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Phytoestrogens: Food or Medicine

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Abstract

Phytoestrogens are metabolites of plants with structural, functional similarity to estradiol along with estrogenic or anti estrogenic effects. Structural similarity with estradiol enables it to bind with estrogen receptors present on the cells which results in agonistic/antagonistic effect of the same. As the name implies these estrogens are products of plants with no or less side effects. Phytoestrogens can be considered as connecting link between nutritional food and medicine i.e. food with medicinal values. A wide range of commonly consumed food contain considerable amount of different phytoestrogens such as soy, soy products, flex, tofu etc. Most of the phytoestrogens present in human diet can be classified into two major classes i.e. isoflavones and lignans. Phytoestrogens have been found to have potential health benefits in the diseases such as cardiovascular, cancers, cognitive health, menopausal symptoms, bone health and maintenance of hormonal balances etc. Rapid and continuous research is needed to better understand nutritional values, medicinal values, potential role, mechanism of action and possible side effects of dietary phytoestrogens.

Keywords: Phytoestrogens, Bioactive Molecules.

Introduction

Phytoestrogens are non-steroidalplant derived bioactive molecules with nutritional constituents or nutraceutical values, capable of binding with estrogen receptors and to induce an estrogenic or antiestrogenic response in targeted tissue. Estrogenic or antiestrogenic response of phytoestrogenes is mainly due to their structural similarity to the mammalian estrogen i.e. estradiol and ability to bind with estrogen receptors (ERs i.e. ERα and ERβ) especially ER β.

Natural estrogens are one of the two main sex hormone of women (another is progesterone) that is responsible for female physical features/ feminism and reproduction. In addition to it other governing functions are to control level of cholesterol, protection of bone health, heart and skin etc. (both in women and men). As natural esrtogens are involved in several programmed events in targeted tissues (uterus, breast, pituitary gland), their optimum level is always desirable. Deviation from its normal level leads to several ailments. Low estrogenic levels causes lessening of menstrual cycle, development of menopausal symptoms such as hot flashes, insomnia, mood swings, dry skin and low libido, whereas high level causes weight gain, cysts in breast, fibroids in uterus and abnormal menstrual. Even in men its low level is responsible for excess belly fat, low libido while higher level may result in growing breast like female and poor erection (Bacciottini et al., 2007).

Phytoestrogens are considered as functional food, a type of nutraceutical product with a combination of nutritive and targeted disease preventive potential. In recent years concept of food with pharmaceutical or medicinal values is gaining much importance due to several side effects and short life span of synthetic drugs. Therefore, a new concept of functional food is being evolved rapidly which relates diet and health, combining the medical, nutritional and food sciences.

Phytoestrogens have 2-phenylnaphthalene-type chemical structures similar to those of estrogens and have been found to bind to estrogen receptors. The rapidly growing body of literature in this area indicates that these plant-derived estrogens may exert both estrogenic and antiestrogenic effects on metabolism, depending on several factors, including their concentration, the concentrations of endogenous estrogens, and individual characteristics, such as gender and menopausal status. Phytoestrogens exhibit weak estrogenic activity on the order of 10^{-2}–10^{-3} that of 17β-estradiol, but may be present in the body in concentrations 100-fold higher than endogenous estrogens. The antiestrogenic activity of phytoestrogens may be partially explained by their competition with endogenous 17β-estradiol for estrogen receptors. This partial

estrogenic/antiestrogenic behavior is a common feature of many weak estrogens (Mostrom and Evans, 2012).

Recent investigations have shown potential health benefits of edible herbal productscontaining phytoestrogenes particularly in reduction of cardiovascular diseases, cancer, osteoporosis, atherosclerosis, hypercholesterolemia, cancer, and osteoporosis, as well as the reduction of menopausal symptoms.A wide range of commonly consumed foods contain good amount of different phytoestrogens such as soy bean, soy products, flax, sesame seeds, oats, barley and tempeh etc. Chemically phytoestrogenes are a vast group of structurally different compounds such as isoflaones, lignans, stilbenes, flavones, flavans, isoflavans and coumestans etc.; among which most investigated are isoflavone and lignans (Michel et al., 2014).

