TABLE OF CONTENTS

PAGE

Acknowledgements----ii
Abstract----iii
Table of Contents----vii
List of Tables----xi
List of Figures----xiv
List of Plates----xviii
Acronyms/Abbreviations used in text----xix

CHAPTER ONE: INTRODUCTION **1**

1.1 OBJECTIVES OF STUDY 1
1.2 BOTANY, DISTRIBUTION AND ETHNOBOTANY OF GENERA STUDIED 2
1.2.1 Annonaceae family *3*
1.2.2 The genus Goniothalamus 5
1.2.2.1 *Goniothalamus andersonii* 7
1.2.2.2 *Goniothalamus dolichocarpus* 7
1.2.2.3 *Goniothalamus malayanus* 10
1.2.2.4 *Goniothalamus velutinus* 10
1.2.2.5 *Goniothalamus macrophyllus* 11
1.2.2.6 *Goniothalamus ridleyi* 11
1.2.2.7 *Goniothalamus uvarioides* 13
1.2.2.8 *Goniothalamus umbrosus* *13*
1.2.3 The Genus Mezzetia 14
1.2.3.1 *Mezzetia umbellata* *14*
1.2.4 The Genus Disepalum 17
1.2.4.1 *Disepalum anomalum* 17
1.3 CHEMISTRY OF THE ANNONACEAE: A LITERATURE REVIEW *17*
1.3.1 Non-alkaloidal constituents of Annonaceae 18
1.3.1.1 Terpenes and aromatic compounds 18
Monoterpenes 18
Sesquiterpenes 19
Diterpenes 19
Triterpenes, sterols and saponins 20
Aromatic compounds *20*
1.3.2 Alkaloids of Annonaceae 20
Oxoaporphines 23
4,5 - Dioxoaporphine 26
Aristolochic acid and aristolactams *31*
1.3.3 Styrylpyrones of the genus Goniothalamus 31
1.3.3.1 Goniothalamin *39*
1.3.4 Annonaceous acetogenins from the family Annonaceae 41
1.3.4.1 Structural classes of acetogenins 48
A. Acetogenins with adjacent bis-tetrahydrofuran ring 50
B. Mono tetrahydrofuran annonaceous acetogenins 54
C. Tri-THF annonaceous acetogenin 54
D. Non-adjacent bis-THF acetogenin 55
E. Non-THF acetogenins 56
1.3.4.2 Extraction, isolation and dosage methods 56

1.3.4.3 Structural elucidation of acetogenins 57
1.3.4.4 Stereochemistry 58
1.3.4.5 Biosynthesis 63
1.3.4.6 Biological activity of annonaceous acetogenins 67
1.3.4.6.1 Cytotoxicity activity and antitumour 68
1.3.4.6.2 Pesticidal activity of annonaceous acetogenins 74
1.3.5 Annonaceous acetogenins from the genus Goniothalamus 76
1.3.6 Alkaloids from the genus Goniothalamus 77
1.3.7 Compounds isolated from the genera Disepalum and Mezzetia 79

CHAPTER TWO: BIOASSAY TECHNIQUES 81

2.1 THE PURPOSE OF BIOLOGICAL ASSAYS 81
2.2 A NEED TO STUDY BIOACTIVITIES OF NATURAL PRODUCTS 82
2.3 BENCHTOP BIOASSAYS COMMONLY USED - A REVIEW 84
2.3.1 Brine shrimp lethality test 85
2.3.2 The Potato disc bioassay (inhibition of crown gall tumours) 85
A. Preparation of *Agrobacterium tumefaciens* (two days before assays) 86
B. Procedure for bioassay 86
2.3.3 Lemna minor (duckweed): A bioassay for inhibitors and promotors of plant growth (McLaughlin et al., 1991) 88
2.3.4 The susceptibility or resistance of mosquito larvae to insecticides tests (WHO/VBC/81.807) 89
A. Establishing the base-line 89
B. Procedure for carrying out bioassays 89
C. Results 91
D. Estimation of the median effective dose 92
E. Fitting a probit regression line 94
2.4 BIOACTIVITIES OF THE STYRYLPYRONES FROM THE GENUS *GONIOTHALAMUS* 98
2.5 BIOACTIVITIES OF ACETOGENINS FROM THE GENUS *GONIOTHALAMUS* 101

CHAPTER THREE: EXPERIMENTAL 105

3.1 PLANT MATERIALS 105
3.2 INSTRUMENTS 105
3.2.1 Melting points 105
3.2.2 Optical rotations 105
3.2.3 Infrared spectroscopy 105
3.2.4 Ultraviolet spectroscopy 105
3.2.5 NMR spectroscopy 106
3.2.6 Mass spectroscopy 106
3.2.7 High performance liquid chromatography 106
3.2.8 Gas chromatography 106
3.2.9 Gas Chromatography-Mass Spectrometry 106
3.3 CHROMATOGRAPHIC METHODS 107
3.3.2 Thin layer chromatography 108
3.3.3 Preparative layer chromatography (PLC) 108
3.3.4 Centrifugal thin layer chromatography (Chromatotron) 109
3.3.5 Spray reagents 110
3.4 BIOASSAY PROCEDURES 110
3.4.1 Culturing of Aedes aegypti mosquitoes 110
3.4.2 Procedure for carrying out the susceptibility or resistance of mosquito larvae to insecticides test 111
3.4.3 Procedure for carrying out an in vitro anti-cancer bioassay 112
3.5 EXTRACTION OF COMPOUNDS 113
3.6 ISOLATION OF BIOACTIVE PRINCIPLES 114
3.6.1 Isolation of bioactive principles from Goniothalamus andersonii 114
3.6.2 Isolation of bioactive principles from Goniothalamus dolichocarpus 116
3.6.3 Isolation of bioactive principles from Goniothalamus malayanus 119
3.6.4 Isolation of bioactive principles from Goniothalamus velutinus 122
3.6.5 Isolation of bioactive principles from Disepalum anomalum 124

