Intake of Dietary Phytoestrogens Is Low in Postmenopausal Women in the United States: The Framingham Study[1–4]

Miriam J.J. de Kleijn, Yvonne T. van der Schouw,[5] Peter W.F. Wilson,* Herman Adlercreutz,† Witold Mazur,† Diederick E. Grobbee and Paul F. Jacques**

*Julius Center for Patient Oriented Research, University Medical Center Utrecht, Utrecht, The Netherlands; *The Framingham Heart Study, Boston University School of Medicine, Boston, MA; †Department of Clinical Chemistry, University of Helsinki and Folkhälsan Research Center, Helsinki, Finland; and **Jean Mayer U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, Boston, MA*

ABSTRACT Many plants that are consumed contain phytoestrogens. Only a few published studies have examined the dietary intake of phytoestrogens in the general Western population. The potentially positive health effects of phytoestrogens might be of relevance to postmenopausal women. The aim of the present study was to estimate the intake of dietary isoflavones, coumestans and lignans by healthy Western postmenopausal women. For this purpose, we studied 964 postmenopausal, Caucasian women who participated in the Framingham Offspring Study and completed the Willett food-frequency questionnaire (FFQ). By searching the medical and agricultural literature and contacting experts, we identified food sources of phytoestrogens. The concentrations of the different isoflavones, coumestrol and lignans in each food in the FFQ were scored in seven categories and multiplied by the serving size of the food and the frequency of its consumption. The estimated daily median intake of the isoflavone daidzein was 39 μg (24–57 μg); of genistein, 70 μg (28–120 μg); of formononetin, 31 μg (13–44 μg); and of biochanin A, 6 μg (2–11 μg). Median total intake of isoflavones was 154 μg (99–235 μg). The main sources of isoflavones were beans and peas. The estimated daily intake of coumestans was 0.6 μg (0.2–1.7 μg), with broccoli as the main source. The estimated daily median intake of matairesinol was 19 μg (12–28 μg) and of secoisolariciresinol 560 μg (399–778 μg). The median total intake of lignans was 578 μg (416–796 μg). The main source of the lignans was fruits. The daily dietary intake of phytoestrogens in healthy postmenopausal Caucasian women in the United States is <1 mg. J. Nutr. 131: 1826–1832, 2001.

KEY WORDS: • *phytoestrogens* • *isoflavones* • *coumestans* • *lignans* • *postmenopausal women*

Postmenopausal estrogen use is associated with a lower cardiovascular disease risk, but also with an increased risk of endometrial cancer, breast cancer and venous thrombosis. Furthermore, postmenopausal women who use estrogen combined with progestagen (to prevent endometrial cancer) experience side effects such as vaginal bleeding. Consumption of plant foods has been associated with a lower risk of cardiovascular disease but also with a lower risk of several types of cancer, which might be ascribed in part to plant estrogenic compounds, the so-called phytoestrogens.

Phytoestrogens are plant substances that are structurally and functionally comparable to 17-β-estradiol and that are capable of producing estrogenic effects (**Fig. 1**). Phytoestrogens bind to the estrogen receptor (ER) at low levels compared with endogenous estrogen (1). By binding to the receptor, phytoestrogens may exert both estrogenic and antiestrogenic effects. It has been shown that in women consuming a phytoestrogen-rich diet, sex hormone binding globulin concentrations were increased (2,3), hot flushes and vaginal dryness were reduced and bone mineral density was increased (4). Animal studies and trials in humans showed that consuming soy, a food containing large amounts of phytoestrogens, improves the plasma lipoprotein profile by decreasing total cholesterol, LDL cholesterol and triglycerides (5,6). Ecological and migrant studies have suggested that phytoestrogens, which are commonly consumed by Asian populations, play a role in preventing cardiovascular disease and certain types of hormonally responsive cancers (7–9). There are indications from observational studies that phytoestrogens protect against breast cancer (10–12) and endometrial cancer (13). Phy-

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[5] To whom correspondence should be addressed.
E-mail: y.t.vanderschouw@jc.azu.nl.

