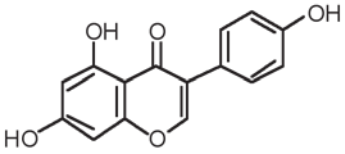
Isolase® Patent Pending

A Formulation From National Enzyme Company

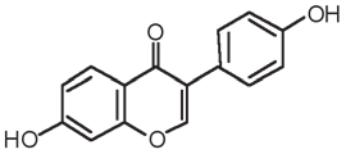
Background Information

The isoflavonoids in soy foods are reported to have numerous medicinal properties. Many studies have shown that these isoflavonoids, which are plant estrogens (phytoestrogens), play an important role in the prevention of cancer[1], cardiovascular disease[2] and osteoporosis.[3a-d] Most important and abundant among these plant estrogens that are found in soy, are genistein and daidzein (Fig. 1).

Figure 1: Chemical structures of genistein and daidzein



Genistein

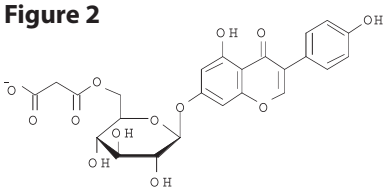


Daidzein

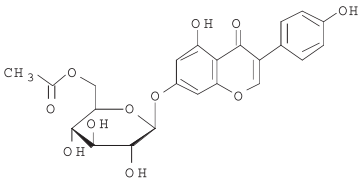
There are a number of hypotheses explaining the health benefits and the biochemical action of genistein and daidzein. Barnes et. al.[4] viewed genistein as a phytoestrogen that exhibits chemopreventive properties by acting as an estrogen antagonist. The anti-cancer drug, tamoxifen, has a similar pharmacological effect. This basic hypothesis was further expanded by Akiyama et. al.,[5] who showed that genistein is an excellent and specific inhibitor of protein tyrosine kinases. Many cellular biochemical pathways, initiated by extracellular growth factors, proceed by the phosphorylation of tyrosine using protein tyrosine kinases. These pathways are especially important in transformed cells since more than half of the protein products of cellular oncogenes undergo uncontrolled tyrosine phosphorylation[6]. In light of these investigations, genistein has been a subject of numerous studies involving protein tyrosine kinase inhibition. Genistein inhibits the proliferative growth of many cancer cells in tissue culture[7a,b] and inhibits the appearance of tumors in animal models of breast cancer[8] and skin cancer,[9a,b] and is active against colonic cancer.[10a,b] Apart from the anti-cancer applications, genistein is also a good inhibitor of α-glucosidase (invertase).[11] Genistein is a reversible, slow binding, non-competitive inhibitor of α-glucosidase with a K_I value of 5.7×10^{-8} M. These results indicate that genistein can be used to treat certain metabolic disorders. Isoflavones are also known to lower the incidence of coronary heart disease and mitigate the effects of hot flashes in postmenopausal women. In many cases treatment of hot flashes by isoflavones has proven safer and more effective than estrogen replacement therapy.

Isoflavones are absorbed in the gut just like any other xenobiotic. The absorption of a xenobiotic through the gastrointestinal tract depends on several factors. The xenobiotic should be hydrophilic enough to dissolve in the aqueous environment but at the same time should be sufficiently hydrophobic to be soluble in the gut membrane. The charge on the xenobiotic also plays a major role in its absorption. This charge is determined by the pH of the medium, which in this case is the small or large intestine, whose pH is close to 7.8. In most non-fermented soy foods, isoflavones exist as conjugates with glucose, as their malonyl or acetyl esters (Fig. 2). In many cases though, the esters are hydrolyzed when soy foods undergo heat treatment. This leaves genistin as the major isoflavone component. Genistin is a very hydrophilic molecule and thus is not absorbed well by the body through the gut. Genistein, on the other hand, has the right balance of hydrophilicity and hydrophobicity to efficiently get absorbed by the body. Experiments on human subjects have shown that the aglycone form, genistein, is absorbed faster and in greater amounts than its glycosylated conjugate, genistin.[12]

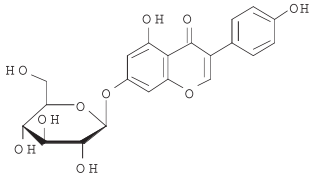
Figure 2



6″-O-Malonylgenistin



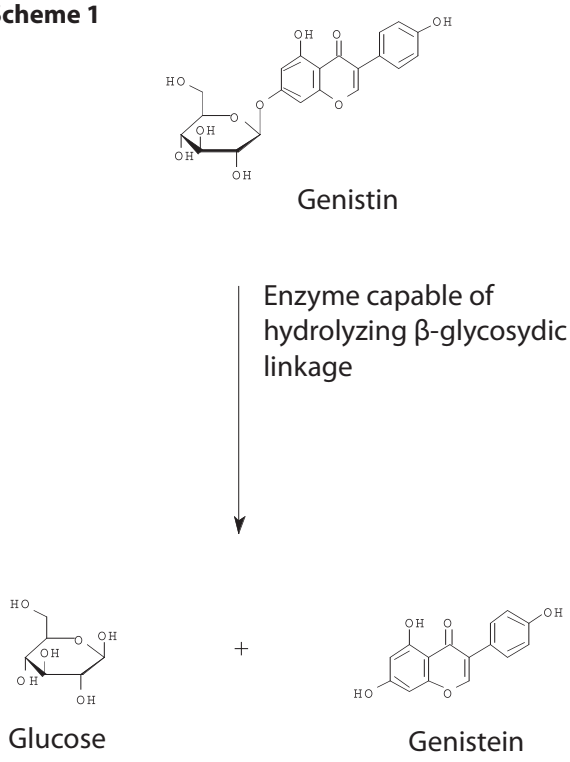
6″-O-Acetylgenistin



Genistin

Enzymes capable of cleaving the β-ether linkage of the glycosylated isoflavones could have applications in soy food and beverage products. Scheme 1 describes the reaction catalyzed by these enzymes.

Scheme 1



The human body does not produce the enzyme that is capable of hydrolyzing the glycosidic linkage between the glucose molecule and the isoflavone. Some bacterial flora present in human gut do produce this enzyme but not all humans carry these bacteria. Consequently many people who ingest soy food are not receiving the benefits of isoflavones. National Enzyme Company has developed a unique blend of enzymes, **Isolase®**, that is capable of hydrolyzing this β-glycosidic linkage and thus release free isoflavones, which are more bioavailable.

To test the efficacy of **Isolase®**, National Enzyme Company conducted a clinical trial in collaboration with Iowa State University. The trial was a double blind study where subjects were administered soy protein drink with and without **Isolase®**. Plasma samples were analyzed after 0, 3 and 24 hours. Analysis of plasma samples taken at 3 hours showed that **Isolase®** doubles the absorption of isoflavones.

Isolase® is stable in gastric juice, has a wide pH range and thus works throughout the GI tract. **Isolase®** is also heat stable up to 85 °C for 5 minutes.

Isolase® can be incorporated into many soy foods and will increase the bioavailability of isoflavones.

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