OPEN 6

brought to you by **CORE**

check

ACCESS Potravinarstvo[®] Scientific Journal for Food Industry



Potravinarstvo, vol. 9, 2015, no. 1, p. 573-579 doi:10.5219/572 Received: 30 November 2015. Accepted: 15 December 2015. Available online: 17 December 2015 at www.potravinarstvo.com © 2015 Potravinarstvo. All rights reserved. ISSN 1337-0960 (online) License: CC BY 3.0

PHYTOESTROGENS DIETARY INTAKE AND HEALTH STATUS OF RETIREE FROM MIDDLE-NORTH SLOVAKIA REGION

Jozef Čurlej, Radoslav Židek, Ľubomír Belej, Peter Zajác, Jozef Čapla

ABSTRACT

Phytoestrogens found in foods of plant origin presents chemical substances that possess a wide range of biochemical benefits. It has been found that they contribute in different health related problems. A wide range of commonly consumed foods contain appreciable amounts of phytoestrogens. Consumption of diet rich to phytoestrogen acts as a protective factor against many diseases such as cardiovascular diseases, post-menopausal symptoms in the context of osteoporosis, cancerous illnesses of colon, prostate and breast. Three main classes of phytoestrogens covers: isoflavones, lignans and coumestans. Selected nine major phytoestrogens had been analyzed simultaneously in the same foods. Questionnaire designed to determine intake frequency as well as amount of selected foods and the most common diseases presented in the population has been realized in cooperation with 140 respondents in retired age (divided into Males – covered by 34 individuals and Females – 106 individuals), comming from middle-north Slovakia region. On the base of collected data it can be concluded, that evaluated population is presented by high values of lignans intake and particularly secoisolariciresinol, mainly caused by relative high proportion of cereals and linseed in the diet. Furthermore, the relationship between phytoestrogens intake and eating habits as well as its contribution in protection against selected diseases was demonstrated.

Keywords: phytoestrogen, nutrition, intake, health

INTRODUCTION

Phytoestrogens presents photochemical substances that are found in foods of plant origin and possess a wide range of biochemical and health benefits. The interest in plant derived estrogens or phytoestrogens has recently been increased by the realization that hormone replacement therapy is not as safe or effective as previously thought (Hays et al., 2003). A wide range of commonly consumed foods contain appreciable amounts of phytoestrogens. Three main classes of phytoestrogens covers: isoflavones, and coumestans. Phytoestrogens lignans exhibits oestrogenic and antioestrogenic effect due to their similarity in structure to oestrogen (Tham et al., 1998; Zava and Duwe, 1997). The antiestrogenic activity of phytoestrogens may be partially explained by their competition with endogenous 17 β-estradiol for estrogen receptors (Martinex-Campos et al., 1986; Martin et al., 1978). One of the most important representantives are isoflavones, natural non-steroidal molecules of similar structure to 17- β oestradiol and selective oestrogen receptor modulators (Yildiz et al., 2005). Isoflavones contains phenolic ring which is essential for binding to oestrogen receptor. According to this, they have lower affinity for serum protein and better bioavailability at receptor site (Mishra, Mishra, and Devanshi 2011). Epidemiological studies have revealed that average intake of isoflavones in Japanese population is about 50 mg.day⁻¹ (Messina, 1995); rest of Asia has an average consumption

