Sveriges lantbruksuniversitet
Swedish University of Agricultural Sciences

Faculty of Natural Resources and Agricultural Sciences
Department of Food Science

Isoflavone sources and bioavailability

– Biological effects of phytoestrogens in the diet

Isoflavonkällor och biotillgänglighet

– Biologiska effekter av fytoöstrogener i mat

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Abstract

Over the last couple of decades non-nutritional bioactive compounds from plants and their biological effects have received attention. Phytoestrogens, also called "plant estrogens", with their similar structure to estradiol, act with estrogenic effects when imbibed. The compounds that have received considerable interest are, among others, the Isoflavones, of which significant quantities can be found in most members of the family Leguminosae (*Fabaceae)*. Soy, a member of the leguminosae, is the main nutritional source to these phytoestrogenic isoflavones. Isoflavones are commonly consumed in East Asia but less so in the western world. It is highly suggested that the health effects of isoflavones are dependent on the consumer's ability to digest the substances. This article reviews these estrogen active, polyphenolic compounds present in soy- and bovine milk for the comparison of isoflavone content, bioavailability, and isoflavone related health effects. The mechanisms are also reviewed. This is done for understanding the eventual importance of these phytoestrogens as a part of the diet, and why variation of sources may be of interest for parts of the population. Preliminary study shows phytoestrogen having a largely positive health effect. But only approximately 30-50% of the population are so called "equol-producers" and for the other half soy may not be an optimal isoflavone source and instead bovine milk may serve as an alternative and/or additional dietary source, as isoflavone metabolites have been traced in cow's milk.

Keywords: Phytoestrogens; isoflavones; legumes; soy; milk; equol; daidzein; genistein; formononentin; biochanin A; content; hormone induced cancer; cardiovascular disease

Sammanfattning

De senaste decennierna har det funnits ett ökat intresse för växters bioaktiva ämnen och biologiska effekt. Fytoöstrogen, eller ”växtöstrogen”, med liknande struktur som östradiol, verkar med likhet på kroppen som dess eget östrogen vid konsumtion. De kemiska föreningarna som det har intresserats mest för har bland annat varit isoflavonerna, vilka höga koncentrationer går att finna i växter från familjen Fabaceae. Soja är medlem i familjen och fungerar också som, för människan, den största nutritionella källan. Isoflavoner konsumeras i högre grad i Ostasien, jämfört med västvärlden. Det har föreslagits att isoflavonernas hälsoeffekter är i stark relation till konsumentens förmåga att bryta ner dessa ämnen till deras metaboliter, bland annat equol som har stark likhet med östradiol. Denna artikel sammanfattar dessa östrogenaktiva polyfenolers förekomst, hälsoeffekt och biotillgänglighet i soja- och komjölk. Mekanismer granskas också. Detta är gjort för att öka förståelsen kring varför det kan vara nödvändigt med fytoöstrogener i dieten och varför det eventuellt skulle vara viktigt med varierande källor till dessa. Vid en preliminär granskning verkar isoflavoners hälsoeffekter överlag vara positiva. Bara ca 30-50% av befolkningen kan producera equol från de isoflavoner som finns i soja, för den andra delen kanske soja trots allt inte är den optimala källan till isoflavoner utan istället kan kanske komjölk vara en alternativ källa. Detta då man har kunnat hitta nivåer av dessa isoflavonmetaboliter i mjölk.

