Phytoestrogens the modulador selective receptor estrogen?

Phytoestrogens el modulador selectivo del receptor de estrógeno?

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Abstract
Flaxseed are particularly abundant source of phytoestrogens, are diphenolic compounds that are present in several plants eaten by human beings. When ingested in relatively large amounts, phytoestrogens have been shown to have significant estrogen agonists/antagonists effects in animals and humans. There is epidemiological, laboratory and clinical evidence which indicates that phytoestrogens, like certain selective estrogen receptor modulators, have an antiproliferative effect on the breast, and positive effects on the lipoprotein profile and bone density. They might also improve some of the climacteric symptoms. This evidence is critically reviewed, and the possible benefit of dietary intervention with phytoestrogen-rich food for woman’s health is discussed.

Keywords: Phytoestrogens. Menopause. Lipoproteins. Selective Estrogen Receptor Modulators.

Resumen
Semilla de linaza son una fuente particularmente abundante de fitoestrógenos, son compuestos difenólicos que están presentes en varias plantas consumidas por los seres humanos. Cuando se ingiere en cantidades relativamente grandes, los fitoestrógenos han demostrado tener importantes agonistas de estrógenos / efectos de los antagonistas en animales y humanos. Hay epidemiológicos, de laboratorio y evidencia clínica que indica que los fitoestrógenos, como ciertos moduladores selectivos de receptores de estrógeno, tienen un efecto antiproliferativo en el pecho, y los efectos positivos sobre el perfil de lipoproteínas y la densidad ósea. También podrían mejorar algunos de los síntomas climatéricos. Esta prueba es un examen crítico, y el posible beneficio de la intervención dietética con alimentos ricos en fitoestrógenos para la salud de la mujer se discute.


INTRODUCTION
Exogenous estrogens and phytoestrogens given to postmenopausal women cause rapid alleviation off menopausal symptoms, and reduce the risk of heart disease¹. Nevertheless, in most western countries only 10–15% of postmenopausal women are current users of hormone replacement therapy (HRT). Women are reluctant to use HRT mainly due to undesirable side-effects (such as irregular bleeding) and concerns about safety (especially possible increased risk of breast cancer). Therefore, there is recently a global effort to develop preparations that would yield the benefits of HRT with minimal inconvenience or risks². Hormonal treatment for postmenopausal women is aimed in two major directions:¹ alleviation of undesired estrogens. This name was given long before SERMs were menopausal symptoms and ² prevention of metabolic identified. Today it seems that there is even higher degree processes which may lead to morbidity in older age. Selective estrogen receptor modulators (SERMs) are possibly a new alternative for postmenopausal therapy³. In this review evidence will be presented that dietary phytoestrogen is a group of compounds with SERM-like activity, that might be considered as another alternative to HRT.

CLASSIFICATION AND BIOLOGICAL ACTIVITY AND EPIDEMIOLOGY
Phytoestrogen (PE) is a general term used to define classes of compounds that are non-steroidal and are either of plant origin or derived from the in vivo metabolism of precursors present in several plants eaten by human beings. The one classe of these compounds are the lignans. Flaxseed is particularly abundant source of phyto-estrogens. In humans, after consumption of plant lignans, enzymatic metabolic conversions occur in the gut, resulting in the formation of heterocyclic phenols⁴,⁵,⁶. These compounds structurally resemble estrogen and were shown to have weak estrogenic activity, and therefore were named phyto (plant) estrogens. This name was given long before SERMs were identified. Today it seems that there is even higher degree of structural resemblance to certain SERMs (e.g. raloxifene).

Phytoestrogens appear to have both estrogenic and antiestrogenic effects, like SERMs, depending on the concentrations of circulating endogenous estrogens and estrogen receptors. The estrogenic effects of phytoestrogens
were first observed as reproductive disturbances in sheep. We recently observed a marked increase in serum levels of SHBG in women who consumed a phytoestrogen rich diet. This increase might be looked upon as a determinant of estrogenic activity. Phytoestrogens were also shown to have estrogen and antiestrogen vitro effects: similar to estrogen they bind to estrogen receptors and increase the synthesis of SHBG by liver cells, but, like antiestrogens, they inhibit aromatase activity, and the proliferation of breast cancer cells.

Lignans are found widely in cereals, fruit and vegetables. They occur in high concentrations in flaxseed, and in lesser concentrations in whole grain and seeds. Vegetarians have the highest excretion values of isoflavones and lignans. The traditional oriental diet is rich in phytoestrogens. In Japan, the typical diet is low-fat with much rice, soy products, fish and vegetables. Japanese men and women consuming a traditional Japanese diet have very high blood and urine concentrations of phytoestrogens, especially isoflavones. Asian populations such as those in Japan, Taiwan and Korea, are estimated to consume 20-150 mg/day of lignans.