of 25 to 45 mg.day⁻¹; while the western consumption is less than 5 mg.day⁻¹ (Coward et al., 1961). Consumption of phytogen rich diet as seen in traditional Asiatic societies is protective against many diseases (Mishra et al., 2011). Phytoestrogens consist of more then 20 compounds, important sources of isoflavones are soy beans, they present the richest source of isoflavones and contains highest concentration of isoflavones, up to 300 mg per 100 mg. Common isoflavone fractions present in soya are genistein (4', 5, 7-trihydroxy-isoflavon) which constitutes 50% of soya isoflavone, diadzein (4', 7- dihydroxy with their betaglycosides isoflavone) 40% along - genistein, diadzein; and glycetein (7, 4'- dihydro-6methoxyisoflavone) remaining 5 to 10%. Wheat, Bengal gram, moong beans, chick peas, cherries, parsley, apples, alfalfa and red clover are other sources of isoflavones. Lignans: are found in oil seeds such as flax seeds (linseed), rye, millet, sesame and sunflower seeds besides legumes, pulses, and whole grains. Sunflower seeds, alfalfa and clover are rich sources besides bean sprouts of coumestans. Soya sprout is a potent source of coumestans (Murkies et al., 1998; Tham et al., 1998). According to a number of epidemiological and clinical studies in this area, phytoestrogens have been generally accepted to have a beneficial, rather than a deleterious effect in humans. Potential health benefits of phytoestrogens may be attributable to metabolic properties that do not involve estrogen receptors, such as influence on enzymes, protein

synthesis, cell proliferation, angiogenesis, calcium transport, Na+/K+ adenosine triphosphatase, growth factor action, vascular smooth muscle cells, lipid oxidation, and cell differentiation (Adlercreutz and Mazur, 1997; Knight and Eden, 1996). Much of the research on the health effects of soyfoods has focused on postmenopausal women. In large part, this is because the soybean is such a rich source of isoflavones, a group of naturally-occurring plant chemicals that possess estrogen-like properties (Franke et al., 1998). As a result, some men are reluctant to eat soyfoods because of the mistaken belief that isoflavones exert feminizing effects. However, not only is this concern without scientific merit, but there is a large amount of evidence suggesting adding soyfoods to the diet can greatly benefit men by reducing the risk of prostate cancer and heart disease. There is also very preliminary evidence that consuming soyfoods might protect against male pattern baldness (Lai et al., 2013). However, it is difficult to recommend specific amounts of dietary phytoestrogen to prevent specific chronic diseases (Tham et al., 1998). Several recent animal studies indicate either teratogenic or protective effects of phytoestrogens with respect to fetal development (Zhao et al., 2010; Xing et al., 2010; Jefferson et al., 2009). Estimating dietary intake of phytoestrogens has been a challenge for various studies. Improvements in analytic techniques (Kuhnle et al., 2007) and published data provided an opportunity to improve estimation of dietary phytoestrogen intake.

The objective of our study was to estimate intake of the phytoestrogens, such as: lignans, isoflavones, coumestans and specific compounds within selected group of retiree from middle-north Slovakia region.

MATERIAL AND METHODOLOGY

Questionaire

A package of 60 questions has been carefully prepared and developed on the basis of literature previously published in scientific journal (**Thompson et al., 2006**). The major questions covers: age; sex; dietary habits (focused to selected foods which are marked as the most common phytoestrogens sources) and health status represented by three major diseases such as cardiovascular disease, cancer and diabetes. A daily intake of selected foods was calculated on the basis of comparison of estimated dose provided by respodents and pattern of the food size published in the literature (**FHCRC, 2015**). A total number of respondents (140) is presented by 34 males and 104 females.

Analysis

Answers according to mentioned questions have revealed several important things. A part devoted to nutrition was processed to detailed list containing daily dosage of selected foods according to which overall daily intake (the values expressed in mg.day⁻¹) of phytoestrogens as well as individual substances (isoflavones: genistein, daidzein, glycitein, formononetin; lignans: secoisolariciresinol, matairesinol, pinoresinol, lariciresinol; coumestan: coumestrol) was calculated individually on the base of age and sex. In this respect, as valuable source of information used to calculate values was published scientific literature. Other importat section of the questionairy was focused to health status of respondents, where the occurence of selected diseases was expressed in percentage.

