Citation:

McVeigh BL, Dillingham BL, Lampe JW, Duncan AM. Effect of soy protein varying in isoflavone content on serum lipids in healthy young men. Am J Clin Nutr. 2006 Feb;83(2):244-51.

PubMed ID: 16469981

Study Design:

randomized crossover trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To ascertain the effects of soy protein varying in isoflavone content on serum lipids in healthy young men.

Inclusion Criteria:

- healthy males
- ages 20 to 40 years
- body mass index (BMI): 19-29 kg/m^2

Exclusion Criteria:

- diagnosis with a disease or serious medical condition
- regular medication use
- antibiotic use within the previous 3 months
- smoking
- vasectomy
- recreational drug use
- soy or milk protein allergy
- vegan diet
- body weight change of >5 kg within the previous 6 months
- elite athletes
- intention to gain or lose weight within the following year

Description of Study Protocol:

Recruitment: subjects recruited from the local community

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Design: randomized crossover trial

Blinding used (if applicable): subjects were blinded to order of treatment; does not appear that investigators were blinded; many outcome variables are laboratory values

Intervention (if applicable):

- habitual diet supplemented with 3 protein powders varying in isoflavone content:
  - milk protein isolate (MPI)
  - ethanol-extracted low-isoflavone soy protein isolate (low-iso SPI)
  - high-isoflavone soy protein isolate (high-iso SPI)
- powders provided on an individual basis based on body weight
  - the high-isoSPI calculated to provide 0.75 mg kg body wt -1 d-1
  - amounts oflow-iso SPI and MPI calculated to provide protein in an amount similar to that provided by hig-iso SPI

Daily isoflavone and protein contribution of study treatment powders

	MPI	Low-iso SPI[1]	High-iso SPI[2]
Isoflavones (mg)	---	1.64±0.19	61.7±7.35
Isoflavones (mg/kg body weight)	0.00±0.00	0.02±0.001	0.75±0.01
Protein (g)	32.1±4.60	31.6±3.60	32.0±3.95

The values are the sums of the individual isomers of each isoflaone (genistein, daidzein, and glycitein) normalized for their molecular-weight differences and presented as total aglycone isoflavones.

[1]The average percentage distribution of isoflavones was 78.9% genistein, 12.7% daidzein, and 8.4% glycitein.
[2]The average percentage distribution of isoflavones was 53.3% genistein, 35.6% daidzein, and 11.1% glycitein.

- three 57 day treatment periods separated by 28-day washout periods
- instructions given to minimize background consumption of phytoestrogens by avoiding soy and soy products, flaxseed, beans and legumes, whole grains, and high-fiber foods, limit consumption of milk and calcium-fortified beverages, tlimit alcohol intake to <7 drinks/week (≤ 2 drinks per sitting); avoid green tea and all dietary supplements

Statistical Analysis

- data not normally distributed was log transformed
- repeated measures analysis of variance (ANOVA) conducted:
  - for day 1 values for serum lipids to ensure washout periods between treatments were sufficient,
  - on calculated change from day 1 to day 57, with control for subject and treatment , then Tukey's test conducted, to evaluate the effect of treatment on serum lipids, lipid ratios, and CRP
  - further analysis after excluding equol excretor status as a covariate
  - on the effects of treatment on anthropometric, food record, and urinary isoflavone data, after control for subject, treatment order, and treatment, then Tukey's test for multiple comparisons

Data Collection Summary:

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Timing of Measurements

- In each treatment period:
  - days 1, 15, 29, 43, and 57: body weight and height
  - days 1 and 57: body composition; blood samples
  - days 54-56: 24-hour urine collection
  - days 1-3, 26-28, and 54-56: 3-day food records

Dependent Variables

- serum lipids:
  - total cholesterol (TC)
  - HDL-cholesterol (HDL-C)
  - triacylglycerols
  - apolipoprotein (apo) B and apo A-I
  - CRP

Independent Variables

- soy isoflavone intake: assessed by food record and by urinary excretion of isoflavones from 24-hour urine collections

Control Variables

- equol excretor status

Description of Actual Data Sample:

Initial N: N=43 males

Attrition (final N): N=35 (4 dropped out and 4 excluded)