Abbreviations

IF, isoflavone

IFA, isoflavone aglycone

IFG, isoflavone glucosides

ERα, estrogen receptor alpha

ERβ, estrogen receptor beta

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1 Introduction

1.1 Background

The soybean originates from China and has been a central part of the traditional East Asian diet. Hormone induced cancers such as colon cancer, breast cancer, prostate cancer, along with cardiovascular diseases and menopausal symptoms have historically been recorded to be fewer in East Asian populations compared to those in the western world (Adlercreutz et., al, 1997). Hence the association of soy being a health food might be possible. The health aspects may be many, likewise the reasons for consumption, such as the bean containing a large amount of unsaturated fatty acids including the essential fatty acid alpha-linolenic acid (He et., al, 2013). Soy also contains significant amounts of all the essential amino acids (Hoffman, 2004). Though more recently interest has fallen on other bioactive compounds, such as those with hormonal activity. One such group of compounds is called phytoestrogens. These "plant-hormones" exist in most plants in different variations, and work as part of the plants own defense mechanism. The most common phytoestrogens are isoflavones (IFs) (Lundh, 1990), a group of compounds that are mostly found in leguminous plants in the Asian diets and less so in the foods of the western world. Though milk based on the legume soy is becoming more popular in the western world as a substitute for its animal counterparts. Despite Euro-American/Asian differences in isoflavone consumption, high levels of these phytoestrogens can be found in animal feed all around the world. The effect of silage type on the IF content in milk may therefore be interesting. The content of IF in milk may even be important when the benefits of milk are discussed (Steinshamn et al., 2008). IFs are found in high concentrations in forage legumes, with high values reached in different types of clover, commonly used as silage. As legumes are nitrogen fixating through bacterial symbiosis they have become a popular organic alternative for nitrogen-binding in soil, as to compared to synthetic fertilizers. The interest for forage legumes as animal feed has therefore increased (Santos-Buelga et al., 2011).

1.2 Aim

The aim of this report was to compare the content, bioavailability and health effects of IFs in soymilk and cow's milk in order to more generally illustrate the health effects and availability of IFs in human nutrition.

1.3 Methods

This is a theoretical report based on information gathered from published scientific articles. There are many published articles regarding soy IFs and their concentrations in soy products, consumption and health benefits. Problematic areas during this work have been that, despite some research on the IF effect on animals, there has only recently been an interest in the IF content in animal products consumed by humans. The literature is therefore limited. Also research on the digestion of IF and mapping of the mechanism of action in the body is also lacking, possibly due to the supposedly wide spread action of the components. The United States Department of Agriculture (USDA), provides the most accessible on-line database for the IF content in different foodstuff.

2 Phytoestrogen and isoflavone characteristics

2.1 Phytoestrogens

Phytoestrogens are a group of naturally occurring, plant-derived compounds that have been shown to have estrogenic properties, binding to the estrogen receptors (ER) and modulating gene expression. They can be divided into three main classes: isoflavones (IFs), coumestans and lignans (Kurzer et. Al., 1997). Although all being non-steroidal they share remarkable resemblance in molecular structures and activity with mammalian estrogens, synthetic estrogens and anti-estrogens and can therefore bind to ERs (Duncan et al., 2003).

Phytoestrogens are found in most plant material, such as berries, grains, nuts and fruits (Patisaul, 2010). Coumestans have been found in many important types of forage, while the IFs are known to be present in red- and subterranean clover (Guggolz, 1961). In the plants they work as an antimicrobial defense to combat pathogens and in legumes the IFs are involved in the nitrogen-fixating abilities, by stimulating the soil-microbe rhizobium to form nitrogen-fixing root nodules (Subramanian et al., 2006). There are many peer-reviewed publications discussing the relationships between health impacts and phytoestrogen consumption and digestion, and the strongest relations have been seen in high IF consuming populations (Bakker, 2004).

2.2 Isoflavones

Isoflavones and their derivatives are similar to 17-beta estradiol both in structure and function (Kleijn et al., 2002). See Figure 1 for a schematic description of the different IFs. They are a group of secondary plant metabolites belonging to the isoflavonoids, which in turn is a subgroup of the flavonoids.

The IF sources are generally more limited as to those of other phytoestrogens, as they are more abundant in plants belonging to the Fabacae family (Patisaul, 2010). Soy is for humans essentially the only relevant nutritional source of IF's compounds. There are however other high content IF sources, although these are not foodstuff for humans, but are rather forage legumes widely used as cattle feed, such as red clover (Messina et al., 2006).