RESULTS AND DISCUSSION

Daily intake of selected nine substances (formononetin, daidzein, genistein, glycitein, matairesinol, lariciresinol, pinoresinol, secoisolariciresinol, coumestrol) belongs to phytoestrogens family had been calculated according to data collected from dietary questionnaire, realised on 140 (divided into Males - covered by 34 individuals and Females - 106 individuals) respondents retired, comming from middle-north Slovakia region. Questionnaire was designed to determine intake frequency as well as amount of selected food, fruits and vegetables and presence of the most common diseases found in population of higher age. According to findings rising from the measured data presented by Table 1 - 4, Secoisolariciresinol has been intended as phytoestrogen compound represented by the highest value irrespective to age range and sex (Table 1). On the other hand, coursestrol was presented by the lowest counts for all age ranges and sex. Integrated part of this population study was screening, focused to evaluation of food, vegetables and fruits intake, those which are reach to phytoestrogens and are typical for local market. Respondents of male sex in the age range 50 - 60 declared high consumption of cereals, this intake considerably falls down with increase of the age (Table 2). According this cereals presents the main proportion fact. of phytoestrogens source for men of the age between 50 and 60 years old. Dietary sources generally marked as others/snacks are considered as other significant part for men of the age between 61 - 70. Partially similar trend was recorded for female respondents of selected years groups, where the high intake of others/snacks brings a high values of phytoestrogen intake as described in the Table 2, except females of the age over 80. As the group marked as others/snacks presents an important dietary source for evaluated individuals from 50 to 80 years old, especially for women, detailed list of evaluated products is posted in the table 3, as well as calculated proportion of these sources on daily intake of phytoestrogens. Sesame seeds present the most important phytoestrogens sources for respondents of male sex except those, who are 61 - 70years old. In that case, linseed was found as major phytoestrogen source. For female significant high intake of linseed brings high values of phytoestrogens daily intake except those, who are older than 80. A separate part of this population study presents questionnaire, which is focused to health status overview, where the most common diseases are listed in the table 4. Cardio-vascular diseases were found as dominant in high percentage (67%) occurrence in the case of 50 - 60 years old male population.

Age	50 - 60	61 - 70	71 - 80	81 - 90
		MALE		
		Value (S.D.)		
FOR	0.013 (0.008)	0.009 (0.011)	0.005 (0.004)	NR
DAI	0.011 (0.007)	0.117 (0.249)	0.005 (0.003)	NR
GEN	0.023 (0.015)	0.227 (0.472)	0.011 (0.008)	NR
GLY	0.007 (0.005)	0.012 (0.021)	0.001 (0.001)	NR
MAT	0.057 (0.03)	0.026 (0.029)	0.012 (0.009)	NR
LAR	0.151 (0.084)	0.169 (0.358)	0.057 (0.036)	NR
PINO	0.387 (0.385)	0.458 (0.982)	0.187 (0.166)	NR
SECO	8.003 (7.279)	10.03 (30.255)	1.109 (1.276)	NR
COU	0.003 (0.002)	0.002 (0.004)	0.001 (0.001)	NR
Phytoestrogens \sum	8.655 (7.815)	11.05 (32.381)	1.388 (1.504)	NR
		FEMALE		
		Value (S.D.)		
FOR	0.012 (0.0142)	0.008 (0.012)	0.011 (0.013)	0.002 (0.001)
DAI	0.582 (1.347)	0.257 (0.658)	0.673 (2.415)	0.004 (0.002)
GEN	1.105 (2.468)	0.533 (1.234)	1.303 (4.518)	0.013 (0.008)
GLY	0.055 (0.103)	0.025 (0.055)	0.07 (0.235)	0.001 (0.001)
MAT	0.051 (0.073)	0.034 (0.082)	0.051 (0.102)	0.015 (0.003)
LAR	0.596 (1.094)	0.307 (1.144)	0.506 (1.295)	0.06 (0.018)
PINO	0.693 (0.847)	0.736 (2.344)	1.324 (3.68)	0.183 (0.12)
SECO	64.701 (136.644)	23.68 (111.525)	39.416 (102.643)	0.046 (0.019)
COU	0.009 (0.017)	0.003 (0.014)	0.006 (0.013)	0.001 (0.001)
Phytoestrogens \sum	67,804 (142,6072)	25.583 (117.068)	43.36 (114.914)	0.325 (0.173)

Note: * Abbreviations: FOR- formononetin; DAI- daidzein; GEN- genistein; GLY- glycitein; MAT- matairesinol; LARlariciresinol; PINO- pinoresinol; SECO- secoisolariciresinol; COU- coumestrol; NR- no respondents.

