

Thawatchai Prabsattroo. 2015. **The Effect of Selected Thai Medicinal Plants on Memory Impairment and Sexual Dysfunction Induced by Stress in Male Rats**. Doctor of Philosophy Thesis in Neuroscience, Graduate School, Khon Kaen University.

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### ABSTRACT

Currently, the stress related disorders especially cognitive deficit and sexual dysfunction are continually increasing. Despite the increasing prevalence and the great burdens on both quality of life and socio-economic status of health care system induced by stress-related disorders, no specific treatments for these conditions are available. Based on the crucial role of oxidative stress on the pathophysiology of cognitive impairment and sexual dysfunction induced by stress and the reputation for cognitive enhancing and sexual enhancing effects of some medicinal plants, the beneficial effects of the medicinal plants reputed for antioxidant, sexual and cognitive enhancing effects on cognitive deficit and sexual dysfunction induced by stress have gained attention. Since no scientific data concerning this issue are available, this study aimed to determine the effect of *Moringa oleifera*, *Anacardium occidentale* and *Nelumbo nucifera* on memory impairment, brain damage and sexual dysfunction in animal model of stress related disorders mentioned earlier.

In the first part of this study, in vitro screening for anti-stress potential of *M.oleifera* leaves, *A.occidentale* leaves and *N.nucifera* flowers extracts was carried out. The results showed that all selected medicinal plants possessed antioxidant effect and inhibitory effects of AChE, MAO-B and PDE-5. Data obtained from acute toxicity study showed that *M.oleifera* and *N.nucifera* were safe up to 5,000 mg/kg BW while *A.occidentale* was safe up to 2,000 mg/kg BW via oral route.

The second part of this study was focused on the determination of sexual enhancing effect of the selected medicinal plants mentioned earlier in stress-exposed rats. Adult male Wistar rats were administered the tested extracts 30-45 minutes prior to the 12 h- immobilization stress exposure once daily throughout the 14-day

experimental period. The doses of *M.oleifera* leaves extract used in this study were 10, 50 and 250 mg/kg whereas *A.occidentale* leaves extract was used at doses of 25, 100 and 200 mg/kg and *N.nucifera* flowers extract was used at doses of 10, 100 and 200 mg/kg BW. After the exposure to immobilization stress, rats were refreshment for 3 h and then the rats were determined sexual behaviors after the single dose administration and at 7-day and 14-day experimental periods. At the end of experiment, they were determined serum corticosterone, testosterone, activities of MAO-B in MPOA and NAc, density of tyrosine hydroxylase immunoposited neurons in VTA and NAc, PDE-5 activity and eNOS expression in penis. The histology of testis was also investigated. All plants extracts could improve sexual behaviors of stress-exposed rats. All extracts could exert the effect both at the central nervous system and at peripheral system. In the central nervous system, all extracts could enhance dopaminergic system in VTA, MPOA and NAc by suppressing the activities of MAO-B and by increasing the density of tyrosine hydroxylase immunoposited neurons. In addition, they also exerted the sexual enhancing effect at the penis by suppressing PDE-5 activity and increased the expression of eNOS. It was found that *M.oleifera* leaves extract decreased serum corticosterone but increased serum testosterone while *A.occidentale* leaves extract could principally enhance serum testosterone and *N.nucifera* could mainly decrease serum corticosterone. Therefore the extracts could modify male sexual behaviors in stress-exposed rats via neuro-endocrine system.

The last part of this study was focused on the neuroprotective and cognitive enhancing effects of all plants mentioned earlier. Adult male Wistar rats were treated with the tested extracts and stress exposure as that mentioned earlier in the previous part except that the animals were determined spatial memory after the single dose of administration and at 7 and 14 days of treatment. At the end of study, they were determined serum corticosterone, the activities of MAO-A and MAO-B, AChE, SOD, CAT, GSH-Px, MDA level and the expression of Ki67, a proliferative markers, in hippocampus. In addition, the densities of survival neurons in CA1, CA2, CA3 and dentate gyrus in hippocampus of stress-exposed rats were also evaluated. The results showed that the extracts of the selected plants improved memory impairment, suppressed AChE, MAO-A and MAO-B, decreased MDA level but increased

scavenger enzymes activities in hippocampus. The enhanced densities of neurons in various subregions of hippocampus and the expression of Ki67 in hippocampus were also observed. Taken all data together, the improved memory impairment might occur partly by increasing the available ACh and monoamine transmitters via the suppression of AChE and MAO-A and MAO-B and by increasing the neuronal density in hippocampus. The enhanced neuron density in hippocampus might occur partly via the decreased neurodegeneration induced by oxidative stress and via the increased proliferation of neuronal cells in the mentioned areas. The decreased oxidative stress in hippocampus induced by *M.oleifera* leaves extract occurred mainly by increasing SOD and CAT activities. It was found that *A.occidentale* leaves extract exerted the effect to decrease oxidative stress mainly by enhancing SOD and GSH-Px activities while *N.nucifera* flowers extract exerted the effect mainly by increasing CAT activity.

Therefore, this study was the first study to provide supporting scientific evidence concerning sexual and cognitive enhancing effects of *M.oleifera*, *A.occidentale* and *N.nucifera*, the plants reputed for both actions in traditional folklore. These plants can be served as the natural resources for developing health products for sexual dysfunction and cognitive impairment induced by stress. However, further researches concerning the possible active ingredients and pharmacokinetic of the extracts are essential before moving forward to the clinical trial.