

Caveat Emptor - Dehydroepiandrosterone (DHEA) Dietary Supplement Products:
Quality Control Discrepancies

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Abstract

Objective.- To analyze dietary supplement DHEA products to assess the accuracy of the manufacturers' label claim of DHEA presence and total content.

Methods.- All products were analyzed by High-Performance Liquid Chromatography (HPLC) with ultraviolet photo diode-array (UV-PDA) detection to establish the presence and content of DHEA by comparing the peak retention time and UV spectrum profile of DHEA reference material. DHEA presence was also confirmed by analyzing extracts of each product by Fourier-Transform infrared (FTIR) spectroscopy.

Results.- Sixteen different DHEA dietary supplement products chosen randomly from freely available health food stores or other commercial sources were tested. On the basis of HPLC retention index, UV-PDA and FTIR spectral analysis, of the 16 products tested, one contained no DHEA, one product contained an average of 150% of label, with a relative standard deviation (RSD) of 32%, and two other products labeled as containing "naturally occurring DHEA" contained only 0.5 mg/dose on the average. Of the remaining 12 products, only 6 contained an average ranging from 95-105% of label claim.

Conclusions.- Only half of products tested were found to meet the manufacturers' label claim using typical release specification of 90-110% as applied to most pharmaceutical products manufactured as per cGMP. In the worst case, one product did not contain any DHEA and in another case, it had 150% of the label claim. This lack of uniformity and predictability has important safety implications for this steroid, which is endogenously converted to potent androgenic and estrogenic sex steroids.

Introduction

DHEA (*dehydroepiandrosterone*, 3-hydroxyandrost-5-en-17-one; also known as prasterone) adrenal hormone is the most abundant steroid hormone in humans. Principally secreted by the adrenal gland, DHEA serves as substrate for conversion into more potent androgens and/or estrogens in peripheral tissues including androstenedione, testosterone, dihydrotestosterone and estrogens estrone (E1) and estradiol (E2)¹. The aromatization of DHEA in peripheral tissue is thought to account for the majority of estrogen biosynthesis in postmenopausal women². Endogenous levels peak at age 20 to 25, declining thereafter. Its biologic function in man is not well understood.

In past few years due to the popularity of DHEA, several commercial products have become available in the United States as so-called "dietary supplements". (DHEA is not a food, however, as it does not occur naturally in the human food chain and no foodstuff can mimic the physiological or pharmacological consequences evoked by DHEA, endogenously secreted or exogenously administered. The safety and efficacy of these DHEA containing dietary supplements have not been evaluated by the US Food and Drug Administration (FDA). As dietary supplements, such products do not have to be manufactured in compliance with FDA current Good Manufacturing Practices (cGMP), nor do these products have to meet quality control standards that all other drugs have to meet. As DHEA clearly has the potential for endogenous conversion to steroids known to be metabolically active, it is important to ascertain whether or not DHEA available as a dietary supplement meets the quality standards expected of drugs.

The purpose of this study was to analyze DHEA products freely available to the public at health food stores or other commercial sources for the presence and total content of DHEA to assess the accuracy of the manufacturers' label claim.

Methods

DHEA Extraction Method

An extraction method consisting of using the HPLC mobile phase was found to be suitable for isolating DHEA from the dosage forms (tablet, capsule, or caplet). The extraction method was standardized for all products by extracting each dosage form into 100 mL of the HPLC mobile phase. Each extract was filtered, and aliquots of each filtered sample were chromatographed.

Analysis by HPLC Method

All dosage form extracts were analyzed by HPLC for their DHEA content using following system conditions:

Column: Regis ODS-II, 5 μ , 4.6 x 250 mm; ambient (~25-30°C)

Mobile Phase: Water : acetonitrile : methyl t-butyl ether (45:45:10, v:v:v)

Flow Rate: 1.0 mL/min

Pump System: Hewlett-Packard (HP) 1100 HPLC System

Injector: HP 1100 Injector; 25 μ L

Detection: HP 1100, PDA-UV, 210 nm

Integration: HP Pentium Vectra with ChemStation Software, Ver. 4.02

Three dosage form units were selected from each formulation. Peak area data were collected for each observable DHEA peak. DHEA content was determined using the external standard method from a standard curve of reference DHEA. PDA-UV spectra and FTIR analyses were also performed to aid in the definitive identification of DHEA in the products.

Analysis by FTIR

The contents from each product were extracted into chloroform. The chloroform extract was evaporated and the residue made into a nujol mull. FTIR spectra were recorded for each product extract on a Perkin-Elmer Paragon 1000 FTIR and compared to a DHEA reference spectrum.

