CHAPTER I

INTRODUCTION

1.1 Background

Neurodegenerative Diseases (NDDs) include specific subsets of disorders that are resulted from the degradation and the succeeding loss of neurons associated with the altered proteins in the human brain. These subsequent changes in the brain give rise to cognitive decline and functional impairment. The mechanism of action in which NDDs are developed is still not fully understood (Pohl & Lin, 2018). However, it is found that the potential risk factors might comprise genetic polymorphism, oxidative stress, inflammation, and many others (Brown, Lockwood, & Sonawane, 2005). Furthermore, as a result of extended health research and improved living conditions, it is found that the average life expectancy of humans has increased in recent years, more specifically in countries like the United States, Canada, western Europe, New Zealand, as well as Australia (Christensen *et al.*, 2009). Consequently, the impact of NDDs could also increase in the coming decades (Berman & Bayati, 2018). Since most NDDs are age-dependent, the increased proportion of older generations poses a great requirement for further research in the neuroscience field.

An increase in the life expectancy of the population could elevate the occurrence of NDDs (Berman & Bayati, 2018). The increased prevalence of Alzheimer's disease (AD), Parkinson's disease (PD), and Huntington's disease have become major health problem and financial constraints for the healthcare system. It is noteworthy that the current treatment available for those particular diseases only alleviates the symptoms. As a result, the threat of these diseases immensely affects public health and poses a larger economic burden (Zahra *et al.*, 2020). There has been an exponential increase in the field of herbal medicine as a more economical alternative due to improvements in its quality, efficacy, and safety (Di Paolo *et al*., 2019). Hence, this study addresses the significance of herbal medicine development for NDDs.

This research is focused on AD, an NDD characterized by dysfunctional cognitive function and behavioral disability. AD is the most common type of dementia identified in older adults which accounts for up to 70% of dementia cases, affecting over 24 million people worldwide (Gaugler, 2020). The pathophysiology of AD is depicted by the development of several pathological changes, such as the establishment of senile plaques containing polymorphous beta-amyloid protein (Aβ), neurofibrillary tangles (NFT), as well as the loss of neurons and synapses (Chen, 2018). Multiple lines of evidence have implicated oxidative stress to the possible etiology of AD (Perry, Cash, & Smith, 2002). This disease gives rise to a deterioration of cognitive performance, including memory, attention, reasoning, language, as well as judgment. Moreover, it is categorized as a progressive disorder that could result in severe cognitive impairment. Besides, it is notable that there is over 5 million AD that cases arise annually, with a 1% increase in incidence for older adults aged between 60 and 70 year-olds, to an 8% increase in incidence for people over the age of 85 years (Bekris *et al.*, 2010).

Market demands of traditional medicine have skyrocketed, in which as many as 95% of drugs are acquired from plants (Maridass & De Britto, 2008). At present, the worldwide market for herbal medicine stands at 60 billion US dollars per year and increases steadily (Nirmal *et al.*, 2014). Indonesia is identified as one of the countries with the highest biodiversity in the world from various unique perspectives, including biogeographical, geological, ecological, along with climatic factors, thus leading to the expansion of a megadiverse flora with numerous endemic and ecologically adapted species. In particular, Indonesia has the second largest number of indigenous medicinal plants after the Amazon rainforest, which comprises about 10% of the world's flowering plant species (Nirmal *et al.*, 2014). Nevertheless, the development of herbal medicine for maintaining the function of the nervous system is still sparse. The approved treatments for AD only improve the symptoms of the patients, including memory and alertness. However, the progression of AD remains unchanged (Weller & Budson, 2018). The ever-increasing prevalence of AD and the ineffectiveness of the currently available treatments highlights the importance of developing herbal medicine specific for

maintaining the function of the nervous system, thus preventing the development of AD. Correspondingly, a high potential opportunity for pharmaceutical and biomedical research can be established in Indonesia to develop medicinal plants into commercial herbal medicine products.

Coriander (*C. sativum*) is an annual herb with many medical benefits due to its rich content of micronutrients and nutritional elements such as dietary fibers, vitamins, and minerals, including potassium, sodium, calcium, as well as magnesium. Previous research have shown that coriander leaves yield a decrease of memory loss in mice models along with a reduction of brain cholinesterase activity, demonstrating its potential protective role for Alzheimer's-like disease treatment (Mani *et al*, 2011). In agreement with this, a study conducted by Liu *et al.* (2016) has shown that coriander leaves suppress cell death, reactive oxygen species, as well as glial cell number induced by amyloid β-peptide. It is also reported that the ethanolic extract of coriander leaves could enhance learning and memory deficits in epileptic rats (Elahdadi-Salman *et al.*, 2015). The increase in reactive oxygen species levels in AD brain of mouse model is also reduced by coriander extract intake, which is shown by a decreased oxidative stress markers (Cioanca *et al.*, 2013). In line with this, donepezil, an acetylcholinesterase inhibitor, which is also the leading compound for AD treatment is suggested to contribute to reduced ROS production (Cacabelos, 2008). Pretreatment using donepezil has been reported to impede the amnesia-induced effect of scopolamine (Lu *et al.,* 2018). These findings indicate that the combinatorial properties of coriander leaves might be favorable for the interventions of Alzheimer's-like diseases.

1.2 Research Objectives

1.2.2 Aim

This study aims to evaluate the anti-Alzheimer's activity of of *C. sativum* leaves extract by means of Y-maze and thiobarbituric acid reactive substance (TBARS) assay using mouse model of Alzheimer's.

1.2.3 Objectives

- To evaluate spatial memory and cognitive function of mouse model of Alzheimer's treated with of *C. sativum* leaves extract using Y-maze.

- To evaluate the levels of lipid peroxidation in hippocampal tissue of mouse model of Alzheimer's treated with of *C. sativum* leaves extract using thiobarbituric acid reactive substance (TBARS) assay.

1.3 Hypothesis

It is hypothesized that of *C. sativum* leaves extract is able to prevent Alzheimer's Disease or dementia as demonstrated by the memory improvement and reduction of lipid peroxidation products.