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FOOD DIVERSIFICATION IN JAPAN: RECENT DEVELOPMENTS IN FUNCTIONAL FOODS

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BACKGROUND

According to the World Health Organization (WHO), food security is built on the following 3 pillars:

a. Food availability: sufficient quantities of food available on a consistent basis.
b. Food access: having sufficient resources to obtain appropriate foods for a nutritious diet.
c. Food use: appropriate use based on knowledge of basic nutrition and care, as well as adequate water and sanitation.

In many countries, health problems related to dietary excess are an ever increasing threat, and malnutrition and food-borne diarrhea are becoming additional burden.

Regarding the situation in Japanese specifically, the food self-sufficiency rate (SSR) is low, for example, 80% of the ingredients for "Tempura-soba (Japanese noodles made from buckwheat flour)" are imported from abroad. Food patterns have changed in Japan with SSR decreasing from 70% in 1965 to 40% in recent years. In particular, rice consumption has reduced and oil consumption has increased in recent years (Fig. 1). Since diets have been westernized, energy intake has become excessive because of an increasing fat to energy ratio; in contrast, the carbohydrate to energy ratio has reduced.

1965 (SSR 70 %)

Fig. 1. Changes in the food consumption pattern in Japan

Recently, production of rice flour has increased for bread production, but the cost of using this product in bread is higher than that for wheat flour. Reduced rice consumption has also led to increased meat and fat intake, reduced vitamin and mineral intake, and reduced exercise levels. This has led to an increased prevalence of lifestyle-related diseases such as dyslipidemia, diabetes, cardiovascular diseases, hypertension, osteoporosis, and cancer in Japan. It is also important to consider the economic effects (primary care and self-medication cost) of lifestyle-related diseases. For example, increase in the prevalence of diabetes would necessitate considerable resources for adequate management (Fig. 2). Therefore, improvement of food quality is an important issue, although increase in food quantity (security) is also required.

In Case of Diabetes

~Medical Expenses~

Treatment for Glycophilia (Nutrition Education & Exercise Prescription)

15 dollars/month

Treatment for Prevention of Diabetic Complication

1750 dollars/month

Dialysis for Diabetic Nephropathy

8750 dollars/month

Fig. 2. Economic effects of primary care and self medication in Japan

Development of Functional Food Science in Japan

The term "physiologically functional food", which first appeared in the Nature journal in 1993 with the headline "Japan explores the boundary between food and medicine" has had a strong international impact. Functional food, is defined as those that have the potential to reduce the risk of lifestyle-related diseases and associated abnormal modalities, have garnered global interest since the 1980s when the systematic research had humble beginnings as a national project in Japan. In 1991, the project led to the launch of the national food for specified health uses (FOSHU) policy; almost 1000 FOSHU products with 8 categories of health claims have been approved up to the present (Tables 1 and 2).

Many FOSHU products claim improvement of gastrointestinal (GI) conditions. The effective component is usually a carbohydrate, which can be divided into oligosaccharides, dietary fiber, and lactic acid bacteria. Approved products containing these components can, for instance, claim that they help to increase intestinal bifidobacteria and thus help to maintain a healthful GI condition.

Other products have been approved for uses concerning blood cholesterol, triacylglycerol, body fat, blood pressure, bone, teeth, and blood glucose (Table 1). The details are as follows:

a. Blood cholesterol: Effective components include soy protein, chitosan, low-molecular-weight sodium alginate, and phytosterols. Approved products that contain these components can claim that they help to decrease blood cholesterol levels.
b. Blood neutral fat: Medium-chain fatty acid, eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and digested globin are believed to decrease blood neutral fat levels after meal consumption. Approved products that contain these constituents claim that they help to reduce postprandial blood triglyceride levels.
c. Body fat: Oolong tea polyphenols are thought to help reduce body fat gain. Approved products that contain these constituents claim that they help to reduce body fat gain.
d. Blood pressure: Effective components that are believed to reduce blood pressure include

lactotripeptide from fermented milk, dodecapeptide from casein, a group of peptides from sardine, dried bonito, seaweed, and γ-aminobutyric acid. Approved products containing these components can claim that they are suitable for people with moderately high blood pressure.

e. Bone health. Vitamin K-2 and soy isoflavone are regarded as promoters of bone calcification. Approved products containing these components can claim such effects.

