

USDA Dietary Supplement Ingredient Database Release 3.0 (DSID-3)

Background and Pilot Study Information

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1. Introduction

The Dietary Supplement Ingredient Database (DSID) evaluates levels of ingredients in dietary supplement products. The Nutrient Data Laboratory (NDL), Beltsville Human Nutrition Research Center, Agricultural Research Service, US Department of Agriculture (USDA), developed the DSID with the Office of Dietary Supplements (ODS) of the National Institutes of Health (NIH) and other federal partners. The other partners are the National Center for Health Statistics of the Centers for Disease Control and Prevention, Food and Drug Administration, National Cancer Institute of NIH 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.

The goals for the DSID are to:

- Develop analytically derived estimates of ingredient content and its variability for vitamins, minerals and other bioactive components in dietary supplement products
- Report analyzed levels of ingredients relative to label values, if available
- Support improved dietary intake assessments in research by providing analytical estimates of the ingredient content of marketed dietary supplements
- Release and maintain a publicly available, online composition database for dietary supplements

The DSID gives researchers and health-care professionals access to information on analytically validated levels of ingredients in a variety of dietary supplements, including multivitamin/mineral (MVM) products, single-ingredient products, fish and plant oil products containing omega-3-fatty acids and botanically based supplements.

The Dietary Supplement Health and Education Act of 1994 defines a dietary supplement as:

- A product (other than tobacco) that is intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients
- Intended for ingestion in pill, capsule, tablet, or liquid form
- Not represented for use as a conventional food or as the sole item of a meal or diet
- Labeled as a "dietary supplement"

A. Prioritization of Supplements for the DSID

In 2004, the consortium of federal agencies listed above determined the priorities for the types of dietary supplement products and the ingredients of public health and research interest to include in the DSID. The product types were initially prioritized based on reports of dietary supplement consumption in 1999-2000 National Health and Nutrition Examination Survey (NHANES; dietary supplement data files). NHANES provides information obtained from nearly 5,000 individuals annually, including food intake records collected in two 24-hour dietary recall reports plus reported dietary supplement intake over the previous month (and within the past 24 hours, in the most recent cycles of the survey).

To set priorities for ingredient analysis, dietary supplement ingredients were ranked using the following factors: population exposure based on frequency of reported use, NIH research interest, availability of valid analytical methods and measurement capabilities and public health importance (Dwyer et. al., 2006). These factors were scored and then weighted to reflect their relative importance. The sums of the weighted scores were then rank-ordered to yield a priority list.

Adult MVM products were identified as a top priority for the DSID because they are the most commonly reported dietary supplements in NHANES. Other high-priority supplement product categories identified for initial chemical analysis due to their high weighted frequency of use in NHANES were children's and prenatal MVMs; calcium supplements; and products containing vitamin E, vitamin C and B-vitamins. Ingredients of lower priority will be considered for study in the future (Dwyer et al., 2007). For DSID studies, MVMs are defined as supplements containing three or more vitamins, with or without minerals or other bioactive components.

2. Pilot Studies

A. Laboratory and Analytical Methods Pilot Study

The goals of this pilot study were to identify key challenges in dietary supplement sampling and sample handling, to evaluate analytical methods and to identify laboratories qualified to analyze dietary supplements. The ingredients selected for analysis were folic acid, vitamin C, vitamin A (retinol and beta-carotene), vitamin E (alpha-tocopherol), calcium, iron, riboflavin, thiamin, niacin, vitamin B-6, vitamin B-12, vitamin D, phosphorus, potassium, copper, selenium, chromium, manganese, magnesium, zinc and iodine.

Four commercial or academic laboratories analyzed each high-priority nutrient in two MVM products five times over several months. One of the products was NIST Standard Reference Material (SRM) 3280, a MVM supplement matrix (under development at the time of the study, 2005-06). The mean content and its measured variability for each nutrient in each laboratory were reviewed, compared to the preliminary NIST results and presented to a federal working group for final review. These assessments for

acceptable laboratory and method variability continue to be performed for each new DSID study.

Research Findings

The expert federal working group concluded that the method variability identified was appropriate and that the laboratories selected were qualified for future DSID analyses. These pilot study findings have been published (Roseland et al., 2008).

