

Hormone hype?

Supplements and foods containing phytoestrogens, it is claimed, can help prevent heart disease, breast & prostate cancer, and relieve the symptoms of the menopause. But do such products live up to the claims, and more worryingly could they pose a risk to health? *Sue Dibb* investigates the hormone hype.

Phytoestrogens are the latest fashion in the world of functional food ingredients. Open a magazine, walk into a health food store and even the supermarket or browse the web and it won't take long to find a product or a company extolling the health-promoting properties of phytoestrogens.

Phytoestrogens are substances found in plants that can mimic, and sometimes block, the hormone oestrogen. There are several different types. The most commonly found in supplements and in phytoestrogen-rich foods are isoflavones such as genistein & daidzein (soya is a rich source) and lignans (found in linseed, also known as flaxseed).

Epidemiological studies show the incidence of certain diseases – cardiovascular disease, osteoporosis and breast cancer, for example – is lower in Asian countries and that the diets of these populations are richer in phytoestrogens compared to traditional western diets. This association is often given as the tenuous basis for promoting the health benefits of phytoestrogens and phytoestrogen-rich foods such as soya. However, traditional diets in countries such as Japan are different from western diets in many respects, not just their phytoestrogen levels. And contrary to western perceptions, foods made from soya typically makes up only a small part of such diets. Furthermore there may be significant genetic, as well as social, economic and cultural differences between populations and societies that can also influence the development of diet-related diseases.

Many researchers are now trying to understand more fully the relationship between phytoestrogens and disease risk. The picture that is emerging is a confused one. While there is some evidence of health benefits, this is not clear cut and it is becoming clear that some of these benefits may have been

overstated. Furthermore there is emerging evidence that high levels of consumption of phytoestrogens could pose risks for some consumers.

For example, phytoestrogens and phytoestrogen-rich foods such as soya are often promoted as being protective against some cancers, such as breast cancer. The Preval cereal bar, which contains both soya and flaxseed, is one example of a product that is being promoted in many countries on this basis. But the science to back up this claim is currently far from conclusive. A recent review¹ concludes that 'the scientific evidence is only modestly supportive' for the claim that phytoestrogens are protective against breast cancer. And other research² suggest that high isoflavone levels in postmenopausal women might actually increase the risk of cancer, particularly breast cancer.

Yet it is just this age group that is being targeted by supplement manufacturers, and some 'functional' food manufacturers, promoting phytoestrogen-rich products for the relief of menopausal symptoms. However there is little substantive evidence to support these claims. A number of studies have not shown that phytoestrogens significantly alleviate hot flushes³. While women often report fewer symptoms during trials, typically so do women taking a dummy pill or placebo.

The prevalence of menopausal hot flushes is reported to be lower in Asia and particularly Japan

Phytoestrogens and the heart

In a decision that has proved controversial, the US Food & Drug Administration has approved a health claim that eating 25g of soya protein a day, as part of a diet low in fat and cholesterol, may reduce the risk of heart disease. The claim was permitted last year despite the lack of understanding of the active constituents in soya responsible for the known cholesterol-lowering effect of soya. The leading soya producer that applied for the health claim, Protein Technologies International Inc, first asserted that it was the phytoestrogens in soya which were provided the heart health benefits. This was charged to soya protein when the FDA was faced with evidence⁴ that extracted phytoestrogens (isoflavones) had no cholesterol-lowering effect. But as Anderson⁵ points out – a favourable impact on cardiovascular disease morbidity and mortality by a soybean-enriched western-type diet remains to be shown.



Some of the phytoestrogen-containing supplements now being sold, particularly to women going through the menopause.

Researchers say that this association does not provide a scientific basis for the claim that phytoestrogens are important for the health and well-being of postmenopausal women⁴ – though this has not deterred companies from developing and marketing new products. Furthermore some researchers now advise that women who may have suffered breast cancer or are at risk of breast cancer should not take such supplements – advice that we believe should be clearly stated on products.

Other evidence⁵ emerging points to a suppression of thyroid function in high soy consumers and those using isoflavone supplements. And new research from Hawaii⁶ suggests a link between higher mid-life tofu consumption with increased risk of Alzheimer's disease in later life.

That phytoestrogens may pose risks as well as benefits has led researchers to urge caution. Dan Sheehan of the US Food & Drug Administration's National Center for Toxicological Research has warned: 'While isoflavones may have beneficial effects at some ages or circumstances, this cannot be assumed to be true at all ages. Isoflavones are like other estrogens in that they are two-edged swords, conferring both benefits and risks'.

In the UK, the Committee on Toxicity's Working Group on Phytoestrogens is currently considering these risks and benefits and is due to report next year. The Food Standards Agency also has an on-going research programme that is investigating some of these risks and benefits. It is also conducting an analysis of phytoestrogen-containing supplements to quantify the type and levels of phytoestrogens they contain and the claims that are being made for products.

