Isoflavone workshop
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Chemistry and isoflavonoids

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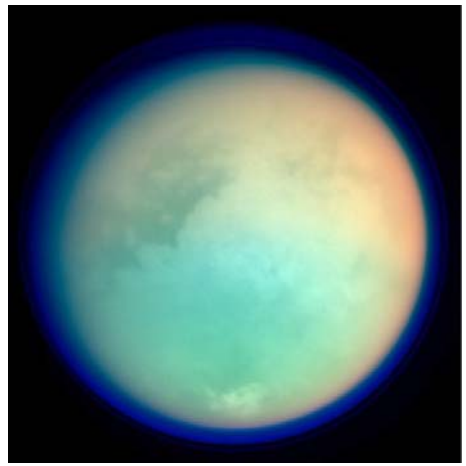
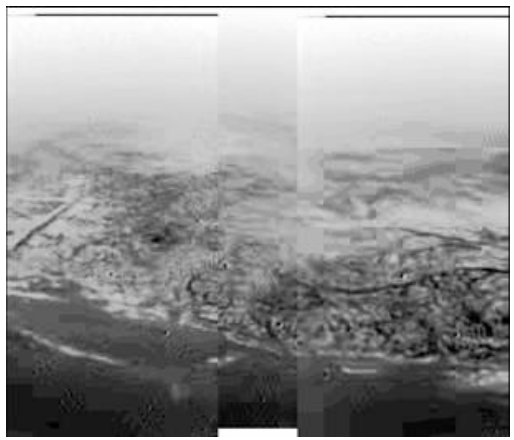
Major issues in use of isoflavones

- **Does it matter which isoflavones (aglycones) are in the product?**
- **Does it matter whether the isoflavones are O- or C-glycosides?**
- **Does it matter whether the isoflavone glycoside conjugates are esters, and if so, should this appear on the label?**
- **Should the weight of isoflavones be given aglycone equivalents?**

Keys to life on planets and moons

Earth and the Saturn moon Titan have atmospheres that are largely nitrogen and smaller amounts of carbonaceous gases - mostly CO_2 on Earth and methane on Titan





So, where is this?

It's not a Swiss lake in winter, but lakeside on Titan (courtesy of NASA-ESA Cassini-Huygens)

Making nitrogen accessible

The key to our form of life was/is converting non-reactive N_2 gas to fixed nitrogen (ammonia, amino acids, etc.). Before life appeared, this occurred from lightning and volcanic action.

The key to life was nitrogen-fixing archeal bacteria and then algae (the latter also fix CO_2).

In the "modern" era, it is the symbiosis between plants (legumes such as clover and the soybean) and soil bacteria that fix nitrogen. Plants also convert CO_2 with the aid of sunlight to carbohydrates and O_2.

Plant-bacterium dilemma

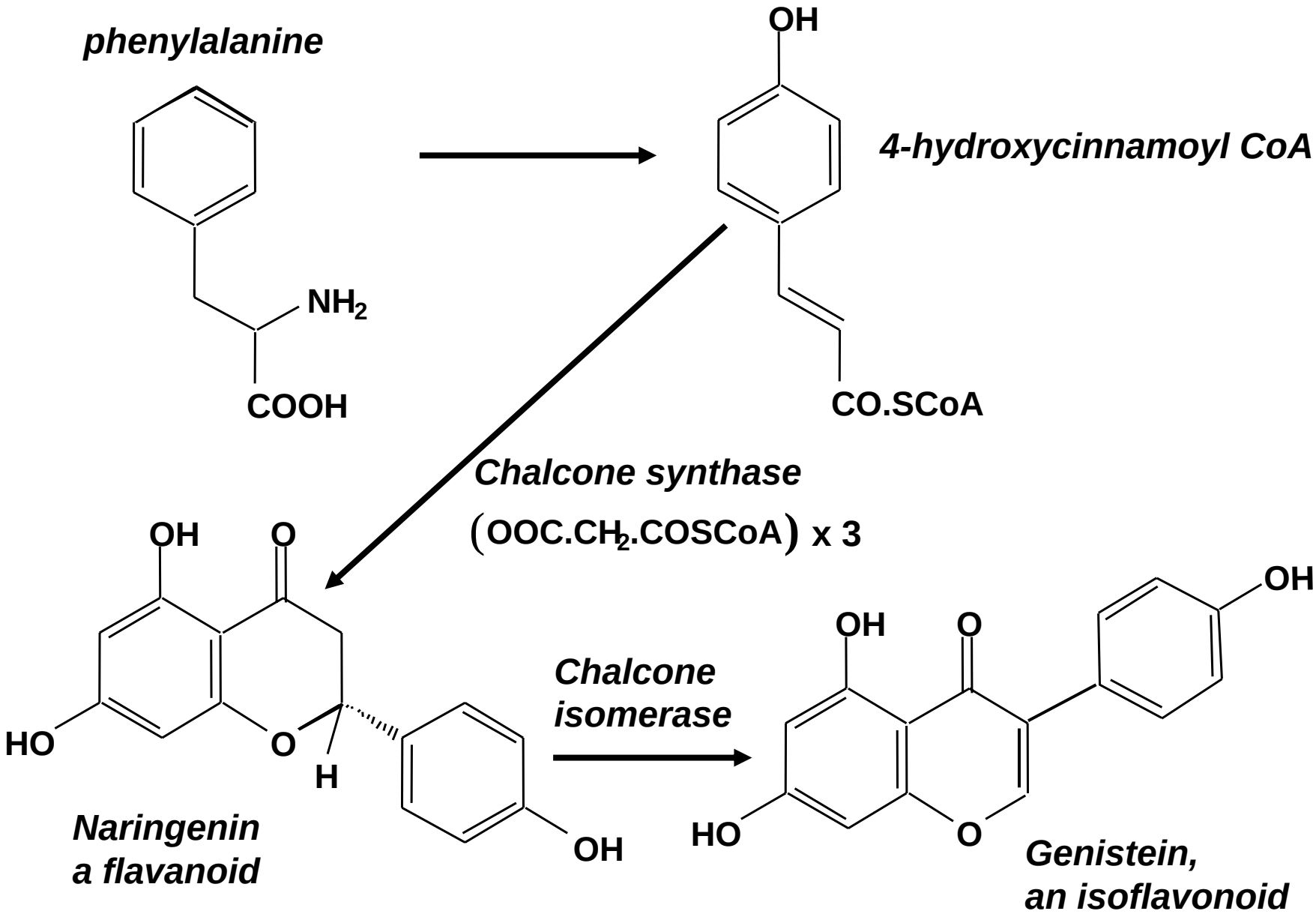
Plants have to defend themselves against microorganisms. But the legumes have a symbiotic relationship with *rhizobia* sp. How does this occur?

