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## Soy isoflavones and cognition

Soy isoflavones have a direct impact on the central nervous system and affect estrogenic activity. Endogenous estrogen levels are important, however, in helping to determine whether soy has an estrogenic or antiestrogenic effect. E.g. in postmenopausal women low levels of endogenous estrogen produce an estrogenic effect of soy, whilst in premenopausal women levels of endogenous estrogen are high and soy has an antiestrogenic effect. There are also established gender differences in cognitive function and estrogen fluctuations are associated with cognitive function. However, there are very few published human intervention studies on soy and cognition and the differences between these studies make it difficult to come to any firm conclusions but generally they suggest that soy may have a beneficial effect in specific cognitive areas.

The results from 3 studies at the University of Leeds, UK were presented which appear to confirm these effects and strongly suggest that soy isoflavones may exert stronger cognitive effects in postmenopausal women compared to premenopausal women. The effects seem to be related to improvements in memory and certain aspects of frontal lobe function which is associated with verbal fluency. Variables such as age, time of exposure, dose and administration of isoflavones are important factors and further long term trials are needed to determine whether these effects in relatively short term interventions will be sustainable in the long term.

A randomised, placebo controlled double blind pilot study from the University of Wisconsin provided some additional data from 30 cognitively healthy older adults (both men and women). Subjects received either 100mg/day of soy isoflavone or placebo for 6 months. Cognitive evaluations were conducted at baseline, 1, 3 and 6 months after initiation of the study. Cognitive data were used to calculate the change from baseline. Using a test category of fluency, women on soy outperformed women on placebo but men on treatment did not differ significantly from men on placebo. In addition to gender differences, a genetic risk factor for Alzheimer's disease, the ApoE gene was also found to influence the response to isoflavone treatment.



## Cancer

Animal (rat) studies (University of Ulster, EU PhytoPrevent Study) suggest that perinatal exposure to isoflavones has no effect on tumour development but post weaning and life-long exposure to isoflavones delays tumour development and reduces tumour incidence.

In humans soy appears to have a protective effect for high soy consumers. In a case controlled study (University of Southern California) of over 1200 Asian American women in Los Angeles County participants provided details on menstrual and reproductive factors, use of HRT, family history, body size, dietary history, and other lifestyle factors. After adjusting for dietary and non-dietary variables it has previously been found that risk of breast cancer is significantly inversely associated with soy intake during adolescence and adult life, with significant risk reduction found in pre- and postmenopausal women. Further analysis in postmenopausal women showed that the benefits of soy intake are found only in women with low body size and non-users of menopausal hormones. However, the benefit of soy does not appear to be high enough to overcome the risk of high body size on breast cancer. These results seem to contradict other studies which have found a protective effect of soy with higher BMI, but the difference could be due to increased amount of weight gain rather than BMI itself.

New lines of research are investigating specific components of soy in respect to cancer. Researchers at the University of California have identified a new cancer preventive peptide in soy (43 amino acids) called Lunasin. They have demonstrated its efficacy in mammalian cells and in a mouse skin cancer model and it appears to be effective against chemical carcinogens and oncogenes. It appears to be absorbed and distributed in various tissues including those that are targets for the most common cancers, and is bioactive in the blood and liver of rats. The next stage is to determine oral bioavailability and its effectiveness in humans.

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A team at Wake Forest University are also investigating the antiestrogenic effects of glyceollins. Glyceollins are phytoalexins present from stressed soybeans. Using postmenopausal monkeys they evaluated the antiestrogenic effects of glyceollin-enriched soy protein on markers for cancer risk. Preliminary findings suggest that glyceollins may enhance the antiestrogenic properties of standard soy protein isolate in the breast and uterus.

Some animal studies have suggested that soy isoflavones may increase the risk of endometrial cancer. However studies in monkeys at Wake Forest University School of Medicine spanning up to 3 years (equivalent to 10 human years) using up to 10 times the dietary exposure of soy isoflavones have shown no uterotrophic effects. In addition, endometrial proliferation data shows that isoflavones are not estrogenic in monkeys. This was confirmed in a two year trial of women given soy protein isolate of up to 58 mg/day which showed no association between serum isoflavone concentrations and endometrial proliferation. These results suggest that there is not a significant uterotrophic effect of dietary soy isoflavones in the humans or monkeys. The researchers hypothesize that there may even be a protective effect in the presence of higher endogenous or exogenous estrogens.



## Cardiovascular disease

A study (Stanford University) of adults with elevated cholesterol concentrations (160-220mg/dL) and not on cholesterol lowering drugs compared plasma lipid responses between two commercially available soy milks, one made using whole soybeans and one using soy protein isolate, with a low fat dairy milk. The results showed a modest 5% LDL cholesterol lowering effect from both types of soy milk relative to the dairy milk when provided in amounts equivalent to 25g protein per day for 4 weeks. However, whilst an LDL cholesterol lowering effect was observed, the question remains as to how much was due to displacement rather than to actual consumption of soy milk.

