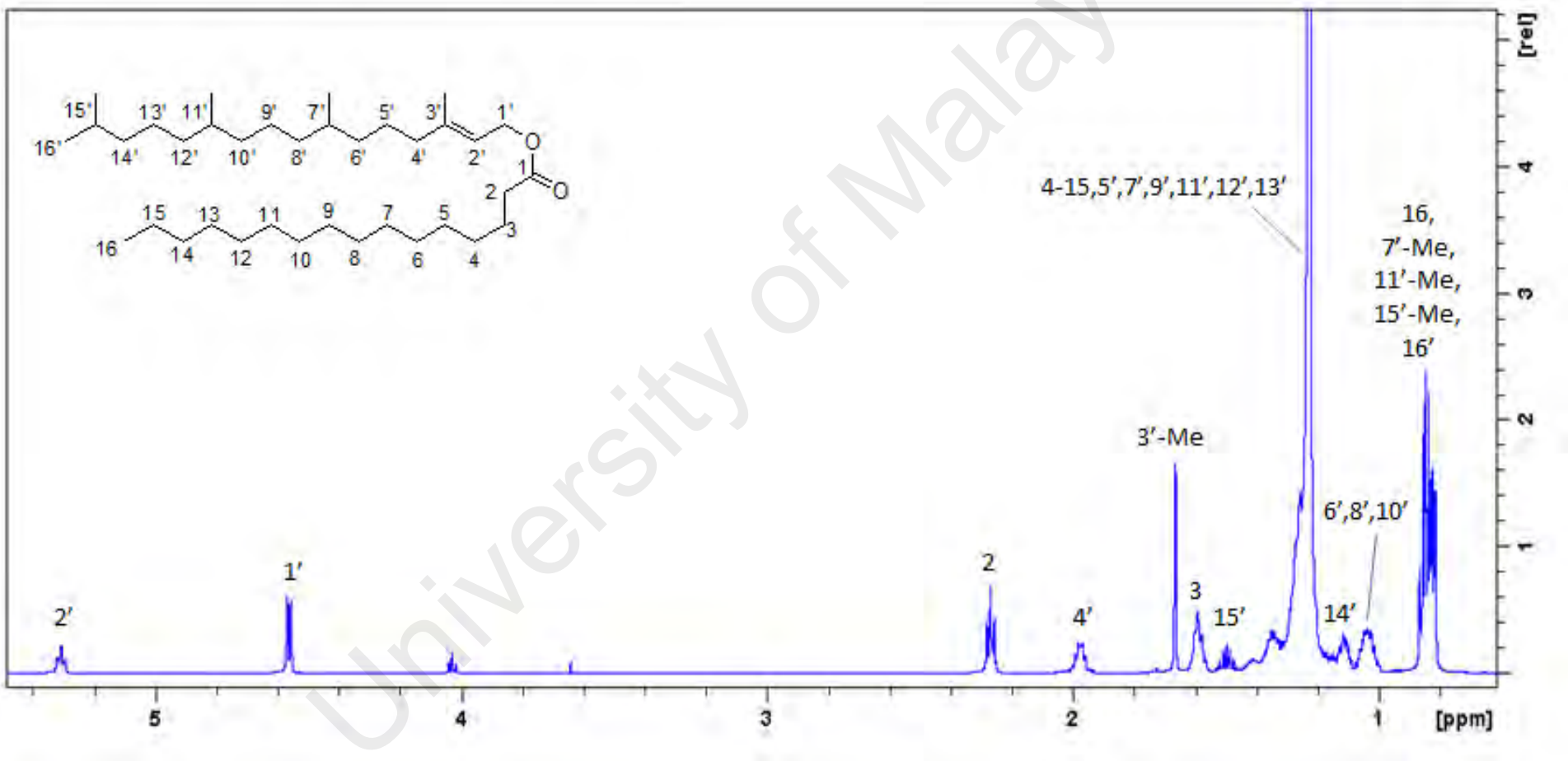


Figure 4.12: ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of **CP4** (*Trans*-phytyl palmitate)

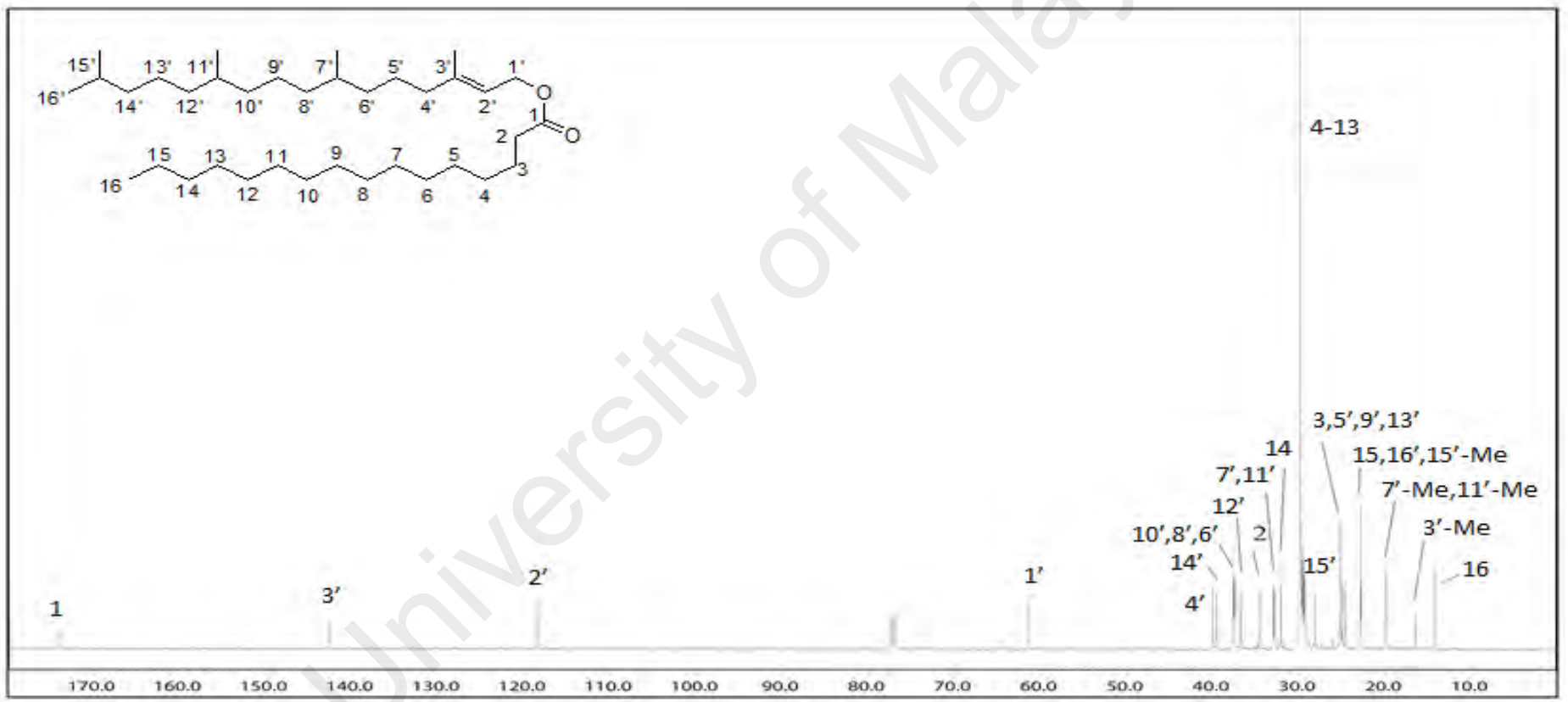
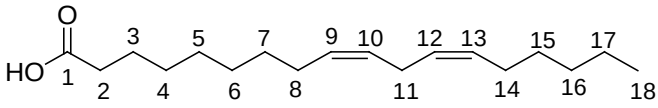


Figure 4.13: ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of **CP4** (*Trans*-phytyl palmitate)

4.1.5 CP5: Linoleic acid



CP5 was isolated as light yellowish amorphous solid with molecular formula $C_{18}H_{32}O_2$, as determined by HRESIMS with m/z 279.2371 $[M-H]^-$ (calculated for $C_{18}H_{32}O_2$ – H m/z 279.2330) (Gunstone & Jacobsberg, 1972). The UV spectrum showed absorption maxima at 224 nm and a shoulder at 272 nm. The IR spectrum showed absorptions for carboxylic acid (3436 and 1710 cm^{-1}), aliphatic (2984, 2918, 2850 cm^{-1}), carbonyl (1741 cm^{-1}) and olefinic (1648 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.13, Table 4.5) revealed the presence of olefinic proton signals at δ_H 5.32 (H-10 and H-12), 5.34 (H-9) and 5.36 (H-13); methylene signals at δ_H 2.79 (H-11a), 2.75 (H-11b), 2.32 (CH_2-2), 2.03 (CH_2-8 and CH_2-14), 1.61 (CH_2-3) and 1.26 [(CH_2-4)-(CH_2-7) and (CH_2-15)-(CH_2-17)]; and a methyl signal at δ_H 0.87 (Me-18). The proton signals of H-9, H-10, H-12 and H-13 appeared most deshielded due to the presence of the olefinic function group, *i.e. cis*-unsaturated fatty acid. The protons of the allylic methylene signals at δ_H 2.03 was assigned to CH_2-8 and CH_2-14 while the *bis*-allylic methylene signals at δ_H 2.75 and 2.79 were assigned to H-11a and H-11b, based on HMBC correlations as discussed below and thereby suggested the presence of non-conjugated double bond.

The ^{13}C NMR spectrum (Figure 4.14, Table 4.5) showed the presence of eighteen carbon atoms including a carbonyl carbon at δ_C 179.8 (C-1). COSY experiment gives one partial structure that is -CH_2-CH=CH-CH_2-CH=CH-CH_2- corresponding to C(8)-C(9)-C(10)-C(11)-C(12)-C(13)-C(14).

The HMBC spectrum (Figure 4.12, Table 4.5) showed correlations of carbonyl carbon to the methylene protons through J^2 correlation (C-1 to CH_2-2) and J^3 correlation (C-1 and CH_2-3). The J^2 HMBC correlations from C-9 to CH_2-8 and C-13 to CH_2-14; J^3 HMBC correlations from C-10 to CH_2-8 and C-12 to CH_2-14 indicated that the position of allylic methylene is at C-8 and C-14. The HMBC correlations from C-9, C-10, C-12 and C-13 to H-11a and H-11b confirmed the position of *bis*-allylic methylene is at C-11. The J^2 HMBC correlations between C-14 and C-16 to CH_2-15, and J^3 HMBC correlation from C-17 to CH_2-15 suggested that the position of the double bonds were between C-9/C-10 and C-12/C-13. The terminal methyl (Me-18) showed J^2 HMBC correlation with CH_2-17 and J^3 HMBC correlation with CH_2-16 confirmed the position of the terminal methyl is at C-18. The experimental data for **CP5** is in agreement with the reported data (Gunstone & Jacobsberg, 1972; Vlahov, 1999).

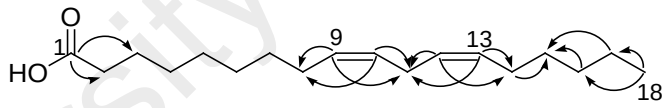


Figure 4.12: Selected HMBC of **CP5** (Linoleic acid)

Table 4.5: The NMR ($CDCl_3$, 600 MHz) data of **CP5** (Linoleic acid)

Position	δ_H	δ_C	HMBC
1	-	179.8	
2	2.32 (t, 8)	34.2	1, 3, 4
3	1.61 (m)	24.9	1, 2, 4
4	1.26 (m)	29.3	
5	1.26 (m)	29.3	
6	1.26 (m)	29.6	
7	1.26 (m)	29.8	
8	2.03 (m)	27.4	7, 9, 10
9	5.34 (m)	130.3	8, 10, 11
10	5.32 (m)	128.1	8, 9, 11
11	2.75 (t, 7) 2.79 (t, 7)	25.9	9, 10, 12, 13
12	5.32 (m)	128.3	11, 13, 14
13	5.36 (m)	130.5	11, 12, 14
14	2.03 (m)	27.4	12, 13, 15
15	1.26 (m)	29.9	14, 16, 17
16	1.26 (m)	31.8	
17	1.26 (m)	22.8	18,
18	0.87 (t, 7)	14.3	16, 17

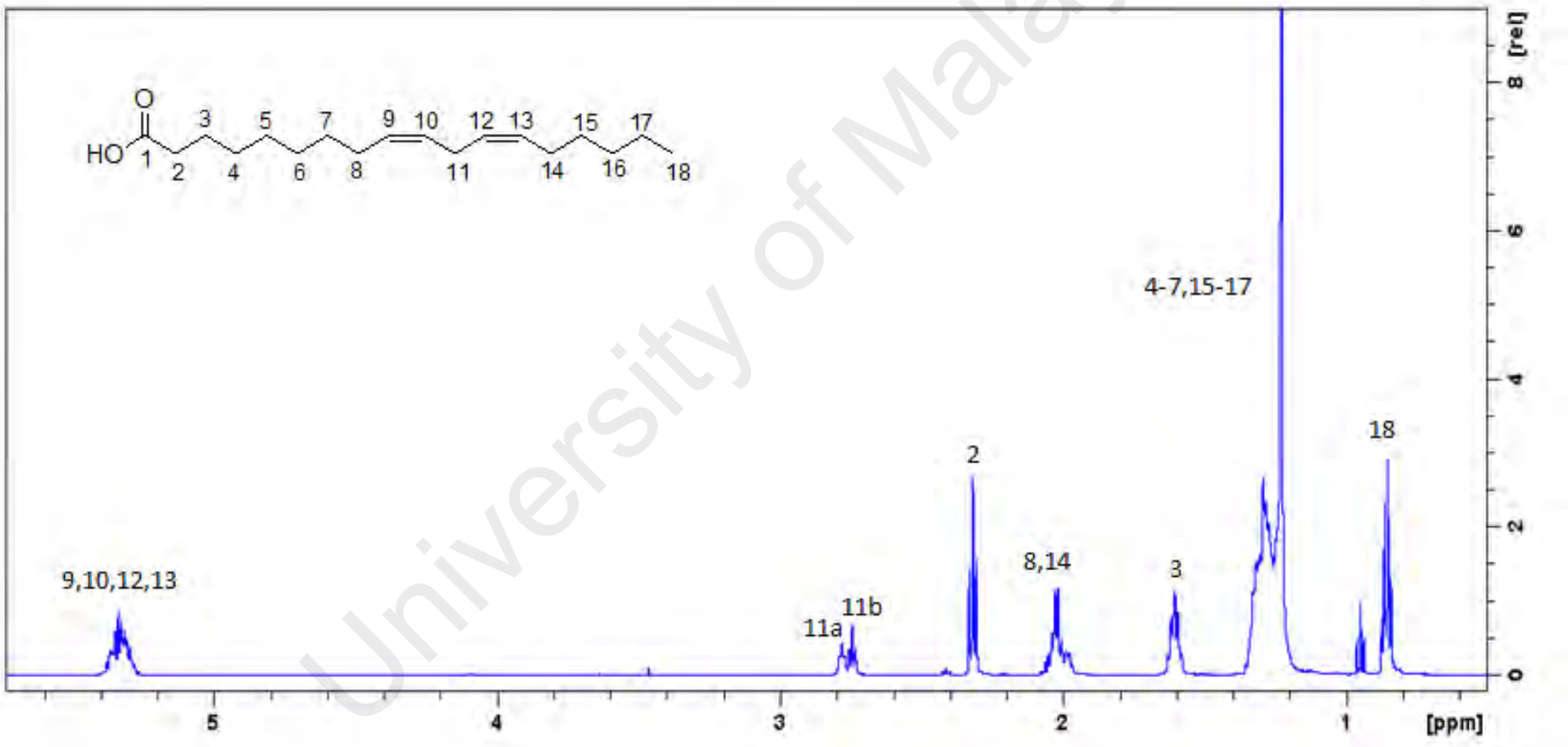


Figure 4.13: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CP5** (Linoleic acid)

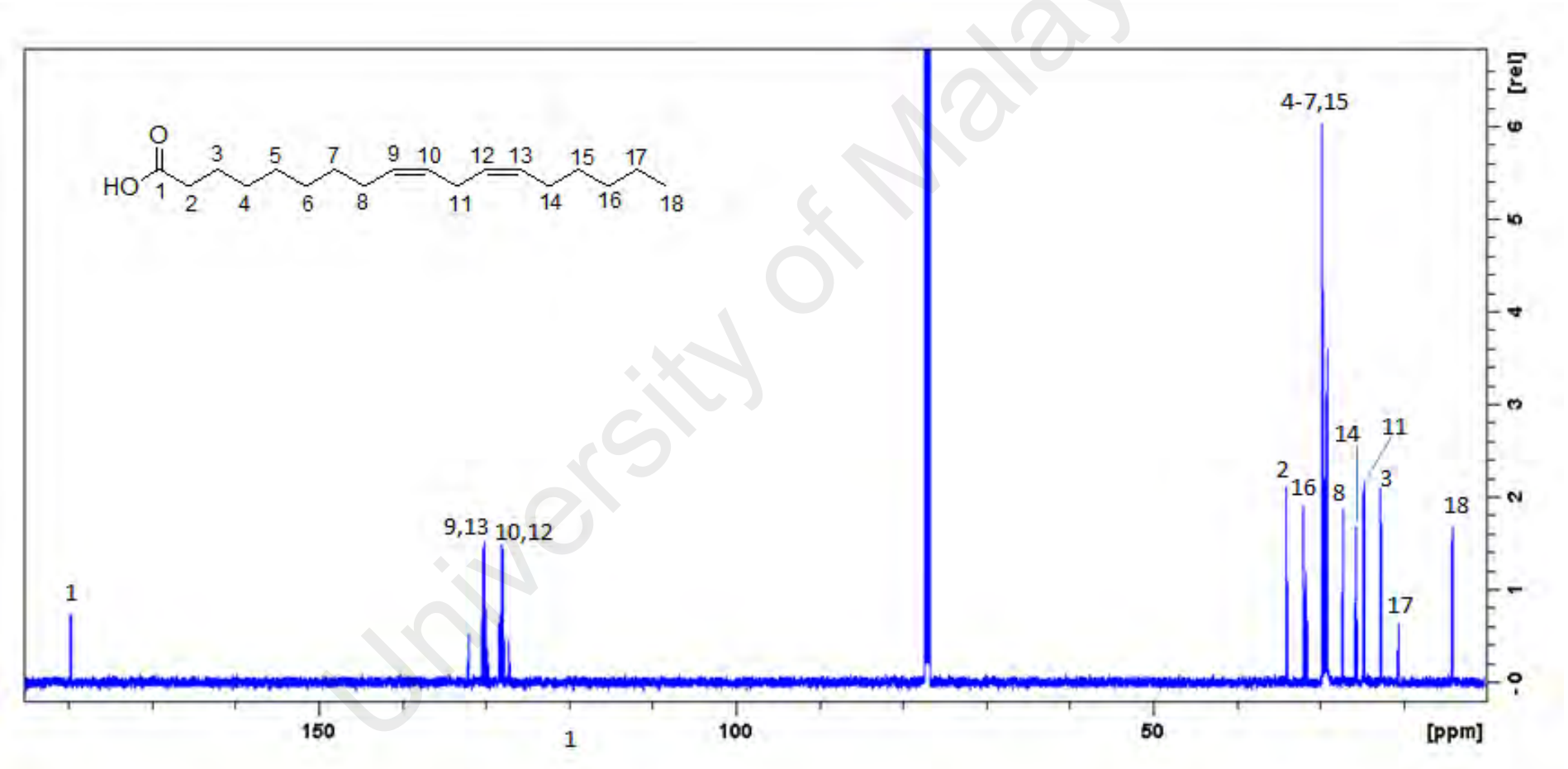
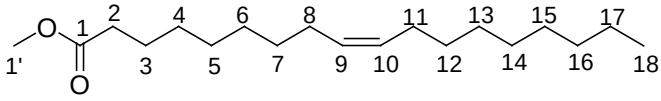


Figure 4.14: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **CP5** (Linoleic acid)

4.1.6 CP6: Methyl oleate



CP6 was isolated as yellowish oil with molecular formula $C_{19}H_{36}O_2$, as determined by GCMS with *m/z* 296 (3) [M^+], 264 (14), 222 (10), 180 (8), 137 (9), 123 (17), 110 (27), 97 (52), 83 (61), 73 (60), 69 (74), 55 (100). The UV spectrum showed absorption maxima at 202 nm with two shoulders at 222 and 277 nm. The IR spectrum showed absorptions for aliphatic (2926 and 2855 cm^{-1}) and carbonyl (1744 cm^{-1}) functionalities (Rakoff et al., 1979).