Epidemiologic data indicate that Japanese women complain much less of climacteric symptoms, especially hot ushes, as compared to western women. Furthermore, the incidence of hormone dependent cancer in Japan is significantly lower than in western countries women have very low incidence of breast cancer. This lower in women in low incidence substantially increases once they westernize their diet. It has been suggested that the high concentrations of phytoestrogen may partially explain the apparently low incidence of hot ushes and breast cancer in Japanese women. This hypothesis was supported by the finding of a case–control study that in western women, an inverse relationship exists between the blood levels of certain phytoestrogens and breast cancer cells.

The climacteric symptoms severity and frequency of vasomotor symptoms, especially hot ushes, are reportedly lower in women in southeast Asia as compared to western women. These differences have been attributed to social and racial characteristics, life-style, and diet. The role of diet is recently attracting increasing interest. It has been hypothesized that the content of natural estrogenic substances such as phytoestrogens in their food may partially explain this phenomenon. There are very few controlled clinical trials which investigated the effects of phytoestrogens on climacteric symptoms. Baird et al. did not find any beneficial effect of the phytoestrogens on menopausal symptomatology in a 4-week study. Such an effect might have been shown if the occurrence of hot ushes when the diet of postmenopausal women was supplemented with phytoestrogens or wheat ours for 12 weeks. At 6 weeks the phytoestrogens diet yielded better results (i.e. reduced the number of hot ushes per day more significantly than the wheat diet). In a more recent study Albertazzi et al. found that phytoestrogens was significantly superior to placebo in reducing the mean number of hot ushes per 24 h after 4, 8 and 12 weeks of treatment.

**Influence of Phytoestrogens and Menopause**

The postmenopause and the climacteric are associated with vasomotor symptoms and increased risk of osteoporosis and cardiovascular disease. The frequency of climacteric symptoms and the incidence of osteoporosis and heart disease are reduced in Asian countries. There are evidence that high intake of phytoestrogens may contribute to these findings.

**Climacteric symptoms**

The climacteric symptoms severity and frequency of vasomotor symptoms, especially hot ushes, are reportedly lower in women in southeast Asia as compared to western women. These differences have been attributed to social and racial characteristics, life-style, and diet. The role of diet is recently attracting increasing interest. It has been hypothesized that the content of natural estrogenic substances such as phytoestrogens in their food may partially explain this phenomenon. There are very few controlled clinical trials which investigated the effects of phytoestrogens on climacteric symptoms. Baird et al. did not find any beneficial effect of the phytoestrogens on menopausal symptomatology in a 4-week study. Such an effect might have been shown if the occurrence of hot ushes when the diet of postmenopausal women was supplemented with phytoestrogens or wheat ours for 12 weeks. At 6 weeks the phytoestrogens diet yielded better results (i.e. reduced the number of hot ushes per day more significantly than the wheat diet). In a more recent study Albertazzi et al. found that phytoestrogens was significantly superior to placebo in reducing the mean number of hot ushes per 24 h after 4, 8 and 12 weeks of treatment.

**Cardiovascular disease**

PE consumption might contribute to the lower incidence of cardiovascular disease in Asian countries and in vegetarians. There is no sufficient evidence to support the observation that phytoestrogen-rich diet has a beneficiary on serum lipoproteins profile. Soy protein supplementation to Rhesus monkeys results in hypcholesterolemic effect when compared with soy diet deplet of phytoestrogens. The HDL: cholesteral ratio increased 50% in female monkeys and 20% in the males. A meta-analysis of 38 published controlled clinical trials soy protein consumption was associated significantly with mean reductions in total cholesterol, LDL-cholesterol and triglycerides. In a our recent study of postmenopausal with PE- women supplemented with 20-mg phytoestrogen capsules may we found a 24% reduction in total cholesterol, and 18% increase in HDL (unpublished). The hypcholesterolemic effect of phytoestrogens may not be
their only mechanism further pursuit of this line of investigation, of cardioprotection. It has been reported that soy isoflavones enhance coronary vascular reactivity in atherosclerotic female macaques, similarly to estrogen postmenopausal women the SPE is. The cardioprotective effect of the phytoestrogen-rich diet has yet to be substantiated by long-term controlled of the soy molasses into a fine dried powder without clinical trails.

CONCLUSIONS

The data presented here indicate that, like SERMs, phytoestrogens have both estrogenic and antiestrogenic effects, depending on the specific tissue and the concentrations of circulating endogenous estrogens. The biological activity of phytoestrogens has been demonstrated mostly in animals and in in vitro studies, but they appear to have physiological effects in humans. The most supportive human data is related to the effects of PE on lipids, lipoproteins, and certain malignant diseases. The evidence we reviewed justifies concluding that phytoestrogens may be among the dietary factors affording the protective effects against heart disease and cancer in vegetarians. Mild estrogenic effects have been observed in postmenopausal women; however, it is too early to determine the clinical value of phytoestrogens in ameliorating the early postmenopausal symptoms. The results of epidemiological and in vitro studies regarding the inhibitory effects of phytoestrogens on the breast, are encouraging but extrapolating from these data to clinical practice must be done with caution. The apparent protective effect of phytoestrogens on the breast should be further examined by long-term clinical trails.

REFERENCE