 Table 2 Daily intake of phytoestrogens (mg) from main sources.

Age	50 - 60	61 - 70	71 - 80	81 - 90
		M	ALE	
		Value	e (S.D.)	
Soy	NA	0.327 (0.739)	NA	NR
Leguminous plants	0.006 (0.000)	0.011 (0.023)	0.003 (0.001)	NR
Vegetable	0.337 (0.237)	0.231 (0.132)	0.205(0.155)	NR
Fruit	0.045 (0.034)	0.041 (0.051)	0.015 (0.010)	NR
Cereals	7.972 (7.285)	1.626 (3.865)	1.079 (1.283)	NR
Others-snack	0.296 (0.319)	8.817 (28.381)	0.087 (0.140)	NR
		FEN	IALE	
		Value	e (S.D.)	
Soy	2.105 (4.390)	0.740 (1.892)	1.988 (7.220)	NA
strukoviny	0.028 (0.065)	0.005 (0.007)	0.003 (0.002)	0.001 (0.000)
Vegetable	0.431 (0.321)	0.320 (0.246)	0.404 (0.270)	0.267 (0.154)
Fruit	0.033 (0.030)	0.035 (0.047)	0.036 (0.059)	0.019 (0.013)
Cereals	3.126 (2.748)	2.005 (3.168)	2.203 (4.333)	0.031 (0.041)
Others-snack	56.876 (144.514)	22.479 (115.043)	38.728 (108.041)	0.007 (0.004)

Note. * NR- no respondents; NA- no answer.

Identical percentage of 29 values was found for the male population of 61 - 70 years old in the case of cardiovascular diseases and others (covers individual/combination of surgery and/or selected diagnosis such as allergy, osteoporosis, etc.). For female presence of cardio-vascular diseases was also found for all selected ages with the highest percentage (39%) occurrence between the age of 71 and 80. A group described as others covers the major value of 58% in the interval 50 to 60 years old.

Present study utilized published data on the phytoestrogen content of foods to estimate phytoestrogen daily intake by the population from selected region. These estimations fill the data gap and concern the effects of phytoestrogen intake on consumers at the age of retirees. On the base of literature sources, the specific foods identified as important phytoestrogen sources and those,

Age	50 - 60	61 - 70	71 - 80	81 - 90
		MAL	Е	
		Value (S	b.D.)	
Green Tea	0.052 (0.037)	0.009 (0.012)	0.004 (0.006)	NR
Beer	NA	0.001 (0.001)	0.001 (0.002)	NR
Red Wine	0.001 (0.001)	0.015 (0.032)	0.008 (0.014)	NR
White Wine	NA	0.002 (0.005)	0.002 (0.005)	NR
Peanuts	0.001 (0.001)	0.002 (0.003)	0.001 (0.005)	NR
Sesame seeds	0.217 (0.307)	0.321 (1.059)	0.056 (0.126)	NR
Linseed	NA	8.448 (27.341)	NA-	NR
		FEMA	LE	
		Value (S	.D.)	
Green Tea	0.008 (0.012)	0.008 (0.013)	0.011(0,011)	0.002 (0.003)
Beer	NA	0.001 (0.001)	0.001 (0.001)	NA
Red Wine	0.001 (0.002)	0.005 (0.012)	0.005 (0.019)	NA
White Wine	0.001 (0.001)	0.001 (0.002)	NA	NA
Peanuts	0.001 (0.001)	0.001 (0.002)	NA	NA
Sesame seeds	0.280 (0.449)	0.554 (2.481)	1.132 (4.048)	NA
Linseed	56.569 (144.133)	21.894 (112.770)	37.564 (104.169)	NA

Table 3 Daily intake of phytoestrogens (mg) from other source	es.
---	-----

* NR- no respondents; NA- no answer.

