Original Article

# Effects of dietary traditional fermented soybean on reproductive hormones, lipids, and glucose among postmenopausal women in northern Thailand

Ratana Sapbamrer PhD[1], Nuwat Visavarungroj PhD[2], Maitree Suttajit PhD[3]

[1]*School of Medicine, University of Phayao, Phayao, Thailand*
[2]*School of Pharmacy, University of Phayao, Phayao, Thailand*
[3]*School of Medical Science, University of Phayao, Phayao, Thailand*

Isoflavone in soybean and its products have numerous beneficial health effects. A number of clinical studies have demonstrated that dietary soy isoflavone can relieve menopausal symptoms, lower risks of breast cancer, and lower cholesterol and glucose. Among the various effects of isoflavone, the role of cholesterol and glucose reduction seems to be well documented; however, other effects such as reproductive hormones were inconclusive and inconsistent. The main objective of the present study was to investigate the effects of six-month dietary traditional fermented soybean intake on BMI, reproductive hormones, lipids, and glucose among postmenopausal women. Subjects were women with their last menstrual period occurring at least 12 months prior to selection by interview and health screening from Baan Tham Village, Phayao Province, Thailand. A total of 60 women were divided into 2 groups: experimental group (n=31) and reference group (n=29). The experimental group was permitted to continue their usual diet, and supplemented with fermented soybean for 6 months. The fermented soybean provided approximately 60 mg of isoflavone per day. The remarkable findings were that dietary fermented soybean had favorable effects on progesterone and cholesterol, but had no effects on estradiol, glucose, and triglycerides. Although estradiol and glucose in the experimental group did not change, a decrease of estradiol and an increase of glucose were found in the reference group. Our results, therefore, suggest that fermented soybean may have beneficial effects on reproductive hormones and cholesterol, and they would be warrant further detail investigations.

**Key Words: isoflavone, estradiol, lipids, glucose, postmenopausal women**

## INTRODUCTION

During menopause, a woman's ovaries stop making eggs and they produce less estrogen and progesterone. The lower hormones may cause menopausal symptoms, and long-term health effects such as osteoporosis, cardiovascular disease, neurological disease, and psychiatric disease.[1] Although most women use hormone replacement therapy (HRT) to reduce menopausal symptoms, several studies have questioned risks of breast cancer, venous thrombo-embolic disease, stroke, and coronary heart disease in relation to HRT.[2]

Soybean and its products are rich in isoflavone compared with the other plants. They are referred as phytoestrogens by binding to estrogen receptor and affecting estrogen mediated process.[3] A number of clinical studies have demonstrated that dietary soy isoflavone can relieve menopausal symptoms, lower risk of breast cancer, and lower cholesterol and blood glucose.[4-6] Among the various effects of isoflavone, the role of cholesterol and glucose reduction seems to be well documented; however available data of other effects such as reproductive hormones were inconclusive and inconsistent.[7-11]

Fermented soybean is a local and traditional northern Thai seasoning food. The process for making fermented soybean is similar to that for Tempe in Indonesia,[12] but there are differences in type of micro-organism for fermentation. Five steps for making fermented soybean are as follows: soaking, boiling, fermenting with Bacillus subtilis, incubating in room temperature for 3-4 days, and packing with banana leaf. There are two forms of the fermented soybean; wet and dried. The elderly people in northern Thailand always eat fermented soybean, especially, the wet form. It is usually used for enhancing flavor in northern Thai soups and some recipes. Therefore, the primary purpose of this study was to investigate the effects of dietary traditional fermented soybean for 6 months on BMI, reproductive hormones, lipids, and glucose among postmenopausal women. In particular, we assessed serum concentrations of estradiol, progesterone, cholesterol, triglycerides and glucose.

