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# Catechins in Dietary Supplements and Hepatotoxicity

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## Abstract

**Background—**Green tea extract (GTE) and its component catechins are found in many herbal dietary supplements (HDS), some of which may not indicate their presence on the product label.

**Aim—**Because GTE and catechins have been implicated in human hepatotoxicity through several case reports, we aimed to determine whether catechins were present in HDS that were implicated in hepatotoxicity even if not identified among the labeled ingredients, and whether these compounds could be associated with liver injury.

**Methods—**We assayed 97 HDS implicated in human hepatotoxicity for catechins.

**Results—**We found that 29 of 73 HDS (39.7%) that did not identify GTE or any of its component catechins on their label contained catechins. Among the patients with confirmed hepatotoxicity, there was no statistically significant association between the presence of catechin or dose consumed and liver injury causality score, severity, or pattern of liver injury. Products used for weight loss tended to have the highest catechin levels, although catechin concentrations were low in most products.

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**Conflict of Interest/Disclosure**

**Victor J. Navarro, MD**- Rottapharm/Madaus – consultant, research support. **Herbert L. Bonkovsky, MD**- Lundbeck S/A:Consulting;Lundbeck S/A:Speaking and Teaching; Merck: Grant/Research Support; Clinuvel, Inc: Consulting; Clinuvel, Inc: Grant/Research Support; Vertex: Grant/Research Support; Amer Porphyria Foundation: Advisory Committees or Review Panels; Iron Disorders Institute: Advisory Committees or Review Panels; Iron Disorders Institute: Board Membership; **Sun-Il Hwang, PhD; Maricruz Vega, MPH; Huiman Barnhart, PhD; and Jose Serrano, MD, PhD**- no conflicts of interest

**Conclusions—**Catechins are commonly present in many HDS that are implicated in hepatotoxicity, even when not identified on the product label. Although our results did not establish an association between GTE or catechin with hepatotoxicity, they highlight some of the many complexities and uncertainties that surround to the attribution of DILI to HDS.

### Keywords

Green Tea extract; hepatotoxin; contamination; EGCG; hepatocellular jaundice

## Introduction

Herbal and dietary supplements (HDS) are commonly consumed in the U.S [1]. The current regulatory environment requires manufacturers to disclose the ingredients of products on the label, adhere to good manufacturing practices and to report serious adverse events when they are made aware of such occurrences [2]. However adulteration of HDS is commonplace and has been reviewed elsewhere [3]. Although products can be removed from the marketplace over concern of toxicity, the precise mechanism of injury or the ingredient within the product responsible for injury remains largely unknown. Even in the unusual circumstance of careful analysis for ingredients, a causal association between the suspected ingredient and the injury can remain elusive [4].

Green tea extract (GTE) is a frequent ingredient in a variety of HDS. It is marketed for health promotion and for its properties as an antioxidant and weight reducing agent. Catechins (CA) are polyphenolic flavonoid compounds that are contained in abundance in GTE. The major catechins include epicatechin (EC), epigallocatechin (EGC), epicatechin-3-gallate (ECG), and epigallocatechin-3-gallate (EGCG) [5]. Much is known about the animal and human pharmacology and toxicology of GTE and EGCG [6–12]. Importantly, several clinical reports of hepatotoxicity attributable to GTE and its component catechins exist in the literature [13–17].

Since GTE is such a common ingredient in dietary supplements, we hypothesized that catechins might sometimes be present in HDS that are associated with hepatotoxicity even when not identified among the ingredients on the package label. Therefore, our primary aim was to determine the catechin concentrations in HDS that were implicated in hepatotoxicity among patients who were enrolled into the U.S. Drug Induced Liver Injury Network (DILIN). As a secondary aim, we explored the relationship between the amount of catechin consumed and liver injury among confirmed cases of hepatotoxicity.

## Methods

### The Drug Induced Liver Injury Network (DILIN) and the Study Population

In 2003, the DILIN was established by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to collect and examine cases of *bona fide* non-acetaminophen drug and dietary supplement induced hepatotoxicity. The network began as five centers in 2003, and expanded to eight in 2008 [18]. Our study population was taken from the cohort of patients who presented to a DILIN investigator within six months of a drug or dietary supplement induced injury. Details of eligibility, data collection, and causality assessment procedures have been previously described [19]. *Confirmed cases* of DILI are those in which the likelihood of a causal association between the liver injury event and an implicated agent is either definite, highly likely, or probable, corresponding with probabilities of 95% or greater, 75–94%, and 50–74% likelihood of causality, respectively.