The key is molecular signals from the plant to the bacteria and bacteria to plant.

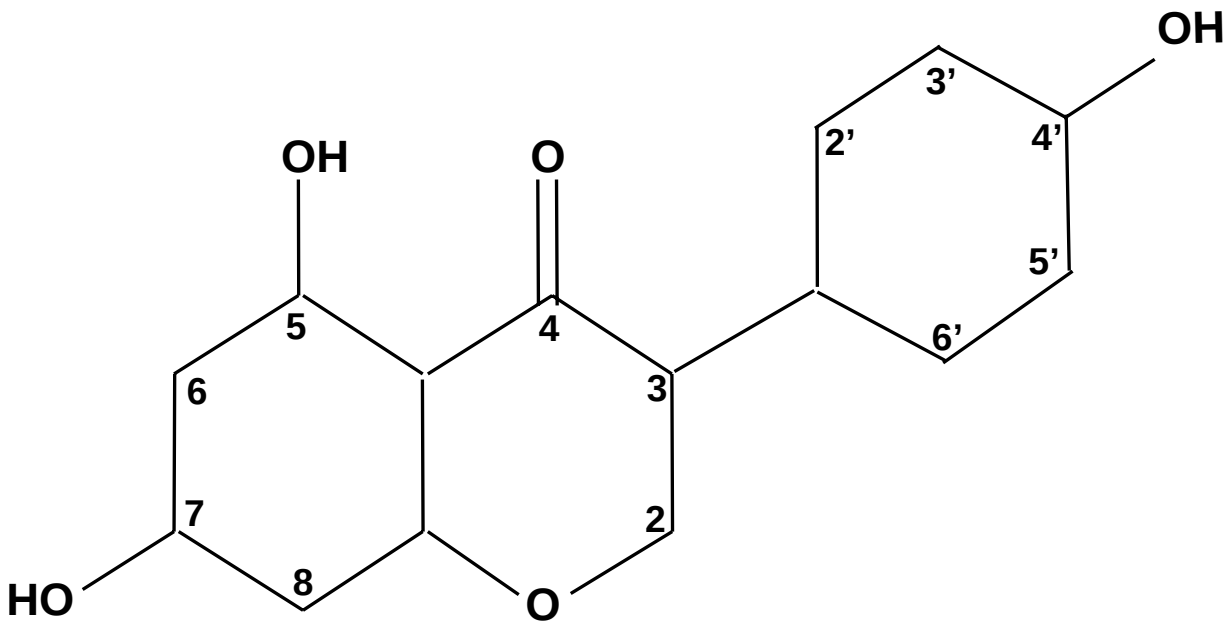
Bacteria have nodulation (Nod) genes. These are activated by compounds released by the root of the legume - for the soybean, these compounds are isoflavonoids.

