Release 2 of the Dietary Supplement Ingredient Database (DSID): Research Protocols and Ingredient Estimates for Children's and Adult Multivitamins

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Abstract

The Dietary Supplement Ingredient Database (DSID) is a federal initiative to provide analytically-derived estimates of ingredients in dietary supplements because the actual content may differ from the labeled amount. Release 2 provides data for children's multivitamins (MVMs), updates adult MVM estimates and is available at http://dsid.usda.nih.gov. Representative children's MVMs were identified and purchased from multiple market channels. These supplements were analyzed for their vitamin and mineral content with certified reference materials. Mean percent differences from label were calculated for each nutrient and compared to labeled levels using regression analysis. The relationship between label and analytical content for each nutrient was identified as either linear (n=12) or quadratic (n=5). Mean % differences from label averaged 1-<10% above label for eight nutrients (zinc, phosphorus, magnesium, copper, iron, vitamin B-6, niacin, riboflavin); 10 to <20% above label for 5 nutrients (thiamin, folic acid, vitamin B-12, manganese, and calcium); 20 to <30% above label for 3 nutrients (iodine and vitamins A and E) and >30% above label for vitamin D. Data estimates were linked to children's MVM products reported in the National Health and Examination Survey and can be used by researchers to more accurately quantify nutrient intake from dietary supplements.

Background

The Nutrient Data Laboratory (NDL), Beltsville Human Nutrition Research Center (BHNRC), Agricultural Research Service (ARS), USDA, in collaboration with the Office of Dietary Supplements, National Institutes of Health (ODS/NIH) and other federal agencies has developed a Dietary Supplement Ingredient Database (DSID) to evaluate levels of ingredients in dietary supplement products. The DSID is funded in large part by the Office of Dietary Supplements. It builds on the well-recognized strengths of the USDA/ARS in developing databases that support the assessment of intake of nutrients from foods. ODS provides leadership, jointly with its federal partners, in making this a reality. The consortium of federal agencies includes ODS and partners at USDA/ARS, the National Center for Health Statistics of the Centers for Disease Control and Prevention (NCHS/CDC), The Food and Drug Administration (FDA), the National Cancer Institute (NCI), NIH and the National Institute of Standards and Technology (NIST) of the Department of Commerce. The goals for this project are :

- To develop reliable estimates, including variability information for nutrients and other bioactive components in DS products
- To support improved dietary intake assessments in research by providing analytical estimates of the ingredient content of marketed DSs
- To release and maintain a publicly available on-line composition database for DSs

Priority dietary supplement product categories and ingredients are determined by a DSID Working Group with members from the collaborating agencies listed above.

DSID Study Steps

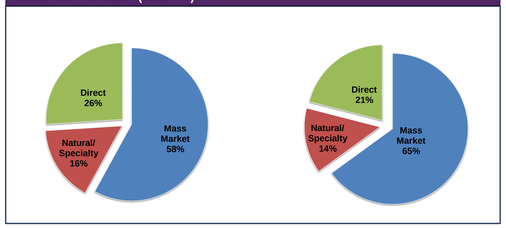
Each DSID study is planned and implemented using these six steps:

1. Identify priority dietary supplement products and ingredients according to prevalence of consumption, public health interest in specific ingredients, and the availability of reliable analytical methods for specific compounds.
2. Design statistically-based sampling plans using national survey data and product market information and including retail and direct channels.
3. Identify appropriate methods and qualified laboratories which demonstrate expertise in the analysis of dietary supplement components and matrices.
4. Procure, process and send samples to laboratories for chemical analysis. Monitor methods of analysis and lab performance using quality control measures and reference materials.
5. Review and evaluate laboratory data. Apply appropriate statistical techniques to lab data and other information.
6. Report results via publicly available releases. Develop data applications and publish results.

Sampling Distribution

A national sampling plan was designed for each study. Representative MVM products (defined for these studies as containing ≥3 vitamins, with or without minerals) were identified using NHANES (National Health and Nutrition Examination Survey) and other surveys. Multiple lots of 109 adult and 64 children's MVMs were purchased from direct marketers and from mass merchandisers and specialty retailers in 6 U.S. locations. These graphs portray the market channel distributions for each study.

Figure 2. Market channel distributions for Adult MVMs (LEFT) and Children's MVMs (RIGHT)



Laboratory Analysis and QC

After purchase, dietary supplement samples were repackaged and sent for laboratory analysis in defined batches. Quality control (QC) materials were added to each batch of MVM products in order to evaluate laboratory precision and accuracy on an on-going basis. Each batch included:

- National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 3280, a MVM matrix with certified values for vitamins and minerals
- In-house control materials (n=2-3), developed from a single lot of a MVM product with a similar matrix to the study samples
- One product sample sent in duplicate

Qualified analytical contract and collaborative laboratories analyzed the sample sets using validated sample-handling protocols and appropriate methods, to obtain analytical information about ingredient levels. Analytical retests for ingredients in specific products were identified to check unusually high or low results, high variability among product lots or questionable data in batches where QC results showed a bias. For each sample analyzed, laboratory results were compared to labeled levels and a percent difference from label was calculated.

