Editorial

Isoflavonoids

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Flavonoids (from the Latin word flavus meaning yellow, their color in nature) are a class of plant and fungus secondary metabolites.

Chemically, flavonoids have the general structure of a 15-carbon skeleton, which consists of two phenyl rings (A and B) and heterocyclic ring (C). According to the IUPAC nomenclature [1,2] they can be classified into:

1. flavonoids or bioflavonoids.
2. isoflavonoids,
3. neoflavonoids,

Isoflavonoids are a class of flavonoid phenolic compounds, many of which are biologically active. Isoflavonoids and their derivatives are sometimes referred to as phytoestrogens, as many isoflavonoid compounds have biological effects via the estrogen receptor. Isoflavonoids are derived from the flavonoid biosynthesis pathway via liquiritigenin or naringenin. [3]

Isoflavonoids are subclass of flavonoids and have been isolated from a wide variety of leguminous and non-leguminous plants. Isoflavones are present in berries, wine, grains, nuts, soybeans, and other legumes including kudzu root (Pueraria lobata), peanuts (Apiosamericana), and chickpeas (Cicer arietinum).

There are many biological activities associated with the isoflavones, including reduction in osteoporosis, cardiovascular disease, and prevention of cancer and for the treatment of menopause symptoms. Recent data indicate that the protective effect of isoflavonoids may extend beyond their antioxidant activity on molecular and cellular levels and modulating activity of many other enzymes.

Biotechnological approaches have been used to produce isoflavonoids through cell cultures of different species grown in shake flasks and bioreactor using normal and transformed cells.

Isoflavonoids are derived from the phenylpropanoid pathway and are synthesized predominantly in leguminous plants [4]. Simple isoflavonoids are dietary phytoestrogens and their glycosides. The isoflavanoid compounds have been studied intensively and about 1,600 isoflavonoids have been identified. [5]

Isoflavones exist in abundance in the natural sources in precursor form, not active form. Isoflavones are inactive in glycosidic form, their aglycosidic form is active and gets absorbed in the intestinal tract however, it is dependent on so many factors like fibre content of the diet and microflora of the gut [6]. After absorption, isoflavones are reconjugated to glucuronides and excreted unchanged in the urine [7].

Soy is recognized as the major dietary source of phytoestrogens, and soy-based products have been shown to contain significant quantities of total isoflavones. Daidzein and genistein are the two most well-characterized isoflavones [8]

Dietary consumption of foods and food additives containing isoflavone phytoestrogens has been associated with several beneficial properties to human health, such as prevention of coronary heart disease and osteoporosis, reduction of menopausal symptoms, and prevention of distinct cancer forms (e.g., breast, prostate, and colon cancer) [9, 10]. The potential health benefits of isoflavones for humans have been the subject of several reviews that have analyzed clinical, animal, and in vitro evidence for biological activity [11].

According to the USDA survey on isoflavone content, lentils do not contain significant amounts of these isoflavonoids [12]. Chickpeas contain daidzein, genistein, and formononetin & biochanin A. Soybeans have significantly higher levels of daidzein and genistein but contain less amount of formononetin and biochanin compared to chickpeas.

Epidemiological data suggest that a diet rich in isoflavones provides protection against several forms of cancer, particularly those that are hormone-dependent, such as breast, prostate, and lung cancer [13] Genistein, the predominant isoflavones found in soy, has been shown to inhibit the carcinogenesis in animal models. There are growing body of experimental evidence that show the inhibition of human cancer cells by genistein through the modulation of genes that are related to the control of cell cycle and apoptosis. Moreover, it has been shown that genistein inhibits the activation of NF-kappa B and Akt (protein kinase also known as PKB) signaling pathways, both of which are known to maintain a homeostatic balance between cell survival and apoptosis [14]. Genistein causes inhibition of cell growth in breast and prostate cancers in vivo and in vitro [15]. Both genistein and genistin induce cell cycle arrest [16] and are able to induce significant apoptosis.

Isoflavones prevent atherosclerosis; the most cited example in this case is the inhibition of LDL oxidation, formation of which is central in atherogenesis [17]. Genistein upregulates the expression of human endothelial nitric oxide synthase and lowers blood pressure in spontaneously hypertensive rats [18].

Soybean isoflavones may exhibit their cancer preventive function through their antioxidant properties. Genistein, the major component of soybean isoflavones, has been demonstrated to inhibit ultraviolet-B (UVB)-induced skin tumorigenesis in hairless mice. Genistein has also been shown to inhibit hydrogen peroxide production and increase the activity of antioxidant enzymes, such as catalase, superoxide dismutase, glutathione peroxidase, and glutathione reductase. Furthermore, genistein and daidzein can inhibit superoxide anion generation by xanthine/xanthine oxidase [7].

Depending on the type of estrogen receptor on the cells, isoflavones may reduce or activate the activity of estrogen. Isoflavones can compete with estrogen for the same receptor sites thereby decreasing the health risks of excess estrogen. They can also increase the estrogen activity.