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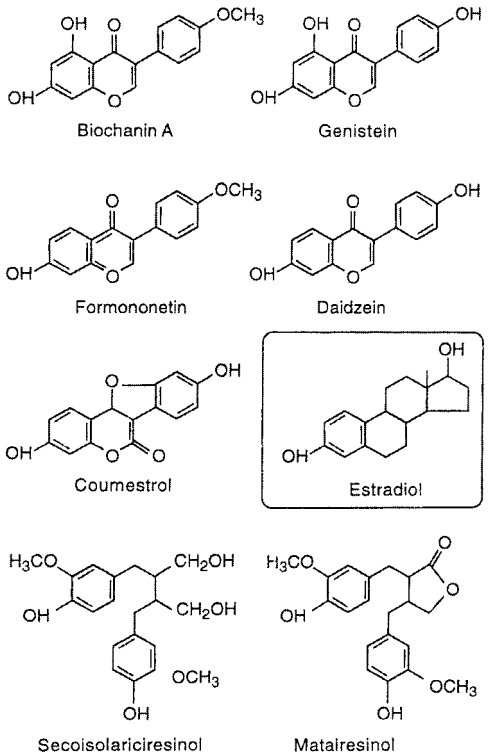

FIGURE 1 Chemical structures of naturally occurring phytoestrogens and endogenous estradiol.

toestrogens can be classified in three groups, i.e., isoflavones, coumestans and lignans. The major isoflavones are genistein, daidzein, formononetin and biochanin A. Coumestrol is the most important coumestan. The major lignans are enterolactone and enterodiol, which are produced by colonic bacteria from their dietary precursors matairesinol and secoisolariciresinol. The highest concentration of isoflavones is found in soybeans, of coumestans in alfalfa and of lignans in linseeds (8). Asian populations consume ~20–50 g of soy daily, which is their major source of phytoestrogens, comparable to a daily intake of 20–80 mg phytoestrogens (7). Consumption of foods high in phytoestrogens is uncommon in most Western countries. However, small concentrations of phytoestrogens have been measured in several fruits and vegetables (14–17), and also in coffee (18), tea (18), beer (19) and wine (17), which are frequently consumed by Western populations.

Thus far, there have been few data on regular dietary phytoestrogen intake by Western populations. To determine the importance of regular phytoestrogen intake in health and disease, more data must be obtained on the mean dietary phytoestrogen intake in these populations. Research in the area of estrogens and more specifically phytoestrogens is concentrated mainly on the health effects in postmenopausal women. These women are at higher risk of cardiovascular disease compared with premenopausal women and in general have an age-related increased cancer risk. In postmenopausal women, endogenous estrogen levels are very low, and phytoestrogens are more likely to bind to estrogen receptors leading to biological effects (1,20).

Our goal was to estimate the mean intake of dietary isoflavones, coumestans and lignans in healthy Western postmenopausal women. For this purpose, we assessed dietary phytoestrogen intake with the Willett food-frequency questionnaire (FFQ) (21) in 964 postmenopausal Caucasian women who participated in the Framingham Offspring Study. All available literature on phytoestrogen concentrations of food was used to extract data on phytoestrogen contents of the food items present in the FFQ.

SUBJECTS AND METHODS

Subjects. The Framingham Heart Study, an epidemiologic study of heart disease, was established in Framingham, MA between 1948 and 1950 with a cohort of 5209 men and women aged 30–59 y (22). By 1971, the original cohort included 1644 husband-wife pairs and 378 individuals who had developed cardiovascular disease. The offspring of these subjects and their spouses were invited to participate, and 5135 of the 6838 eligible individuals participated in the first Framingham Offspring Study examination (23). This study was approved by the Human Investigations Review Committee at New England Medical Center and by the Institutional Review Board for Human Research at Boston University Medical Center. The offspring cohort has undergone repeat examinations at ~3- to 4-y cycles. Between January 1991 and December 1994, 3799 members of the offspring cohort, of whom 1061 (27.9%) were postmenopausal women (at least 1 y after last menses), participated in the fifth examination cycle. For this analysis, we excluded women who did not fill in a FFQ, who left 12 or more items blank on this questionnaire and those with an implausibly high (≥16.7 kJ) or low (<2.5 kJ) total energy intake (n = 97). After these exclusions, 964 postmenopausal women remained for analysis.