Summary of DSID-2 Results

Table 1: Predicted Mean % Differences from Label for Vitamins and Minerals in Adult and Children's MVMs

	ADULT MVMs		CHILDREN'S MVMs	
	Predicted Mean % Differences from Label			
Ingredient	Range	at Most Common Label Level	Range	at Most Common Label Level
Vitamins				
Folic Acid	7.7 to 18	13	14 to 22	14
Niacin	0.4 to 5.8	0.9	5.4 to 14	5.4
Riboflavin	3.5 to 14	14	4 to 11	14
Thiamin	-6.5 to 8.6	-6.4	2.4 to 16	11
Vitamin A	*	*	-0.1 to 24	23
Vitamin B-12	8.6	8.6	7.6 to 25	15
Vitamin B-6	-5.4 to 5.8	5.4	4.1 to 19	6.1
Vitamin C	8.3 to 9.1	8.3	*	*
Vitamin D	*	*	34 to 49	34
Vitamin E	5 to 6.2	6.0	14 to 46	14
Minerals				
Calcium	7.2 to 29	14	3.8 to 31	19
Copper	0.73 to 16	7.4	4.8 to 11	4.8
Iodine	26	26	1.9 to 64	24
Iron	-1 to 16	0.9	1.7 to 13	1.7
Magnesium	1.7 to 9.4	2.3	3.5 to 5.9	4.2
Manganese	4.3 to 7.2	6.5	*	*
Phosphorus	8.2 to 8.4	8.4	1.2 to 4.5	1.2
Potassium	6.9 to 12	8.2	*	*
Selenium	13 to 25	25	*	*
Zinc	-1.1 to 9.5	4.3	0.3 to 20	0.9

* These ingredients are not reported in the study.

Statistical Analysis

Ingredient data from laboratory analysis were prepared for statistical analysis by averaging duplicate observations and obtaining market share product weights for weighted regression analysis. Market share weights were based on data from NHANES and from an independent marketing firm.

Regression analysis was used to compare the label to analytical values across a range of labeled levels. A regression equation was derived for each supplement type and ingredient using the label value as the independent variable and the percent difference from the label (based on the laboratory results) as the dependent variable. The resulting equations predict mean analytical levels in the product category (expressed as a predicted percent difference from the label). In addition, the standard error of the predicted mean and the standard error for prediction of an individual observation were calculated at each labeled level and are available on the DSID website (www.dsid.usda.nih.gov). The predictions are linked to labeled levels for each ingredient in a product category and are not brand or supplement-specific. Data applications to NHANES DS files are also provided.

Discussion

Table 1 lists the range of mean predictions for each ingredient in each study across the labeled levels analyzed and at the most common labeled levels. These results indicate that for many ingredients the labeled levels reflect the ingredient levels and the overages seen are very similar for the two types of MVMs. Only Thiamin showed mean predictions below label at the most common labeled level and only for adult MVMs. The ingredients with predicted means significantly above label are iodine for both studies, selenium for the adult MVM study and vitamins A and D for the children's study, with predicted % differences from label ranging from +22 to +34% of label. The information in this database can be used to more accurately estimate intake contributed by DS ingredients. These estimates can then be combined with nutrient intakes from foods to evaluate total dietary intake as it relates to health and disease outcomes.

Future Plans

DSID-3

In 2014, DSID-3 will be released and it will include data from studies evaluating the levels of omega-3 fatty acids in fish, plant and fish/plant blend DSs and levels of vitamins and minerals in over-the-counter prenatal MVM products.

Botanical DSID Studies

Green tea and flavonoid-containing DSs will be the first botanical supplements to be analyzed for the DSID. Green tea DSs are among the most common botanicals purchased in the U.S. and they contain flavan-3-ols, including epicatechin, epigallocatechin, epicatechingallate, and epigallocatechingallate (EGCG), as well as caffeine. Commercial green tea dietary supplements may be dried leaves or extracts and may be chemically standardized to levels of total polyphenols, total catechins, or EGCG. In addition, many botanical DSs contain flavonoids. More than half of the top 100 DSs reported by the Nutrition Business Journal (NBJ, 2012), based on volume of sales, are botanical supplements containing one or more flavonoid ingredient. Flavonoids are divided into subclasses including flavonols, flavones, flavanones, flavan-3-ols, anthocyanidins, and isoflavones. The DSs most likely to contain high levels of flavonoids contain plant material or extracts from green tea, *Ginkgo biloba*, *Echinacea spp*, red clover, berries, wine, cocoa, citrus and soy. These studies are planned:

1. **Pilot Study: Catechins and caffeine in green tea DSs**
2. **Pilot Study: Flavonoids in botanical DSs**

Scientific Purpose: Assess methods of analysis by testing representative and top-selling products. Identify quantitative issues in extracts and mixed herbal blends and for various label formats and ingredient levels.

Plans: This study will be carried out in consultation and collaboration with Food Composition and Methods Development Laboratory, BHNRC and other contracted laboratories. A sampling plan will be developed. Products will be purchased locally and from direct channels. Products with a single ingredient, with multiple ingredients and with labeled and unlabeled ingredient levels will be analyzed. Pilot studies for the DSID typically include multiple lots of 40-60 products.

1. **National Study: Catechins and caffeine in green tea DSs**
2. **National Study: Flavonoids in botanical DSs**

Scientific Purpose: In a national study, examine the relationship between labeled level (if available), other label factors and analytical levels of ingredients of interest in these DS botanical product/ingredient categories.

Plans: A national sampling plan will be developed and representative products purchased for analysis. National studies for the DSID typically include multiple lots of 60-125 products. Criteria for the products to be purchased, ingredients to be analyzed and methods for sample handling and analysis will be established from the pilot study. Analytical results will be statistically evaluated for ingredient level information that would be useful to researchers and published in DSID releases. NHANES and DSLD applications will be developed.