

# CHAPTER I

## INTRODUCTION

### 1.1 Rationale and Background

Stress, a regular accompaniment and an important part of normal daily living, tones the body, sharpens the mind, and enables the organism to cope with changes in the environment or other external stressors. Although, it is not an illness, it can produce numerous deleterious disorders including neuropsychological disorders and sexual dysfunction. Since the prevalence of stress exposure in the current daily lifestyle is increasing (Intarakamhang, 2009), the prevalence of stress related disorders such as memory and sexual dysfunction are continually increasing. Both the memory impairment and sexual dysfunction have been regarded as the important health problems which disturb the quality of life. The annual health care budget of each condition is also very high. Therefore, both stress related memory impairment and stress related sexual dysfunction produce a great economic burden.

It has been reported that stress exerts the deleterious effects on several cellular functions through impairment of antioxidant defenses, leading to oxidative damage, a key factor of numerous pathological disorders (Torres *et al.*, 2006). It decreases antioxidant defense status in the brain, which may form the basis for impaired memory (Mats, 1999; Onodera *et al.*, 2003). In addition, stress can also interfere with spermatogenesis, fertility rate, and sexual disturbances which express as erectile dysfunction, ejaculatory disorders, loss of libido and a decrease in the frequency of intercourse (Lenzi *et al.*, 2002). It has been reported that oxidative stress also plays a critical role on the pathophysiology of sexual dysfunction especially in erectile dysfunction (ED), the most important sexual dysfunction problem (Mishra and Singh, 2013).

Complementary alternative medicine especially herbal medicine has been long term used for treating various disorders. In addition, many herbs are also used for increasing sexual function and known as aphrodisiac. According to the traditional folklore, numerous herbs are reputed for both cognitive enhancing effect and

aphrodisiac properties. In addition, most of them also possess antioxidant effect. Based on the reputations of the herbs according to traditional folklore, the antioxidant effect of the herbs and the crucial role of oxidative stress on the pathophysiology of memory impairment and sexual dysfunction induced by stress, there is a growing interest to develop the functional food to protect against both conditions.

*Moringa oleifera* Lam or Marum in Thai, *Anacardium occidentale* L. and *Nelumbo nucifera* Gaertn are the plants that are widely available in the Northeast of Thailand. They were consumed both as food and as medicine. According to the traditional folklore, these plants are reputed for aphrodisiac effect. In addition, they also possess antioxidant effect (Faizi *et al.*, 1998; Lalas and Tsaknis, 2002; Sheikh *et al.*, 2014). Therefore, the potentials to protect against stress related memory impairment and sexual dysfunction of these plants have been focused. Currently, no scientific evidence concerning this issue is available. Therefore, this study was set up to determine the protective effect against memory impairment and sexual dysfunction induced by stress of these plants.

## **1.2 Experimental Aims and Objectives**

### **1.2.1 General experimental aim**

This study was designed to determine the protective effect against memory impairment and sexual dysfunction induced by stress of *Moringa oleifera* Lam. or Marum in Thai, *Anacardium occidentale* Linn. and *Nelumbo nucifera* Gaertn.

### **1.2.2 Specific objectives**

1.2.2.1 To screen the potential of selected Thai medicinal plants to protect against stress related disorders including memory impairment and sexual dysfunction.

1.2.2.2 To evaluate the effect of the potential selected Thai medicinal plants to mitigate memory impairment and sexual dysfunction induced by stress.

1.2.2.3 To investigate the possible underlying mechanism of the selected Thai medicinal plants including the following parameters:

- (1) The alteration of monoamine transmitters in hippocampus, nucleus accumbens and medial preoptic area of hypothalamus
- (2) The alteration of cholinergic function in hippocampus

- (3) The alteration of oxidative markers including superoxide dismutase, catalase and glutathione peroxidase and malondialdehyde in hippocampus
- (4) The alteration of phosphodiesterase activity in penis
- (5) The alteration of serum testosterone and corticosterone
- (6) The alteration of neurons density and proliferative marker (Ki-67) in hippocampus
- (7) The effect on endothelial nitric oxide synthase (eNOS) in penis
- (8) The alteration of dopaminergic function in ventral tegmental area and nucleus accumbens

### **1.3 Hypothesis**

1.3.1 If the selected Thai medicinal plants possess the potential to mitigate the stress related disorders, the extract should exhibit the antioxidant activity and the suppression effect on acetylcholinesterase, monoamine oxidase and phosphodiesterase activities.

