

Thesis Title	Study on Immunostimulating Effect of a Well-Known Thai Folkloric Remedy in Breast Cancer Patients
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### ABSTRACT

Traditional medicine is very popular as an alternative treatment for cancer apart from modern medicine in Thailand. One of the most well-known prescription of Thai folkloric remedies has been increasingly accepted by many cancer patients. Previous studies showed the interesting anticancer activity of the extract of this remedy, that is, *in vitro* study in KB-cytotoxic system, the extract could inhibit cell growth under the standard criteria of cytotoxic activity. The antitumor activity showed more noticeable significance *in vivo* that is daily administration of the extract could increase body weight and survival rate, prolong survival time, slow down tumor growth rate and decrease the rate of metastasis in experimental animals. In addition, recent study indicated the immuno-stimulating effect of the extract via increasing natural killer (NK) cell activity in tumor-bearing nude mice. Whether the extract of this folkloric remedy could stimulate human immune effector mechanism(s) against cancer i.e. NK cell and monocyte/macrophage function is interesting and should be investigated.

This study initially examined the NK cell activity of breast cancer patients compared to normal subjects. Breast cancer patients were divided to 2 groups. The first group were composed of 18 patients, ages between 35-68 years from Ramathibodi Hospital and the other group 13 patients with the age of 32-60 years from Dr. Sommai Thongprasert's private clinic in Sinhaburi province. Fifteen healthy women, ages between 30-43 years were the control group. The results showed the tendency of lower NK cell cytotoxic activity in breast cancer patients as compared to normal healthy controls. Although the significance was demonstrated only in terms of percent cytotoxicity at E:T 100:1 and 25:1 in the Ramathibodi group, this may be due to the stress effect because these patients had to undergo mastectomy on the day that their blood specimens were drawn.

Immunostimulating effect of the extract treatment on NK cell activity was studied in 13 breast cancer patients of Singhaburi group and 8 normal subjects. The response of NK cell to the extract were as follows: eight normal subjects demonstrated no significant change in percent cytotoxicity and insignificant increase in lytic unit of NK cells after 1 week administration of the extract. The lytic unit subsequently declined after extension of treatment to 2 weeks. Nevertheless, the significant increase in NK cell binding activity ( $p < 0.05$ ) presented at this period also increased the host's immunity.

The two weeks' extract treatment of breast cancer patients significantly increased NK cell cytotoxic activity in both percent cytotoxicity and lytic unit ( $p < 0.05$ ) while having no effect on binding activity. This may suggest that the extract has the capability in enhancing NK cell cytotoxicity independently to binding events. The stimulating effect on NK cell cytotoxicity only in breast cancer patients indicated that cancer may be one of the factor(s) that challenged the response of NK cells to extract treatment. The following addition of chemotherapeutic drugs to the

treatment regimen for breast cancer patients decreased NK cell cytotoxicity. This indicated the immunosuppressive effect of chemotherapy in contrast to the immunostimulating effect of the extract.

The two weeks' treatment with the extract could also stimulate the release of TNF- $\alpha$  from monocytes/macrophages of breast cancer patients which previously inactive to LPS stimulation. This response of monocytes/macrophages to the extract treatment was better in patients who had tumor cells in their bodies than patients without tumor. The addition of chemotherapeutic drugs to the treatment schedule abolished this effect. This confirmed the immunosuppressive effect of chemotherapy which is contrary to the immunostimulating effect of the extract not only on NK cell but also on monocyte/macrophage function. The presence of tumor cells may be required as well.

All findings in this study suggest that the extract of Thai folkloric remedy is beneficial to the host's immunity via enhancing or restoring the activity of NK cells and monocytes/macrophages which are the important effector cells in cancer immunity. So it is worthwhile to use this remedy as an adjuvant therapy in the treatment of breast cancer or supportive treatment for the untreatable or immunosuppressive patients. Further study should be carried out on the immunostimulating effect of this remedy in more subjects and various types of cancer, in immune deficient host, e.g. AIDS, or study on other effector mechanism(s) that relate to the anticancer activity.