which are available on local market and known as ingredients or a part of traditional meals, were analyzed according to published data and personalized questionnaire. Measurements nine different of phytoestrogens on different sets of foods have been made. The advantage of the study is that it could utilize recent data generated by single laboratories, on a wide range of foods common to Slovak diet. The mechanism of phytoestrogen action to human body is based on structural similarities between estradiol and the isoflavones, lignans, and coumestans. It suggests that these compounds may exert their effects through binding with estrogen receptors, acting estrogenically or antiestrogenically depending on endogenous estrogen levels and the type of receptor (α or β) in specific body tissues (Kinjo et al., 2004). Individual phytoestrogens may differ in activities such as inhibition of tyrosine kinase (Youngren et al., 2005), DNA topoisomerases II and growth factors (Gordaliza et al., 2000), alteration of enzymes involved in estrogen synthesis and metabolism, such as aromatase (Brooks and Thompson 2005) as well as antioxidant activities (Kitts et al., 1999) or antiangiogenesis (Fotsis et al., 1995). Thanks to above mentioned facts, Webb and McCullough (2005) and couple of other authors point to potential health benefits of phytoestrogens obtained from food in reducing the risk of cancer, cardiovascular disease, osteoporosis, and menopausal symptoms. When the presence of selected diseases is compared to overall phytoestrogens intake measured individually for male and female respondents divided into four age intervals (Table 1 vs. Table 4), it is clear, that counting effect of phytoestrogens intake and eating habits partially protects the population against selected diseases, which are typically found at the retirees of slovak population. Moreover, this is in accordance to various studies such as the study presented by Adlercreutz (2007).where the author is describing how phytoestrogens, especially the ligans playes a defensive role against human cancer diseases. For a more precise determination of selected or total phytoestrogen daily intake value it is important to keep it in mind, that although some foods such as beverages, vegetables or fruits contain low concentrations for example of lignans, they are consumed in large amounts so they can contribute significantly to lignan intake. In respect of these,

Age	50 - 60	61 - 70	71 - 80	81 - 90
		MALE		
Cardio-vascular	67%	29%	20%	NR
Cancer	NA	5%	NA	NR
Diabetes	NA	10%	20%	NR
Others	NA	29%	30%	NR
		FEMALE		
Cardio-vascular	25%	34%	39%	33%
Cancer	NA	4%	NA	NA
Diabetes	8%	4%	9%	NA
Others	58%	25%	22%	NA

* NR- no respondents; NA- no answer.

Horn-Ross et al., (2000) described that, coffee and orange juice contributed about 40% of total lignan intake in postmenopausal women of the United States. A fruit, vegetables and beverages presents 7%, 24% and 37% of total lignan intake in the Dutch population (Milder et al., 2005). Relatively low amounts of soy intake presented by our respondents is in accordance to the fact, that in western diets soy beans do not contribute substantially to the diet (Keinan-Boker et al., 2004). Low doses of coumestrol intake were recorded by the present study, what is caused by naturaly lower concentrations. The same conclusion in relation to this substance was published by Thompson et al., (2006). Average intake (summary for male & female) of isoflavones at retirees of selected Slovakia region is represented by following values: 0.0226 (50 - 60 age intervals); 0.1485 (61 - 70 age intervals); 0.2599 (71 - 80 age intervals) and 0.005 mg.day⁻¹ (over 81). Presented values are in accordance to conclusion identified by Coward et al., (1961) about the intake of western consumers less than 5 mg.day⁻¹ and apparently lower than those found in Japanese population (50 mg.day⁻¹) presented by Messina (1995); or population of Asia (a range between 25 to 45 mg.day⁻¹) (**Coward et al., 1961**).

CONCLUSION

In conclusion, the present study summarized eating habits and health status of selected Slovak population in combination with estimation of potential effect of phytoestrogen sets intake to diseases frequency. Selected major phytoestrogens had been analyzed nine simultaneously in the same foods. Moreover, according to data reached from questionnaire it is clear, that cereals and linseed are the major contributors to phytoestrogen intake of evaluated consumers. This fact is in relation to high values of lignans and particularly secoisolariciresinol, which contributes significantly on phytoestrogen intake of evaluated population. This information packages we developed can be applied directly by future studies focused to personalizing the nutrition of retirees or designing high phytoestrogen diets in clinical trials that are related not only to cancer but also to other hormone-related diseases. If such knowledge is combined by more details like genetical backgroung and metabolism of consumer, possitive effect of diet optimalised in phytoestrogens content may brings a useful tool for reaching of desired health status.