Identifying food sources of phytoestrogens. To locate published laboratory analysis data for the phytoestrogen content of food items, we conducted a search of the medical (Medline) and agricultural (Agricola) scientific literature and contacted several experts in the field of phytoestrogens. We searched for data on measurements of the phytoestrogens daidzein, genistein, formononetin, biochanin A, coumestrol, matairesinol and secoisolariciresinol in foods. We also searched the literature with the terms phytoestrogens, plant estrogens, isoflavones, coumestans, isoflavones, lignans, enterolactone and enterodiol. We expanded our database with unpublished measured data (W. Mazur and H. Adlercreutz, Department of Clinical Chemistry and Folkhälsan Research Center, University of Helsinki, Finland) on lignan contents of some food items using an isotope dilution gas chromatography/mass spectrometry method (24).

Food-frequency questionnaire. The self-administered FFQ on dietary intake developed by Willett and colleagues (21) was used to assess usual food consumption. This questionnaire lists 130 individual food items with specified portion sizes; study participants were asked how often, on average, they had consumed these food items during the previous year. Nine responses were possible, ranging from "never or less than once per month" to "more then six times per day." The questionnaire also requested information about the use of specified vitamin and mineral supplements, the brand of breakfast cereal and included open-ended sections for information on foods and supplements not specified on the questionnaire.

Scoring phytoestrogen intake. Using the information from our review of the literature, we calculated and assigned for each food item in the FFQ values for the isoflavones daidzein, genistein, formononetin, biochanin A, coumestrol, and for the lignans matairesinol and secoisolariciresinol, according to the following protocol. All values

TABLE 1

Scoring of phytoestrogen concentrations of food items

Phytoestrogen, *mg/100 g wet weight*	Score, *mg/100 g*
Nondetectable, 0	0
$0 < * < 0.001$	0.0005
$0.001 \leq * < 0.01$	0.005
$0.01 \leq * < 0.1$	0.05
$0.1 \leq * < 1$	0.5
$1 \leq * < 10$	5
≥ 10	50

TABLE 2

Phytoestrogen concentrations of food items in the Willett food-frequency questionnaire

