USDA Dietary Supplement Ingredient Database

Adult Multivitamin/mineral (AMVM-2009) Dietary Supplement Study

Research Summary

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1. Introduction

Nearly half of US adults report taking dietary supplements (DS) (1). A single serving of a DS may contain amounts of nutrients or other bioactive compounds that exceed their concentration in foods. During the manufacturing of DS, ingredients may be added in amounts exceeding the label claims in order to compensate for losses during shelf life. However, these amounts are not standardized for specific ingredients or among the different manufacturers. DSID pilot studies have also identified a number of ingredients in a variety of product categories with mean content below label claims. Thus, actual ingredient amounts are unknown to consumers and researchers. Epidemiological studies of nutrient intake and health currently use the manufacturer's label as the source of information on ingredient content in dietary supplements.

In order to provide a tool to more accurately estimate intakes from dietary supplements, an analytically validated database for high priority ingredients in dietary supplement products has been developed. The Dietary Supplement Ingredient Database (DSID; https://dsid.usda.nih.gov) is a collaboration of the Agricultural Research Service (ARS)/ Nutrient Data Laboratory (NDL), and the National Institutes of Health (NIH)/Office of Dietary Supplements (ODS) with other federal partners (National Center for Health Statistics of the Centers for Disease Control and Prevention, Food and Drug Administration, National Cancer Institute of the National Institutes of Health and National Institute of Standards and Technology [NIST] of the Department of Commerce). ODS is the primary funder of the DSID, which builds on the well-recognized strengths of the NDL in developing databases that support assessments of intakes of nutrients from foods. For national DSID studies, representative supplement products are purchased and tested by experienced laboratories for their ingredient content.

2. Overview of the Adult Multivitamin/mineral (MVM) study

A study of adult MVMs (dietary supplements containing three or more vitamins with or without minerals or other bioactive components) was conducted to estimate the relationship between label values and analytical values for 18 vitamins and minerals.

Products identified as representative of the US market were purchased from nationwide retail outlets and through direct-to-consumer sales channels. Samples of multiple lots of these products were sent to qualified laboratories for the analysis of ingredients using validated methods and appropriate quality assurance measures. The final analytical dataset was statistically analyzed using regression techniques to estimate relationships between label claims and analytically measured ingredient content at a range of label levels. These study results and their National Health and Nutrition Examination Survey (NHANES) application tables were **originally released in 2009** and have been updated in DSID-2 in 2012 and DSID-3 (http://dsid.usda.nih.gov) in 2015. For more information, please visit the DSID Release History page.

3. Sampling Plan

A national sampling plan for adult MVMs was developed to identify and purchase dietary supplement product samples that represent the US market. A national sampling of adult MVMs was conducted for two purposes:

- To provide representative estimates for ingredients in products commonly reported by the US population (top market share [TMS] products).
- To obtain additional data on lower-market share (LMS) products identified as representative and purchased in different regions of the country.

Information on frequency of intake (market share estimate) for reported supplements was derived from the 2001-02 NHANES dietary supplement data files, which are population weighted to indicate reported usage trends. Adult MVM products were defined in NHANES as “standard and mature formulations” (indicating that they were designed for adults and seniors) and containing three or more vitamins, with or without minerals or other bioactive components. Information about the most commonly purchased adult MVMs was verified and updated based on nationally representative market data provided by an independent marketing firm. In addition, supplement use information from the Multiethnic Cohort study of supplements that adults reported using in Hawaii and California conducted in 2005-06 (2) and from the *Nutrition Business Journal Supplement Business Report* (3) was reviewed. Supplement use information from all of these sources was combined so that products currently on the market would be included along with products that respondents commonly reported using in national surveys.

Thirty-five products were identified as TMS products, representing over 55% of the market share of adult MVM products reported in the United States. Samples (n=210) of the retail products were purchased in six US states (California, Georgia, Maryland, Minnesota, Texas and Virginia) from a variety of retail channels, including mass merchandisers (e.g., Safeway, Target and Wal-Mart) and natural/ specialty stores (e.g., Whole Foods and GNC). In addition, some products were purchased from direct marketers (e.g., Amway, Herbalife, or internet-based retailers).

LMS adult MVM products were identified using NHANES 2003-04 dietary supplement data. LMS adult MVM products were defined as products with a market share below that of the TMS products. Samples of approximately 80 representative LMS products were obtained from various market channels, including mass merchandisers, natural/ specialty stores and direct marketers. Retail products were purchased in the same six geographic locations as the TMS products.