f. Absorption of minerals: Fructooligosaccharides in the colon and casein phosphopeptide in the small intestine are thought to improve calcium absorption. Approved products containing these components can claim that they help in improved absorption of calcium.

g. Dental health: Some sugar alcohols such as xylitol, maltitol, erythritol, and palatinose are considered to be hypocariogenic, whereas green tea polyphenol is regarded as noncariogenic. Approved products contain these sugar alcohols can claim that these products are low or noncariogenic. In addition, some FOSHU-approved products can claim that these aid in maintaining strong and healthy teeth.

h. Blood glucose: Effective components include indigestible dextrin, wheat albumin, and L-arabinose. Approved products that contain these components can claim that these materials are helpful for those who are concerned about their blood glucose level.

Table 1. Approved Health Claims on FOSHU **(**as of 2011/04/01)

Health Uses	Food category	Ingredients (Example)	Model Claim, statements	Number approved
GI function	Table sugar	Oligosaccharides	• Helps maintain good GI condition • Helps improve bowel movement	350
Cholesterol level	Powdered beverage Oil	Soy protein, Chitosan, Phytosterol,	• Helps lower cholesterol level	142
Triacyglycerol Body Fat	Refined oil	Medium-chain fatty acids, DHA, EPA	• Helps resist body fat gain	70
	Oolong tea	Polyphenol	• For those concerned about	

Health Uses	Food category	Ingredients (Example)	Model Claim, statements	Number approved
			body fat	
Blood pressure	Instant powder soup, candy	Peptides	• For those with high blood pressure	120
Mineral absorption Bone health	Table sugar Beverage	Oligosaccharides Casein pospho-peptide Soy isoflavone	• Promotes calcium absorption • Supports bone health	53
Dental health	Chewing gum	Mixture of Xylitol, Calcium Phosphate and Fukuronori extract	• Helps maintain strong and healthy teeth	79
Blood glucose level	Beverage Instant Miso soup	Indigestible dextrin	• For those concerned about blood glucose level	141

To reduce disease risk there are additional approved FOSHU health claims (Table 2).

Table 2. Additional approved FOSHU health claim for reduction of disease risk

Functional ingredients	Health claim approved	Precautions in ingestion
Calcium Daily intake of calcium from the FOSHU products should be between 300 and 700 mg.	This product contains adequate calcium. Intake of a proper amount of calcium contained in healthy meals with appropriate exercise may support healthy bones of young women and reduce the risk of osteoporosis when aged.	Diseases are generally caused by various factors. Excessive ingestion of calcium will not eliminate the risk of developing osteoporosis.
Folic acid	This product contains adequate folic acid.	Diseases are generally

Daily intake of folic acid from the FOSHU products should be between 400 and 1000 mg.	Healthy meals containing an appropriate amount of folic acid may support healthy fetal development in pregnant women and allow them to bear healthy babies by reducing the risk of neural tube defects such as spina bifida.	caused by various factors. Excessive ingestion of folic acid will not eliminate the risk of giving birth to a child with a neural tube defect.

Since 1991, food functionalities have been extensively researched, and novel functional food genomics based on nutrigenomics have also been introduced. The availability of these functional foods is evaluated by using the "omics" techniques to cyclopedically analyze how gene expression fluctuates in each intravital tissue after consuming a functional food or its component.

Safety Evaluation of Soybean Isoflavones

Since the availability of functional foods has been adequately assessed, the focus has now turned to the evaluation of safety and the necessity of risk assessment.

The Food Safety Commission of the Cabinet Office assesses the risk and safety of foods, including the so-called "health foods" and FOSHU. Soybean isoflavone was approved in 2001 as the principle ingredient in FOSHU, as targeted to individuals concerned about bone health. After the shapes of the tablets and capsules were finalized and brought into effect by the health-promoting food system in April 2001, the assessment of safety was specifically emphasized. As an initiative, the Food Safety Commission of the Cabinet conducted a safety evaluation of soy isoflavones.

Soybean isoflavones are structurally similar to estrogen; have the ability to bind to the estrogen receptor, exhibit weak estrogen activity; and have anti-oxidative and anti-inflammatory efficacies relevant to prevention of chronic diseases, including lifestyle-relate diseases such as cancer, cardiovascular disease, diabetes, and osteoporosis (Fig. 3).

