HOW EFFECTIVE AND SAFE ARE COMPLEMENTARY AND ALTERNATIVE MEDICATIONS: AN EVIDENCE BASED ANSWER

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Phytoestrogens are a diverse group of polyphenolic non steroidal plant compounds. They can be classified into flavonoids and non-flavonoids. Flavonoids include isoflavones, coumestans, and prenyl flavonoids. Non-flavonoids are called lignans, which include lariciresinol, isolariciresinol, matairesinol, secoisolariciresinol, enterodiol, and enterolactone.
- 17β-Estradiol
- Genistein
- Coumestrol
- Secoisolariciresinol
- 8-prenyl-naringenin
- Daidzein
- Equol
Influence of phytoestrogens:

On vasomotor symptoms: Studies were grouped into broad categories. Five trials used Promensil (Novogen, Sydney, Australia), a red clover extract; these trials were combined in a meta-analysis, and summary effect measures were calculated.

There is no evidence of effectiveness in the alleviation of menopausal symptoms with the use of phytoestrogen treatments (dietary soy, soy extracts, red clover extracts, and other types of phytoestrogen). Cohrane Update (maart 2008, obst Gyn vol 111, 3)

On the cardiovascular system: no evidence

On the breast:
DUCTLOBULAR UNIT
P-1 breast cancer prevention trial van de National Surgical Adjuvant Breast and Bowel Project NSABP

results:

in the tamoxifen arm there was a reduction of 49% of invasive breast cancer.
Total Cases = 77
*P<.001

RR = 0.38 (95% CI = 0.24-0.58)*

Placebo 5.3 per 1000 woman-years

Raloxifene 1.9 per 1000 woman-years
PARTIAL AGONIST

hERβ-LBD + GEN

Genistein
Relative affinity for the alfa and beta receptor

<table>
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<th>HOP</th>
<th>FLAX</th>
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GENISTEIN, DAIDZEIN, AND EQUOL AND CELL-CELL ADHESION IN MCF-7/6 CELLS

SLOW AGGREGATION ASSAY

DMSO

Equol

Equol + MB2

Equol + ICI 182,780
FAST AGGREGATION ASSAY

Differential Volume

- Genistein 10
- Genistein 130
- Genistein + IC1 130
- Genistein + MB2 130

Volume (%)

Particle Diameter (μm)

0.4 0.6 1 2 4 6 10 20 40 60 100 200 400 1000 2000
The major problem is the large variation in results in studies with phyto estrogens due to the large variation in resorption in human.
WORK PACKAGE I

Large interindividual variation
WORK PACKAGE I

- Individual phytoestrogens – SHIME run
WORK PACKAGE I

- Individual phytoestrogens – SHIME run
  - Daidzein metabolism (Decroos et al. (2006) J Nutr 136, 946-52)
    - Weak equol-producing inoculum + EPC4
    - Standard SHIME feed + 175 µM daidzein aglycon eq.
    - Strong 8-PN-producing inoculum
    - Weak 8-PN-producing inoculum + E. limosum
    - Standard SHIME feed + 70 µM IX

- Stable EQUOL production in colon transversum
- Stable 8-PN production in colon transversum
### BREAST TISSUE HOMOGENATE

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MATERIAL & METHODS - BREAST

**MATERIAL & METHODS**

- FFQ, BMI, age, antibiotic use, etc.
- Breath methane
- Blood spot urine
- Breath methane
- GC-FID
- WASHOUT
- Treatment

**AESTHETIC BREAST SURGERY**

- Breast biopsies
- Enzymatic deconjugation
- Extraction
- HPLC-UV-MS

**Bio-activity**
- Biodistribution
- Concentration
- Molecular form

**SOY**

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**HOP**

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**CTL**

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WP 2 - Distribution in breast tissue

Molecular form
Aglycones or conjugated? (Gu et al. 2005)

ISOLATION

HYDROLYSIS

Biodistribution
Glandular or adipose tissue?

CONCENTRATION

KWANTIFICATION

EXTRACTION
Soy products could be used as an alternative to classical hormonal therapy if the resorption problem could be solved. Adding strains of bacteria can improve absorption in vitro to 100%. In vivo studies need to prove safety of these bacteria in all circumstances.

Gut bacteria play an important role in the absorption and metabolisation of phyto estrogens. 8-PN is by far the most potent phyto estrogen. Xanthohumol has antitumoral properties. Iso xanthohumol can be a precursor of 8-PN.

The ultimate goal is to obtain sufficient phyto estrogen concentration in target tissues such as breast, brain, cardiovascular system and the bone.