

## Important Facts You Should Know

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### RESEARCH SHOWS THAT DHEA MAY SUPPORT

#### WEIGHT CONTROL<sup>2, 3, 4, 13, 14, 16</sup>

- stimulates fat burning, reduces abdominal fat storage
- increases metabolic rate through the stimulation of thermogenesis and by supporting the lean body mass
- reduces insulin resistance

#### STRESS SUPPORT

- reduces the stress hormone cortisol and reduces some of its catabolic effects on bone and muscle<sup>9</sup>

#### DRUG TREATMENT SUPPORT

- reduces the side-effects from corticosteroid therapy<sup>17</sup>

#### SEXUAL HEALTH

- enhances female libido<sup>8</sup>
- supports erectile function through improved nitric oxide levels and facilitated testosterone binding to albumin<sup>11, 15</sup>

#### SKIN HEALTH<sup>10</sup>

- increases epidermal thickness and hydration, sebum production, decreases facial skin pigmentation

#### IMMUNE FUNCTION

- improves immune response to infections and reverses its age-related decline<sup>4</sup>
- may reduce the severity of auto-immune diseases such as lupus, arthritis, psoriasis<sup>1</sup>
- alleviates allergies<sup>1</sup>

#### BRAIN<sup>1</sup>

- improves the sense of well being and reduces certain types of depressions
- has a mental stimulating effect (counteracts the inhibitory effects of GABA neurotransmitter)

#### MENOPAUSE/PERIMENOPAUSE

- reduces hot flashes, supports vaginal tissue<sup>9</sup>
- supports bone health<sup>1</sup>
- sense of well being, libido<sup>7</sup>

#### AGE-RELATED CHANGES

- restores declining IGF-1 levels
- corrects age related changes in immune system, skin, bone & muscle strength and sexual health.

#### OTHER CONDITIONS

- may alleviate chronic fatigue<sup>12</sup>
- has a mild blood thinning effect<sup>6</sup>

DHEA is a fat soluble steroid hormone which is synthesized in the body, mostly in the adrenal glands, and in small amounts in ovaries/testes, the brain and various other peripheral tissues, such as skin. It is a derivative of cholesterol metabolism as seen below:

#### Acetyl-CoA ⇌ Cholesterol ⇌ Pregnenolone ⇌ DHEA ⇌ DHEA-S

A great portion of DHEA in the body is derived from adrenal synthesis, which is controlled by ACTH (a signal from the brain), and can be severely reduced when the stress hormone cortisol is high or due to treatment with corticosteroids. The adrenals secrete DHEA in the bloodstream, where it is converted back and forth to DHEA-Sulfate, which is considered the body's circulating reservoir of DHEA. Circulating DHEA is taken up by many tissues such as skin, bone, ovaries or testes and converted to various estrogens and testosterone (which can be further converted to dihydrotestosterone [DHT] or estrogen). See figure below:

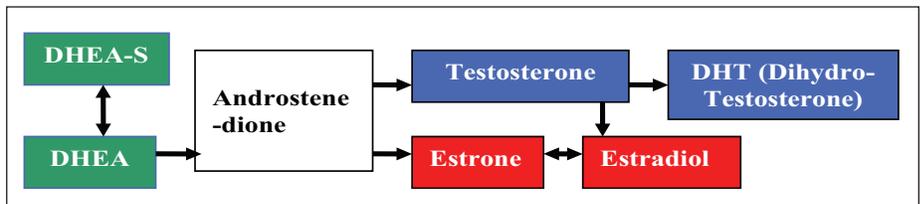


Fig. 1 - DHEA conversions in adrenals, ovaries, testes, skin, bone, brain

For females, supplementation with approximately 25-50 DHEA for 3 months can double baseline testosterone levels for subjects that have a low baseline DHEA level to begin with (which often occurs after the age of 40, during menopause/perimenopause). DHEA supplementation can also cause small (approximately 10%) increases in the estrogen hormones estrone and estradiol, which may be significant only for postmenopausal women.

For males, DHEA supplementation with approximately 25-50mg DHEA may not significantly increase serum testosterone levels, when the baseline testosterone is in the typical normal male range, but may significantly increase their estrogen levels, based on biochemical individuality. Males with increased body fat tend to have higher baseline estrogens and a more marked increase in estrogen levels in response to DHEA supplementation.

Whether male or female, at any age, supplementation with DHEA has to be monitored by a health care practitioner for baseline and subsequent levels of DHEA, testosterone, DHT, estradiol and estrone.