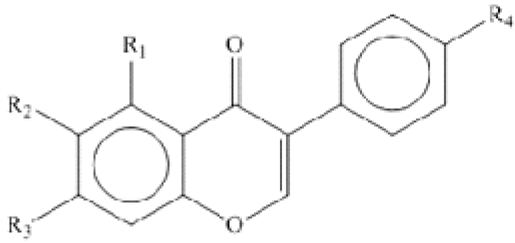
2.3 Chemical structure of the isoflavones in soy and clover

There are three main IFs in soy; genistein (4',5,7-trihydroxyisoflavone), daidzein (4',7-dihydroxyisoflavone), and glycitein (4',7-dihydroxy-6-methoxyisoflavone), (Figure 1)(Kurzer, 1997). They can be found in different conjugated forms depending on conditions, e.g. digestion, product handling and processing. The forms of the IFs in soy are the more biologically active aglycones (IFA) (genistein, daidzein and glycitein), and the non-active 7-*O*-glucosides (IFG) (genistin, daidzin and glycitin) (Heinonen et al., 1999). The IFGs in soy and other plants are conjugated mainly with glucose, and 6"-*O*-malonyl or 6"-*O*-acetylglucose.

Soy and clover have different IF profiles. The commonest IFs in clover are the less estrogenic precursors and 4'-methyl ethers of daidzein and genistein; biochanin A (5,7-dihydroxy-4'methoxyisoflavone) and formononetin (7-hydroxy-4'-methoxyisoflavone), respectively (Kurzer, 1997; Heinonen, 1999). IFAs described above have similar biological activities, though at different degree, of which daidzein can be converted into a highly active metabolite (Jia, 2004).

2.4 Isoflavone metabolites

By the colonic microflora genistein may be metabolized primarily into *p*-ethyl phenyl and daidzein to equol (4',7-dihydroxyisoflavan) and/or to O-desmethylangolensin (O-DMA), *p*-ethylphenol being non-estrogenic (Tham et al., 1998). Equol is the phytoestrogen of special interest, as it is similar in structure to estradiol, (Figure 2), and is suggested to have, among other positive health effects, strong cancer preventative effects (Setchell, 2006). With its chiral center positioned at C-3, equol is a molecule that exists as the enantiomers *R*-equol and *S*-equol, where *S*-equol has high affinity to the estrogen receptor β (ER- β), therefore having a strong estrogenic effect on the organisms (Setchell, 2005). It is this molecule´s ability to exist in two enantiomer forms that distinguishes it from the other IFs mentioned. Other IF metabolites do however exist, but with less activity than equol (Heinonen et al., 1999).



Compounds	R1	R2	R3	R4
Genistein	OH	H	OH	OH
Daidzein	H	H	OH	OH
Glycitein	H	OCH_3	OH	OH
Genistin	OH	H	O-glucoside	OH
Daidzin	H	H	O-glucoside	OH
Glycitin	H	OCH_3	O-glucoside	OH
Biochanin A	OH	H	OH	OCH_3
Formonoetin	H	H	OH	OCH_3

Figure 1. Chemical structure of isoflavones, as aglycones, glucosides, and the precursors of the aglycones genistein and daidzein; biochanin A and formonoetin, respectively.

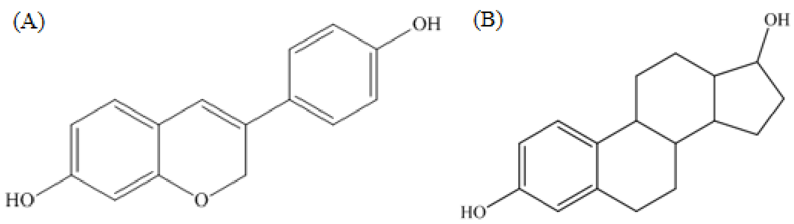


Figure 2.Chemical structure of (A) equol and (B) estradiol.

