



CHAPTER I

INTRODUCTION

Breast cancer is the most common cancer in women, especially in Western countries. In Thailand, breast cancer is the second cause of death in cancer patients. Very low rates of incidence are reported for most Asian and African populations, however, the rates in Asian countries are increased considerably (Coleman et al., 1993). Considering, when the women who migrated at a young to the United States, higher breast cancer rates are found in their next generations, especially those born in the United States. This suggests that social and environmental risk factors for breast cancer are not only more important than genetic risk factors, but also can change relatively rapidly, with equally rapid increases in breast cancer risk (Kelsey, 1993).

The international epidemiological comparisons have linked the semi-vegetarian diet and soy intake in some Asian countries with a low risk of chronic diseases (i.e. cancer and coronary heart disease). Interestingly, people in Asian countries especially Japanese women who commonly consumed soy foods, the low breast cancer mortality rate was found. Report indicating that some non-nutrient compounds, lignans and isoflavonoids in the diet may contribute to homeostasis and thus have a role in the maintenance of health. These compounds have molecular weights or structures similar to those of steroids, both of plant origin and implying that they could be such important dietary modulators of the human hormonal system (Markies et al., 1998 and Adlercreutz, 1999). These naturally occurring compounds have structurally and functionally similar to estrogen that are defined as phytoestrogen.

Many reports showed that phytoestrogen could inhibit the growth of cancer cell lines while some reports mentioned about their ability to stimulate the proliferation of the estrogen sensitive cancer cell lines, such as human mammary carcinoma, MCF-7 (Wang et al., 1996; Wang and Kurzer, 1997 and Zawa and Duwe, 1997). The mechanisms of phytoestrogens may influence sex hormone production, metabolism and biological activity. It could depend, at least in part, on mixed estrogen agonist/antagonist properties and binding to estrogen receptors. Furthermore, phytoestrogen have been demonstrated to affect intracellular enzymes, protein synthesis, growth factor action, malignant cell proliferation, cell differentiation,

cell adhesion, angiogenesis, and apoptosis. Experimental studies in animals suggest that phytoestrogen in the group of lignans and isoflavonoids are among the dietary factors affording protection against atherosclerotic vascular disease and cancers (Clarkson et al., 1995; Adlercreutz and Mazur, 1997; Murkies et al., 1998; Tham et al., 1998; Bingham et al., 1998 and Lamartiniere et al., 1998).

Results from animal studies suggested that phytoestrogen isoflavones may inhibit chemically induced mammary gland tumorigenesis (Murkie et al., 1998; Messina et al., 1994; Yang et al., 2001; Knight et al. 1996; Constantinou et al., 1996; Lamartiniere et al., 1998; Ohta et al., 2000 and Pollard and Luckert, 1997) and tumor metastasis (Bylund et al., 2000; Dalu et al., 1998 and Zhou et al., 1998) when administered in sufficient amounts. Isoflavones containing glycoside are converted by complex enzymatic system in human gastrointestinal tract that produce the biologically active compounds as aglycoside isoflavones (Murkie et al., 1998). These compound exhibit weak estrogenic activity when present in low concentrations (Markiewicz et al., 1993) and act as estrogen antagonists when present in high concentrations (Wang et al., 1996 and Sathyamoorthy et al., 1994). It is likely that the estrogen antagonist activity of plant phytoestrogen isoflavones is not mediated by the estrogen receptor and therefore is capable of inhibiting the expression of the weak estrogenic effects (Peterson and Barnes, 1993; Murkie et al., 1998 and Knight et al., 1996).

Pueraria mirifica and *Butea superba* have been long recorded consumption as folklore remedies among Thai peoples with the rejuvenating and neurotonic purposes. *P. mirifica* is used to improve human physical appearance such as busting breast firmness, re-growing hair, promoting black hair and improving body complexion. In northern Thailand, *P. mirifica* powder was consumed in women for rejuvenation and aphrodisiac purpose. Interestingly, *P. mirifica* consumption can induce the recovering of menstruation in menopause women (60-88 years of age). It was believed to rejuvenate and prolong life after orally taking the pill consisted of *P. mirifica* and honey (Suntara, 1931). However, some side effects i.e. headache, malaise and vomiting were reported when taking overdose (Kerr, 1932). These symptoms were remained for two weeks after stop consuming the herb (Wanandorn, 1933). Many inactive glycosides of the plant phytoestrogen i.e. miroestrol, deoxymiroestrol, puerarin, genistin and daidzin are found in *P. mirifica* root extracts. The bioassays of *P. mirifica* were confirmed with high estrogenicity. The reported

experiments were generally in estrogenic activity or toxicity test. It could exhibit effect on both physical and mental change (human) or mating behavior (animal). *B. superba* was also used in Thai remedies as well as *P. mirifica* but mostly specific for man and the dosage was two third of *P. mirifica* amount (Suntara, 1931).

Due to the widely consumption of *P. mirifica* and *B. superba* in Thailand. The plants in the form of extract have been introduced just recently. With modern extraction technology, the extract from dried roots is standardized and prepared in the form of powder and solution. The extract solution is used in cosmetic industry such as preparation of breast cream, eye gel, and skin moisturizer. Topical uses of *P. mirifica* have been known to include: breast cream and cataplasm/ patches for breast firming or enhancement, eye gel, body gel and day & night cream for wrinkles reduction (Dweck, 2002). Topical use of *B. superba* have been known to include: gel for aphrodisiac. Food supplement derived from tubers of *B. superba* is also popular.

In vitro and *in vivo* animal studies have revealed interesting properties of phytoestrogens and food containing these compounds by showing that they inhibit carcinogenic. It is noticed that the application of *P. mirifica* is related to breast directly. It might be do positive effect as a chemoprevention or negative effects on the breast cancer. Moreover, the effects of these plants have not been fully evaluated in rodent breast cancer model. Thus, it is interesting to study the effect of the plants upon the carcinogen-induced tumor in rats which were performed in order to clarify these effects. The results of this study will benefit as the additional data in cancer prevention.

Aims of the study are as followed:

1. To study the prevention roles of *P. mirifica* and *B. superba* in DMBA-induced mammary carcinoma in female rats.
2. To study the antitumor efficacy of *P. mirifica* and *B. superba* in DMBA-induced mammary carcinoma in female rats.