

CHAPTER 1

INTRODUCTION

1.1 Problem Background

Neurodegeneration disease (ND) is a condition of progressive loss of neuron structure and function that leads to significant decreased life quality (Batista and Pereira, 2016). The most consistent risk factor is increasing age, especially elderly aged 60 years and above. In 2016, there are more than 631 million people around the world are suffer from ND risk factor, and over the next 20 years the proportion of elderly will be doubled with higher possibility of people suffering ND (Przedborski, Vila and Jackson-Lewis, 2003).

ND patients having problems with body movement and brain function which leads to a complete inability to carry out any type of everyday activity. This disease is one of the most important medical and socio-economic problem in the world, but the cause of the disease is still unknown. Examples of ND are: Alzheimer's disease (AD), Parkinson's disease (PD), Amyotrophic Lateral Sclerosis (ALS), Multiple Sclerosis (MS), and Huntington's disease (HD) (Batista and Pereira, 2016).

People with AD are having significant memory loss, obviously it hve concequences on daily life in many aspects. Leading to communication and behavioral problems, and safety hazards. Moreover, people with PD are experiencing tremor in hand and finger, slow movement, rigid muscle, impaired posture and balance, loss of automatic movement, speech changes, and writing problems. On top of that, approximately €130 billion per year is dedicated to care people with dementia across Europe (Goedert, 2015).

In this modern society, there are many treatments available for neurodegenerative disease, such as: [dopaminergic treatments for PD and movement disorders,] [cholinesterase inhibitors for cognitive disorders,] [antipsychotic drugs for behavioral and psychological symptoms of dementia,] [analgesic drugs for pain,] [anti-inflammatories for infections,] [and even the use of deep brain stimulation to stop tremor and refractory movement disorders] (Chen and Pan, 2015). However, none of the treatments above are effective and able to treat ND patients because the main focus of the available treatments is to reduce the symptoms, not regenerating the degenerated neurons. Moreover, due to numerous adverse effects, current ND treatment is inaccessible to many patients.

Neurite outgrowth is a process to maintain neuronal cell volume or to promote recovery from neurodegeneration, while neuroprotection is an intervention process to decelerate the neurodegradation process. Those processes are essential to slow down the onset of neurodegenerative disease and to stop degeneration of neuron in people with ND (Hu *et al.*, 2015). In its application, the mushroom is expected to promote recovery of damaged neuron. In the past decade, neurite outgrowth and neuroprotection becoming a popular research topic because it can be a promising alternative treatment for people with damaged or impaired neuron (McConeghy *et al.*, 2012).

In the past decade, natural product become a popular alternative treatment and showed a promising result for the serious problems of many neurodegenerative diseases (Pan, Kwak, *et al.*, 2011; Pan, Liu, *et al.*, 2011; Pan *et al.*, 2014). *Lignosus rhinocerus* is one of natural product that shows an excellent result in promoting neurite outgrowth in PC-12 cell lines (Eik *et al.*, 2012; Seow *et al.*, 2015). A study by Eik *et al.* showed 24.4% and 42.1% neurite outgrowth of 20 µg/mL aqueous extract alone and a combination of 20 µg/mL aqueous extract and 30 ng/mL NGF. Although there is no study about neuroprotection properties of this macro mushroom according to online literature, but this mushroom has a diverse and unique properties such as, nutrient and mineral, phenolic content, antioxidant activity, ferric reducing

antioxidant power (FRAP), radical scavenging activity, anti-proliferative activity, and many more that make it as a suitable treatment for many kinds of diseases (Yap *et al.*, 2013).

Therefore, with the help of macro fungus regenerating damaged neuron by stimulating neurite outgrowth and neuroprotection could be an alternative approach to prevent the development of ND in the future. Thus, the uses of *Lignosus rhinocerus* extracts to promote neurite outgrowth and neuroprotection is the main focus in this study.

1.2 Problem Formulation

Current treatment for ND is limited and not all of the patients could gain an expected result due to numerous adverse effects. Moreover, once people suffer ND, they will most likely to get worse, and it is difficult to detect this disease in the early stage. Therefore, *Lignosus rhinocerus* as a macro fungus that has been proven to have a neurite outgrowth properties, as well as, highly diverse and unique composition. Tiger milk mushroom could be an alternative compound for a researcher to find a treatment for people with neurodegenerative disease.

1.3 Research Objectives

The objectives of this study are:

- i. To observe and compare neurite outgrowth in PC-12 cells with and without *Lignosus rhinocerus* extracts treatment.
- ii. To investigate neuroprotection properties of *Lignosus rhinocerus* extract in PC-12 cell.

1.4 Research Scope

The research scope for this research are: cell culture and maintenance, cytotoxic assay, neurite outgrowth assay, and neuroprotection assay (pre, post, and concurrent treatment).