3.6.6 Isolation of bioactive principles from Mezzetia umbellata ... 126
3.6.7 Gas chromatography screening of the stem bark of the various Goniothalamus species ... 127
3.7 SYNTHESES ... 128
3.7.1 Synthesis of goniothalamin epoxide and isogoniothalamin epoxide ... 128
3.7.2 Synthesis of goniodiol ... 128
3.7.3 Synthesis of threo-goniodiol ... 129
3.7.4 Synthesis of goniodiol diacetate ... 129
3.7.5 Synthesis of (-)-iso-5-deoxygoniopypyrone ... 129
3.7.6 Synthesis of 5β-hydroxygoniothalamin and 5α-hydroxygoniothalamin ... 129
3.7.7 Acetylation of 5α-hydroxygoniothalamin and 5β-hydroxygoniothalamin ... 130
3.7.8 Silylation of disepalin ... 130
3.7.9 Acetylation of disepalin ... 131
3.7.10 Acetylation of (-)-iso-5-deoxygoniopypyrone ... 131

CHAPTER FOUR: RESULTS AND DISCUSSION-LARVICIDAL PRINCIPLES ... 132

4.1 ISOLATION OF LARVICIDIAL PRINCIPLES FROM THE STEM BARK OF THE VARIOUS SPECIES STUDIED ... 132
4.2 ISOLATION OF LARVICIDAL PRINCIPLES FROM THE STEM BARK OF VARIOUS INSECTICIDAL PLANTS FROM THE ANNONACEAE FAMILY ... 133
4.2.1 Goniothalamus andersonii ... 133
4.2.2 Goniothalamus dolichocarpus ... 134
4.2.3 Goniothalamus malayanus ... 134
4.2.4 Goniothalamus velutinus ... 135
4.2.5 Mezzetia umbellata ... 135
4.2.6 Disepalum anomalum ... 135
4.2.7 Characterisation of GA-1 as goniothalamin ... 136
4.2.8 Characterisation of GA-2 as (+)-goniothalamin epoxide ... 144
4.2.9 Characterisation of (+)-isogoniothalamin epoxide ... 149
4.2.10 Synthesis of goniothalamin epoxide and isogoniothalamin epoxide ... 158
4.2.11 Characterisation of GA-4 as (+)-goniodiol ... 158
4.2.11.1 Synthesis of goniodiol ... 165
4.2.12 Characterisation of GA-5 as (+)-goniodiol diacetate ... 174
4.2.13 Characterisation of LB5 as pinocembrin ... 180
4.2.14 Characterisation of LB6 as naringenin ... 188
4.2.15 Characterisation of EELA 25 as (-)-iso-5-deoxygoniopypyrone ... 197
4.2.15.1 Synthesis of (-)-iso-5-deoxygoniopypyrone ... 213
4.2.16 Characterisation of GMg and GV9b as (+)-goniothalenol ... 215
4.2.16.1 Synthesis of goniothalenol ... 224
4.2.17 Characterisation of LB21C1 as (+)-5β-hydroxygoniothalamin ... 225
4.2.18 (-)-5β-Acetoxygoniothalamin ... 231
4.2.18.1 Syntheses of 5β-hydroxygoniothalamin and 5α-hydroxygoniothalamin ... 236
4.2.19 (+)-5α-Hydroxygoniothalamin ... 238
3.2.19.1 Mechanism of reaction ... 248
4.2.20 (-)-5α-Acetoxygoniothalamin ... 249
4.2.21 Characterisation of LBMF 8b, GMC, KHP13b and GV260R as (+)-annonacin ... 255
4.2.22 Characterisation of F7 as a new acetogenin, disepalin ... 270
4.2.23 Characterisation of GM5-7 and GV3b-2 as aristolactam BII ... 289
4.2.24 Characterisation of LS13-4y-13 as liriodenine ... 296
4.2.25 Characterisation of GV26SF2 and GMf as ouregidione ... 301

CHAPTER FIVE: RESULTS AND DISCUSSION-BIOASSAY RESULTS ... 311

5.1. INTRODUCTION ... 311
5.2. BIOASSAY OF CRUDE PLANT EXTRACTS ... 311
5.3. LARVICIDAL ACTIVITY FOR CRUDE PLANT EXTRACTS OF VARIOUS PLANT SPECIES OF THE GENERA *GONIOTHALAMUS*, *DISEPALUM* AND *MEZZETIA* ... 312
5.3.1. Crude hexane extracts of the stem bark from the plants of the genera Goniothalamus, Disepalum and Mezzetia ... 313

5.3.1.1 *Goniothalamus andersonii* 314
5.3.1.2 *Goniothalamus dolichocarpus* 314
5.3.1.3 *Goniothalamus velutinus* 314
5.3.1.4 *Goniothalamus malayanus* 315
5.3.1.5 *Goniothalamus macrophyllus* 315
5.3.1.6 *Goniothalamus ridleyi* 316
5.3.1.7 *Goniothalamus gigantifolius* 316
5.3.1.8 *Goniothalamus sinclairinius* 316
5.3.1.9 *Goniothalamus montanus* 317
5.3.1.10 *Goniothalamus macranii* 317
5.3.1.11 *Goniothalamus uvarioides* 317
5.3.1.12 *Disepalum anomalum* 318
5.3.1.13 *Mezzetia umbellata* 318
5.3.2 Conclusions *318*
5.3.3 Crude ethanol extracts of the stem bark from the plants of the genera Goniothalamus, Disepalum and Mezzetia *320*
5.3.3.1 *Goniothalamus andersonii* 321
5.3.3.2 *Goniothalamus dolichocarpus* 321
5.3.3.3 *Goniothalamus velutinus* 321
5.3.3.4 *Goniothalamus malayanus* 321
5.3.3.5 *Goniothalamus macrophyllus* 322
5.3.3.6 *Goniothalamus ridleyi* 322
5.3.3.7 *Goniothalamus gigantifolius* 322
5.3.3.8 *Goniothalamus sinclairinius* 322
5.3.3.9 *Goniothalamus montanus* 323
5.3.3.10 *Goniothalamus macranii* 323
5.3.3.11 *Goniothalamus uvarioides* 323
5.3.3.12 *Mezzetia umbellata* 323
5.3.3.13 *Disepalum anomalum* 324
5.3.4 Conclusions *324*
5.3.5 Crude methanol soluble fractions of the ethanol bark extracts of the genera Goniothalamus, Mezzetia and Disepalum *326*
5.3.5.1 *Goniothalamus andersonii* 328
5.3.5.2 *Goniothalamus dolichocarpus* 328
5.3.5.3 *Goniothalamus velutinus* 328
5.3.5.4 *Goniothalamus malayanus* 329
5.3.5.5 *Goniothalamus macrophyllus* 329
5.3.5.6 *Goniothalamus ridleyi* 329
5.3.5.7 *Goniothalamus gigantifolius* 330
5.3.5.8 *Goniothalamus sinclairinius* 330
5.3.5.9 *Goniothalamus montanus* 330
5.3.5.10 *Mezzetia umbellata* 330
4.3.5.11 *Disepalum anomalum* 331
5.3.6 Conclusions *331*
5.4 LARVICIDAL ACTIVITY OF SOME COMPOUNDS ISOLATED FROM THE VARIOUS PLANT SPECIES STUDIED 333
5.5 CONCLUSIONS 334