What level is safe?

In the light of inconclusive evidence to support many of the claimed health benefits and increasing evidence pointing to potential risks of high phytoestrogen consumption, many researchers are now urging caution about their increased consumption. The Food Commission, too, is concerned about the way in which products are marketed, the lack of information provided about levels of phytoestrogens in some products and lack of warnings for groups for whom products may be unsuitable. Such concerns have led one researcher⁷ to write to the *Lancet* earlier this year about the 'potential dangers of an unregulated distribution of poorly studied products'.

For infant feeding, the current government advice is that soya infant formula is not recommended, unless on the advice of a health professional and for a diagnosed medical condition.

■ Sue Dibb is a member of the CoT Working Group on Phytoestrogens

- 1 Anderson et al, Effects of phytoestrogens on tissues, *Nutrition Research Reviews*, 1999, 12, 75-116.
- 2 Wu et al, Tofu and risk of breast cancer in Asian-Americans, *Cancer Epidemiology, Biomarkers and Prevention*, 901-906, 1996
- 3 Ginsburg J & Prelevic GM, Lack of significant hormonal effects and controlled trials of phytoestrogens, *The Lancet*, Vol 555, January 15, 2000.
- 4 Ginsburg J & Prelevic GM, Is there a proven place for phytoestrogens in the menopause? *Climacteric*, 2:75-78, 1999.
- 5 Fitzpatrick M, Soy formulas and the effects of isoflavones on the thyroid, *New Zealand Medical Journal*, 11 February 2000: 113, 24-2226.

Government enquiry calls for submissions

The Committee on Toxicity of Chemicals, Working Group on Phytoestrogens is calling for written submissions of relevant evidence. The Working Group has been asked 'to advise on the health implications of dietary phytoestrogens through review of published scientific research and the Food Standards Agency's Phytoestrogen Research Programme.'

The Working Group will address the following key points:

- On the basis of current evidence, does ingestion of soya-based infant formula pose any risk for human infants;
- Are there health implications to other sub-groups of the population from the ingestion of dietary phytoestrogens;
- To consider the evidence of beneficial effects of dietary phytoestrogens;
- To make recommendations for further research.

Submissions should be sent to Ms Jennifer Lamothe, Food Standards Agency, Po Box 30077, Room 651C, Skipton House, 80 London Road, London SE1 6XZ, tel 020 7972 1612.

- 6 White L, et al Brain ageing and midlife tofu consumption, *Journal of the American College of Nutrition*, 19, 2000.
- 7 Sirtori, R, Dubious benefits and potential risk of soy phytoestrogens, *The Lancet*, 355: 849, March 4, 2000.
- 8 See for example, Nestel PJ et al (1997) Soy isoflavones improve systemic arterial compliance but not plasma lipids in menopausal and perimenopausal women. *Arteriosclerosis, Thrombosis and Vascular Biology* 17, 3392-3398.

Supplement company 'misrepresented scientific evidence'

Redclover, from Novogen, is aimed at menopausal and postmenopausal women. But in Australia Novogen has been found guilty of making false claims for the product, where it is sold under the name Promensil. The claim made in advertisements that the product's effectiveness in reducing menopausal symptoms such as hot flushes, night sweats and mood swings 'had been proven in clinical trials around the world' was successfully challenged by Professor Alastair MacLennan, from the University of Adelaide and the editor-in-chief of *Climacteric*, the journal of the International Menopause Society. Almost three years after the product's launch, there were still no published peer-reviewed study showing Promensil to be any better than a placebo in reducing hot flushes. In finding Novogen guilty of misrepresenting scientific evidence and in breach of the Therapeutic Goods Advertising Code, the Australian advertising regulators concluded this was 'a particularly serious breach of the standards'.



Questions are now being asked, not only about the way in which Novogen's ads may have misled consumers, but also how the company may have misled the financial market. In November 1999 Novogen announced there was now 'incontrovertible evidence' that Promensil was effective in managing symptoms of menopause⁸.

This and similar statements made by the company have been described as 'scientifically dishonest' and 'misleading' by Monash University's Professor Henry Burger in an opinion statement to the Australian Stock Exchange.

Novogen also makes a phytoestrogen supplement called **Trinovin** that claims to help men with prostate problems. This has also fallen foul of the advertising regulators. Last year the New Zealand Advertising Standards Complaints Board found Novogen breached their 'therapeutics' code in its advertisement for Trinovin. The Board considered that the claim 'Trinovin improves the general health outlook for men over 50' could not be substantiated.



Promoted for the relief of menopausal symptoms, the 'Sheila Slice' was first developed in Australia. In the UK both **Bürgen Bread** and the newly launched **Nutribread** are manufactured to contain phytoestrogens from soya and linseed. No clinical trials of the products have been conducted to establish whether claims can be substantiated. Although both products contain phytoestrogens neither states the levels contained, nor how much you should eat.