The TMS and LMS products analyzed for this study were purchased in 2006-07. The analytical content of vitamins and minerals for up to six lots of each TMS product and up to three lots of each LMS product was measured in 2007-08.

4. Laboratory Analysis and Quality Control

The purchased products were sent to NDL for processing. Relevant information on each product purchased (e.g., ingredient names and levels, lot number, purchase location and date, and expiration date) was recorded in NDL's in-house database. Samples were repackaged and sent for laboratory analysis in defined batches. Each product sample sent to labs contained at least 20 units (tablets, capsules or liquid serving amounts) of the MVM product. Labs were instructed to homogenize at least 20 sample units before sub-sampling for analysis (per the United States Pharmacopeia (USP) recommendations for the analysis of dietary supplements).

Qualified analytical contract laboratories analyzed the sample sets using validated sample-handling protocols and appropriate methods to obtain analytical information about ingredient levels (Table 1).

Table 1. Analytical Methods

Nutrients	Analytical Method Used
Calcium Copper Iron Magnesium Manganese Phosphorus Potassium Zinc	Multi-element inductively coupled plasma spectrometry after wet ashing
Selenium	Hydride generation/atomic absorption spectroscopy
Iodine	Thiosulfate titration
Niacin Riboflavin Thiamin Vitamin B6 Vitamin C	High-performance liquid chromatography (HPLC) with ultraviolet detection
Folic acid Vitamin B-12	Microbiological methods
Vitamin E	HPLC with fluorescence detection

Some data were received for vitamin A (beta-carotene and retinol), vitamin D and chromium, but concerns about methodological issues prevent the reporting of final data for these ingredients. Laboratory methods for these ingredients have improved since 2007-08, and national estimates for these ingredients are reported for children's MVMs in DSID-3. NDL's monitoring study of adult MVMs, which began in 2012, will provide data for these ingredients in DSID-4.

Quality control (QC) materials were added to each batch of adult MVM products to evaluate laboratory precision and accuracy on an ongoing basis. NIST Standard Reference Material (SRM) 3280, an MVM matrix with certified values for vitamins and minerals, was also sent in each batch to monitor laboratory measurement accuracy. In addition, each batch included a set of product duplicates (two sets of 20 tablets of the same MVM product with different test sample identification numbers) that were analyzed for all ingredients in the study and at least two in-house control materials. For each in-house control material, a case of a single lot of an adult MVM product was purchased. These control materials were added to each batch to evaluate the precision of laboratory methods over time in a similar product matrix.

Analytical retests for ingredients in specific products were conducted to check unusually high or low results, high variability among product lots, and questionable data in batches where QC results showed a bias. For each sample analyzed, laboratory results reported in mg/g or µg/g were compared to label levels and a percent difference from the label levels was calculated.

5. Statistical Analysis

Ingredient data from laboratory analysis were prepared for weighted regression analysis by applying market share estimates as product weights. Market share estimates were based on data from NHANES and from an independent marketing firm, as previously discussed in Section 3. To identify overly influential supplement observations, a jackknife technique was used to calculate Cook's distances and restricted likelihood distances.

Relationships between the label and percent difference from label across the range of label levels analyzed were estimated by regression with SAS® mixed model procedure. For each supplement ingredient, the label value was the independent variable and the percent difference from the label level (based on the laboratory analysis) was the dependent variable. Percent differences from label were calculated: ((analytical value – label value)/label value) × 100%. The selected regression equations were used to predict mean analytical levels for each ingredient in adult MVMs: label value × (1 + predicted percent difference/100). In the DSID files, these mean predictions are shown in application tables as predicted percent differences from the label level or as predicted values in international units (IU), mg, or µg per serving.

In addition, the standard error of the mean (SEM), 95% confidence intervals (CI) for the mean, and the standard error (SE) of an individual observation were calculated at each label level. Because the regression equation could be used to predict ingredient values of independent supplement samples, SE were adjusted to reflect this expected greater prediction variability.

6. Results

Detailed results for this study, including all regression equations and applications to NHANES dietary supplement data files, are listed in the data files released in the DSID. Regression results are reported for 18 vitamins and minerals: folic acid, niacin, riboflavin, thiamin, vitamin B-12, vitamin B-6, vitamin C, vitamin E, calcium, copper, iodine, iron, magnesium, manganese, phosphorus, potassium, selenium and zinc. Regression results for mean predicted percent differences from the label amount and the associated SE varied by ingredient and, in some cases, by ingredient level.