**Corresponding Author:** Dr Ratana Sapbamrer, School of Medicine, University of Phayao, 19 Moo2, Mae Ka Subdistrict, Muang District, Phayao, 56000 Thailand.
Tel: +6654 466-666 ext.3314; Fax: +6654-466-698
Email: lekratana56@yahoo.com
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## MATERIALS AND METHODS

### *Isoflavone in fermented soybean*

Isoflavone was investigated in fermented soybean among 15 villages in Phayao Province. Seventy-five fermented soybean samples were randomized from the markets in each village for analysis of genistein and daidzein. Standards of genistein and daidzein were obtained from Sigma-Aldrich, USA. All solvents for extraction were HPLC grades (JT Baker, USA). Sample extraction and analysis were performed according to the method of Nakamura *et al.*[13] Briefly, one gram of each sample was placed in a centrifuge tube. One mL IS solution (flavone 210 $\mu$g), 10 mL 10 N HCl solution, and 40 mL 0.05% BHT solution were added to the centrifuge tube and sonicated for 30 minutes. The tube was cooled and centrifuged at 1000×*g* for 20 minutes at 5°C, and the volume was adjusted to 50 mL with ethanol. Cleanup of sample solution was performed using C18 ODS cartridges (Agilent, USA) before HPLC analysis. One mL of each sample solution was diluted with 10 mL water and applied to the cartridge column preconditioned with 2 mL 20% methanol and 20 mL water. Isoflavone and internal standard (flavone) were eluted with the exactly 2 mL methanol and analysed by HPLC (Prostar, Varian).

The LC conditions were as follows: Omnisphere C18, 250×4.6 mm column (Varian); mobile phases (A) water–phosphoric acid 1,000 + 1 (v/v) and (B) acetonitrile–water–phosphoric acid 800 + 200 + 1 (v/v/v); linear gradient program, 35°C column oven temperature; UV detector; 10 $\mu$L injection volume; and 260 nm monitoring wavelength. Recovery was 118.9% for genistein and 109.9% for daidzein. The quantitation limit was 0.951 $\mu$g/g for genistein and 0.881 $\mu$g/g for daidzein. The intra-batch coefficient of variation (% CV) was 8.96% for genistein and 6.41% for daidzein. The inter-batch % CV was 10.77% for genistein and 9.71% for daidzein.

### *Health effects of dietary fermented soybean among postmenopausal women*

The present study protocol was approved by the Human Experimentation Committee, Naresuan University, Phitsanulok, Thailand (Certificate of Ethical Clearance No. 53 03 01 0001), February 23, 2010. The study was conducted between October 2011 and May 2012.

Subjects were selected after interview and health screening. Inclusion criteria were: women living in Baan Tham Village of Phayao Province from northern Thailand and had last menstrual period at least 12 months prior to the participation in the study. Exclusion criteria included: vegetarian, diabetes, cigarette smoking, treated with HRT, had history of cancers and cardiovascular disease, menstrual bleeding within 12 months, and had a conflict with the intervention. Of 444 women in the study area, 226 (50.9%) met the criteria, 64 (28.3%) signed informed consent form, and 4 (6.25%) dropped out during intervention period. A total of 60 women were divided into 2 groups: experimental group (n=31) and reference group (n=29). The women preferring to eat fermented soybean were chosen as an experimental group. The women not preferring to eat fermented soybean and eat soy or soy products less than three meals per week were chosen as a reference group. An average age was 55.7$\pm$2.6 years for the experimental group and 55.6$\pm$2.7 years for the reference group. The experimental group was permitted to continue their usual diet, and was supplemented with fermented soybean for six months. The fermented soybean was provided in uncooked form to be used as ingredients. It was provided in daily package for a week, and refrigerated until the day it was to be consumed. The fermented soybean provided approximately 60 mg of isoflavone a day which was the range of recommended for daily isoflavone intake.[14,15] The reference group was permitted to continue their usual diet, but was not permitted to diet fermented soybean. They were permitted to consume soy or soy products no more than three meals per week. During intervention period, the experimental group was asked to record whether or not they consumed and how they consumed fermented soybeans weekly. The reference group was also asked weekly about the frequency of soy and soy product consumption.

Five mL of fasting blood was obtained on the first day of the study (baseline) and after six months of intervention. The parameters investigated at baseline and after 6 months of intervention were as follows: BMI, reproductive hormones (estradiol and progesterone), lipids (cholesterol and triglycerides), and glucoses. Estradiol and progesterone were measured using chemiluminescent competitive immunoassay (Elecsys 1010, Roche, USA). Cholesterol and triglycerides levels were determined using an enzymatic method (Synchron Synchron CX systems, Beckman, Germany). Glucose was measured using an enzymatic method (Accu-Check, Roche, USA).