REFERENCES

Adlercreutz, H., Mazur, W. 1997. Phyto-oestrogens and western diseases. *Annals of Medicine*, vol. 29, no. 2, p. 95-120. <u>http://dx.doi.org/10.3109/07853899709113696</u> <u>PMid:9187225</u>

Adlercreutz, H. 2007. Lignans and human health. *Critical Reviews in Clinical Laboratory Sciences*, vol. 44, no. 5-6, p. 483-525. <u>http://dx.doi.org/10.1080/10408360701612942</u> PMid:17943494

Brooks, J. D., Thompson, L. U. 2005. Mammalian lignans and genistein decrease the activities of aromatase and 17 beta-hydroxysteroid dehydrogenase in MCF-7 cells. *The Journal of Steroid Biochemistry and Molecular Biology*, vol. 94, p. 461-467.

http://dx.doi.org/10.1016/j.jsbmb.2005.02.002 PMid:15876411

Coward, L., Barnes, N. C., Setchell, K. D. R., Barnes, S. 1961. The isoflavone genestein diadzein soyabean foods from American and Asian diets. *Journal of Agricultural and Food Chemistry*, vol. 41, no. 11, p. 1961-1967. http://dx.doi.org/10.1021/jf00035a027

Fotsis, T., Pepper, M., Adlercreutz, H., Hase, T., Montesano, R., Schweigerer, L. 1995. Genistein, a dietary ingested isoflavonoid, inhibits cell proliferation and in vitro angiogenesis. *Journal of Nutrition*, vol. 125, p. 790S-797S. <u>PMid:7533831</u>

Franke, A. A., Custer, L. J., Wang, W., Shi, C. Y. 1998. HPLC analysis of isoflavonoids and other phenolic agents from foods and from human fluids. *Proceedings of The Society for Experimental Biology and Medicine*, vol. 217, no. 3, p. 263-273. <u>http://dx.doi.org/10.3181/00379727-</u> 217-44231 PMid:9492334

Gordaliza, M., Castro, M. A., del Corral, J. M., Feliciano, A. S. 2000. Antitumor properties of podophyllotoxin and related compounds. *Current Pharmaceutical Design*, vol. 6, p. 1811-1839.

http://dx.doi.org/10.2174/1381612003398582 PMid:11102564

Hays, J., Ockene, J. K., Brunner, R. L., Kotchen, J. M., Manson, J. E., Patterson, R. E., Aragaki, A. K., Shumaker, S. A., Brzyski, R. G., LaCroix, A. Z., Granek, I. A., Valanis, B. G. 2003. Women's Health Initiative InvestigatorsEffects of estrogen plus progestin on healthrelated quality of life. *The New England Journal of Medicine*, vol. 348, p. 1835-1837. http://dx.doi.org/10.1056/NEJMoa030311

PMid:12642637

Horn-Ross, P. L., Lee, M., John, E. M., Koo, J. 2000. Sources of phytoestrogen exposure among non-Asian women in California, USA. *Cancer Causes Control*, vol. 11, p. 299-302. http://dx.doi.org/10.1023/A:1008968003575

PMid:10843441

Jefferson, W. N., Padilla-Banks, E., Goulding, E. H., Lao, S. P., Newbold, R. R., Williams, C. J. 2009. Neonatal exposure to genistein disrupts ability of female mouse reproductive tract to support preimplantation embryo development and implantation. *Biology of Reproduction*, vol. 80, no. 3, p. 425-431. http://dx.doi.org/10.1095/biolreprod.108.073171 PMid:19005167

Keinan-Boker, L., van Der Schouw, Y. T., Grobbee, D. E., Peeters, P. H. M. 2004. Dietary phytoestrogens and breast cancer risk. *The American Journal of Clinical Nutrition*, vol. 79, p. 282-288. <u>PMid:14749235</u>