B. Adult MVM Common Level Pilot Study

The adult MVM common level pilot study had the following objectives:

- determine whether consistent relationships exist between label and analytical values for nutrients
- assess nutrient variability between the products with up to four of the most common label levels for each priority vitamin and mineral
- evaluate usefulness of nutrient variability assessment based on the most common labels for planning future studies

To identify the most common label levels for high-priority vitamins and minerals in adult MVMs, the NHANES 2001-02 data was researched. The nutrients evaluated were vitamins C, E, B-6, B-12, folic acid, niacin, riboflavin, thiamin, calcium, iron, copper, iodine, magnesium, manganese, phosphorus, potassium, selenium and zinc. Based on the MVM definition, 541 supplements were identified as adult MVM products. The market share for each product was estimated using NHANES information and applied to that product's labeled ingredients. The estimated market share for each labeled level within each ingredient was then calculated and distribution graphs were evaluated. In most cases, three or four label levels were most common per ingredient for adult MVMs. The most frequent common level for many of the vitamins and minerals was at 100% of the Daily Value.

Representative adult MVM products with ingredients at these three or four most common levels were identified for analysis with a sampling plan using a probability-proportional-to-size approach (in this case, proportional to estimated market share). A total of 219 different MVM products were purchased from local retail outlets, including six products from each common level for each ingredient.

After being purchased, products were repackaged and sent to analytical laboratories in defined batches for the analysis of 8 vitamins and 10 minerals. Quality control (QC) materials, including SRMs, blinded duplicates and in-house control materials, were added to each batch of samples for the evaluation of laboratory precision and accuracy. Qualified analytical contract and academic laboratories analyzed the sample sets using validated sample-handling protocols and appropriate methods to obtain analytical data on levels of nutrients in adult MVM supplements. Most of the vitamins were analyzed by high-performance liquid chromatography methods and most of the minerals were analyzed by inductively coupled plasma spectrometry techniques. Six products at each common level were analyzed; over 500 nutrient analyses were completed.

The analysis of pilot study results focused on comparing analytical results to labeled nutrient levels. Laboratory results were statistically evaluated for each nutrient (typically n=18 or 24) at each of the (usually three or four) common levels.

Research Findings

For 12 nutrients analyzed in this study (magnesium, iron, niacin, zinc, phosphorus, potassium, calcium, manganese, thiamin, vitamin B-6, vitamin C and riboflavin), the mean differences from label level and standard deviation were both less than 10%. These findings indicated that the analytical results for these nutrients in MVM products were consistently close to label levels across the common levels evaluated. One ingredient, selenium, had a mean analytical level that was more than 20% higher than the label level, and analytical levels were significantly different from all label levels analyzed. Results were more variable for the five other vitamins and minerals studied (copper, folic acid, iodine and vitamins B-12 and E).

In addition to evaluations of the analytical results for this study, the product sampling, laboratory methods and QC plan were assessed. Because only one lot of each product was purchased, questions about the results could not be answered by analyzing a sample from a second lot. It was unclear whether low or high percent differences from label levels were accurate or resulted from a laboratory error. More importantly, it became clear that distributing the number of products evenly across three or four levels was not the best way to produce data that could be extrapolated to the whole population.

With this approach, label levels representing more than 25% of the total market share were not analyzed for 13 of the 18 vitamins and minerals. In addition, for 14 of the ingredients tested, the most common label level represented over 50% (and sometimes over 80%) of the market share. Only six of 18 or 24 products were purchased and analyzed at this label level. In order to analyze a more representative selection of nutrients in adult MVM products, it was concluded that analyzing representative products would be a better approach than a common level approach.

For this study, QC was evaluated by batch. If the QC results for a batch were acceptable, the entire set of data was accepted. If the QC results were unacceptable, the entire batch was reanalyzed. This approach led to the identification of a few systemic problems for a few nutrients. However, the approach did not take into account random laboratory errors, including dilution or calculation errors for specific samples.

This pilot study provided important information about best practices for sampling and analysis of dietary supplements for the DSID and facilitated development of a comprehensive analytical study of adult MVMs.