Present investigation is an effort to review sources of phytoestrogenes, their potential health benefits, estrogenic/antiestrogenic effects. Article also discusses future of plant derived estrogens as functional food in the present life style which root cause of several ailments.

Types of Phytoestrogen

Plants vary intra- and inter-species in the types and concertrations of phytoestrogens due to variability in plant growth, soil, weather conditions and age of the plants. Chemically phytoestrogens are phenolic phytochemicals or polyphenols. These are the largest catogery of phytochemicals and the most widely distributed in plant kingdom. Phytoestrogens can be divided into four main classes: flavonoids (flavones and isoflavones), lignans, coumenstans and stilbenes.

Flavonoids

Flavonoids are the largest group of plant phenols and contain 4000 different compounds which are largely studied phytochemicals. The basic flavonoid structure varies which gives rise to flavanols (quercetin, kaempferol, myricetin), flavones (apigenin, luteolin), flavanones (catechins, epicatchin), anthocyanadins and isoflavonoids (glycitein, genistein, daidzein) (UCLA 2004). The isoflavonoids from legumes including genistein and diadzeinare most studied phytoestrogens. Genistein has one third the potency of estradiol and it may produce similar effects to estradiol in several different tissues as breast, ovarian, endometria, prostrate, vascular, bone tissues and cell lines.(Wang et al 2003, Zhou et al 2003). Genistein also induces inhibition of tyrosine kinase and DNA topoisomerase (Bacciottini 2007).

Lignans

lignans are present in higher plants, such as whole grains, legumes, vegetables and seeds like flaxseed. Enterlactone and enterdiol are metabolites of the plant lignans (Tham et al 1998). Lignans serves as an antioxidant in plant defenses against biotic and abiotic factors. Lignans also shows anti-inflammatory , antioxidative and anticarcinogenic activity.

Coumestans

Coumestans are polycyclic aromatic plant secondary metabolites containing a coumestan moiety, which consists of a benzoxole fused to a chromen-2-one to form 1-Benzoxolo [3,2-c]chromen-6-one. Legumes are the main source of coumestrol, the coumestan showing the higest estrogenic activity (Bacciottini 2007).

Stilbenes

Stilbene may refer to one of the two isomers of 1,2-diphenylethene: (E)-Stilbene (trans-isomer), (Z)-Stilbene (cis-isomer). Stilben resveratrol has been identified as phytoestrogen. It is a natural compound produced by peanuts and grapevines in response to injury. Polygonium cuspidatum roots are the major active source of stlben phytoalexins. Resveratol possess anticancer, antioxidant, antherosclerosis and cardiovascular diseases (Bertelli 1998).

Sources of Phytoestrogens

The study of phytoestrogen started in the 1950's when it was realized that some plant derived substances could cause an estrogenic effect. Sheep that were grazing in the pastures containing red clover had multiple fertility problemsand it was shown that the clover present in the pasture had very high amount of isoflavones, in particular formononetinand biochanin (Rossiter and Beck 1996).

Phytoestrogens are known to be present in fruits, vegetables, whole grains and are commonly consumed by humans. They are abundant in several edible and/or medicinal plants, belonging mostly to the Leguminosae family (Dixon, 2004; Michel et al., 2013). Phytoesrtrogens involves variety of structurally diverse compounds such as isoflavones mainly found in soy, lignans found in gram, stilbenes found in skin of grapes. Until recently, most of the available information on concentrations of phytoestrogens in foods is related to isoflavone aglucones. This is due to the limitations in the analytical methods used. Data on the concentrations of isoflavone glucosides or glucones, prenylated flavonoids, coumestans and lignans are more limited.

