

# CHAPTER I

## INTRODUCTION

### Rationale for the study

Due to the longevity of the world population than the past, geriatric health care become higher important in the present medicine. Dementia, especially with the Alzheimer's disease, is one of the major problems in geriatric medicine. In Thailand, the caring cost for 1 dementia patient is 4,000 – 6,000 bath/ month or up to 8,000 - 16,000 bath/ month in case of the severe patient. For attenuating the cost of medication, researching for herbal medicine beneficial for improving cognitive and memory function is recently reasonable alternation for the disease treatment.

Two outstanding characters of Alzheimer's disease, neurofibrillary tangles and neuritic plaques, are the most putative pathologies of the disease. Although both neuritic plaques and neurofibrillary tangles are found in all association areas of the cortical cortex, comparatively, neurofibrillary tangles (NFTs) and quantitative neuronal losses, not the neuritic plaques, correlate best with the severity of dementia (Arriagada, et al., 1992a). Moreover, neuronal atrophy is also the prominent macroscopic character of the disease. Correlatively, recent findings reported elevated tau hyperphosphorylation in apoptotic cells by both DNA damage (Mookherjee and Johnson, 2001) and by removal of trophic factor (Davis and Johnson, 1999a, b; Nuydens *et al.*, 1997; Shelton and Johnson, 2001; Zhang and Johnson, 2000). The accumulation and aggregation of the tau protein was recently proposed to be attributed to the inhibition of the autophagy protein degrading system (Hamano, et al., 2008)

*Bacopa monnieri* or Brahmi (BM) is a versatile traditional Ayurvedic herb used for centuries as an anti-inflammatory, analgesic, antipyretic, antiepileptic, and sedative agent. The most important of these is especially the use of the plant, plant extract and isolated important component bacosides as an enhancing agent for cognition and memory function. Several findings suggest that the cognition-promoting functions of BM may be partially attributed to the antioxidant effect of the bacosides. BM could exert a neuroprotective effect by inhibiting Acetylcholinesterase (AChE)

and by being the antioxidant relieving neuronal oxidative stress (Limpeanchob, et al., 2008), which could be in turn contributed to neuronal apoptosis. With this reason, this antioxidant property of BM is tempting to be applicable for decreasing tau protein aggregation, the one more prominent pathology of Alzheimer's disease. Further, this advantage may alleviate the medication cost of this disease.

### **Propose of the study**

This study is aimed to measure the effect of alcoholic BM extract on the viability and the amount of tau protein from NGF-deprived PC12 or human SH-SY5Y neuroblastoma cells brought up in apoptotic-induced media.

#### **Specific objectives**

To measure the effect of alcoholic BM extract on the viability of the neuronal cells brought up in normal-serum RPMI1640 medium.

To measure the effect of alcoholic BM extract on the viability of the neuronal cells brought up in normal-serum medium and in apoptotic-induced condition.

To measure the effect of alcoholic BM extract on the amount of total-tau expression (at Tau 5 site) from the neuronal cells brought up in normal-serum medium and apoptotic-induced condition.

To measure the effect of alcoholic BM extract on the amount of dephosphorylated-tau expression (at Tau-1 site) from the neuronal cells brought up in normal-serum medium and apoptotic-induced condition.

To measure the effect of alcoholic BM extract on the expression of total-tau gene in the neuronal cells brought up in normal-serum medium and apoptotic-induced condition.

### **The research hypothesis**

The hypothesis of this study is that BM antioxidant property can be applicable for reducing tau protein aggregation so alcoholic BM extract will increase the viability of and decrease tau protein from NGF-deprived PC12 or differentiated human SH-SY5Y neuroblastoma cells brought up in apoptotic-induced media.

**Significance of the study**

This research can be the scientific advocating data for alternative medicine for enhancing memory function with a versatile traditional Ayurvedic herb BM.

**Scope of the study**

1. This study is used alcoholic BM extract generously provided by Assoc. Prof. Dr. Kornkanok Ingkaninan's laboratory, Department of Pharmaceutical Chemistry and Pharmacognosy, Faculty of Pharmaceutical Science, Naresuan University, Muang, Phitsanulok, Thailand.

2. This research is studied on NGF-deprived PC12 cells and differentiated human SH-SY5Y neuroblastoma cells brought up in control normal-serum and apoptotic-induced serum-free media with either no or with alcoholic BM extract ranging from 50-200  $\mu$ M.