USDA Dietary Supplement Ingredient Database Release 4.0 (DSID-4)

Green Tea Dietary Supplement Pilot Study

Research Summary and Results

Prepared by

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1. Introduction

The Dietary Supplement Ingredient Database (DSID) reports levels of ingredients in dietary supplement (DS) products based on chemical testing. The Methods and Application of Food Composition Laboratory (MAFCL), Beltsville Human Nutrition Research Center, Agricultural Research Service (ARS), US Department of Agriculture (USDA), developed the DSID with the Office of Dietary Supplements (ODS) of the National Institutes of Health and 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 ARS in developing databases that support assessments of intakes of nutrients from foods.

The DSID provides analytically-derived estimates of the ingredient content in DS commonly sold and purchased in the US. DSID 4.0 includes estimates of ingredient content in 4 categories of DS: adult, children's and non-prescription prenatal multivitamin/mineral products (MVM) and omega-3 fatty acid DS. These mean estimates can replace label information in studies assessing the dietary intake of the US population from foods and DS.

According to the 2007-10 NHANES, 7.5% of the United States population reports taking botanical DS (the 4th most common supplement type reported). A single serving of a botanical extract may provide amounts of bioactive components (e.g., flavonoids) equal to or significantly exceeding their daily intake from foods. However accurate intake estimation of ingredients is difficult. The DS label information is not sufficient because of the way DS are manufactured and regulated.

Supplement labels may provide only partial information about the actual content of bioactive components in botanicals. For botanicals, current label regulations require information on the total weight of each botanical or botanical extract present in a DS. Label information on the ingredient concentration or standardization of extracts is not required However, many extracts are microencapsulated with maltodextrin or other powdered material (extracts are sprayed into a fine powder and coated) and thus total weight of these extracts will also include the weight of the coating material. Although some companies voluntarily list information about the concentration of phytochemical constituents, many do not. For researchers to more accurately estimate the phytochemical intakes from botanicals, analytical testing is necessary to determine ingredient actual concentration and amount in the products.

A botanical initiative for the DSID is now underway to evaluate levels of ingredients and ingredient constituents in botanical DS. The DSID Working Group identified non-vitamin/mineral bioactive ingredients in DS for analysis and inclusion based on these criteria: public exposure (intake and sales), the availability of validated analytical

methods and analytical reference materials, research interest and economic and safety concerns. The top scoring 11 ingredients from this ranking process were: CoQ10, garlic, saw palmetto, ginkgo biloba, glucosamine, ginseng, green tea catechins (EGCG and other catechins), milk thistle, echinacea, flaxseed, and turmeric (curcumin).

Green tea botanical supplements were chosen for initial study. Pilot studies are evaluating ingredient and constituent levels by testing representative and top-selling products for prioritized ingredients of interest. The analytical data are being compared to label claims.

2. Overview of the green tea dietary supplement study

Green tea is a botanical product that is commonly consumed and frequently studied for its health benefits and thus was chosen as the first botanical for the DSID. Since the botanical constituents in GT are also commonly found in foods and beverages, the data from these studies will complement the data on the phytochemical intake from foods.

The major goal of the pilot study was to analyze representative and top-selling products to obtain information about the content and variability of individual catechins and caffeine in GT DS. Three experienced laboratories were chosen for participation. Seven catechins (including (+)-catechin, (–)-epicatechin, (–)-epicatechingallate, (–)-epigallocatechin, (–)-epigallocatechingallate (EGCG), (–)-gallocatechin, (–)-gallocatechingallate) and caffeine were measured in a variety of green tea supplements. Three NIST green tea Standard Reference Materials® (SRMs) were sent for analysis with product samples in order to evaluate the accuracy and precision of the laboratory methods. The ingredient data for 2 lots of 32 green tea DS were combined for each product and the mean results compared to label information, if available.

3. Sampling Plan

A sampling plan was developed to identify representative products for purchase and analysis. The scope and variety of GT DS reported in NHANES 2009-2010 and the Office of Dietary Supplement Dietary Supplement Label Database (DSLD; https://dsld.nlm.nih.gov/dsld/) were evaluated for information about GT composition, component levels and health claims. In addition, we conducted a detailed survey of GT products sold via various channels including local stores, the internet and multi-level marketing companies in 2013-14.

