

Does the lipid lowering effect of soy foods differ based on equol status?

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Project title

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Abstract

Soy isoflavones (daidzein, genistein, glycitein) are a family of plant-derived polyphenolic compounds with similar structure and properties to mammalian estrogen, and possess weak estrogenic activity. Once ingested, gut microbiota biotransform the β -glucosides to their active form, which in turn could be further biotransformed to various metabolites, including equol. Soy has been considered an effective lipid lowering food, but only 30-40% of the Western population have the ability to produce equol. Given this, we examined the inter-individual variation in microbial biotransformation of soy isoflavones as the cause of the variance in its lipid lowering effect. The process of a systematic review and meta-analysis was quite extensive and a conclusion was not reached. The studies to be included have passed the title and abstract phase for eligibility and will be processed through thorough examination for statistical analysis.

Introduction

The global burden of diseases such as cardiovascular and metabolic syndromes is immense. Coronary heart disease (CHD) remains the leading cause of death worldwide. International efforts have been made to implement dietary strategies (1,2) for the prevention and treatment of hyperlipidemia, specifically low-density lipoprotein-cholesterol (LDL-C), the primary modifiable lipid risk factor for CHD. As a result of such efforts, the US FDA has approved a number of health claims for CHD risk reduction, one of which is for soy foods (soy protein) (3). Similarly, increased consumption of plant protein, including soy, is a recommendation in current national dietary guidelines for CHD risk reduction. However, there has been conflicting evidence from other clinical trials in regards to the reductions shown by those used to support the health claim for soy (4-6).

Soy isoflavones (daidzein, genistein, glycitein) are a family of plant-derived polyphenolic compounds with similar structure and properties to mammalian estrogen and possess weak estrogenic activity. Once ingested, gut microbiota biotransform the β -glucosides to their active form, which in turn could be further biotransformed to various metabolites, including equol. Interestingly, it has been observed that only approximately 30-40% of adults in Western populations have the ability to produce equol.

We therefore hypothesize that one of the reasons for the inconsistencies in the current literature examining the effectiveness of soy as a lipid-lowering food may be explained by inter-individual variation in microbial biotransformation of soy isoflavones. Current literature examining the role of equol status on serum lipid reductions is inconclusive and has not yet been systematically reviewed.

We aim to conduct a systematic review and meta-analysis.

Methodology

The planning and conduct of this meta-analysis were carried out according to the Cochrane Handbook for Systematic Reviews of Interventions, and the reporting of results will follow the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (7). A search of MEDLINE (1950-), EMBASE (1980-), CINAHL(1982-) and the Cochrane Library (including The Cochrane Central Register of Controlled Trials[Clinical Trials; CENTRAL] database [1800-]), using appropriate search terms and Boolean operators was conducted. The search was limited to inclusion and exclusion criteria set out to include humans and clinical studies with no limit on language. Studies that were <14d follow-up, administered soy isoflavone supplements, lacked an adequate control group, or lacked determination of equol status will be excluded. In cases where multiple publications with duplicate data exist for the same study, the article with the most information will be included. The identified studies were then analysed by title and abstract for appropriateness for the study individually by the included investigators. The reasons for exclusion were matched and reviewed to maintain accuracy. The studies that were deemed suitable were retrieved in full text and will be reviewed for statistical analysis.

The described process encompassed more time than originally set out and thus the final statistical analysis has not been completed. The initial review of the studies using title and abstract and the hurdles with retrieval of full texts due to university subscription took the majority of the allocated time.

Results

From the initial search of MEDLINE, EMBASE, Cochrane, CINAHL a total of 1754 papers were identified. The 1754 studies were analysed by two independent investigators and specific reasons for exclusion was identified. The reasons for exclusion, and the count of the studies that fit for each reason is tabulated below.

	Reason	Number of Studies
1	Included systematic reviews of soy, other nutrition interventions, commentaries, guideline statements, some of which did not focus exclusively on soy	167
2	Included studies of soy feeding in animals	43
3	Were not randomized soy interventions (cross sectional studies, cohorts)	3
4	Were interventions of soy <14 d	16
5	Did not include a control group	7
6	Include Total Parenteral Nutrition, lipid emulsions or soybean oil, soy sterols, soybean lecithin, phospholipids, fish oils, other non-soy interventions such as , coconut oil, red rice yeas, pinotol; majority was use of a) soy oil based TPN; b) soy oil interventions; c) infant soy formulae, black cohosh	93
7	Had a soy intervention arm, but clearly did not measure lipids (e.g. oxidation products, arterial stiffness)	3
8	Administered soy product parenterally or enterally	8
9	Designs were not balanced	0
10	Duplicate records in multiple databases PUBMED used as primary	842

11	Clearly identifiable co-intervention without single intervention arm (e.g. exercise + soy, soy+beta-sitosterol, soyprotein+ nopal+ chia seed+ oat, soy+high PUFA, soy+DHA, low-GI +soy, fermented-soy based yogurt)	16
12	Conflicting reasons between investigators, including marked duplicates	556

Of the 1754 studies identified from the searches, 232 met eligibility criteria based on title and abstract, as assessed by both investigators independently. The full articles were retrieved through various search engines. The articles will then be read to determine if eligibility criteria are still met. Those which remain eligible will be read to extract the details for statistical meta-analysis. The results from this phase are not complete.

Conclusion and outcome

The rapidly increasing global burden of non-communicable diseases, such as cardiovascular disease, has provided the impetus for a United Nations high-level meeting in September 2011 to set a new international agenda. Dietitians are at the forefront of synthesizing and disseminating the current evidence to support current dietetic practice, yet are often faced with literature that is inconclusive at best and contradictory at worst. At a time when the availability of high biological value protein alternatives to soy foods for the prevention and management of hyperlipidemia are lacking, determining which segments of the population may derive the greatest benefit from dietary approaches are essential for dietetic resource allocation. This drove me to engage in this project, meticulously extracting information from large spreadsheets.

Completing this project with the funding from IATL helped me gain a better understanding of not only use of soy isoflavones in the reduction of LDL, but more importantly the hard work that goes into preparation of a systematic review and meta-analysis. I was presented with large numbers of search results set out in a spread sheet that I then had to sift through to make logical sense of it all. I was primarily involved with matching the reasons for eligibility determined by the independent investigators, and identifying duplicates in the search outcome. Once that was done I faced my next barrier with attaining the full published articles, as most journals only make their abstracts available for viewing.

I originally set out to have the systematic review and meta-analysis completed by the end of the study year, but due to the mentioned obstacles soon realised the process is much more time consuming than I imagined. The funding of IATL allowed me to understand this approach to research while gaining a better understanding of the study topic itself. Due to this, I was able to give presentations to students at the research special study modules at WMS regarding the process in conducting large scale research, and the details one has to consider when undertaking projects.

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