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Content of Commercially Available, Single-Ingredient Vitamin D Dietary Supplements

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Abstract

With the increased Institute of Medicine recommendation for vitamin D, more consumers are taking vitamin D from over-the-counter or prescription sources. The purpose of this study was to determine the content of commercially available, single-ingredient vitamin D supplements. Eleven commercially available dietary supplement calciferol products were purchased, repackaged, and analyzed for vitamin D content in a laboratory that was blinded to brand or manufacturer of the supplement. Vitamin D was extracted and isolated for analysis by a high-performance liquid chromatography method. Measured vitamin D content was compared with the stated label amount of vitamin D. The percentage of actual vitamin D contained in the supplements ranged from 82% and 119% of the stated label amount. Despite anecdotal reports of products with substantial content deviations from the labeled amount, no remarkable departures from labeled content were found in this set of vitamin D preparations.

Keywords

vitamin D, dietary supplements, nutrition, drug information

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Introduction

Vitamin D is a unique vitamin. Although technically not a vitamin, as it is produced by the skin when exposed to ultraviolet B (UV-B) light, it is treated as a vitamin by regulatory entities and by supplement manufacturers.

As a dietary supplement, all vitamin D products or combinations with other vitamins or minerals are regulated by the US Food and Drug Administration (FDA). The role of the FDA in regulating dietary supplements is mainly to monitor postmarketing safety. Proof of safety and effectiveness is not required for dietary supplements as it is for prescription drugs, which undergo premarket approval by the FDA to treat and prevent disease. Also, unlike prescription drugs, the quality of dietary supplements is primarily the responsibility of the manufacturer. Dietary supplements are now required to follow current good manufacturing practices.[1] However, the standards for dietary supplements are not as stringent as they are for conventional prescription drugs. There are a few commercial organizations that test the potency and purity of supplements and manufacturers can voluntarily have their products tested; however, participation in these programs is not mandated by FDA.

With the increased popularity of vitamin D among consumers and the increased Institute of Medicine recommendation for vitamin D, more consumers are taking and will be taking vitamin D from over-the-counter or prescription sources. The purpose of this study was to determine the vitamin D content of commercially available, single-ingredient vitamin D supplements.

Methods

Supplements

Eleven different calciferol products were purchased from 5 retail stores, pharmacies, or Web sites from August 16 to September 9, 2010 (see Table 1). The supplements were kept away from light and repackaged in number labeled pill containers. They were shipped to Heartland Assays where they were analyzed in blinded fashion in 2010. We have used 4 additional vitamin D products in previous clinical trials and measured their content in the same lab with the same method. These results are also listed in Table 1 and are identified with the manufacturers name and an Arabic numeral to differentiate them.

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Table 1. Description of Calciferol Products

Brand/Manufacturer	Pill Type	Labeled Dose (μg)[a]	Lot No.	Expiration	Date of Analysis	% of Label Dose
Carlson Labs	Oil capsule	25 D_3	1000251	12/1/2013	11/2010	0.97
Douglas Labs 1	Tablet	25 D_3	7945209	10/2012	11/2010	0.90
Douglas Labs 2	Tablet	25 D_3	6970109	10/2011	4/2010	0.91
NatureMade	Tablet	25 D_3	1008092	4/1/2013	11/2010	1.01
Spring Valley	Oil capsule	25 D_3	373303-01	6/2013	11/2010	0.91
Walgreen	Oil capsule	25 D_3	251416	12/2012	11/2010	0.91
Carlson Labs	Oil capsule	50 D_3	1004451	4/2014	11/2010	1.02
Finest Natural	Oil capsule	50 D_3	254061	2/2013	11/2010	1.18
Whole Foods	Oil capsule	50 D_3	006063	2/2013	11/2010	0.89
Maximum D3 1	Oil capsule	250 D_3	01-091109	10/2012	11/2010	1.05
Maximum D3 2	Oil capsule	250 D_3	050106-02	2/2007	4/2009	1.03
Maximum D3 3	Oil capsule	250 D_3	080701-02	6/2011	4/2010	1.19
Replesta	Wafer	1250 D_3	41660	8/2011	11/2010	0.93
Barr Labs^{USP} 1[b]	Oil capsule	1250 D_2	312838	6/2011	11/2010	0.82
Barr Labs^{USP} 2[b]	Oil capsule	1250 D_2	312367	6/2011	4/2010	0.94

[a]To convert to international units multiply by 40.
[b]USP indicates that it subscribes to the USP (United States Pharmacopeia) Dietary Supplement Verification Program.

Analysis Method

Vitamin D was extracted and isolated for analysis by a high-performance liquid chromatography (HPLC) method developed at Heartland Assays for food[2] and modified for vitamin supplements.[2] Briefly, 5 to 10 representative pills were homogenized. Approximately 0.25 g of the homogenized sample was saponified in 5 mL (1 volume) of methanolic KOH. The sample was spiked with an internal standard [^{3}H]-vitamin D_3 (30 Ci/mmol) to estimate recovery losses. After 60 minutes at 60°C, 1 volume of H_2O was added and the mixture was extracted 3 times with 1 volume of hexane/ethyl acetate (85/15). The extract was washed with water (1 volume), collected, and dried under vacuum. The dried extract was resuspended in 1.0 mL of hexane/methylene chloride 90/10 v/v), applied to a hand-packed solid-phase extraction cartridge (0.5 g of 10-40 μm silica, Varian, Palo Alto, CA, part A8501, equipped with a top stainless steel frit), eluted with methylene chloride/2-propanol (99.8/0.2) and dried. The residue was resuspended in hexane/methylene chloride/alcohols (85/15/0.2; the alcohols consisted of 2/1 (v/v) isopropanol/methanol), applied to Agilent HPLC ZORBAX SIL column (5μ, 0.9 × 25 cm, Agilent Technologies, Santa Clara, CA), and the vitamin D fraction was collected and dried. The residue was resuspended in hexane/alcohols (99.5/0.5), again applied to an HPLC ZORBAX NH2 column (5μ, 0.0.45 × 25 cm, Agilent Technologies, Santa Clara, CA), and the fraction containing the vitamin D was collected and dried for final purification.