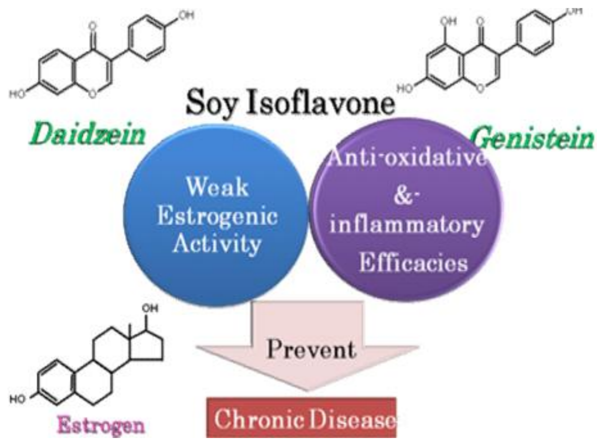


Fig. 3. Chemical structures of soy isoflavones and estrogen

In 2001, soybean isoflavone was approved as the principle ingredient in FOSHU targeted to individuals concerned about bone health. There are tea, soymilk and soft drink products that contain 40 mg of isoflavone conjugate, which is equivalent to 25 mg of the aglycone form. In 2004, applications for a tablet containing soy isoflavone aglycones as its principal ingredient, and a fermented food containing isoflavone aglycone in amounts exceeding the usual amounts in FOSHU were filed for approval. Foods with fortified or condensed isoflavones have not been consumed before, and there is a possibility that the tablets and capsules would be excessively consumed. Thus, the Food Safety Commission issued a Notice, "Basic approaches to evaluating the safety of FOSHU containing soy isoflavones" in 2006. According to this evaluation, the maximum recommended level for safe isoflavone aglycone intake in the daily diet was set at 70 to 75 mg/day. Table 3 shows quantities of foods containing around 75 mg of isoflavone. These indicate that it will be easy to exceed 75 mg of isoflavones in a standard Japanese daily diet.

Table 3. Food equivalents of 75 mg of isoflavone

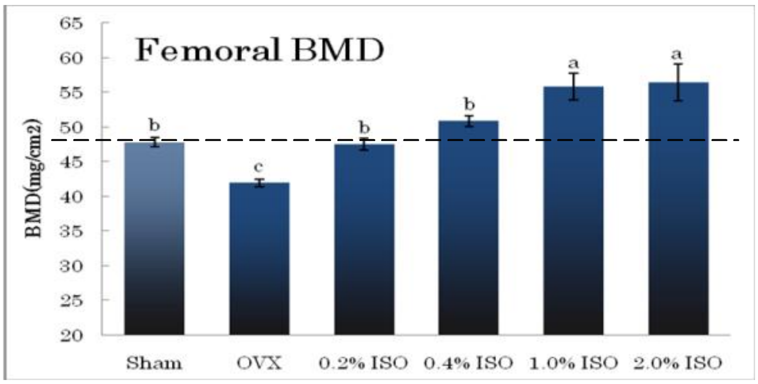
Commodity	**Equivalencies**
Natto fermented soybeans (46 g/package)	2 packages = 71 mg
Tofu	1 piece (300g) = 80 mg
Soy milk, 200 g/ package	2 packages = 82 mg

Soy flour, 6 g/ spoon	8 spoons = 77 mg

In the USA, The Food and Drug Administration (FDA) indicated that, "25 grams of soy protein daily in a diet low in saturated fatty acid and cholesterol may reduce a risk of heart disease.". This amount of soy protein (25 g) daily is very likely to equate to more than 75 mg of isoflavone. Which should we then choose, reducing the risk of heart disease or consuming a safe level of isoflavone? It appears that maximum recommended safe levels of safe isoflavone intake are not easy to evaluate and 75 mg of isoflavones may be low when considering daily diets in Japan.

RiskJbenefit Analysis of Functional Foods: The Case of Soy Isoflavones

We conducted an animal experiment to examine the dose–response relationship between isoflavone supplementation and bone and uterine weights in ovariectomized (OVX) mice, a model for postmenopausal osteoporosis. The results indicated that administration of 0.2% isoflavone prevented bone loss and inhibited uterine hypertrophy, a risk factor for uterine cancer, in the OVX mice The results suggest that the appropriate dose of isoflavones to prevent uterine hypertrophy might be less than 0. 2%. (Fig. 4).