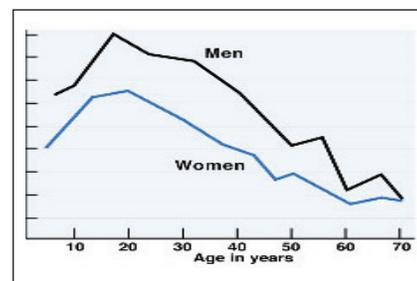
The serum levels of estrogens or testosterone are only a partial indicator of the DHEA hormonal derivatives in the body. A significant amount of DHEA conversions occur inside ovaries, testes, brain and various peripheral cells such as skin and bone and the resulting hormones are metabolized locally, inside the cells/tissues. [8] Also, note that DHEA supplements on the market have been found to have a wide discrepancy in contents compared to label claims [15], hence it is important to get DHEA from a reliable, trusted supplier.

**Conditions that may lower DHEA production:** excessive mental or physical stress (usually characterized by increased cortisol level), alcohol consumption, dieting, malnutrition, vegetarian diets (especially soy consumption)

**Drugs that may lower DHEA production include:** corticosteroids (cortisone, dexamethasone), insulin, central nervous system agents (carbamazepine, phenytoin, danazol)

**DHEA plasma levels drop steadily with aging, which may be due to (see figure 2):**

- lowered availability of the precursor pregnenolone (also declines with age)
- lowered ACTH (stimulation signals from the brain)
- inadequate sensitivity of adrenals or other tissues that manufacture DHEA
- adrenal gland atrophy



**Fig. 2** - Decline of DHEA with aging

“The steroid hormone intermediate, DHEA, has been proposed as a therapeutic agent for the treatment of obesity. Its effects on lipogenesis, substrate cycling, peroxisome proliferation, mitochondrial respiration, protein synthesis, and thyroid hormone function have been reported. The results of these studies suggest that the antiobesity function of DHEA is not simply one of inhibiting fat synthesis and deposition but is one of affecting a number of pathways that contribute to the maintenance of the isoenergetic state rather than the promotion of positive energy balance.” [16]

“In postmenopausal women, all estrogens and nearly all androgens are made locally in peripheral target tissues from DHEA. In adult men, approximated 50% of androgens are made locally. In fact, all the enzymes required to make androgens and estrogens are expressed in a cell-specific fashion, thus permitting local control of steroid formation and action.. On the other hand, exogenous DHEA provides important advantages in postmenopausal women because it compensates for the declining secretion of DHEA by the adrenals with age. The benefits of DHEA include increased bone mineral density, muscle mass, well-being, and libido, as well as beneficial effects against skin atrophy, type 2 diabetes, and obesity.” [8]

“DHEA-S is reduced in chronic inflammatory diseases. Since DHEA-S is the pool for peripheral sex steroids, such as testosterone and 17 beta-estradiol, lack of this hormone leads to a significant sex hormone deficiency in the periphery. The importance of DHEA-S deficiency will be demonstrated with respect to osteoporosis. As a consequence, we suggest a combined therapy with corticosteroids plus DHEA in chronic inflammatory diseases.” [17]

**Suggested use of DHEA:** 25-50-mg DHEA may be administered in one or two divided doses in the morning and at the latest in the afternoon, due to its stimulatory effect on metabolism and the brain. DHEA is best absorbed with a fatty meal or snack. The bigger the size of the meal and the higher its fat content, the slower will be the delivery of DHEA to the plasma, which mimics the body's own production of DHEA. However, a rapid increase in DHEA plasma levels might be desired for a sharp rise in libido and/or support of erectile function. In this case oral DHEA should be taken with a small fatty snack (may add some phosphatidylcholine) 2-4 hours before the expected result.

- In females, the increased libido is due to a fast rise in plasma testosterone levels
- In males, DHEA is believed to improve NO (nitric oxide) production. DHEA is also known to help with the testosterone binding to plasma albumin and with testosterone delivery to tissues for its effects. It also increases conversion to DHT (dihydrotestosterone), which may play a role in a male's libido. [11,15]

**Conditions where DHEA may be contraindicated:** PCOS (until excessive insulin levels are corrected, because testosterone levels are elevated), hirsutism (excessive facial hair), acne, males with excessive estrogen levels, prostate enlargement, hormonal sensitive cancers (breast, prostate, adenomas). In premenopausal women, DHEA supplementation, when it is not deficient, may increase androgens to the point of interference with ovulation and fertility.

DHEA supplementation may increase DHT (dihydrotestosterone) levels. This is due to both its conversion to testosterone and the fact that DHEA upregulates the activity of 5AR (5-alpha-reductase) enzyme, which further converts testosterone to DHT. As a consequence, some women may experience a slight increase in hair loss, especially if their estrogen levels are low. In this case it is recommended to also administer saw palmetto or green tea (standardized for EGCG) because these two compounds were shown to inhibit the activity of the 5AR enzyme.

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