

UPDATE ON PHYTOESTROGENS

Phytoestrogens are plant-derived molecules of non-steroidal structure, capable of binding to the oestrogen receptor. Depending on their concentration, endogenous sexual steroid levels and the target organ concerned, phytoestrogens may behave agonistically or antagonistically toward oestrogens. On the other hand, a certain number of their properties seem to result from non-genomic mechanisms. There are many phytoestrogens, and their concentration varies considerably from one plant to another and from one preparation to another. Phytoestrogens are considered as food supplements: they are also sometimes called nutrients or nutraceuticals. The products currently most in use come from soya beans. Isoflavones are most often used. Their main active compounds are daidzein and genistein. Several questions arise regarding these OTC products in pharmacies.

Must phytoestrogens be considered as oestrogens?

With the exception of coumestrol, phytoestrogens are characterized by:

- A greatly reduced affinity for oestrogen receptors than E2 (Oestradiol),
- A greater affinity for the β receptor than for the α ⁽¹⁾.

Overall, they have a significantly lower biological effect than oestrogens.

Are phytoestrogens effective against hot flushes?

The reduced frequency of hot flushes in Asia: 20% in China and 25% in Japan, compared to the West: 75 % in the USA, has raised the issue of benefits of a soy-rich diet vis-a-vis climacteric symptoms.

But a number of uncertainties persist despite numerous publications on this subject, explained by the importance of variations in individual bioavailability and the great diversity of usable products, in terms of quality as well as dosage. After an extensive review of the literature, Tempfer et al.⁽²⁾ maintain that isoflavones are especially effective in women who have had a recent natural menopause and suffer from moderate disorders. In contrast, the effects are modest in cases of idiopathic premature menopause, menopause induced by cancer treatment, prolonged HRT or if isoflavones

are started more than three years after menopause. On the other hand, soy-based products do seem more effective than those derived from red clover.

Are phytoestrogens effective against bone loss in postmenopausal women?

Despite several publications having arrived at a favourable conclusion on markers of bone restructuring or on bone density, most authors do not consider phytoestrogens to have a preventive effect against osteoporosis in postmenopausal women⁽³⁾.

Do phytoestrogens entail a carcinogenic risk?

Endometrium

The incidence of endometrial cancer is low in countries where consumption of isoflavones is high⁽⁴⁾. The vast majority of authors agree in recognizing that as far as usual therapeutic doses are concerned, the use of phytoestrogen does not induce any endometrial risk. A recent publication by Palacios⁽³⁻⁵⁾ et al.⁽⁶⁾ has confirmed the absence of any deleterious effects after three years of treatment: endometrial biopsy study of the thickness of the mucous membrane shows that its dimensions remain identical to those at the beginning of treatment.

Breast

Mammographic density

Taking phytoestrogens does not alter breast density, a phenomenon confirmed by the recent study by Palacios et al. After 3 years of treatment, the ACR (American College of Radiology) classification, a universally accepted criterion, remained unchanged.

Epidemiological data

The incidence of breast cancer is lower in several Asian countries: Japan, China, Korea and Indonesia, than in the West⁽⁷⁾.

The study of Asians who immigrated to the U.S. is particularly interesting: the incidence of breast cancer is lower among women who immigrated at a later age than among those who immigrated during their youth⁽⁸⁾. It remains low among those who maintained their eating habits⁽⁹⁾ while it increases in cases of changing dietary behaviour⁽¹⁰⁾. Thus the incidence of breast cancer in Asians catches up with that of Westerners from the first generation of immigrants onwards⁽¹¹⁾.



Epidemiological studies

in women taking phytoestrogens

Several observational, case-control or cohort studies were conducted, again with conflicting results: some authors have observed a protective effect induced by a soy-rich consumption, others have not. A meta-analysis⁽¹²⁾ involving 14 case-control studies and 7 cohort studies results in an RR = 0.75 (0.59 to 0.95), representing a 25% reduction in the risk of breast cancer in women who in the past have consumed soya beans, tofu, miso or isoflavones.