The ^1H NMR spectrum (Figure 4.16, Table 4.6) revealed the presence of an olefinic proton signal at δ_H 5.32 which was integrated for two protons and attributed to H-9 and H-10; a methoxyl signal at δ_H 3.64 (OMe-1'); four group of methylene signals at δ_H 2.28 (CH_2-2), δ_H 1.98 (CH_2-8 and CH_2-11), δ_H 1.59 (CH_2-3), δ_H 1.28 [(CH_2-4)-(CH_2-7) and (CH_2-12)-(CH_2-17)]; and methyl signals at δ_H 0.86 (Me-18). The ^{13}C NMR spectrum (Figure 4.17, Table 4.6) showed the presence of 19 carbon signal including a carbonyl signal at δ_C 174.6 (C-1). COSY experiment give one partial structure that is CH_2-CH=CH-CH_2 corresponding to C(8)-C(9)-C(10)-C(11).

The HMBC spectrum (Figure 4.15, Table 4.6) showed J^3 correlation from C-1 to OMe-1', hence confirming the position of the terminal methyl ester. The carbonyl carbon at C-1 showed J^2 and J^3 HMBC correlations with the α-methylene proton (CH_2-2) and β-methylene proton (CH_2-3), respectively. The J^2 and J^3 HMBC correlations from C-2 to CH_2-3 and CH_2-4, respectively indicated the position of α-methylene signal is at C-2. While the J^2 and J^3 HMBC correlations from C-3 to CH_2-2 and CH_2-4 indicated the position of β-methylene signal is at C-3. The J^2 HMBC correlations from

C-8 to CH_2-7 and H-9, C-11 to H-10 and CH_2-12; J^3 HMBC correlations from C-8 to H-10 and C-11 to H-9 indicated that the position of allylic methylene is at C-8 and C-11. The partial structure from COSY experiment (CH_2-CH=CH-CH_2) connecting with C-7 and C-12 providing the fragment of CH_2-CH2-CH=CH-CH_2-CH_2. The terminal methyl (Me-18) showed J^2 HMBC correlation with CH_2-17 and J^3 HMBC correlation with CH_2-16 confirmed the position of the terminal methyl is at C-18. The experimental data of **CP6** is in agreement with the reported data (Knothe et al., 1995; Lie et al., 1995; Rakoff et al., 1979).

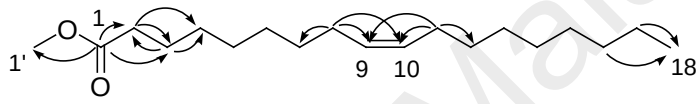


Figure 4.15: Selected HMBC of **CP6** (Methyl oleate)

Table 4.6: The NMR ($CDCl_3$, 600 MHz) data of **CP6** (Methyl oleate)

Position	δ_H	δ_C	HMBC
1’	3.64 (s)	52.7	1
1	-	174.6	
2	2.28 (t, 8)	34.3	1, 3, 4
3	1.59 (m)	25.2	1, 2, 4
4	1.28 (m)	29.4	
5	1.28 (m)	29.3	
6	1.28 (m)	29.3	
7	1.28 (m)	29.9	
8	1.98 (m)	27.4	7, 9, 10
9	5.32 (m)	130.0	8, 11
10	5.32 (m)	130.2	8, 11
11	1.98 (m)	27.4	9, 10, 12
12	1.28 (m)	30.0	
13	1.28 (m)	29.5	
14	1.28 (m)	29.7	
15	1.28 (m)	29.5	
16	1.28 (m)	32.1	
17	1.28 (m)	22.9	16
18	0.86 (t, 7)	14.3	16, 17

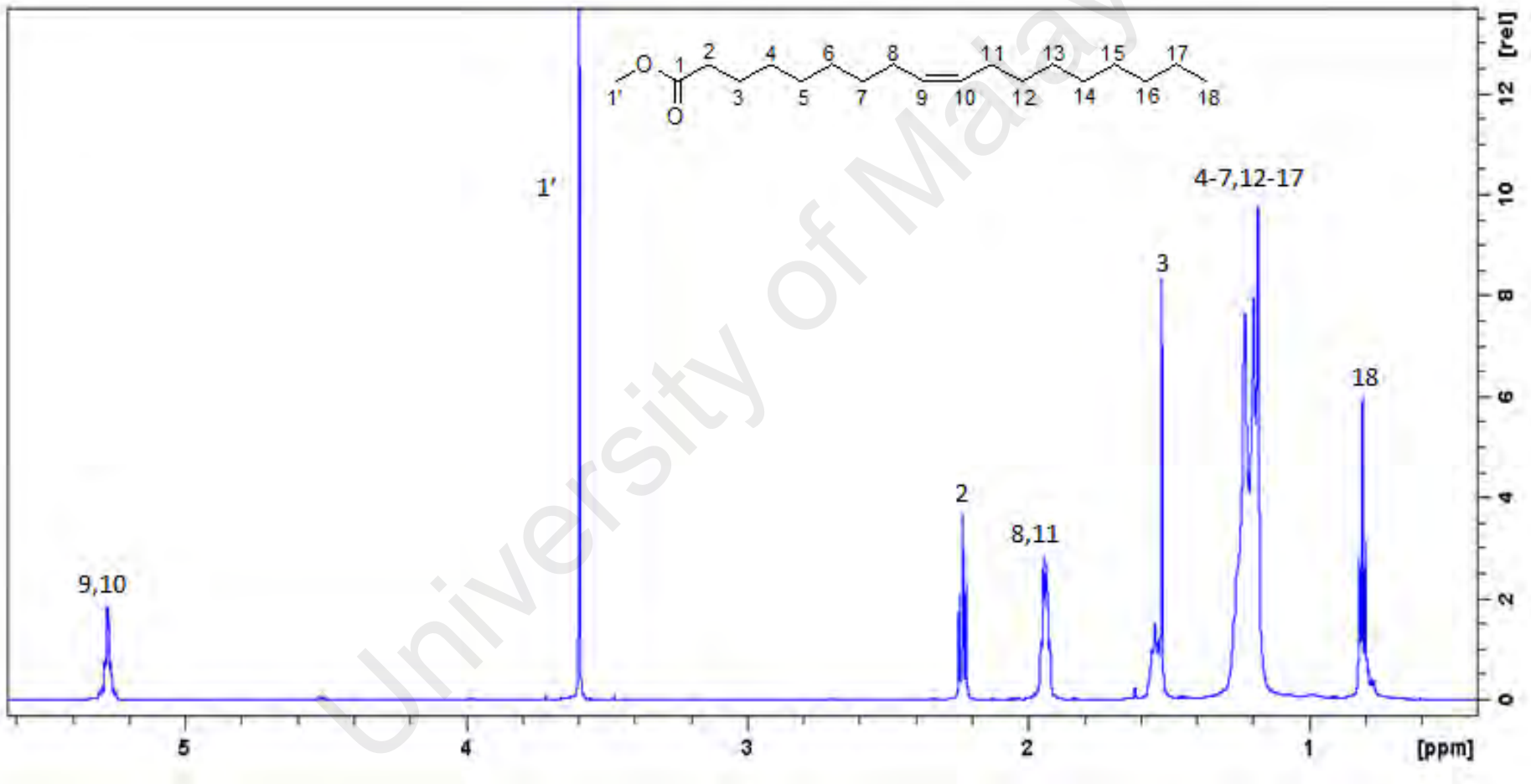


Figure 4.16: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CP6** (Methyl oleate)

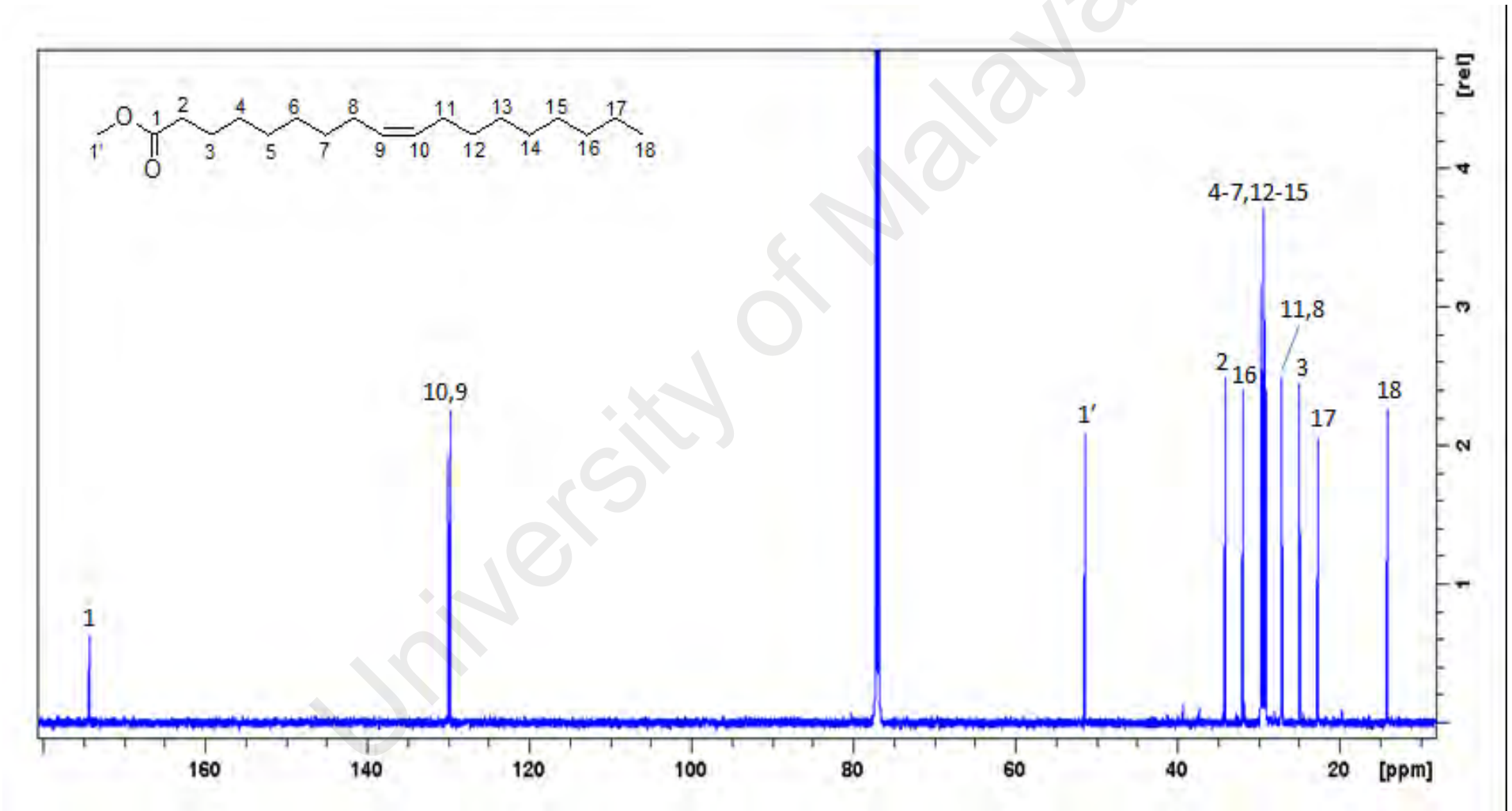
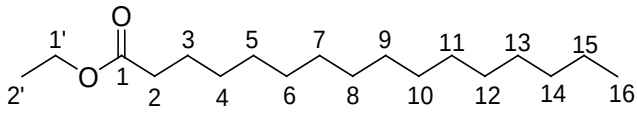


Figure 4.17: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **CP6** (Methyl oleate)

4.1.7 CP7: Ethyl palmitate



CP7 was isolated as yellowish oil with molecular formula $C_{18}H_{36}O_2$, determined by GCMS *m/z* 284 (4) $[M]^+$, 255 (2), 241 (6), 157 (11), 101 (53), 88 (100), 70 (26), 55 (27) (Joshi et al., 2009). The UV spectrum showed absorptions at 206 and 274 nm. The IR spectrum showed absorptions for aliphatic (2924 and 2853 cm^{-1}) and carbonyl (1740 cm^{-1}) functional groups.

The ^1H NMR spectrum (Figure 4.19, Table 4.7) showed OCH_2- signal at δ_H 4.08 (CH_2-1'); methylene signals at δ_H 2.38 (CH_2-2), 1.57 (CH_2-3), 1.24 [(CH_2-4)-(CH_2-15)], and two methyl signals at δ_H 1.21 (Me-2') and 0.84 (Me-16). The DEPT-135 NMR spectrum (Figure 4.20, Table 4.7) showed the presence of 17 carbon signals which corresponded to the two methyl and fifteen methylene functionalities. COSY experiment gives two partial structures that are OCH_2-CH_3 corresponding to C(1')-C(2') and CH_2-CH_2-$(CH_2)_{12}$-CH_3 corresponding to -C(2)-C(3)-C(4-15)-C(16). The observe pattern of these protons suggested the presence of ethyl ester functionality in the compound.

The presence of the ethyl ester moiety was confirmed by the HMBC experiment. The HMBC spectrum (Figure 4.18, Table 4.7) indicated the presence of the ethyl ester bond through J^3 correlation from C-1 to CH_2-1'. Meanwhile, the presence of the ethyl moiety was indicated through J^2 HMBC correlation from C-1' to Me-2'.In addition, the carbonyl carbon at C-1 showed J^2 and J^3 HMBC correlations to CH_2-2 and CH_2-3. The C-2 methylene showed J^2 and J^3 HMBC correlations to CH_2-3 and CH_2-4, respectively; C-3 methylene carbon showed J^2 HMBC correlations to CH_2-

2 and CH_2-4. The terminal methyl (Me-16) showed J^2 and J^3 HMBC correlations to CH_2-15 and CH_2-14, respectively, suggesting the position of the terminal methyl is at C-16. The experimental data of **CP7** is in agreement with the reported data (Joshi et al., 2009).

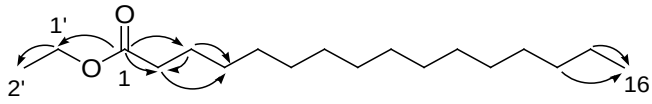


Figure 4.18: Selected HMBC of **CP7** (Ethyl palmitate)

Table 4.7: The NMR ($CDCl_3$) data of **CP7** (Ethyl palmitate)

Position	δ_H	δ_C	HMBC
1	-	173.8[a]	
1’	4.08 (q, 7)	60.4	1
2	2.38 (t, 8)	34.6	1, 3,4
2’	1.21 (t, 7))	14.5	1’
3	1.57 (p, 8)	25.3	2, 4
4	1.24 (m)	29.4	
5	1.24 (m)	29.6	
6	1.24 (m)	29.8	
7	1.24 (m)	29.9	
8	1.24 (m)	30.0	
9	1.24 (m)	30.0	
10	1.24 (m)	30.0	
11	1.24 (m)	29.9	
12	1.24 (m)	29.9	
13	1.24 (m)	29.7	
14	1.24 (m)	32.2	
15	1.24 (m)	23.0	14
16	0.84 (t, 7)	14.4	14, 15

[a] Value obtained from HMBC spectrum.

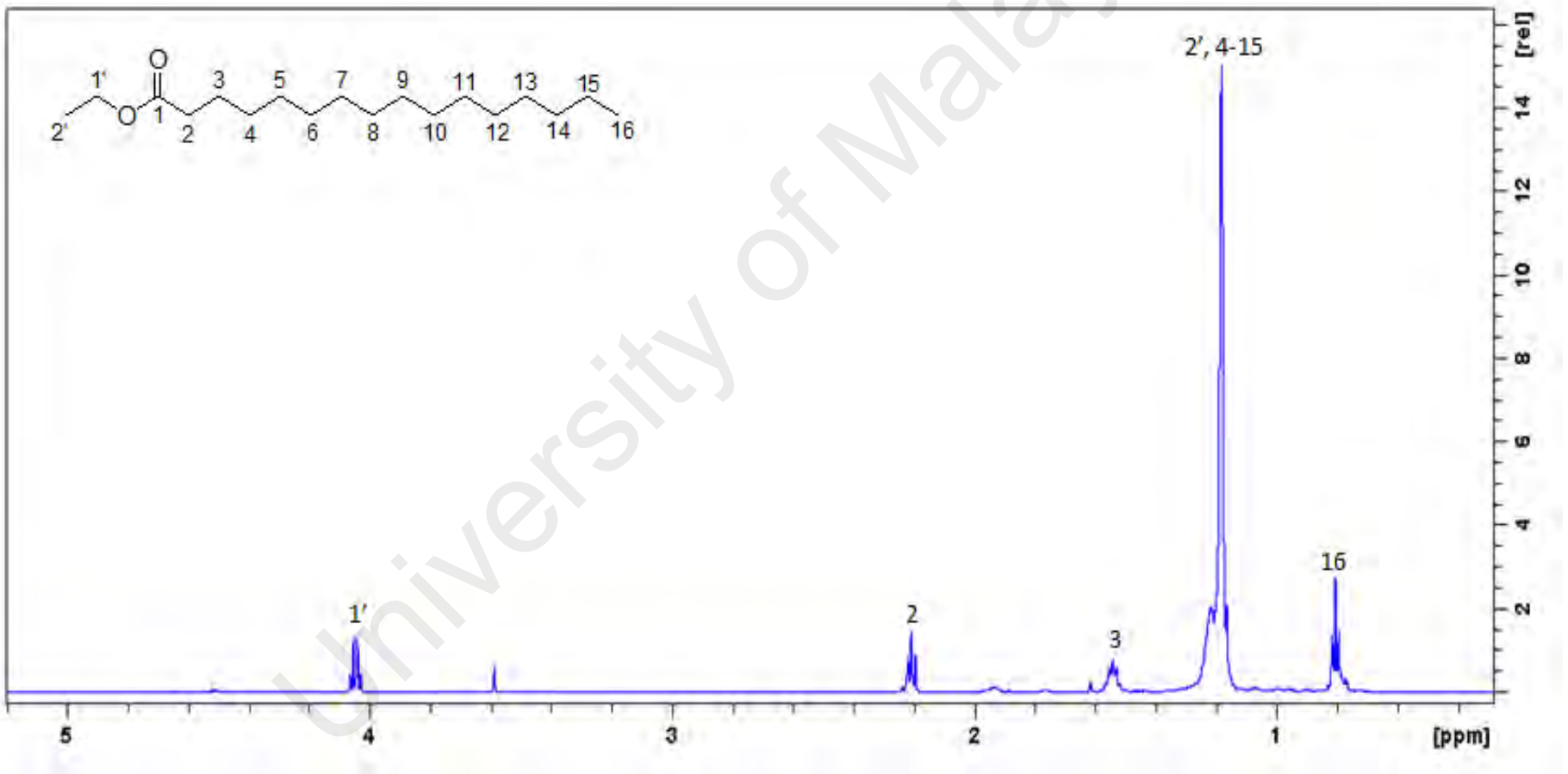


Figure 4.19: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CP7** (Ethyl palmitate)