Each case of DILI is given a severity grade. These grades include mild (elevated liver enzymes and total bilirubin < 2.5 mg/dL and INR < 1.5), moderate (elevated liver enzymes with total bilirubin > 2.5 mg/dL or INR > 1.5), moderate-hospitalized, severe (fulfills moderate criteria and also has signs of hepatic failure or organ failure related to the DILI event), and fatal (patient dies or undergoes transplantation).

### Herbal Dietary Supplements

To facilitate studies of hepatotoxicity attributable to HDS, the DILIN established a repository for dietary supplements that were implicated in hepatotoxicity [20]. Products are obtained from subjects enrolled at any DILIN site and entered into the repository. Herbal and dietary supplements were assayed if consumed by any subject who fulfilled criteria for entry into the DILIN between 2004 and 2010. HDS were classified according to the intended purpose for use, as ascertained by patient reporting and/or packaging and marketing materials. Samples submitted for catechin assay were blinded to the investigators with regards to the original labeled ingredients.

### Catechin Assays

Catechins were extracted and quantified as described previously [21], and as detailed in the supplemental on-line material.

**Statistical Analysis—**Frequency and percentage are used to describe categorical data and mean and standard deviation are used to describe the continuous data. Chi-square test was used to test the association between two categorical variables.

## Results

### Characteristics of the Study Population

Forty-seven DILIN subjects consumed a total of 97 products that were available for analysis. The mean age of the patients was 44 years; 51% were female. Of the 47 subjects, 38 (81%) had confirmed DILI; the remaining 9 patients either had liver injury deemed to be possible (causality score of 25–50%) (5 patients), unlikely (causality score of less than 25%) (3 patients), or the liver injury was not determined yet (1 patient). The age and gender distributions differed slightly from the DILIN cases attributed to non-HDS (ie, prescribed medications) where the non-HDS cases were significantly older with mean age of 50 years (P=0.01) and had slightly more females, 60% (P=0.24).

### Catechin Profiles

Of the 97 products assayed for catechins, 49 (50.5%) contained at least one catechin. Seventy-three products had no GTE or catechins identified on the label, but 29 (39.7%) products, listed in table 1, had detectable catechins. The highest concentrations of individual catechins were for EGCG and GCG, with CA and EGCG being the most commonly found, in 18 and 16 of the 29, respectively. Eighteen products, also listed in table 1, identified GTE or one its component catechins on the label; of these, all but two contained catechins and EGCG tended to be the most abundant. The remaining six products had no label; half contained total catechin in low concentrations (< 50 mcg/g product) (data not shown). Most of the catechins in this group comprised EGCG, CA, and EC.

Table 2 shows the accuracy of catechin labeling in each of the categories of HDS. Of the catechin containing products within each category, bodybuilding supplements comprised the largest single group, followed by products marketed for weight loss, as multivitamins, and for immune support as well as Chinese herbs. Among all categories that did not identify

catechins or GTE on the product labels, more than half contained catechins, with frequencies ranging from 29 to 100% of products within these categories. Interestingly, even when labeled as containing catechin or GTE, they were not present uniformly, except in weight loss products; specifically, 6 of 18 contained either no or negligible catechin.

### Relationship Between Catechin Consumption and Hepatotoxicity in Confirmed DILI Cases

We assessed for associations between categories of catechins and DILI causality score, clinical patterns of disease, and disease severity. For this analysis, we focused on the 38 patients with confirmed DILI. We compared the 26 patients who consumed catechin-containing HDS (ranging from 1 to 8 supplements consumed per patient), to the 12 in which the HDS implicated in injury did not contain catechin or GTE. As shown in table 3, there were no differences in the DILI causality assessment scores, clinical patterns of injury, or disease severity.

We had sufficient information on dose of supplement consumed to assess the relationship between the catechin dose (calculated from catechin concentration in the supplements) and liver injury in 19 patients with confirmed DILI. As shown in table 4, we found no correlation between daily or total catechin dose and causality score, peak liver enzyme values, or disease severity; in three patients the total dose of catechin consumed was unavailable due to incomplete patient reporting. Products for weight loss had the highest catechin concentration; however, the daily catechin dose was small, with the highest estimated daily dose being 40 mg/kg in the patient who consumed HDS-066.