Food name as in Willett food-frequency questionnaire[1]	Food name as in literature (Reference)	*g/100 g dry weight*	Daidzein	Genistein	Formononetin	Biochanin A	Coumestrol	Matairesinol	Secoiso—lariciresinol
					mg/100 g or *g/L*				
Prunes	Plums (14)	67.6 (40)	0	0	0	0	0	0	0.005
Bananas	Bananas (14)	29.8	0	0	0	0	0	0	0.010
Cantaloupe	Cantaloupe (17)	6.7	0	0	0	0	0	0	0.1839
Watermelon	Watermelon[2]	8.5 (40)	—	—	—	—	—	0.0022	0.050
Fresh apples or pears	Apples (17)	18.3	0.0124	trace	0	0	0	0	trace
Apple juice or cider	Apples (17)	18.3	0.0124	trace	0	0	0	0	trace
Oranges	Oranges (17)	14.7	0	0	0	0	0	0	0.0768
Orange juice	Oranges (17)	14.7	0	0	0	0	0	0	0.0768
Grapefruit	Grapefruit[2]	9.9 (40)	—	—	—	—	—	0	0.2193
Grapefruit juice	Grapefruit[2]	9.9 (40)	—	—	—	—	—	0	0.2193
Other fruit juice	Cranberry (8)	14.5	0	0	0	0	0	0	1.510
Strawberries	Strawberries (17)	12.4	trace	trace	0	0	0	0.0781	1.5
Blueberries	Blueberries (14)	26.6	0	0	0	0	0	0	0.835
Peaches, apricots or plums	Plums (14)	14.8	0	0	0	0	0	0	0.005
Tomatoes	Tomatoes (17)	5.0	0	0	0	0	0	0.0065	0.0516
Tomato juice	Tomatoes (17)	6.0	0	0	0	0	0	0.0065	0.0516
Tomato sauce	Tomatoes (17)	11.0	0	0	0	0	0	0.0065	0.0516
Red chili sauce	Red peppers[2]	25.0 (40)	—	—	—	—	—	0	0.0515
Tofu or soybeans	Tofu (15)		25.34[3]	42.15	ND	ND	ND	0	0
String beans	Green beans fresh; boiled (15)	36.8 (40)	ND	ND	0.0001[3]	0.000001[3]	ND	0.04[4]	0.056[4]
Broccoli	Broccoli (14)	7.8	0.006	0.008	0	0	0.008	0.023	0.414
Cabbage or coleslaw	Red cabbage (14)	18.9	0.005	0.014	0.011	0	0	trace	0.141
Cauliflower	Cauliflower (14)	8.5	0.005	0.009	0	0	0	trace	0.097
Carrots, raw	Carrots (8, 14)	12.5	0.0016	0.0017	0	0	0	trace	0.370
Carrots, cooked	Carrots (8)	12.5	0.0016	0.0017	0	0	0	0.00286	0.192
Corn	Corn[2]	18.6 (40)	0	0	0	0	0	0	0.0416
Peas or lima beans	Peas (17)	92.7	0.0529	0.0497	0	0	0	0	0.013
Mixed vegetables	corn (17)	18.6 (40)	0	0	0	0	0	0	0.0416
	peas (17)	92.7	0.0529	0.0497	0	0	0	0	0.013
	carrots (8)	12.5	0.0016	0.0017	0	0	0	0.00286	0.192
Beans or lentils	Navy beans (haricot) (41)	36.8 (40)	0.0137	0.408	0	0.044	0		0.0588
Yellow (winter) squash	Squash (16)		—	—	—	—	—	0.271[4]	0.110[4]
Eggplant, zucchini, summer squash	Zucchini with peel (14)	7.9	0	0	0	0	0	trace	0.817
Yams or sweet potatoes	Yams (16)		—	—	—	—	—	0.24[4]	0.055[4]
Iceberg or head lettuce	Iceberg lettuce (16)		—	—	—	—	—	0.058[4]	0.063[4]
Celery	Celery (17)	27.5	0	0	0	0	0	0.0035	0.1114
Beets	Beetroot (14)	22.5	0	0	0	0	0	trace	0.1
Alfalfa sprouts	Alfalfa sprouts (17, 41, 40)	8.5	0.062	0.005	261	0.124	4.68	0.0007	0.033
Garlic	Garlic (8)	45.0	0.00145	0.00208	0	0	0	0.00362	0.379
Cold breadkfast cereal	Wheat bran (8)		0.0035	0.0069	0	0	0	0	0.110
	Rye bran (8)		0	0	0	0	0	0.167	0.132
Cooked oatmeal	Oatmeal (8)		0	0	0	0	0	0.0003	0.0134
Other cooked breakfast cereal	Wheat bran (8)		0.0035	0.0069	0	0	0	0	0.110
	Rye bran (8)		0	0	0	0	0	0.167	0.132
Dark bread	Nine-grain bread (24)		0.0076	0.0105	0.0024	0	0	0.0110	0.0707
Brown rice	Rice (16)	28.5 (40)	0	0	0	0	0	0.169[4]	0.128[4]
White rice	Rice (17)	28.5 (40)	0	0	0	0	0	trace	0.016
Pasta (spaghetti, noodles)	Spaghetti = 35.8% tomatoes (17)	11.0 (40)	0	0	0	0	0	0.0065	0.0516
	3.7% onions (14)		0	0	0	0	0	0.0080	0.0830

continued

TABLE 2 (*continued*)