Descriptive statistic parameters, including arithmetic mean,SD, minimum (Min), maximum (Max) were computed. The variables with non-normal distribution were natural logarithm transformed (*ln*) before parametric test. Two-independent student's t-test was used to analyse the difference in BMI, reproductive hormones, lipids, and glucose between the experimental and the reference groups. Paired student's t-test was used to analyze the mean differences between the baseline and the intervention after six months.

## RESULTS AND DISCUSSION

### *Isoflavone in fermented soybean*

Table 1 shows the average of isoflavone contents in fermented soybean (n=75). All samples had genistein and daidzein. Genistein was found in the highest level (132$\pm$95.4 $\mu$g/g), followed by daidzein (63.0$\pm$44.6 $\mu$g/g). The results were in agreement with several studies reporting that genistein was the major content of isoflavone in fermented soybean.[8-11] It has been known that isoflavone aglycones were absorbed faster and in greater amounts than their glucosides in humans; however, data regarding the bio-availability of genistein and daidzein were inconsistent.[16] Two previous studies reported that daidzein was

**Table 1.** Isoflavone levels in fermented soybean (n = 75)

| Isoflavones | Mean | SD | Min | Max |
|---|---|---|---|---|
| Genistein, $\mu$g/g | 132 | 95.4 | 1.74 | 364 |
| Daidzein, $\mu$g/g | 63.0 | 44.6 | 1.34 | 216 |

Min = minimum; Max = maximum

more bio-available than genistein.[17,18] On the other hand, the study of Izumi *et al* [16] reported that genistein was more bio-available than daidzein. Genistein has also been reported to be the most potent growth inhibitor in both MCF-7 breast cancer cells, anti-oxidant and, anti-promotional effects among soy isoflavone, followed by daidzein.[19] Their possibility is that gut microflora in human was a crucial factor influencing bio-availability of isoflavone.[20]

In comparing with other countries, Thai fermented soybean had higher isoflavone level than Meju (130 $\mu$g/g) and Doenjang (193 $\mu$g/g) from Korea,[21] but lower than Douchi (530 $\mu$g/g) from China,[22] Tempeh (660 $\mu$g/g), and Miso (1,260 $\mu$g/g) from Japan, respectively.[23,24] Whereas the highest isoflavone was found in Miso from Japan which was higher than Thai fermented soybean by approximately 6.4 times. Soybean cultivars and cooking process for producing fermented soybean in each country were different. Therefore, it is suggested that soybean cultivars and cooking process may affect the isoflavone contents in fermented soybean.

***Health effects of dietary fermented soybean among postmenopausal women***

Mean value of BMI, reproductive hormones, lipids, and glucose found in the subjects at baseline and after six months of intervention are shown in Table 2. The baseline of all variables (except estradiol) between experimental group and reference group were not significantly different.

BMI did not significantly change in the experimental group and the reference group. The results were in agreement with several studies indicating that isoflavone had no effects on body composition and physical performance.[25-28]

Reproductive hormones: Estradiol in the experimental group did not change, but there was a significant decrease in the reference group ($p$=0.014). Progesterone in the experimental group increased significantly ($p$=0.001). The amount of dietary soy isoflavone might be an important factor affecting reproductive hormone mechanism.[29] Previous studies demonstrated that daily intake with 20-90 mg/day of isoflavone had no effects on estradiol and progesterone.[8-11] On the other hand, daily intake with 132 mg of isoflavone was approximately 2.2 times higher than the present study, and modest hormonal effects were found (Table 3).[7]

