Continuing education

Phytoestrogens: Dietary sources and metabolism

Continuing education and the APD program

This quiz is an ideal activity for APD members to include in your CPD log, where it relates to personal learning goals. Record the time taken, to the nearest hour, to complete the quiz and any associated research.

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Introduction

The phytochemical family includes a diverse array of biologically active substances that occur in plant foods such as fruits, vegetables, legumes, cereals, nuts and seeds. Phytoestrogens are members of the phytochemical family with naturally occurring oestrogenic activity. Particularly high concentrations of phytoestrogens are found in soybeans. A notable feature of the distribution of phytoestrogens in foods is the wide variability in content within the same item. This reflects genetic variation, as well as the fact that unlike more stable structural components such as proteins, phytoestrogens are part of the plant’s natural response to stress and are synthesised in direct response to microbial or insect damage.

Phytoestrogens achieved notoriety in the 1940s in Western Australia when sheep fed large quantities of subterranean clover fodder developed a reproductive abnormality called clover disease, which resulted in substantial losses in productivity—phytoestrogens in the clover were subsequently identified as the bioactive factor responsible for the reproductive abnormality.1 In recent years, phytoestrogens have received increasing public attention in Australia and overseas regarding the possible health benefits of moderate quantities in the human diet.

The following quiz is designed to enhance your understanding of phytoestrogens from a nutritional science perspective. It will test your knowledge of basic concepts including the main types of phytoestrogens and major food sources, their absorption, metabolism, excretion and possible toxicity.

1. Besides soy, what are some of the identified food sources of isoflavonoid phytoestrogens?
   a. Broccoli, Brussels sprouts
   b. Rye, linseed
   c. Chickpeas, lentils
   d. Onions, leeks

2. What are some of the main phytoestrogens in the human diet?
   a. Daidzein, genistein, glycitein
   b. Formononetin, biochanin A
   c. Zearalanone
   d. All of the above

3. Which of the structures shown in Figure 1 is a phytoestrogen?

4. What are the distinguishing features of isoflavonoid metabolism?
   a. Hydrolysis of glycosidic conjugate to produce an aglycone form
   b. Structural transformation by colonic microflora
   c. Enterohepatic recycling
   d. All of the above

5. Equol:
   a. Is an isoflavonoid metabolite.
   b. Has a sweeter taste than other isoflavonoids.
   c. Is an isoflavonoid found in soybeans.
   d. Is not an isoflavonoid.

6. Which of the following factors has been shown to specifically affect bioavailability of phytoestrogens?
   a. Antibiotics
   b. Tannins
   c. Alcohol
   d. All of the above
7. What symptoms could arise from overconsumption of phytoestrogens?
   a. Dermatitis
   b. Anaemia
   c. Menstrual cycle irregularity
   d. Bowel irregularity

8. What is the recommended intake of phytoestrogens (mg/day)?
   a. 1
   b. 10
   c. 100
   d. There is no recommended intake

9. Binding of phytoestrogens to oestrogen receptors:
   a. Can result in both oestrogenic and anti-oestrogenic effects.
   b. Is dependent on circulating levels of endogenous oestrogens.
   c. Is tissue-specific.
   d. All of the above.

Answers

1. c.

The three classes of phytoestrogens of importance in the human diet are the isoflavonoids, lignans and coumestans. Isoflavonoids are widely distributed in the legume family, with concentrations approximately 50-fold higher in soybeans (37.3–131 mg/100 g) than other legumes such as chickpeas, peanuts and lentils; one striking exception is Kudzu root (Japanese arrowroot), in which isoflavonoid concentrations exceed those in the soybean (197 mg/100 g). Lignans are the basic monomer units for lignin, a polyphenolic constituent of dietary fibre. Therefore, they are found widely in plant foods in small amounts, including nuts, seeds, legumes, cereals, vegetables and fruits (0.01–0.9 mg/100 g). An analysis of 19 tea samples reported relatively high concentrations in tea infusions (up to 2.9 mg/100 g); uniquely high concentrations of lignans are reported in linseed (67–369 mg/100 g). Coumestans are found in highest amounts in sprouted beans, including alfalfa and clover, with only trace amounts in non-sprouted legumes.

2. a.

Soybeans and soy products provide the main sources of phytoestrogens in the human diet. Soy phytoestrogens belong to the isoflavonoid class and comprise mainly genistein (about 60%) and daidzein (30%), with smaller quantities of glycitein (10%); glycitein is found in relatively high concentrations in the hypocotyls of the soybean. Isoflavonoids are stable to heating and processing, but are lost with certain extraction procedures, for example, leaching with alcohol in the preparation of soy protein concentrates removes isoflavonoids into the extraction solvent, whereas the original isoflavonoids are retained with aqueous extraction procedures. Dehulling or defatting soybeans has little effect on concentrations because relatively small amounts are found in the outer hull and there are no isoflavonoids associated with the lipid moiety.

Formononetin and biochanin A are methylated precursors of daidzein and genistein, respectively, found in high concentrations in phytoestrogen supplements derived from red clover; only small amounts are found in foods. Zearalanone is a phytoestrogen derived from Fusarium moulds that flourish in warm moist conditions; it is found as a contaminant in poorly stored grains and other produce.

3. a.

Genistein (Figure 1a) is a plant oestrogen with a similar molecular weight and structure to the mammalian oestrogen, oestradiol (Figure 1d). The presence of a hydroxyl group (–OH) attached to the phenolic ring is a prerequisite for binding to oestrogen receptors, and the distance between the two opposing hydroxyl groups on the phenolic rings of the isoflavonoid is almost identical to the distance between the hydroxyl groups of oestradiol. These structural features permit binding to mammalian oestrogen receptors, but with lower affinity than oestradiol.