Age: 27.9±5.7 years

Ethnicity: Not specified

Other relevant demographics: None specified

Anthropometrics and other subject characteristics (mean±SD, N=35)

- Age: 27.9±5.7 years
- Body weight: 82.5±9.5 kg
- Height: 1.81±0.07 m
- BMI: 25.4±3.0 kg/m^2
- Body fat: 16.4±4.6%
- Total cholesterol: 4.50±1.25 mmol/L
- LDL-cholesterol: 2.74±1.06 mmol/L
- HDL-cholesterol: 1.07±0.17 mmol/L
- Triaclyglycerols: 1.45±1.07 mmol/L

Location: Canada

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Summary of Results:

Key Findings

- The three treatments did not differ significantly for TC, HDL-C, non-HDL-C, triacylglycerols, apo B, and apo A-I, or for serum CRP.
- Ratios of TC:HDL-C, LDL:HDL, and apoB:apoA-I were significantly lower with consumption of the low-iso SPI (4.01± 0.06, P=0.031; 2.45±0.05, P= 0.006, and 0.60±0.01, P=0.011, respectively) and the high-iso SPI (4.00±0.06, P=0.054; 2.41±0.05, P=0.012, and 0.60±0.06, P=0.005) than with that of the MPI (4.22±0.06; 2.66±0.05; 0.64±0.01).
- When equol status (excretor versus non-excretor) was included, only LDL-C was significantly lower with consumptio of the low- (P=0.035) and high-iso SPI (P=0.04) than with that of the MPI.

Energy, macronutrient, dietary fiber, cholesterol, and calcium intakes

	Before study[2]	MPI r[3]	Low-iso SPI[3]	High-iso SPI[3]
Energy (kcal)	2647±97.4	2564±58.1	2536±58.1	2587±58.1
Protein (g)	105.7±4.91[a]	123.5±2.78[b]	122.8±2.78[b]	125.6±2.78[b]
Carbohydrate (g)	339.2±13.7	334.9+8.31	320.1±8.31	326.9+8.31
Fat (g)	96.4±4.79[a]	81.2±3.00[b]	84.9±3.00[b]	86.3±3.00[b]
SFA (g)	27.9±1.82	25.6±1.13	25.1±1.13	25.5±1.13
MUFA (g)	12.9±1.38	11.7±0.80	11.3±0.80	13.0±0.80
PUFA (g)	6.70±0.67	5.55±0.41	6.12±0.41	6.53±0.41
Dietary fiber (g)	14.9±0.78	13.7±0.46	13.9±0.46	13.4±0.46
Cholesterol (mg)	292.0±22.5	268.7±12.9	265.9±12.9	291.4±12.9
Calcium (mg)	770.6±94.0[a]	1905±54.5[b]	1856±54.5[b]	2004±54.5[b]

[1]All values are least-squares mean±SE, N=35. Vlaues in a row with different letter superscripts are significantly different, P≤ 0.05 (repeated-measures ANOVA followed by Tukey's test).

[2]Values are based on the results of one 3-day food record completed before the study.

[3]Values are based on the average results of three 3-day food records completed on days 1-3, 26-28, and 54-56; these data include the contributions from the study treatment protein powders.

Other Findings

There were no significant effects of treatment or treatment order on anthropometric measurements, including body weight, BMI, and percentage body fat.

Comparison of prestudy and study food records showed that subjects consumed significantly more protein (P=0.0005), more calcium (P<0.001), and less fat (P=0.015).

Urinary excretion of genistein and daidzein, and equol and O-desmethyl-angolensin, was significantly greater with the consumption of the high-iso SPI than with that of the low iso SPI and the MPI (P<0.0001)

The day 1 concentrations of TC, LDL-C, HDL-C, non-HDL-C, triacylglycerols, apoB, apoA-1, and CRP did not differ significantly among the 3 treatments, indicating that washout periods

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between treatments were sufficient.

Author Conclusion:

Soy protein, regardless of isoflavone content, modulates serum lipid ratios in a direction beneficial for cardiovascular disease risk in healthy young men.

Reviewer Comments:

study included men only

unclear if subjects were compliant with dietary recommendations for food intake (exclusive of powder)

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes

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2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes

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5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes

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8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

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