One study suggests only modest effects of isoflavones on plasma hormones in postmenopausal women, and no significant effects on vaginal cytology or endometrial biopsy results. Thus, effects of isoflavones on plasma hormones per se are not likely to be significant mechanisms by which soy exerts estrogen-like effects in postmenopausal women [19].

In October 1999, the US Food and Drug Administration authorized the use on food labels of health claims associated with soy protein and the reduced risk of coronary heart disease. Several studies have indicated that a total daily intake of 25 g of soy protein paired with a low-fat diet resulted in clinically important reductions of total cholesterol and low-density lipoprotein (LDL) cholesterol levels. So far, there is no evidence for a stimulatory effect of isoflavones on the endometrium. A few studies reveal a minimal effect of soy on hot flashes, with soy reducing hot flashes 45% and placebo causing a 30% reduction compared with an approximate 70% reduction in hot flashes with estrogen replacement therapy.

Data available from human studies on the effect of isoflavones on osteoporosis are limited, and additional studies are needed to support a role in osteoporosis prevention. To date, no adverse effects of short- or long-term use of soy proteins are known in humans [20].

Current data are insufficient to draw definitive conclusions regarding the use of isoflavones as an alternative to estrogen for hormone replacement in postmenopausal women. Although epidemiological and basic laboratory studies allude to the possible protective effects of soy isoflavones at specific target tissues, randomized, placebo-controlled clinical trials are necessary to address these important issues.

References

1. McNaught, Alan D; Wilkinson, Andrew; IUPAC (1997), "IUPAC Compendium of Chemical Terminology (2 ed.), Oxford: Blackwell Scientific.
2. "The Gold Book". 2009. doi:10.1351/goldbook. ISBN 0-9678550-9-8. Retrieved 16 September 2012.
3. Isoflavonoid biosynthesis on www.ncbi.nlm.nih.gov/biosystems/
4. Du H, Huang Y, Tang Y (2010) Genetic and metabolic engineering of isoflavonoids biosynthesis. Appl Microbiol Biotechnol 86:1293–1312.
5. Dixon RA (2004) Phytoestrogens. Annu Rev Plant Biol 55:225–261.
6. Lund TD, Blake C, Bu L, Hamaker AN, Lephart ED (2011) Equol an isoflavonoid: potential for improved prostate health, in vitro and in vivo evidence. Reprod Biol Endocrinol 9:4
7. Wroblewski LL, Cooke JP (2000) Phytoestrogens and cardiovascular health. J Am Coll Cardiol 35:1403–1410.
8. Patisaul HB, JeffersonW(2010) The pros and cons of phytoestrogens. Front Neuroendocrinol 31:400–419.
9. Oldoni TLC, Cabral ISR, Arcea MAB, Rosalenb PL, Ikegaki M, Nascimentoa AM, Alencara SM (2011) Isolation and analysis of bioactive isoflavonoids and chalcone from a new type of Brazilian propolis. Sep Purif Technol 77:208–213.
10. Watanabe S, Uesugi S, Kikuchi Y (2002) Isoflavones for prevention of cancer, cardiovascular diseases, gynecological problems and possible immune potentiation. Biomed Pharmacother 56:302–312.
11. Rochfort S, Panozzo J (2007) Phytochemicals for health, the role of pulses. J Agric Food Chem 55:7891–7994.
12. USDA (2002) USDA-Iowa state university database on the isoflavone content of foods. Agriculture Research Service, U.S. Department of Agriculture, Washington, DC.
13. Ren MQ, Kuhn G, Wegner J, Chen J (2001) Isoflavones, substances with multi-biological and clinical propertie. Eur J Nutr 40:135–146.
14. Sarkar FH, Li Y (2003) Soy isoflavones and cancer prevention. Cancer Invest 21:744–757.
15. Helferich WG, Andrade JE, Hogland MS (2008) Phytoestrogen and breast cancer: a complex story. Inflammopharmacology 16:219–226.
16. Choi EJ, Kim T, Lee MS (2007) Pro-apoptotic effect and cytotoxicity of genistein and genistin in human ovarian cancer SK-OV-3 cells. Life Sci 80:1403–1408.
17. Patel RP, Barnes S (2010) Isoflavones and PPAR signaling: a critical target in cardiovascular, metastatic, and metabolic disease. PPAR Res. doi:10.1155/2010/153252.
18. Si H, Liu D (2008) Genistein, a soy phytoestrogen, upregulates the expression of human endothelial nitric oxide synthase and lowers blood pressure in spontaneously hypertensive rats. J Nutr 138:297–304.
19. Alison M. Duncan Kerry E.W. Underhill Xia Xu June LaValleur William R. Phipps Mindy S. Kurzer. Modest Hormonal Effects of Soy Isoflavones in Postmenopausal Women. The Journal of Clinical Endocrinology & Metabolism, Volume 84, Issue 10, 1 October 1999, Pages 3479–3484.
20. Vincent A1, Fitzpatrick LA. Soy isoflavones: are they useful in menopause? Mayo Clin Proc. 2000 Nov;75(11):1174-84.