Table 1: Different Classes of Phytoestrogens

Phytoestrogen Class	Source
isoflavones	legumes, lentils, chickpeas, soybean
Coumestans	young sprouting legumes
Lignans	most cereals, linseed, fruit and vegetables
prenylated flavonoids	some beers (hops)

Table 2: Main Chemical Categories of Phytoestrogens

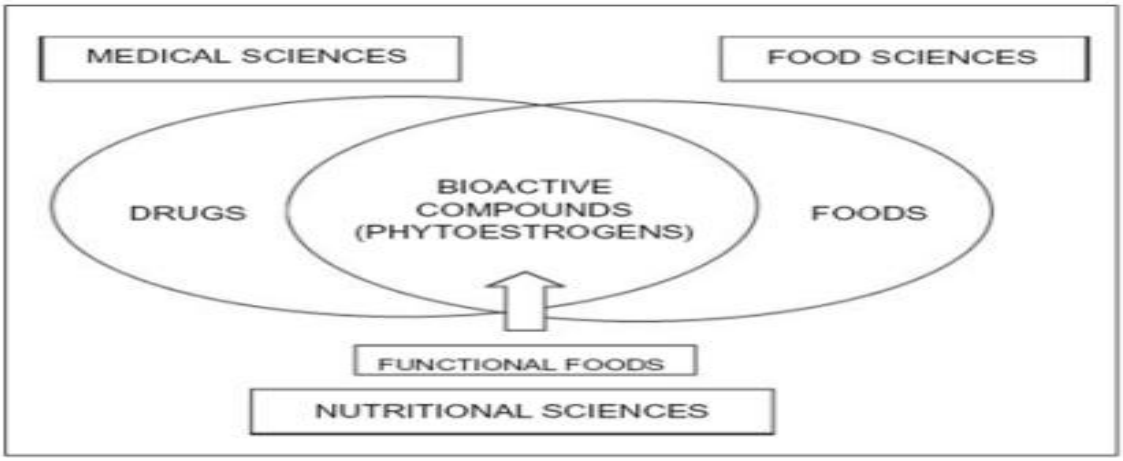
Lignans	Flavonols	Coumestans	Isoflavones	Stilbenes
Enterolactone Enterodiol	Quercetin Rutin	Cumestrol	Glycitein Genistein Daidzein	Resveratrol

Isoflavones are primarily found in legumes where they often occur as glucosides. Soybeans and soy-based foodstuffs are a particularly rich source of isoflavones, especially genistein and daidzein and to a lesser extent glycitein. Biochanin A and formononetin (which are derivatives of genistein and daidzein) are generally less prevalent in soy and are found mostly in clover and alfalfa sprouts. The coumestans of which coumestrol is the most common form, have been found in high concentrations in clover and fresh alfalfa sprouts as well. Lignans are a class of phytoestrogens that exist as minor constituents in many cereals, vegetables and fruit. Linseed (flaxseed) is the richest known source of lignans. Prenylated flavonoids have been found in high concentrations in hops, which are used in some beers. The concentration of these compounds can be influenced by a number of factors including species, strain, crop year and environmental conditions. Processing can also alter the phytoestrogen content of foodstuffs. For example fermentation of soy into products such as tempeh, miso and bean paste reduces the isoflavone content. Cooking has also been shown to reduce phytoestrogen concentrations. However, baking or frying does not appear to alter the total isoflavone content of foodstuffs.(Schneider et al., 1997; Meagher and Beecher, 2000).

Potential Health Benefits

Recent clinical and epidemiological studies have been performed to test the health effects of foods and supplements rich in phytoestrogens. Present review summarizes some of the potential health benefits due to intake of phytoestrogens by humans. Phytoestrogens lowers risk of cardiovascular disease and thought to be hypocholestrolemic, anticarcinogenic, antiproliferative, theantiosteoporetic and also hormone altering.