Another more recent study that analyzed 174 randomized controlled trials, observed no increased risk of breast cancer among consumers of phytoestrogens⁽⁵⁾.

It is actually a complex problem because of the diversity of phytoestrogens and the many differences between Western and Asian food, which do not concern only food content in phytoestrogens but also in red meat and animal fats, fish, notable Vitamin D sources, etc.

On the other hand, the period in which soy is consumed may play a significant role; originally discovered in animals, this fact has recently been observed in human clinical practice, with several studies showing a decrease in further risk of breast cancer among adolescents who received significant soya bean contributions⁽¹³⁻¹⁴⁾.

In practice however, given the current state of our knowledge, it appears inadvisable to use phytoestrogens in cases of personal history of breast cancer, especially if treatment with aromatase inhibitors is underway.



CONCLUSION

Phytoestrogens, at least some of them, may be useful for treating hot flushes. Though their efficiency with respect to the prevention of bone loss is not proven, we can confirm their safety with respect to the endometrium and breast.

BIBLIOGRAPHY

¹KUIPER G.G., CARLSSON B., GRADIEN K. ET AL.

Comparison of the ligand binding specificity and transcript tissue distribution of oestrogen receptor and β Endocrinology, 1997 ; 138 : 863-870.

²TEMPFER CL.B., BENTZ E.K., LEODOLTER S. ET AL.

Phytoestrogens in clinical practice : a review of the literature Fertil. Steril. 2007 ; 87 : 1243-9

³ROZENBAUM Henri

In La Ménopause, 1 vol., Eska édit., Paris, 2008 : pp. 315-330

⁴PARKIN D.M.

Cancers of the breast, endometrium and ovary : geographic correlations Eur. J. Cancer Clin. Oncol. 1989 ; 25 : 1917-25

⁵TEMPFER CL. B., FROESE G., HEINZE G. ET AL.

Side effects of phytoestrogens: a meta analysis of randomized trials American J. Med. 2009 ; 122 : 939-946

⁶PALACIOS S., PORNEL B., VASQUEZ F. ET AL.

Long-term endometrial and breast safety of a specific, standardized soy extract Climacteric 2010 ; Early Online 1-8

⁷ROSE D.P., BOYAR A.P., WYNDER E.L.

International comparisons of mortality rates for cancer of the breast, ovary, prostate and colon, and per capita food consumption Cancer 1986 ; 58 : 2363-71

⁸ZIEGLER R.G., HOOVER R.N., PIKE M.C. ET AL.

Migration patterns and breast cancer risk in Asian-American women J. Nat. Cancer Inst., 1993 ; 85 : 1819-27

⁹WU A.H., ZIEGLER R.G., NOMURA A.M. ET AL.

Soy intake and risk of breast cancer in Asians and Asian Americans Am. J. Clin. Nutr., 1998 ; 68 (6 Suppl) : 1437S-43S.

¹⁰LEE H.P., GOURLEY L., DUFFY S.W., ESTEVE J., LEE J., DAY N.E.

Dietary effects on breast-cancer risk in Singapore Lancet 1991 ; 337 : 1197-200

¹¹SHIMIZU H., ROSS R.K., BERNSTEIN L., YATANI R., HENDERSON B.E., NACK T.M.

Cancers of the prostate and breast among Japanese and white immigrants in Los Angeles Country Br. J. Cancer., 1991, 63 : 963-966

¹²QIN L., XU J., WANG P., HOSHI K.

Soyfood intake in the prevention of breast cancer risk in women: a meta analysis of observational epidemiological studies J. Nutr. Sci Vitaminol. 2006 ; 52 : 428-36

¹³SHU X.O., JIN F., DAI Q. ET AL.

Soyfood intake during adolescence and subsequent risk of breast cancer among chinese women. Cancer Epidem. Biomarker Prev., 2001 ; 10 : 483-88.

¹⁴WU A.H., WAN P., HANKIN J., TSENG C.C., YU M.C., PIKE M.C.

Adolescent and adult soy intake and risk of breast cancer in Asian-Americans