REFERENCES **337**

COMPOUND/STRUCTURE INDEX **346**

APPENDICES **348**

APPENDIX 1 348
APPENDIX 2 350
APPENDIX 3 352
APPENDIX 4 354
APPENDIX 5 356
APPENDIX 6 359
APPENDIX 7 367

LIST OF TABLES

Table 1. 1: *Goniothalmus* species available in Malaysia 5
Table 1. 2: Occurrence of oxoaporphines in Annonaceae 21
Table 1. 3: Goniothalamin contents in different morphological parts of *Goniothalamus* species 33
Table 1. 4: Diagnostic ^{1}H and ^{13}C NMR chemical shifts for the γ-lactone moiety 58
Table 1. 5: Diagnostic NMR chemical shifts of different subunits with various relative configuration in acetogenins 60
Table 1. 6: Cytotoxicity and antitumour activity of annonaceous acetogenins 71
Table 1. 7: *In vivo* antitumour activities of bullatacin, bullatacinone, bullatalicinone and squamocin against i.p.-implanted L1210 leukaemia 73
Table 1. 8: Antitumour efficacy of bullatacin, bullatacinone and bullatalicin in athymic mice bearing s.c.-implanted A2780 human ovarian carcinoma xenografts 74
Table 1. 9: Pesticidal activity of tested acetogenins 76
Table 2. 1: Some novel antitumour prescreens 84
Table 2. 2: A test of the toxicity of rotenone to *Macrosiphoniella sanborni* 92
Table 2. 3: Empirical probits and approximate expected probits for data of Table 2.2 94
Table 2. 4: Transformation of percentages to probits 97
Table 2. 5: Comparison of observed and expected mortality in eye estimation for rotenone - *Macrosiphoniella sanborni* test 97
Table 4. 1: Larvicidal principles present in the stem bark of various plant species studied 132
Table 4. 2: ^{1}H NMR (δ) assignments and *J*(Hz) values for goniothalamin (270 MHz, $CDCl_3$) 137
Table 4. 3: Proton-proton connectivities obtained from ^{1}H-^{1}H COSY experiment for (+)-goniothalamin (270 MHz and 67.8 MHz) 142
Table 4. 4: Proton and carbon connectivities obtained from ^{1}H-^{13}C HETCOR experiment for (+)-goniothalamin (270 MHz and 67.8 MHz) 142
Table 4. 5: ^{13}C NMR (δ) assignments for goniothalamin (67.8 MHz, $CDCl_3$) 142
Table 4. 6: ^{1}H NMR (δ) assignments and coupling constant values (Hz) for goniothalamin epoxide 145
Table 4. 7: ^{1}H - ^{1}H connectivities (^{1}H -^{1}H COSY) for goniothalamin epoxide 145
Table 4. 8: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for goniothalamin epoxide 149
Table 4. 9: ^{13}C NMR (δ) assignments for goniothalamin epoxide 149
Table 4. 10: ^{1}H NMR (δ) assignments and *J*(Hz) values for (+)-isogoniothalamin epoxide 150
Table 4. 11: ^{1}H - ^{1}H connectivities (^{1}H - ^{1}H COSY) for (+)-isogoniothalamin epoxide 156
Table 4. 12: ^{1}H - ^{13}C connectivities (^{1}H - ^{13}C HETCOR) for (+)-isogoniothalamin epoxide 156
Table 4. 13: ^{13}C NMR (δ) assignments for isogoniothalamin epoxide 156
Table 4. 14: ^{1}H NMR (δ) assignments and *J*(Hz) values for (+)-goniodiol (270 MHz, $CDCl_3$) 159
Table 4. 15: ^{1}H - ^{1}H connectivities (^{1}H - ^{1}H COSY) for (+)-goniodiol 160
Table 4. 16: ^{1}H-^{13}C connectivities (^{1}H-^{13}C HETCOR) for (+)-goniodiol 160
Table 4. 17: ^{13}C NMR (δ) assignments for (+)-goniodiol (67.8 MHz, $CDCl_3$) 160
Table 4. 18: ^{1}H NMR (δ) assignmemts and *J*(Hz) values for *threo*-goniodiol (270 MHz, $CDCl_3$) 167
Table 4. 19: ^{1}H -^{1}H connectivities obtained from ^{1}H -^{1}H COSY experiment for *threo*-goniodiol 167
Table 4. 20: ^{1}H - ^{13}C connectivities obtained from ^{1}H- ^{13}C HETCOR experiment for *threo*-goniodiol 167
Table 4. 21: ^{13}C NMR assignments (δ) for *threo*-goniodiol (67.8 MHz, $CDCl_3$) 172
Table 4. 22: ^{1}H NMR (δ) assignments and *J* values (Hz) for goniodiol diacetate 175
Table 4. 23: ^{1}H - ^{1}H connectivities (^{1}H - ^{1}H COSY) for goniodiol diacetate 175
Table 4. 24: ^{1}H - ^{13}C connectivities (^{1}H - ^{13}C HETCOR) for goniodiol diacetate 175
Table 4. 25: ^{13}C NMR (δ) assignments for goniodiol diacetate (67.8 MHz, $CDCl_3$) 175
Table 4. 26: ^{1}H NMR (δ) assignments and *J*(Hz) values for pinocembrin (270 MHz, CD_3COCD_3).. 181
Table 4. 27: ^{1}H - ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for pinocembrin 181
Table 4. 28: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for pinocembrin.. 181