Figure 1: Phytoestrogens as Connecting Link between Food and Drugs (Bacciottini et al., 2007)



Phytoestrogen and Cancer

The incidence of hormone related cancer in the reproductive tract their accessory tissues and breast cancer was found to be low in Asian and Eastern Europe as compared to US and western Europe because of their eating habitsand lifestyle which includes plant based diet with high content of phytoestrogens (Parkin 1969, Rose *et al*. 1993). The positive effect of phytoestrogens on cancer may be due to their role in lowering circulating levels of unconjugated sex hormones. Estrogens mainly circulate as inactive conjugates of sex hormone binding globulins (SGHBG) and albumin (Dotsch *et al*. 2001). Dietary supplementation with soy isoflavonoids or lignans produced an increase of the levels of SGHBG in post-menopausal women, lowering the serum level of estradiol (Hutchins *et al*. 2001, Dotsch *et al*. 2001). Furthermore, higher intake of soy products and flaxseeds produced a significant decrease of urinary excretion of genotoxic estrogen metabolites. The role of phytoestrogens in preventing breast cancer in women may be related to changes in menstrual cycle length (Nagata et. al. 1998). Increase in menstrual cycle length together with eating a diet rich in phytoestrogens correlate with a decreased rate of hormone- dependent cancers development, including endometrial, ovarian and breast cancer (Tsourounis 2004). It has been studied that soy intake prevents prostrate cancer in men. This can be attributed by the ptotective effects that can be related to the reduction of androgen production, through inhibition of 5α-reductase. (Paul Cos 2003).

Phytoestrogen and Bone

Estrogens are known to promote bone formation. It is studied that their effect can promote osteoporosis. Estrogen receptors are found to be present in osteoblast cells and decrease the resorption capacity of osteoclasts. It is suggested to intake phytoestrogen rich diet that prevent osteoporosis. (Wutte et. al. 2002: Cassidy 2003: Branca and Lorenzi 2005). Soy phytoestrogen genistein was shown to enhance osteoblastic differentiation and maturation and an inhibitor of osteolclast formation and bone resorption (Ming *et. al*. 2013).

Phytoestrogen and Cardiovascular Health

Phytoestrogens have beneficial effects on endothelial cells, vascular smooth muscle and etracellular matrix. (Alexander 2014). Cholesterol homeostasis is an estrogen sensitive phenomena. In rhesus monkey, studies using diets made from soy isolates (20%) with and without isoflavones showed that phytoestrogens contributed to hypocholestrolemic effect. These studies showed relatively large

reduction in total LDL and VLDL cholesterol in both male and female animals without any effects on the reproductive tract (Setchell and Olsen, 2003).

Conclusion

Phytoestrogens can contribute towards nonsteroidal estrogen of dietary origin that may have potential health effects that are especially related to women health and hormone associated diseases. Phytosestrogens share many similarities with endogenous estrogens which can bind to estrogen receptors. Clinical trials and animal studies have shown that health benefits of phytoestrogens may extend into several areas including cardiovascular diseases by lowering the levels of cholesterol, enhancing endothelial function, inhibiting several stages of cancer initiation, promotimg the conservation of bone mass and influencing menstrual and menopausal symptoms. Thsese findings are consistent with the high intake of soy products which is the main source of phytoestrogens. Phytoestrogens also play role in protection against hormone dependent cancers and diseases.

In contrast to health benefits few risks also may arise due to excess intake of plant based phytoestrogens. More research is needed to resolve about the optimal dosage and gender difference in context to the intake of phytoestrogens.The intake of phytoestrogen will be successful to humans only after changing their lifestyle by taking low fat, low calorie and fresh fruits and vegetables in combination with daily physical activities. Although large gaps still exist in our understanding of phytoestrogensand theirimpactonhumanhealth, therefore immense research is required towards this direction. Phytoestrogens can be a significant contributor of nonsteroidal estrogens of dietary origin that may have several health effects.

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