The regression results and SEM for the most common label level for each ingredient in the adult MVM study are summarized in Tables 2 and 3 below. Table 2 lists the predicted mean percent difference from the label level for vitamins, and Table 3 does the same for minerals. If a linear or quadratic regression model was selected, a range of label levels was predicted. If a means model was selected, the predicted mean percent difference was not dependent on the label level.

Table 2. Predicted Mean Values for Vitamins in Adult MVMs

Ingredient	Range of Predicted Mean Percent Differences from Label Levels	Most Common Label Level per Serving	Predicted Mean Percent Difference at Most Common Label Level	Predicted SEM at Most Common Label Level
Folic acid	13.2%	400 mcg	13.2%	1.6%
Niacin	1.5%*	20 mg	1.5%*	1.3%
Riboflavin	12.6%	1.7 mg	12.6%	2.5%
Thiamin	-6.5% to 8.6%	1.5 mg	-6.4%	1.7%
Vitamin B-12	9.0%	6 mcg	9.0%	2.2%
Vitamin B-6	-3.5% to 21%	2 mg	4.9%	1.8%
Vitamin C	8.38%	60 mg	8.38%	1.0%
Vitamin E	5.4%	27 IU	5.4%	1.1%

* Not significantly different from label

Table 3. Predicted Mean Values for Minerals in Adult MVMs

Ingredient*	Range of Predicted Percent Differences from Label Levels	Most Common Label Level per Serving	Predicted Percent Difference at Most Common Label Level	Predicted SEM at Most Common Label Level
Calcium	7.1% to 29.3%	162 mg	14.1%	1.9%
Copper	9.0%	2 mg	9.0%	1.6%
Iodine	26.2%	150 mcg	26.2%	2.1%
Iron	-0.5% to 16.4%	18 mg	0.93%	0.9%
Magnesium	3.35%	100 mg	3.35%	0.8%
Manganese	6.25%	2 mg	6.25%	0.8%
Phosphorus	8.13%	109 mg	8.13%	0.9%
Potassium	8.7%	80 mg	8.7%	1.5%
Selenium	24.6%	20 mcg	24.6%	1.8%
Zinc	-1.9% to 8.1%	15 mg	4.39%	0.6%

These results show that nine ingredients (niacin, vitamin B-12, vitamin C, vitamin E, copper, magnesium, manganese, phosphorus and potassium) had predicted mean percent differences from label levels of between 0% and 10% above label level at the most common label level and across the entire regression range. For four ingredients (thiamin, vitamin B-6, zinc and iron), predicted percent differences from label levels ranged from slightly below (-6.5% to -0.5%) to 8.1% to 21% above label level across the regression ranges. For riboflavin and folic acid, predicted percent differences were approximately 13% higher than label level for all label levels analyzed. For calcium, the predicted percent differences from label levels ranged from 7% to 29.3% higher. For two ingredients (iodine and selenium), the predicted percent difference from label levels was well above label level (26.2% and 24.6%, respectively) for all levels reported. One ingredient, thiamin, had predicted means slightly below label level for the regression range representing a majority of products. At the most common label level, 1.5 mg/serving, the mean analytical content was predicted to be 6.4% below label level.

7. Use of DSID data

The regression equations for the adult MVM-2009 study predict the mean percent differences from label levels for 18 ingredients in dietary supplements consumed in the United States. The predicted amounts are linked to label levels for each ingredient and are not specific to any brand or supplement. These predictions (predicted mean values) are intended for research purposes and are not meant to provide analytical estimates for ingredients in individual products.

The predicted SEM is the SE for this mean prediction. The regression equations also estimate the SE for an individual sample at specific label levels. The SE and 95% CI for an individual observation are much larger than the SEM and 95% CI of the means because they represents the error of prediction for an individual product vs. the error of prediction of a mean value for many products.

Results predicted by regression for the mean percent difference from label level and the SE have been assigned linking codes that may be applied to NHANES DS data files or used for other studies of DS intake. The predicted analytical content from the DSID can be used to replace information from labels to more accurately assess ingredient intakes from dietary supplements in *large* population surveys.

Documentation about the DSID-4 data files and instructions for appropriate use of the files are described in the report, *DSID-4 Data File Documentation,* available on the "Data Files" page of the website. Please refer to that report for additional information on how best to interpret and use each data file.

An online, interactive, *Adult MVM-2009 Calculator* is available on the DSID website. This calculator allows the user to enter ingredient information from MVM labels and generate the appropriate predicted mean values, SE and CI at those label levels.

9. References

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