PHYTOESTROGENS

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The term phytoestrogen is used loosely in the herbal community. There is no current agreed upon definition for this term. Basically the term is used for any plant that has one or more constituents with similar chemical structure to estrogen or is changed into a similar compound in vivo or clinically produces effects that the clinician would expect from giving exogenous estrogens.

Plants may have compounds that are structurally similar to human endogenous estrogens that mimic estrogenic activity or effect estrogen metabolism. Some plants may show an estrogenic effect in laboratory studies, animal studies or in clinical settings but the specific constituent or mode of action has not been identified. It is thought that the weaker phytoestrogens can compete for estrogen receptors with the more potent endogenous estrogens thereby decreasing the overall estrogenic activity when it is deemed to be too high. When endogenous estrogens are low and phytoestrogens are used in large quantities phytoestrogens have been shown to exert an estrogenic effect in animals.[236,237] The phytoestrogens can take up receptor sites that are empty due to low estrogen levels. Most of the identified phytoestrogen constituents consist of sterols, coumestans and isoflavones. There are more than 300 plants, which have been identified as possessing estrogenic or uterotropic activity.[282]

Phytoestrogens compete with estradiol for estrogen binding sites in the reproductive tracts of animals in vivo and in human breast cancer cells in vitro.[220-2222, 223] Phytoestrogens will produce similar results to estrogens such as growth and increased weight of the uterus. Research measuring weight increase of uteri in mice showed sterols to have the most activity, followed by coumestans and then isoflavones.[224, 291]

Coumestans have a high affinity for the human estrogen receptor.[283] They are estimated to be 200 times less potent than estrone and 3000 times less potent than diethylstilbestrol, and 30-100 times more potent than isoflavones. Animal studies have shown coumestans can reduce follicle-stimulating hormone and lutenizing hormone levels. Coumestans produce uterine growth in rats at natural dietary levels and competitively inhibit binding to the estrogen receptors.[284] Not all isoflavones have estrogenic effects, but many of them do.[285] Some of them need to be converted by gut bacteria to other compounds to be effective. If a person is using antibiotics or ingesting other substances that destroy gut flora, there would be decreased isoflavone conversion in the gut, and the herb would not work as expected. The isoflavone, Genistein, has shown antiproliferative effects against estrogen-dependent and independent human breast carcinoma cell lines. There were synergistic effects when used with the anticancer drug adriamycin.[286] Isoflavones have very weak estrogenic activity compared with natural estrone or synthetic DES.[180]

Phytoestrogens can act as anti-estrogens to compete with estradiol for cytoplasmic receptors in estrogen-sensitive tissues.[181-182]

Soybeans, which also contain estrogenic isoflavones, have been implicated as being responsible for the low incidence of breast and other female reproductive cancers in Japanese woman who consume large amounts of soybean products.[183] Studies show a correlation between high levels of urninary lignans and isoflavonoid phytoestrogens, specifically genistein, and a low incidence of hormone-dependent cancers such as breast and prostate cancer. In vitro studies show genistein and daidzein inhibit growth of both estrogen receptor-positive and estrogen receptor-negative human breast cancer cell lines (IC50=24-44um).[432] Dietary phytoestrogenes dilute xenoestrogen-type carcinogens by binding at the receptor sites and acting as antiestrogens.[433]

The phytoestrogens genistein and daidzein tend towards normalizing estrogen and progesterone levels.[434] Lignans are phenolic compounds with weak estrogenic activity. They have been linked to a lowered incidence of breast cancer.[287, 294] The highest concentrations of estrogenically-active lignans are in the defatted portion of flax seeds. They are converted by gut bacteria to mammalian lignans, the primary ones being enterolactone and enterodiol. They are structurally similar to estrogen and bind with low affinity to estrogen receptors. They also increase sex hormone binding protein.[294]
The most potent phytoestrogens are the phytosterols. Common foods, which contain phytosterols, are chestnuts, sesame, safflower, sunflower and pumpkin seeds.

Phytosterols are most common in whole grains, nuts, seeds and legumes. The sterol, beta-sitosterol has phytoestrogen activity as well as anti-inflammatory activity and antipyretic activity.[228,229] It can be found in Achillea millefolium, Anemone pratensis, Angelica sinensis, Calendula officinalis, Glycyrrhiza glabra, Hypericum perforatum, Larrea spp., Panax spp., Piscidia erythrina, Plantago psyllium, Serenoa repens, Symphytum spp., Taraxacum officinale, Trifolium pratense, Turnera spp., Tussilago farfara, Valeriana officinalis, Viburnum prunifolium.[289, 290] A fat soluble extract of Humulus lupus was found to contain small amounts of estradiol.[225] Water-soluble glycoproteins from Hops strobiles are antigonadotropic and suppress progesterone production by luteal cells in rats.[226,227]

Dioscorea species contain the steroidal sapogenin called diosgenin. Diosgenin is manipulated chemically in laboratories to create estrone, testosterone, and progesterone as well as adrenocortical hormones. In current research on animals, it appears that diosgenin usually turns into smilagenin due to action on it by gut flora.[230] Both animals and humans poorly absorb diosgenin itself.[231] When diosgenin was given orally to female rats they had an increase in uterine weight, vaginal opening and vaginal cornification.[232] When injected into ovariectomized mice there was a growth of mammary epithelium.[233] Chamaelirium and Aletris both contain diosgenin and have produced estrogenic activity in rats.[234]

Cimicifuga (Black cohosh) contains the isoflavone formononetin and two other unidentified endocrine-active compounds, which appear to have estrogenic activity via competition for estrogen receptors.[235] Black cohosh has been shown to suppress luteinizing hormone secretion in menopausal woman and competes in vitro with 17-beta-estradiol for estrogen receptor binding sites.[37] Black Cohosh has an inhibitory activity in vitro and in vivo on bone resorption in ovariectomized rats as well as rats on low calcium diets.[265, 266]

The active constituents in black cohosh are thought to be:

1.) Triterpene glycosides, principally actein, 27-deoxyactein, cimicifugoside and cimigenol 3-O-alpha-L-arabinopyranoside and related aglycones,

2.) Isoflavones including formonoetin,
3.) Aromatic acids including isoferulic acid, ferulic acid, and salicylic acid.[281]

Legumes are a good source of edible phytoestrogens. Soybeans are one of the most highly researched source of phytoestrogens. They are currently thought to be one of the best sources of edible phytoestrogens. Additionally, soybean sprouts have the highest concentration of isoflavones. Health care practitioners have been concerned about giving plants with phytoestrogens to patients that have estrogen sensitive breast cancer. Research has shown that women consuming high amounts of phytoestrogens in their diet have had a decreased incidence of breast cancer rates. [292, 293, 294]

Practitioners should be cautious giving phytoestrogens to patients on tamoxifen or other anti-estrogenic drugs since the phytoestrogens could (theory, not known) interfere with the drug therapy.

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