Table 4. 29: ^{13}C NMR assignments for pinocembrin (67.8 MHz, CD_3COCD_3) 187
Table 4. 30: ^{1}H NMR (δ) assignments and J(Hz) values for naringenin (270 MHz, CD_3COCD_3)..... 189
Table 4. 31: ^{1}H - ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for naringenin 189
Table 4. 32: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for naringenin..... 189
Table 4. 33: ^{13}C NMR assignments for naringenin (67.8 MHz, CD_3COCD_3) 197
Table 4. 34: ^{1}H NMR assignments for (-)-iso-5-deoxygoniopypyrone acetate (270 MHz, $CDCl_3$)..... 201
Table 4. 35: ^{1}H - ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for
(-)-iso-5-deoxygoniopypyrone acetate 201
Table 4. 36: ^{1}H NMR assignments for (-)-iso-5-deoxygoniopypyrone (270 MHz, $CDCl_3$) 207
Table 4. 37: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for
(-)-iso-5-deoxygoniopypyrone acetate 207
Table 4. 38: ^{13}C NMR assignments for (-)-iso-5-deoxygoniopypyrone acetate (67.8 MHz, $CDCl_3$) . 207
Table 4. 39: ^{1}H NMR (δ) assignments and J(Hz) values for (+)-goniothalenol (270 MHz, $CDCl_3$)... 216
Table 4. 40: ^{1}H- ^{1}H connectivities (^{1}H - ^{13}C HETCOR) for (+)-goniothalenol..... 216
Table 4. 41: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for
(+)-goniothalenol 223
Table 4. 42: ^{13}C NMR (δ) assignments for goniothalenol (67.8 MHz, $CDCl_3$) 223
Table 4. 43: ^{1}H NMR (δ) assignments for (+)-5β-hydroxygoniothalamin (270 MHz, $CDCl_3$)..... 226
Table 4. 44: ^{1}H- ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for (+)-5β-
hydroxygoniothalamin 226
Table 4. 45: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for (+)-5β-
hydroxygoniothalamin 227
Table 4. 46: ^{13}C NMR (δ) assignments for (+)-5β-hydroxygoniothalamin (67.8 MHz, $CDCl_3$)..... 227
Table 4. 47: ^{1}H NMR (δ) assignments and J(Hz) values for (-)-5β-acetoxygoniothalamin
(270 MHz, $CDCl_3$) 233
Table 4. 48: ^{1}H- ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for
(-)-5β-acetoxygoniothalamin 233
Table 4. 49: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for
(-)-5β-acetoxygoniothalamin 233
Table 4. 50: ^{13}C NMR assignments for (-)-5β-acetoxygoniothalamin (67.8 MHz, $CDCl_3$)..... 236
Table 4. 51: ^{1}H NMR (δ) assignments and J values for (+)-5α-hydroxygoniothalamin
(270 MHz, $CDCl_3$) 239
Table 4. 52: ^{1}H- ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for
(+)-5α-hydroxygoniothalamin 239
Table 4. 53: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for
(+)-5α-hydroxygoniothalamin 240
Table 4. 54: ^{13}C NMR (δ) assignments for (+)-5α-hydroxygoniothalamin (67.8 MHz, $CDCl_3$)..... 246
Table 4. 55: ^{1}H NMR (δ) assignments and J(Hz) values for (-)-5α-acetoxygoniothalamin 250
Table 4. 56: ^{1}H- ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for
(-)-5α-acetoxygoniothalamin 254
Table 4. 57: ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment for
(-)-5α-acetoxygoniothalamin 254
Table 4. 58: ^{13}C NMR (δ) assignments for (-)-5α-acetoxygoniothalamin (67.8 MHz, $CDCl_3$)..... 254
Table 4. 59: ^{1}H NMR (δ) assignments and J(Hz) values for (+)-annonacin (270 MHz, $CDCl_3$)..... 260
Table 4. 60: ^{1}H - ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for (+)-annonacin..... 260
Table 4. 61: Structure and ^{1}H - ^{13}C connectivities obtained from ^{1}H - ^{13}C HETCOR experiment
for (+)-annonacin 269
Table 4. 62: ^{13}C NMR (δ) assignments for (+)-annonacin (67.8 MHz, $CDCl_3$)..... 270
Table 4. 63: Structure and proton NMR spectral data for disepalin ($CDCl_3$, 500 MHz) and
annonacin ($CDCl_3$, 470 MHz) (McCloud *et al.*, 1987) 277
Table 4. 64: Proton-proton connectivities obtained from ^{1}H- ^{1}H COSY experiment for disepalin 287
Table 4. 65: Proton and carbon connectivities and their ^{2}J and ^{3}J interactions obtained from
^{1}H - ^{13}C HETCOR and HMBC experiments for disepalin 287
Table 4. 66: ^{13}C NMR spectral data for disepalin ($CDCl_3$, 67.8 MHz) and annonacin
(McCloud *et al.*, 1987)..... 288

