

Table of Contents

	Page
List of Figures	vii
List of Schemes	ix
List of Structures	x
List of Tables	xiii
List of Abbreviations	xiv
Research Goals	xv
I. Medicinal Natural Products	1
1.1 History and Representative Structures	1
1.2 Natural Products In Medicine	4
1.2.1 Natural Products and Anti-infectives	4
1.2.2 Natural Products and Anticancer Agents	7
1.3 Natural Products As a Source of Chemical Diversity	13
1.4 Natural Products and Biodiversity	14
1.5 The ICBG Program	15
1.5.1 Biodiversity Loss and the ICBG Program	15
1.5.2 Plant Collection in the ICBG Program	17
1.6 The Use of Bioassays in Natural Products Research	18
1.6.1 Bioassay Guided Fractionation	18
1.6.2 Operation of the Bioassay	19
1.7 Structure Elucidation	21
1.7.1 Mass Spectrometry	22

1.7.2	Nuclear Magnetic Resonance	22
II.	Cytotoxic benzophenones from <i>Garcinia macrophylla</i> (Clusiaceae)	25
2.1	Introduction	25
2.1.1	Chemical Investigation of <i>Garcinia</i>	25
2.1.2	Structural and Medicinal Properties of Benzophenones	28
2.2	Results and Discussion	30
2.2.1	Isolation of Compounds A , B , and C from <i>Garcinia macrophylla</i>	30
2.2.2	Structural Elucidation of Compound A	33
2.2.3	Structure Elucidation of Compound B	36
2.2.4	The Structure Elucidation of Compound C	58
2.2.5	Biological Evaluation of Friedelin and Guttiferones A and G	60
2.3	Experimental Section	60
III.	The Isolation of Deoxypodophyllotoxin from <i>Bridelia tulasneana</i> (Euphorbiaceae)	64
3.1	Introduction	64
3.1.1	Chemical Investigation of <i>Bridelia</i>	64
3.1.2	The Podophyllotoxins	69
3.2	Results and Discussion	71
3.2.1	Isolation of Compound A from <i>Bridelia tulasneana</i>	71
3.2.2	Structure Elucidation of Compound A from <i>Bridelia tulasneana</i>	73
3.2.3	Biological Evaluation of Deoxypodophyllotoxin	76
3.3	Experimental Section	77

IV. Conclusions	80
Appendix	81
<i>Vita</i>	101

List of Figures

Figure 1.1	The role of natural products in modern medicine.	3
Figure 1.2	The role of natural products in anticancer and anti-infective drugs.	3
Figure 2.1	<i>Garcinia macrophylla</i> .	25
Figure 2.2	Bicyclo[3.3.1]nonane ring system.	28
Figure 2.3	Six possible tautomers of aristophenone.	29
Figure 2.4	HMBC fragment 1.	38
Figure 2.5	HMBC fragment 2.	39
Figure 2.6	HMBC fragment 3.	39
Figure 2.7	HMBC fragment 4.	40
Figure 2.8	HMBC fragment 5.	41
Figure 2.9	HMBC fragment 6.	41
Figure 2.10	HMBC fragment 7.	42
Figure 2.11	Compound B with carbon numbering.	43
Figure 2.12	HMBC correlations of compound B in d ₅ -pyridine.	44
Figure 2.13	Selected NOESY correlations for compound B .	47
Figure 2.14	Selected NOESY correlations for guttiferone A (2.7).	48
Figure 2.15	C23 axial/C24 equatorial chair configuration of guttiferone A.	49
Figure 2.16	C23/C24 axial chair configuration of guttiferone A.	50
Figure 2.17	C23/C24 equatorial boat configuration of compound B .	53
Figure 2.18	C23 equatorial/C24 axial boat configuration of compound B .	54
Figure 2.19	C23 equatorial/C24 axial chair configuration of compound B .	55

Figure 2.20	C23/C24 equatorial chair configuration of compound B .	55
Figure 3.1	The <i>cis</i> -fused ring of picropodophyllin.	70
Figure 3.2	Numbering scheme for deoxypodophyllotoxin.	74

List of Schemes

Scheme 2.1	Fractionation tree for <i>Garcinia macrophylla</i> .	32
Scheme 3.1	Fractionation tree for the isolation of compound A from <i>Bridelia tulasneana</i> .	72