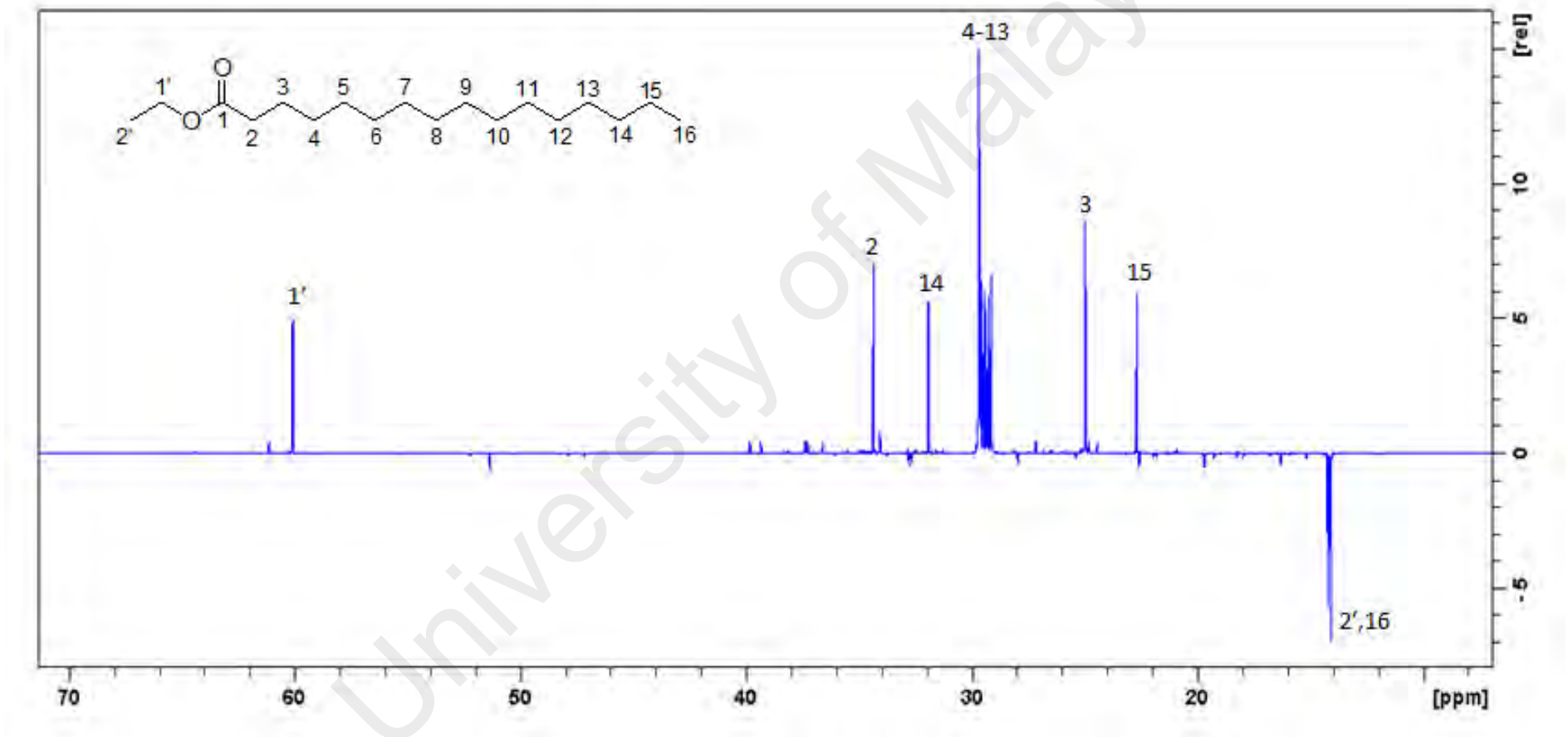
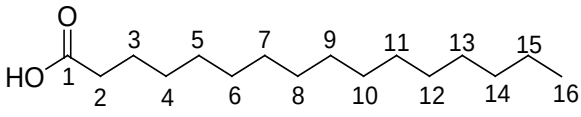


Figure 4.20: DEPT-135 NMR spectrum ($CDCl_3$, 150 MHz) of **CP7** (Ethyl palmitate)

4.1.8 CP8: Palmitic acid



CP8 was isolated as white amorphous solid with molecular formula $C_{16}H_{32}O_2$ as determined by HRESIMS with *m/z* 255.2369 $[M-H]^-$ (calculated for $C_{16}H_{32}O_2$ - H *m/z* 255.2330) (Miranda-Vilela & Grisolia, 2009). The UV spectrum showed absorption maxima at 208 and 268 nm. The IR spectrum showed absorptions for carboxylic acid (3409 cm^{-1}), aliphatic (2917 cm^{-1} and 2850 cm^{-1}) and carbonyl (1707 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.22, Table 4.8) revealed the presence of methylene signals at δ_H 2.33 (CH_2-2), 1.61 (CH_2-3), 1.28 [(CH_2-4)-(CH_2-15)], and methyl signal at δ_H 0.86 (Me-16). The ^{13}C NMR spectrum (Figure 4.23, Table 4.8) showed the presence of 16 carbon signals corresponded to a methyl and fourteen methylene and a carbonyl carbon at δ_C 178.7 (C-1).

The HMBC spectrum (Figure 4.21, Table 4.8) showed J^2 correlation from the carbonyl C-1 to CH_2-2. The C-2 methylene carbon showed J^2 and J^3 HMBC correlations to CH_2-3 and CH_2-4; and the C-3 methylene carbon showed J^2 HMBC correlation to CH_2-2. The terminal Me-16 showed J^2 and J^3 HMBC correlations to CH_2-15 and CH_2-14, respectively, suggesting the position of terminal methyl is at C-16. The experimental data of **CP8** is in agreement with the reported data (Miranda-Vilela & Grisolia, 2009).

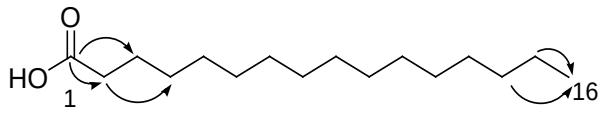


Figure 4.21: Selected HMBC of **CP8** (Palmitic acid)

Table 4.8: The NMR ($CDCl_3$, 600 MHz) data of **CP8** (Palmitic acid)

Position	δ_H	δ_C	HMBC
1	-	178.7	
2	2.33 (t, 8)	34.0	1, 3, 4
3	1.61 (m)	24.9	1,2
4	1.28 (m)	29.3	
5	1.28 (m)	29.5	
6	1.28 (m)	29.7	
7	1.28 (m)	29.9	
8	1.28 (m)	29.9	
9	1.28 (m)	29.9	
10	1.28 (m)	29.9	
11	1.28 (m)	29.9	
12	1.28 (m)	29.8	
13	1.28 (m)	29.6	
14	1.28 (m)	32.1	
15	1.28 (m)	22.9	
16	0.86 (t, 7)	14.2	14, 15

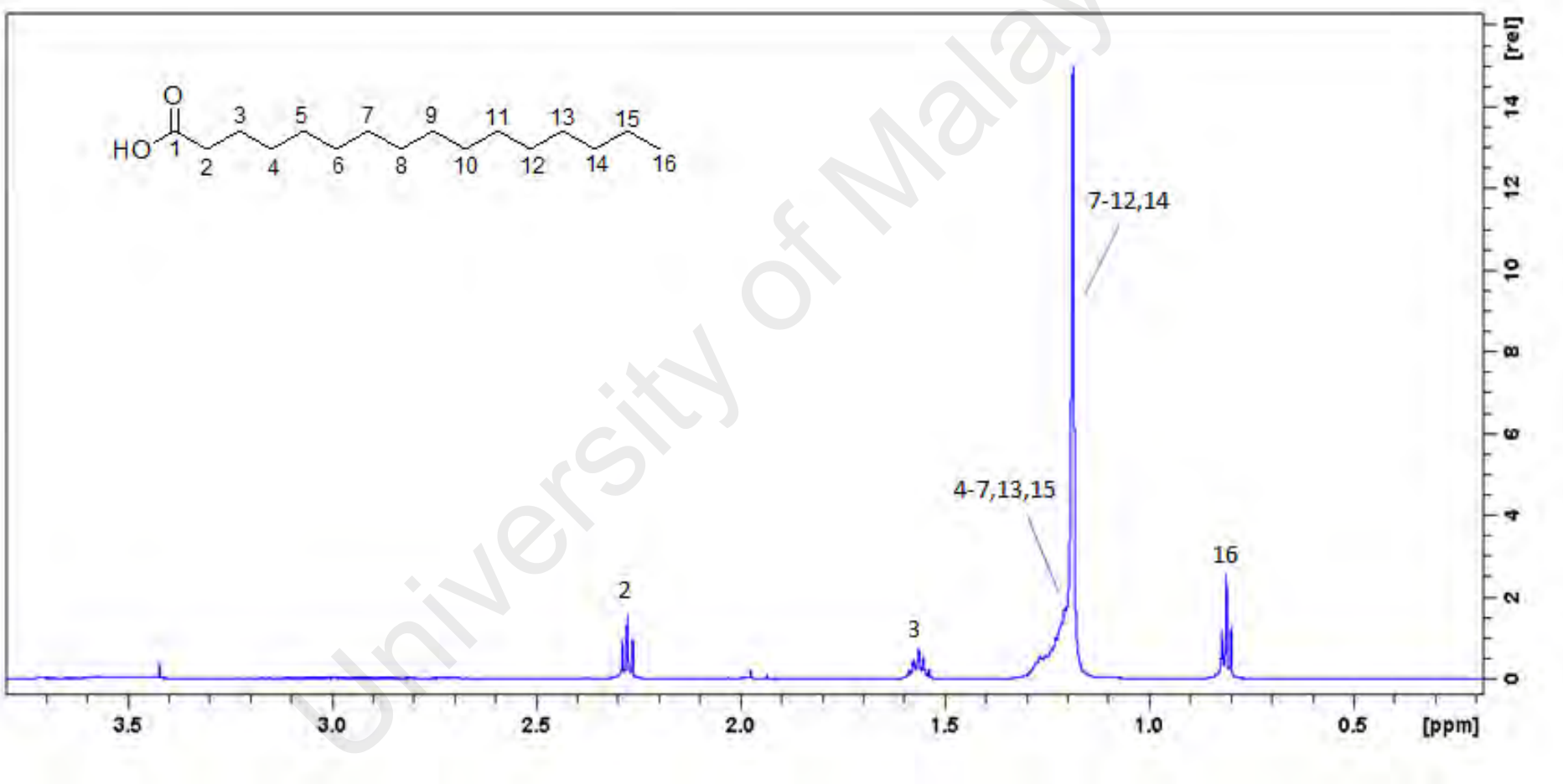


Figure 4.22: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CP8** (Palmitic acid)

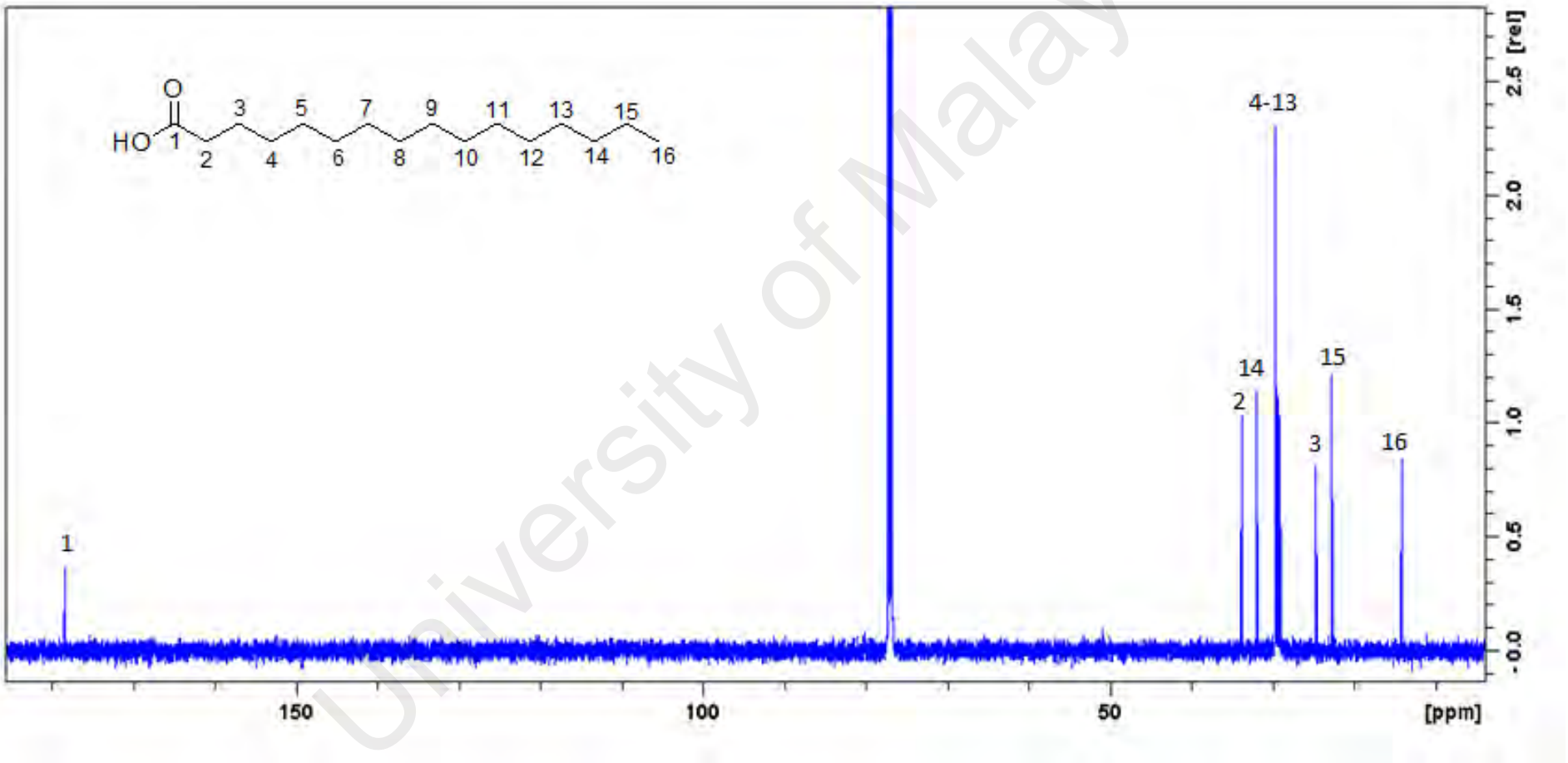
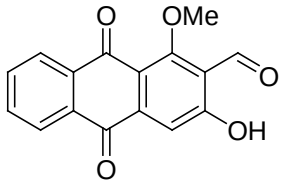


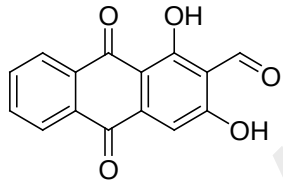
Figure 4.23: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **CP8** (Palmitic acid)

4.2 Compounds isolated from *Morinda citrifolia*

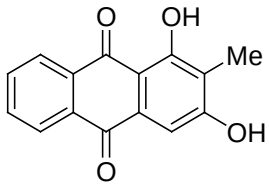
Six compounds were isolated from the chloroform extract of the roots of *M. citrifolia*. The isolated compounds are summarized below.



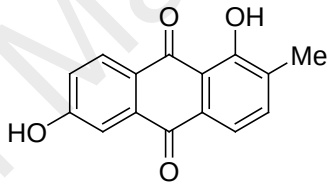
Damnacanthal (**MC1**)



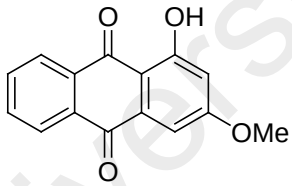
Nordamnacanthal (**MC2**)



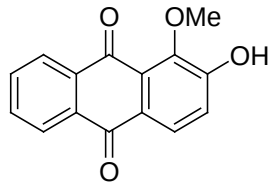
Rubiadin (**MC3**)



1,6-Dihydroxy-2-methylanthraquinone (**MC4**)

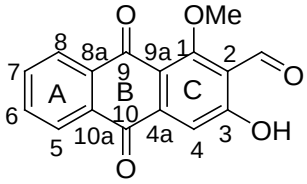


1-Hydroxy-3-methoxyanthraquinone (**MC5**)



1-Methoxy-2-hydroxyanthraquinone (**MC6**)

4.2.1 MC1: Damnacanthal



MC1 was isolated as yellow amorphous powder with molecular formula $C_{16}H_{10}O_5$ as determined by ESI-MS with m/z 281.0 $[M-H]^-$ (calculated for $C_{16}H_{10}O_5$-H, 281.0). The UV spectrum showed absorption maxima at 400, 285, 255, and 210 nm. The IR spectrum indicated the presence of hydroxyl group (3462 cm^{-1}), conjugated carbonyl group (1678 cm^{-1}), and aromatic ring (1575, 1457 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.25 and Table 4.9) revealed the presence of one methoxyl signal at δ_H 4.13 (1-OMe), five resolved aromatic signals at δ_H 7.67 (H-4), 7.77 (H-6), 7.82 (H-7), 8.24 (H-5) and 8.29 (H-8); an aldehyde signal at δ_H 10.46 (2-CHO), and a hydroxyl signal at δ_H 12.27 (3-OH). A set of doublet of doublet (dd) at δ_H 8.24 and δ_H 8.29, integrating for two protons and were assigned to H-5 and H-8, respectively. Another set of triplet of doublets (td) at δ_H 7.77 and δ_H 7.82, integrating for two protons and were assigned to H-6 and H-7, respectively. The COSY experiment gave a partial structure of -CH=CH-CH=CH-, corresponding to (C-5)-(C-6)-(C-7)-(C-8). The observed pattern of these four proton signals in the aromatic region suggested the presence of unsubstituted aromatic moiety at ring A. The isolated aromatic proton at δ_H 7.67 was assigned to H-4 of ring C. Meanwhile, a hydroxyl, a methoxyl and a formyl group were accounted as substituents in ring C.

The ^{13}C NMR spectrum (Figure 4.26 and Table 4.9) showed the presence of 16 carbon signals which included three carbonyl signals at δ_C 195.5 (2-CHO), 181.9 (C-10), and 180.2 (C-9); and one methoxy carbon at δ_C 64.8 (1-OMe). The carbon signal

at δ_C 166.9 (C-1) and 166.7 (C-3) suggested the position of these carbons were adjacent to an oxygen atom.

The HMBC spectrum (Figure 4.24 and Table 4.9) showed the connectivity between ring A and ring B through J^3 correlations from C-5 to H-7, C-6 to H-8, C-7 to H-5, C-8 to H-6, C-8a to H-7, C-9 to H-8, C-10 to H-5, C-10a to H-6; indicating that the connection points of benzene ring with the aliphatic ring were at C-8a and C-10a. While the connectivity between ring C and ring B were observed through J^2 HMBC correlations from C-3 to H-4 and C-4a to H-4; and J^3 HMBC correlations from C-10 to H-4, C-9a to H-4, C-2 to H-4; indicating that the connection points of benzene ring with the aliphatic ring were at C-4a and C-9a. The J^3 HMBC correlations between C-1 and C-3 to 2-CHO, and J^4 HMBC correlation from C-4 to 2-CHO suggested that the position of the carbonyl group were at C-2. The J^3 HMBC correlation from C-1 to 1-OMe suggested that the position of the methoxyl group was at C-1. The experimental data of **MC1** is in agreement with the reported data (Kamiya et al., 2010).