3 Absorption, metabolism and mechanism of action

3.1 Absorption and metabolism

The metabolism of the IFs is primarily carried out by intestinal bacteria. There has been no observation of absorption by the epithelium of the intact IFGs, as they have higher molecular weight and hydrophilicity than their aglycones (Hendrich, 2002; Yuan et al., 2007). When ingested, the inactive IFGs are exposed to acidic and enzymatic hydrolysis by glycosidases in the small intestine (Figure 3)(Heinonen et al., 1999). The IFAs may be metabolized further through demethylation and reduction by gut bacteria.

Biochanin A can be demethylated in the liver to genistein that may continue tometabolize in the intestine to *p*- ethylphenol and other organic acids, e.g. acetic and melonic acids, by ring cleavage (Pfitscher et al., 2008). Formononetin is mainly demethylated to daidzein, which may subsequently be converted through reduction to become equol in the intestine. An alternative path that does not include the demethylation, involves reduction and ring fission to O-DMA. Other pathways may exist.

The IFAs and metabolites formed are then excreted via the urine or absorbed in the intestine and transported in the blood plasma (Heinonen et al., 1999). A small part of the aglycones enters the enetrohepatic circulation. In the liver they go through hydroxylation and conjugation to other more hydrophilic metabolites that can be secreted via the urine.

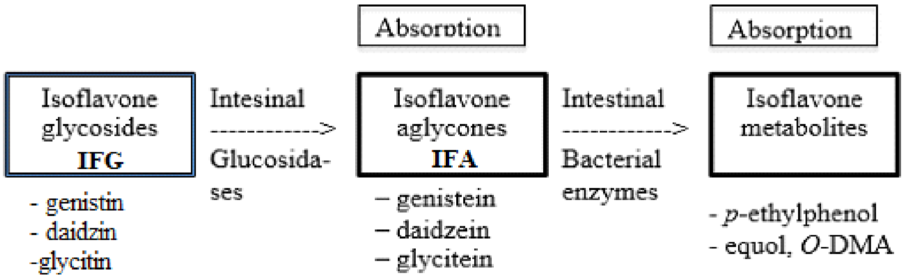


Figure 3. Schematic description of the metabolism and absorption of the IFAs and IFGs. O-DMA= 0-desmethylangolensin.

Since the metabolism of the IFs varies there is a limitation when quantifying the content in urine and/or plasma as a determination of soy ingestion (Hendrich, 2002). Individuals that can metabolize IFs into equol are referred to as “equol producers”. The extent of the metabolic capacity varies among individuals as only about 30-50% of the total human population has the bacteria able to metabolize equol. Other mammals have not shown the same variety as humans in the ability to produce equol. This variation among the populations is believed to depend on multiple factors such as the bacterial composition in the intestinal tract, pH and redox potential in the small- and large intestine (Tärnvik, 2001). Antibiotic treatments have been recorded to eliminate equol production in individuals and germfree animals do not excrete the IF metabolites (Wiseman et al., 2004)

The nature of the diet influences the microflora diversity and their activity on metabolizing the IFs. It has ben suggested that a high total intake of dietary lipids may decrease the capacity to synthesize equol by the microbial flora (Rowland, 1999). The relationship between IFs and food matrix has however not been studied in any greater extent (Hendrich, 2002).

3.2 Mechanisms of action

Genistein is the most studied phytoestrogen, as it is also the most biological active one (Tärnvik et al., 2001). To what extent the IFs can provide health effects depend on absorption, metabolism, cellular distribution and bioavailability (Hendrich, 2002). The metabolites have gained lots of interest as it is strongly suggested that those who are equol producers may have particular or extensive benefit from soy (Heinonen, 2003). The health effects are caused by different mechanisms of which can be described as those binding to ERs causing estrogenic or antiestrogenic effects, and those inhibit enzyme activity affecting production of hormones or hormone binding protein (Tärnivik et al., 2001). But there are also effects that are not hormone related, such as being antioxidants.