4. d.

In the original plant, isoflavonoids and lignans occur as conjugates to a range of sugars that renders them stable, water-soluble and inactive for storage in the plant. When consumed in the diet, conjugates are readily hydrolysed, mainly by bacterial β-glucosidases in the proximal colon, to the unconjugated (or aglycone) form that can be absorbed. Hydrolysis is essential for absorption.

A distinctive feature of dietary isoflavonoids and lignans is their capacity to undergo structural transformations, by colonic microflora in the proximal colon, to a range of hormone-like compounds. These compounds can be absorbed and have the ability to bind with low affinity to oestrogen receptors and exert weak oestrogenic activity. As the metabolites differ in their biological activity, individual differences in these transformations could have important consequences for potential health benefits.

After absorption, isoflavonoids and lignans are transported to liver where they are conjugated with glucuronic acid and sulfate by hepatic phase II enzymes. These conjugates can enter the systemic circulation and be finally excreted in urine; or be resecreted with bile, deconjugated once again and reabsorbed to undergo enterohepatic circulation. Unabsorbed conjugates are lost in faeces.

5. a.

The isoflavonoid daidzein can be transformed by colonic bacteria to at least three metabolites: dihydrodaidzein, O-desmethylangolensin (O-DMA) and equol. Interest has focused on equol as this metabolite has greater oestrogenic potency than either daidzein or O-DMA and, therefore, excretor status could have physiological implications. Equol excretion in women has been associated with a hormonal profile of reduced risk for breast cancer. However, only about one in three individuals are able to synthesise equol. It has been proposed that diet could facilitate equol synthesis by selectively modifying the growth of intestinal bacteria involved in the transformation, by influencing either intestinal pH or availability of substrates for the bacteria to utilise. However, results of studies are conflicting. Intervention studies with a soy protein beverage or textured soy protein have reported that the ability to excrete equol is associated with significantly more carbohydrate and dietary fibre, or less fat and more carbohydrate.
consumed in the habitual diet; whereas an observational study reported that equol excretors had a significantly lower intake of protein. 10

6. a.

The colonic microflora are essential for hydrolysis of the glucose moiety of the dietary phytoestrogens to produce the biologically available aglycone forms. Antibiotics reduce the activity of colonic microflora and thereby promote increased faecal losses of phytoestrogens; individuals without an intact colon also have low plasma and urinary lignan concentrations demonstrating the importance of the microflora in the bioavailability of phytoestrogens. 6 Data on antibiotics were collected from a nationwide prescription database and compared with serum concentrations of enterolactone, the major mammalian lignan derived from the colonic bacterial metabolism of the plant lignan, matairesinol. Concentrations of enterolactone were significantly lower in those who had used oral antimicrobials up to 12–16 months before serum sampling, than in non-users; the concentration was associated with the number of treatments and the time from the last treatment. 11 Whether taking antibiotics could lower the possible beneficial effects of phytoestrogens on risk of chronic diseases, remains to be investigated.

7. c.

Overconsumption of phytoestrogens could lead to menstrual cycle irregularity due to competition between the phytoestrogens and endogenous oestrogens for binding to oestrogen receptors. Reported effects in premenopausal women at doses of 45 mg/d have included lengthening of the menstrual cycle, specifically the preovulatory follicular phase, and suppression of the normal midcycle surge in luteinizing and follicle stimulating hormone in premenopausal women. 12 Infertility has resulted in sheep after high consumption of leguminous fodder. These effects have been seen with phytoestrogen intakes of about 1–9 g/day and are unlikely to arise by incorporating soy items within a variety of plant foods—but could possibly be attained by sustained high intake of concentrated phytoestrogen supplements.

8. d.

There is no recommended intake because there is no specific deficiency disease associated with a lack of isoflavone intake; nor is it possible to ascribe a specific role to any particular isoflavonoid in maintaining optimal health. Estimates of average isoflavone intakes in communities consuming traditional soy staples have been between 11 and 54 mg isoflavones per day. 13,14 These values have been used as a guide to optimal intake by virtue of the association between higher isoflavone intakes and the observed lower rates of degenerative diseases such as hormone sensitive cancers and coronary heart disease in these communities. They can be achieved by regular consumption of one or two serves of soy foods on a daily basis. This recommendation must be made in the context of the dietary guidelines for Australians to ensure that increasing soy intake does not reduce exposure to a large variety of plant foods that provide an array of protective nutrients and phytochemicals. 15

9. d.

One of the defining characteristics of phytoestrogens is their ability to bind with low affinity to oestrogen receptors and exert weakly oestrogenic effects. Where concentrations of endogenous oestrogens are relatively high, as in premenopausal women, they can exclude the more potent oestrogen from binding to the receptor and, therefore, the overall effect is anti-oestrogenic. The presence of two types of oestrogen receptors, the classic ERα and the more recently discovered ERβ, is of special relevance to the mechanism of action of phytoestrogens. Some phytoestrogens bind to ERβ with higher affinity than to ERα. The proportion of ERα to ERβ varies between different body tissues, for example the uterus and breast have more ERα receptors whereas the blood vessels, bone, urinary tract and brain have higher proportions of ERβ. 16 An implication of these findings is that dietary phytoestrogens could demonstrate tissue-specific effects, according to the proportion of ERα or ERβ present, with greater oestrogenic potency in the ERβ-expressing tissues.

Binding to oestrogen receptors provides a potential mechanism to explain influences of phytoestrogens in prevention of hormone-related diseases. However, phytoestrogens exhibit other biological effects unrelated to their oestrogenic activity, which could also protect against chronic diseases. These include a range of anti-oxidant activities to inhibit free radical-mediated cytotoxicity and lipid peroxidation, and antiproliferative activities to inhibit tumour growth.

References