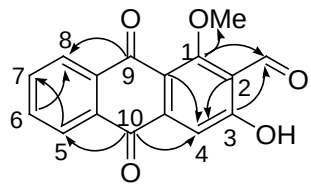


Figure 4.24: Selected HMBC correlations of **MC1** (Damnachantal)

Table 4.9: The NMR ($CDCl_3$, 600 MHz) data of **MC1** (Damnacanthal)

Position	δ_H	δ_C	HMBC
1	-	166.9	1-OMe, 3-OH, 2-CHO
2	-	118.1	4, 3-OH
3	-	166.7	4, 2-CHO
4	7.67 (s)	113.1	3-OH, 2-CHO
4a	-	141.6	4, 3-OH
5	8.24 (dd, 8, 1)	127.4	7
6	7.77 (td, 8, 1)	133.7	8
7	7.82 (td, 8, 1)	134.9	5
8	8.29 (dd, 8, 1)	127.2	6
8a	-	134.9	7
9	-	180.2	8
9a	-	117.7	4
10	-	181.9	4, 5
10a	-	132.5	6
1-OMe	4.13 (s)	64.8	
3-OH	12.27(s)	-	
2-CHO	10.46 (s)	195.5	3-OH

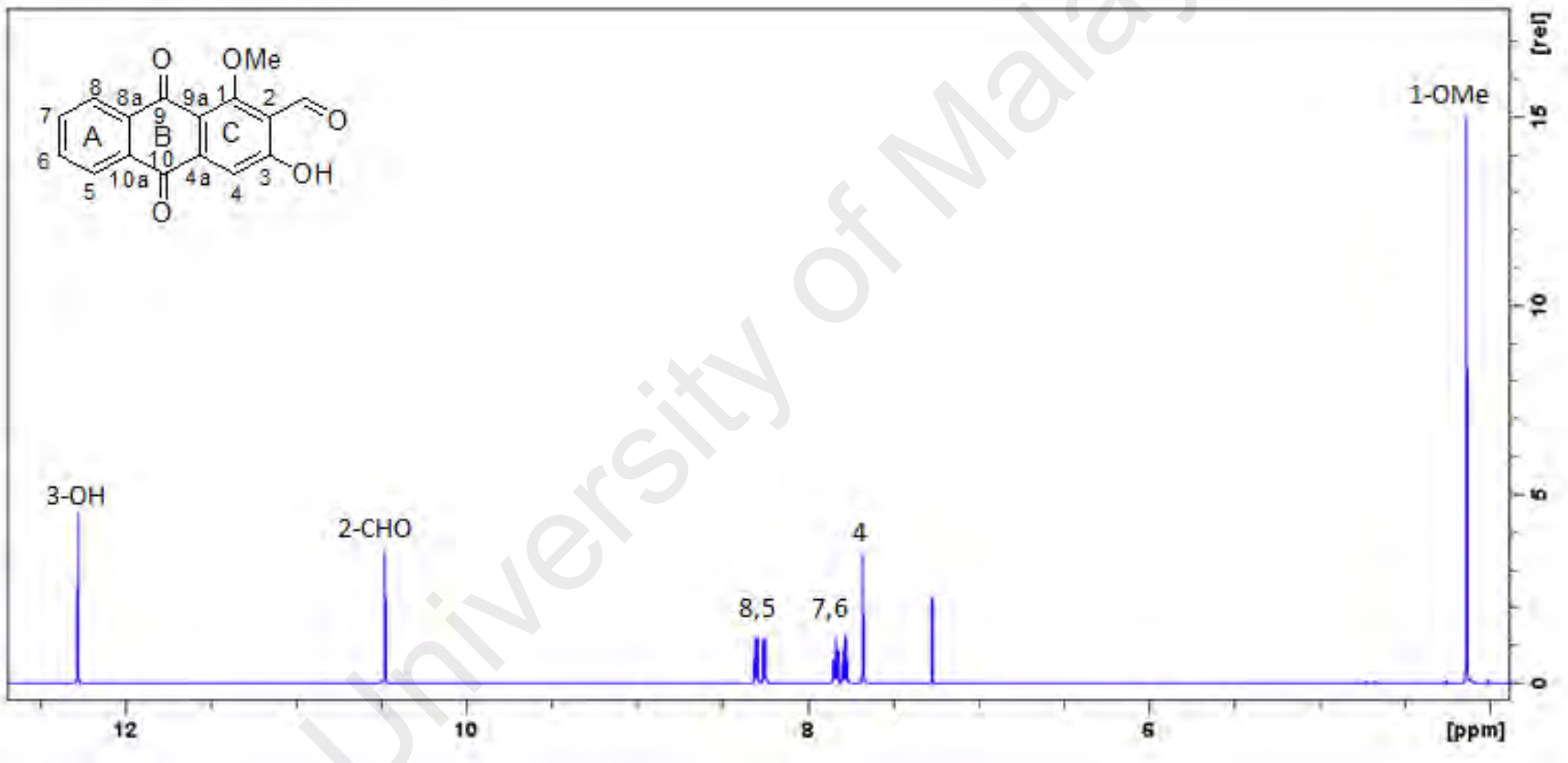


Figure 4.25: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **MC1** (Damnacanthal)

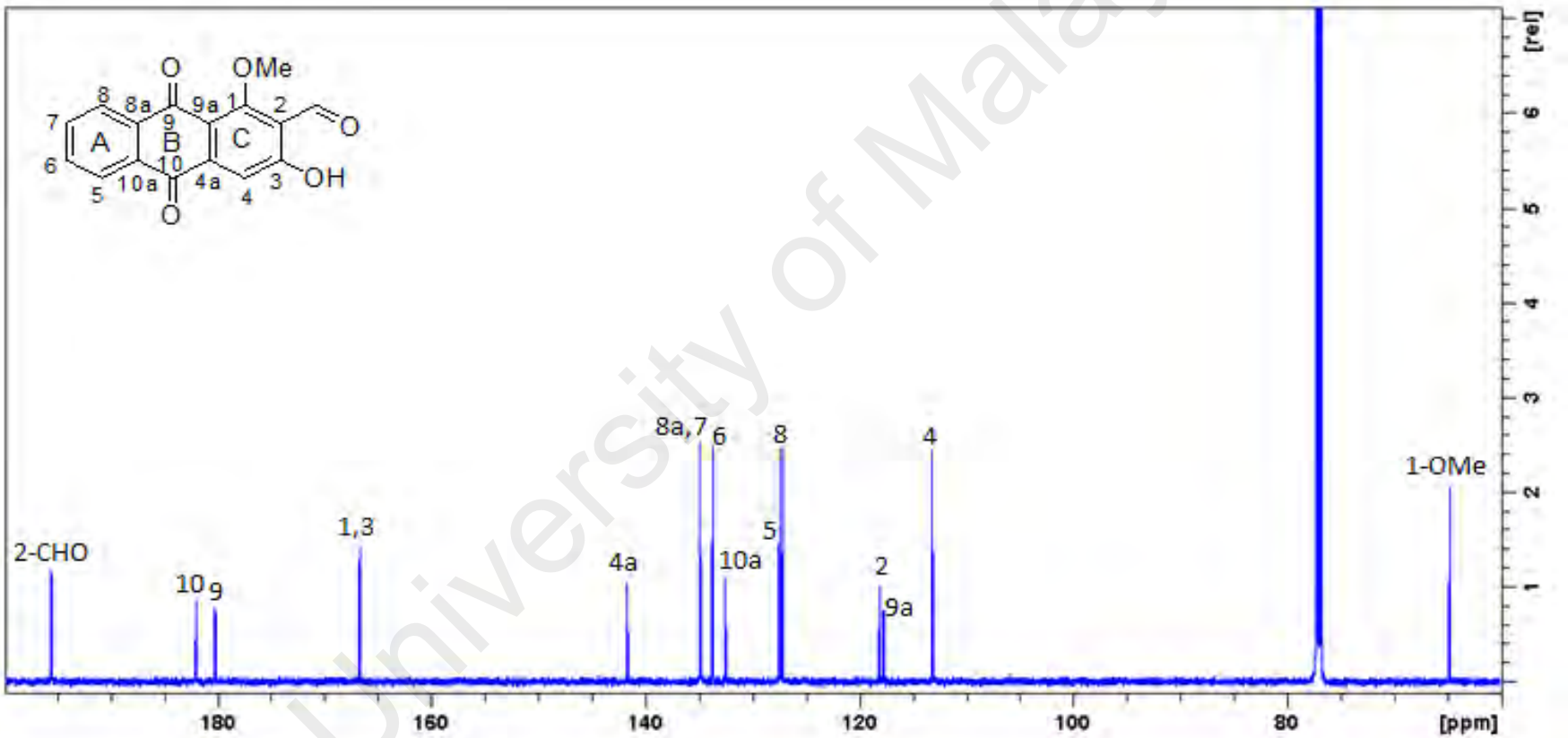
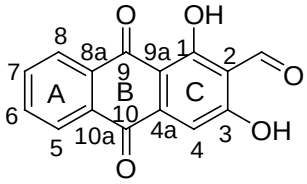


Figure 4.26: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **MC1** (Damnacanthal)

4.2.2 MC2: Nordamnacanthal



MC2 was isolated as yellowish-orange needles with molecular formula $C_{15}H_8O_5$ as determined by ESI-MS with *m/z* 267.0 $[M-H]^-$ (calculated for $C_{15}H_8O_5$-H, 267.0). The UV spectrum showed absorption maxima at 430, 290, 265, and 210 nm. The IR spectrum indicated the presence of hydroxyl group (3075 cm^{-1}), conjugated carbonyl group (1674 cm^{-1}), and aromatic ring (1593, 1574 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.28 and Table 4.10) revealed the presence of four sets of resolved aromatic signals: Two sets of doublet of doublet (dd) at δ_H 8.28 and δ_H 8.31 integrating for two protons and were assigned to H-5 and H-8, respectively; multiplet (m) at δ_H 7.83, integrating for two protons and were assigned to H-6 and H-7, respectively; singlet at δ_H 7.33 (H-4). In addition, an aldehyde proton was observed at δ_H 10.50 (2-CHO), and two hydroxyl signals at δ_H 12.67 (3-OH) and 14.05 (1-OH). The COSY experiment gave a partial structure of -CH=CH-CH=CH-, which corresponds to (C-5)-(C-6)-(C-7)-(C-8). The observed pattern of these four proton signals in the aromatic region suggested the presence of unsubstituted aromatic moiety at ring A. The isolated aromatic proton at δ_H 7.33 (H-4) was assigned to ring C, as well as two hydroxyls and a formyl group. The ^{13}C NMR spectrum (Figure 4.29 and Table 4.10) showed the presence of 15 carbon signals which include three carbonyl signals at at δ_C 194.1 (2-CHO), 186.9 (C-9), and 181.5 (C-10). The carbon signal at δ_C 169.2 (C-1) and 168.3 (C-3) suggested the position of these carbons were adjacent to an oxygen atom.

The HMBC spectrum (Figure 4.27 and Table 4.10) showed the connectivity between ring A and ring B through J^3 correlations from C-5 to H-7, C-6 to H-8, C-7 to H-5, C-8 to H-6, C-8a to H-7, C-8a to H-5, C-9 to H-8, C-10 to H-5, C-10a to H-6 and C-10a to H-8; indicating that the connection points of benzene ring with the aliphatic ring were at C-8a and C-10a. While the connectivity between ring C and ring B were observed through J^3 HMBC correlations from C-10 to H-4, C-9a to H-4, and C-2 to H-4; indicating that the connection points of benzene ring with the aliphatic ring were at C-4a and C-9a. The J^3 HMBC correlations between C-1 and C-3 to 2-CHO; and J^4 HMBC correlations from C-4 and C-9a to 2-CHO suggested that the position of the carbonyl group were at C-2. The experimental data of **MC2** is in agreement with the reported data (Kamiya et al., 2010).

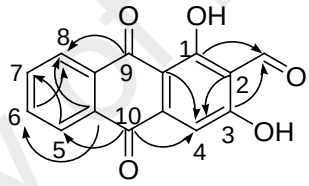


Figure 4.27: Selected HMBC correlations of **MC2** (Nordamnachantal)

Table 4.10: The NMR ($CDCl_3$, 600 MHz) data of **MC2** (Nordamnacanthal)

Position	δ_H	δ_C	HMBC
1	-	169.2	4, 3-OH, 2-CHO
2	-	112.2	4, 1-OH, 3-OH
3	-	168.3	1-OH, 2-CHO
4	7.33 (s)	109.4	1-OH, 3-OH, 2-CHO
4a	-	139.5	3-OH
5	8.28 (dd, 8, 1)	127.8	7
6	7.83 (m)	134.7	8
7	7.83 (m)	134.8	5
8	8.31 (dd, 8, 1)	127.0	6
8a	-	133.2	5, 7
9	-	186.9	8
9a	-	109.1	4, 1-OH, 3-OH, 2-CHO
10	-	181.5	4, 5
10a	-	133.3	6, 8
1-OH	14.05 (s)	-	
3-OH	12.67 (s)	-	
2-CHO	10.50 (s)	194.1	

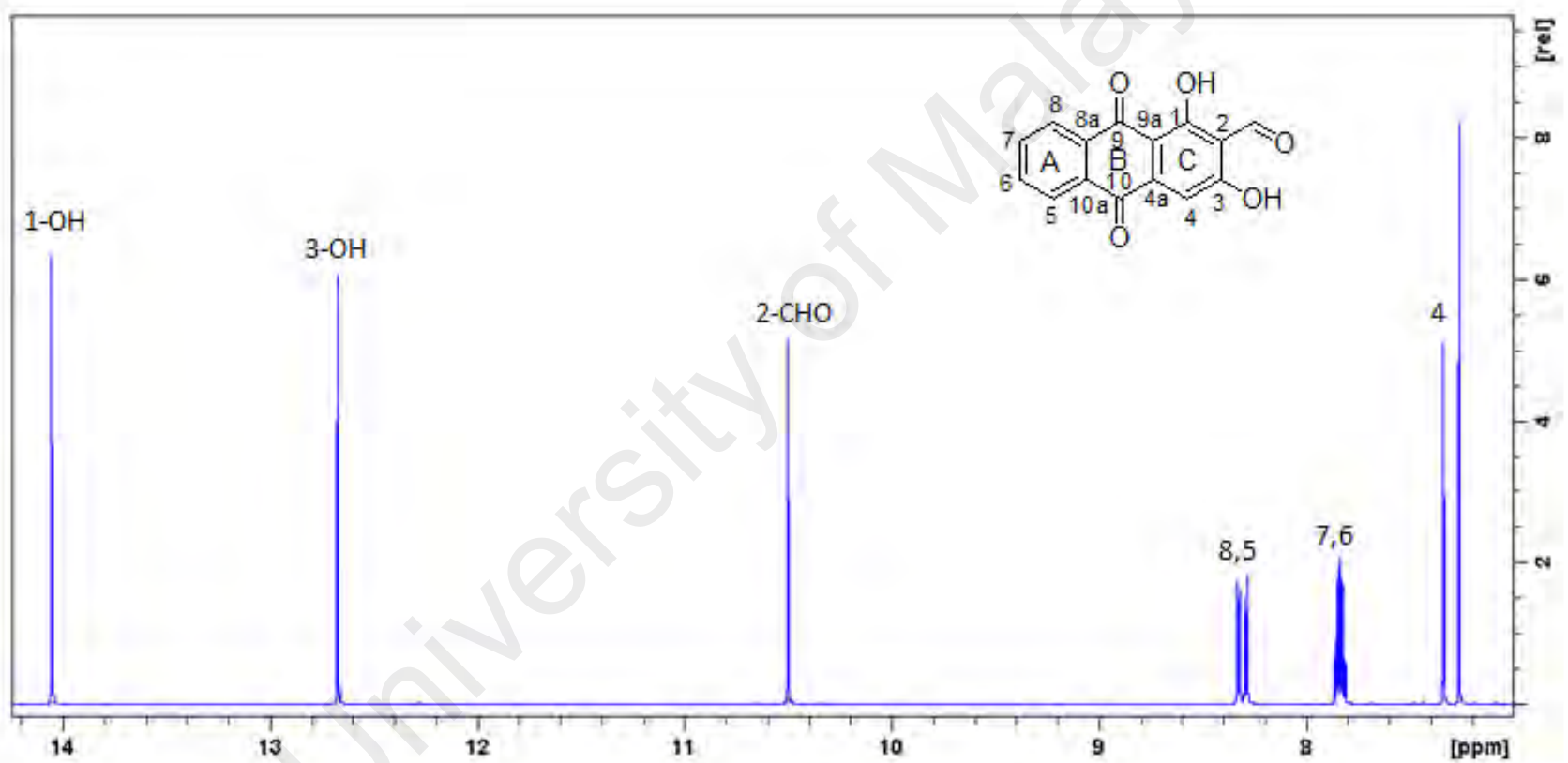


Figure 4.28: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **MC2** (Nordamnacanthal)

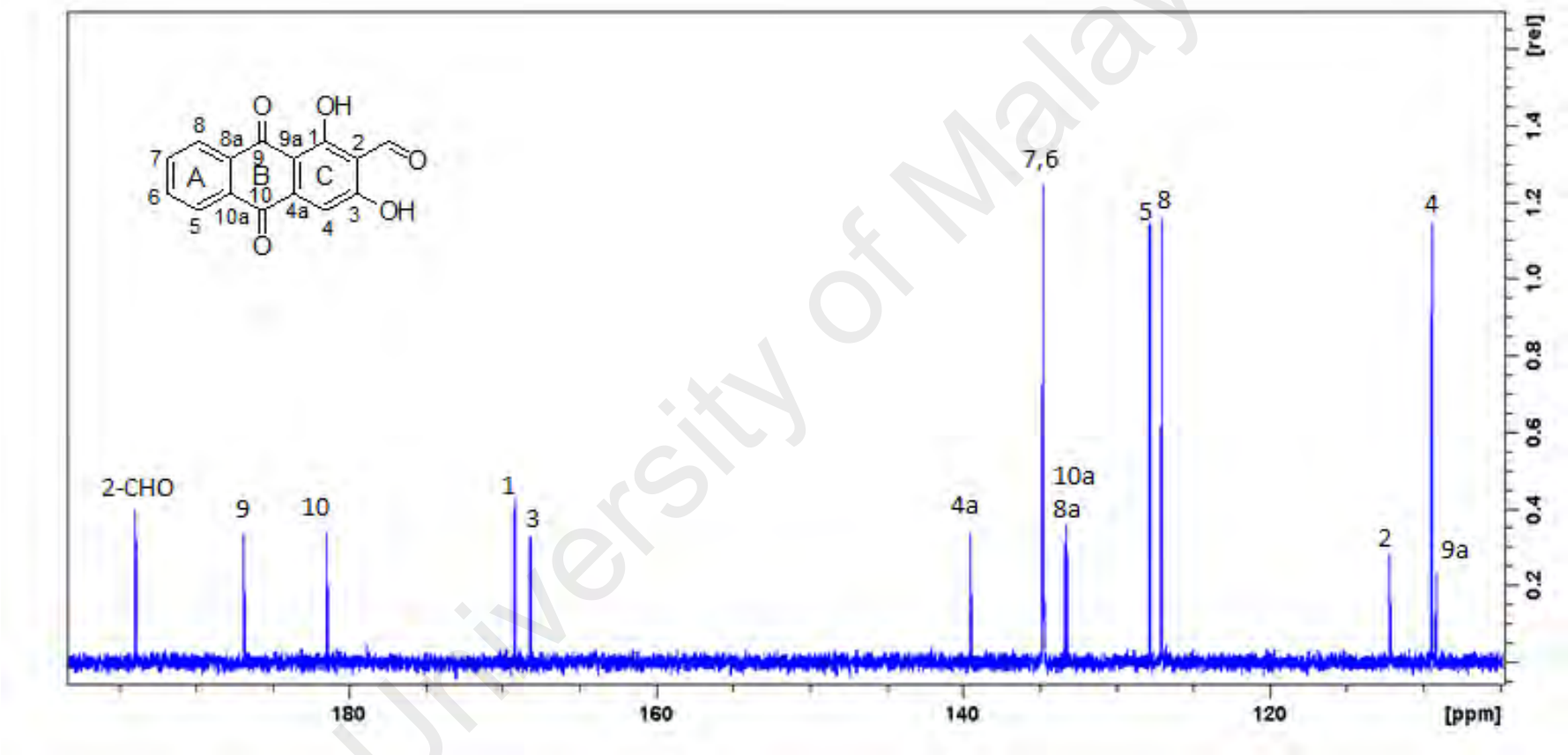
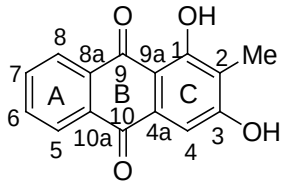


Figure 4.29: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **MC2** (Nordamnacanthal)

4.2.3 MC3: Rubiadin



MC3 was isolated as yellow amorphous powder with molecular formula $C_{15}H_{10}O_4$ as determined by ESI-MS with *m/z* 253.0 $[M-H]^-$ (calculated for $C_{15}H_{10}O_4$-H, 253.1). The UV spectrum showed absorption maxima at 425, 280, 245, and 210 nm. The IR spectrum indicated the presence of hydroxyl group (3391 cm^{-1}), conjugated carbonyl group (1629 cm^{-1}), and the aromatic ring (1593 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.31 and Table 4.11) revealed the presence a methyl signal at δ_H 2.11(2-Me) and one hydroxyl signal at δ_H 13.07 (1-OH). In addition, two sets of doublet of doublet (dd) at δ_H 8.11 and δ_H 8.18, integrating for two protons and were assigned to H-5 and H-8, respectively. Another set of triplet of doublet (td) at δ_H 7.64 and δ_H 7.68, integrating for two protons and were assigned to H-6 and H-7, respectively. The COSY experiment gave a partial structure of -CH=CH-CH=CH-, corresponding to (C-5)-(C-6)-(C-7)-(C-8). The observed pattern of these four proton signals in the aromatic region suggested the presence of unsubstituted aromatic moiety at ring A.

The ^{13}C NMR spectrum (Figure 4.32 and Table 4.11) showed the presence of 15 carbon signals which include two carbonyl signals at δ_C 186.8 (C-9) and 183.7 (C-10); and one methyl signal at δ_C 8.3 (2-Me). The carbon signal at δ_C 163.3 (C-1) and 162.7 (C-3) suggested the position of these carbons were adjacent to an oxygen atom.

