Ginseng as a Complementary and Alternative Medicine for Postmenopausal Symptoms

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Abstract: Ginseng is a popular herbal medicine that has been used for thousands of years. A number of its components have been isolated and characterized, including ginsenosides, polysaccharides, peptides, polyacetylenic alcohols, and fatty acids. The lipophilic characteristics of ginsenosides have raised the possibility of their efficacy as steroid hormones. Several in-vitro studies have reported their pharmacological function as steroid hormones, especially estrogen, but no human study to date has confirmed their efficacy as alternatives to synthetic estrogen.

Key words: ginseng, complementary medicine, postmenopausal symptoms

INTRODUCTION

Ginseng has been used for over 2000 years in oriental countries as a tonic, to fight to enhance stamina and immune function, where it has been suggested to have pharmacological activities in the cardiovascular, endocrine, immune, and central nervous systems. Its use has expanded to Western countries, and continues to rise with the increasing popularity of complementary and alternative medicine. It is one of the best-selling herbs in the United States with gross retail sales of $US62 million in 2000 with current sales being estimated to be over $300 million US per year. In the United States, ginseng is used as an alternative herb for postmenopausal women, as are black cohosh (Cimicifuga racemosa), chastetree berry (Vitex agnus-castus), dong quai (Angelica sinensis), evening primrose oil (Oenothera biennis), motherwort (Leonurus cardiaca), red clover (Trifolium pratense), and licorice (Glycyrrhiza glabra). Here in this review, the reports on ginseng usages targeting post-menopausal symptomms is discussed.

1. Hormone replacement therapy

Menopause is known as the cessation of menstrual periods and normally occurs at a mean age of 51.4 years in healthy women. The failure of the ovaries to produce estrogens results in hot flushes and/or sleep disturbances in many women, as well as accelerated bone loss, increased risk of colon cancer, and weight gain accompanied by shifts in plasma lipoprotein cholesterol profiles associated with a higher incidence of cardiovascular disease. Hormone replacement therapy is used to prevent or combat heart disease, stroke, osteoporosis, Alzheimer’s disease, and postmenopausal symptoms such as hot flashes and depression. However, such uses of synthetic estrogens and progestereones are associated with side effects, increased risks of uterine and breast cancer (perhaps ovarian cancer as well) and clotting disorders as was demonstrated in The Women’s Health Initiative Study, which was abruptly ceased in 2002 because of an increased incidence of breast cancer, and increases in cardiovascular complications such as coronary heart disease, stroke, and venous thromboembolism. Owing to these problems, public interest in alternative medicines for hormone replacement therapy has increased, which is believed to carry less risk when associated with the management of menopausal symptoms.

As stated, the most commonly used alternative herbal medicines for estrogen replacement are soy, black cohosh, dong quai, chastetree berry, and ginseng. Phytoestrogens that include isoflavones, lignans, and coumestans are found in some of these herbs. This is assumed to be one reason for the lower prevalence of menopausal symptoms in countries like Korea, Japan, and China, where...
consumption of soy is high. Although accumulating studies suggest important potential health benefits, both the clinical efficacies and mechanisms of action of these herbs are still not fully known.

2. Experimental Ginseng studies in animals and in vitro
The major pharmacologically active components of ginseng are ginsenosides, which are steroidal saponins comprising 3-6% of ginseng. It has been shown that ginsenosides decrease the levels of total cholesterol and triglyceride via cAMP production, and inhibit the accumulation of calcium ions in liver cells. Ginsenosides potentiate analgesia and inhibit analgesic tolerance. The cardioprotective action of ginsenosides is due to effects on vasodilatation via nitric oxide (NO) release. Other activities, such as anticarcinogenic and neurologic effects, have also been reported for ginsenosides. In addition to the above beneficial effects, triterpene saponin has been hypothesized to be a type of phytoestrogen, which is a plant-based compound with estrogen-like activity. accumulating evidence suggests that ginseng contains either direct or indirect estrogenic activity. Ginseng extracts activate estrogen-responsive genes and regulate the growth of human breast cancer cells. Recent studies by Chan et al. showed that picomolar ginsenoside-Rg1 from Panax notoginseng activated ER-mediated transcription without direct receptor interaction mediated by mitogen-activated protein kinase pathway. Two ginsenosides with estrogenic activity, ginsenoside-Rb1 and -Rh1, had been identified previously by screening panel of ginsenosides by our group. Cho et al. showed that ginsenoside-Rb1 activated both ERα and ERβ, leading to the transactivation of estrogen-responsive genes. However, this activation occurred in the absence of direct receptor binding, as examined using receptor competition assays. This indicated that ginsenoside-Rb1 activates ER via a mechanism or mechanisms other than that of classical, hormone-mediated activation. The results from other studies in different systems indirectly suggest the regulation of estrogen-responsive genes by ginsenoside-Rb1 as well. It was shown to decrease cardiac contraction in adult rat ventricular myocytes, in part through an increase in NO production. While a correlation between the increase in NO and ER activation was not evaluated, estrogen is known to enhance NO production. Ginsenoside-Rb1 also regulates adrenal tyrosine hydroxylase, which is known to be under estrogen regulation. These in vitro studies provide a scientific foundation for potential clinical development. However, it should be noted that, as with other phytoestrogens, these reported ginsenosides contain biologic activities that are independent of ER, such as antioxidant, antiproliferative, and antiangiogenic effects.

3. Human ginseng studies on postmenopausal symptoms
There are several published randomized trials of phytoestrogen and menopause symptoms. One recent randomized controlled clinical trial showed that black cohosh had a beneficial effect on postmenopausal hot flashes. However, recent data showed that black cohosh increased metastatic mammary cancer in transgenic mice expressing c-erbB2. This indicates that black cohosh should be cautiously used. Although, various in vitro studies have indicated that ginseng has estrogenic activity, no clinical trials have demonstrated real efficacy as an estrogen-replacement therapy.

A placebo-controlled multi-centre randomized trial of 384 post-menopausal women with 200 mg of ginseng per day showed ginseng had no significant effect in reducing the frequency of hot flushes after 4 months. However, the study noted ginseng had a favorable effect on psychological well-being. A further trial did not show ginseng to be effective for improving in mood. Although in vivo experiments have suggested that ginseng does not have estrogenic activity, its use is not recommended in the presence of breast cancer. However, it should be noted that no claimed phytoestrogen has been demonstrated to be effective against postmenopausal symptoms. There are insufficient data to confirm its inefficacy. Well designed, in vitro data based large scale studies are needed to develop herbal products targeting female-related diseases.

CONCLUSION
There is no convincing evidence for any herbal medical product in the treatment of menopausal symptoms as well as ginseng. More research is required to clearly define the pharmacological effects of ginseng as dietary phytoestrogen. Considering well reported anticancer effects of ginseng, if proven to be effective as a phytoestrogen, it will greatly benefit menopausal women suffering from post-menopausal symptoms without increasing the risk of breast cancer.