UNIVERSITI TEKNOLOGI MARA

EFFECT OF STIGMASTEROL ON LIPOPOLYSACCHARIDE-INDUCED NEUROINFLAMMATION IN MICE

SITI NOR AMIRAH BINTI ZAINAL AZWAN

Dissertation submitted in partial fulfilment of the requirements for the Bachelor of Pharmacy (Hons.)

Faculty of Pharmacy

July 2017

ACKNOWLEDGEMENT

First and foremost, praise to Allah SWT for the perseverance, good health and wellbeing given to complete this research thesis. I would like to express my special gratitude to my project supervisor, Dr Mizaton bt Hazizul Hasan, for the continuous support of this research project, for her endless guidance, patience, motivation and immense knowledge. Her guidance helped me in all the time of research and writing of this thesis. I could not have imagined having a better supervisor for my final year project.

I would like to thank Prof. Dr Aishah Adam, and also Universiti Teknologi MARA (UiTM), for providing the necessary facilities and equipments which ease me while conducting this project. My sincere thanks also go to the postgraduate students, laboratory assistants and everyone in the Department of Pharmaceutical Pharmacology & Chemistry for sharing expertise and gave endless guidance. I take this opportunity to express gratitude to all of the Department faculty members for their help and support. I also thank my project research members who have endured and guide me throughout completing this research. In addition, I am very grateful to have my friends who helped me a lot in finalizing this project within the limited time frame.

Last but not least, my warmest gratitude to my beloved parents for all the support they have provided me and it was the greatest gift anyone has ever given me. Without these people above, I would not be able to finish this research project. Thank you.

TABLE OF CONTENTS

ABSTRACT

Neuroinflammation is the combination of the responses of all cells in the CNS. The long term regulation of inflammation can cause degeneration of neurons which lead to neurodegenerative disease such as Alzheimer's disease and Parkinson's disease. Since these diseases are incurable, many researches were conducted to find cure and prevention for these diseases especially Alzheimer's disease. Stigmasterol, a type of phytosterol, which can be found in many plants, possesses anti-cholesterol effect due to its structure similarity with cholesterol. However, there are not many studies on the effect of stigmasterol against neuroinflammation. In the present study, the effect of stigmasterol on LPS-induced memory impairments using the Morris water maze and probe tests was investigated. The efficacy of the prophylactic treatment of stigmasterol (10, 20 and 40 mg/kg, p.o.) were determined by measuring the escape latency, distance travelled, swimming speed and the average swimming time in target quadrant of LPS-induced ICR mice model. LPS (3 mg/kg, i.p.) was administered 3 days after the daily administration of stigmasterol (p.o.). The mice were given trainings for three days and Morris water maze test was conducted on the fourth day. On the last day, probe test was conducted to assess the spatial learning of the mice, in which the platform was removed. Results showed that there were no significant differences between the groups ($p>0.05$) in the escape latency. For the distance travelled as well as swimming speed, only the mice treated with 10 mg/kg of stigmasterol showed significant difference compared to LPS-induced mice ($p<0.05$). However, in probe test, the untreated mice showed a significant difference ($p<0.05$) compared to the normal and treated groups. The treated groups showed longer time spent in the target quadrant compared to the LPS-induced group. In conclusion, stigmasterol may have the potential in attenuating LPS-induced memory impairment and further studies are necessary to determine the mechanism of action.

CHAPTER 1

INTRODUCTION

1.1 Background of study

The innate immune system protects the central nervous system (CNS) against the process of inflammation. Neuroinflammation is the combination of the responses of all cells in the CNS. Temporary up regulation of CNS inflammation is natural and has no detrimental effect on neuronal cells (Khan et al., 2016). However, long-term up regulation of the inflammation may cause the degeneration of neurons which can lead to neurodegenerative diseases such as Parkinson's disease (PD), multiple sclerosis, Alzheimer's disease (AD) and many others. Neuroinflammation as well as the accumulation of proteins are the characteristics of age-related neurodegenerative diseases (Pintado et al., 2012). Neuroinflammation is also related to depression which is characterized by the nuclear factor-kappa B (NF-κB) pathway activation and the release of proinflammatory cytokines (Jiang et al., 2016). Patients who suffer from depression have high levels of proinflammatory cytokines as well as other inflammatory mediators in the cortex and hippocampus.

Neuroinflammation involves the brain immune cell and various inflammatory mediators, including cytokines as well as free radicals (Behairi et al., 2016). The activation of microglia and astrocytes induce the neuroinflammatory process