Genistein
Daidzein
Glycitein

Biosynthesis of isoflavonoids

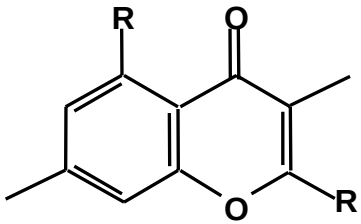


Numbering scheme for isoflavonoids

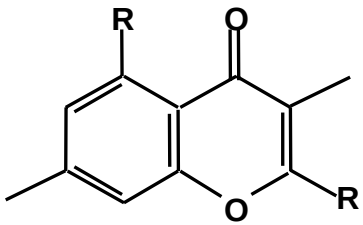


Genistein = 5,7,4'-trihydroxyisoflavone

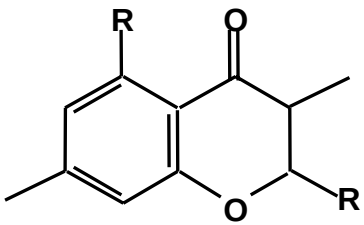
Classes of isoflavonoids



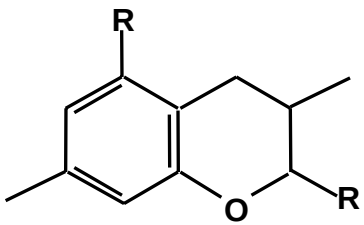
Isoflavone, R=H
daidzein, genistein



Isoflavonol, R=OH



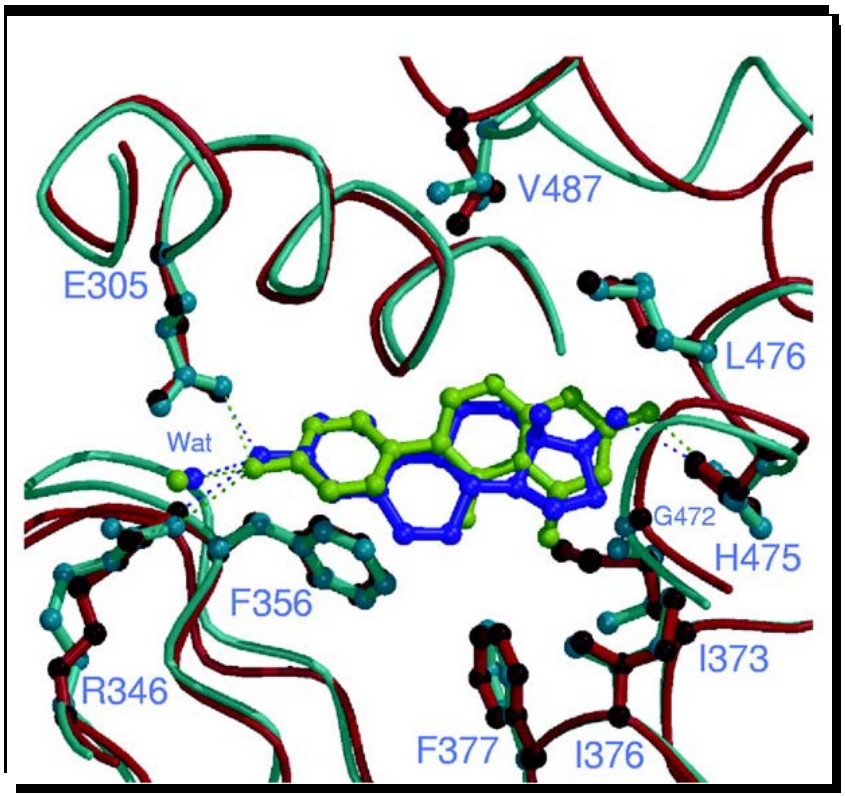
Isoflavanone, R=H
Isoflavanol, R=OH



Isoflavan, R=H
Equol, bacterial metabolite

Note that these compounds have an assymetric carbon atoms and are optically active

What's up duck?

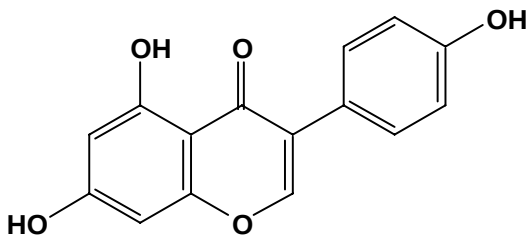


Superposition of genistein (green) and 17β-estradiol (blue) in the ligand binding pocket of ERβ

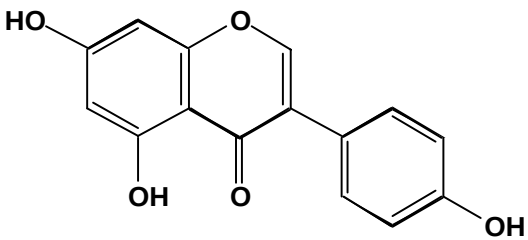
– note that the phenolic B-ring of this isoflavone is in the position occupied by the aromatic A-ring of 17β-estradiol

From Pike et al. (1999)

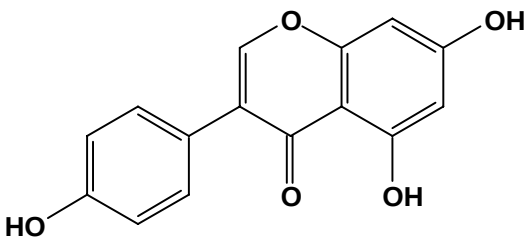
Genistein “flipped and spun around” is the right way