Results

Analytical HPLC method for analysis of DHEA was developed and validated. Each product HPLC profile was compared to the reference standard profile for selectivity and specificity. A standard curve of reference DHEA was generated to verify the linearity, relative accuracy, and acceptable concentration range. A system suitability test was conducted by injecting reference DHEA six times. Six injections gave a relative of precision of 0.2%, which meets USP XXIII (United States Pharmacopoeia) guidelines.

HPLC results for all formulations are summarized in Table 1 and Figure 1. All formulations except one (product no. 7) were found to contain DHEA on the basis of HPLC retention index. Of the 15 formulations found to contain DHEA, PDA-UV spectral analysis confirmed the presence of DHEA in 13 of the formulations, 2 products failed to yield a PDA-UV spectrum to corroborate the presence of DHEA.

Seven products (no. 2,5,6,11,14,15 and 16) were found to contain average amounts of DHEA ranging from 90% to 110% of their labeled value with a %RSD range from 1.8 to 13.8. Product 1, 9, and 13 were found to have average amounts within 75% to 125% of label; %RSD's for these three formulations were 18%, 8% and 3%, respectively. Of the remaining products, no DHEA was detected in product no. 7, and trace amounts of DHEA were detected in 4 and 8 (0.6 mg, RSD 78%, and 0.5 mg, RSD 80%, respectively). These latter two products were labeled as containing "naturally occurring DHEA" with no specific amount indicated on the label. Product no. 10 was found to contain an average of 150% of label, RSD 32%.

Each formulation extract spectrum was examined for the presence of -OH, C=O, and C=C near frequencies of 3430, 1728, 1068 cm^{-1} , respectively; bands that were found to be prominent in the DHEA spectrum. Products except for no. 4 and 7 indicate bands that are consistent with the presence of DHEA.

Discussion

Although DHEA is widely available for self-administration as a "nutritional food supplement," the metabolic effects of exogenously administered DHEA in normal children, men and pre-menopausal women are largely unknown. During chronic administration of DHEA to normal postmenopausal women, serum levels of male and female sex hormones have been observed to increase^{3,4}, suggesting possible risks to hormonally dependent tissues including endometrium, breast, and prostate gland⁵⁻⁷. Clinically meaningful increases in sex steroids including serum androstenedione, testosterone, dihydrotestosterone, estradiol, and estrone have been reported following single oral doses of as little as 50 mg DHEA⁸. In some individuals, long-term DHEA administration may have the potential to cause insulin resistance⁴, hypertension⁹⁻¹¹ and reduce HDL-cholesterol^{4,12-14}.

The variability of content (range of 0% to 150%) observed in analyses of sixteen DHEA products available, as nutritional supplements should raise concerns over availability of this potent drug or hormone as non-cGMP product in a medically unsupervised setting.

Conclusions

In conclusion, only half of products tested were found to meet the manufacturers' label claim using typical release specification of 90-110% as applied to most pharmaceutical products manufactured as per cGMP. In the worst case, the product did not contain any DHEA and in one case, it had 150% amount of the label claim. This wide range of variation of actual DHEA content in comparison to labeled content has important safety implications for this steroid, which is endogenously converted to potent androgenic and estrogenic sex steroids.

Acknowledgment

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Table 1. Analysis Results of DHEA Dietary Supplement Products.