Table 4. 67: Structure and comparison of ^{1}H NMR values of the acetate derivatives of disepalin and annonacin 288
Table 4. 68: ^{1}H NMR assignments (δ) and *J* values (Hz) for aristolactam BII (270 MHz, $CDCl_3$)..... 290
Table 4. 69: ^{1}H - ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for aristolactam BII.... 290
Table 4. 70: ^{1}H -^{13}C connectivities obtained from ^{1}H -^{13}C HETCOR experiment for aristolactam BII..... 295
Table 4. 71: ^{13}C NMR (δ) assignments for aristolactam BII (67.8 MHz, $CDCl_3$) 295
Table 4. 72: ^{1}H NMR (δ) assignments and *J*(Hz) values for liriodenine (270 MHz, $CDCl_3$) 297
Table 4. 73: ^{1}H - ^{1}H connectivities (^{1}H - ^{1}H COSY) for liriodenine 297
Table 4. 74: ^{13}C NMR (δ) assignments for liriodenine (67.8 MHz, $CDCl_3$) 301
Table 4. 75: Structure and ^{1}H NMR (δ) assignments and *J*(Hz) values for ouregidione in different solvents (270 MHz) 303
Table 4. 76: ^{1}H - ^{1}H connectivities obtained from ^{1}H - ^{1}H COSY experiment for ouregidione 304
Table 4. 77: Proton and carbon connectivities and their ^{2}J and ^{3}J interactions obtained from HMQC and HMBC experiments for ouregidione ($CDCl_3$, 270 MHz and 67.8 MHz)..... 305
Table 4. 78: ^{13}C NMR (δ) assignments for ouregidione 305
Table 5. 1: Larvicidal (*Aedes aegypti*) activity of crude hexane extract..... 313
Table 5. 2: Larvicidal (*Aedes aegypti*) activity of crude ethanol extracts..... 320
Table 5. 3: *In vitro* cytotoxicity activity of crude ethanol extracts 326
Table 5. 4: Larvicidal (*Aedes aegypti*) activity of methanol soluble fractions of crude ethanol extracts..... 327
Table 5. 5: *In vitro* cytotoxicity activity of methanol soluble fractions..... 333
Table 5. 6: Larvicidal (*Aedes aegypti*) activity of compounds 334

LIST OF FIGURES

Figure 1. 1: Some recently identified oxoaporphines 22
Figure 1. 2: Structures of dihydropontevedrine and corydione 23
Figure 1. 3: Structures of some 4,5-dioxoaporphines 24
Figure 1. 4: Originally assigned and revised structures for pontevedrine 25
Figure 1. 5: Synthesis of aristolactam 26
Figure 1. 6: Structures of some aristolochic acids 27
Figure 1. 7: Structures of some aristolactams 28
Figure 1. 8: Degradation sequences of aristolochic acid-I into phenanthrene and aristolactam 29
Figure 1. 9: Structures of five phenanthrene derivatives 30
Figure 1. 10: Structures of some aristolactam alkaloids 30
Figure 1. 11: Structure of (+)-goniothalamin 31
Figure 1. 12: Structures of *threo* and *erythro*-7,8-dibromogoniothalamin 32
Figure 1. 13: Synthesis of 6*R*-(+)-goniothalamin 34
Figure 1. 14: Syntheses of (6*S*)-goniothalamin and (6*R*)-goniothalamin 35
Figure 1. 15: Structures of some styrylpyrone derivatives 38
Figure 1. 16: Structures of five tetrahydrofuran subunits 41
Figure 1. 17: Structures of γ-lactone units of acetogenins 43
Figure 1. 18: Structure of bullatacinone 43
Figure 1. 19: Structures of some bis-THF annonaceous acetogenins 44
Figure 1. 20: Structure of reticulatacin 45
Figure 1. 21: Structures of some novel bis- and mono-THF acetogenins 46
Figure 1. 22: Two novel acetogenins with epoxy rings 47
Figure 1. 23: Acetogenins with adjacent bis-THF rings 48
Figure 1. 24: Some mono-THF annonaceous acetogenins 50
Figure 1. 25: Structure of goniocin, a tri-THF acetogenin 54
Figure 1. 26: Structures of some non-adjacent bis-THF acetogenin 54
Figure 1. 27: Structures of some non-THF acetogenins 55
Figure 1. 28: Mosher's model for the (*R*)-MTPA and (*S*)-MTPA derivatives 62
Figure 1. 29: The MTPA plane of an MTPA ester and $H_{a,b,c}$ and $H_{x,y,z}$ on the right and left sides of the plane, respectively 62
Figure 1. 30: Model A for the determination of the absolute configuration of secondary alcohols (Ohtani *et al.*,1991) 62
Figure 1. 31: Hypothesis for the biosynthesis of the THF rings of annonaceous acetogenins 64
Figure 1. 32: Biogenetic pathways leading to the acetogenins from *G. giganteus*. 65
Figure 1. 33: Biogenetic pathways leading to the acetogenins from *G. giganteus* 66
Figure 1. 34: A possible role of diepomuricanin in the biogenesis of solamin (Laprevote *et al.*, 1992) 67
Figure 1. 35: Structures of (-)- anolobine, (-)-annonaine and liriodenine 77
Figure 1. 36: Structures of goniopedaline, aristolactam AII and taliscanine 78
Figure 1. 37: Structures of velutinam and aristolactam BII 78
Figure 1. 38: Structure of scorazanone 79
Figure 1. 39: Structures of asimilobine and (-)-sculerine 80
Figure 2. 1: Relation between percentage kill of *Macrosiphoniella sanborni* and doses of rotenone, showing normal sigmoid curve represented by equation Y = 2.25 + 4.01x (Source: Finney, 1971: 30) 95
Figure 2. 2: Relation between probit of kill of *Macrosiphoniella sanborni* and dose of rotenone, showing probit regression line from equation Y = 2.25 + 4.01x (Source: Finney, 1971: 31) 96
Figure 2. 3: Styrylpyrones and their biological activities (McLaughlin *et al.*, 1991). 99
Figure 2. 4: Annonaceous acetogenins from *Goniothalamus giganteus* and their cytotoxicities. 102
Figure 3. 1: Scheme of extraction of the bark of *Goniothalamus andersonii* 116
Figure 3. 2: Scheme of extraction of the bark of *Goniothalamus dolichocarpus* 119
Figure 3. 3: Scheme of extraction for the bark of *Goniothalamus malayanus* 121

