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Isoflavones

Soyfoods are Rich in Isoflavones

Author
Mark Messina, Ph.D.

Reviewers
Stephen Barnes, Ph.D.
Clare Hasler, Ph.D.
Anne Patterson, RD
Kim Galeaz, RD

Introduction

All plant foods are complex mixtures of chemicals including both nutrients and biologically active nonnutrients, referred to as nutraceuticals or phytochemicals. Soy is known for having high concentrations of several physiologically–active phytochemicals, including isoflavones, phytate (inositol hexaphosphate), saponins, phytosterols and protease inhibitors. The isoflavones, however, are what make soy unique.[1,2]

Soybeans and soyfoods are the only natural dietary sources that provide nutritionally relevant amounts of isoflavones. Furthermore, clinical data suggest that modest amounts of soy provide sufficient isoflavones to exert physiological effects. Therefore, understanding the health effects of soyfoods requires an understanding of isoflavones.

Chemical Structure

Isoflavones are a subclass of a larger and more ubiquitous group of nutraceuticals called flavonoids. In comparison to most flavonoids, isoflavones have a very limited distribution in the plant kingdom. While flavonoids are found in many plant foods such as onions, apples, and grapes, soybeans are the only food to contain nutritionally relevant amounts of isoflavones.

The primary isoflavones in soybeans are genistein (4' 5, 7–trihydroxyisoflavone) and daidzein (4', 7–dihydroxyisoflavone), and their respective ß–glycosides (glucose is attached at the 7 position of the A ring, figure), genistin and daidzein. Typically, more genist(e)in exists in soybeans and soyfoods than daidz(e)in.[3] There are also small amounts of a third isoflavone in soybeans, glycitein (7, 4'–dihydroxy–6–methoxyisoflavone) and its glycoside, glycitin.

There are actually 12 different soybean isoflavone isomers. In addition to the six described above, each of the isoflavone glycosides can have an acetyl or malonyl group attached at carbon six of the A ring (figure).

In soybeans and nonfermented soyfoods, isoflavones are present primarily as beta–glucosides, esterified with malonic or acetic acid.[4] In fermented soy products such as tempeh and miso, due to microorganism–induced fermentation and hydrolysis more of the isoflavones are present in aglycone (unconjugated) form. Isoflavones are quite heat stable. Baking or frying does not alter total isoflavone content and although the chemical structure of the isoflavone is very slightly changed, this change is not thought to be nutritional relevant.[4]

Isoflavones as Phytoalexins

Isoflavones, like many phytochemicals of interest to nutritionists, are phytoalexins – substances formed by the host tissue in response to physiological stimuli, infectious agents or their products – that accumulate to levels that inhibit

the growth of micro–organisms.[5] Isoflavones possess properties (antifungal, antimicrobial, antioxidant, etc.) that enhance the survival of the soybean.[5] For this reason, soybean isoflavone concentrations increase greatly in times of stress, such as when moisture is limited, and are influenced by the environmental conditions under which the soybean is grown.[6,7]

In contrast to many phytoalexins, isoflavones are always present in significant quantities in soybeans, because one of their primary functions is to stimulate nodulation genes in soil bacteria called Rhizobium. Rhizobia have the ability to induce the formation of structures called nodules on legume (soybean) roots.[8] The rhizoba within these nodules reduce atmospheric nitrogen to ammonia, which the soybean can then use as a source of nitrogen for growth. This property of soybeans has been used extensively by the American farmer in crop rotation to naturally restore nitrogen to their fields

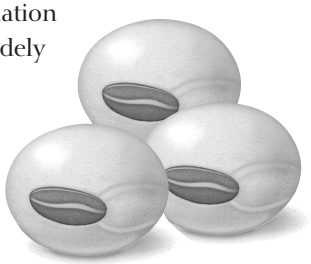
Soy Isoflavone Content

There is as much as a eightfold variation in isoflavone content among the many different varieties of soybeans. Thus, the soyfoods made from these beans also have a large variation in isoflavone content. However, most of the variation in isoflavone content of soyfoods results from the effects of food processing.[9] The U.S. Department of Agriculture, in conjunction with Iowa State University, recently established an online database (http://www.nal.usda.gov/fnic/) of the isoflavone content of soyfoods.[10]

According to this database, the isoflavone content of dry uncooked soybeans is approximately 1.0 mg/g, with a range of about 0.4 – 2.4 mg/g. Traditional soyfoods such as tofu and miso typically provide 0.2 – 0.4 mg/g (fresh weight) product, and about 2 – 4 mg/g protein. Isolated soy proteins vary in isoflavone content (range 0.5 – 2.0 mg/g), although the average is about 1 mg/g. As a result of losses through processing, the isoflavone content of alcohol–washed soy protein concentrates (the most common type of concentrate), is only 5 percent to 20 percent that of the water–washed concentrates. Typically, one serving of a traditional soyfood provides about 20 – 35 mg of isoflavones.