The final purification for vitamin D_2 by HPLC was achieved using a Vydac ODS column (Vydac part 201TP54, Chrom Tech, Inc, Apple Valley, MN) using a mobile phase of acetonitrile/methylene chloride (65/35) and UV detection at 265 nm. Vitamin D_2 was quantified by comparison of the UV peak areas with standards that were also spiked with [^{3}H]-vitamin D_3. Using this HPLC system, vitamin D_2 was baseline resolved from vitamin D_3. Samples and standards were collected for quantitation of [^{3}H]-vitamin D_3. Vitamin D_2 was quantified by comparison of the UV peak areas at 265 nm with known standards using the sample to [^{3}H]-vitamin D_3 to correct for losses. The inter-assay coefficient of variation was 13.2%, and intra-assay coefficient of variation was 9.1%.

Results

We tested 15 different vitamin D supplements from 10 manufacturers. Of these, 9 of the supplements contained vitamin D_3 (cholecalciferol) and 2 contained vitamin D_2 (ergocalciferol). Eight of these were oil capsules, 2 were tablets, and 1 was a wafer formulation. The description of the supplement manufacturer, formulation type, and labeled dose for each product is presented in Table 1.

The percentage of vitamin D contained in the supplements ranged from 82% to 119% of the stated label amount. Four of the 11 products sampled contained at least 100% of the labeled amount. One of these products was measured 2 years after the labeled expiration date, but it still contained at least 100% of the labeled amount.

One of the products sampled was labeled "USP" indicating compliance with the United States Pharmacopeia standards. It contained 84% of the labeled amount in one sample and 94% of the labeled amount in another sample.

Discussion

The United States federal government requires manufacturers to follow "current good manufacturing practices" to ensure that food, pharmaceuticals, and cosmetics are safe, are processed consistently, and meet quality standards. Most recently, this has also been applied to dietary supplements, including vitamin D. As of June 2010, all manufacturers of dietary supplements are required to fulfill the requirements for good manufacturing practices.[3] There are also several independent organizations that will test dietary supplements and provide approval seals for products that fulfill their requirements. This is only done on a volunteer basis though and is not required by the federal government. One such organization is the US Pharmacopeia Dietary Supplement Verification Program (USP).

One of the products we tested was verified by this organization and carries their approval seal (see Table 1). The standard that USP uses for vitamin D products differs between the 2 forms of vitamin D. Finished vitamin D_2 (ergocalciferol) products should contain between 100% and 120% of the labeled amount. The standard for vitamin D_3 is less clear as the raw ingredients should contain between 97% and 103% of the labeled amount of vitamin D_3, but this does not apply to finished supplement products.[4] Therefore, no finished vitamin D_3 supplements can carry a USP verification.

Despite anecdotal reports of products with substantial content deviations from the labeled amount,[5] we found no remarkable departures from labeled content in this set of vitamin D preparations. Overall, most of the products that we tested contained within 10% of the labeled amount, although if we apply the USP standard for vitamin D_2, only 6 of these products met that particular standard. The supplement that had the lowest level was the vitamin D_2 product, which was also nearest to its expiration date.

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Author Contributions

Study design: LAGA. Study conduct: LAGA, RLH. Data collection: LAGA, RLH. Data analysis: LAGA. Data interpretation: LAGA, PG. Drafting article: LAGA. Revising article content: LAGA, RLH, PG. Approving final version of article: LAGA, RLH, PG.

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: RLH is owner and CEO of Heartland Assays, Inc.

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Ethical Approval

This study is exempt from oversight by human subjects research protection as there were no human subjects involved.

References

1. US Food and Drug Administration. Dietary supplement current good manufacturing practices (CGMPs) and interim final rule (IFR) facts. June 22, 2007. http://www.fda.gov/Food/DietarySupplements/GuidanceComplianceRegulatoryInformation/RegulationsLaws/ucm110858.htm. Accessed July 8, 2011.
2. Phillips KM, Byrdwell WC, Exler J, et al. Development and validation of control materials for the measurement of vitamin D3 in selected US foods. *J Food Compos Anal*. 2008;21:527-534.
3. US Food and Drug Administration. FDA issues dietary supplements final rule, June 2007. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108938.htm. Accessed June 4, 2011.
4. US Pharmacopeial Convention. U.S. Pharmacopeia National Formulary 2011: USP 34 NF 29. *Rockville, MD: United States Pharmacopeial; Har/Pap Su edition; 2011.*
5. Eckstein C, Bandaru V, Haughey N, Calabresi PA. Vitamin D3 content in commercially available oral supplements (abstract P3). *The Joint Consortium of Multiple Sclerosis Centers and America's Committee on Treatment and Research in Multiple Sclerosis Meeting*. 2010;33-34.