The remarkable finding was a significant increase of progesterone in the experimental group. The previous studies demonstrated that soy supplementation induced progesterone receptor. Progesterone receptor expression is regulated by estrogen via estrogen receptor. Since soy isoflavone exerts as either a weak estrogen agonist or a weak antagonist, the increased progesterone was suggested as a possible weak estrogenic stimulus of fermented soybean.[30,31] Although soy isoflavone had weak estrogenic affinity, the high circulating levels may affect estrogen and progesterone receptors. Alternatively, isoflavone may alter enzymes involved in steroid metabolism.[32-34] In this study, there was no significant effect on estradiol. It could be hypothesized that the amount of soy isoflavone supplementation might not be high enough to compete completely at the receptor level, or to affect endogenous estrogen synthesis. However, estradiol in the reference group significantly decreased. It is possible that decreased estradiol was caused by aging, and they did not obtain soy isoflavone supplementation as hormone replacement. Our results, therefore, suggested that the amount of dietary fermented soy may affect reproductive hormonal status. It is also suggested that isoflavone in fermented soybean may mimic estrogen by binding to its receptor sites, and consequently elevate or maintain circulating reproductive

**Table 2.** Mean BMI, reproductive hormones, lipids, and glucose in the subjects after six months of intervention (experimental group = 31, reference group = 29)

| Parameters | Baseline (Pre) | After 6 months (Post) | Mean difference (Post-Pre) | $p$-value intra-group differences [§] |
|---|---|---|---|---|
| BMI, kg/m$^2$ [†] | | | | |
| Experimental group | 23.8 $\pm$ 2.54 | 23.1 $\pm$ 4.55 | -0.66 | 0.342 |
| Reference group | 23.3 $\pm$ 3.05 | 23.0 $\pm$ 2.99 | -0.28 | 0.327 |
| Estradiol, pg/mL [‡] | | | | |
| Experimental group | 12.1 $\pm$ 6.43 | 12.1 $\pm$ 14.9 | 0.055 | 0.257 |
| Reference group | 28.2 $\pm$ 52.7 | 17.0 $\pm$ 35.0 | -11.1 | 0.014* |
| Progesterone, ng/mL [†] | | | | |
| Experimental group | 0.168 $\pm$ 0.157 | 0.205 $\pm$ 0.130 | 0.037 | 0.001** |
| Reference group | 0.234 $\pm$ 0.439 | 0.374 $\pm$ 0.975 | 0.139 | 0.110 |
| Cholesterol, mg/dL [†] | | | | |
| Experimental group | 216 $\pm$ 51.3 | 192 $\pm$ 31.1 | -24.7 | <0.001** |
| Reference group | 200 $\pm$ 59.6 | 182 $\pm$ 39.7 | -18.0 | 0.102 |
| Triglycerides, mg/dL [†] | | | | |
| Experimental group | 142 $\pm$ 90.1 | 161 $\pm$ 63.9 | 18.4 | 0.109 |
| Reference group | 150 $\pm$ 85.1 | 157 $\pm$ 95.6 | 6.59 | 0.544 |
| Fasting glucose, mg/dL [†] | | | | |
| Experimental group | 86.9 $\pm$ 26.9 | 85.5 + 39.6 | -1.00 | 0.633 |
| Reference group | 79.4 $\pm$ 32.5 | 90.9 $\pm$ 51.5 | 14.3 | 0.015* |

Data are presented as mean$\pm$SD; [†] Baseline between experimental group and reference group were not significantly different ($p$>0.05); [‡] Baseline between experimental and reference groups were significantly different ($p$<0.05); [§] was obtained from pair student's t-test comparing the mean difference (last minus baseline measurement) in experimental and reference groups; *$p$ <0.05; ** $p$ <0.01

**Table 3.** Effects of dietary soy isoflavone on reproductive hormones, lipids, and glucose in postmenopausal women from other studies

