

# CHAPTER I



## INTRODUCTION

Oophorectomized and post-menopausal women suffer from many menopausal symptoms such as emotional instability, hot flushes that may alternate with chilling sensation and drying vaginal epithelium etc. Moreover, important abnormalities including osteoporosis (Campston, 2005) and cardiovascular diseases (CVDs) (Arnal et al., 2004) have been reported. The incidences of cardiovascular diseases, atherosclerosis and coronary artery diseases (CADs), and osteoporosis in post-menopausal women are higher than women at the age before menopause (Lissin and Cooke, 2000). Endogenous estrogen deficiency is considered to be the main cause of these abnormalities, especially due to the loss of protective effects of estrogen on bone and cardiovascular system.

The observational studies suggested that estrogen replacement therapy (ERT) can reduce the risks of cardiovascular diseases and osteoporosis in post-menopausal women (Gass and Dawson, 2006). Estrogen replacement therapy is considered to be an effective method to prevent menopausal symptoms and restore the protective effects on cardiovascular system and bone (Ruggiero and Likis, 2002). However, many serious side effects in long term ERT used including cancerous events (breast cancer and endometrial cancer etc.) and thromboembolic events (causes of death by coronary artery diseases and strokes etc.) have been reported (Staren and Omer, 2004).

Many researchers have been attempting to study the alternative hormone replacement therapy (HRT) in order to find the safer therapeutic agents and “phytoestrogens” is the interesting one. Phytoestrogens, plant-derived estrogen like substances, possess the varying degree of estrogenic activity and estrogen-like molecular structure. Phytoestrogens such as genistein, daidzein and coumestrol exhibit

the protective effects on cardiovascular system including atherosclerotic preventing effects, lipid lowering effects and also can prevent osteoporosis in post-menopausal women (Lotke, 1998).

*Pueraria mirifica* (white “Kwao-Keur”) is an indigenous herb of Thailand which possesses estrogenic activity. This medicinal plant has been used in Thai traditional medicine and known well as “rejuvenating” folk medicine for over a hundred year. It’s recommended for both aged men and women for improve complexion, blood circulation, energy balance and vigor leading to more reflexive movement, grow and strengthen hair (หลวงอนุสารสุนทร, 1931). The phytoestrogens that possess the highest estrogenic activity in tuberous root of *P. mirifica* are chromene derivative compounds, deoxymiroestrol and miroestrol (Chansakaow et al., 2000a). A previous study reported that the tuberous root extract of *P. mirifica* exhibit lipid-lowering effects in hypercholesterolemic rats and vascular protective effects in ovariectomized rabbits (Auttapongpaiboon, 2002).

Despite evidences linking phytoestrogens of *P. mirifica* exhibit strong estrogenic activities, beneficial effects of *P. mirifica* using as ERT in particular on bone remain poorly defined. According to previous studies, ovariectomized rat is an appropriate model for evaluation of estrogen replacement therapy.

Therefore, the objectives of this study were to determine the subchronic effects of *P. mirifica* preparation on vascular functions in isolated thoracic aorta preparations in ovariectomized rat model. In parallel sets of experiment, the bone sparing effects as well as its effects on clinical blood biochemistry parameters of *P. mirifica* preparation were also examined.

## **Hypothesis**

Tuberous root extract of *Pueraria mirifica* exhibits vascular protective effect and osteoporotic preventive effect in ovariectomized rats.

### **Benefit gained from the study**

1. A supporting data of *P. mirifica* preparation on vascular functions (endothelium-dependent and/or endothelium-independent vascular responses on isolated aortic rings) and pathogenicities of thoracic aorta in ovariectomized rats.
2. A preliminary data of *P. mirifica* preparation on bone sparing (inductive and/or reductive effects on bone mass and biological marker of bone turnover rate) and pathogenicities of femoral bones in ovariectomized rats.
3. Evidences linking NO production and lipid parameters to abnormal endothelial dependent arterial relaxation and atherogenesis in *P. mirifica* treated ovariectomized rats.