Kinjo, J., Tsuchihashi, R., Morito, K., Hirose, T., Aomori, T., Nagao, T., Okabe, H., Nohara, T., Masamune, Y. 2004. Interactions of phytoestrogens with estrogen receptors alpha and beta (III): estrogenic activities of soy isoflavone aglycones and their metabolites isolated from human urine. *Biological and Pharmaceutical Bulletin*, vol. 27, p. 185-188. <u>http://dx.doi.org/10.1248/bpb.27.185</u> <u>PMid:14758030</u>

Kitts, D. D., Yuan, Y. V., Wijewickreme, A. N., Thompson, L. U. 1999. Antioxidant activity of the flaxseed lignan secoisolariciresinol diglycoside and its

Available

mammalian lignan metabolites enterodiol and enterolactone. *Molecular and Cellular Biochemistry*, vol. 202, p. 91-100. http://dx.doi.org/10.1023/A:1007022329660

PMid:10705999

Knight, D. C., Eden, J. A. 1996. A review of the clinical effects of phytoestrogens. *Obstetrics & Gynecology*, vol. 87, p. 897-904. <u>PMid:8677131</u>

Kuhnle, G. G., Dell-Aquila, C., Low, Y. L., Kussmaul, M., Bingham, S. A. 2007. Extraction and quantification of phytoestrogens in foods using automated solid-phase extraction and LC/MS/MS. *Analytical Chemistry*, vol. 79, no. 23, p. 9234-9239. <u>http://dx.doi.org/10.1021/ac701732r</u> <u>PMid:17975893</u>

Lai, C. H., Chu, N. F., Chang, C. W., Wang, S. L., Yang, H. C., Chu, C. M., Chang, C. T., Lin, M. H., Chien, W. C., Su, S. L., Chou, Y. C., Chen, K. H., Wang, W. M., Liou, S. H. 2013. Androgenic alopecia is associated with less dietary soy, higher blood vanadium and rs1160312 1 polymorphism in Taiwanese communities. *PLoS One*, vol. 8, no. 12, p. e79789. http://dx.doi.org/10.1371/journal.pone.0079789 PMid:24386074

Martin, P. M., Horwitz, K. B., Ruyan, D. S., McGuire, W. L. 1978. Phytoestrogen interaction with estrogen receptors in human breast cancer cells. *Endocrinology*, vol. 103, no. 5, p. 1860-1867. <u>http://dx.doi.org/10.1210/endo-103-5-1860</u>

PMid:570914

Martinex-Campos, A., Amara, J., Dannies, P. 1986. Antiestrogens are partial estrogen agonists for prolactin production in primary pituitary cultures. *Molecular and Cellular Endocrinology*, vol. 48, p. 127-133. http://dx.doi.org/10.1016/0303-7207(86)90035-3

Messina, M. 1995. Isoflavone intake by Japanese were overestimated (letter to the editor). *The American Journal of Clinical Nutrition*, vol. 62, p. 645. <u>PMid:7661128</u>

Milder, I. E., Feskens, E. J., Arts, I. C., Bas Bueno de Mesquita, H. B., Hollman, P. C., Kromhout, D. 2005. Intake of the plant lignans secoisolariciresinol, matairesinol, lariciresinol and pinoresinol in Dutch men and women. *Journal of Nutrition*, vol. 135, p. 1202-1207. <u>PMid:15867304</u>

Mishra, N., Mishra, V., Devanshi, N. 2011. Natural Phytoestrogens in Health and Diseases. *Journal, Indian Academy of Clinical Medicine*, vol. 12, no. 3, p. 205-211.

Murkies, A. I., Wilcox, G., Davis, S. R. 1998. Phytoestrogens. *Journal of Clinical Endocrinology & Metabolism*, vol. 83, p. 297. http://dx.doi.org/10.1210/jc.83.2.297

Tham, D. M., Gardener CD, Haskell WL. 1998. Potential health benefits of dietary phytoestrogens: a review of clinical, epidemiological and mechanistic evidence. *Journal of Clinical Endocrinology & Metabolism*, vol. 83, no. 7, p. 2223. <u>http://dx.doi.org/10.1210/jc.83.7.2223</u>

Thompson, L. U., Boucher, B. A., Liu, Z., Cotterchio, M., Kreiger, N. 2006. Phytoestrogen content of foods consumed in Canada, including isoflavones, lignans, and coumestan. *Nutrition and Cancer*, vol. 54, p. 2, p. 184-201.

