

## Table of Contents

<b>Contents</b>	<b>Page No</b>
Certificates	iii
Acknowledgments	ix
List of Figures	xiv
List of tables	xvi
List of abbreviations	xvii
Preface	xix
<b>Chapter 1. Introduction</b>	<b>1</b>
1. Introduction	2
1.1. Biodiversity inspired chemical diversity of natural products	3
1.2. Exploration of natural products from plant source	3
1.3. Dereplication strategy	4
1.3.1. Data acquisition by hyphenated techniques	5
1.3.2. Data mining via natural products database	9
<b>Chapter 2. Objectives and Plan of work</b>	<b>13</b>
2. Objectives and Plan of work	14
2.1. Objectives	14
2.2. Plan of work	15
2.2.1. Phytochemical investigation and cytotoxic evaluation of <i>Dysoxylum malabaricum</i> Bedd. bark	15
2.2.2. Chemical modification of isolated compound (beddomeilactone)	15
<b>Chapter 3. Phytochemical investigation of <i>Dysoxylum malabaricum</i> bark using LC-MS-based dereplication strategy and cytotoxic evaluation</b>	<b>17</b>
3. Phytochemical investigation of <i>Dysoxylum malabaricum</i> bark using LC-MS-based dereplication strategy and cytotoxic evaluation	18
3.1. Literature review	18
3.2. Experimental section	22
3.2.1. General experimental procedures	22
3.2.2. Plant material	24
3.2.3. Extraction and isolation	24
3.2.4. Cell line and cell culture	25
3.2.5. Apoptosis analysis by acridine orange/ethidium bromide staining	26
3.2.6. Apoptosis analysis by DAPI staining	26
3.2.7. DNA content and cell cycle phase distribution	27
3.2.8. Western blot analysis	27
3.3. Result and discussion	28
3.3.1. LC-MS-based dereplication for identification and isolation of metabolites present in the bark extract using the DNP database	28
3.3.1.1. LC-MS analysis of bark extract	29
3.3.1.2. DNP-based dereplication using LC-MS data	31
3.3.2. Structure elucidation and cytotoxicity screening of compounds isolated from fractions I and II	32

3.3.2.1. Structure elucidation of compounds targeted and isolated fractions I and II	32
3.3.2.2. Cytotoxicity screening of isolated compounds from fractions I and II	45
3.3.2.3. Apoptotic cell death induced by dihydrobeddomeilactone	45
3.3.3. Structure elucidation and cytotoxicity screening of compounds from fraction III	47
3.3.3.1. Structure elucidation of compounds targeted and isolated from fraction III	47
3.3.3.2. Cytotoxicity screening of isolated compounds from fractions III	54
3.3.3.3. Microscopic assessment of nuclear morphology	55
3.3.3.4. Effect of dihydrobinectarilactone on cell cycle distribution of MCF-7 cells	56
3.3.4. Structure elucidation and cytotoxicity screening of compounds from fraction IV	58
3.3.4.1. Structure elucidation of compounds targeted and isolated from fraction IV	58
3.3.4.2. Cytotoxicity screening of isolated compounds from fractions IV	65
3.3.4.3. Glucose uptake inhibition in breast cancer cells after treatment	66
3.3.4.4. Enhanced nitric oxide production in breast cancer cells after treatment	67
3.3.4.5. Apoptosis cell death induced by mahamanalactone C	68
3.4. Outcomes	69
<b>Chapter 4 Chemical modification of isolated metabolites and cytotoxic evaluations</b>	<b>71</b>
4. Chemical modification of isolated metabolites and cytotoxic evaluations	72
4.1. Introduction	72
4.2. Rationale designed	75
4.3. Experimental section	76
4.3.1. General experimental procedure	76
4.3.2. General method of amide synthesis	77
4.3.3. General method of halogenation reactions	77
4.3.4. General method of oxidative esterification	77
4.4. Result and Discussion	78
4.4.1. Series 1: Synthesis of nitrogenous derivatives	78
4.4.1.1. Optimization of reaction condition for amide synthesis	79
4.4.1.2. Synthesis of amide derivatives	81
4.4.1.3. Plausible reaction mechanism of amide synthesis	85
4.4.1.4. Outcomes	87
4.4.2. Series 2: Synthesis of halogenated derivatives	88
4.4.2.1. Optimization of reaction condition	89
4.4.2.2. Synthesized products of halogenation and esterification	91
4.4.2.3. Plausible reaction mechanism	97

4.4.2.4. Outcomes	98
<b>Chapter 5 Summary and conclusion</b>	99
5. Summary and conclusion	100
<b>References</b>	103
<b>Appendix</b>	117
<b>List of publications</b>	154