



# DHEA:

## The “**Youth**” Hormone

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# Dehydroepiandrosterone

(DHEA) and its ester metabolite dehydroepiandrosterone sulfate (DHEAS) are steroid hormones produced by the adrenal glands (DHEAS is also the blood marker for measuring DHEA).

Under normal physiologic conditions, these hormones are precursors that are transformed to estrogen and testosterone. DHEA and DHEAS are thought to affect mood and well-being, have neurosteroid effects and may influence the immune system. Animal experiments suggest that DHEA has many other effects, including anticancer, immune-enhancing, neurotropic and general anti-aging effects. Perhaps no other hormone is more associated with youthfulness and aging as DHEA.

## DHEA's decline with age

DHEA levels start relatively low at birth, and gradually increase until puberty, when levels increase markedly, reaching a peak around 20 to 24 years of age. From there, serum and tissue DHEA levels decline at a rate of 2 to 3% per year, with a steep decline occurring around middle age. In fact, human clinical research has shown that DHEA and DHEAS levels were 40% lower in women than men between the ages of 50-89. Although levels of these hormones declined 60% across the 40-yr age range for both men and women, the pattern of the change differed. For men, DHEA(S) fell in a curvilinear fashion, with the degree of change decreasing with each decade. In contrast, DHEA(S) levels in women fell 40% from the 50s to 60s, were unvarying from 60-80 yr of age, and declined an additional 18% in the 80s. Despite these differences in the effect of aging, levels of DHEA(S) remained lower in women than men throughout the 50-89-yr age range. These results were independent of adiposity, smoking, and alcohol consumption. In any case, by age 75, humans exhibit 10 to 20% of young adult DHEA levels.

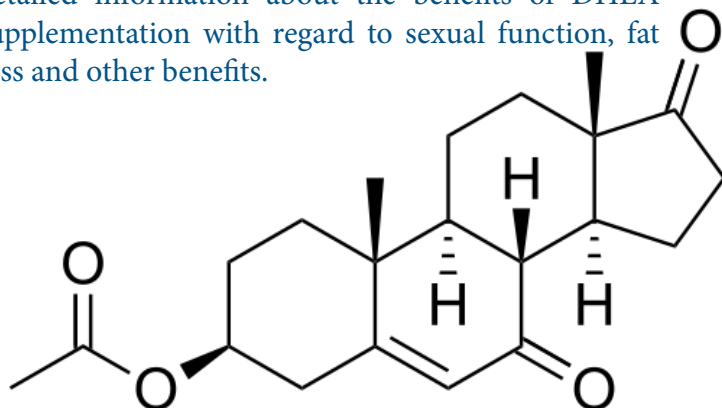
## The effect of DHEA decline on health

With this decline comes a host of age-related

syndromes and diseases. A number of review articles have summarized the available observational data showing that in older individuals serum DHEA levels are inversely related to incidence and prevalence of disease. Low levels of DHEA are associated with aging and cardiovascular disease in men, and an increased risk of premenopausal breast and ovarian cancer in women, impaired cognitive function, and compromised immune function. With this decline may also come a concurrent reduction in protein formation, a decrease in muscle mass, and an increase in body fat.

## The Benefits of DHEA Supplementation

Results from various studies indicate that DHEA supplementation may benefit older individuals. More than 50 published human studies show that supplementation in elderly and those with endocrine deficiencies can safely restore DHEA levels to those typical of healthy younger adults. Furthermore, research has shown that DHEA supplementation is effective at supporting immune function (25, 26), maintaining cognitive function, elevating mood and sense of well-being (27-35), improving sleep patterns (36), providing, peri- and postmenopausal support (37, 38), reducing fat mass and maintaining lean body mass (39-42), maintaining bone health (41, 43-47), maintaining healthy lipid levels and overall cardiovascular health (48-51), and normalizing glucose metabolism (40, 49, 51-53). Following is more detailed information about the benefits of DHEA supplementation with regard to sexual function, fat loss and other benefits.



## **Low levels of DHEA are associated with poor sexual function**

In a study involving 348 male patients, DHEAS levels were significantly lower in the men with aging male symptoms (e.g., decrease in sexual desire/libido), and the DHEAS was significantly lower in men with sexual dysfunction. In another study of 442 male subjects, serum levels of DHEAS in patients with erectile dysfunction were lower than in healthy volunteers until 60 years of age. An additional study with 53 patients found that erectile dysfunction is associated with a lower level of serum DHEAS.

## **Supplementation with DHEA promotes healthy sexual function**

A prospective study was conducted on erectile dysfunction (ED) patients with different organic etiologies. The study patients comprised 27 patients (group 1) with hypertension, 24 patients (group 2) with diabetes mellitus, six patients with neurological disorders (group 3) and 28 patients (group 4) with no organic etiology. All were treated with 50 mg DHEA for 6 months. The effectiveness was assessed by using the responses to question 3 (frequency of penetration) and question 4 (maintenance of erections after penetration) of the 15-question International Index of Erectile Function (IIEF). DHEA treatment was associated with statistically significantly higher mean scores compared to baseline values for question 3 and question 4 of the IIEF in groups 1 and 4 after a period of 24 weeks. The researchers concluded that oral DHEA-treatment may be of benefit to patients with ED who have hypertension or to patients with ED without organic etiology.