When studying the health effects of phytoestrogens, the ligands ability to antagonize the growth- promoting action of 17β- estradiol has received interest (Matsumura et,al., 2005). Genistein has at low concentrations been observed to enhance cell growth through ER, whilst at high concentrations (>10uM) cell growth is inhibited. IFs are generally weaker compared to the endogenous estrogen, but may be found in plasma concentrations 100-fold higher (Tham et al., 1998). The competition that arises between the phytoestrogens and the endogeneous estrogen for the ER may explain the antiestrogenic activity. This activity is a common behavior for many weak estrogens, and means that they bind to block estrogen activity that may cause hormone related diseases. IFs bind to ERβ and ERα with a diverse affinity compared to the endogenous estrogens that generally show no difference to affinity (Tärnvik et al., 2001). This could mean a targeting effect on body tissue with higher proportion ERβ such as bone and thymus in female, and prostate and vascular in male.

Evidence supports that the IFs metabolites act with greater effect than those of their parent compounds (Rowland, 1999). Equol has been found to be three times as estrogenic in an endometrial tumor line as its parental compound daidzein. Also, equol decreased the estrogen-responsive *pS2* gene expression in MCF7 (a breast cancer cell line), daidzein did not show this activity. The *S*-equol enantiomer selectively binds to the ERβ with ca20% as much affinity as 17β- estradiol (Setchell et al., 2005). Equol is unique as it has selective estrogen action while also having the ability to be an antagonist of androgen action. The mechanisms are however not fully understood. The degree of effect and biological behavior by the IFs consumed has been shown to depend on the consumption amount and the individual's levels of endogenous estrogen (Setchell, 1999). Equol is also a more potent antioxidant compared to daidzein.

Further studies upon the mechanism of action are necessary in order to pin point the exact activity providing the eventual health effects caused by the discussed Isoflavones, as there is some confusion within the discussion of the subject (Matsmura, 2005).

4 Occurrence of isoflavones and their metabolites in soymilk

4.1 Isoflavone content in soybean

As mentioned, the IFs come in different chemical forms, but the IFs in soy occur primarily as β-glucosides in non-fermented soy foods. Only 2% occur as the biologically active aglycones. The distribution of IFs in soy is 50% genistein, 40% daidzein and 10% glycitein (Messina, 2010).

According to USDA (U.S Department of Agriculture) the genistein, daidzein and glycitein content in unprocessed mature soybeans is 81 mg/100g, 62 mg/100g and 15 mg/100g edible portion, respectively (USDA Database for the Isoflavone Content of Selected Foods, 2008). The data presented by USDA is collected from articles published in referred journals since 1999 containing analytic data for IFs in food. All data presented is converted to represent values for the biologically active IFAs. Mazur (1998) presents phytoestrogen levels in plant-derived foods given from a method using isotope dilution gas chromatography- mass spectrometry (ID-GC-MS-SIM), recognizing this method for being more specific when quantifying small concentrations of phytoestrogens compared to the commonly used high-performance liquid chromatography (HPLC) (Mazur, 1998).

IF concentrations in soy beans as well as in the soy end product will vary depending on several factors, such as location, daylight, stress and conditions of harvest as well as storage and product handling. In any plant material the IF content will vary depending on several factors. As Seguin et al. (2004) suggests; environmental factors do have great impact on IFs concentrations in soybean seeds (Seguin et al., 2004).

4.2 Occurrence in soymilk

The IFGs generally remain unmodified during food processing (Heinonen et al., 2003). Most IFs consumed in non-fermented soy foods, such as soymilk, are therefore not in the biologically active aglycone form.

The genistein, daidzein and glycitein content in soymilk (low fat, with added calcium, vitamins A and D) are 1.51 mg/100g, 1.01 mg/100g, 0.4 mg/100g edible portion respectively, reaching a total content of 2.56 mg IFs/100g. Nonfat soymilk contains less, with a total of 0.7mg IFs/100g (USDA Database for the Isoflavone Content of Selected Foods, 2008).