| Amount of dietary Isoflavone | Numbers of subjects | Duration of intervention | Effects | Reference |
|---|---|---|---|---|
| Effects on reproductive hormones | | | | |
| 20 mg/day | 16 | 24 weeks | Estradiol ~ | Foth and Nawroth, 2003 [8] |
| 50 mg/day | 92 | 2 years | Estradiol ~, Progesterone ~ | Maskirinec et al., 2004 [9] |
| 60 mg/day | 31 | 24 weeks | Estradiol ~, Progesterone ↑ | The present study, 2012 |
| 90 mg/day | 47 | 24 weeks | Estradiol ~ | Persky et al., 2002 [10] |
| 90 mg/day | 60 | 16 weeks | Estradiol ~ | Carmignani et al.,2010 [11] |
| 132 mg/day | 35 | 12 weeks | Modest estradiol ↓ | Duncan et al., 1999 [7] |
| Effects on lipids and glucose | | | | |
| 40 mg/day | 47 | 24 weeks | Cholesterol ~, Triglycerides ~ | Rios et al., 2008 [35] |
| 40 mg/day | 20 | 24 weeks | Cholesterol ↓, Triglycerides ~ | Yildiz et al., 2005 [28] |
| 50 mg/day | 10 | 16 weeks | Cholesterol ↓, Triglycerides ~ | Maesta et al., 2007 [26] |
| 50 mg/day | 117 | 8 weeks | Cholesterol ~, Triglycerides ~, Glucose ~ | Hall et al., 2006 [36] |
| 60mg/day | 25 | 48 weeks | Cholesterol ~, Triglycerides ~ | Petri et al., 2004 [37] |
| 60 mg/day | 31 | 24 weeks | Cholesterol ↓, Triglycerides ~, Glucose ~ | The present study, 2012 |
| 96 mg/day | 33 | 12 weeks | Cholesterol ~, Triglycerides ~, Glucose ~ | Christie et al., 2010 [42] |
| 100 mg/day | 17 | 12 weeks | Cholesterol ~, Triglycerides ~, Glucose ↓ | Cheng et al., 2004 [5] |
| 100 mg/day | 30 | 1 year | Cholesterol ~, Triglycerides ~, Glucose ↓ | Huang et al., 2006 [43] |
| 138 mg/day | 40 | 14 weeks | Cholesterol ↓, Triglycerides ~ | Appt et al., 2008 [44] |

~ no effect; ↑ increase; ↓ decrease

hormones. However, it would be warrant further detail investigations.

Lipids: Cholesterol in the experimental group reduced significantly ($p$=0.000), but triglycerides did not change ($p$=0.109). The results of several studies were consistent with our results; however, some studies found no effects on cholesterol and triglycerides (Table 3). For example, Yildiz *et al* [28] evaluated postmenopausal women supplemented with 40 mg/day of isoflavone for 24 weeks, and they found the effect on cholesterol. The study of Rios *et al* [35] evaluated at the same conditions, and no significant effects were found. The study of Maesta *et al* [26] investigated the women supplemented with 50 mg/day of isoflavone, and they found effect on cholesterol, but the study of Hall *et al* [36] found no significant effects. Similarly, our study investigated the women supplemented with 60 mg/day of isoflavone and the results showed a significant decrease of cholesterol, whereas the study of Petri *et al* [37] found no significant effects. The conflicting results were therefore due to the differences in terms of the form of soy supplementation, intake amount, duration of supplementation, individual absorption ability, and genetic factor.[26]

Glucose: Glucose in the experimental group did not change ($p$=0.633), but the glucose in the reference group increased significantly ($p$=0.015). Previous studies demonstrated that daily intake with 100 mg of isoflavone reduced glucose levels, but daily intake with isoflavone less than 100 mg had no significant effects (Table 3). It seems that the amount of isoflavone consumed was an important factor influencing glucose level. Although studies on human were few, the results of the previous studies have demonstrated that dietary isoflavone may reduce insulin level, alleviate insulin resistance, impaired glycemic control.[38,39]

Several limitations should be considered. Firstly, gonadotropins, follicle stimulating hormone (FSH) and luteinizing hormone (LH), were not determined in the study. Phytoestrogens in food may have estrogenic activity and affect gonadotropins (FSH and LH). The gonadotropins are crucial hormones for stimulating estrogen and progesterone secretion.[40] Secondly, the only lipids determined were cholesterol and triglycerides. Cholesterol is divided into two groups, HDL-C and LDL-C. Lowering HDL-C levels have a strong relation with increased cardiovascular risk, whereas lowering LDL-C may reduce the risk.[41] However, HDL-C and LDL-C were not determined in this study. Thus, it is difficult to conclude which profile of cholesterol reduced in this study. Finally, both experimental and reference groups were not randomized, this may cause a limitation in interpretation.