In this presentation

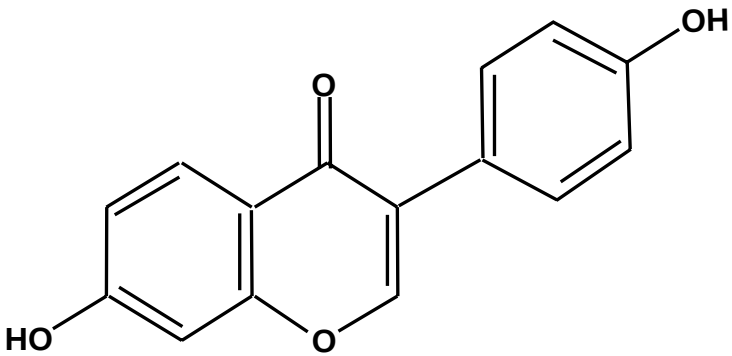


In plant journals

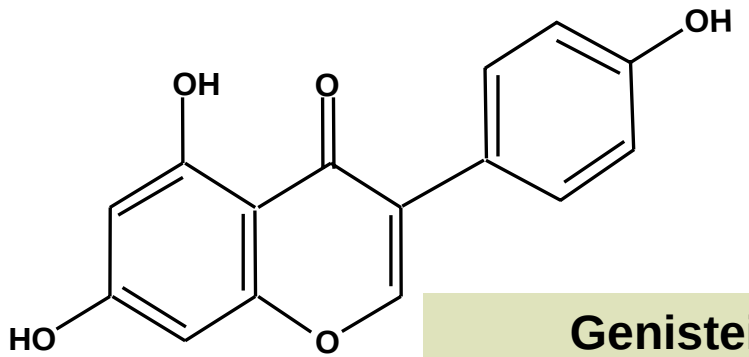


If genistein is an estrogen

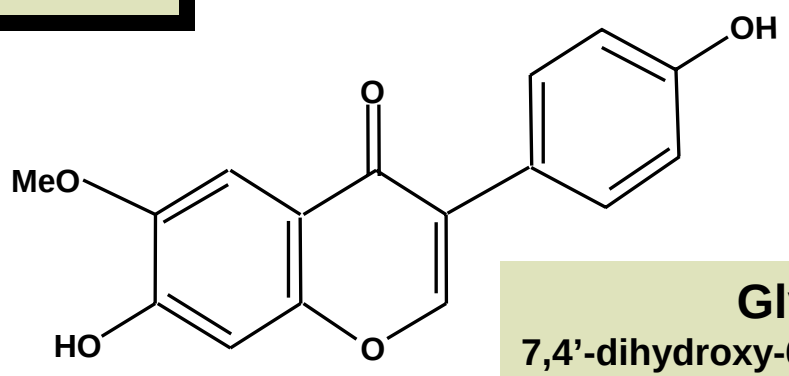
Soy isoflavones



Daidzein
7,4’-dihydroxyisoflavone



Genistein
5,7,4’-trihydroxyisoflavone

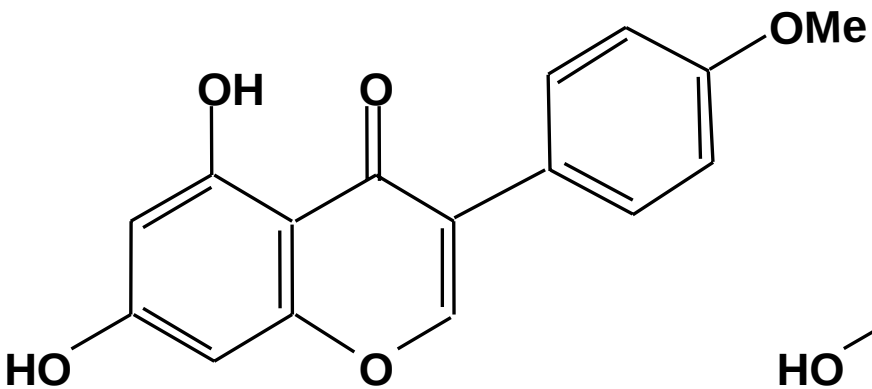


Glycitein
7,4’-dihydroxy-6-methoxyisoflavone

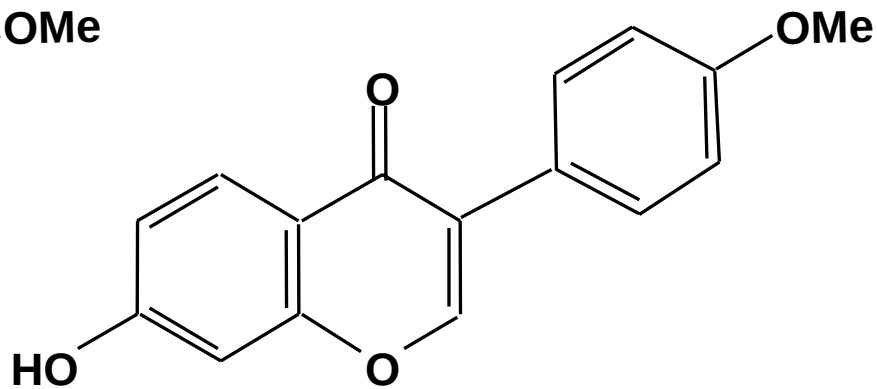
Methylated isoflavonoids

Red clover (*Trifolium pratense*)