5 Occurrence of isoflavones and their metabolites in cow's milk

5.1 Occurrence in animal feed

Most crops that are commonly used in large amounts as animal feed contain relatively high amounts of IFs (Lundh, 1990). The pasture forage legumes containing large amounts of IF are subterranean clover (*Trifolium subterraneum*), red clover (*Trifolium pratense*), soybean (*Glycine max*), and field bean (*Vicia faba*). In red clover the IF content is 0.5-2.5% of the dry matter. In green subterranean clover the content can be as much as 5% of the dry matter. The most common IFs in animal feed are formonoetin and biochanin A, followed by daidzein, genistein, glycitein, all mainly occurring as water-soluble glycoside conjugates. An increased interest for nitrogen-fixating crops within the organic agriculture has resulted in the increased IF content in the animal feed.

5.2 Occurrence in cow milk

According to USDA there is no formononetin present in milk with 2% fat. The same finding is documented for the other IFs (USDA Database for the Isoflavone Content of Selected Foods, 2008).

The phytoestrogens consumed by cattle are highly metabolized in the rumen (Steinshamn et al., 2008). IFs metabolites may therefore be present in the milk (Mustonen et al., 2009). The bovine's digestion of IFs allows for equol production. The concentration varies greatly, and as a result of the feed fed to organically raised cows there may be higher concentration of the IF metabolites in organic milk compared to non-organic.

The equol content has been measured to be 600-700µg/L in milk produced by cows given red clover silage feeding. These levels can be manipulated by harvest and feeding strategy. Biochanin A and formononetin are not found in any significant amount in soy. They are the main IFs in some clover, especially in clover grown in nitrogen poor soil. Depending on the conditions genistein is known to stimulate nitrogen-fixing bacteria (Bingham et, al., 1997).

In Finland, Hoikkala et al. (2007) quantified the equol concentration commercial skimmed Finnish milk and found concentration levels to be ca six times larger in organic milk compared to conventionally produced milk (411µg/L and 62µg/L, respectively) (Hoikkala et al., 2007). The higher content probably a result of higher legume content in the leys. Biochanin A and formonoetin were traced in the organic milk samples.

5.3 Effects on the animal

Phytoestrogens and their estrogenic activities were recognized first in the 1940's when an outbreak in Australia occurred with infertility in ewes grazing on subterranean clover. It has been suggested that cattle are less sensitive to plant estrogens as they have not been recorded to show symptoms in the same degree as those seen in sheep (Lundh, 1990). This probably depends on the differences in metabolism and the degradation and conjugation rates affecting the sensitivity of the animal. The IF effect on cattle are of interest and should be taken into consideration when evaluating the effect of feed and harvest strategies.

6 Dietary intakes of phytoestrogens and isoflavones

Dietary intakes of phytoestrogens vary among populations. China and Japan have been known to have a higher intake of IFs (Setchell, 2006). The ability to produce equol has also ben seen to vary among the populations.

Consumers with traditional East Asian diets have the highest intake phytoestrogens, of which the majority is IFs (ca25-100mg/d), compared to those consuming traditional west diets (Bakker, 2004). Ca 50-55% of adults in Asian countries produces *S*-equol (Setchell, 2006). A diet that provides such high levels phytoestrogens causes plasma levels much higher than the endogenous estrogen (Tärnvik et al., 2001).

In standard Western diets, phytoestrogen content as a total is low. The IF intake of the average Western consumer is therefore also low (ca1-2mg/d) (Bakker, 2004). Only ca20-35% of Western adults produces *S*-equol from soy food or IFs supplements (Setchell, 2006). However, vegans in Western countries have a relatively high IF intake (ca75mg/d) (Bakker, 2004). Vegetarians in the same regions have higher frequencies of equol producers, ca 59% (Setchell, 2006). Consumers taking dietary phytoestrogen containing supplements are also recorded to have a higher IF intake.

In Scandinavia the total intake of phytoestrogens is relatively low, just a few hundred µg/day of which the majority is lignans from cereal, fruit, berries and vegetables (tärnvik, 2001).