### *Conclusion*

Dietary traditional fermented soybean had favorable effects on progesterone and cholesterol, but had no effects on estradiol, glucose, triglycerides, and BMI. Although estradiol and glucose levels in the experimental group did not change, the decrease of estradiol and the increase of glucose were found in the reference group. It is likely that fermented soybean consumption may maintain circulating estrogen hormone and glucose levels. The amount of dietary fermented soybean might be an important factor influencing favorable effects of reproductive hormones, lipids, and glucose. Therefore, more studies in larger scale and higher amounts of dietary fermented soybean are needed to confirm these results.

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## AUTHOR DISCLOSURES

The authors declare no conflict of interest.

## REFERENCES


1. Shuster LT, Rhodes DJ, Gostout BS, Grossardt BR, Rocca WA. Premature menopause or early menopause: long-term health consequences. Maturitas. 2010;65:161-6.
2. Anagnostis EA. Menopausal Hormone Therapy (MHT): Refining our understanding of MHT research, optimally applying results, and considering the future of MHT. J Pharm Pract. 2012;25:324-30.
3. Cederroth CR, Zimmermann C, Nef S. Soy, phytoestrogens and their impact on reproductive health. Mol Cell Endocrinol. 2012;355:192-200.
4. Cornwell T, Cohick W, Raskin I. Dietary phytoestrogens and health. Phytochemistry. 2002;18:379-402.
5. Cheng SY, Shaw NS, Tsai KS, Chen CY. The hypoglycemic effects of soy isoflavones on postmenopausal women. J Women Health. 2004;13:1080-6.
6. Baber R. Phytoestrogens and post reproductive health. Maturitas. 2010;66:344-9.
7. Duncan AM, Underhill KE, Xu X, Lavalleur J, Phipps WR, Kurzer MS. Modest hormonal effects of soy isoflavones in postmenopausal women. J Clin Endocrinol Metab. 1999;84: 3479-84.
8. Foth D, Nawroth F. Effect of soy supplementation on endogenous hormones in postmenopausal women. Gynecol Obstet Invest. 2003;55:135-8.
9. Maskarinec G, Franke AA, Williams AE, Hebshi S, Oshiro C, Murphy S, Stanczyk FZ. Effects of a 2-year randomized soy intervention on sex hormone levels in premenopausal women. Cancer Epidemiol Biomarkers Prev. 2004;13:1736-44.
10. Persky VW, Turyk ME, Wang L, Freels S, Chatterton R Jr, Barnes S, Erdman J Jr, Sepkovic DW, Bradlow HL, Potter S. Effect of soy protein on endogenous hormones in postmenopausal women. Am J Clin Nutr. 2002;75:145-53.
11. Carmignani LO, Pedro AO, Costa-Paiva LH, Pinto-Neto AM. The effect of dietary soy supplementation compared to estrogen and placebo on menopausal symptoms: a randomized controlled trial. Maturitas. 2010;67:262-9.
12. Astuti M, Meliala A, Dalais FS, Wahlqvist ML. Tempe, a nutritious and healthy food from Indonesia. Asia Pacific J Clin Nutr. 2000;9:322-5.
13. Nakamura Y, Tsuji S, Tonogai Y. Determination of the levels of isoflavonoids in soybeans and soy-derived foods and estimation of isoflavonoids in the Japanese daily intake. J AOAC Int. 2000;83:635-50.
14. Kang HJ, Ansbacher R, Hammoud MM. Use of alternative and complementary medicine in menopause. Int J Gynaecol Obstet. 2002;79:195-207.
15. Messina M, Messina V. Provisional recommended soy Protein and isoflavone intakes for healthy adults: rationale. Nutr Today. 2003;38:100-9.
16. Izumi T, Piskula MK, Osawa S, Obata A, Tobe K, Saito M et al. Soy isoflavone aglycones are absorbed faster and in higher amounts than their glucosides in humans. J Nutr. 2000;130:1695-9.
17. King RA. Daidzein conjugates are more bioavailable than genistein conjugates in rats. Am J Clin Nutr. 1998;68: 1496S-9S.