The HMBC spectrum (Figure 4.30 and Table 4.11) showed the connectivity between ring A and ring B through J^3 correlations from C-5 to H-7, C-6 to H-8, C-7 to H-5, C-8 to H-6, C-8a to H-5, C-9 to H-8, C-10 to H-5, and C-10a to H-8; indicating that the connection points of benzene ring with the aliphatic ring were at C-8a and C-10a. While the connectivity between ring C and ring B were observed through J^2 HMBC correlations from C-4a to H-4 and J^3 HMBC correlations from C-10 to H-4, C-9a to H-4, and C-2 to H-4; indicating that the connection points of benzene ring with the aliphatic ring were at C-4a and C-9a. The J^3 HMBC correlations between C-1 and C-3 to 2-Me, and J^4 HMBC correlation from C-9a to 2-Me suggested that the position of the methyl group were at C-2. The experimental data of **MC3** is in agreement with the reported data (Lv et al., 2011).

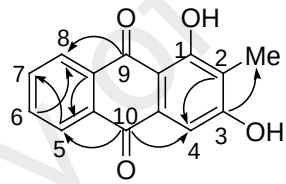


Figure 4.30: Selected HMBC correlations of **MC3** (Rubiadin)

Table 4.11: The NMR ($CDCl_3$, 600 MHz) data of **MC3** (Rubiadin)

Position	δ_H	δ_C	HMBC
1	-	163.3	2-Me
2	-	109.9	4
3	-	162.7	2-Me
4	7.13 (s)	107.8	
4a	-	132.1	4
5	8.11 (dd, 8, 1)	127.2	7
6	7.64 (td, 8, 1)	134.0	8
7	7.68 (td, 8, 1)	134.4	5
8	8.18 (dd, 8, 1)	126.9	6
8a	-	134.4	5
9	-	186.8	8
9a	-	119.2	4, 2-Me
10	-	183.7	4, 5
10a	-	133.5	8
1-OH	13.07 (s)	-	
2-Me	2.11 (s)	8.3	

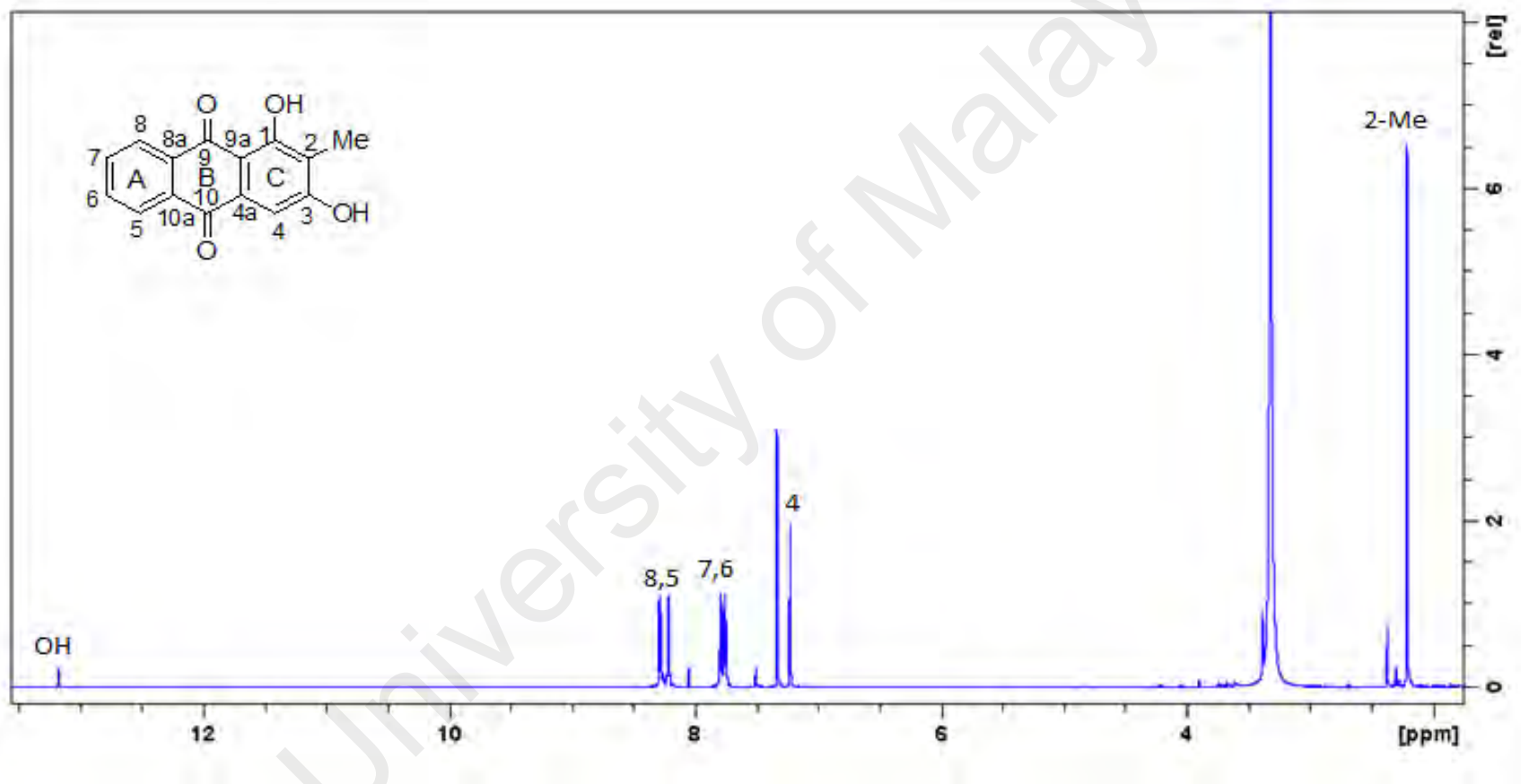


Figure 4.31: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **MC3** (Rubiadin)

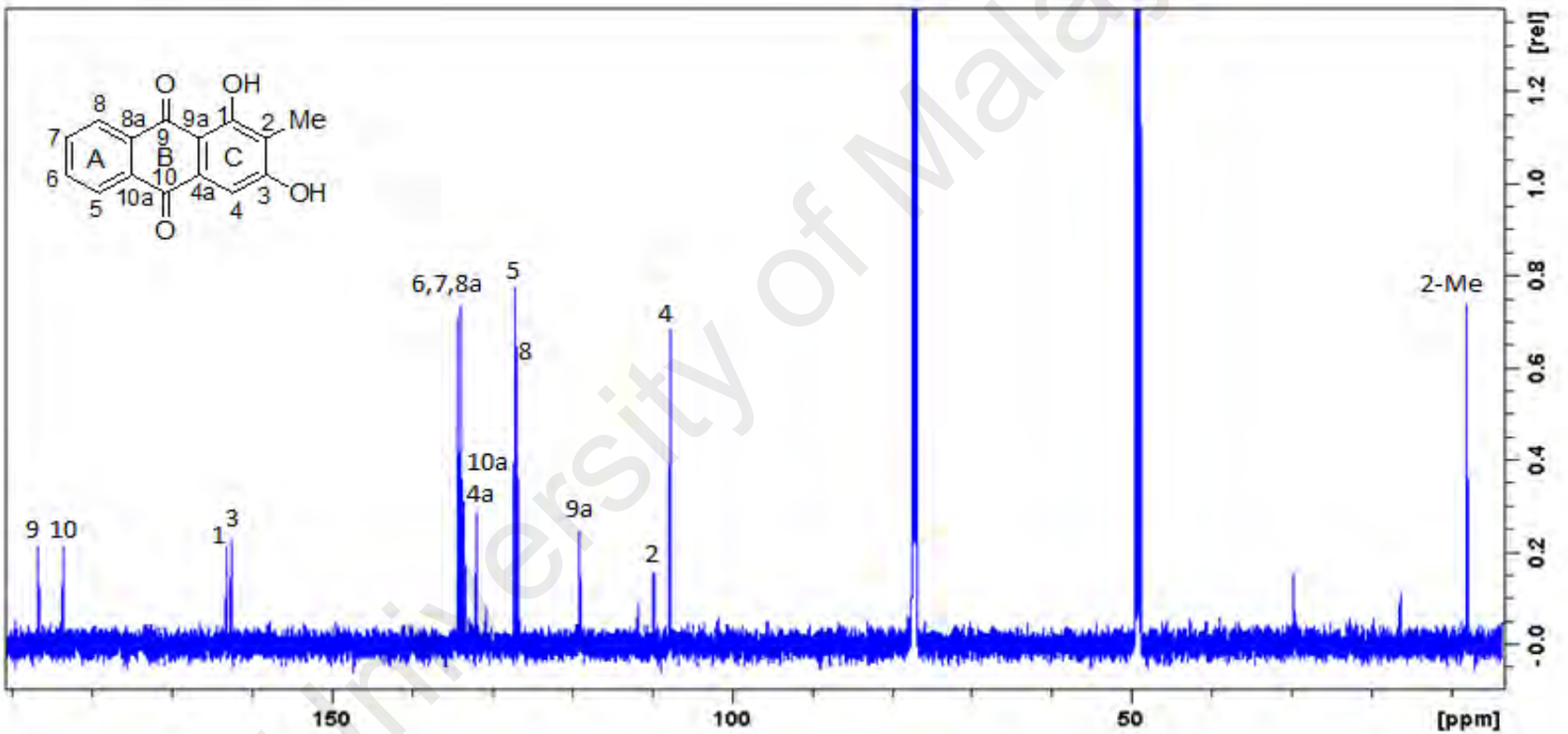
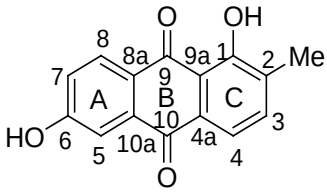


Figure 4.32: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **MC3** (Rubiadin)

4.2.4 MC4: 1,6-Dihydroxy-2-methylanthraquinone



MC4 was isolated as yellowish-orange amorphous powder with molecular formula $C_{15}H_{10}O_4$ as determined by ESI-MS with *m/z* 253.0 $[M-H]^-$ (calculated for $C_{15}H_{10}O_4$-H, 253.1). The UV spectrum showed absorption maxima at 420, 270, and 220 nm. The IR spectrum indicated the presence of hydroxyl group (3419 cm^{-1}), conjugated carbonyl group (1641 cm^{-1}), and aromatic ring (1596, 1451 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.34 and Table 4.12) revealed the presence a methyl signal at δ_H 2.31 (2-Me) and a hydroxyl signal at δ_H 13.11 (1-OH). Two doublets (d) at δ_H 7.11 and δ_H 8.3, integrating for two protons and were assigned to H-7 and H-8, respectively. Two other doublets (d) at δ_H 7.41 and δ_H 7.63, integrating for two protons and were assigned to H-3 and H-4, respectively. The aromatic proton at δ_H 7.49 was assigned to H-5. The COSY experiment confirmed the presence of two partial structures of -CH=CH-, corresponding to (C-3)-(C-4) and (C-7)-(C-8).

The ^{13}C NMR spectrum (Figure 4.35 and Table 4.12) showed the presence of 13 carbon signals which include one carbonyl signal at δ_C 187.5 (C-9); and one methyl signals at δ_C 16.4 (2-Me). The C-8a and C-10 quaternary carbons were not detected in the spectrum due to the minute amount of **MC4** sample. The carbon signals at δ_C 169.1 (C-1) and 170.8 (C-6) suggested that the hydroxyl groups are attached to these carbons.

The HMBC spectrum (Figure 4.33 and Table 4.12) showed the connectivity between ring A and ring B through J^2 correlations from C-6 to H-5 and C-6 to C-7 and J^3 correlations from C-5 to H-7, C-6 to H-8, C-7 to H-5, and H-7, C-9 to H-8, C-10 to H-5, and C-10a to H-8; indicating that the connection points of benzene ring with the aliphatic ring were at C-8a and C-10a. The connectivity between ring C and ring B were observed through J^2 HMBC correlations from C-3 to H-4 and C-4 to H-3 and J^3 HMBC correlations from C-4a to H-3, and C-9a to H-4; indicating that the connection points of benzene ring with the aliphatic ring were at C-4a and C-9a. The J^2 HMBC correlation from C-2 to 2-Me; and J^3 HMBC correlations from C-1 and C-3 to 2-Me suggested that the position of the methyl group were at C-2. The experimental data of **MC4** is in agreement with the reported data (Kamiya et al., 2010).

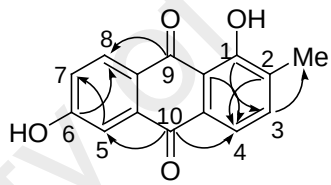


Figure 4.33: Selected HMBC correlations of **MC4** (1,6-Dihydroxy-2-methylanthraquinone)

Table 4.12: The NMR ($CDCl_3$, 600 MHz) data of **MC4** (1,6-Dihydroxy-2-methylanthraquinone)

Position	δ_H	δ_C	HMBC
1	-	169.1	3, 2-Me
2	-	136.6	4, 1-OH, 2-Me
3	7.41 (d, 8)	136.6	4, 2-Me
4	7.63 (d, 8)	119.3	3
4a	-	131.3	3
5	7.49 (s)	113.2	7
6	-	170.8	5, 7, 8
7	7.11 (d, 8)	121.7	5
8	8.13 (d, 8)	130.0	
8a	-	n.d[a]	5, 7
9	-	187.5	8
9a	-	118.5	4
10	-	n.d[a]	4, 5
10a	-	136.7	8
1-OH	13.11 (s)	-	
2-Me	2.31 (s)	16.4	3

[a] n.d. Not detected.

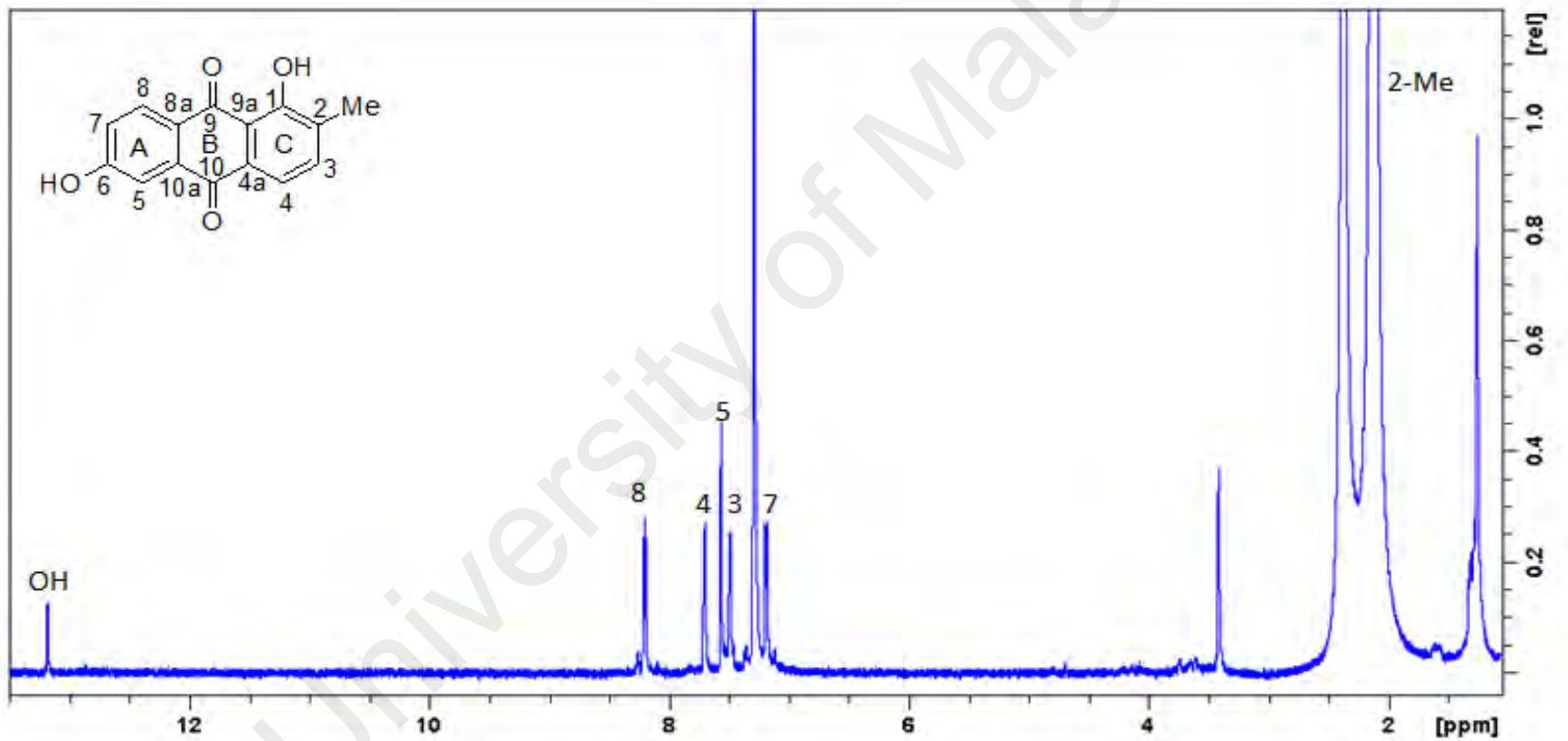


Figure 4.34: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **MC4** (1,6-Dihydroxy-2-methylanthraquinone)

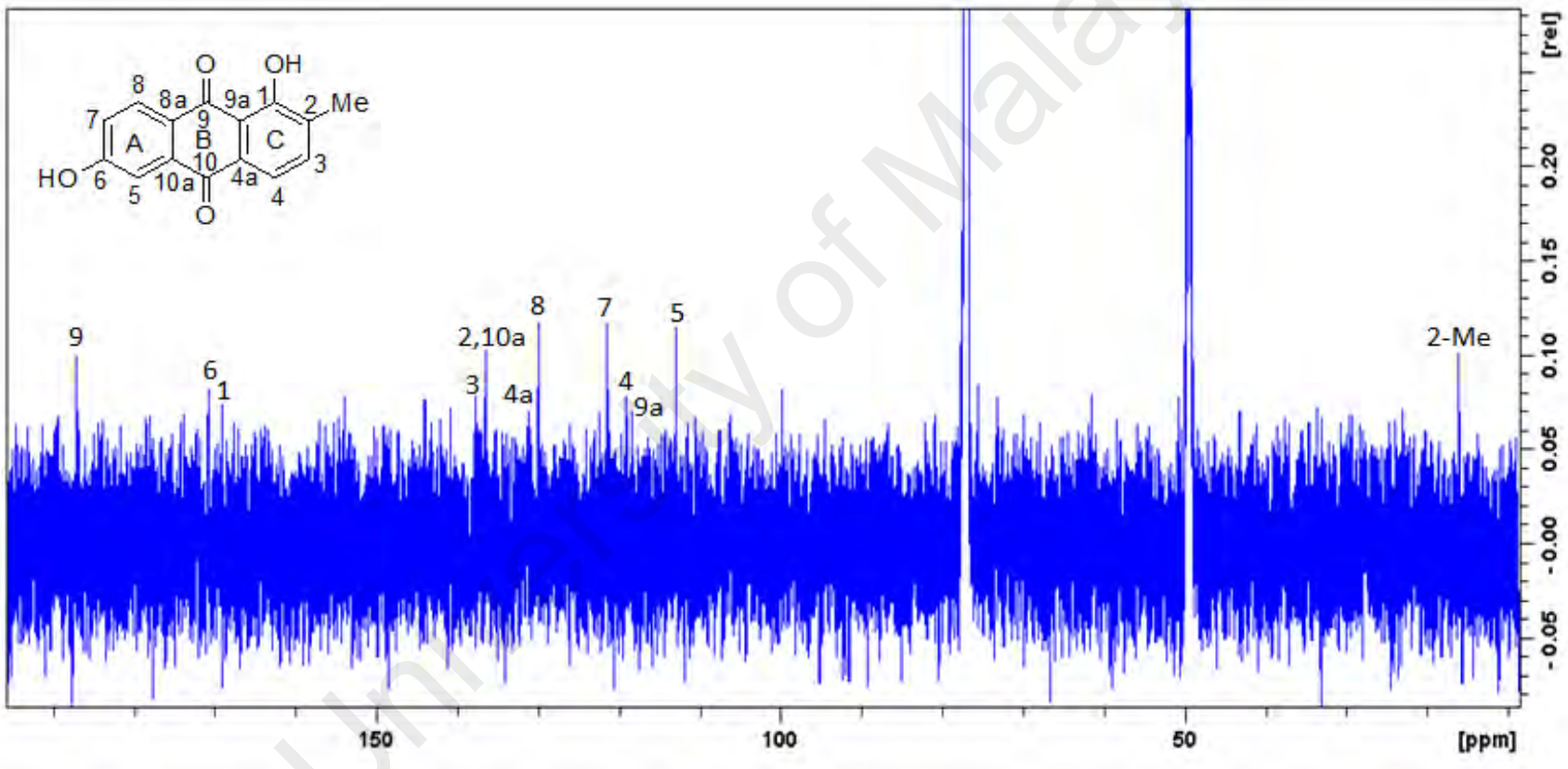
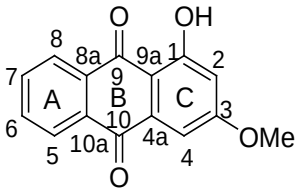


Figure 4.35: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **MC4** (1,6-Dihydroxy-2-methylanthraquinone)

4.2.5 MC5: 1-Hydroxy-3-methoxyanthraquinone



MC5 was isolated as yellow amorphous powder with molecular formula $C_{15}H_{10}O_4$ as determined by ESI-MS with *m/z* 253.0 $[M-H]^-$ (calculated for $C_{15}H_{10}O_4$-H, 253.1). The UV spectrum showed absorption maxima at 420, 340, 255, and 205 nm. The IR spectrum indicated the presence of hydroxyl group (3400 cm^{-1}), methyl group (2926 cm-1), conjugated carbonyl group (1674 cm^{-1}), and aromatic ring (1455 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.36 and Table 4.13) revealed the presence a methoxyl signal at δ_H 3.42 (3-OMe) and a hydroxyl signal at δ_H 13.33 (1-OH). A multiplet (m) signal at δ_H 8.33, integrating for two protons and were assigned to H-5 and H-8. Another multiplet (m) signal at δ_H 7.85, integrating for two protons were assigned to H-6 and H-7. The observed pattern of these four proton signals in the aromatic region suggested the presence of unsubstituted aromatic moiety at ring A. Two aromatic protons at δ_H 6.26 and 7.53 were assigned to H-2 and H-4, respectively on ring C. The hydroxyl and a methoxyl groups were accounted as substituents on ring C. Due to the minute amount of **MC5** sample, a number of the carbon signals were not detected in the ^{13}C NMR spectrum (Table 4.13). Out of 15 carbon atoms, only five carbon signals were detected in the spectrum which are C-4, C-5, C-6, C-7 and C-8.

