

VITAMINS / SUPPLEMENTS

Dehydroepiandrosterone

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Dehydroepiandrosterone (DHEA) remains a very controversial supplement. Some studies indicate that it may slow and reverse certain aspects of the aging process, and provide therapeutic value for a number of health conditions; other studies suggest it may promote the growth of latent breast, prostate and other cancers. Many patients ask our professional advice regarding the use of various supplements, including DHEA. As such, health practitioners should be aware of the research on this supplement and its potential effects on human health. The following is brief review of DHEA, outlining its synthesis, metabolism, effects on various health conditions, adverse side effects and key drug-nutrient interactions

General Features

DHEA is an intermediate steroid hormone produced mostly by the adrenal glands. All steroid hormones are derived from cholesterol. In the synthesis of adrenal androgen hormones, cholesterol is converted to pregnenolone and then to DHEA. From DHEA, the adrenal glands can synthesize androstenedione, which is further converted to testosterone. In fat tissue, androstenedione can be converted to estrone hormone by the aromatase enzyme, which also is known as estrogen synthase enzyme. Thus, DHEA supplementation can lead to increased production of androstenedione, testosterone and estrogen.

DHEA is the most abundant hormone made by the adrenal glands. Some DHEA is secreted by the adrenal glands and circulates in the bloodstream, where it is picked up by other tissues (i.e., adipose, testis, ovaries) and further converted into other androgens or estrogens. The serum concentration of DHEA (DHEA-sulfate), is used as a measure of adrenal androgen production when monitoring various conditions.¹

DHEA supplements can be made in the laboratory from diosgenin, a steroid compound found in wild yams. However, the body is unable to convert diosgenin into DHEA or any other hormone.

Thus, supplementing with wild yam as a means to affect hormone levels is unsubstantiated.²

In humans, DHEA blood levels peak in early adulthood and then start a lifelong descent. By the age of 70, DHEA levels have declined by up to 75 percent compared with young adult levels. By age 90, we make 90 percent less DHEA than a young adult.^{3,4}

These findings have led some researchers to investigate whether returning DHEA levels to those of a young adult (through supplementation) can serve as an anti-aging and degenerative disease prevention strategy. Preliminary reports in this regard are conflicting. Some evidence suggests DHEA supplementation (25-200 mg per day) can reverse some parameters of aging and improve well-being. Other reports correlate higher blood DHEA levels (and supplementation in some cases) with increased risk of prostate cancer, postmenopausal breast cancer and ovarian cancer. ⁵⁻¹³

As a result, many health authorities are cautious about recommending DHEA supplementation as an anti-aging intervention. Individuals with a history or family history of breast, ovarian or prostate

cancer should not supplement with DHEA indiscriminately until further studies are completed.¹⁴ The average male produces 31 mg of DHEA per day, while the average woman produces approximately 19 mg.¹⁵

Supplementation Studies and Clinical Applications

Systemic Lupus Erythematosus (SLE): In a Stanford Medical Center study, DHEA supplementation (200 mg per day) decreased the SLE Disease Activity Index by nearly two points, while the placebo group increased by almost a full point. DHEA patients had significantly fewer flare-ups and their required dosage of corticosteroid drug used to control symptoms decreased by 35 percent, whereas the placebo group increased their dose of corticosteroids by 40 percent. This was a three-month study only. Long-term benefits are still unknown, and the major side effect in this study was mild to severe acne in women in the DHEA group. 16,17

Dementia (Age-Related): DHEA is found in high concentrations in the brain; declining levels with aging may affect memory and cognitive functions. DHEA supplementation shows promise in enhancing memory and improving cognitive function (men: 25-50 mg per day; women: 15-25 mg per day). ^{18,19}

Erectile Dysfunction: A double-blind research study provided evidence that 50 mg of DHEA per day (six months) improved erectile function in men presenting with erectile dysfunction problems.²⁰ Be aware that other phytonutrients can correct erectile dysfunction and are known to have fewer potential side effects than DHEA (i.e., *Tribulus terrestris*, ginkgo biloba, muira puama).

