UNIVERSITI TEKNOLOGI MARA

MECHANISM OF ANTI-HYPERTENSIVE EFFECT OF STANDARDISED AQUEOUS ETHANOLIC EXTRACT OF *FICUS DELTOIDEA TRENGGANUENSIS* IN SPONTANEOUSLY HYPERTENSIVE RATS

ZURAIN BINTI RADJENI

MSc

September 2019

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student	:	Zurain binti Radjeni		
Student I.D. No.	:	2015455814		
Programme	:	Master of Medical Science (Physiology) - MD 754		
Faculty	:	Medicine		
Thesis Title	:	Mechanism of Anti-hypertensive Effect of Standardised Aqueous Ethanolic Extract of <i>Ficus</i> <i>deltoidea Trengganuensis</i> in Spontaneously Hypertensive Rats		
Signature of Student	:			

Date : September 2019

ABSTRACT

The leaves of *Ficus deltoidea* are often used in traditional medicine for the treatment of a number of ailments. However, evidence about its anti-hypertensive activity remains undetermined although its extract has been shown to have angiotensin converting enzyme (ACE) inhibitory activity in vitro. This study therefore investigates the anti-hypertensive effect of a standardised aqueous ethanolic extract of the leaves of Ficus deltoidea Trengganuensis (FDT) in Spontaneously Hypertensive Rats (SHRs). Thirty, male SHRs, aged 12 to 14 weeks, weighing 220 to 270g and with a systolic blood pressure (SBP) of greater than 150 mmHg were divided into 5 groups (n=6). Each group was treated daily, via the oral route, for 4 weeks either with 800, 1000 or 1200 mg/kg body weight of standardised aqueous ethanolic extract of leaves of FDT. Controls were given either 10 mg/kg body weight of losartan or 0.5 ml of distilled water. Blood pressure was measured weekly using tail cuff plethysmography. Urinary and serum calcium, sodium, potassium and total protein concentrations were analysed. Endothelial nitric oxide synthase (eNOS), endothelin 1 (ET-1) concentrations, total antioxidant status (TAS) and major components of the reninangiotensin-aldosterone system (RAAS), including renin, ACE, angiotensin (Ang) I, ACE2, Ang II and aldosterone were determined using ELISA. Data were analysed using ANOVA. SBP was significantly lower at week 4 in rats receiving 1200 mg FDT (p<0.05) or losartan (p<0.001) when compared with that in the controls. No significant differences were evident in body weight and urine output between the groups. There were also no significant differences in urinary and serum calcium, sodium, potassium and total protein excretion rates between the groups. No significant differences were evident in concentrations of components of RAAS when compared with that in the control groups. However, the concentrations of ET-1, eNOS and TAS were significantly lower in FDT treated rats. In conclusion, daily oral administration of 1200 mg FDT for four weeks significantly lowers blood pressure in SHR. However, it is unlikely to involve the RAAS or electrolyte excretion as no differences were detected in any of these between control and treated rats. The precise mechanism therefore remains to be determined.

ACKNOWLEDGEMENT

In the Name of Allah, the Most Gracious, the Most Merciful.

Glory be to Allah in the highest, whose grace and strength has enabled me to complete this thesis in spite of many obstacle faced throughout the project. Indeed, without His help and will, nothing is accomplished and this study would never come into this present form.

I would like to express my deepest appreciation to my dedicated and helpful supervisors, Prof. Dr. Harbindar Jeet Singh for his continuous support, comments, advice, suggestions, patience and guidance in regard to research and during the completion of this thesis. Without his guidance and persistent help this thesis would not have been possible. I would like to thank Dr. Mardiana Abdul Aziz for her supervision, support and guidance. I would also like to thank Dr. Sergey Gupalo for his supervision, valuable advice, support and assistance.

I would like to express my gratitude to Dr. Effat Omar for her assistance and guidance in conducting the histolopathological analysis, and also Dr. Damayanthi Durairajanayagam for her assistance along this journey. I would also like to thank the members and staffs of IMMB and LACU, UiTM Sungai Buloh for helping me in this research.

I would also like to extend my thanks to Prof. Dr. Abdul Manaf Ali of UniSZA for initiating this project, his help in obtaining the research funds from MOA, and supplying the leaves of *Ficus deltoidea Trengganuensis*.

In addition, I am grateful to all my precious friends for being very supportive and helpful in the field from the beginning until the completion of this study. I also wish a million thanks to my beloved family whose true love, support and inspiration made this work possible.

Last but not least, I would like to thank everyone who had been involved either directly or indirectly in guiding me through to the completion of this thesis.

TABLE OF CONTENTS

CON	ii		
AUT	'HOR'S DECLARATION	iii	
ABS'	iv		
ACK	KNOWLEDGEMENT	v	
TAB	vi		
LIST	Γ OF TABLES	X	
LIST	Γ OF FIGURES	xi	
LIST	xii		
LIST	Γ OF ABBREVIATIONS	xiii	
СНА	APTER ONE: INTRODUCTION	1	
1.1	Research Background	1	
1.2	Problem Statement	4	
1.3	Research Questions	5	
1.4	Research Objectives	5	
1.5	Hypotheses	6	
1.6	Significance of Study	6	
1.7	Scope and Limitation of Study	6	
CHA	7		
2.1	Hypertension and Its Risk Factors	7	
2.2	Pathophysiology and Complications of Hypertension	10	
2.3	Drugs Therapy of Hypertension	14	
2.4	Renin-Angiotensin-Aldosterone System	17	
	2.4.1 Angiotensinogen	18	
	2.4.2 Renin	18	
2.5	Endothelial Nitric Oxide Synthase		
2.6	Endothelin 1		
2.7	Oxidative Stress	21	