Phytoestrogen concentrations of food items in the Willett food-frequency questionnaire

Food name as in Willett food-frequency questionnaire[1]	Food name as in literature (Reference)	*g/100 g dry weight*	Daidzein	Genistein	Formononetin	Biochanin A	Coumestrol	Matairesinol	Secoiso—lariciresinol
			mg/100 g or g/L						
French fried potatoes	Potato peeled (14)	74.2	0	0	0	0	0	0.006	0.010
Potatoes, baked, boiled, mashed	Potato peeled (14)	74.2	0	0	0	0	0	0.006	0.010
Potato or corn chips	Potato peeled (14)	74.2	0	0	0	0	0	0.006	0.010
Pizza	Tomatoes (34.6%) (17)	11.0 (40)	0	0	0	0	0	0.0065	0.0516
Decaffeinated coffee	Coffee (18)	1.5 (40)	0.066	0.029	0.078	0	0	0	0.716
Coffee	Coffee (18)	1.5 (40)	0.066	0.029	0.078	0	0	0	0.716
Tea	Black tea (8, 18)	0.3 (40)	0.029	0	0	0	0	0.305	2.418
Beer	Beer (19)		0.0000646	0.0001821	0.0004024	0.0001376	0	—	—
Red wine	Red wine (17)		0	0	0	0	0	0.0098	0.1280
White wine	White wine (17)		0	0	0	0	0	0.0022	0.0174
Cookies, ready made	6% peanuts/ground nut (14, 17, 41)		0.058	0.811	0.0068	0.031	0	trace	0.333
Peanut butter	Peanut/ground nut (14, 17, 41)		0.058	0.811	0.0068	0.031	0	trace	0.333
Popcorn	Corn[2]		0	0	0	0	0	0	0.0416
Nuts	Peanut/ground nut (14, 17, 41)	98.1	0.058	0.811	0.0068	0.031	0	trace	0.333
Bran, added to food	Wheat bran (14)	97.0	0.004	0.007	0	0	0	0	0.110
Wheat germ	Wheat whole grain (8)	97.0	0	0	0	0	0	0.0026	0.0329

[1] Dairy products (skim or lowfat milk, whole milk, crem, sour cream, nondairy coffee whitener, sherbert or ice milk, ice cream, yogurt, cottage or ricotta cheese, cream cheese, other cheese, margarine, butter)/raisins or grapes/brussels sprouts/spinach, raw and cooked/kale, mustard, chard greens/romaine or leaf lettuce/eggs/meat and fisch (chicken/turkey, bacon, hot dogs, processed meat, liver, hamburger, beef, pork, lam, canned tuna fish, dark meat fish, other fish, shrimp, lobster, scallops)/english muffins, bagels, rolls/muffins or biscuits/other grains (bulgar, kasha, couscous)/pancakes or waffles/crackers, triskets, wheat thins/soft drinks (cola or other carbonated beverage, low calorie or with sugar, with or without caffeine, non carbonated beverage with sugar)/liquid/chocolate/candy bars/candy without chocolate/cookies home baked/white bread, including pita bread/liquor/chocolate/candy bars/candy without chocolate/cookies homemade/other sweets (brownies, doughnuts, cake home baked or ready made, sweet roll home baked or ready made, pie home baked or ready made, jams/jellies/preserves/syrup/honey)/crackers, triskets, wheat thins/chowder or cream soup/oil and vinegar dressing/mayonnaise or creamy dressing/mustard, dry or prepared/pepper/salt are all food-items of the Willett food-frequency questionnaire with no data available on phytoestrogen concentrations.

[2] Personal communication.

[3] Wet weight.