List of Structures

1.1	Strychnine	1
1.2	Morphine	1
1.3	Atropine	2
1.4	Colchicine	2
1.5	Penicillin G	4
1.6	Streptomycin	4
1.7	Chlortetracycline	5
1.8	Erythromycin A	5
1.9	Quinine	6
1.10	Chloroquine	6
1.11	Artemisinin	6
1.12	Spongouridine	7
1.13	Spongothymidine	7
1.14	AZT	7
1.15	Podophyllotoxin	9
1.16	Etoposide	9
1.17	Teniposide	9
1.18	4'-Demethylepipodophyllotoxin	9
1.19	Vinblastine	10
1.20	Vincristine	10
1.21	Paclitaxel (Taxol®)	11

1.22	(+)-Discodermalide	12
1.23	Epothilone A	12
2.1	Aristophenone A	27
2.2	Aristophenone B	27
2.3	Mangostin	27
2.4	Garcinisidone-A	27
2.5	α Methyl (24 <i>E</i>)-3 α ,23-dihydroxy-17,14-friedolanostan-8,14,24-trien-26-oate	28
2.6	Nervosin	28
2.7	Guttiferone A	35
2.8	Guttiferone B	51
2.9	Guttiferone G	56
2.10	Friedelin	59
3.1	Friedelin	65
3.2	Friedelan-3 α -ol	65
3.3	Friedelan-3 β -ol	65
3.4	Sitosterol	65
3.5	Glochidone	66
3.6	24-Methylstanosta-9(11),25-dien-3-one	66
3.7	<i>trans</i> -Triacontyl-4-hydroxy-3-methoxycinnamate	66
3.8	(-)-Ovatolide	66
3.9	Rutin	67
3.10	Myricetin	67
3.11	Gallocatechin-(4'-O-7)-epigallocatechin	67

3.12	3,5-Dicaffeoylquinic acid	67
3.13	1,3,4,5-Tetracaffeoylquinic acid	67
3.14	Deoxypodophyllotoxin	68
3.15	β -Peltatin	68
3.16	β -Peltatin-5- <i>O</i> - β -D-glucopyranoside	68
3.17	5'-Demethoxy- β -peltatin-5- <i>O</i> - β -D-glucopyranoside	68
3.18	Etoposide	69
3.19	Teniposide	69
3.20	Podophyllotoxin	70
3.21	Picropodophyllin	70

List of Tables

Table 2.1	^1H and ^{13}C NMR data for compound A and guttiferone A .	35
Table 2.2	Distances in Å between selected protons for the C23 axial, C24 equatorial configuration.	49
Table 2.3	Distances in Å between selected protons for the C23, C24 equatorial chair configuration.	50
Table 2.4	Distances in Å between selected protons for the C23, C24 equatorial boat configuration.	53
Table 2.5	Distances in Å between selected protons for the C23 equatorial, C24 axial boat configuration.	54
Table 2.6	Distances in Å between selected protons for the C23 equatorial, C24 axial chair configuration.	55
Table 2.7	Distances in Å between selected protons for the C23, C24 equatorial chair configuration.	55
Table 2.8	Summary of expected and observed correlations.	56
Table 2.9	^1H and ^{13}C NMR data for compound A and compound B .	57
Table 2.10	^{13}C NMR data and selected ^1H NMR data of friedelin and compound C .	59
Table 3.1	^1H NMR of Compound A .	75
Table 3.2	^{13}C NMR of Compound A .	75

List of Abbreviations

APT	Attached Proton Test
cc	Column Chromatography
DEPT	Distortionless Enhancement by Polarization Transfer
EtOAc	Ethyl acetate
FABMS	Fast Atom Bombardment Mass Spectrometry
HMBC	Heteronuclear Multiple Bond Correlation
HMQC	Heteronuclear Multiple Quantum Correlation
HRFABMS	High Resolution Fast Atom Bombardment Mass Spectrometry
HSQC	Heteronuclear Single Quantum Correlation
MeOH	Methanol
NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser Enhancement Spectroscopy
ppm	Parts Per Million

Research Goals

The following research is carried out on extracts of higher plants that show cytotoxicity. The goal of this research is to isolate the compound(s) that are responsible for this activity. Following isolation, compound structures are determined using various spectroscopic techniques.

Under the ICBG program, if the compound isolated is of significant interest and goes into clinical use, a percentage of the profits would be returned to the source country as an incentive for biological conservation.