## Discussion

In this study, we hypothesized that catechins were commonly present as unidentified ingredients in HDS that had been implicated in human hepatotoxicity. Indeed, we found that nearly 40% of HDS contained catechins among those not listing green tea as ingredients on their labels. The most abundant species were EGCG, CA, and EC, with EGCG being the most frequent among products failing to identify GTE or catechins on the label. By contrast, we also found that some products labeled as containing GTE or its component catechins actually contained no detectable catechins. Therefore, packaging and labels of HDS appear to be unreliable as regards GTE and catechin content.

Our secondary aim was to explore the relationship between catechins and liver injury. The rationale for this analysis arises from prior case reports of hepatotoxicity attributed to GTE. This assessment relied on matching the clinical histories with the analysis for catechins. We could find no convincing relationship between the catechin dose and causal likelihood score, severity, or type of liver injury; notwithstanding these findings, there was a non-statistically significant tendency toward fatal liver injury with catechin containing HDS; a larger sample size would be required to further explore a potential association. Green tea extract is a common ingredient in several HDS that have been withdrawn from the market due to safety concerns [22–23]. Case series and a systematic review by the United States Pharmacopeia (USP) catalogued evidence for GTE's hepatotoxicity [24]. Since 1966, at least 216 case reports of toxicity attributed to green tea extracts exist. Doses in case reports that involved hepatic injury ranged from 0.7 to 3 g per day [24]. The majority of cases presented with an acute hepatocellular injury pattern and most recovered with cessation of use [13–17, 24]. In most case reports, it was unclear whether the toxicity was due to the GTE per se or possibly related to chemicals introduced during the extraction process, to concomitant medications, or to other herbs in the supplements. Based on the review by the U.S. Pharmacopeia, it was concluded that, when HDS containing green tea extracts are formulated and used appropriately, the potential for significant safety issues should be low [2,24]. These clinical

data must be viewed in the context of work by Lambert et al who found EGCG, the most abundant catechin in GTE, to be a dose-dependent hepatotoxin in mice [25].

The usual doses of GTE required to lead to hepatotoxicity in humans are not clearly established. They are likely quite variable, depending upon nutritional, genetic, and other factors. A review of reported cases in humans in 2006 indicated that cumulative doses of GTE from as little as 5.9 g over 5 days to maximum of 240 g over 120 days may be harmful, underscoring the potential wide range of toxic doses [26].

Herbal dietary supplements were implicated in 10% of cases of human drug induced hepatotoxicity in the DILIN [18]. In fact, HDS represented the second largest single group of implicated agents among all potential culprits, with antibiotics being the most commonly implicated group. But it is the hardest group of agents to implicate for many reasons. The myriad available and often multiple implicated products, batch-to-batch and product-to product-variability, the potential for interaction among ingredients within a product or with other medications, and the possibility of contamination frequently confound attribution of injury to any one product or ingredient.

Our findings support the assertion that herbal dietary supplement labels are unreliable, a consideration that is germane when evaluating hepatotoxicity attributable to HDS since the inclusion of unidentified dietary ingredients or other adulterants in HDS confounds the process of causality assessment. Most adulterants in dietary supplements are pharmaceuticals and heavy metals. Bacterial contamination has also been implicated in hepatotoxicity from HDS [27–28]. Despite the purported benefits of GTE and its component catechins [29–30], the inclusion of these compounds may also be considered adulteration, given the clinical and experimental supporting their hepatotoxic potential.

Our study highlights an important question that deserves further investigation; namely, did GTE or its component catechins play a role in liver injury in these cases? We cannot exclude that some other adulterant was the cause for injury, particularly since the concentrations of catechins were usually low and the doses lower than those found to be toxic in animals. Given the low catechin doses, as well as the widespread use of these compounds in teas and extracts, it is also possible that toxicity may be idiosyncratic, that is non-dose dependent in nature. These considerations underscore the need for additional research in this area to confirm or refute the as yet empirical evidence linking GTE and its component catechins to hepatotoxicity