In a prospective, double-blind, randomized, placebo-controlled study, forty ED patients were randomly divided into two groups of 20 patients each. Group 1 was treated with an oral dose of 50 mg DHEA and group 2 with a placebo one time a day for 6 months. The International Index of Erectile Function (IIEF), a 15-item questionnaire, was used to rate the success of this therapy. The results were that DHEA treatment was associated with higher mean scores for all five domains of the IIEF, including the ability to achieve or maintain an erection sufficient for satisfactory sexual

performance. The researchers concluded that oral DHEA treatment may be of benefit in the treatment of ED.

Two hundred and eighty healthy individuals (women and men 60-79 years old) were given DHEA, 50 mg, or placebo, orally, daily for a year in a double-blind, placebo-controlled study. Besides the reestablishment of a “young” concentration of DHEAS, a small increase of testosterone and estradiol was noted, particularly in women, and may be involved in the significantly demonstrated physiological-clinical manifestations here reported. A significant increase in most libido parameters was also found in women over 70 years old. The authors concluded that 50 mg/day DHEA administration over one year normalized some effects of aging. In a double-blind study, 24 women with adrenal insufficiency randomly received 50 mg of DHEA orally each morning for four months and placebo daily for four months, with a one-month washout period. The results were that treatment with DHEA raised the initially low serum concentrations of DHEA, DHEAS, androstenedione, and testosterone into the normal range. As compared with placebo, DHEA significantly increased the frequency of sexual thoughts ( $P=0.006$ ), sexual interest ( $P=0.002$ ), and satisfaction with both mental and physical aspects of sexuality ( $P=0.009$  and  $P=0.02$ , respectively). DHEA also significantly improved overall well-being as well as scores for depression and anxiety. For the global severity index, the mean change from base line was  $-0.18 \pm 0.29$  after four months of DHEA therapy, as compared with  $0.03 \pm 0.29$  after four months of placebo ( $P=0.02$ ).

## **Supplementation with DHEA and fat loss**

In a randomized, double-blind, placebo-controlled trial fifty-six elderly persons (28 women and 28 men aged 71 [range, 65-78] years) with age-related decrease in DHEA level were randomly assigned to receive 50 mg/d of DHEA or matching placebo for 6 months. Of the 56 men and women enrolled, 52 underwent follow-up evaluations. Compliance with the intervention was 97% in the DHEA group and 95% in the placebo group. The results were that DHEA therapy compared with placebo induced significant decreases in visceral fat area ( $-13 \text{ cm}^2$  vs  $+3 \text{ cm}^2$ , respectively;  $P = .001$ ) and subcutaneous fat ( $-13 \text{ cm}^2$  vs  $+2 \text{ cm}^2$ ,  $P = .003$ ).

Insulin was also significantly reduced after 6 months of DHEA therapy compared with placebo ( $P = .007$ ). Despite the lower insulin levels, the glucose response was unchanged, resulting in a significant increase in an insulin sensitivity index in response to DHEA compared with placebo ( $P = .005$ ). The researchers concluded that DHEA replacement could play a role in prevention and treatment of the metabolic syndrome associated with abdominal obesity.

In a prospective 6 month trial, 10 women and eight men, aged 73  $\pm$  1 years, received 50 mg DHEA daily. Control subjects were 10 women and eight men, aged 74  $\pm$  1 years. The results were that fat mass decreased (-2.86 lbs;  $P < 0.01$ ) and fat-free mass increased (1.98 lbs;  $P \leq 0.05$ ) in response to DHEA replacement.

Research has also shown that women with polycystic ovary syndrome (PCOS) who had the highest levels of DHEAS also had the lowest risk of abdominal obesity.

### Some Other DHEA Benefits

Two hundred and eighty healthy individuals (women and men 60-79 years old) were given DHEA, 50 mg, or placebo, orally, daily for a year in a double-blind, placebo-controlled study. Bone turnover improved selectively in women over 70 years old. Improvement of the skin status was observed, particularly in women, in terms of hydration, epidermal thickness, sebum production, and pigmentation.

In a prospective 6 month trial, 10 women and eight men, about 73 years old received 50 mg DHEA daily. Control subjects were 10 women and eight men about 74 years old. The results were that bone mineral density (BMD) of the total body and lumbar spine increased (both  $P \leq$

0.05), in response to DHEA replacement. DHEA replacement also resulted in an increase in total serum testosterone concentrations (from 10.7 to 15.6 nmol/l in the men and from 2.1 to 4.5 nmol/l in the women; both  $P \leq 0.05$ ).

### DHEA Safety

In animal studies, DHEA has been found to inhibit breast cancer development and growth and to stimulate bone formation. In clinical studies, DHEA has been found to increase bone mineral density and to stimulate vaginal maturation without affecting the endometrium, while improving well-being and libido with no significant side effects. The advantage of DHEA over other androgenic compounds is that DHEA, at physiological doses, is converted into androgens and/or estrogens only in the specific target tissues that possess the appropriate physiological enzymatic machinery, thus limiting the action of the sex steroids to those tissues possessing the tissue-specific profile of expression of the genes responsible for their formation, while leaving the other tissues unaffected and thus minimizing the potential side effects observed with androgens or estrogens administered systemically.

Two hundred and eighty healthy individuals (women and men 60-79 years old) were given DHEA, 50 mg, or placebo, orally, daily for a year in a double-blind, placebo-controlled study. No potentially harmful accumulation of DHEAS and active steroids was recorded. A number of biological indices confirmed the lack of harmful consequences of this 50 mg/day DHEA administration over one year, also indicating that this kind of replacement therapy normalized some effects of aging, but does not create "supermen/women" (doping).