But due to the limited amount of the compound, the authenticity of this compound was then determined by comparison of the NMR data with the literature.

The experimental data of **MC5** is in agreement with the reported data (Iwao & Kuraishi, 1987).

Table 4.13: The NMR ($CDCl_3$, 600 MHz) data of **MC5** (1-Hydroxy-3-methoxyanthraquinone)

Position	δ_H	δ_C
1	-	n.d.[a]
2	6.26 (s)	n.d.[a]
3	-	n.d.[a]
4	7.53 (s)	108.5
4a	-	n.d.[a]
5	8.33 (m)	127.5
6	7.85 (m)	134.9
7	7.85 (m)	134.9
8	8.33 (m)	127.5
8a	-	n.d.[a]
9	-	n.d.[a]
9a	-	n.d.[a]
10	-	n.d.[a]
10a	-	n.d.[a]
3-OMe	3.42 (s)	n.d.[a]
1-OH	13.33 (s)	

[a] n.d. Not detected.

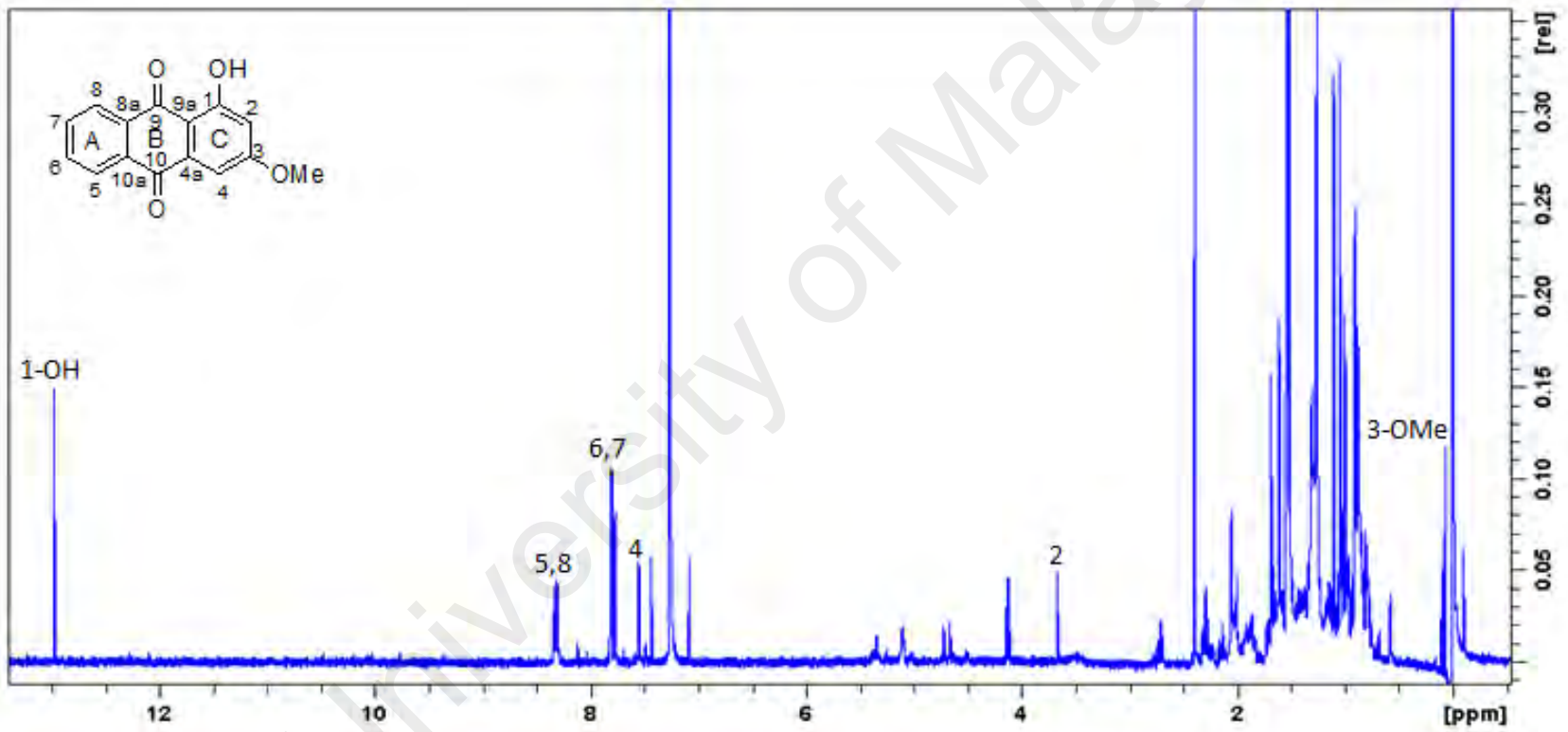
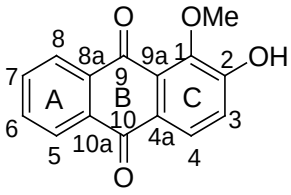


Figure 4.36: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **MC5** (1-Hydroxy-3-methoxyanthraquinone)

4.2.6 MC6: 1-Methoxy-2-hydroxyanthraquinone



MC6 was isolated as yellow amorphous powder with molecular formula $C_{15}H_{10}O_4$ as determined by ESI-MS with *m/z* 253.0 $[M-H]^-$ (calculated for $C_{15}H_{10}O_4$-H, 253.1). The UV spectrum showed absorption maxima at 405, 275, 245, and 205 nm. The IR spectrum indicated the presence of hydroxyl group (3370 cm^{-1}), conjugated carbonyl group (1671 cm^{-1}), and aromatic ring (1573 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.38 and Table 4.14) revealed the presence a methoxyl signal at δ_H 4.01 (1-OMe) and a hydroxyl proton signal at δ_H 13.01 (2-OH). In addition, a set of multiplet (m) at δ_H 8.24, integrating for two protons and were assigned to H-5 and H-8, respectively. Another set of multiplet (m) at δ_H 7.75, integrating for two protons and were assigned to H-6 and H-7, respectively. The COSY experiment gave partial structure -CH=CH-CH=CH-, corresponding to (C-5)-(C-6)-(C-7)-(C-8), suggested the presence of unsubstituted aromatic moiety at ring A. Two sets of doublet (d) aromatic protons at δ_H 7.34 and 8.12 were assigned to H-3 and H-4, respectively on ring C. While the hydroxyl and a methoxyl group were accounted as substituents on ring C. The ^{13}C NMR spectrum (Figure 4.39 and Table 4.14) showed the presence of carbonyl signal at δ_C 181.7 (C-10); and a methoxyl signal at δ_C 62.5 (1-OMe). Carbon signal for C-9 was not detected in the ^{13}C NMR spectrum due to minute amount of **MC6** sample. The carbon signal at δ_C 146.6 (C-1) and 155.3 (C-2) suggested that these carbons are located adjacent to an oxygen atom.

The HMBC spectrum (Figure 4.37, Figure 4.40, and Table 4.14) showed the connectivity between ring A and B through J^3 correlations from C-8a to H-8; and J^3 correlations from the C-5 to H-7, C-6 to H-8, C-8a to H-5, C-10 to H-5, and C-10a to H-8; indicating that the connection points of benzene ring with the aliphatic ring were at C-8a and C-10a. The connectivity between ring C and ring B were observed through J^3 HMBC correlations from C-10 to H-4, C-9a to H-4, and C-2 to H-4; indicating that the connection points of benzene ring with the aliphatic ring were at C-4a and C-9a. The J^3 HMBC correlation from C-1 to 1-OMe suggested that the position of the methoxyl group were at C-1. The experimental data of **MC6** is in agreement with the reported data (Lv et al., 2009).

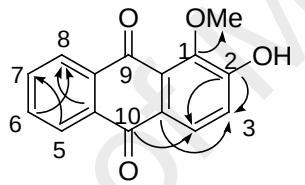


Figure 4.37: Selected HMBC correlations of **MC6** (1-Methoxy-2-hydroxyanthraquinone)

Table 4.14: The NMR ($CDCl_3$, 600 MHz) data of **MC6** (1-Methoxy-2-hydroxyanthraquinone)

Position	δ_H	δ_C	HMBC
1	-	146.6	3, 1-OMe
2	-	155.3[a]	3, 4
3	7.34 (d, 9)	120.4	
4	8.12 (d, 9)	125.9	
4a	-	127.2	3
5	8.24 (m)	126.9	
6	7.75 (m)	134.1	8
7	7.75 (m)	134.2	5
8	8.24 (m)	127.7	
8a	-	134.1	5, 8
9	-	n.d.[b]	
9a	-	125.9	4
10	-	181.7[a]	4
10a	-	134.1	8
1-OMe	4.01 (s)	62.6	
2-OH	13.01 (s)	-	

[a] Value obtained from HMBC spectrum.
[b] n.d. Not detected.

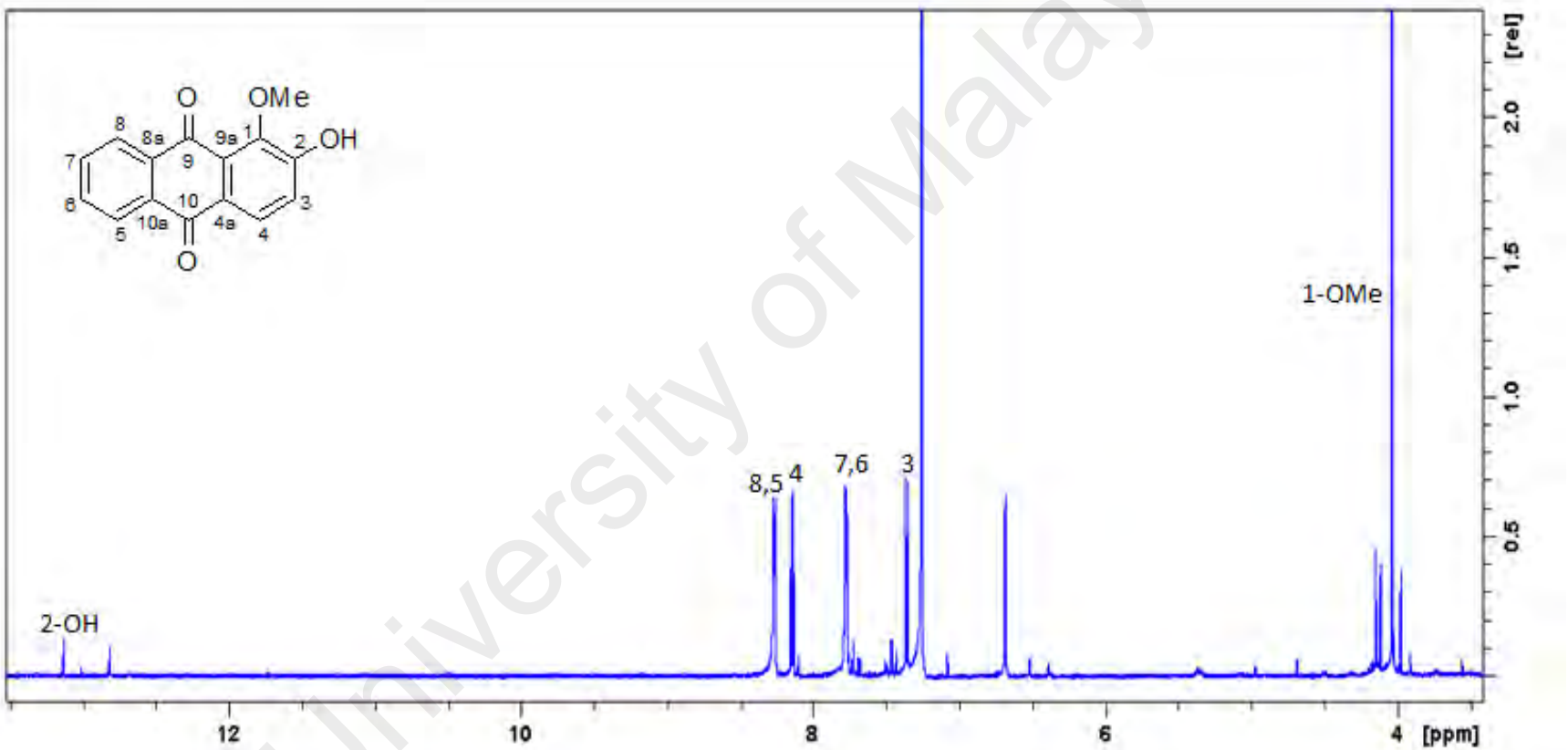


Figure 4.38: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **MC6** (1-Methoxy-2-hydroxyanthraquinone)

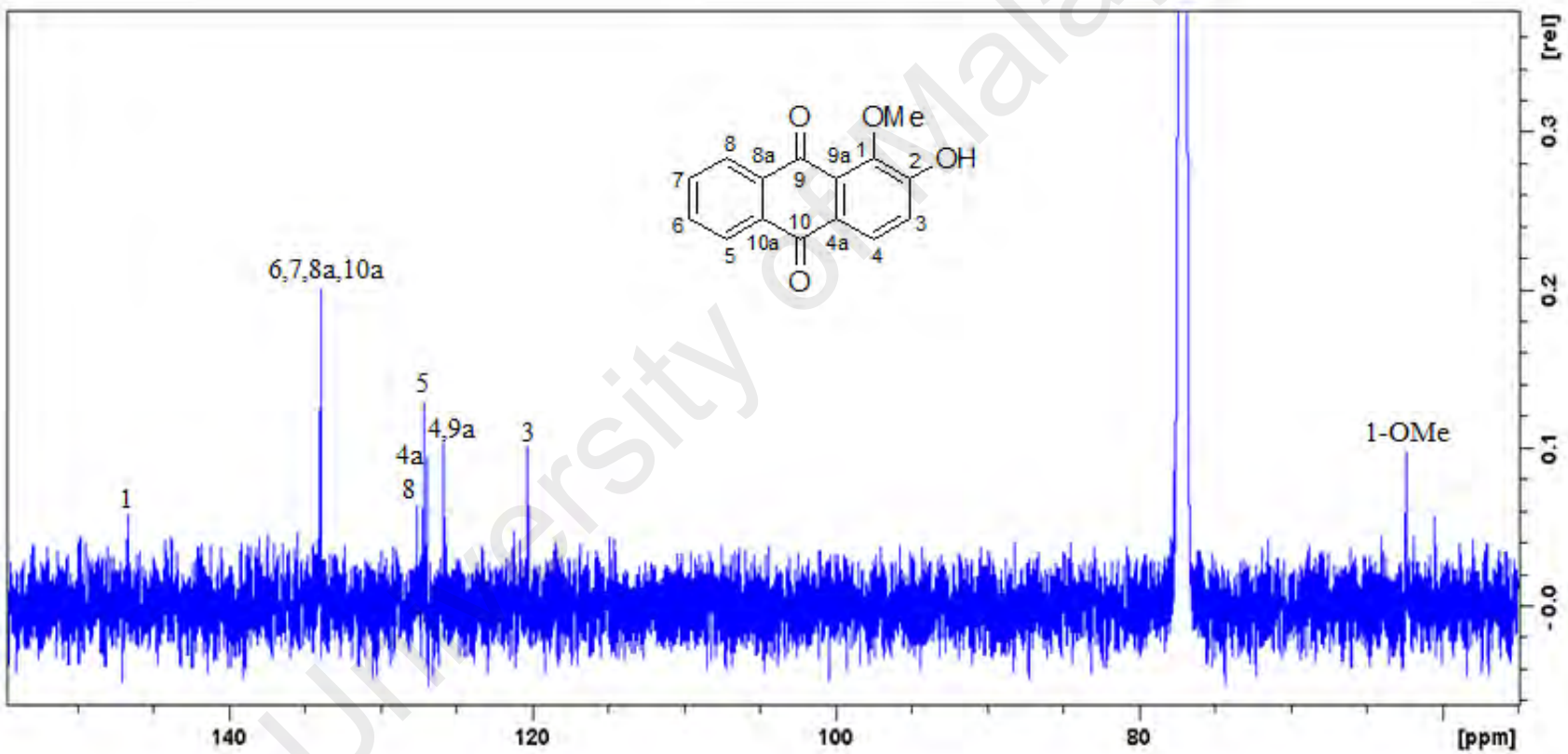


Figure 4.39: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **MC6** (1-Methoxy-2-hydroxyanthraquinone)

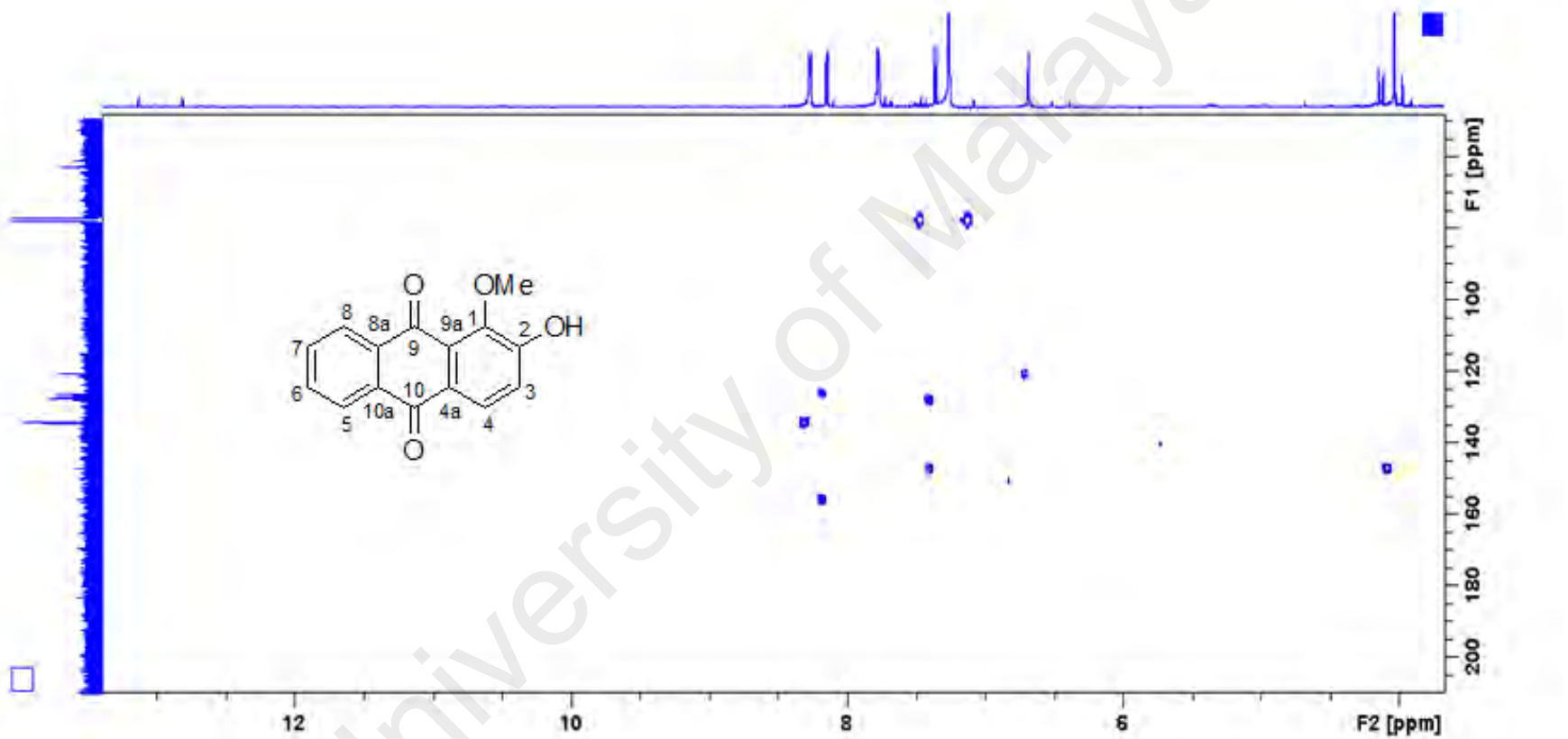
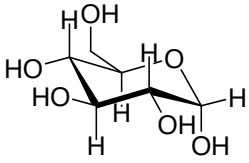


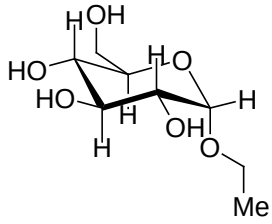
Figure 4.40: HMBC spectrum ($CDCl_3$, 600 MHz) of **MC6** (1-Methoxy-2-hydroxyanthraquinone)

4.3 Compounds isolated from *Chlorophyllum molybdites*

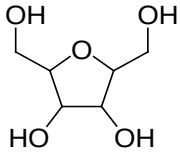
Four compounds were isolated from the ethyl acetate extract of the fruit bodies of *C. molybdites*. The isolated compounds are summarized below.