Diabetes: Two short-term (three-week duration) studies have shown that DHEA supplementation increases insulin sensitivity at a daily dosage of 25-50 mg. There are no long-term human studies to indicate whether DHEA is appropriate for diabetics at this time. ^{21,22}

Dosage Ranges

- Systemic Lupus Erythematosus: 100-200 mg per day for three months; maintenance dose unknown.
- Dementia: Men: 25-50 mg per day; women: 15-25 mg per day.
- Erectile Dysfunction: 50 mg per day.
- Diabetes: 25-50 mg per day, but requires substantiation.

Adverse Side Effects and Toxicity

At doses of 50-200 mg, patients often experience acne, increased facial hair and increased perspiration. Less frequently reported side effects are breast tenderness, weight gain, mood alteration, headache, oily skin and menstrual irregularity.²³

Contraindications

Any personal history or family history of breast, ovarian or prostate cancer (extreme caution should be used in these cases)¹⁴ precludes indiscriminate use of DHEA supplementation. Males taking DHEA should have their PSA (prostate-specific antigen) levels monitored to screen for prostate cancer development. Females taking DHEA should be monitored for breast, ovarian and endometrial cancer development.²⁶⁻³³

Drug-Nutrient Interactions

Methyltestosterone: DHEA supplementation has been shown to increase blood levels of testosterone, as does methyltestosterone. Thus, the addition of DHEA supplementation to methyltestosterone treatment may result in an excessive increase of blood testosterone and increase the risk of related side effects.^{24,25}

References

- 1. Marks M, Marks A, Smith C. *Basic Medical Biochemistry: A Clinical Approach*. Baltimore, MD: Williams & Wilkins;1996, p. 675-88.
- 2. Araghiniknam M, Chung S, Nelson-White T, Eskelson C, Watson RR. Antioxidant activity of dioscorea and dehydroepiandrosterone (DHEA) in older humans. *Life Sce* 1996;59:147-57.
- 3. Migeon C, et al. DHEA and androsterone levels in human placenta. Effect of age and sex: day-to-day and diurnal variations. *J Clin End Met* 1957;17:1051-62.
- 4. Ravaglia G, et al. The relationship of DHEAS to endocrin-metabolic parameters and functional status in the oldest old. *J Clin Endocrinol Metab* 1996;81:1173-7.
- 5. Diamond P, Cusan L, Gomez J-L, Belanger A, Fabrie F. Metabolic effects of 12-month percutaneous DHEA replacement therapy in post menopausal women. *J Endocrinol* 1996;150(Suppl):43S-50S.
- 6. Villareal DT, Holloszy JO, Kohrt WM. Replacement of DHEA in aging men and women. *Ann NY Acad Sci* 1995;774:128-42.
- 7. McNeil C. Potential drug DHEA hits snags on way to clinic. J Natl Cancer Inst 1997;89:681-3.
- 8. Jones JA, Nguyen A, Straub M, Leidich R, Veech RL, Wolf S. Use of DHEA in a patient with advanced prostate cancer; a case report and review. *Urology* 1997;50:784-8.
- 9. Zumoff B, Levin J, Rosenfeld RS, Marksham M, Strain GW, Fukushima DK. Abnormal 24-hr mean plasma concentration of DHEA and DHEAS in women with primary operable breast cancer. *Cancer Res* 1981;41:3360-3.
- Dorgan JF, Longcope C, Stephenson HE Jr, Falk RT, Miller R, Franz C, et al. Relationship of prediagnostic serum estrogen and androgen levels to breast cancer risk. *Cancer Epidemiol Biomarkers Prev* 1996;5:533-9.
- 11. Gordon GB, Bush TL, Helzlsouer KJ, et al. Relationship of serum levels of DHEA and DHEAS to the risk of developing postmenopausal breast cancer. *Cancer Res* 1990;50:3859-62.
- 12. Morales AJ, et al. The effect of six months treatment with a 100mg daily dose of DHEA on circulating sex steroids, body composition and muscle strength in age-advanced men and women. *Clin Endocrinol* 1998;49: 421-32.
- 13. Skolnick AA. Scientific verdict still out on DHEA. JAMA 1996;276:1365-7.
- 14. Balch J. The Super Antioxidants. New York, NY: M. Evans and Company, Inc.; 1998, p. 143-9.
- 15. Aksoy IA, et al. Human lives DHEA- sulfotransferase: nature and extent of individual variation. *Clin Parmacol Therapeutics* 1993;54:498-506.
- 16. van Vollenhoven RF, Engleman EG, McGuire JL. An open study of DHEA in system lupus erythermatosus. *Arthritis Rheum* 1994;37;9:1305-10.
- 17. van Vollenhoven RF, Engleman EG, McGuire JL. DHEA in systemic lupus erythematosus: results of a double-blind, placebo-controlled, randomized clinical trial. *Arthritis Rheum* 1995;38:1826-31.
- 18. Yen SS, Morales AJ, Khorram O. Replacement of DHEA in aging men and women: potential remedial effects. *Ann NY Acad Sci* 1995;774:128-42.
- 19. Morales AJ, Nolan JJ, Nelson JC, Yen SSC. Effect of replacement dose of DHEA in men and women of advancing age. *J Clin Endocrinol Metab* 1994;78,6:1360-7.
- 20. Reiter WJ, Pycha A, Schatzl G, et al. DHEA in the treatment of erectile dysfunction: a prospective double-blind reandomised, placebo-controlled study. *Urology* 1999;53:590-5.
- 21. Bates CW, Bates CW, Egerman RS, Umstot ES, Buster JE, Casson PR. DHEA attenuates study-induced declines in insulin sensitivity in postmenopausal women. *Ann NY Acad Sci*