7 Effects on human health

Prevalent western diseases such as hormone induced cancers, cardiovascular diseases and osteoporosis, and menopausal symptoms have been documented to be fewer in groups who consume more high IF content foods (Coward et al., 1993). Epidemiological studies regarding the associations between IF consumption and health benefits have however, despite many supportive studies, not ben consistently positive. Ingested IFs have been linked to beneficial effects regarding cell growth, and there are many studies presenting positive effects with animal as test objects.

7.1 Cancer

Isoflavones have been suggested to decrease the risk of hormone induced cancers such as breast cancer and colon cancer.

7.1.1 Breast cancer

In western populations, breast cancer is the most common cancer in woman (Bingham et, al., 1997). Estrogen levels and breast cancer risk has ben strongly associated with each other, levels that will vary depending estrogen activity related to ovarian function. Short menstrual cycles, elevated age of first pregnancy- and menopause are factors that determine an increased risk. These factors do vary between women in east- and western populations (Tärnvik et al., 2001). Women in Asia have even been recorded to have 20-30% lower plasma concentrations of the endogenous estrogens.

There are epidemiological observations that show a significant lower risk of breast cancer in women from Asian populations compared to women in Western populations (Adlercreutz and Mazur, 1997). Focused observational studies have shown an inversed relationship between soy IFs consumption and breast cancer risk. Further support is the observation that after adaption of western diets in Asian woman who emigrated to the U.S.A the lower breast cancer risk is lost. Indicating that the differences between the populations are about environmental- rather than genetic factors (Tham et al., 1998). Other support is that vegetarians, who in general consume more soy products and less animal products, also have a lower risk of gaining breast cancer (Duncan et al., 2003).

7.1.2 Colon and prostate cancer

Like breast cancer, colon and prostate cancer is also less frequent in men from Asian populations compared to those in western countries. High intake of IFs is proven by the higher concentration found in biological fluids of Asian men compared to European and western counterparts (Duncan et al., 2003).

7.2 Cardiovascular disease

There are many risk factors for development of cardiovascular disease, and hormonal status is one that is known (Bakker 2004). Many studies have ben able to show a relationship between IF consumption and low risk of cardiovascular disease (Tham et al., 1998). Consumption of soy may lower cholesterol levels, but if the IFs are responsible for this is still unclear (Bakker, 2004).

8 Discussion

The aim of this article was to review the most common isoflavones and metabolites. Since we have seen that these substances vary amongst themselves in metabolic fates and nutritional sources it is relevant to observe closer the consumer patterns of these phytochemicals. Research on soybean and soy foodstuffs is extensive due to their high IF content. That IFs have the ability to generate effects on the host post ingestion seems to be out of discussion. However there are many contradictory results wheatear these are negative or positive, and to which extent. Given that the consumption levels vary to be high in the east and the fact that hormone related conditions are low in the populations, it is important to discuss the bioavailability and content in different foodstuffs.

Evaluation of the IF's health effects is complex and observation studies can be difficult, as it is not only the consumed IFs contents that differ between the populations, but entire diets. Further research is needed to evaluate the absolute effects of these compounds as well as the attributes of the individuals who would perhaps benefit from these. Many, if not most, studies discuss the positive health effects generated from IFs and their metabolites. There are many discussing the positive health effects regarding prevention of hormone induced cancers, such as breast cancer and prostate cancer, also other hormone related diseases and conditions such as cardiovascular diseases, osteoporosis, and menopausal difficulties. The studies that present negative health effects should also be investigated further.

When analyzing the effects of a single component in a foodstuff it is important to consider its complexity and that other factors may be responsible for any positive or negative health effect.

Since much interest has fallen on the metabolites for their activity it seems only reasonable that sources for these are discussed. Bovine milk could be a source for eqoul for non-equol producers. Other foodstuff of animal origin could also be discussed as a potential source of IF metabolites.

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