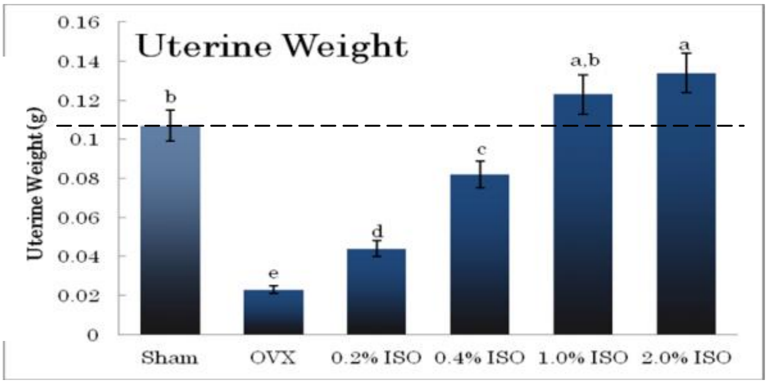


Fig. 4. Dose –response relationship between isoflavone supplementation and bone-mineral density (BMD) or uterine weight in ovariectomized (OVX) mice.

It is thought that the clinical effectiveness of isoflavones might be attributable to their ability to produce equol, a metabolite of daidzein (a major isoflavone), in the gut , although only 50% of Asians can produce equol from daidzein (Fig. 5).

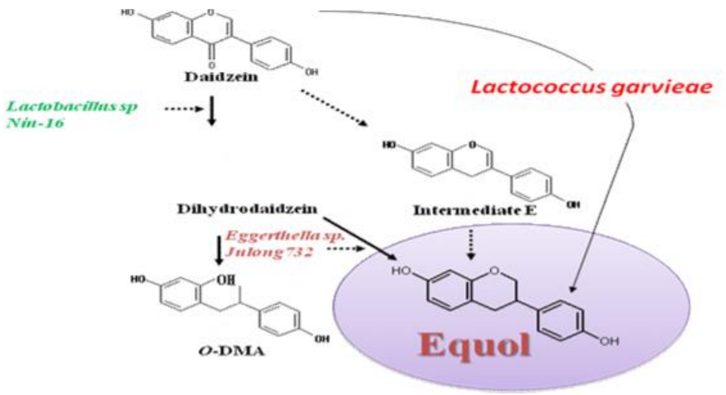
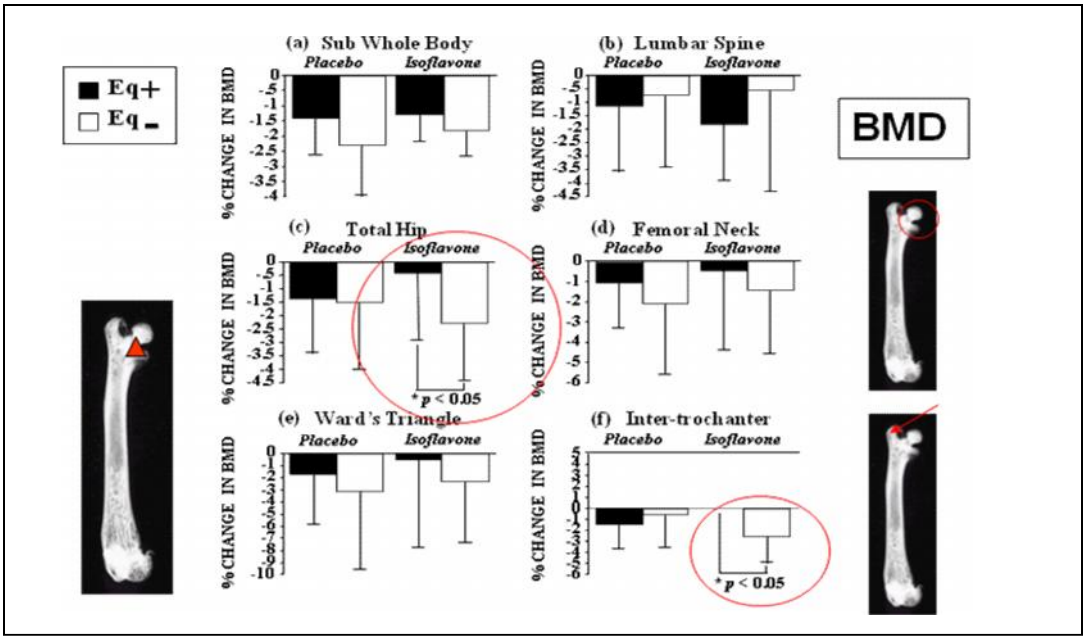


