UNIVERSITI TEKNOLOGI MARA

DOSE-RESPONSE EFFECTS ON SPATIAL LEARNING AND MEMORY AFTER SUBACUTE EXPOSURE OF HAB10R12 ENDOPHYTIC EXTRACT IN MICE

RADHIA AZIA BINTI REDZUAN

Dissertation submitted in partial fulfillment of the Requirements for the degree of Bachelor of Pharmacy (Hons)

Faculty of Pharmacy

November 2008

ACKNOWLEDGEMENT

I am very grateful and thankful to almighty Allah S.W.T in giving me the patience and strength to complete this thesis. In the process of accomplishing this task, I was fortunate enough to work with people who had contributed greatly to the success of this research project. Firstly, I would like to take this opportunity to express my gratitude and appreciation to my supervisor, Prof. Dr. Abu Bakar B. Abdul Majeed for his guidance, invaluable advice and courage, constructive comments and patience during the course of this subject. Thousands thanks to Mr Richard Muhammad Johari James, postgraduate student for his guidance and priceless opinions which are very much appreciated. My appreciation also goes to my lab mates, Norhidayah Bte Kasiman @ Kamisan and Shaira Shuwari Sha-Aladin, who gave copacetic cooperation and companionship in the progress of this project. Besides, I would also to express my heartfelt thanks to all postgraduate students, lab assistants and research assistants who helped me regarding materials and methods required for this study. Many thanks to Dr. Zainul Amiruddin Zakaria as the coordinator for PHM555 (Research Instrumentation) for his guidance on the write-up of my thesis. I would like to express my appreciations to all the lecturers and my colleagues for their comments and opinions. Last but not least, special thanks to my family members for all their love, patience and helping hands in completing this thesis.

TABLE OF CONTENTS

TITLE PAGE APPROVAL FORM ACKNOWLEDGEMENT TABLE OF CONTENTS LIST OF TABLE LIST OF FIGURES LIST OF PLATES LIST OF ABBREVIATIONS ABSTRACT	Page ii iii vi vii viii ix xi
CHAPTER ONE (INTRODUCTION)	1
CHAPTER TWO (LITERATURE REVIEW)	6
2.1 Endophytes	6
2.2 Morris water maze	7
2.3 Spatial learning and memory	9
2.3.1 Hippocampus	10
2.3.2 NMDA receptors	13
2.3.2.1 Long term potentiation (LTP)	15
2.3.2.2 Long term depression (LTD)	16
2.3.2.3 NMDA-R1 subtype	17
2.3.2.4 Gene expression of NMDA-receptor	18
2.4 Pathophysiology influencing in spatial learning and memory	21
2.4.1 Alzheimer's disease	22
2.4.2 Amnesia	24

ABSTRACT

THE DOSE RESPONSE EFFECT ON SPATIAL LEARNING AND MEMORY AFTER SUBACUTE EXPOSURE OF HAB10R12 OF ENDOPHYTIC EXTRACT IN MICE.

An endophyte is an endosymbiont, often a bacterium or fungus, which lives within a plant for at least part of its life without causing apparent disease. Endophytes may benefit host plants by preventing pathogenic organisms from colonizing them. Our strain of interest is HAB10R12, which is found in local forest. Preliminary studies have shown that extract from this strain might have some neuroprotective properties. This study was aimed to investigate the dose-response effects of endophytic extract of HAB10R12 on spatial learning and memory after subacute exposure in mice. For the evaluation of the dose-response effects on spatial learning and memory, the Morris Water Maze (MWM) test is performed. The endophytic extract dose of 5, 10, 20 mg/kg were subacutely administered through the intraperitoneal route to mice (n = 6 per group) everyday for 14 days. Normal saline was administered intraperitoneally as a control and memantine (an NMDA receptor antagonist) as a positive control. The Morris Water Maze test was carried out on day 3, 6, 9, 12, 15 (after 15 minutes of treatment). From the result obtained only memantine showed a significant difference in enhancing the spatial learning and memory compared to the blank control. The 5mg/kg, 10 mg/kg of the HAB10R12 endophytic extract did not show statistically significant difference (P > 0.05) towards the spatial learning and memory. Further studies should be conducted to uncover the possible action of HAB10R12 endophytic extract on the human pathophysiology.

Keywords: endophyte; HAB10R12 endophytic strain; memantine; spatial memory and learning; Morris Water Maze.

CHAPTER 1

INTRODUCTION

It is speculated that there may be thousands of endophytes useful to mankind. Sometimes endophytes not only work to the advantage of their traditional host plants but could also be used to combat pathogens and even cancers in animals including humans. An endophyte is an endosymbiont, often a bacterium or fungus, which lives within a plant for at least part of its life without causing any apparent disease. It may benefit host plants by preventing pathogenic organisms from colonizing them. Extensive colonization of the plant tissue by endophytes creates a "barrier effect", where the local endophytes outcompete and prevent pathogenic organisms from taking hold. Endophytes may also utilize chemicals which inhibit the growth of competitors, including pathogenic organisms. In this research, the endophytic strain of interest is HAB10R12. Several studies have been done on this strain found in the local forest. While the HAB10R12 endophytic extract is claimed to have antiepileptic properties, it might have an effect on spatial memory and learning located in hippocampus as well. One of the studies is on the potential of this strain to treat epilepsy. The compounds present in the strain may have actions on the nerves associated with spatial learning and memory especially in the hippocampus, which this study will focus on.

Spatial memory is the part of memory responsible for recording information about one's environment and its spatial orientation. Spatial memories are formed after an organism