Leung & Foster, 1996

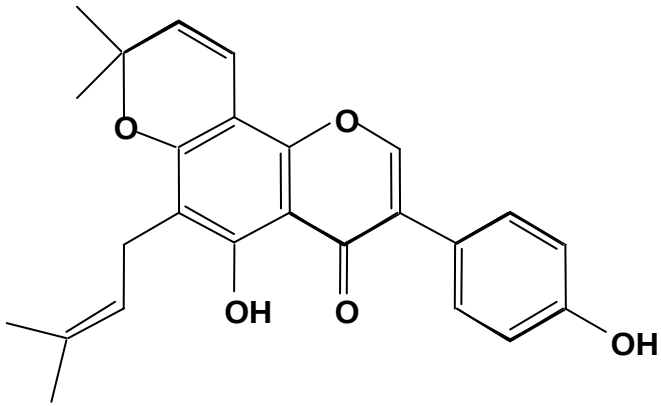


Biochanin A



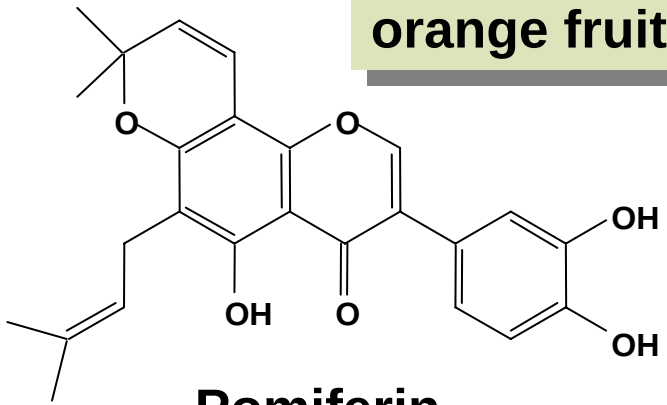
Formononetin

Prenylated isoflavones

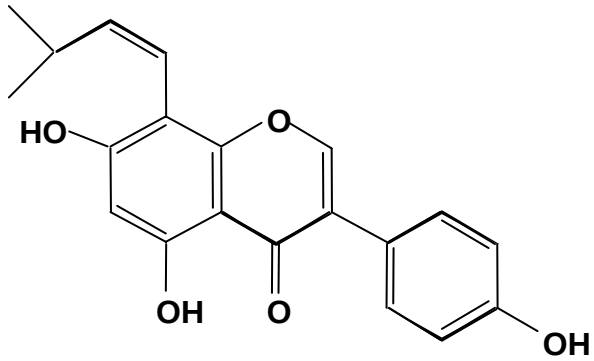


Osajin

From the Osange orange fruit



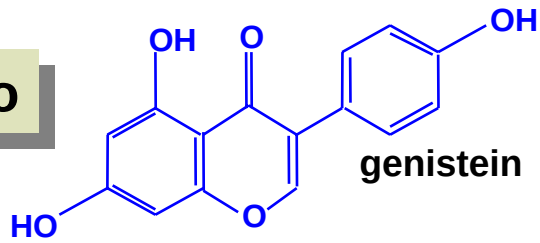
Pomiferin



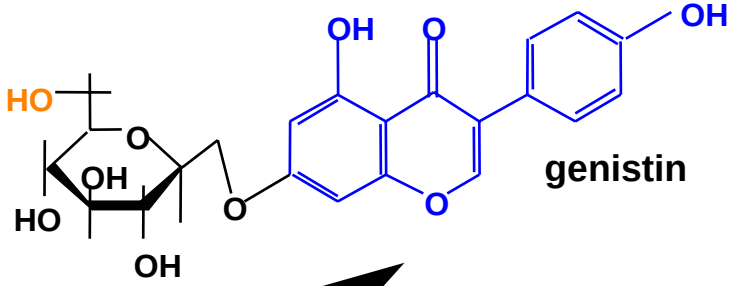
8-prenyldaidzein in hop-based beer

Genistein glucosides in soy products and supplements

Miso



genistein

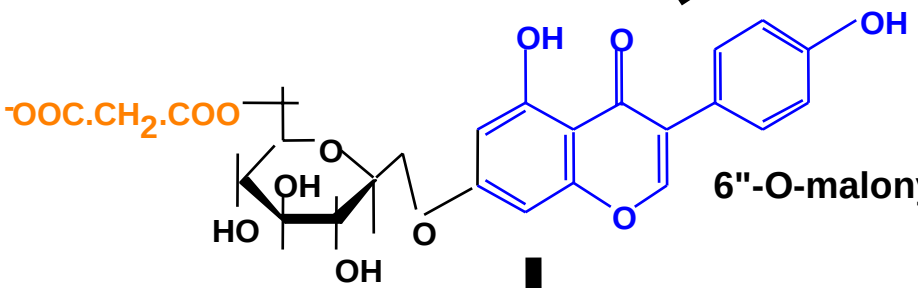


genistin

Tofu and soy milk

fermentation

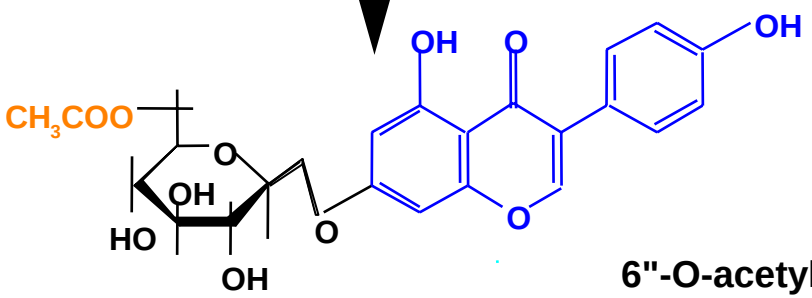
hot water extraction



6"-O-malonylgenistin

Whole soybean or unheated soy flour

dry heat (100°C); $-CO_2$



6"-O-acetylgenistin