18. Xu X, Wang HJ, Murphy PA, Cook L, Hendrich S. Daidzein is a more bioavailable soymilk isoflavone than is genistein in adult women. J Nutr. 1994;124:825-32.
19. Brooks JD, Thompson LU. Mammalian lignans and genistein decrease the activities of aromatase and 17beta-hydroxysteroid dehydrogenase in MCF-7 cells. J Steroid Biochem Mol Biol. 2005;94:461-7.
20. Rowland I, Faughnan M, Hoey L, Wahala K, Williamson G, Cassidy A. Bioavailability of phyto-oestrogens. Br J Nutr. 2003;89(Suppl 1):S45-S58.
21. Shin D, Ahn E, Kim Y, Oh J. Changes in physicochemical characteristics of Gochujang prepared with different Koji during fermentation. Korean J Food Sci Technol. 2001;33: 256-63.
22. Liu Y, Wang L, Cheng Y, Saito M, Yamaki K, Qiao Z, Li L. Isoflavone content and anti-acetylcholinesterase activity in commercial Douchi (a traditional Chinese salt-fermented soybean food). JARQ. 2009;43:301-7.
23. Haron H, Ismail A, Azlan A, Shahar S, Peng LS. Daidzein and genistein contents in tempeh and selected soy products. Food Chem. 2009;115:1350-6.
24. Liggins J, Bluck LJ, Runswick S, Atkinson C, Coward WA, Bingham SA. Daidzein and genistein content of fruits and nuts. J Nutr Biochem. 2000;11:326-31.
25. Kok L, Kreijkamp-Kaspers S, Grobbee DE, Lampe JW, van der Schouw YT. Soy isoflavones, body composition, and physical performance. Maturitas. 2005;52:102-10.
26. Maesta N, Nahas EA, Nahas-Neto J, Orsatti FL, Fernandes CE, Traiman P, Burini RC. Effects of soy protein and resistance exercise on body composition and blood lipids in postmenopausal women. Maturitas. 2007;56:350-8.
27. Pino AM, Valladares LE, Palma MA, Mancilla AM, Yanez M, Albala C. Dietary isoflavones affect sex hormone-binding globulin levels in postmenopausal women. J Clin Endocrinol Metab. 2000;85:2797-800.
28. Yildiz MF, Kumru S, Godekmerdan A, Kutlu S. Effects of raloxifene, hormone therapy, and soy isoflavone on serum high-sensitive C-reactive protein in postmenopausal women. Int J Gynaecol Obstet. 2005;90:128-33.
29. Wood CE, Register TC, Franke AA, Anthony MS, Cline JM. Dietary soy isoflavones inhibit estrogen effects in the postmenopausal breast. Cancer Res. 2006;66:1241-9.
30. McMichael-Phillips DF, Harding C, Morton M, Robert SA, Howell A, Potten CS. Effects of soy-protein supplementation on epithelial proliferation in the histologically normal human breast. Am J Clin Nutr. 1998; 68(suppl):1431S-6S.
31. Stevenson LM, Oates SH, Doernte AL, Hess JB, Berry WD. Soy phytoestrogen effects on progesterone receptor and ovalbumin synthesis in the chic oviduct. 12th European Poultry Conference, Verona, Italy, 10-14 September 2006: 47-51.
32. Hooper L, Ryder JJ, Kurzer MS, Lampe JW, Messina MJ, Phipps WR, Cassidy A. Effects of soy protein and isoflavones on circulating hormone concentrations in pre- and post-menopausal women: a systematic review and meta-analysis. Hum Reprod Update. 2009;15:423-40.
33. Rice S, Mason HD, Whitehead SA. Phytoestrogens and their low dose combinations inhibit mRNA expression and activity of aromatase in human granulosa-luteal cells. J Steroid Biochem Mol Biol. 2006;101:216-25.
34. Xu X, Wang HJ, Murphy PA, Cook L, Hendrich S. Daidzein is a more bioavailable soymilk isoflavone than is genistein in adult women. J Nutr. 1994;124:825-32.
35. Rios DR, Rodrigues ET, Cardoso AP, Montes MB, Franceschini SA, Toloi MR. Lack of effects of isoflavones on the lipid profile of Brazilian postmenopausal women. Nutrition. 2008;24:1153-8.
36. Hall WL, Vafeiadou K, Hallund J, Bugel S, Reimann M, Koebnick C et al. Soy-isoflavone-enriched foods and markers of lipid and glucose metabolism in postmenopausal

