CHAPTER I
INTRODUCTION

1. Rationale and Background

The number of elderly in Asia and the Pacific region including Thailand is expected to rise dramatically. It has been reported that the elderly population in Thailand increased from 4.02 million in 1990 to 65 million in 2001 and will reach 82 million in 2040 (Knodel and Chayovan, 2008). The increased long life span leads to the increase in age-related neurodegenerative disorders such as Alzheimer's disease (AD) and Parkinson's disease (PD). Alzheimer's disease and Parkinson's disease are the most common age-related neurodegenerative disorders. The extrapolated number of Alzheimer's disease and Parkinson's disease worldwide in 2005 and 2006 were approximately 26.6 million and 4.1 million respectively. These numbers are still continually increased (Dorsey *et al.*, 2007; Vossius *et al.*, 2011).

Neurodegenerative diseases including Alzheimer's disease and Parkinson's disease contribute the important role to the substantial medical and public health burdens on populations throughout the world. They also produce both financial and psychological burdens on the society. It has been reported that Alzheimer's disease is a high cost disease that affects families, caregivers, medical resources, and the economy (Hurd *et al.*, 2013;Prince *et al.*, 2013). In 2010, nearly 15 million families and other unpaid caregivers provided an estimated 17 billion hours of care to people with AD and other dementias, a contribution valued at more than $202 billion. (Association, 2012). Currently, it has been known that not only AD but also PD produces a great impact on the annual health budget as mentioned above. In the United States, it was reported that both direct and indirect costs associated with PD exceed $20 billion annually and it was likely to exceed $50 billion in 2040 (Huse *et al.*, 2005). To the best of my knowledge, there is no effective treatment to terminate the neurodegeneration. The current therapeutic efficacy is still limited and the adverse effects are commonly found (Fox *et al.*, 2010; Hong *et al.*, 2008; Kuan and Barker, 2005).

Complementary and alternative medicines (CAMs) has been long-term used for treating numerous ailments for a long time. Currently, it has been reported that abundant of population worldwide still used alternative medicine (World Health Organization 2001). In the developing countries such as some countries in Africa and Asian, approximate 80% of the populations still used the complementary alternative medicine. Although, there are numerous modalities of alternative medicine, herbal medicine and acupuncture appear to be the most famous.

Medicinal plants are long-term used for longevity promotion, neuroprotection and memory enhancer in traditional folklore. The herbal medicine can be used either by single herb or polyherbal recipes. However, the polyherbal recipes have been very much widely used than the single plant based on the concept that the synergistic effect of the plants can provide more beneficial effects (Jayakumar, 2010). Numerous studies have demonstrated that numerous plants possess longevity promotion effect. These also included *Anethum graveolens* Linn, *Anacardium occidentale* Linn, *Moringa oleifera* Lam, *Zingiber officinale* Roscoe and *Cyperus rotundus* Linn. In order to optimize the benefit of the plant extracts, the positive modulation effects on the interaction of these medicinal plants to protect against neurodegenerative diseases such as AD and PD have gained attention.

In addition to herbal medicine, acupuncture is also recognized as one of the effective therapy against neurodegenerative diseases. According to the theories of Traditional Chinese Medicine, meridians of the body are responsible for all the body's major organ systems. It is believed that meridians carry energy throughout the body and similar to the way the arteries carry blood. This energy is referred to as "Qi" or "Chi". According to Traditional Chinese Medicine (TCM), the stimulations of acupoints (acupuncture points) are implemented to balance the movement of energy (qi) in the body to restore health condition. Traditionally, the stimulation of acupoint was performed at numerous points simultaneously. Therefore, it produced a great burden to a patient due to tits invasive technique.

Acupuncture has been used for treating neurological disorders for a long time. Numerous acupoints have been stimulated to improve various neurological disorders. Among various acupoints, "HT7" or "shenmen"is scientifically shown to improve the cognitive function (Lee *et al*, 2011). Since needle acupuncture is invasive and painful,

the stimulation this acupoint by using non-invasive technique including laser acupuncture has been developed. However, no scientific evidence about the effect of laser acupuncture at only one single point especially at HT7.

Due to the continually increase in AD and PD prevalence and the limitation of current therapy, the alternative choices to protect and to mitigate the disorders in both conditions are required. Therefore, the current study was carried out to determine the effective of therapy with potential herbs and laser acupuncture against neurodegenerative disease including AD and PD.

2. Experiment Aims and Objectives

2.1 General experimental aim

This study was designed to develop an innovation in complementary alternative medicine for treating neurodegenerative disease especially in Alzheimer's disease and Parkinson's disease.

2.2 Specific objectives

2.2.1 To develop and to test the efficacy of the neuroprotective product in animal model of Alzheimer's disease and Parkinson's disease.

2.2.2 To determine the effect of laser acupuncture and neuroprotective product against Alzheimer's disease and Parkinson's disease.

2.2.3 To determine the possible underlying mechanism of the laser acupuncture and neuroprotective product.

1) To determine the alteration of oxidative stress damage markers including the level of malondialdehyde (MDA) and the alteration of scavenging enzymes activities including superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px).

2) To determine the alterations of acetylcholinesterase and monoamine oxidase activities.

3) To determine the neuron densities in substantia nigra and hippocampus.

4) To determine the alteration of pERK 1/2.

3. Scope and Limitation of the Study

3.1   Male Wistar ratswere used as experimental animals in this study and the ages were approximately at 8 weeks old.

3.2   All stresses should be avoided to prevent the influence effect of stress.

3.3   All interventions should be performed at the same period to avoid an influence of circadian rhythm.

3.4   In all experiments, control and experimental groups should be performed in parallel at the same period to avoid effect of seasonal changes.

4. Hypothesis

4.1   If the developed neuroprotective product is the potential neuroprotective product, the polyherbal recipe should exhibit the highest potential benefit on antioxidant and memory enhancing effects in vitro.

4.2   If laser acupuncture or the neuroprotective product could effectively treat Alzheimer's disease, at least one of the following changes should be observed.

4.2.1   The rat which were induced memory deficit induced by AF64A and obtained either laser acupuncture or neuroprotective product should show better memory performance than the non-treated group.

4.2.2   The rat which were induced memory deficit induced by AF64A and obtained either laser acupuncture or neuroprotective product should show the higher neurons density in hippocampus than the non-treated group.

4.2.3   The rat which were induced memory deficit induced by AF64A and obtained either laser acupuncture or neuroprotective product should show higher density of pERK 1/2 in hippocampus than the non- treated group.

4.3   If laser acupuncture or the neuroprotective product could effectively treat Parkinson's disease, at least one of the following changes should be observed.

4.3.1   The rat which were induced Parkinson-like condition by 6-OHDA and obtained either laser acupuncture or neuroprotective product should show better motor and memory performance than the non-treated group.

4.3.2   The rat which were induced Parkinson-like condition by 6-OHDA and obtained either laser acupuncture or neuroprotective product should show the higher neurons density in hippocampus than the non-treated group.

4.3.3 The rat which were induced Parkinson-like condition by 6-OHDA and obtained either laser acupuncture or neuroprotective product should show higher density of tyrosine hydroxylase positive neuron in substantia nigra than the non- treated group.

5. Anticipated Outcome

5.1 To develop the innovation in complementary alternative medicine for treating neurodegenerative disease including Alzheimer's disease and Parkinson's disease.

5.2 To provide the evidence based for the therapeutic efficacy against neurodegenerative disease including Alzheimer's disease and Parkinson's disease and the possible underlying mechanism of laser acupuncture and neuroprotective product.