[4] Enterolactone (matairesinol)/enterodiol (secoisolariciresinol).

found in the literature were converted to mg per 100 g food. Values expressed on a dry weight basis were converted to a wet weight basis either by using moisture content provided by the author, by assuming commonly expected moisture content for that particular food (25), or by using adjustments for the method of preparation (26) (**Table 1**). When the specific phytoestrogen content was reported as "a trace" or "traceable," the value of 0.00001 mg/100 g was assigned, which was based on the sensitivity of the method used (24). When more values were reported from the same or different original sources in the literature we used the highest value to score the phytoestrogen content of a food. If wet and dry weights were reported from different original sources in the literature, we used the reported wet weight value. If the questionnaire listed similar food items on the same line, we used the phytoestrogen data for the food most commonly eaten. If values for the most common food were unavailable, any value found on one of the other food items in the line was used. When there was no information available on the lignan precursors matairesinol and secoisolaraisinol we estimated these values by using data on the biologically active products enterolactone and enterodiol (16). If we did not have any information about the phytoestrogen content of a food item, we assigned a value using data of a similar food item if available. If no data were available, we assumed the value to be zero. We estimated the amount of the phytoestrogens in breakfast cereals by using the fiber content of the cereal as a proxy for the phytoestrogen content, using the Nutrition Data system of the University of Minnesota [University of Minnesota, Nutrition Data System (1998); http://www.ncc.umn.edu (March 2001; data not freely accessible)]. The average phytoestrogen content of wheat bran and rye bran was used to estimate the amount of phytoestrogen per gram fiber. Each phytoestrogen content of a food item was then scored in seven categories (**Table 2**). Finally, we multiplied the score of each food item in milligrams by the serving size of the food. This final phytoestrogen amount of each food item was multiplied by the frequency of the consumption of that food and then summed across foods to obtain the total individual intake of each phytoestrogen.

Data analyses. Mean intake with standard deviation and median intake with interquartile range are presented for each phytoestrogen. The percentage of intake of isoflavones, coumestans and lignans from different food sources are presented.

RESULTS

Table 2 lists the phytoestrogen level per 100 g of the food item in the Willett FFQ. The richest sources of daidzein

(mg/100 g dry weight) are tofu, peas, alfalfa, nuts, tea and coffee. Genistein, another isoflavone, is found in tofu, nuts, beans, dark bread and coffee. The isoflavone formononetin is present mainly in alfalfa sprouts, nuts and beer. The isoflavone biochanin A is also found in alfalfa sprouts and nuts, although in a lower concentration compared with formononetin. Coumestrol, the dietary coumestan, is found mainly in alfalfa sprouts and broccoli. Lignans concentrate in berries and some vegetables; matairesinol is found mainly in broccoli, strawberries, blackberries, dark bread and tea, and the richest sources of secoisolaraisinol are grapefruits, cranberries, blueberries, zucchini, coffee and tea.

The estimated daily median intake (25th–75th percentiles) of the isoflavone daidzein was 39 μg (24–57 μg); of genistein, 70 μg (28–120 μg); of formononetin, 31 μg (13–44 μg); and of biochanin A, 6 μg (2–11 μg) (**Table 3**). Median total intake of isoflavones was 154 μg (99–235 μg). The main sources of dietary isoflavones in this population were beans and peas, tea and coffee, and nuts (**Table 4**). The estimated daily intake of coumestans was 0.6 μg (0.2–1.7 μg). The main source of coumestan was broccoli. The estimated daily median intake of matairesinol was 19 μg (12–28 μg) and of secoisolariciresinol, 560 μg (399–778 μg). The median total intake of lignans was 578 μg (416–796 μg). The main source of lignan in this population was "other fruits" (plums, bananas, cantaloupe, watermelon, and apples or pears), breads, cereals, rice and grain, and berries.

DISCUSSION

With the growing interest in the potential health benefits of phytoestrogens, more and more data are being published on the phytoestrogen content of foods commonly eaten in Western countries. We used this literature to determine the daily intake of isoflavones, coumestans and lignans in postmenopausal Caucasian women in the Framingham Heart Study (USA). Intake was low compared with that of Asian populations, but was not zero. The total dietary intake of phytoestrogens in our study population was <1 mg/d. Dietary lignan intake was high (median 578 μg) compared with isoflavone intake (median 154 μg), and coumestan intake was extremely low (median 0.6 μg).