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1**

Catechin profiles

| A. Profiles for products with detectable catechins, but with no GTE or catechins identified on the product label (n=29) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **HDS #** | **Product Name** | **CA (MW 290) (mcg/g)** | **EC (MW 290) (mcg/g)** | **GC (MW 306) (mcg/g)** | **EGC (MW 306) (mcg/g)** | **ECG (MW 442) (mcg/g)** | **EGCG (MW 458) (mcg/g)** | **GCG (MW 458) (mcg/g)** | **Total Catechin (mcg/g)** |
| HDS-100 | Grapefruit Seed extract | * | * | * | * | 16.0 | 4509 | 1668 | 6193 |
| HDS-083 | Gluco-Ease Plus | 721.0 | 137.3 | 19.5 | 58.3 | 58.3 | 69.6 | * | 1064 |
| HDS-049 | PCT Advanced | 728.9 | 128.7 | * | 12.5 | 17.2 | 24.5 | * | 911.8 |
| HDS-040 | Gaia's Delight | 71.6 | 823.4 | * | 7.0 | * | * | * | 902.0 |
| HDS-092 | Isotonix | 211.4 | 108.9 | * | 8.1 | 19.3 | 32.6 | * | 380.3 |
| HDS-082 | Multi-Cleanse Formulas: Cleansing Complex with Fibers (Part II) | 25.0 | 6.2 | * | 21.0 | 56.0 | 28.4 | * | 277.2 |
| HDS-010 | HERBALIFE Shapeworks Cell Activator | 54.8 | * | * | 7.7 | 15.7 | 18.3 | * | 113.2 |
| HDS-047 | CKLS | 9.1 | 4.1 | * | 11.2 | * | * | * | 81.7 |
| HDS-075 | Traditional Medicinals, Gypsy Cold Care | * | 3.3 | * | 15.9 | 15.7 | 27.2 | * | 56.3 |
| HDS-043 | Ultracolloid Silver | 2.7 | * | * | 10.5 | 13.5 | 23.2 | * | 52.7 |
| HDS-016 | Axobecal | 17.0 | 1.9 | * | 11.0 | * | 18.3 | * | 45.7 |
| HDS-090 | Super Colon Cleanse | * | * | * | 21.8 | 11.4 | * | * | 40.7 |
| HDS-004 | Reishi D. dietary supplement | 12.6 | 10.8 | * | 7.5 | * | 17.8 | * | 36.7 |
| HDS-017 | Muscle Milk | * | * | * | * | * | * | * | 23.4 |
| HDS-044 | Niacin | * | * | * | * | * | 19.9 | * | 19.9 |
| HDS-032 | Sunflower Supreme | * | * | * | * | * | 18.9 | * | 18.9 |
| HDS-048 | Super-Test mass | * | * | * | * | * | 19.3 | * | 19.3 |
| HDS-093 | Saw Palmetto Extract | 8.5 | 6.1 | * | * | * | 15.8 | * | 15.8 |
| HDS-009 | HERBALIFE Shapeworks Nutritional Supplement Shake mix | 2.1 | * | * | * | 12.8 | * | * | 14.6 |
| HDS-012 | HERBALIFE Shapeworks Multivitamins | 4.8 | 1.6 | * | * | * | * | * | 14.9 |
| HDS-067 | TokkyoTren | * | * | 6.1 | 2.2 | * | * | * | 14.7 |
| HDS-063 | Infinit nutrition supplement | * | * | * | * | * | 12.3 | * | 12.3 |
| HDS-064 | 1, 4 AD Bold 200 | * | * | * | * | * | 11.8 | * | 11.8 |
| HDS-065 | H-Drol | 13.7 | * | * | * | * | 11.9 | * | 11.9 |
| HDS-074 | Dual-Action Cleanse, Colon Clear Formula | * | 7.3 | * | * | * | * | * | 13.7 |
| HDS-056 | Leg Cramps with Quinine | * | * | * | * | * | * | * | 7.3 |

**A. Profiles for products with detectable catechins, but with no GTE or catechins identified on the product label (n=29)**

| HDS # | Product Name | CA (MW 290) (mcg/g) | EC (MW 290) (mcg/g) | GC (MW 306) (mcg/g) | EGC (MW 306) (mcg/g) | ECG (MW 442) (mcg/g) | EGCG (MW 458) (mcg/g) | GCG (MW 458) (mcg/g) | Total Catechin (mcg/g) |
|---|---|---|---|---|---|---|---|---|---|
| HDS-060 | MIT | 1.2 | 1.8 | * | 7.5 | * | * | * | 7.5 |
| HDS-079 | Acai Extract | 1.1 | 1.3 | * | * | * | * | * | 3.0 |
| HDS-029 | Testron SX by Neutraceutics | | | * | * | | * | * | 2.4 |