The first GT study was limited to products containing GT in a relatively simple matrix (products with green tea as the only ingredient or with green tea as the primary ingredient with no other botanicals), to minimize interferences for analytical results and to compare to label claims for GT components.

Products with a wide range of dosage forms were purchased: hard-shell capsules, softgels, tablets, caplets (smooth-coated tablets), liquids and powders. Two lots of each

product (n=32) were purchased from the three major sales channels: mass market retail (e.g., Walmart, CVS, Target), natural and specialty retail (e.g., GNC or Whole Foods), and direct sales (products sold exclusively via the web or by multi-level marketers like Amway or Herbalife). Two DS were purchased in bulk for use as in-house control materials to monitor laboratory performance over time. Samples were repackaged and sent for laboratory analysis in defined batches.

4. Laboratory Analysis and Quality Control

Laboratories analyzed the sample sets using validated sample-handling protocols and appropriate methods to obtain analytical information about ingredient levels. For the catechin monomers, high-performance liquid chromatography (HPLC) using a reversed phase column with either ultraviolet absorbance (UV) or mass spectrometric (MS) detection was used. For caffeine, HPLC with UV detection was used. Samples were sent for retesting if there was a large discrepancy among lab results or to confirm unusually high or low values.

Quality control (QC) materials, including three certified reference materials (NIST® SRM® 3255 “Green Tea Extract”, 3254 “Green Tea Leaves” and 3256 “Green Tea Solid Oral dosage”) were analyzed with each batch of samples to evaluate laboratory precision and accuracy. In addition, product duplicates and in-house control materials were included. The consistent results seen in the catechin and caffeine values for these quality control materials gave confidence in the results for these constituents in the commercial GT DS under study.

5. Statistical Methods

The final laboratory data reported by the three laboratories for two lots of each product were statistically evaluated. Least squares means and standard deviations (SDs) were computed for each product using a mixed model procedure. Results for EGCG (the most prevalent catechin), total catechins (TC) and Caffeine (Caf) are reported as “amount per serving”, “amount per day” and “percent difference from label”, if applicable.

Data are reported for this study as per serving (**Table 1**) and per day (**Table 2**). The most useful comparison of content among GT DS products is accomplished by using per day amounts rather than per serving because, for many products, the label recommends more than one serving per day. Of the thirty-two products included in this study twenty had a suggested use of more than on serving per day. Suggested use was one serving per day for twelve products, two servings per day for fourteen products and three servings per day for six products. Analytically measured amounts for catechins and caffeine in green tea are reported as mg/serving and as mg/day in order to facilitate accurate comparisons between GT DS products. The suggested use for some products was a range of servings per day (for example, 1-2 servings per day). In this case the maximum servings per day was used to calculate per day amounts.

6. Results and Discussion

The product based mean values for analytically measured concentrations of EGCG, total catechins, and caffeine showed wide ranges (0.5-562, 1.4-1070, and 0.1-130 mg/serving, respectively; Table 1**,** page 7). Median per serving values for product based EGCG, total catechin, and caffeine content were 113, 205, and 11 mg/serving, respectively. The product based analytical mean per day ranges for EGCG, total catechins, and caffeine were (2.0-630, 4.2-1070, and 0.25-130 mg/day, respectively; Table 2**,** page 8). Median per day values for EGCG, total catechin, and caffeine content were 141, 280, and 22 mg/day, respectively.

The labeled levels for the amount of GT in the 32 products (information required by FDA) ranged from 150-2000 mg/serving and 300-6000 mg/day. At the most commonly labeled level for GT material (500 mg/serving; n=9), the analytical mean values for total catechin ranged from 1.4 to 410.6 mg/serving, and from 0.5 to 314.8 mg/serving for EGCG.

For the 23 products that voluntarily provided label claims for total catechins, EGCG or caffeine, we compared the mean percent difference from labels with label claim. For the 18 products with EGCG label claims, percent differences from label ranged from 35% below label to 186% above label, with 10 products within ± 20% of label claim. For the 10 products with total catechin label information, the percent differences from label ranged from 36% below label to 45% above label and for the 9 products with a label claim for caffeine, the ranges were 84% below to 70% above label (**Table 3,** page 9).

Seven products contained green tea from two different sources. Five of these had a claim for EGCG, TC or Caf for only one of the sources (usually the green tea extract). Not surprisingly, the analytical results for these products are all above label claims (Table 3). The two liquid GT DS (GTP07; GTP11) had the lowest levels of total catechins of all the products (results: 1.4 and 10.8 mg/serving). The analytical content of eight products labeled as decaffeinated (or below 4 mg) averaged 2.9 mg/day (range 0.4-12).