women: interactions with genotype and equol production. Am J Clin Nutr. 2006;83:592-600.
37. Petri NE, Nahas NJ, De LL, Traiman P, Pontes A, Dalben I. Benefits of soy germ isoflavones in postmenopausal women with contraindication for conventional hormone replacement therapy. Maturitas. 2004;48:372-80.
38. Kavanagh K, Jones KL, Zhang L, Flynn DM, Shadoan MK, Wagner JD. High isoflavone soy diet increases insulin secretion without decreasing insulin sensitivity in premenopausal nonhuman primates. Nutr Res. 2008;28: 368-76.
39. Lu MP, Wang R, Song X, Chibbar R, Wang X, Wu L et al. Dietary soy isoflavones increase insulin secretion and prevent the development of diabetic cataracts in streptozotocin-induced diabetic rats. Nutr Res. 2008;28: 464-71.
40. Wilcox G, Wahlqvist ML, Burger HG, Medley G. Oestrogenic effects of plant foods in postmenopausal women. BMJ. 1990;301:905-6.
41. Barter P, Gotto AM, LaRosa JC, Maroni J, Szarek M, Grundy SM et al. HDL cholesterol, very low levels of LDL cholesterol, and cardiovascular events. N Engl J Med. 2007; 357:1301-10.
42. Christie DR, Grant J, Darnell BE, Chapman VR, Gastaldelli A, Sites CK. Metabolic effects of soy supplementation in postmenopausal Caucasian and African American women: a randomized, placebo-controlled trial. Am J Obstet Gynecol. 2010;203:153-9.
43. Huang HY, Yang HP, Yang HT, Yang TC, Shieh MJ, Huang SY. One-year soy isoflavone supplementation prevents early postmenopausal bone loss but without a dose-dependent effect. J Nutr Biochem. 2006;17:509-17.
44. Appt SE, Tormala R, Franke AA, Mikkola TS, Tikkanen MJ, Ylikorkala O et al. Soy-tibolone combination - effect on lipids in postmenopausal monkeys and women. Maturitas. 2008;60:216-22.

Original Article

# Effects of dietary traditional fermented soybean on reproductive hormones, lipids, and glucose among postmenopausal women in northern Thailand

Ratana Sapbamrer PhD[1], Nuwat Visavarungroj PhD[2], Maitree Suttajit PhD[3]

[1]*School of Medicine, University of Phayao, Phayao, Thailand*
[2]*School of Pharmacy, University of Phayao, Phayao, Thailand*
[3]*School of Medical Science, University of Phayao, Phayao, Thailand*

# 傳統發酵黃豆食物對泰國北部停經婦女生殖性荷爾蒙、血脂和血糖之影響

黃豆及其製品中的異黃酮有許多健康效益。一些臨床研究顯示，飲食中的黃豆異黃酮可以緩解停經症狀、降低乳癌發生風險、降低血膽固醇及血糖。在異黃酮產生的多種效益中，降低膽固醇和血糖似乎已被充分證實，然而，其他例如對生殖性荷爾蒙的影響則不確定且不一致。本篇研究主要目的是探討，停經婦女攝取 6 個月的傳統發酵黃豆後，對於其 BMI、生殖性荷爾蒙、血脂質、和血糖之影響。受試者來自泰國 Phayao 省 Baan Tham 村，透過訪問及健康篩檢挑選出停經至少一年之婦女。將 60 位婦女分成實驗組(31 人)與對照組(29 人)。實驗組持續平常飲食，並額外補充發酵黃豆食品 6 個月，這些食品每天約供給 60 毫克的異黃酮。值得注意的結果是，飲食中發酵黃豆對於黃體素和血膽固醇是有健康效益的，但對雌二醇、血糖和三酸甘油酯則沒有影響。雖然實驗組的雌二醇與血糖值並未改變，然而對照組的雌二醇降低、血糖則增加。因此，本篇研究結果顯示，發酵黃豆食物對於生殖性荷爾蒙、血膽固醇可能有效益，值得進一步探討。

**關鍵字：異黃酮、雌二醇、脂質、葡萄糖、停經婦女**