**B. Profiles for products with GTE or catechin on the label (n=18)**

| HDS # | Product Name | CA (MW 290) (mcg/g) | EC (MW 290) (mcg/g) | GC (MW 306) (mcg/g) | EGC (MW 306) (mcg/g) | ECG (MW 442) (mcg/g) | EGCG (MW 458) (mcg/g) | GCG (MW 458) (mcg/g) | Total Catechin (mcg/g) |
|---|---|---|---|---|---|---|---|---|---|
| HDS-066 | Green tea fat burner | 2,785 | 52,900 | * | 87,770 | 132,360 | 210,640 | * | 486,460 |
| HDS-059 | Slimquick female fat burner | 2,705 | 27,350 | * | 12,310 | 22,380 | 49,900 | 14,900 | 129,600 |
| HDS-071 | Hydroxycut | 19,200 | 68,060 | * | 7,792 | 14,610 | 11,740 | * | 121,400 |
| HDS-042 | resVpure | 399.3 | 7,590 | * | 17,040 | 24,020 | 57,780 | * | 106,800 |
| HDS-030 | Slimquick | 324.5 | 4,312 | 557.1 | 13,370 | 24,410 | 24,500 | 32,480 | 99,950 |
| HDS-011 | HERBALIFE Shapeworks Total Control | 3,356 | 5,714 | 219.6 | 7,100 | 22,360 | 31,810 | 19,500 | 90,060 |
| HDS-061 | Tight | 1,438 | 27,320 | 56.8 | 33.3 | 16,000 | 22,510 | * | 67,360 |
| HDS-058 | Slimquick 6 ways | 374.6 | 4,977 | * | 441.3 | 10,750 | 15,970 | * | 32,510 |
| HDS-091 | Xenadrine RFA-X | 758.3 | 11,880 | * | 5,001 | 2,731 | 7,712 | * | 28,080 |
| HDS-028 | Hydroxycut | 1,091 | 9,822 | * | 1,797 | 4,690 | 5,152 | 1,905 | 24,460 |
| HDS-081 | Multi-Cleanse Formula: Cleansing Complex with Herbs (Part I) | 130.4 | 684.4 | * | 667.9 | 3,454 | 7,258 | * | 12,200 |
| HDS-073 | Dual-Action Cleanse, Total Body Purifier | 7.5 | 19.3 | * | 36.9 | 367.5 | 598.7 | 89.5 | 1,119 |
| HDS-084 | Ultra Vitality, Citrus powder packs | 20.7 | 17.0 | * | * | * | * | * | 37.7 |
| HDS-041 | Relacore | 5.6 | * | * | * | * | * | * | 5.6 |
| HDS-038 | Nano Vapor | * | * | * | 3.8 | * | * | * | 3.8 |
| HDS-076 | Men's Mega Men 50 Plus | 1.2 | 0.1 | * | * | * | * | * | 1.3 |
| HDS-036 | Optimum Opti-Men | * | * | * | * | * | * | * | * |
| HDS-089 | Life's Fortune, Multi-Vitamin and Mineral | * | * | * | * | * | * | * | * |

* LOQ: Limit of quantification on the day of analysis.