In summary, the GT DS in the simple matrices analyzed in this study have a variety of label formats and a wide range of labeled amounts for GT. The information about the total weight of GT may not permit accurate predictions for the content of specific phytochemical constituents, because green tea extracts may or may not be highly concentrated and they are often microencapsulated (adds additional weight) for improved shelf life. Voluntary label information (e.g., listing amounts of EGCG or caffeine) is associated with a higher level of the actual phytochemical content, on average, compared to products without such information. The caffeine content in these products was usually low for a DS (<50 mg/day; n=28/32 products).

It is important to track the intake of phytochemicals, especially those that have intakes from foods and supplements to evaluate their health effects. In a recent evaluation of flavonoid intake in NHANES 2007-08 using the USDA Flavonoid Values for Survey Foods and Beverages 2007–2008 (Bhagwat and Haytowitz, 2015), the mean U.S. daily intake of flavonoids was estimated to be 251 mg (with 81% from catechins) (Sebastion, et. al, 2015). If you compare that number to the analytical results for total catechins in the GT DS studied, 19 products would provide more flavonoids per day than the average daily estimate of 251 mg from foods and beverages.

9**. Future Research**

A second GT pilot study (GT-2) is in progress to evaluate the content of catechins and caffeine in complex matrices that include several botanical ingredients along with minerals, vitamins and/or other compounds. These botanical products were marketed for the purposes of weight loss, increasing energy, sports performance or increasing intake of antioxidants or bioflavonoids. Approximately half of the 36 products listed a label claim for green tea on the label. The other half listed green tea as part of a blend (these products are not required to list the amounts of ingredients within a blend—only the weight of the total blend).

The efficacy of a DS is determined not only by the amount of one or more active ingredients but also by the design and performance of the formulations into which they are incorporated. Currently, we are studying whether commercially sold single- and multi-ingredient green tea dietary supplements meet the United State Pharmacopeia general chapter specifications for disintegration and dissolution for immediate release formulations.

9. References

Bhagwat, S., Haytowitz, D.B. 2015. USDA Database for the Flavonoid Content of Selected Foods, Release 3.2. U.S. Department of Agriculture, Agricultural Research Service. Methods and Application of Food Composition Laboratory Home Page: https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/methods-and-application-of-food-composition-laboratory/

Sebastion, Rhonda S, Wilkinson, Cecilia E, Goldman Joseph D, Martin Carrie L, Steinfeldt, Lois C, Murayi, Theophile, and Moshfegh, Alanna J. 2015. A New Database Facilitates Characterization of Flavonoid Intake, Sources, and Positive Associations with Diet Quality among US Adults. J Nutr 145:1239–48.

Table 1. EGCG, Total Catechin and Caffeine in 32 Green Tea DS: label claims and measured amounts per serving