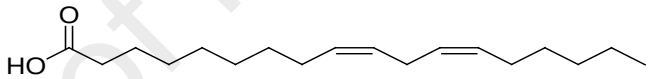
α-D-glucose (**CM1**)



Ethyl-*β*-D-glucopyranoside (**CM2**)



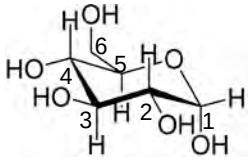
2,5-Anhydro-D-hexitol (**CM3**)



Linoleic acid (**CP5**)

*Note: Linoleic acid (**CP5**) was isolated from both *Crotalaria pallida* and *Chlorophyllum molybdites*. Compound description and data of **CP5** are presented in section 4.1.5 under *Crotalaria pallida* section.

4.3.1 CM1: *α*-D-glucose



CM1 was isolated as white amorphous powder with molecular formula $C_6H_{12}O_6$ as determined by ESI-MS with *m/z* 197.1 $[M\text{-}OH]^+$ (calculated for $C_6H_{12}O_6$+OH, 197.0). The UV spectrum showed absorption maxima at 220 and 260 nm. The IR spectrum indicated the presence of hydroxyl group (3362 cm^{-1}), and hemiacetal group (1049 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.42 and Table 4.15) showed the presence of five methine signals, including an anomeric proton at δ_H 5.13, and two methylene protons at δ_H 3.80 (H-6a) and δ_H 3.84 (H-6b). Of the five methine signals, one signal was observed as doublet (d) at δ_H 5.13 (H-1), two were observed as multiplet (m) at δ_H 3.82 (H-5) and δ_H 3.32 (H-4); and the last two signals were observed as doublet of doublet (dd) at δ_H 3.70 (H-3) and 3.50 (H-2). The ^{13}C NMR spectrum (Figure 4.43 and Table 4.15) showed the presence of six carbon signals consisted of five methine and one methylene carbons. The carbon signal at δ_C 93.61 is typical of an anomeric carbon (C-1) of the glucose moiety. This carbon signal appears as most the deshielded signal which suggested that this carbon is attached to two oxygen atoms.

COSY experiment give a partial structure of -CH(OH)-CH(OH)-CH(OH)-CH-CH(OH)- corresponding to C(2)-C(3)-C(4)-C(5)-C(6). The observed pattern of these protons indicated the presence of pyranosyl ring. The HMBC spectrum (Figure 4.41and Table 4.15) showed J^2 correlations from C-2 to H-1, C-3 to H-4, C-4 to H-5, and C-5 to H-6; and J^3 correlations from C-1 to H-5, C-2 to H-4, C-3 to H-1, C-4 to H-

2, C-5 to H-1 and C-6 to H-4, establish the six membered ring of pyranose and hence confirming the structure of **CM1**. The experimental data of **CM1** is in agreement with the reported data (Agrawal, 1992; Philip & Mytosk, 1974).

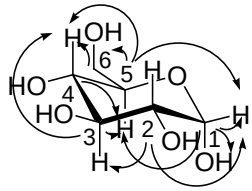


Figure 4.41: Selected HMBC correlations of **CM1** (α-D-glucose)

Table 4.15: The NMR ($CDCl_3$, 600 MHz) data of **CM1** (α-D-glucose)

Position	**δ_H**	**δ_C**	**HMBC**
1	5.13 (d, 4)	93.6	5
2	3.50 (dd, 10, 4)	72.3	1, 3, 4
3	3.70 (dd, 11, 5)	73.1	1, 2, 4, 5
4	3.32 (m)	70.5	2, 3, 5, 6
5	3.82 (m)	71.8	1, 3, 4, 6
6	3.80 (m)	61.2	4, 5
	3.84 (m)		

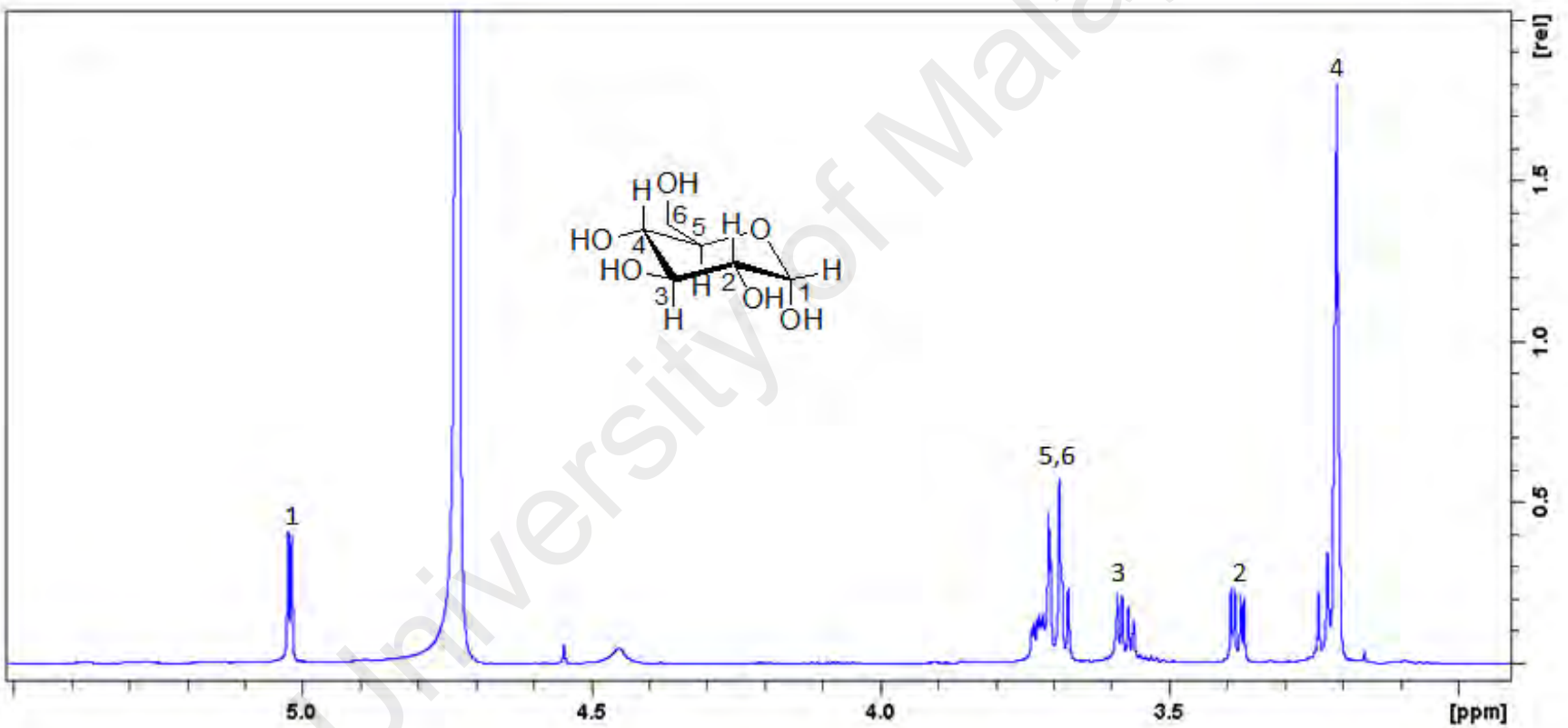


Figure 4.42: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CM1** (α-D-glucose)

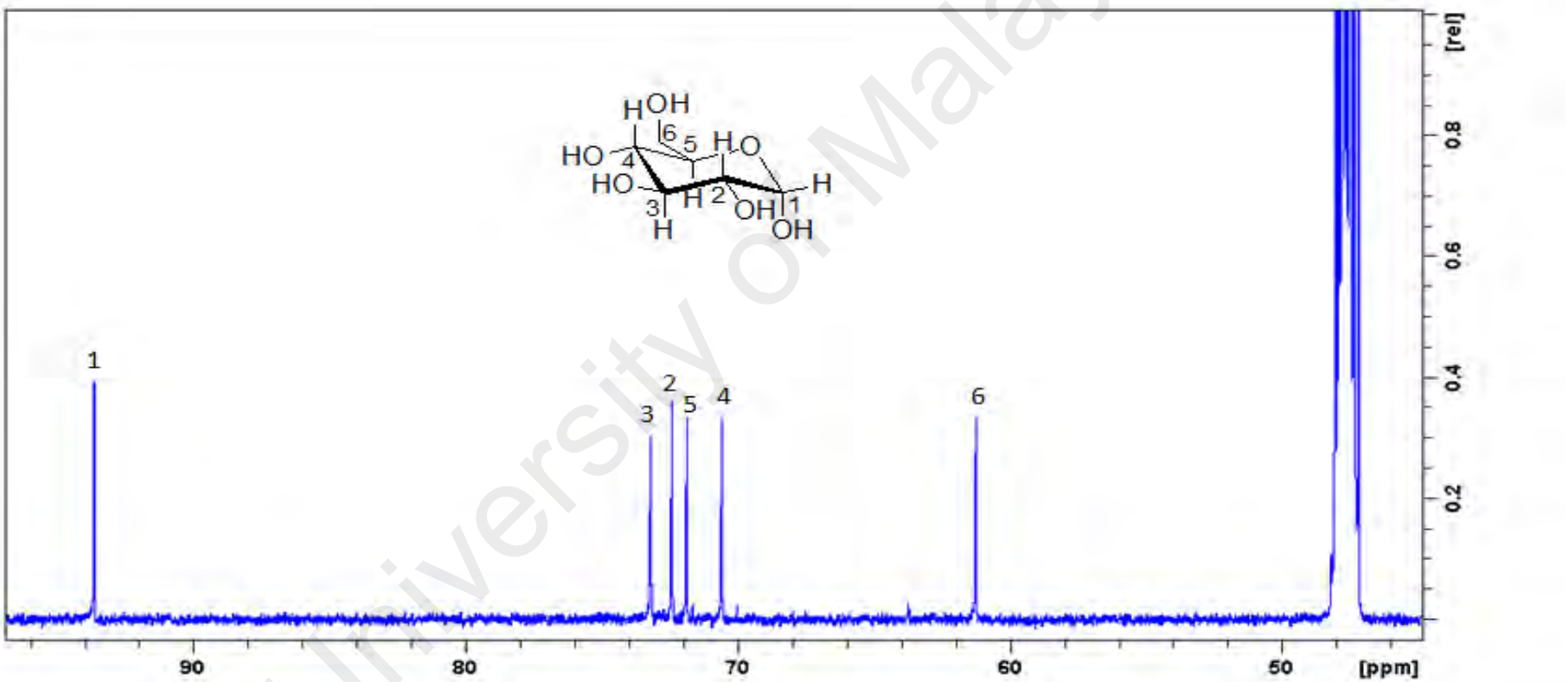
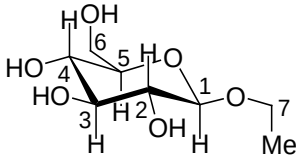


Figure 4.43: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **CM1** (α-D-glucose)

4.3.2 CM2: Ethyl-*β*-D-glucopyranoside



CM2 was isolated as white amorphous powder with molecular formula $C_8H_{16}O_6$ as determined by ESI-MS with *m/z* 225.2 $[M\text{-}OH]^+$ (calculated for $C_8H_{16}O_6$+OH, 225.2). The UV spectrum showed absorption maxima at 223 and 256 nm. The IR spectrum indicated the presence of hydroxyl group (3352 cm^{-1}), and hemiacetal group (1077 cm^{-1}) functionalities.

The ^1H NMR spectrum (Figure 4.45 and Table 4.16) showed the presence of five methines including an anomeric proton at δ_H 4.28, four methylene protons at δ_H 3.97 (H-7a), δ_H 3.63 (H-7b), δ_H 3.87 (H-6a), δ_H 3.68 (H-6b), and one methyl at δ_H 1.25 (7-Me). Of the methine, one signals were observed as doublet (d) at δ_H 4.28 (H-1), one triplet (t) at δ_H 3.36 (H-3), two signals were observed as multiplet (m) at δ_H 3.30 (H-2) and δ_H 3.28 (H-5); and one signal were observed as doublet of doublet (dd) at δ_H 3.18 (H-4).

The ^{13}C NMR spectrum (Figure 4.46 and Table 4.16) showed the presence of eight carbon signals consisted of five methine, two methylenes and one methyl. The carbon signal at δ_C 102.78 is typical of an anomeric carbon (C-1) of the glucose moiety. This carbon appears as the most deshielded carbon which is flanked by two oxygen atoms. The carbon signal at δ_C 14.05 (7-Me) suggested the presence of a methyl group.

COSY experiment give a partial structure of -CH(OH)-CH(OH)-CH(OH)-CH- corresponding to C(2)-C(3)-C(4)-C(5). The observed pattern of these protons indicated the presence of pyranosyl ring. The HMBC spectrum (Figure 4.44 and Table 4.16) showed J^2 correlations from C-1 to H-2, C-2 to H-3, C-3 to H-4, C-4 to H-5, and C-5 to H-6; and J^3 correlations from C-1 to H-5, C-2 to H-4, C-3 to H-1, C-4 to H-2, C-5 to H-1, and C-6 to H-4, establish the six membered ring of pyranose and hence confirming the structure of **CM2**. The J^2 HMBC correlation from C-7 to 7-Me suggested that the position of the methyl group were at C-7. The experimental data of **CM2** is in agreement with the reported data (Agrawal, 1992; Philip & Mytosk, 1974).

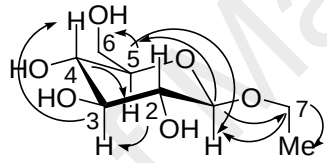


Figure 4.44: Selected HMBC correlations of **CM2** (Ethyl-*β*-D-glucopyranoside)

Table 4.16: The NMR ($CDCl_3$, 600 MHz) data of **CM2** (Ethyl-*β*-D-glucopyranoside)

Position	δ_H	δ_C	HMBC
1	4.28(d, 8)	102.7	2, 5, 7
2	3.30 (m)	73.7	1, 3, 4
3	3.36 (t, 9)	76.7	1, 2, 4, 5
4	3.18 (dd, 9, 1)	70.2	2, 3, 5
5	3.28 (m)	76.5	1, 4, 6
6	3.87 (dd, 12, 3) 3.68 (dd 12, 6)	64.8	4, 5
7	3.97 (dd, 10, 2) 3.63(dd, 7, 3)	61.3	1, 7-Me
7-Me	1.25 (t, 7)	14.0	7

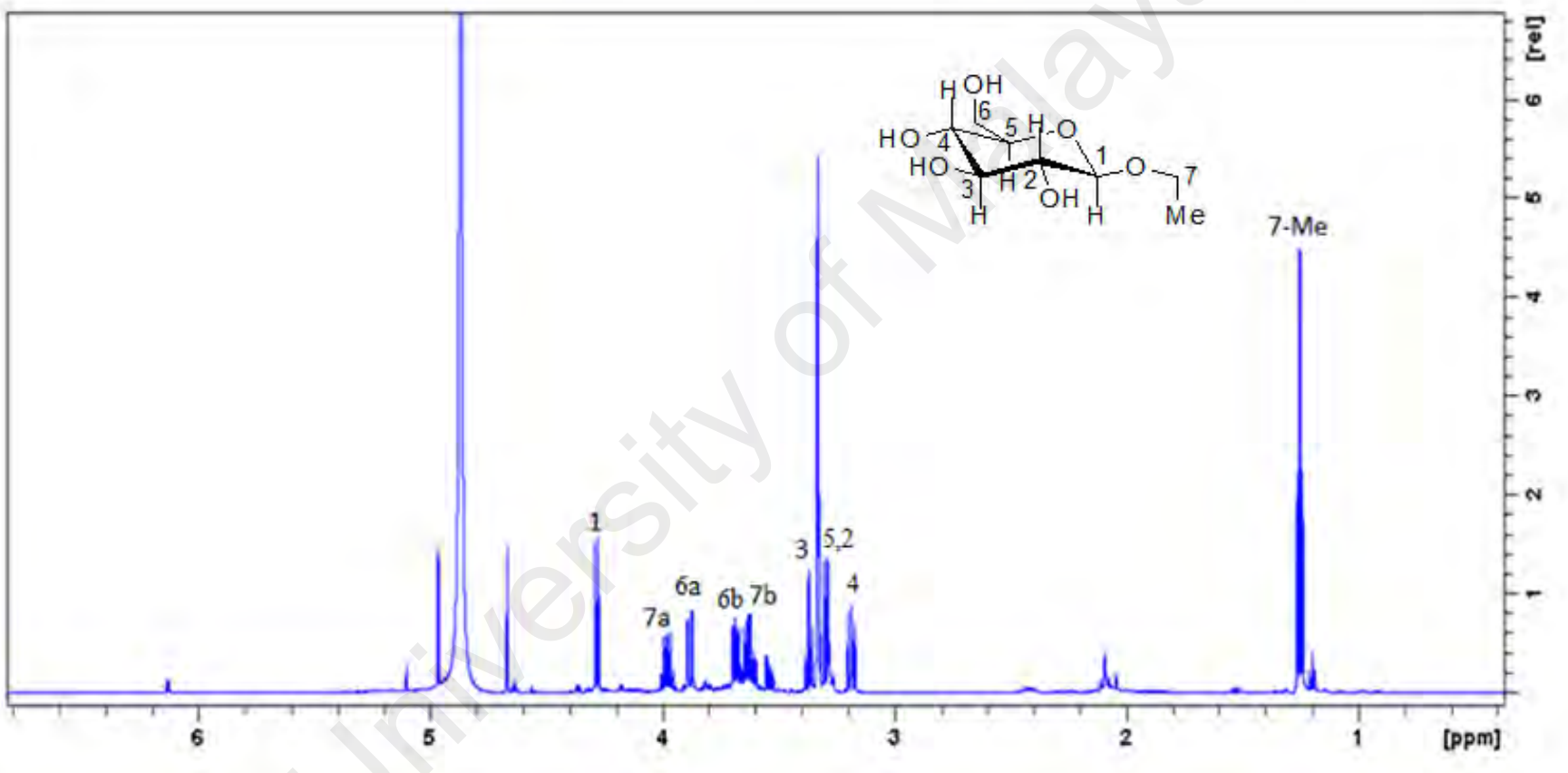


Figure 4.45: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CM2** (Ethyl-*β*-D-glucopyranoside)

