CHAPTER I

INTRODUCTION

The accumulation of reactive oxygen species (ROS), caused by enhancement of ROS production or by suppression of ROS destruction, may result in an imbalance between cellular production of ROS and the ability of cells to defend themselves against ROS. This is referred to as oxidative stress (Simonian and Coyle, 1996). Oxidative stress may cause lipid peroxidation, protein oxidation, DNA damage and finally cell death. The organ most vulnerable to ROS damage is the brain because of its high oxygen consumption, abundant lipid content and relative paucity of antioxidants (Coyle and Puttfarcken, 1993). There is increasing data from experimental models and human brain studies that suggest oxidative stress may play an important role in neuronal degeneration in diseases such as Parkinson's and Alzheimer's diseases, and amyotrophic lateral sclerosis (Simonian and Coyle, 1996). Furthermore, excessive or persistent activation of glutamate-gated ion channels may cause neuronal degeneration in stroke, trauma, and seizures. Oxidative stress and excessive activation of glutamate receptors appear to be converging, sequential, interacting processes that provide a final common pathway for cell vulnerability in the brain (Coyle and Puttfarcken, 1993).

The antioxidants that could intercept and react with free radicals at a rate faster than the substrate, and are able to attack a variety of targets including lipids, fats, and proteins are believed that they are implicated in a number of important degenerative diseases including aging itself (Harman, 1981, Ozawa, 1997, Beckman and Ames, 1998).

Among various plant compounds, phytoestrogens have been proposed to have many health benefits such as isoflavone protection against breast cancer (Lof and Weiderpass, 2006), antioxidant protection against oxidatively-induced DNA damage (Sierens et al., 2001) and protection of neuronal cells against oxidative stress (Sonee et al., 2004). Phytoestrogens are plant substances producing estrogen activities that can be divided into three main classes; isoflavones, lignans and coumestran. It has been suggested that some of the beneficial effect of isoflavones might be, at least in part, mediated by their antioxidative activity (Wu and Chan, 2007, Zeng, Chen and Zhao, 2004).

Among plant sources, *Pueraria candollei* var. *mirifica* (*P. miriifica*) has long been used as a rejuvenating/anti-aging supplement in Thailand and Myanmar (Cain, 1960). *P. mirifica* has been found to alleviate menopausal symptoms in women (Muangman and Cherdshewasart, 2001) and inhibit bone loss in the long and axial bones in sex hormone-deficient male rats (Urasopon et al., 2007). Various isoflavonoids have been isolated and characterized from its tuberous root extracts. The major active compounds proposed to play apart in are phytoestrogens such as genistein, daidzein, miroestrol, deoxymiroestrol (Chansakow, et al., 2000a and 2000b).

In this study, various *P. mirifica* extracts were screened for their antioxidative activities against DPPH radical. The extracts exhibiting antioxidative activity were further studied for their neuroprotictive activity. The experiments were conducted by using a model of glutamate-induced cell death in HT-22 mouse hippocampal neuronal cells. Additionally, the types of radical that the extract could scavenge also were identified by the ORAC and DCFH-dA assay.