## Table 2

Categories of 97 Assayed Herbal Dietary Supplements: Accuracy of Labeling

| | Total n | Catechins detected/GTE or Catechin identified on label (%) | Catechins detected/GTE or Catechin NOT identified on label (%) |
|---|---|---|---|
| **Body Building** | 22 | 1/2 (50%) | 7/20 (35%) |
| **Weight Loss** | 18 | 11/11 (100%) | 4/7 (57.1%) |
| **Multivitamin** | 10 | 2/3 (66.7%) | 2/7 (28.6%) |
| **Immune Support** | 9 | 0 | 4/9(44.4%) |
| **Chinese Herbs** * | 9 | 0 | 0/3 (0%) |
| **Colon Cleanse** | 7 | 1/2 (50%) | 5/5 (100%) |
| **Menopause Support** | 3 | 0 | 0/3 (0%) |
| **Analgesic** | 3 | 0 | 1/3 (33.3%) |
| **Cardiovascular Health** | 3 | 0 | 0/3 (0%) |
| **Sleep Aid** | 2 | 0 | 0/2 (0%) |
| **Diabetes Control** | 2 | 0 | 1/2 (50%) |
| **Cough & Cold** | 1 | 0 | 1/1 (100%) |
| **Digestive Health** | 1 | 0 | 0/1 (0%) |
| **Energy Booster** | 1 | 0 | 1/1 (100%) |
| **Herbal Incense** | 1 | 0 | 1/1 (100%) |
| **Joint Support** | 1 | 0 | 0/1 (0%) |
| **Other** | 4 | 0 | 2/4 (50%) |
| | **Total** | **15/18 (83.3%)** | **29/73 (39.7%)** |

* No label available for six Chinese herbs

## Table 3

Clinical Characteristics of Enrolled Cases

| Clinical Characteristics | | Catechin Free HDS N=12 | Catechin Containing HDS* N=26 | Total N=38 |
|---|---|---|---|---|
| Type of Liver Injury, P=0.44 | Cholestatic | 2 (16.7%) | 4 (15.4%) | 6 |
| | Mixed | 0 (0.0%) | 4 (15.4%) | 4 |
| | Hepatocellular | 10(83.3%) | 18 (69.2%) | 28 |
| Severity of Liver Injury**, P=0.89 | Mild | 2 (16.7%) | 3 (11.5%) | 5 |
| | Moderate | 5 (41.7%) | 9 (34.6%) | 14 |
| | Moderate-Hospitalized | 3 (25.0%) | 8 (30.8%) | 11 |
| | Severe | 1 (8.3%) | 1 (3.8%) | 2 |
| | Fatal | 1 (8.3%) | 5 (19.2%) | 6 |
| Causality Score**: Likelihood of Drug Induced Liver Injury, P=0.74 | Definite Greater than 95% | 4 (33.3%) | 6 (23.1%) | 10 |
| | Very likely 75–95% | 6 (50.0%) | 12 (46.2%) | 18 |
| | Probable 50–75% | 2 (16.7%) | 8 (30.8%) | 10 |

*Subjects took at least one HDS product with catechin concentration >=1 mcg/g.

**One subject with missing severity and causality score in Catechin containing HDS group

**Table 5**

Clinical Characteristics of Patients in Whom Catechin Consumption Could be Quantified

| Cases N=19 | Gender Age Wt (kg) | Daily Catechin Consumed (mcg) | Total Catechin Consumed (mcg) | Intended Use | Likelihood of DILI | Severity Score | Peak Liver Enzymes | | | | Peak INR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ALT | AST | Alk P | T.Bili | |
| HDS-066 | Female | 2,918,757 | 207,231,747 | Weight Loss | Definite | Moderate | 1592 | 1447 | 141 | 9.7 | 1.1 |
| | 34 | | | | | Hosp | | | | | |
| | 72.7 | | | | | | | | | | |
| HDS-028 | Male | 199,577 | 8,581,811 | Weight Loss | Definite | Moderate | 3099 | 3005 | 144 | 11.3 | 2.0 |
| | 32 | | | | | Hosp | | | | | |
| | 100.7 | | | | | | | | | | |
| HDS-060* | Male | 25,258 | 2,475,284 | Bodybuilding | Definite | Moderate | 435 | 279 | 130 | 8.8 | 7.2 |
| HDS-061 | 29 | | | | | | | | | | |
| | 88.5 | | | | | | | | | | |
| HDS-090 | Male | 28,165 | 1,918,462 | Weight Loss | Very likely | Moderate Hosp | 2327 | 2057 | 165 | 22.1 | 1.2 |
| HDS-091 | 27 | | | | | | | | | | |
| | 126.7 | | | | | | | | | | |
| HDS-092 | Female | 6465 | 1,183,095 | NR | Very likely | Moderate | 203 | 118 | 1323 | 8.0 | 1.5 |
| | 57 | | | | | | | | | | |
| | 93 | | | | | | | | | | |
| HDS-073 | Female | 26,796 | 309,877 | Constipation | Very likely | Fatal | 92 | 123 | 399 | 15.7 | 1.7 |
| HDS-074 | 62 | | | | | | | | | | |
| HDS-081 | 59.9 | | | | | | | | | | |
| HDS-082 | | | | | | | | | | | |
| HDS-100 | Female | 7927 | 301,226 | Lyme Disease | Very likely | Mild | 1589 | 989 | 241 | 1.2 | 1.0 |
| | 66 | | | | | | | | | | |
| | 56.5 | | | | | | | | | | |
| HDS-009 | Female | 750 | 182,250 | Weight Loss | Very Likely | Severe | 2310 | 2398 | 179 | 13.8 | 1.7 |
| HDS-012 | 22 | | | | | | | | | | |
| HDS-013* | 55.8 | | | | | | | | | | |
| HDS-037* | Male | 275 | 42,350 | Bodybuilding | Very likely | Moderate | 313 | 149 | 96 | 9.0 | 1.0 |