1.3.2 If the selected Thai medicinal plants can mitigate the stress related disorders, the animals which receive the plant extract should show either better memory performance or better copulatory behavior than the vehicle treated animals.

1.3.3 In order to investigate the possible underlying mechanism, the hypotheses have been set up as following:

1.3.3.1 If the selected Thai medicinal plants exhibit their beneficial effects to mitigate memory impairment and sexual dysfunction via the alteration of monoamine transmitters, the animals which received the plants extract should show less activities of monoamine oxidase in hippocampus, nucleus accumbens and medial preoptic area of hypothalamus than vehicle treated rats.

1.3.3.2 If the selected Thai medicinal plants exhibit their beneficial effects to mitigate memory impairment via the enhanced cholinergic function, the animals which received the plants extract should show less activity of acetylcholinesterase in hippocampus than vehicle treated rats.

1.3.3.3 If the selected Thai medicinal plants exhibit their beneficial effects to mitigate memory impairment via the enhanced oxidative stress markers and

reduced malondialdehyde, the animals which received the plants extract should show higher level of oxidative stress markers and lower level of malondialdehyde in hippocampus than vehicle treated rats

1.3.3.4 If the selected Thai medicinal plants exhibit their beneficial effects to mitigate sexual dysfunction via the alteration of phosphodiesterase type 5 in penis, the animals which received the plants extract should show less activity of phosphodiesterase type 5 in penis than vehicle treated rats

1.3.3.5 If the selected Thai medicinal plants exhibit their beneficial effects to mitigate sexual dysfunction via the alteration of testosterone or corticosterone, the animals which received the plants extract should show higher level of serum testosterone and lower level of serum corticosterone than vehicle treated rats.

1.3.3.6 If the selected Thai medicinal plants exhibit their beneficial effects to mitigate memory impairment via the enhanced neurons density and proliferation in hippocampus, the animals which received the plants extract should show higher expression of neurons density and proliferative marker (Ki-67) in hippocampus than vehicle treated rats.

1.3.3.7 If the selected Thai medicinal plants exhibit their beneficial effects to mitigate sexual dysfunction via nitric oxide, the animals which received the plants extract should show higher endothelial nitric oxide synthase (eNOS) level in penis than vehicle treated rats.

1.3.3.8 If the selected Thai medicinal plants exhibit their beneficial effects to mitigate sexual dysfunction via dopaminergic neurons, the animals which received the plants extract should show higher density of tyrosine hydroxylase reactive neurons in ventral tegmental area and nucleus accumbens than vehicle treated rats.

## **1.4 Scope and limitation of the study**

1.4.1 Male Wistar rats used in this study were approximately 8-12 weeks old.

1.4.2 Female rats used in this study were virgin rats and they were induced estrous cycle and served as receptive female rats during the compulsory assessment.

1.4.3 The administration of the interventions for all groups should be performed parallel at the same period to avoid the effect of circadian rhythm and seasonal changes.

1.4.5 Other stresses besides mobilization stress used in this study should be avoided to prevent the confounding effects.

## **1.5 Anticipated Outcomes**

1.5.1 To provide the knowledge about bioactivities of *Moringa oleifera* Lam, *Anacardium occidentale* Linn and *Nelumbo nucifera* Gaertn.

1.5.2 To provide the knowledge concerning aphrodisiac activity and learning and cognitive enhancer of *Moringa oleifera* Lam, *Anacardium occidentale* Linn and *Nelumbo nucifera* Gaertn in stress male rats.

1.5.3 To provide the knowledge about the possible underlying mechanism of *Moringa oleifera* Lam, *Anacardium occidentale* Linn and *Nelumbo nucifera* Gaertn against stress condition in male rats.

1.5.4 To provide the alternative choice to increase the value of *Moringa oleifera* Lam, *Anacardium occidentale* Linn and *Nelumbo nucifera* Gaertn as food supplement against stress related memory impairment and sexual dysfunction.