An update of James Anderson's (University of Kentucky) 1995 meta analysis indicated that in the last 10 years most studies have reported smaller reductions in LDL cholesterol than the 12.9% suggested by the meta analysis. In reviewing the 57 studies published since 1995, Anderson concluded that most of the studies report serum lipoprotein changes with average reductions from baseline of 7.8% compared to reductions in the controls of 4.1%. However, there are differences in the dose and duration of soy consumption as well as differences in the type of soy protein used in these studies. This appears to affect cholesterol lowering. For example, some studies used baked soy protein rather than non-baked and whilst this still lowers cholesterol, the effect appears to be much reduced. One reason for this is that intact soy peptides have a significantly greater cholesterol lowering effect than fragmented preparations; baking may fragment the most active peptides. To achieve a daily consumption of 16-50mg isoflavone and a 5-7% reduction in LDL cholesterol it is recommended to consume at least 10g soy protein twice per day. The best choices are soy milk, tofu, yogurt, edamame soy beans, soy nuts or soy foods such as smoothies.

## Immune Function

Researchers at the Mount Sinai School of Medicine, New York are investigating the effectiveness of ImmuSoy, a koji fungus (*Aspergillus oryzae*) and lactobacteria soybean fermentation product based on traditional Japanese fermentation technology, as a potential novel treatment for peanut allergy. Experiments using peanut allergic mice showed that ImmuSoy has a dose dependent protective effect against peanut anaphylaxis in the mouse peanut allergic model.

In a study of postmenopausal women (Washington State University) soymilk and isoflavone supplements were found to modulate beta cell populations, plasma interferon gamma concentrations (both markers of immunity and oxidative stress) and appeared protective against DNA damage.

## Glycemic control

Two studies were presented that showed improved glycemic control with soy in healthy subjects. The first study, carried out at the University of Hong Kong, on 173 community based postmenopausal Chinese women showed that habitual soy intake improves glycemic control in women with a higher base line fasting glucose level. Surprisingly a Japanese study on 43 healthy men (fire fighters) also showed a beneficial effect of soy rich diets on insulin resistance.

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# conference highlights



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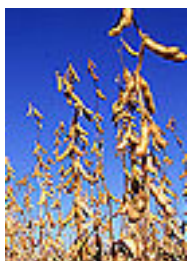
### **Obesity**

Researchers at the University of Kentucky compared soy vs casein meal replacements for the weight management of obese women. In a 16 week randomised controlled trial, 35 women (BMI 30-40) following an intensive weight loss programme achieved a steady weight loss of about 2 lbs per week. There was no difference between the casein or soy-based diets in the amount of weight lost or in body fat loss. Those on the soy diet had a slight tendency to bigger blood pressure reductions and lipid reductions than those on the casein-based diet but the differences were not statistically significant.

### **Inflammatory disease**

An interesting study from the Manitoba Institute of Child Health suggested that maternal soy exposure may have long term beneficial benefits on renal inflammation and disease progression in young adult offspring. Using a rat model of genetically determined renal disease the researchers compared rats on a soy-based diet with a casein based diet. They found maternal soy protein resulted in less proteinuria indicating better renal function. They also found that soy protein in the weaning diet of these rats reduced inflammation.

### **Equol**



Debate continues over the significance of equol, a metabolite of diadzein, and its role in the biological effects of soy. Some studies indicate that there may be possible benefits to health if you are one of the 20-40% of the population who produce equol after consuming soy while other studies show no differences between equol and non equol producers. Recognising the essential role of gut microflora in isoflavone metabolism, particularly equol, a study from Australia (University of Wollongong) investigated the role of a probiotic (yogurt) or a prebiotic (resistant starch) in conjunction with soy on isoflavone metabolism and lipids. In a randomised crossover study 31 hyperlipidemic men and postmenopausal women were studied. Intake of soy alone was compared with either soy + probiotic or soy + prebiotic treatments for effects on plasma and urinary isoflavones and plasma lipids following a test soy meal. Five weeks of soy intake significantly increased circulating plasma genistein and daidzein levels, but did not affect plasma or urinary isoflavones after the test meal. There was a trend towards increased plasma daidzein and genistein levels with the probiotic and prebiotic treatments but no overall statistically significant effects. Neither treatment induced or increased equol production, although there was a trend with probiotic treatment for increased plasma equol in equol producing subjects. Despite the lack of significant effects on isoflavone bioavailability, total cholesterol was significantly decreased with both probiotic and prebiotic treatments and LDL cholesterol was most significantly decreased with prebiotic treatment indicating a synergistic action between soy and prebiotic and probiotic intake for lipid lowering.

A Japanese study examining the association between urinary excretion of equol and the risk of breast cancer in Japanese women (Gifu University Graduate School of Medicine) found that excretion of equol was moderately positively associated with urinary levels of daidzein. This was higher in those women with cancer than in the controls suggesting that the ability to produce equol may be associated with the risk of breast cancer.

### **Infant feeding**

A separate one day workshop was held before the main symposium to explore the state of our current knowledge on the effects of soy on growth and development. The aim of this symposium entitled "Effects of soy on growth and development: how much do we know?" was to identify the important health issues related to early soy exposure and the research needs aimed at resolving unanswered questions. The symposium covered important issues such as the the role of estrogens in development, clinical safety, the usefulness and appropriateness of animal models in this kind of research, the role of equol, and information on pilot and other studies currently underway in the USA and Japan.