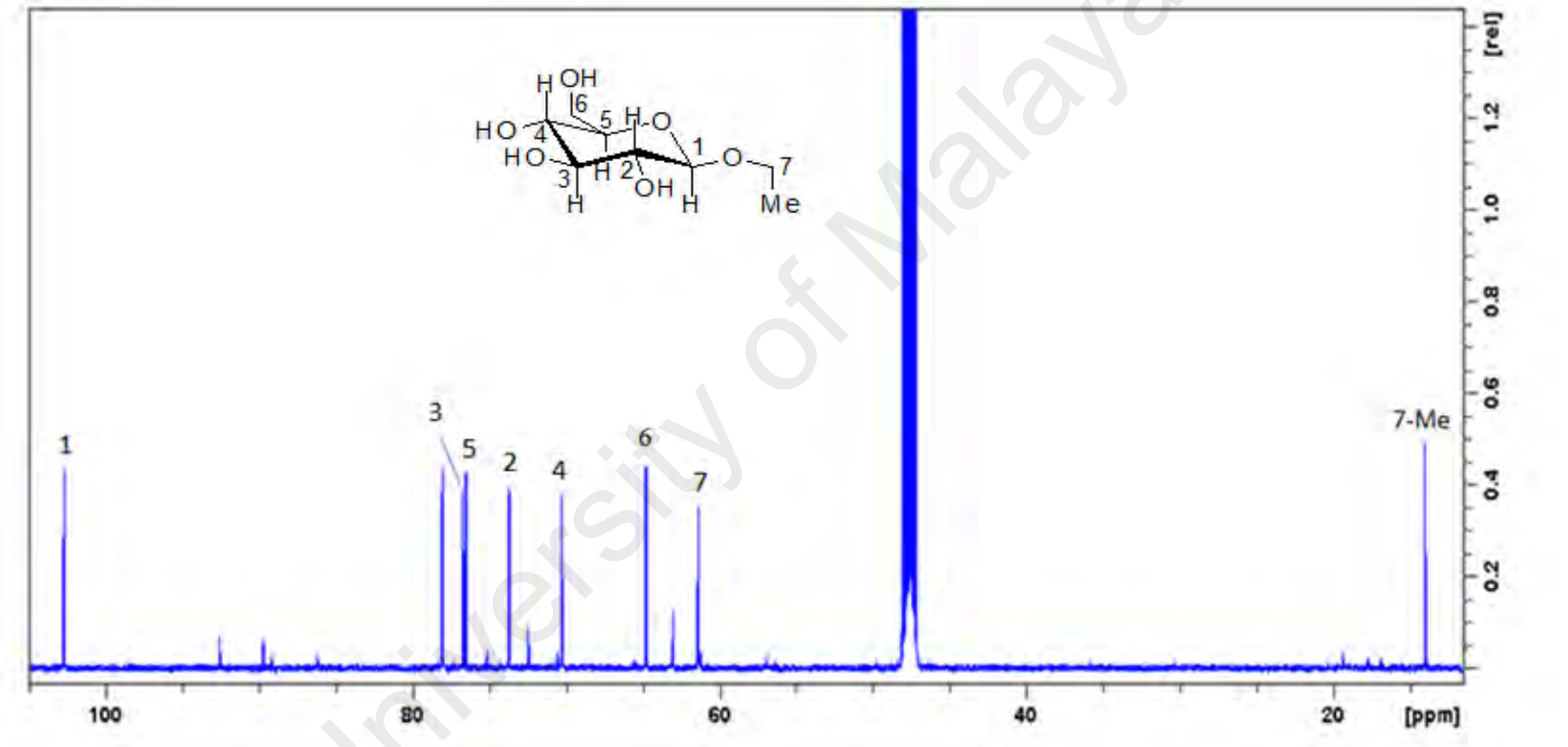
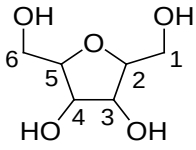


Figure 4.46: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **CM2** (Ethyl-*β*-D-glucopyranoside)

4.3.3 CM3: 2,5-Anhydro-D-hexitol



CM3 was isolated as white amorphous powder with molecular formula $C_{16}H_{12}O_5$. The UV spectrum showed absorption maxima at 220 and 262 nm. The IR spectrum showed absorptions for ether (1081 cm^{-1}) and hydroxyl group (3334 cm^{-1}).

The ^1H NMR spectrum (Figure 4.48 and Table 4.17) showed the presence of two set of methylene signals at δ_H 3.80 (H-1a and H-6a), δ_H 3.64 (H-1b and H-6b) and two methine signals at δ_H 3.77 (H-2 and H-5), δ_H 3.69 (H-3 and H-4). Both methine signals were observed as multiplet (m) while the two methylene signals were observed as doublet of doublet (dd). The ^{13}C NMR spectrum (Figure 4.49 and Table 4.17) showed the presence of three carbon signals consisted of two methines and a methylene. Only three out of the six carbon resonances are visible suggesting **CM3** possesses an axis of symmetry. The HMBC NMR spectrum (Figure 4.47 and Table 4.17) showed J^2 correlations from C-1 to H-2, C-2 to H-1, C-2 to H-3, C-3 to H-2; and J^3 correlations from C-1 to H-3, C-3 to H-1, establish half structure of the **CM3**. The experimental data of **CM3** is in agreement with the reported data (Bock et al., 1981).

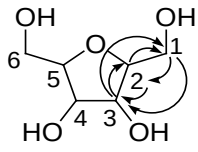


Figure 4.47: Selected HMBC correlations of **CM3** (2,5-Anhydro-D-hexitol)

Table 4.17: The NMR ($CDCl_3$, 600 MHz) data of **CM3** (2,5-Anhydro-D-hexitol)

Position	δ_H	δ_C	HMBC
1	3.80 (dd, 11, 6) 3.64 (dd, 11, 6)	63.7	2, 3, 4, 5
2	3.77 (m)	71.6	1, 3, 4, 6
3	3.69 (m)	69.9	1, 2, 5, 6
4	3.69 (m)	69.9	1, 2, 5, 6
5	3.77 (m)	71.6	1, 3, 4, 6
6	3.80 (dd, 11,6) 3.64 (dd, 11,6)	63.7	2, 3, 4, 5

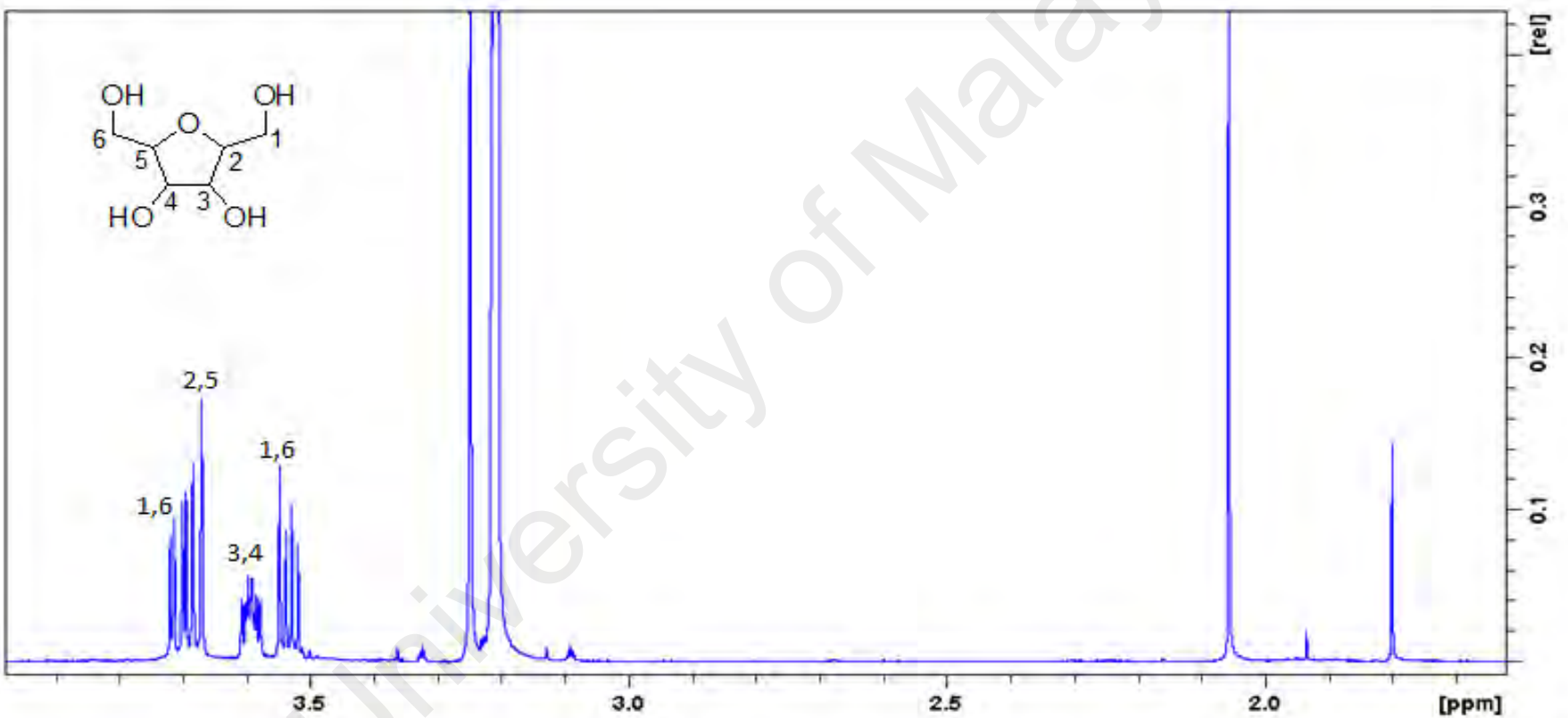


Figure 4.48: ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of **CM3** (2,5-Anhydro-D-hexitol)

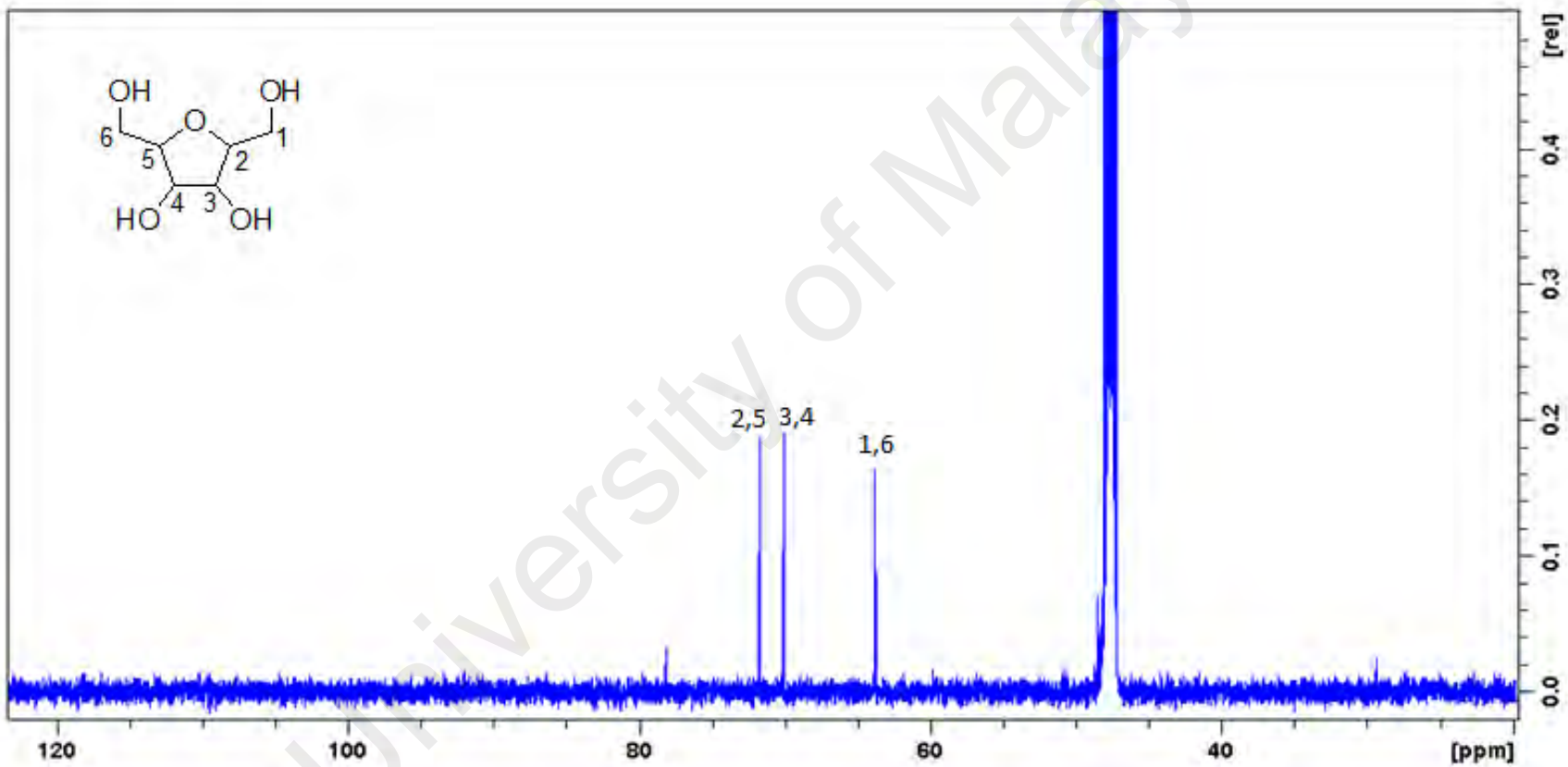


Figure 4.49: ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of **CM3** (2,5-Anhydro-D-hexitol)

CHAPTER 5: CONCLUSION

The chemical constituents of the Malaysia plant *Crotalaria pallida, Morinda citrifolia* and *Chlorophyllum molybdites* were studied. Various classes of compounds were obtained and characterized through a few spectroscopic methods namely NMR, LCMS, UV, and IR.

The phytochemical study on the hexane extract of the plant *Crotalaria pallida* yielded a new compound cyclopentyliene **CP1**, a known furanone derivative **CP2**, and six fatty acids (**CP3**, **CP4**, **CP5**, **CP6**, **CP7**, and **CP8**). This is the first report of the occurrence of **CP2** in this plant species. On the other hand, the phytochemical study on the chloroform extract of the plant *Morinda citrifolia* yielded six known anthraquinones which are **MC1, MC2, MC3, MC4, MC5, and MC6**.

Lastly, the phytochemical study on the ethyl acetate extract of the plant *Chlorophyllum molybdites* yielded three carbohydrate derivatives **CM1**, **CM2** and **CM3,** and a known fatty acid **CP5**. This is the first report of the occurrence of **CM1**, **CM2** and **CM3** in this plant species.

All the eightteen isolated compounds from the hexane extract of *C. pallida,* the chloroform extract of root *M. citrifolia* and the ethyl acetate extract of fruit body *C. molybdites* are summarized in the Table 5.1.

Table 5.1: Compounds isolated from *Crotalaria pallida, Morinda citrifolia* and *Chlorophyllum molybdites*.

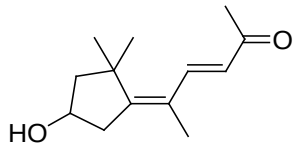
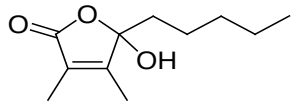
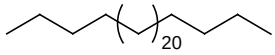
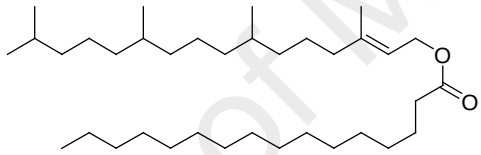
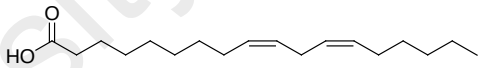
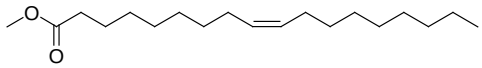
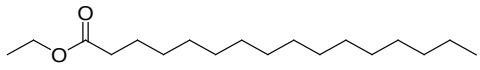
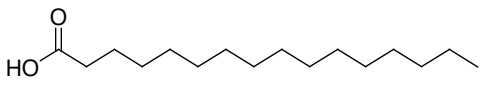
Comp. ID.	Source	Compound structure	Compound name
CP1	*C. pallida*		Crotolidene
CP2			Hydroxydihydrobovolide
CP3			Octacosane
CP4			*Trans*-phytyl palmitate
CP5			Linoleic acid
CP6			Methyl oleate
CP7			Ethyl palmitate
CP8			Palmitic acid

Table 5.1, continued

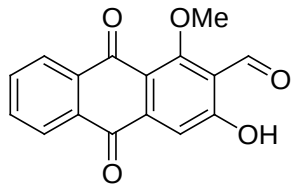
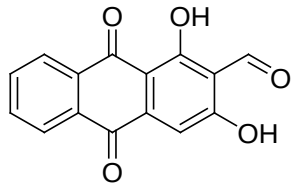
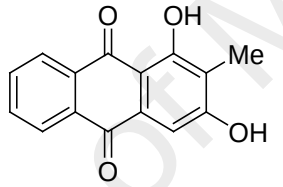
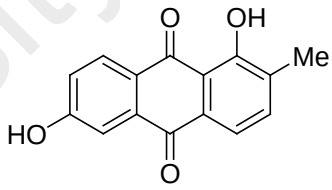
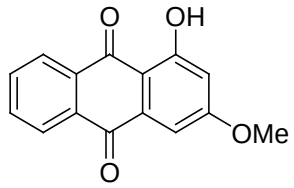
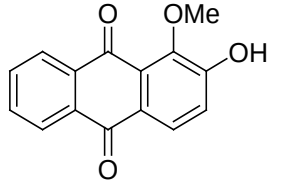
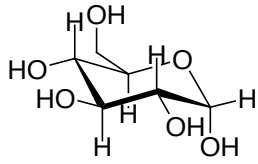
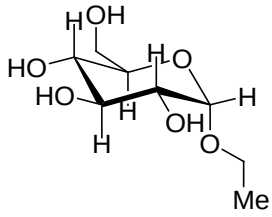
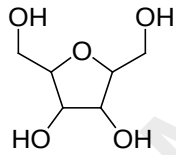
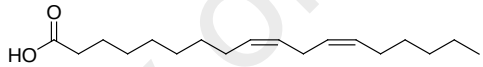
MC1	*M. citrifolia*		Damnacanthal
MC2			Nordamnacanthal
MC3			Rubiadin
MC4			1,6-Dihydroxy-2-methylanthraquinone
MC5			1-Hydroxy-3-methoxyanthraquinone
MC6			1-Methoxy-2-hydroxyanthraquinone

Table 5.1, continued

CM1	*C. molybdites*		α-D-glucose
CM2			Ethyl-β-D-glucopyranoside
CM3			2,5-Anhydro-D-hexitol
CP5			Linoleic acid

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LIST OF PUBLICATIONS AND PAPERS PRESENTED

(a) List of publications

Fadzil, S. R., Yap, A. C., Choo, Y. M. (2017). A new cyclopentylidene and other chemical constituents from Malaysian *Crotalaria pallida*. *Sains Malaysiana, 46*(9), 1581-1586.

(b) List of papers presented

Siti Rabeah Fadzil, Choo Yeun Mun. Chemical constituents from Malaysia *Chlorophyllum molybdites*. 5th International Conference for Young Chemists (ICYC), August 5-7, Penang, Malaysia.