Product ID	Form	Matrix	Amount of GT	EGCG (mg/serving)			Total Catechin (mg/serving)			Caffeine (mg/serving)		
			mg/serving									
			Label	Label	Measured	SD	Label	Measured	SD	Label	Measured	SD
GTP01	powder	GT leaf	1000	83	54.2	6.8	179	115	11	25	17.9	0.7
GTP02	capsule	GTE[&]	300	-	134	5.5	150	218	7.5	24	3.76	0.1
GTP03	capsule	GTE	600	180	225	14	360	384	24	36	40.9	2.4
GTP05	capsule	GTE, GT leaf	1565	50	143	9.9	-	265	24	30	51.2	5.8
GTP06	capsule	GTE	500	75	113	4.2	150	207	7.5	Decaf	2.08	0.2
GTP07	liquid extract	GTE	500	-	0.512	0.2	-	1.39	0.3	-	1.3*	0.2
GTP08	capsule	GTE	630		27.6	1.3	-	58.4	3.1	-	32.9	2.2
GTP10	capsule	GTE	500	225	234	2.7	375	391	5.6	-	10.8	0.2
GTP11	liquid extract	GTE	2000	-	4.25	2.2	-	10.8	4.8	-	9.0*	0.02
GTP12	capsule	GTE	150	19.5	50.5	1.2	-	96.0	3.7	Caffeine Free	1.62	1.2
GTP13	capsule	GTE	696	-	165	19	-	283	46	-	14.3	7.1
GTP14	capsule	GTE	500	350	315	17	-	411	15	Decaf	0.406	0.05
GTP15	capsule	GTE	725	326	339	15	-	623	23	Decaf	3.15	0.4
GTP17	capsule	GTE	687.5	275	297	15	-	506	34	-	0.928	0.1
GTP18	capsule	GTE, GT leaf	450	137.5	171	2.6	187.5	246	6.8	Low Caf (not decaf)	5.76	0.3
GTP19	capsule	GTE	500	-	74.5	5.0	125	146	6.6	35	41.0	10.4
GTP20	capsule	GTE, GT leaf	450	200	227	5.7	320	386	7.5	Decaf (up to 4 mg)	1.57	0.2
GTP21	capsule	GTE, GT leaf	470	75	98.4	1.8	-	165	3.1	-	13.2	4.6
GTP22	capsule	GTE	630	-	20.8	0.9	-	56.0	3.2	40	17.7	1.3
GTP23	capsule	GTE	300	39	39.7	1.3	-	67.7	2.8	Decaf	0.380	0.1
GTP24	capsule	GTE, caffeine	1500	525	562	27	1050	1069	57	120	130	9.4
GTP27	softgel	GTE, caffeine	250	-	73.4	7.3	-	155	8.9	65	41.1	2.3
GTP28	capsule	GTE	630	-	22.7	2.0	-	54.8	2.8	-	19.2	2.7
GTP30	capsule	GTE, GT leaf	500	-	66.2	2.0	-	149	24	32	36.5	1.9
GTP31	capsule	GTE	350	157	168	22	262	290	35	-	4.09	1.2
GTP32	capsule	GTE	750	-	21.2	1.7	-	45.0	6.2	-	20.9	5.8
GTP33	capsule	GTE	500	125	130	12		205	16	-	22.1	3.3
GTP37	tablet	GTE, mineral, GT leaf	333	90	133	9.5	-	222	19	-	13.5	1.8
GTP38	capsule	GTE	250	-	36.0	4.1	-	62.5	6.7	-	0.082	0.02
GTP39	capsule	GTE	500	-	139	1.4	-	254	2.5	-	4.9*	0.1
GTP40	capsule	GTE	500	350	314	4.9	-	406	5.3	Decaf	0.44	0.1
GTP43	capsule	GTE	250	-	42.2	11	-	90.3	4.6	-	14.2	11.9

[&]GTE = green tea extract

*Caffeine data were available only from two laboratories.

Table 2. EGCG, Total catechin and Caffeine in 32 Green Tea DS: label claims and measured amounts per day[#]