Before interpreting these data, some issues must be addressed. By using a FFQ, we were able to quantify the average intake of dietary phytoestrogens in the previous year. This is particularly important for a study of dietary phytoestrogen intake because foods containing high amounts of phytoestrogens are most likely to be consumed weekly or monthly, not on a daily basis. Biochemical indicators are found in urine and blood specimens (27,28) and can be used as a measure of dietary phytoestrogen intake; however, these measurements often represent only a short period of intake, i.e., several to 24 h before sampling (29–31). Biochemical indicators might provide an index of intake and subsequent metabolism by the gut flora, and therefore serve as a measure of bioavailability. Unfortunately the usefulness of these biochemical indicators of dietary intake is restricted; isoflavone excretion in the urine is substantial only in Asian populations (7,31) and until now, only lignans can be measured reliably in blood (32).

Dietary assessment methods such as 24-h dietary recall and food record methods also represent a relatively short period of intake. The underlying principle of the FFQ approach is that average long-term diet is the conceptually important exposure rather than intake of a few days (33).

Instead of using the exact measurements of phytoestrogen concentration reported in the literature, we decided to score the highest literature values into seven categories (Table 1). By doing so, we avoid the suggestion of a degree of precision for which the reported data in the literature are too limited and too preliminary. By using this method, we decreased considerably the degree of misclassification of our determinant of interest, phytoestrogen intake. Differences in the phytoestrogen concentration of food items between types, brands or different countries are not taken into account in this data set because the number of measurements reported in the literature is limited. Most measurements have been performed in one country (Finland), using only a few types or brands. By using categories instead of exact amounts of phytoestrogen content, these differences also do not bias our results as long as they are within a 10-fold range of the data we used for our classification. Our main concern is error in measurement of phytoestrogen intake produced by missing data on some of the food items consumed in the Western diet. We did have data on almost all vegetable and fruit items in the FFQ, which are the food groups most likely to contain phytoestrogens. The industrial use of soy flour could result in the presence of phytoestrogens in food items such as donuts and white bread;

TABLE 3

Phytoestrogen intake in the diet of 964 postmenopausal women participating in the Framingham Offspring Study

	Mean ± SD	Median (interquartile range)
	μg/d	
Daidzein	289 ± 2104	39 (24–57)
Genistein	338 ± 2119	70 (28–120)
Formononetin	124 ± 485	31 (13–44)
Biochanin A	9 ± 47	6 (2–11)
Coumestrol	11 ± 49	0.6 (0.2–1.7)
Matairesinol	23 ± 19	19 (12–28)
Secoisolariciresinol	622 ± 357	560 (399–778)
Total isoflavones	760 ± 4345	154 (99–235)
Total lignans	645 ± 363	578 (416–796)

TABLE 4

Sources of intake of phytoestrogens (isoflavones, lignans, coumestans) in the daily diet of 964 postmenopausal women participating in the Framingham Offspring Study

Food groups	Isoflavones	Lignans	Coumestans
	% total daily intake		
Beans and peas	26.2	2.0	
Tea, coffee	17.1	0.2	
Nuts	15.4	4.6	
Alfalfa	6		10.5
Soy	3.3		
Breads, cereals, rice and grain	2.4	10.5	
Other fruit (no citrus or berries)	2	12.7	
Broccoli, cabbage, cauliflower, lettuce, spinach	0.4	2.3	89.4
Alcohol	0.3		
Other vegetables	0.2	6.4	
Berries	0.1	8.3	
Potatoes		2.1	
Tomatoes		0.7	
Citrus fruits		2.8	

however, the processing of soy flour likely reduces the amounts of phytoestrogens in these products.

The results indicate that the intake of lignans with the Western diet is much higher then the intake of isoflavones. Recent findings in the laboratory of one of the authors (H.A.) indicated that the presence of several enterolactone precursors is much more abundant than of the two (secoisolariciresinol and matairesinol) measured until now. When methods for the measurements of these precursors become available, the true lignan values will increase at least 10-fold in foods such as cereals. This means that the lignans are the most abundant phytoestrogen in the Western diet.

