## Complementary medicine update

# Phytoestrogens for menopause

## **ELIZABETH FARRELL** FRANZCOG, FRCOG

Phytoestrogen supplements are popular complementary medicines for the treatment of menopausal symptoms and for general wellbeing.

Phytoestrogens are present in many of the plants that have been used for centuries as foods and medicines. Interest in these compounds increased when epidemiological data from various countries and specific community groups with high phytoestrogen dietary intakes showed reduced incidences of menopausal symptoms, cardiovascular disease and some malignancies (such as breast cancer), compared with communities with low phytoestrogen diets. Supplements containing phytoestrogens derived from plants are now widely used by women in mid-life as a popular over-the-counter substitute for hormone therapy.

The daily intake of phytoestrogen-containing food required to protect against illness and to maintain health has not been quantified because of the complexity and variability within food sources and in their absorption and metabolism. It is believed that the whole food may provide greater beneficial health effects than extracts of phytoestrogens.

## Actions of phytoestrogens

Phytoestrogens are weak oestrogen-like chemicals found in a wide variety of plants and foods derived from these plants. Their potency is much less than that of the biological oestrogens.

Phytoestrogens exhibit both oestrogenic and antioestrogenic activity. They act like oestrogen receptor modulators, binding mainly to the oestrogen receptor, and are agonistic in the brain, bone and cardiovascular system, and antagonistic in the breast and uterus. They also have antioxidant properties and inhibit angiogenesis.

Dr Farrell is Head, Menopause Unit, Southern Health, Clayton, and a Director of the Jean Hailes Foundation, Clayton, Vic.



## Sources of phytoestrogens

The three major groups of phytoestrogens are the isoflavones, the lignans and the coumestans. Sources of isoflavones include soybeans (and the various soy foods derived from them) and pulses such as lentils, beans and chickpeas. Lignans are found in wholegrain cereals and in many fruits, vegetables and seeds, such as apples, carrots, garlic and linseed, and cournestans are found in alfalfa, soy and clover sprouts. A plant may, however, contain more than one phytoestrogen; soy and red clover, for example, contain both isoflavones and coumestans.

The phytoestrogen content of a plant depends on many different factors, including the plant variety, the time of harvesting and the climate conditions and soil where the plant was grown. The content in a derived food depends on the part of the plant used and the refining or processing involved in the manufacture of the food.

## Phytoestrogen bioactivity

The bioactivity of a phytoestrogen is dependent on many factors and is unpredictable because of individual diversity in absorption and metabolism.

Phytoestrogens are converted to active compounds in the gastrointestinal tract by the intestinal flora. These active compounds are subsequently metabolised in the liver and excreted in the urine, although they can be excreted back into the bile,

reactivated by the intestinal flora and then metabolised again in the liver. Many factors may alter the absorption and metabolism of phytoestrogens. These include modification of the intestinal flora composition by, for example, antibiotics, and a change in intestinal transit time by, for example, bowel disease or stress. Concurrent intake of fat, alcohol, dietary fibre and protein in the diet may also alter absorption and, therefore, metabolism.<sup>1</sup>

## Phytoestrogen supplements

There has been an enormous increase recently in the use of over-the-counter phytoestrogen supplements by middle-aged women for the treatment of menopausal symptoms and for general wellbeing. These supplements are regarded as alternatives to prescriptive hormone therapy, because of concern about the risks of hormonal therapy. There is also a popular belief that the taking of these products is 'natural', and therefore harmless and free of side effects.

Most of the supplements available contain isoflavones, mainly derived from soy but also from red clover. Many preparations also contain herbs (such as black cohosh) or other botanicals, and possibly other nutrients and vitamins.<sup>2</sup> These preparations are primarily listed as food supplements and manufacturers are legally not able to make medical claims that include effects on specific symptoms or medical conditions.

## **Evidence for effects**

## Menopausal symptoms

A systematic review of phytoestrogens for the treatment of menopausal symptoms (Cochrane Library and Medline, 1966 to 2004) suggests that soy foods, soy extracts and red clover do not improve menopausal symptoms.<sup>3</sup>

Studies using black cohosh extracts have shown variable results, mainly without significant improvement of symptoms except when using the maximum recommended dose.<sup>4</sup>

## Cardiovascular health

In 1999, the US Food and Drug Administration approved a health claim that 25 g/day of soy protein or more in a low fat, low cholesterol diet may reduce the risk of heart disease.<sup>2</sup> A meta-analysis of 38 studies showed that soy protein significantly reduced total cholesterol and LDL cholesterol, and there was a trend towards increasing HDL cholesterol.<sup>5</sup> The average amount of soy protein required to show these effects was 47 g/day. Arterial compliance has been found to improve with soy and red clover supplements.<sup>67</sup> There are no long term studies of cardiovascular events.

#### Osteoporosis

The evidence that suggests soy isoflavones and soy protein are beneficial to bone and therefore reduce the risk of osteoporosis is inconclusive and further research is needed.<sup>8</sup> There is no evidence of fracture reduction.

## **Cancer prevention**

There are still inadequate data to prove that phytoestrogens reduce breast cancer risk. It may be exposure of the breasts to phytoestrogens at the time of breast development in childhood and adolescence that reduces the breast cancer risk. There is also inadequate data on the use of phytoestrogens in women with breast cancer, although two studies have shown weak oestrogenic effects on the breast.<sup>9,10</sup>

## Conclusion

Phytoestrogens are oestrogenic bioactive compounds that appear to have positive effects on cardiovascular function but inconsistent effects on menopausal symptoms. More research is needed to clarify the appropriate dosages, their benefits and risks in breast cancer, their long term effects and their effects on bone health. MT

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