Daily per capita isoflavone intake in Asia varies among countries. It also varies among regions and subsets of the population within the same country, but surveys suggest the range is from 15 – 50 mg.[11]

Because of the surge in interest in the health benefits of isoflavones, isoflavones extracted from soybeans are being to both soy and nonsoy products, and many companies now provide information about the isoflavone content of their products. Isoflavones supplements are also widely available.



Isoflavone Bioavailability and Serum Levels

Over the past decade, scientists have conducted considerable research on the absorption and metabolism of isoflavones. Serum isoflavone levels increase in response to soyfood consumption in a dose–dependent fashion,[12,13] and can reach the low micromolar level.[14,15] Plasma levels among free–living Asians are typically around 500 nmol/l, but measurements are typically taken after an overnight fast.[16,17] Since the half–life (the time required for serum levels to decrease by 50%) of isoflavones is approximately six hours, fasting levels are much lower than postprandial (following a meal) levels.[15,18,19,20] Studies suggest that approximately 30 percent to 50 percent of the isoflavone dose ingested is absorbed.[12, 19,21]

Some research suggests isoflavones in aglycone (without sugar) form, as in fermented soyfoods, are absorbed more efficiently than isoflavone glycosides.[22,23] However, recent research suggests this is not the case,[24] although aglycones may be absorbed somewhat faster.[25] Since physiological effects have been observed in humans in response to both the consumption of isolated isoflavones in glycoside form[26] and soyfoods in which the isoflavones are present primarily as glycosides,[27] it is clear humans have the ability to absorb isoflavones regardless of form.

Isoflavones – Physiology

Isoflavones have a strikingly similar chemical structure to mammalian estrogens. Therefore, it is not surprising that isoflavones bind to estrogen receptors and affect estrogen–regulated gene products.[28,29]

Traditionally, isoflavones have been considered to be very weak estrogens, possessing between 1 x 10–4 and 1 x 10–2 the activity of 17ß–estradiol on a molar basis.[28,29,30] Even these estimates of estrogenic activity suggest isoflavones likely exert physiological activity in vivo, since people who consume soyfoods may have serum isoflavone levels up to 10,000 fold higher than endogenous estrogen levels.[15] The high serum and tissue isoflavone concentrations compensate for their relative weakness. However, for several reasons, these older views of the relative estrogenicity of isoflavones may need to be revised.

First, genistein binds with almost the same affinity to the recently discovered second estrogen receptor, estrogen receptor beta (ERb), as 17b–estradiol.[31,32] Until recently, estimates of the estrogenic activity of isoflavones were based largely on estrogen receptor alpha (ERa), for which genistein has much less affinity. Second, isoflavones may bind less tightly than estrogen to serum proteins making them more available to the tissues.[30] Third, isoflavones may be tissue–selective, exerting quite pronounced estrogenic activity in some tissues,[33] but not in others.[34]

The ability to exert tissue–selective effects likely stems in part from the different tissue distribution of ERb and ERa.[35] This observation has prompted speculation that isoflavones are natural selective estrogen receptor modulators (SERMs), like the drugs tamoxifen and raloxifene,[36] and therefore might provide the benefits of estrogen without the disadvantages – but this is still speculative.

Although isoflavones possess estrogenic and possibly antiestrogenic activity,[37] the physiological effects of isoflavones, especially genistein, are likely only partially related to direct interaction with or binding to estrogen receptors. This is evidenced by the finding that genistein inhibits the growth of a wide range of both hormone–dependent and independent cancer cells in vitro[38,39,40] – a result thought to be due to the ability of genistein to influence signal transduction.[41] In vitro, genistein inhibits the activity of many enzymes and cellular factors that control the growth of cells.[42,43,44,45] Isoflavones also possess antioxidant activity.[46] The myriad biological effects of isoflavones accounts for their possible beneficial roles in diseases as diverse as osteoporosis,[47, 48] coronary heart disease,[33] malaria,[49] cystic fibrosis,[50] and alcoholism.[51]

In clinical studies demonstrating the health benefits of soyfood consumption, subjects typically ingest between 40 and 150 mg of isoflavones per day. Some studies report average Japanese consumption may be as high as 50 mg/day. Obviously, a sizeable portion of the population consumes more than this amount. In fact, several studies reported that isoflavone intake by approximately five percent of the Japanese population is 100 mg/day.

Therefore, a reasonable upper adult daily limit for isoflavone intake is considered to be about 100 mg (aglycone units), an amount found in approximately three servings of traditional soyfoods. Consuming three servings of soyfoods per day is much more than most Americans currently consume, but still consistent with recommendations to choose a variety of foods. Furthermore, clinical studies conducted for as long as one year in which subjects have consumed more than 100 mg of isoflavones per day have not reported any adverse effects.

Conclusions

Soybeans are a unique natural dietary source of isoflavones. Much of the interest in the health effects of soyfoods is due to the presence of isoflavones in soybeans. Even modest amounts (one or two servings per day) of soyfoods may provide a sufficient level of isoflavones to exert physiological effects in humans. The biological effects of isoflavones may be due to both hormonal and non–hormonal properties.

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