



Review

The pros and cons of plant estrogens for menopause

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ARTICLE INFO

Article history:

Received 28 November 2012

Received in revised form 4 December 2012

Accepted 5 December 2012

Keywords:

Isoflavone

Lignan

Coumestan

Phytoestrogen efficacy

HRT alternatives

ABSTRACT

Concerns pertaining to the risk of estrogen exposure through HT have prompted an increase in the use of natural alternatives. Phytoestrogens may provide postmenopausal women with a practical alternative and many women have already begun to utilize phytoestrogen supplements. However, research regarding the efficacy of phytoestrogens as a hormone therapy alternative has been previously pessimistic or questionable at best. This review scrutinizes the most current research regarding the efficacy of three types of phytoestrogens, isoflavones, lignans and coumestans, and their specific effect on the reduction of climacteric symptoms, specifically vasomotor symptoms, vaginal atrophy, insomnia and osteoporosis. A discussion of the research pertaining to the relative safety of each phytoestrogen in terms of breast and endometrial health is also included. Overall, current research demonstrates that phytoestrogens are effective in reducing the intensity of hot flushes, and some phytoestrogen combinations result in a decreased frequency. Certain phytoestrogens have also been shown to decrease vaginal atrophy, improve sleep and cognition, and positively affect bone health. Even though initial research was generally unconvincing, the more recent evidence reviewed here is rather positive. In terms of safety and reports of adverse reactions, trials have not shown an increase in breast cancer risk or increase in endometrial hyperplasia following phytoestrogen use, but trials explicitly designed to find neoplasia have not been reported. Moreover, unlike hormone therapy, lignans may not increase clotting risk in postmenopausal women, thus supplements may serve as a treatment option for patients who have contraindications to hormone therapy. Phytoestrogens may provide a safe and partially effective alternative to HT. However, because research regarding phytoestrogens is relatively new, pharmaco-vigilance is still required, as these products are not yet FDA-approved.

This article is part of a Special Issue entitled 'Phytoestrogens'.

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1. Introduction

Menopause is inevitable. Advances in healthcare and public initiatives toward healthy living have increased the number of women in the menopausal age group. This exposure to age-related diseases presents not only a distinctive challenge for patients, but health-care providers are called on to offer alternatives that are preventive and improve quality of life. The menopausal transition results from declining ovarian function and leads to dramatic decreases in estrogen, which is clinically seen as several physical and mental conditions including vasomotor symptoms, histological changes to estrogen sensitive tissues, dyspareunia, vaginal atrophy, increased risk of developing osteoporosis and insomnia. Because climacteric symptoms result from a decrease in estrogen it naturally follows, and has been clinically proven, that replacing estrogen through hormone therapy (HT) is effective against menopausal symptoms. HT is the most effective treatment for conditions faced by postmenopausal women and has consistently demonstrated to reduce both the frequency and intensity of hot flashes, is effective against vaginal atrophy and insomnia, and positively affects bone loss and risk of fracture. HT may also prevent cardiovascular disease.

Despite the above responses to HT, more than 80% of women who may benefit from it are unwilling or unable to undergo treatment due to various medical or personal reasons, including increased clotting risk, liver disease or fear of cancer [1]. Concerns pertaining to the risk of estrogen exposure through HT have prompted an increase in the use of non-steroidal estrogen mimetic agents. Food sources rich in phytoestrogens, or naturally occurring estrogen-like compounds found in plants, for example, may provide postmenopausal women with a practical alternative. Women have in fact already begun to utilize phytoestrogen supplements. Despite inconsistencies amongst the data, there is growing evidence supporting the efficacy of phytoestrogens in the reduction of menopausal symptoms. As the commercial popularity and availability of phytoestrogen supplements begins to grow, however, so does concern regarding safety of long-term exposure to levels exceeding those obtained from diet alone; phytoestrogen supplement tablets allow for the possibility of ingesting large amounts of phytoestrogens per day [2]. It is thus vital to assess data regarding both the efficacy and safety of phytoestrogen therapies. This review will assess isoflavones, lignans and coumestans;

we will not specifically address soy protein, except to account for its use in conjunction with isoflavones. However, it is important to note that soy protein has been shown to have similar effects as soy and that most commercial products contain both soy and soy protein.

2. Biochemistry

The term phytoestrogen is generally used to define a class of compounds that is non-steroidal and is either of plant origin or metabolically derived from plant precursors [3]. Hundreds of foods have been shown to contain phytoestrogens. Most belong to one of three classes: isoflavones, lignans or coumestans. Isoflavones are found in beans from the legume family with soybeans and soy products being the major dietary source. Lignans are found in high fiber foods such as unrefined grains, cereal brans and beans, with flaxseed containing the largest amount. Foods containing the highest amount of coumestans include alfalfa and clover sprouts, with lesser amounts also found in split peas, pinto beans and lima beans [4]. Dietary consumption by national groups naturally follows agricultural patterns of growth and cuisines.

After the consumption of plant isoflavones, lignans and coumestans, enzymatic metabolic conversions occur in the gut, resulting in the formation of heterocyclic phenols; isoflavones are metabolized to aglycones, genistein and daidzein, lignans to secoisolariciresinol-diglucoside (SDG), and coumestans to coumestrol [5]. The breakdown products all contain the presence of a phenolic ring that can compete for binding to the “pocket” of estrogen receptors. These compounds thereby structurally resemble estrogen and have weak estrogenic activity; therefore they are termed phytoestrogens. However, all are selective estrogen receptor modulators and each has a profile of action of its own.

2.1. Phytoestrogens as selective estrogen receptor modulators

SERMs are defined as a group of compounds that behave like estrogen agonists in certain tissues, and like antagonists in others [6]. All estrogens, including steroidal estrogens, such as estradiol, and many xenobiotics are SERMs, and their properties depend on both the tissue in which they are acting, and the relative

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