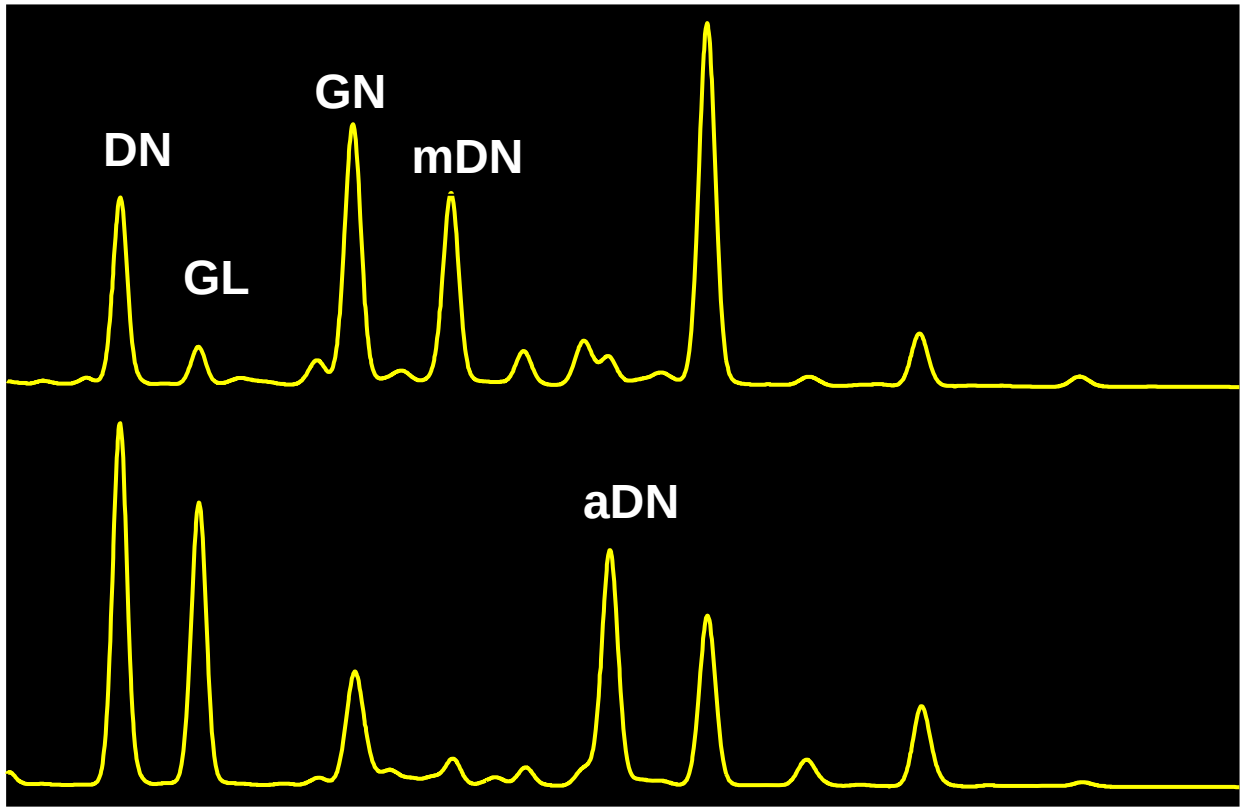
SoyLife™ or TVP

Two non-identical soy protein products

Both different with regard to proportion of isoflavones and in glucoside composition

Soy flour
Defatted, low heat

SoyLife™
Roasted soy hypocotyl



Lessons in labeling

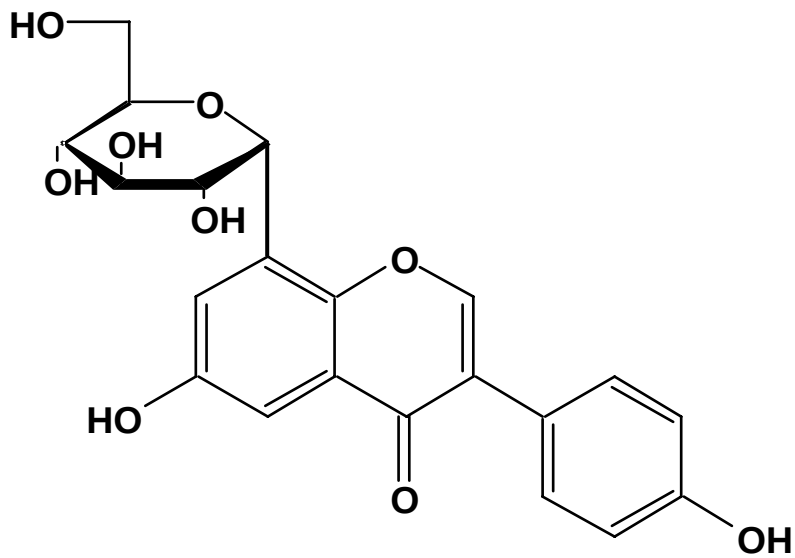
- **The problems with the equine estrogens extract (Premarin™) have led women to turn to "soy" estrogens for estrogen replacement therapy**
- **But soy estrogens are not what's in the bottle - it's the kudzu isoflavones**

*"Purified Isoflavones (from GMO-Free Soybeans and **Other Plants**) 80.0 mg"*

*"Soy and **other plants**, sources of natural estrogens, for hormonal balance."*