Figure 3. 4: Scheme of extraction for the bark of *Goniothalamus velutinus* 123
Figure 3. 5: Scheme of extraction for the bark of *Disepalum anomalum* 125
Figure 3. 6: Scheme of extraction for the bark of *Mezzetia umbellata* 127
Figure 4. 1: Structure of (+)-goniothalamin 136
Figure 4. 2: ^{1}H NMR spectrum of (+)-goniothalamin (270 MHz, $CDCl_3$) 138
Figure 4. 3: ^{1}H - ^{1}H COSY spectrum of (+)-goniothalamin 139
Figure 4. 4: ^{13}C NMR spectrum of (+)-goniothalamin (67.8 MHz, $CDCl_3$) 140
Figure 4. 5: ^{1}H - ^{13}C HETCOR spectrum of (+)-goniothalamin 141
Figure 4. 6: EIMS spectrum of (+)-goniothalamin 143
Figure 4. 7: EIMS fragmentation of (+)-goniothalamin 144
Figure 4. 8: Structure of (+)-goniothalamin epoxide 144
Figure 4. 9: ^{1}H NMR spectrum of (+)-goniothalamin epoxide (270 MHz, $CDCl_3$) 146
Figure 4. 10: ^{1}H - ^{1}H COSY spectrum of (+)-goniothalamin epoxide 147
Figure 4. 11: ^{13}C NMR spectrum of (+)-goniothalamin epoxide 148
Figure 4. 12: Structure of (+)-isogoniothalamin epoxide 149
Figure 4. 13: ^{1}H NMR spectrum of (+)-isogoniothalamin epoxide (270 MHz, $CDCl_3$) 151
Figure 4. 14: ^{1}H - ^{1}H COSY spectrum of (+)-isogoniothalamin epoxide 152
Figure 4. 15: ^{13}C NMR spectrum of (+)-isogoniothalamin epoxide (67.8 MHz, $CDCl_3$) 153
Figure 4. 16: ^{1}H - ^{13}C HETCOR spectrum of (+)-isogoniothalamin epoxide 154
Figure 4. 17: EIMS spectrum of (+)-isogoniothalamin epoxide 155
Figure 4. 18: A perspective view of (+)-isogoniothalamin epoxide 157
Figure 4. 19: Synthesis of goniothalamin epoxide 158
Figure 4. 20: Structure of (+)-goniodiol 158
Figure 4. 21: ^{1}H NMR spectrum of (+)-goniodiol (270 MHz, $CDCl_3$) 161
Figure 4. 22: ^{1}H-^{1}H COSY spectrum of (+)-goniodiol 162
Figure 4. 23: ^{13}C NMR spectrum of (+)-goniodiol 163
Figure 4. 24: ^{1}H-^{13}C HETCOR spectrum of (+)-goniodiol 164
Figure 4. 25: Synthesis of (+)-goniodiol 165
Figure 4. 26: Mechanism for the synthesis of (+)-goniodiol 165
Figure 4. 27: Synthesis of *threo*-goniodiol 166
Figure 4. 28: ^{1}H NMR spectrum of *threo*-goniodiol (270 MHz, $CDCl_3$) 168
Figure 4. 29: ^{1}H-^{1}H COSY spectrum of *threo*-goniodiol 169
Figure 4. 30: ^{13}C NMR spectrum of *threo*-goniodiol (67.8 MHz, $CDCl_3$) 170
Figure 4. 31: ^{1}H-^{13}C HETCOR spectrum of *threo*-goniodiol 171
Figure 4. 32: Cyclisation of of *threo*-goniodiol and *erythro*-goniodiol 172
Figure 4. 33: Synthesis of (+)-goniopypyrone 173
Figure 4. 34: Structure of (+)-goniodiol diacetate 174
Figure 4. 35: ^{1}H NMR spectrum of (+)-goniodiol diacetate (270 MHz, $CDCl_3$) 176
Figure 4. 36: ^{1}H-^{1}H COSY spectrum of (+)-goniodiol diacetate 177
Figure 4. 37: ^{13}C NMR spectrum of (+)-goniodiol diacetate (67.8 MHz, $CDCl_3$) 178
Figure 4. 38: ^{1}H-^{13}C HETCOR spectrum of (+)-goniodiol diacetate 179
Figure 4. 39: Structure of pinocembrin 180
Figure 4. 40: ^{1}H NMR spectrum of pinocembrin (270 MHz, CD_3COCD_3) 182
Figure 4. 41: ^{1}H-^{1}H COSY spectrum of pinocembrin 183
Figure 4. 42: ^{13}C NMR spectrum of pinocembrin (67.8 MHz, CD_3COCD_3) 184
Figure 4. 43: ^{1}H-^{13}C HETCOR spectrum of pinocembrin 185
Figure 4. 44: EIMS spectrum of pinocembrin 186
Figure 4. 45: EIMS fragmentations of pinocembrin 187
Figure 4. 46: Structure of naringenin 188
Figure 4. 47: ^{1}H NMR spectrum of naringenin (270 MHz, CD_3COCD_3 190
Figure 4. 48: ^{1}H-^{1}H COSY spectrum of naringenin 191
Figure 4. 49: ^{13}C NMR spectrum of naringenin (67.8 MHz, CD_3COCD_3) 192
Figure 4. 50: ^{1}H-^{13}C HETCOR spectrum of naringenin 193
Figure 4. 51: DEPT spectra of naringenin 194
Figure 4. 52: EIMS spectrum of naringenin 195
Figure 4. 53: GC-MS spectrum of naringenin 196
Figure 4. 54: Structure of (-)-iso-5-deoxygoniopypyrone 197
Figure 4. 55: Structure of (-)-iso-5-deoxygoniopypyrone 200