| Cases N=19 | Gender Age Wt (kg) | Daily Catechin Consumed (mcg) | Total Catechin Consumed (mcg) | Intended Use | Likelihood of DILI | Severity Score | Peak Liver Enzymes | | | | Peak INR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ALT | AST | Alk P | T.Bili | |
| HDS-038 | 24 | | | | | Hosp | | | | | |
| | 96.9 | | | | | | | | | | |
| HDS-048 | Male | 1739 | 10,985 | Bodybuilding | Definite | Moderate | 198 | 98 | 166 | 30.0 | 1.1 |
| HDS-049 | 37 | | | | | Hosp | | | | | |
| HDS-050* | 99.3 | | | | | | | | | | |
| HDS-075 | Male | 201 | 4531 | Diabetes | Probable | Moderate | 374 | 333 | 938 | 9.5 | 0.9 |
| HDS-076 | 56 | | | | | Hosp | | | | | |
| | 78 | | | | | | | | | | |
| HDS-093 | Male | 20 | 1980 | NR | Very likely | Moderate | 1648 | 1049 | 300 | 2.7 | 1.0 |
| HDS-098* | 47 | | | | | | | | | | |
| | 83.6 | | | | | | | | | | |
| HDS-054* | Female | 25 | 1950 | Sleep | Probable | Mild | 703 | 281 | 109 | 1.3 | 1.1 |
| HDS-055* | 61 | | | Cramps | | | | | | | |
| HDS-056 | 124.3 | | | | | | | | | | |
| HDS-064* | Male | 3 | 555 | Bodybuilding | Definite | Moderate | 187 | 93 | 170 | 15.7 | 0.9 |
| HDS-065 | 32 | | | | | | | | | | |
| | 102.3 | | | | | | | | | | |
| HDS-041 | Female | 26 | 416 | Weight Loss | Probable | Moderate | 1717 | 1193 | 364 | 20.8 | 1.1 |
| | 41 | | | | | | | | | | |
| | 90.5 | | | | | | | | | | |
| HDS-067 | Male | 1 | 25 | Bodybuilding | Definite | Moderate | 173 | 89 | 211 | 22.0 | 1.0 |
| | 35 | | | | | | | | | | |
| | 81.8 | | | | | | | | | | |
| HDS-032 | Male | 168 | NR | EnergyBoost | Probable | Moderate | 1614 | 573 | 254 | 8.0 | 1.0 |
| HDS-033 | 45 | | | | | Hosp | | | | | |
| | 83.8 | | | | | | | | | | |
| HDS-084 | Female | 354 | NR | Multivitamin | Probable | Fatal | 58 | 162 | 258 | 28.8 | 1.9 |
| | 58 | | | | | | | | | | |
| | 75 | | | | | | | | | | |



*Dig Dis Sci*. Author manuscript; available in PMC 2014 September 01.

| Cases N=19 | Gender Age Wt (kg) | Daily Catechin Consumed (mcg) | Total Catechin Consumed (mcg) | Intended Use | Likelihood of DILI | Severity Score | Peak Liver Enzymes | | | | Peak INR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | ALT | AST | Alk P | T.Bili | |
| HDS-030 | Female<br>27<br>58.5 | 419,814 | NR | Weight Loss | Probable | Fatal | 1778 | 3543 | 283 | 22.7 | 7.0 |

*No catechin found

NR = Not Reported



*Dig Dis Sci*. Author manuscript; available in PMC 2014 September 01.