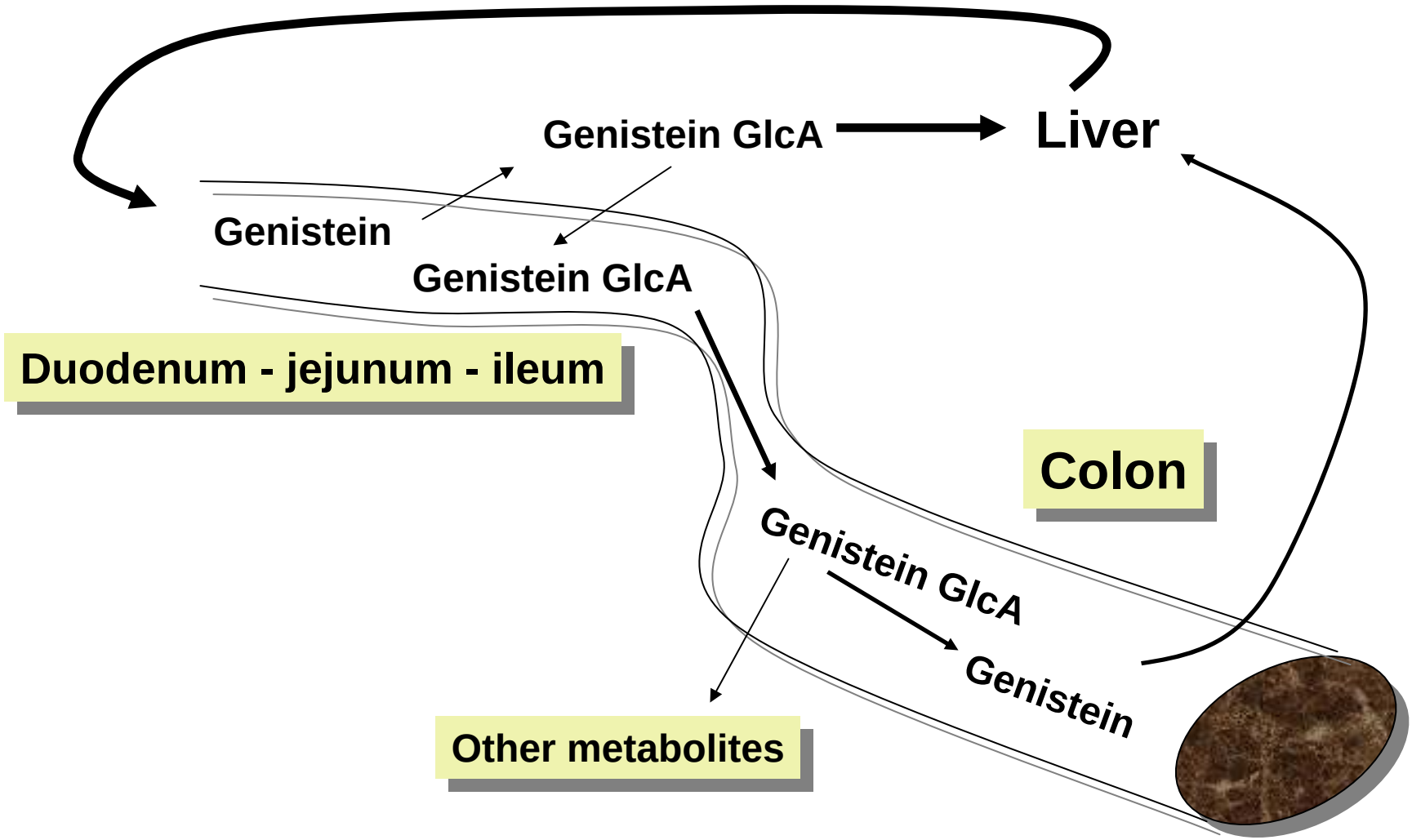
The new player on the shelves

Kudzu (*Pueraria lobata*)