Figure 4. 56: Structure of (+)-5-deoxygoniopypyrone 200
Figure 4. 57: NOE enhancements of (-)-iso-5-deoxygoniopypyrone acetate 200
Figure 4. 58: ^{1}H NMR spectrum of (-)-iso-5-deoxygoniopypyrone (crude) (270 MHz, $CDCl_3$) 202
Figure 4. 59: ^{1}H-^{1}H COSY spectrum of (-)-iso-5-deoxygoniopypyrone (crude) 203
Figure 4. 60: ^{13}C NMR spectrum of (-)-iso-5-deoxygoniopypyrone (crude) (67.8 MHz, $CDCl_3$) 204
Figure 4. 61: ^{1}H-^{13}C HETCOR spectrum of (-)-iso-5-deoxygoniopypyrone (crude) 205
Figure 4. 62: EIMS spectrum of (-)-iso-5-deoxygoniopypyrone 206
Figure 4. 63: ^{1}H NMR spectrum of (-)-iso-5-deoxygoniopypyrone acetate (270 MHz, $CDCl_3$) 208
Figure 4. 64: ^{1}H-^{1}H COSY spectrum of (-)-iso-5-deoxygoniopypyrone acetate 209
Figure 4. 65: ^{13}C NMR spectrum of (-)-iso-5-deoxygoniopypyrone acetate (67.8 MHz, $CDCl_3$) 210
Figure 4. 66: ^{1}H-^{13}C HETCOR spectrum of (-)-iso-5-deoxygoniopypyrone acetate 211
Figure 4. 67: DEPT spectra of (-)-iso-5-deoxygoniopypyrone acetate 212
Figure 4. 68: Synthesis of (-)-iso-5-deoxygoniopypyrone 213
Figure 4. 69: Postulated synthesis of goniopypyrone 214
Figure 4. 70: Structure of (+)-goniothalenol 215
Figure 4. 71: ^{1}H NMR spectrum of (+)-goniothalenol (400 MHz, $CDCl_3$) 217
Figure 4. 72: ^{1}H-^{1}H COSY spectrum of (+)-goniothalenol (400 MHz, $CDCl_3$) 218
Figure 4. 73: Long-range ^{1}H-^{1}H COSY spectrum of (+)-goniothalenol 219
Figure 4. 74: ^{13}C NMR spectrum of (+)-goniothalenol (400 MHz, $CDCl_3$) 220
Figure 4. 75: HSQC spectrum of (+)-goniothalenol 221
Figure 4. 76: EIMS spectrum of (+)-goniothalenol 222
Figure 4. 77: Cyclisation of 5β-hydroxyisogoniothalamin epoxide 224
Figure 4. 78: Cyclisation of 5β-hydroxygoniothalamin epoxide 224
Figure 4. 79: Structure of (+)-5β-hydroxygoniothalamin 225
Figure 4. 80: ^{1}H NMR spectrum of (+)-5β-hydroxygoniothalamin (270 MHz, $CDCl_3$) 228
Figure 4. 81: ^{13}C NMR spectrum of (+)-5β-hydroxygoniothalamin (67.8 MHz, $CDCl_3$) 229
Figure 4. 82: EIMS spectrum of (+)-5β-hydroxygoniothalamin 230
Figure 4. 83: Structure of (-)-5β-acetoxygoniothalamin 231
Figure 4. 84: ^{1}H NMR spectrum of (-)-5β-acetoxygoniothalamin (270 MHz, $CDCl_3$) 234
Figure 4. 85: ^{13}C NMR spectrum of (-)-5β-acetoxygoniothalamin (67.8 MHz, $CDCl_3$) 235
Figure 4. 86: Attempted syntheses of 5-hydroxygoniothalamin (Smith, 1994) 237
Figure 4. 87: Structure of (+)-5α-hydroxygoniothalamin 238
Figure 4. 88: NOE enhancement for 5α-hydroxygoniothalamin 240
Figure 4. 89: ^{1}H NMR spectrum of (+)-5α-hydroxygoniothalamin (270 MHz, $CDCl_3$) 241
Figure 4. 90: ^{1}H-^{1}H COSY spectrum of (+)-5α-hydroxygoniothalamin 242
Figure 4. 91: ^{13}C NMR spectrum of (+)-5α-hydroxygoniothalamin (67.8 MHz, $CDCl_3$) 243
Figure 4. 92: ^{1}H-^{13}C HETCOR spectrum of (+)-5α-hydroxygoniothalamin 244
Figure 4. 93: NOE difference spectra of (+)-5α-hydroxygoniothalamin 245
Figure 4. 94: A perspective view of (+)-5α-hydroxygoniothalamin 247
Figure 4. 95: Mechanism for the oxidation of goniothalamin to (+)-5β-hydroxygoniothalamin 248
Figure 4. 96: Structure of(-)-5α-acetoxygoniothalamin 249
Figure 4. 97: ^{1}H NMR spectrum of (-)-5α-acetoxygoniothalamin (270 MHz, $CDCl_3$) 251
Figure 4. 98: ^{13}C NMR spectrum of (-)-5α-acetoxygoniothalamin (67.8 MHz, $CDCl_3$) 252
Figure 4. 99: NOE difference spectrum of (-)-5α-acetoxygoniothalamin 253
Figure 4. 100: Structure of (+)-annonacin 255
Figure 4. 101: EIMS and CIMS for (+)-annonacin 257
Figure 4. 102: EIMS for the silated derivative of (+)-annonacin 258
Figure 4. 103: Structure of the α,β-unsaturated lactone 259
Figure 4. 104: ^{1}H NMR spectrum of (+)-annonacin (270 MHz, $CDCl_3$) 261
Figure 4. 105: ^{1}H-^{1}H COSY spectrum of (+)-annonacin 262
Figure 4. 106: ^{13}C NMR spectrum of (+)-annonacin (67.8 MHz, $CDCl_3$) 263
Figure 4. 107: DEPT spectra of (+)-annonacin 264
Figure 4. 108: ^{1}H-^{13}C HETCOR spectrum of (+)-annonacin 265
Figure 4. 109: CIMS spectrum of (+)-annonacin 266
Figure 4. 110: EIMS spectrum of (+)-annonacin 267

