

**UNIVERSITI TEKNOLOGI MARA**

**ANTIPLASMODIAL ACTIVITIES OF  
*GONIOTHALAMUS LANCEOLATUS*  
AGAINST *PLASMODIUM*  
*FALCIPARUM* AND *PLASMODIUM*  
*BERGHEI*-INFECTED MICE.**

**FATIN AMELINA BINTI KAHARUDIN**

Thesis submitted in fulfilment  
of the requirement for the degree of

**Master of Science**

**Faculty of Pharmacy**

**November 2022**

## ABSTRACT

Malaria remains a global health problem with the emergence and spread of drug-resistance parasites thwarts the successful treatment of the infection. To address this challenge, increased efforts are directed in discovering new agents against malaria. The current study was designed to investigate the antiplasmodial activities of *Goniothalamus lanceolatus* Miq. crude extracts and major compounds using *Plasmodium falciparum* in *in vitro* culture and *Plasmodium berghei*-infected mice. The *in vitro* antiplasmodial activity was determined by parasite lactate dehydrogenase (pLDH) assay on chloroquine-sensitive *P. falciparum* (3D7) and chloroquine-resistant *P. falciparum* (K1) strains. The cytotoxicity effect was evaluated using a tetrazolium salt MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) on normal liver (WRL-68) cell line. The results revealed that root methanol extract and Parvistone D of *G. lanceolatus* possessed potent and promising antiplasmodial activity against both *P. falciparum* (3D7) and (K1) strains, respectively without causing cytotoxicity effect against WRL-68 cell line. Therefore, root methanol extract and Parvistone D were selected to be further investigated for its acute oral toxicity profile prior to the *in vivo* antiplasmodial activity using 4-day suppressive test. A total of 105 Institute of Cancer Research (ICR) mice were used in this study. The mice treated with extract and compound showed no sign of toxicity and mortality up to a single dose of 2000 mg/kg and 500 mg/kg, respectively. In addition, the extract and compound prolonged the mean survival time and demonstrated significant ( $p < 0.05$ ) chemosuppression activity at the dose of 300 mg/kg and 30 mg/kg, respectively. Furthermore, oral administration of the extract and compound also showed ameliorative effects with references to the haematological, biochemical and histopathological changes in the infected mice. In conclusion, the root methanol extract and Parvistone D of *G. lanceolatus*, are relatively safe with active antiplasmodial activities which could further develop into new antimalarial lead structure.

## **ACKNOWLEDGEMENT**

In the name of Allah, the Most Gracious and the Most Merciful.

All praises to Allah and His blessing for the completion of this thesis. I thank God for all the opportunities, trials and strength that have been showered on me to finish writing the thesis. His continuous grace and mercy were with me throughout my life and ever more during the tenure of my research.

First and foremost, I would like to sincerely thank my supervisor Dr. Rozaini Mohd Zohdi for her guidance, understanding, patience and most importantly, she has provided positive encouragement and a warm spirit to finish this thesis. It has been a great pleasure and honour to have her as my supervisor. I would also like to express my gratitude to my co-supervisors, Prof. Nor Hadiani Ismail and Prof. Hasidah Mohd Sidek for their support and knowledge regarding their topics.

My deepest gratitude goes to all my parents; Kaharudin Suboh, and Norhayati Ayob, and to my beloved sisters Fatin Nur Haziqah and Fatin Nur Qasrina for their endless love, prayers and encouragement. I offer my special thanks to all my colleagues; Shahida Mukhtar, Nurliana, Akmal Arif, Hadzrul Hisham, Jemain, Atiqah Jusril, and Madam Evana, for their motivation, prayers and their sincere help during my studies.

Finally, thanks to all staffs in Faculty of Pharmacy UiTM Puncak Alam who indirectly contributed in this study. I thank them wholeheartedly. May God shower the above cited personalities with success and honor in their life.

## TABLE OF CONTENTS

	<b>Page</b>
<b>CONFIRMATION BY PANEL EXAMINERS</b>	<b>ii</b>
<b>AUTHOR'S DECLARATION</b>	<b>i</b>
<b>ABSTRACT</b>	<b>ii</b>
<b>ACKNOWLEDGEMENT</b>	<b>iv</b>
<b>LIST OF TABLES</b>	<b>viii</b>
<b>LIST OF FIGURES</b>	<b>viii</b>
<b>LIST OF SYMBOLS</b>	<b>ix</b>
<b>LIST OF ABBREVIATIONS</b>	<b>xii</b>
<b>LIST OF NOMENCLATURE</b>	<b>xiii</b>
<b>CHAPTER ONE: INTRODUCTION</b>	<b>1</b>
1.1 Research Background	1
1.2 Problem statement	5
1.3 Objectives	5
1.3.1 General objective	5
1.3.2 Specific objectives	6
1.4 Research questions	7
1.5 Hypothesis	7
1.6 Significance of the study	8
1.7 Limitation of the study	8
<b>CHAPTER TWO: LITERATURE REVIEW</b>	<b>9</b>
2.1 Malaria	9
2.1.1 Malaria epidemiology	9
2.1.2 Malaria in Malaysia	13

2.2 Plasmodium life cycle	14
2.2.1 Murine model in malaria research	17
2.3 Clinical signs and symptoms	18
2.4 Malaria prevention and control	20
2.4.1 Vector control	20
2.4.2 Vaccination	21
2.5 Antimalarial drugs	22
2.5.1 Quinine	22
2.5.2 Chloroquine	23
2.5.3 Pyrimidine derivatives	24
2.5.4 Mefloquine	25
2.5.5 Artemisinin combination therapy (ACTs)	25
2.6 Antimalarial drug resistance	27
2.7 <i>Goniothalamus lanceolatus</i> Miq.	29
<b>CHAPTER THREE: <i>IN VITRO</i> ANTIPLASMODIAL AND CYTOTOXICITY</b>	<b>31</b>
<b>ACTIVITIES OF <i>G. LANCEOLATUS</i></b>	
3.1 Introduction	31
3.2 Materials and methods	32
3.2.1 Plant materials	32
3.2.2 Parasite cultivation technique	35
3.2.3 <i>In vitro</i> antiplasmodial study	39
3.2.4 Cytotoxicity study	43
3.2.5 Selectivity index (SI)	47
3.3 Results	47
3.3.1 <i>In vitro</i> antiplasmodial activity of <i>G. lanceolatus</i> crude extracts and major compounds against <i>P. falciparum</i> .	47
3.3.2 Cytotoxicity activity of <i>G. lanceolatus</i> crude extracts and major compounds against WRL-68 cell line	52
3.3.3 Selectivity index (SI)	54
3.4 Discussion	56
3.5 Conclusion	59