Fred Hutchinson Cancer Research Center, 2015. Sample Serving Size Booklet [online] s.a. [cit. 12.11.2015]

http://sharedresources.fhcrc.org/content/sample-serving-size-booklet.

at:

Webb, A. L., McCullough, M. L. 2005. Dietary lignans: potential role in cancer prevention. *Nutrition and Cancer*, vol. 51, p. 117-131. http://dx.doi.org/10.1207/s15327914nc5102_1 PMid:15860433

Xing, L., Xu, Y., Xiao, Y., Shang, L., Liu, R., Wei ,X., Jiang, J., Hao, W. 2010. Embryotoxic and teratogenic effects of the combination of bisphenol A and genistein on in vitro cultured postimplantation rat embryos. *Toxicological Sciences*, vol. 115, no. 2, p. 577-588. http://dx.doi.org/10.1093/toxsci/kfq081 PMid:20299547

Yildiz, M. F., Kumru, S., Godekmerdan, A., Kutlu, S. 2005. Effects of raloxifene, hormone therapy, and soy isoflavone on serum high-sensitive C-reactive protein in postmenopausal women. *International Journal of Gynecology & Obstetrics*, vol. 90, no. 2, p. 128-133. http://dx.doi.org/10.1016/j.ijgo.2005.05.005 PMid:15970291

Youngren, J. F., Gable, K., Penaranda, C., Maddux, B. A., Zavodovskaya, M., Lobo, M., Campbell, M., Kerner, J., Goldfine, I. D. 2005. Nordihydroguaiaretic acid (NDGA) inhibits the IGF-1 and c-erbB2/HER2/neu receptors and suppresses growth in breast cancer cells. *Breast Cancer Research and Treatment*, vol. 94, p. 37-46. http://dx.doi.org/10.1007/s10549-005-6939-z PMid:16142439

Zava, D. T., Duwe, G. 1997 Estrogenic and antiproliferative properties and other flavonoids in human breast cancer cells in vivo. *Nutrition and Cancer*, vol. 27, p. 31-40. <u>http://dx.doi.org/10.1080/01635589709514498</u> PMid:8970179

Zhao, H., Liang, J., Li, X., Yu, H., Xiao, R. 2010. Folic acid and soybean isoflavone combined supplementation protects the post-neural tube closure defects of rodents induced by cyclophosphamide in vivo and in vitro. *Neurotoxicology*, vol. 31, no. 2, p. 180-187. http://dx.doi.org/10.1016/j.neuro.2009.12.011 PMid:20060418

Acknowledgments:

This work was supported by the Slovak Research and Development Agency of the Slovak Republic under Grant no. APVV-0629-12.

Contact address:

Jozef Čurlej, Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Department of Hygiene and Food Safety, Tr. Andreja Hlinku 2, 949 01 Nitra, Slovakia, E-mail: jozef.curlej@uniag.sk.

Radoslav Židek, Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Department of Hygiene and Food Safety, Tr. Andreja Hlinku 2, 949 01 Nitra, Slovakia, E-mail: radoslav.zidek@uniag.sk.

L'ubomír Belej, Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Department of Hygiene and Food Safety, Tr. Andreja Hlinku 2, 949 01 Nitra, Slovakia, E-mail: lubomir.belej@uniag.sk. Peter Zajác, Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Department of Hygiene and Food Safety, Tr. Andreja Hlinku 2, 949 01 Nitra, Slovakia, E-mail: peter.zajac@uniag.sk. Jozef Čapla, Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Department of Hygiene and Food Safety, Tr. Andreja Hlinku 2, 949 01 Nitra, Slovakia, E-mail: jozef.capla@uniag.sk.