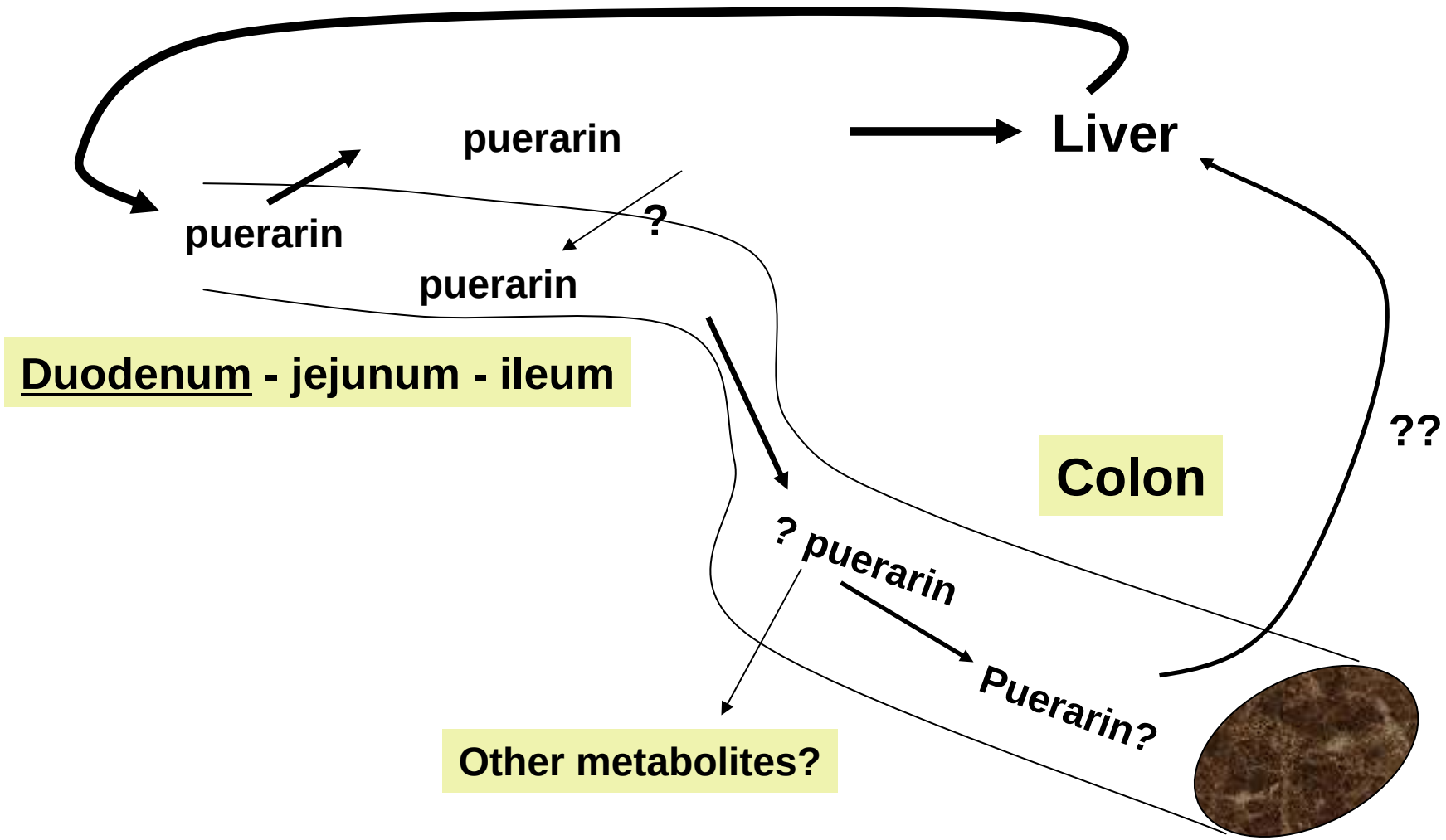


Puerarin - daidzein 8-C-glucoside

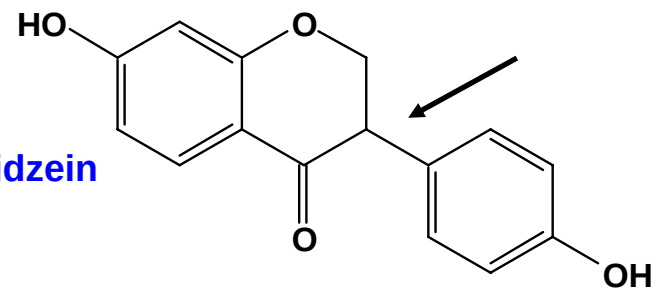
Overall view of isoflavonoid uptake and metabolism



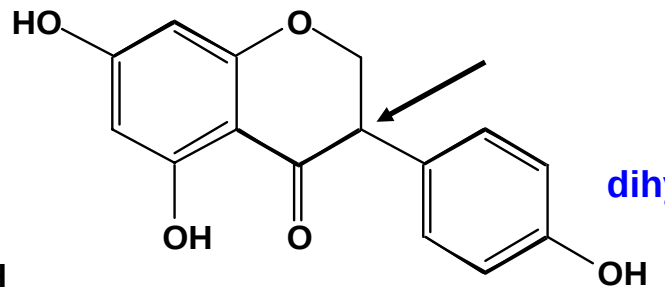
Possible puerarin uptake and metabolism



Isoflavone bacterial metabolism

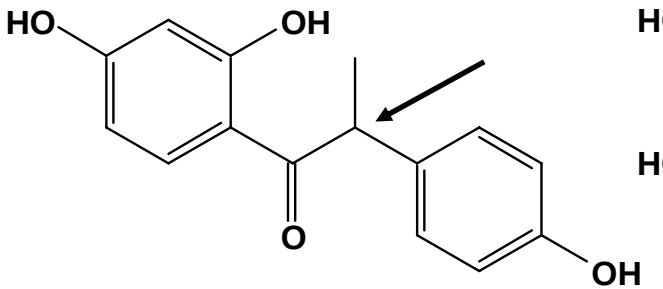


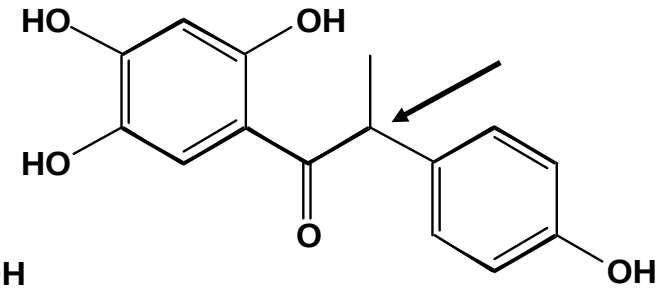
dihydrodaidzein



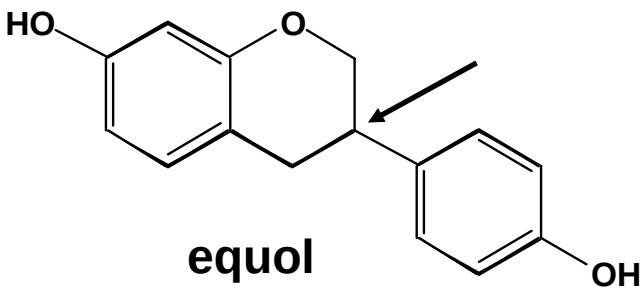
dihydrogenistein

Dihydro metabolites





***O*-desmethylangolensins**



equol

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