- 1995;291-3.
- 22. Casson PR, Faquin LC, Stentz FB, Straughn AB, Anderson RN, Abraham GF, Buster JE. Replacement of DHEA enhancer T-lymphocyte insulin binding in postmenopausal women. *Fertil Steril* 1995;63:1027-31.
- 23. Regelson W, et al. DHEA A Pleiotropic Steroid: How Can One Steroid Do So Much? In: Klatz RM: *Advances in Anti-Aging Medicine*. Larchment, NY: Mary Ann Liebert Publ; 1996, vol. 1.
- 24. Wolf OT, Neumann O, Hellhammer DH, Geiben AC, Strasburger CJ, Dressendorfer RA, et al. Effects of a two-week physiological DHEA substitution on cognitive performance and wellbeing in healthy elderly women and men. *J Clin Endocrinol Metab* 1997;82:2263-7.
- 25. Labrie F, Bélanger A, Simard J, Luu-The V, Lebrie C. DHEA and peripheral androgen and estrogen formation: intracinology. *Ann NY Acad Sci* 1995;774:16-28
- 26. McNeil C. Potential drug DHEA hits snags on way to clinic. J Natl Cancer Inst 1997;89:681-3.
- 27. Jones JA, Nguyen A, Straub M, Leidich RB, Veech RL, Wolf S. Use of DHEA in a patient with advanced prostate cancer: a case report and review. *Urology* 1997;50:784-8.
- 28. Zumoff B, Levin J, Rosenfeld RS, Markham M, Strain GW, Fukushima DK. Abnormal 24-hr mean plasma concentrations of DHEA and DHEA-sulfate in women with primary operable breast cancer. *Cancer Res* 1981;41:3360-3.
- 29. Helzlsouer KJ, Gordon GB, Alberg AJ, Bush TL, Comstock GW. Relationship of prediagnostic serum levels of dehydroepiandrosterone and dehydroepiandrosterone sulfate to the risk of developing premenopausal breast cancer. *Cancer Res* 1992;52:1-4.
- 30. Berrino F, Muti P, Micheli A, Bolelli G, Krogh V, Sciajno R, et al. Serum sex hormone levels after menopause and subsequent breast cancer. *J Natl Cancer Inst* 1996;88:291-6.
- 31. Barrett-Connor E, Friedlander NJ, Khaw KT. Dehydroepiandrosterone sulfate and breast cancer risk. *Cancer Res* 1990;50:6571-4.
- 32. Bernstein L, Ross RK, Pike MC, Brown JB, Henderson BE. Hormone levels in older women: a study of post-menopausal breast cancer patients and health population controls. *Br J Cancer* 1990;61:298-302.
- 33. Heinonen PK, Koivula T, Pystynen P. Decreased serum level of dehydroepiandrosterone sulfate in postmenopausal women with ovarian cancer. *Gynecol Obstet Invest* 1987;23:271-4.

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