C. Caffeine Pilot Study

To gather some preliminary information on the prevalence of caffeine in selected dietary supplements, the NDL conducted a pilot study to identify representative dietary supplement products containing caffeine and determine their analytical caffeine content (Andrews et al., 2007). This study was designed to provide a snapshot of the products currently sold in the United States. The products identified for analysis were predominantly sports-performance and weight-loss supplements which represent the segment of the dietary supplement market whose products are most likely to contain caffeine.

Caffeine-containing dietary supplements were identified based on labels listing one or more of the following ingredients: caffeine, citrus aurantium, cocoa, green tea, guarana, kola, or yerba mate. The products analyzed were selected based on the estimated market share for three sales channels determined from *Nutrition Business Journal* report (NBJ, 2004) and information provided by ACNielsen (Schaumburg, IL, USA):

- Natural/specialty retailers (e.g., Whole Foods and GNC, accounting for 30.1% of the dietary supplements market)
- Mass merchandisers, including supermarkets and drug stores (25.4% of the market)
- Direct-to-consumer sales, including multilevel marketers (e.g., Amway and Herbalife), internet vendors and health-care practitioners (44.5% of the market)

Approximately 50 dietary supplements sold in all of these channels were purchased and analyzed for their caffeine content. Two to three lots of each product were purchased over nine months.

An independent laboratory with experience in caffeine analysis and botanical matrices analyzed the caffeine content in the dietary supplements. QC measures, including analyses of standard reference materials (SRMs), were implemented. Two SRMs were analyzed with each batch of supplements. One SRM, NIST SRM 3243 (ephedra-containing solid oral dosage form), was a diet pill mixture with a certified level of 76.5 mg/g caffeine. The other SRM, NIST SRM 3244 (ephedra-containing protein powder), was a cocoa-protein powder with a certified level of 2.99 mg/g caffeine. Analytical caffeine values for both reference materials were within the certified range of the materials, indicating acceptable accuracy and precision for the product results.

Results were calculated in mg caffeine/day because label instructions varied widely among the products (from one tablet per day to four tablets three times a day).

Research Findings

For all 53 products, product mean content ranged from 0.07 to 307 mg caffeine/tablet and 1 to 829 mg caffeine/day. According to the USDA food composition database (USDA, 2011), one cup of brewed coffee contains approximately 95 mg/caffeine. When this value was used as a reference, the 53 products analyzed provided a range of

caffeine levels that corresponded to the caffeine levels in up to eight cups of brewed coffee/day.

Daily caffeine intakes from the dietary supplement products analyzed in this study ranged from 1 mg to greater than 800 mg, if taken at maximum recommended dosages. For most (89%) of the caffeine-containing dietary supplements that listed a level of caffeine on the label, the mean analyzed level calculated on a per-day basis was similar (within 20%) to the label amount. Most products (72%) had a lot-to-lot variability of less than 10%.

Many consumers may not realize that in the United States, dietary supplement products may contain caffeine in proprietary blends or from botanical sources (e.g., cocoa, green tea extract, guarana, kola nut, or yerba mate) even if caffeine is not listed as an ingredient on the label.

3. Studies of Nationally Representative MVMs

After the completion of these pilot studies, three studies were completed to estimate the mean analytical content and variability of ingredients in adult, children's and nonprescription prenatal MVM dietary supplements. The study of adult MVMs estimated the relationships between label and analytical values for 18 vitamins and minerals in adult MVMs representative of the US marketplace. For more information about this study, please read the 'Adult MVM Research Summary', available on the DSID-3 website. Updated statistical results for this study and NHANES application tables were released in DSID-3 in 2015.

The study of children's MVMs assessed the relationships between label and analytical values for high-priority vitamins and minerals in products representing the US market. For more information about this study, please read the 'Children's MVM Research Summary', available on the DSID-3 website. Updated statistical results for this study and NHANES application tables were released in DSID-3 in 2015.

A study of non-prescription prenatal MVM products assessed the relationships between label and analytical values for high-priority vitamins and minerals in products representing the national market. For more information about this study, please read the 'Non-prescription Prenatal MVM Research Summary', available on the DSID-3 website. Statistical results for this study and NHANES application tables were reported for the first time in DSID-3 in 2015.

4. References

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