To our knowledge, this study is the first to determine daily food intake of phytoestrogens in postmenopausal Western women. Until now, only one research group also quantified the dietary intake of phytoestrogens to address the association between dietary intake of phytoestrogens and prostate cancer in a case-control study (34,35). This group used an adapted Block FFQ to measure the intake of several phytoestrogens (36). The Block FFQ was modified to include frequently consumed ethnic foods and foods that were previously reported to be important sources of phytoestrogens. Furthermore, adjustments were made for cooking and preparation, and the original values as reported in the literature were used to determine the intake. These values in general correspond to the values reported in our study (Table 3) because this research group was using the same published sources. The median dietary intakes of genistein, daidzein, secoisolariciresinol and matairesinol reported in the prostate cancer study were comparable to the intakes in our study among postmenopausal women. In our study, we used the 130-item Willett FFQ. No relevant differences in ability to detect associations between nutrient intake and disease have been reported for the Willett and Block FFQ (37). Biochanin A and coumestrol intakes were higher and formononetin intake was lower in the earlier study among men compared with our study. This higher intake of some of phytoestrogens could be explained in part by the addition of several specific food items (i.e., soy sauce, soy cheese, green tea) containing high amounts of phytoestrogens to the Block FFQ used in the study among men. Furthermore, a difference in the dietary pattern between men and women is a possible explanation for the differences found. In this study, mean (and sometimes median) values of phytoestrogen contents were used instead of a scoring of the highest reported value in categories. This could also explain in part the differences between the intake of phytoestrogens in our study and the intake measured in the prostate cancer study.

Estrogens act by binding to the ER, an intranuclear binding protein; two types have now been identified, ERα and ERβ. These receptors, like all steroid hormone receptors, are transcription factors that modify gene expression when they are activated (38). Phytoestrogens bind to ER with low affinity compared with endogenous estrogens and, depending on the tissue, may exert either estrogenic or antiestrogenic effects. These effects are comparable to the effects of Selective Estrogen Receptor Modulators such as Tamoxifen and Raloxifen. With both estrogenic and antiestrogenic effects, it is possible to reduce the risk of cardiovascular diseases as well as the risk of breast cancer. The use of traditional hormone replacement therapy is related to a lower cardiovascular risk but also with an increased risk of breast cancer.

Antiestrogens are thought to exert their effect by decreasing the concentration of cytoplasmic ER and by complexing with the receptor, thus preventing biosynthetic processes associated with tissue development (39). In postmenopausal women, endogenous estrogen levels are very low and phytoestrogens are more likely to bind to ER, leading to biological effects (20). Postmenopausal women are at high risk of cardiovascular disease and breast cancer, and effective preventive treatments could have a major effect on morbidity and mortality.

The effects of phytoestrogens on different hormone-related diseases have been studied primarily in Asian populations, who consume ~20–50 g soy/d, or in trials with soy supplements given to people consuming a Western diet. For the former group, the high level of phytoestrogens contained in soy is comparable to an intake of 20–80 mg phytoestrogens (7). The effects of daily intakes of low dietary phytoestrogens have not yet been studied. To be able to study dietary phytoestrogen intake more precisely in relation to disease risk and incidence, a comprehensive and complete database of isoflavonoid, coumestan and lignan contents of the most common foods in the Western diet should be developed, including data on milk products and "fast food"(possibly containing soymilk or soy flour), to increase the comprehensiveness and accuracy of the nutrient database. The data that have been collected for this study together with the existing database on isoflavones can be used as a basis for an expanded database. Availability of such data will enable longitudinal studies of the health effects of dietary phytoestrogen intake in populations consuming a Western diet.

This study shows that dietary intake of isoflavones, coumestans and lignans in healthy postmenopausal Caucasian women in the United States is low. In spite of the low intakes, recommendations for changes in the diet of postmenopausal women to increase dietary phytoestrogens may be premature before the health benefits of phytoestrogens are clearly demonstrated.

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