Fig. 5. Daidzein metabolism and candidate microflora for producing equol

Among postmenopausal Japanese women, individuals who are able to produce equol experience beneficial effects on bone loss (Fig. 6). Effects of 1 year isoflavone conjugate intake (47mg aglycone equivalent) in addition to the normal diet (average: 28 mg/day) on changes in bone mineral density (BMD) in postmenopausal Japanese women stratified according to their equol status. Mean (SD) percentage changed in the BMD of the sub-whole body, lumbar spine, total hip, femoral neck, Ward's triangle, and inter-trochanteric region after the 1-year intervention in the study groups.



The subjects were stratified by their equol status in both the study groups and were referred to as equol producers (■) and nonproducers (□). Significant differences were observed in the total hip and inter-trochanteric BMD between the equol producers and nonproducers in the isoflavone group (Student's t test *p = 0.05).

Fig. 6. Effects of 1 year isoflavone conjugate intake (47mg aglycone equivalent) in addition to the normal diet (average: 28 mg/day) on changes in bone mineral density (BMD) in postmenopausal Japanese women stratified according to their equol status.

To examine the effects of isoflavone intake on hormone levels in the postmenopausal women in the same intervention study, we measured serum concentrations of estrogen, FSH, LH, progesterone, and thyroid hormones. The results indicated that, in equol producers, around 75 mg of daily isoflavone intake shows beneficial effects on the bones after 1 year without any harmful effect (risk) on the level of sex and thyroid hormones.

Table 4. Effects of 1 year isoflavone conjugate intake (47mg aglycone equivalent) in addition to the normal diet (average: 28 mg/day) on serum sex- and thyroid- hormone concentrations in postmenopausal Japanese women.

		Placebo (n = 29)	Isoflavone (n = 25)	Placebo vs Iso
Estradiol (pg/ mL)	Baseline	12.66(4.03)	12.32(3.34)	NS
	After 1 year	12.98(7.31)	11.98(2.94)	NS
	% change	6.09(57.71)	1.20(23.80)	NS
FSH (U/L)	Baseline	70.36(26.02)	68.19(18.66)	NS
	After 1 year	60.00(19.83) *	58.12(17.86) *	NS
	% change	-12.36(8.40)	-14.05(9.01)	NS
LH (U/L)	Baseline	26.68(13.87)	27.70(9.32)	NS
	After 1 year	22.43(11.12) *	22.33(7.90) *	NS
	% change	-12.16(15.98)	-19.10(14.44)	NS
Progesterone (ng/mL)	Baseline	0.27(0.11)	0.29(0.16)	NS
	After 1 year	0.21(0.10) *	0.24(0.12) *	NS
	% change	-24.54 (29.47)	-14.07(18.08)	NS
T3 (ng/mL)	Baseline	1.13 (0.16)	1.08 (0.13)	NS
	After 1 year	1.10 (0.16)	1.03 (0.16)	NS
	% change	-1.60 (6011)	-3.92 (7.96)	NS
T4 (µg/dL)	Baseline	8.57 (1.12)	8.19 (1.28)	NS
	After 1 year	8.46 (1.13)	7.54 (1.42) *	NS
	% change	-1.85 (7.46)	-4.48 (6.23)	NS
TSH (mU/L)	Baseline	2.34 (1.10)	2.30 (0.74)	NS
	After 1 year	2.75 (2.81)	2.25 (1.10)	NS
	% change	12.71 (69.59)	-9.22 (32.74)	NS

* Significantly different from baseline by paired *t*-test, $p < 0.05$

CONCLUSIONS

Although it is necessary to have food in sufficient quantity, improvement of food quality is also important. Functional foods and FOSHU have been developed in Japan for improving the health status of individuals and preventing lifestyle-related diseases.

The maximum recommended safe level for isoflavone intake is not easy to evaluate and 75mg daily may be too low an amount in the for daily diets.

During the past few years, only the validity, that is the benefits, of FOSHU were evaluated. More recently, risk evaluation has been promoted in Japan. Risks and benefits posed by functional foods should be collaterally evaluated in the near future, and risk–benefit analyses should be performed to investigate the correlation between these two factors.

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