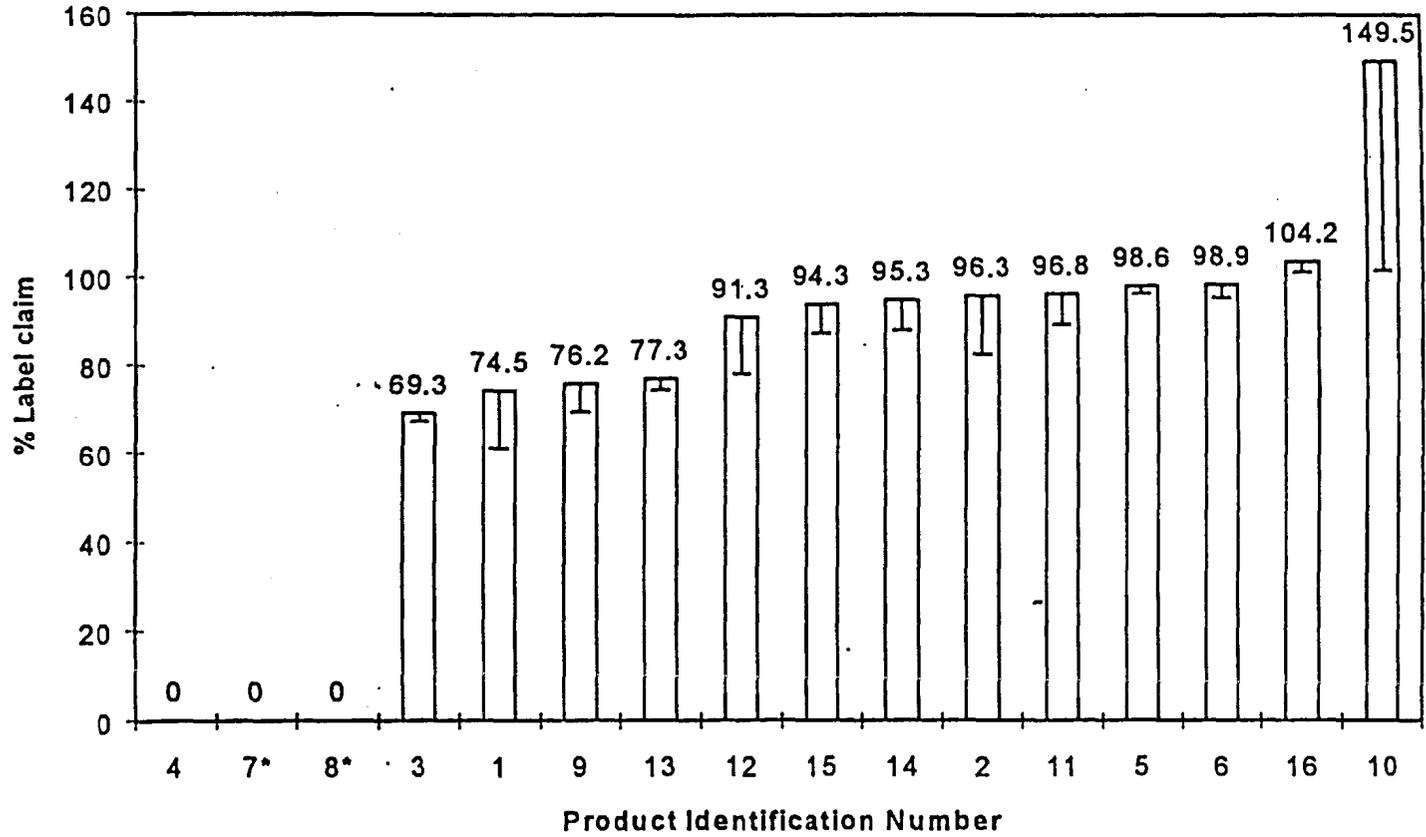
| Product No. | DHEA Label Claim (mg/unit) | Amount Found Average (mg/unit) | % of Label claim | ID Confirmed by | |
|-------------|----------------------------|--------------------------------|----------------------|------------------------|------|
| | | | | UV-PDA | FTIR |
| 1 | 25 | 18.6 (15.5-22.1***) | 74.5 (*13.2, **17.7) | YES | YES |
| 2 | 25 | 24.1 (21.6-27.9) | 96.3 (13.3, 13.8) | YES | YES |
| 3 | 50 | 44.6 (43.8-45.7) | 89.3 (1.9, 2.1) | YES | YES |
| 4 | Not indicated | 0.6 (0.2-1.2) | N/A | NO (not definitive) | NO |
| 5 | 50 | 49.2 (48.6-50.2) | 98.5 (1.7, 1.8) | YES | YES |
| 6 | 25 | 24.7 (23.9-25.2) | 98.9 (3.0, 3.0) | YES | YES |
| 7 | 0.5 | None | N/A | NO | NO |
| 8 | Not indicated | 0.5 (0.1-1.0) | N/A | NO (not definitive) | YES |
| 9 | 25 | 19.1 (17.8-20.9) | 76.2 (6.4, 8.4) | YES | YES |
| 10 | 25 | 37.4 (23.7-44.7) | 149.5 (47.5, 31.8) | YES | YES |
| 11 | 5 | 4.8 (4.5-5.2) | 96.8 (7.1, 7.3) | YES | YES |
| 12 | 25 | 22.8 (19.2-25.4) | 91.3 (12.9, 14.2) | YES | YES |
| 13 | 25 | 19.3 (18.6-19.9) | 77.3 (2.6, 3.4) | YES | YES |
| 14 | 25 | 23.8 (22.0-25.4) | 95.3 (6.9, 7.2) | YES | YES |
| 15 | 25 | 23.6 (22.5-25.5) | 94.3 (6.6, 7.0) | YES | YES |
| 16 | 25 | 26.0 (25.5-26.7) | 104.2 (2.5, 2.4) | YES | YES |

* Std. dev.

** % RSD

***Range

Figure 1. Analysis Results as % Label Claim of DHEA Dietary Supplement Products with standard deviation bars. *Product 7 and 8 claim to contain naturally occurring DHEA with no label amount specified.



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