



TABLE OF CONTENT

COVER	i
DISSERTATION	ii
STATEMENT	iii
PREFACE	iv
TABLE OF CONTENT	v
TABLE LIST	viii
FIGURE LIST	x
SUPPLEMENTARY DATA	xiv
ABBREVIATIONS	xv
ABSTRACT	xvii
ABSTRAK	xviii
CHAPTER I. INTRODUCTION	1
1.1. Background.....	1
1.2. Novelty	4
1.3. The Objective of Research	6
CHAPTER II. LITERATURE REVIEW	7
2.1. Literature Review	7
2.1.1. Biology of <i>Plasmodium</i>	7
2.1.2. Cancer Cells.....	11
2.1.3. Antimalarial and Anticancer Resistance.....	13
2.1.4. Antibiotic-Anticancer as Antiplasmodial	18
2.1.5. Antiplasmodial Assay	21
2.1.6. The Cytotoxicity Assay	23
2.1.7. Biology of <i>Streptomyces</i>	26
2.1.8. <i>Streptomyces</i> Metabolites	29
2.1.9. Biosynthetic Gene Clusters (BGCs)	32
2.1.10. Genome Mining	33
2.1.11. Liquid Chromatography Mass Spectrometry Analysis in Drug Discovery	36
2.1.12. <i>In silico</i> Molecular Docking for Drug Discovery	40



2.2. Theoretical Framework	43
2.3. Hypothesis	45
CHAPTER III. MATERIALS AND METHODS	46
3.1. Materials	46
3.1.1. Biological Materials.....	46
3.1.2. Microbiological Medium	47
3.1.3. Chemical Reagent	47
3.1.4. Antiplasmodial and Cytotoxicity Reagent.....	48
3.2. Research Instruments.....	48
3.3. Research Framework.....	49
3.4. Methods	51
3.4.1. Bacterial Identification	51
3.4.2. Morphological Analysis.....	53
3.4.3. Genome Mining Analysis	54
3.4.4. Genome Annotation and Average Nucleotide Identity (ANI) Analysis.....	54
3.4.5. Fermentation and Extraction	55
3.4.6. Metabolite Profiling	56
3.4.7. Bioassay-guided Fractionation.....	58
3.4.8. <i>In vitro</i> Antiplasmodial Assay	59
3.4.9. Cytotoxicity Assay	62
3.4.10. <i>In silico</i> Molecular Docking	63
3.4.11. The Analysis of Biosynthetic Gene Cluster Encoding Active Metabolites	64
3.5. Data Analysis	64
3.5.1. Extraction Yield	64
3.5.2. Antiplasmodial Assay	65
3.5.3. Cytotoxicity Assay.....	65
3.5.4. Metabolite Analysis	65
3.6. Ethical Clearance.....	66
CHAPTER IV. RESULT AND DISCUSSION.....	67
4.1. Morphological Characterization of <i>Streptomyces</i>	67
4.2. Molecular Identification of <i>Streptomyces</i>	70



4.3. Genome Annotation and Average Nucleotide Identity (ANI) Analysis	73
4.4. Genome Mining Analysis.....	76
4.5. The Extraction Yield	96
4.6. Metabolite Profiling using LC-MS/MS.....	97
4.7. Antiplasmodial Activity	106
4.8. Anticancer Activities	110
4.9. Metabolite Profiling Using Targeted LC-HRMS	113
4.10. Bioassay-guided Fractionation	116
4.11. Active Metabolite Profiling using LC-MS/MS Analysis	125
4.12. The Analysis of Gene Cluster Encoding Active Metabolites.....	136
4.13. <i>In silico</i> Molecular Docking on Target Proteins of <i>P. falciparum</i> and Cancer Cells.....	142
CHAPTER V. CONCLUSION AND RECOMMENDATION	161
5.1. Conclusion.....	161
5.2. Recommendation.....	162
REFERENCES.....	163
SUPPLEMENTARY DATA	186
PUBLICATION	248