Figure 4. 111: EIMS spectrum of the silated derivative of (+)-annonacin 268
Figure 4. 112: Structure of disepalin 270
Figure 4. 113: FAB MS of disepalin 273
Figure 4. 114: FAB MS and EIMS for the silated derivative of disepalin 273
Figure 4. 115: NOE enhancements observed for disepalin 275
Figure 4. 116: ^{1}H NMR spectrum of disepalin (500 MHz, $CDCl_3$) 278
Figure 4. 117: ^{1}H NMR spectrum of disepalin (500 MHz, $CDCl_3$) (expanded) 279
Figure 4. 118: ^{13}C NMR spectrum of disepalin (67.8 MHz, $CDCl_3$) 280
Figure 4. 119: ^{1}H-^{1}H COSY spectrum of disepalin (500 MHz, $CDCl_3$) 281
Figure 4. 120: NOE difference spectrum of disepalin 282
Figure 4. 121: NOE difference spectra of disepalin (500 MHz, $CDCl_3$) 283
Figure 4. 122: HMBC spectrum of disepalin (500 MHz, $CDCl_3$) 284
Figure 4. 123: FAB MS spectrum of disepalin 285
Figure 4. 124: FAB MS spectrum of the silylated derivative of disepalin 286
Figure 4. 125: Structure of aristolactam BII 289
Figure 4. 126: ^{1}H NMR spectrum of aristolactam BII (270 MHz, $CDCl_3$) 291
Figure 4. 127: ^{1}H-^{1}H COSY spectrum of aristolactam BII 292
Figure 4. 128: ^{13}C NMR spectrum of aristolactam BII (67.8 MHz, $CDCl_3$) 293
Figure 4. 129: EIMS spectrum of aristolactam BII 294
Figure 4. 130: Structure of liriodenine 296
Figure 4. 131: ^{1}H NMR spectrum of liriodenine (270 MHz, $CDCl_3$) 298
Figure 4. 132: ^{13}C NMR spectrum of liriodenine (67.8 MHz, $CDCl_3$) 299
Figure 4. 133: EIMS spectrum of liriodenine 300
Figure 4. 134: Structure of ouregidione 302
Figure 4. 135: ^{1}H NMR spectrum of ouregidione (270 MHz, $CDCl_3$) 306
Figure 4. 136: ^{1}H-^{1}H COSY spectrum of ouregidione 307
Figure 4. 137: ^{13}C NMR spectrum of ouregidione (67.8 MHz, $CDCl_3$) 308
Figure 4. 138: NOE difference experiments for ouregidione 309
Figure 4. 139: EIMS spectrum of ouregidione 310

LIST OF PLATES

Plate 1: Fruits, flowers, leaves (top), and stem (bottom) of *Goniothalamus andersonii* 6
Plate 2: Flower (top), fruits (middle), and leaves (bottom) of *Goniothalamus dolichocarpus* 8
Plate 3: Fruits and flowers of *Goniothalamus malayanus* 9
Plate 4: Leaves of *Goniothalamus velutinus* (top), and leaves and shoot of *Goniothalamus macrophyllus* (bottom) 12
Plate 5: Fruits, leaves and stem of *Goniothalamus umbrosus* (top), flowers and leaves of *Disepalum anomalum* (bottom) 15
Plate 6: Flowers on branches (top) and leaves (bottom) of *Mezzetia umbellata* 16

ACRONYMS/ABBREVIATIONS USED IN TEXT

α	alpha
β	beta
δ	chemical shift in ppm
γ	gamma
μg	micro gram
^{0}C	degree in celsius
ATP	adenosine triphosphate
brd	broad doublet
brs	broad singlet
BSTFA	N,O-bis (trimethylsilyl)-trifluoroacetamide
CIMS	Chemical ionization mass spectroscopy
cm	centimetre
COSY	Correlated Spectroscopy
^{13}C	carbon-13
CL	confidence limit
d	doublet
DBU	1,8-diazabicyclo [5.4.0] undec-7-ene
dd	doublet of doublet
ddd	doublet of doublet of doublet
dddd	doublet of doublet of doublet of doublet
DEPT	Distortionless enhancement by polarization transfer
DMSO	dimethylsulfoxide
DNP	dinitrophenol
dt	doublet of triplet
ED	effective dose
EIMS	Electron impact-mass spectroscopy
FAB	Fast Atom Bombardment
Fe-S	ferrous sulphide
FI	fluorescence inhibition
FP	frond proliferation
g	gram(s)
GC	Gas Chromatography
GC-MS	Gas Chromatography-mass spectroscopy
GI	growth inhibition
^{1}H	proton
HETCOR	Heteronuclear chemical shift-correlation
HMBC	Heteronuclear Multiple Bond Connectivity by 2D Multiple Quantum NMR
HMQC	^{1}H-Detected Heteronuclear Multiple-Quantum Coherence via Direct Coupling
HOAc	acetic acid
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrum
Hz	hertz

id	internal diameter
IR	infrared
J	coupling constant in Hz
l	litre
LC	lethal concentration
LD	lethal dose
Lit.	literature
LPRL	log-probit regression lines
LR	long range coupling constant
m	multiplet
MCPBA	*m*-chloroperoxybenzoic acid
MHz	megahertz
ml	millilitre(s)
mm	millimetre(s)
mol	moles
Mol. wt.	molecular weight
m.p.	melting point
MS	mass spectrum/spectra/spectrometer/spectroscopy
MTBE	methyl tert-butyl ether
MTPA	methoxytrifluoromethylphenylacetate
NA	not available
NADH	nicotinamide adenine dinucleotide, reduced form
NCI	National Cancer Institute
nm	nanometre(s)
NMR	Nuclear Magnetic Resonance
NOE	Nuclear Overhauser Enhancement
NOESY	Nuclear Overhauser and Exchange Spectroscopy
OAc	acetate
PCN	propionitrile
Ph	phenyl
PLC	preparative layer chromatography
ppm	parts per million
q	quartet
dq	doublet of quartet
[R]	corresponding alkyl group
RI	refractive index
S	singlet
SE	standard error
t	triplet
td	triplet of doublets
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	tetramethylsilane
TMPD	N,N,N,N'-tetramethyl-p-phenylenediamine
UV	ultra violet
WHO	World Health Organization