Product ID	Form	Matrix	Amount of GT	EGCG mg/day			Total catechin, mg/day			Caffeine, mg/day		
			mg/day									
			Label	Label	Measured	SD	Label	Measured	SD	Label	Measured	SD
GTP01	powder	GT leaf	1000	83	54.2	6.8	179	115	11	25	17.9	0.70
GTP02	capsule	GTE	600		268	11	300	435	15	48	7.52	0.23
GTP03	capsule	GTE	600	180	225	14	360	384	24	36	40.9	2.4
GTP05	capsule	GTE, GT leaf	1565	50	143	9.9		265	24	30	51.2	5.8
GTP06	capsule	GTE	500	75	113	4.2	150	207	7.5	Decaf	2.08	0.22
GTP07	liquid extract	GTE	1500		1.53	0.53		4.18	0.82	-	3.9*	0.6
GTP08	capsule	GTE	1260		55.3	2.7		117	6.2	-	65.7	4.4
GTP10	capsule	GTE	1000	450	468	5.4	750	781	11	-	21.5	0.43
GTP11	liquid extract	GTE	6000		12.7	6.7	-	32.3	14	-	27.0*	0.06
GTP12	capsule	GTE	300	39	101	2.3	-	192	7.5	Caffeine Free	3.25	2.4
GTP13	capsule	GTE	1392		330	39	-	565	93	-	28.6	14
GTP14	capsule	GTE	1000	700	630	34	-	821	31	Decaf	0.81	0.09
GTP15	capsule	GTE	725	326	339	15	-	623	23	Decaf	3.15	0.44
GTP17	capsule	GTE	1375	550	594	30	-	1012	68	-	1.86	0.28
GTP18	capsule	GTE, GT leaf	900	275	341	5.2	375	492	14	Low Caf (not decaf)	11.5	0.64
GTP19	capsule	GTE	500		74.5	5.0	125	146	6.6	35	41.0	10
GTP20	capsule	GTE, GT leaf	450	200	227	5.7	320	386	7.5	Decaf (up to 4)	1.57	0.22
GTP21	capsule	GTE, GT leaf	940	150	197	3.7	-	331	6.2	-	26.3	9.2
GTP22	capsule	GTE	1260		41.5	1.9	-	112	6.4	80	35.4	2.7
GTP23	capsule	GTE	300	39	39.7	1.3	-	67.7	2.8	Decaf	0.380	0.05
GTP24	capsule	GTE, caffeine	1500	525	562	27	1050	1069	57	120	130	9.4
GTP27	softgel	GTE, caffeine	750	-	220	22	-	466	27	195	123	7.0
GTP28	capsule	GTE	1260	-	45.3	3.9	-	110	5.7	-	38.4	5.3
GTP30	capsule	GTE, GT leaf	1000	-	132	3.9	-	298	47	64	73.0	3.8
GTP31	capsule	GTE	350	157	168	22	262	290	35	-	4.09	1.2
GTP32	capsule	GTE	1500		42.4	3.4	-	89.9	12	-	41.8	12
GTP33	capsule	GTE	500	125	130	12	-	205	16	-	22.1	3.3
GTP37	tablet	GTE, mineral, GT leaf	999	270	399	29	-	665	57	-	40.6	5.3
GTP38	capsule	GTE	750		108	12	-	188	20	-	0.246	0.05
GTP39	capsule	GTE	500		139	1.4	-	254	2.5	-	4.9*	0.1
GTP40	capsule	GTE	1000	700	628	9.7	-	812	11	Decaf	0.89	0.19
GTP43	capsule	GTE	750		127	34	-	271	14	-	42.5	36

[#]Per day values were calculated by multiplying per serving amounts by number of servings per day from the manufacturer suggested use given on the product label.
[&]GTE = green tea extract
*Caffeine data were available only from two laboratories.

Table 3. Mean percent differences from label for EGCG, Total catechin, and Caffeine in green tea DS

Product ID	Form	Matrix	EGCG		Total Catechin		Caffeine	
			Percent Differences from Label					
			mean	SD	mean	SD	mean	SD
GTP01	powder	GT leaf	-34.7	8.2	-36.0	6.4	-28.4	2.8
GTP02	capsule	GTE			45.1	5.0	-84.3	0.47
GTP03	capsule	GTE	25.0	7.8	6.67	6.6	13.5	6.5
GTP05*	capsule	GTE, GT leaf	186	20			70.5	19
GTP06	capsule	GTE	51.0	5.7	38.0	5.0	–	-
GTP10	capsule	GTE	4.10	1.2	4.20	1.5	-	-
GTP12	capsule	GTE	158	6.0	-	–	-	–
GTP14	capsule	GTE	-10.1	4.8	-	-	-	-
GTP15	capsule	GTE	3.96	4.5	-	–	-	-
GTP17	capsule	GTE	7.95	5.5	-	–	-	-
GTP18*	capsule	GTE, GT leaf	24.1	1.9	31.2	3.6	-	-
GTP19	capsule	GTE			16.9	5.3	17.0	29.8
GTP20	capsule	GTE, GT leaf	13.3	2.8	20.6	2.3	-	-
GTP21*	capsule	GTE, GT leaf	31.2	2.5	-	-	–	-
GTP22	capsule	GTE	-	-	-	–	-55.7	3.3
GTP23	capsule	GTE	39	1.9	–	–	-	-
GTP24	capsule	GTE, caffeine	6.97	5.1	1.83	5.5	8.58	7.8
GTP27	softgel	GTE, caffeine	-	–	-	-	-36.8	3.6
GTP30	capsule	GTE, GT leaf	-	-	-	–	14.1	6.0
GTP31	capsule	GTE	7.21	13	10.7	13	–	-
GTP33*	capsule	GTE	3.90	9.5	–	-	-	-
GTP37*	tablet	GTE, mineral, GT leaf	47.7	11	-	-	-	–
GTP40	capsule	GTE	-10.2	1.4	–	–	–	-

*These products contain more than one source of green tea, but label claims are based on one source only.