

Life Extension Magazine December 2010

Report

New Research Substantiates the Anti-Aging Properties of DHEA

By Kirk Stokel

In 2007, *Life Extension*® led the battle against Congress's ill-conceived campaign to re-classify **DHEA** (dehydroepiandrosterone) as an "anabolic steroid drug"—an act that would have made this life-sustaining compound unavailable to the American public without a prescription.

Thanks in no small part to the efforts of **Life Extension**® members, the battle was won.

Today, less than **three years later**, scientists have uncovered *even more research substantiating* DHEA's remarkable health-promoting benefits.

Sometimes called the "**youth hormone**," DHEA is the most abundant hormone precursor in the human body and a source of the sex hormones.

Its steady and precipitous decline is an inevitable consequence of aging, ¹ and contributes to the onset of degenerative disease.

The latest scientific discoveries indicate that as little as **50 mg** of DHEA per day may:

1. Inhibit multiple factors implicated in **metabolic syndrome** by favorably altering **gene expression**;
2. Boost **bone strength** and ward off **osteoarthritis**;
3. Enhance **memory**.²⁻⁵

Daily intake of **90 mg** per day and higher has been shown to **improve cognitive function** and **alleviate depression** both in the elderly and among individuals suffering from debilitating mental illness.^{6,7}

First introduced to Americans in **1981** by the **Life Extension Foundation**®, the anti-aging effects of DHEA have been described in medical textbooks starting in the early **1990s**.

In this article, you will discover the most up-to-date evidence of DHEA's *profoundly* beneficial impact across multiple systems of the body.

Potent Cognitive Support

DHEA deficiency is implicated in numerous age-related conditions, including declines in brain and nervous system function. The latest research suggests that DHEA supplementation may exert powerful neuroprotective effects.

In fact, **2009** witnessed *extraordinary* advances in our understanding of the cognitive and memory-enhancing benefits of DHEA.



Two large studies showed that levels of DHEA-S in elderly patients correlated significantly and positively with cognitive function. (Chemically similar to DHEA, DHEA-S is the sulfated *form* of DHEA.)^{8,9} Prior research had shown that higher DHEA-S levels were directly associated with improved concentration, working memory, and executive (decision-making) function.¹⁰

Israeli scientists found that the cognitive dysfunction that occurs in **schizophrenia** is also partly associated with levels of DHEA-S and other neurosteroids.¹¹ Supplementation with **200 mg per day** of DHEA in schizophrenic patients improved attention and motor skills compared with placebo.⁶ Although the direct symptoms of schizophrenia were unaffected, DHEA's ability to provide relief from the cognitive deficits associated with this severe psychiatric condition may significantly improve quality of life in these individuals.



The last few years have also yielded new pre-clinical data on DHEA's neuroprotective, memory-enhancing effects. In one noteworthy study, DHEA significantly improved memory retention and consolidation in mice—especially when the experimental equivalent of an emotional stimulus was involved.¹² This may be related to DHEA's ability to stimulate the proliferation of key brain cell receptors specifically associated with memory processing.¹³

When given to aging rats, DHEA was shown to enhance brain cell utilization of ATP—the body's fundamental energy-storage molecule—thereby protecting the cell membranes from age-related damage.⁴ Impaired energy utilization and reduced production of ATP contribute to the “neuronal energy crises” that underlie Alzheimer's and other neurodegenerative diseases.¹⁵

A landmark 2007 study showed that DHEA supplementation of **150 mg twice daily** improved memory recall and mood in healthy young men, specifically increasing activity in the hippocampus, the region of the brain most closely associated with mnemonic function (memory).⁵

Enhance Your Mood—*Naturally*

Depression often accompanies aging, frequently emerging in older individuals.^{16,17} Fortunately, we now recognize depression as an essentially physiological condition—one that can be treated. Low DHEA levels are known to render aging humans more vulnerable to depression in the presence of triggers such as rejection or isolation.¹⁸ Negative emotional stimuli have been shown to *lower* DHEA levels even further.¹⁹

Supplementation with DHEA can powerfully *mitigate* depression and its effects. A *National Institute of Mental Health* study of depressive men and women aged **45-65 years** showed significant improvement over 6 weeks among those who took **90 mg of DHEA per day for 3 weeks** and then **450 mg per day for 3 weeks**, compared with placebo.⁷ The study also showed significant improvements in sexual functioning scores in supplemented patients, but not among control patients. In a rare admission from the generally conservative National Institute of Mental Health, their conclusion was, “*We find DHEA to be an effective treatment for midlife-onset major and minor depression.*”

In a set of studies, DHEA was found to improve both mood and energy while alleviating depression.²⁰⁻²² Israeli researchers also demonstrated *minimal* effects on other hormonal profiles, alleviating concerns about adverse events with DHEA.²³

A remarkable 2006 study demonstrated reduction in depressive symptoms in an especially challenging population—patients with HIV/AIDS.²⁴

Several 2009 studies revealed associations of low DHEA levels with a number of neuropsychiatric conditions and were able to show that DHEA influences **gene expression** in the brain.²⁵ For example, DHEA modulates expression of genes directly involved in **appetite regulation, energy utilization, and alertness**.²⁶ Another study demonstrated that DHEA acted in

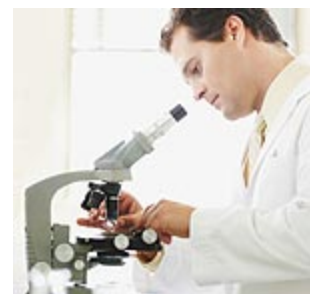
synergy with the antidepressant fluoxetine (Prozac®), leading researchers to suggest DHEA as “a useful adjunct therapy for depression.”²⁷

Support for Aging Bones and Joints

A 2000 study demonstrated improved bone turnover—more marked in women than in men—during a year-long study of daily **50 mg** supplementation with DHEA.²⁸ (Bone turnover is the natural process by which the body replaces old bone from the skeleton and replaces it with new bone.) By 2003, laboratory evidence emerged suggesting that DHEA could potentially *enhance* joint function and ward off **osteoarthritis** (OA).²

DHEA treatment of cartilage tissue taken from patients with OA increased production of healthy, flexible type II collagen protein, while reducing production of the less flexible type I collagen associated with scar formation.² DHEA also modified the imbalance between cartilage-destroying enzymes and those that protect cartilage from damage. These impressive effects were the direct result of DHEA’s capacity to favorably modulate gene expression.

DHEA’s effects on bone structure are no less significant. A double-blind, randomized, controlled trial of **50 mg per day** of DHEA administered orally versus placebo for 12 months showed improved hip bone mineral density (BMD) in older men and women with low DHEA-S levels, with additional improvements in spine BMD in women.^{3,29} A larger study in 2008 showed that DHEA not only improved lumbar spine BMD in women (not men) taking **50 mg per day** for a year, but it also reduced blood-borne markers of bone resorption,³⁰ an important measure of overall bone health and bone aging. Not surprisingly, the addition of **vitamin D** and **calcium** supplements to a DHEA regimen may afford further benefit.³¹



WHAT YOU NEED TO KNOW: DHEA

- DHEA, the most common hormone precursor in the body, is intimately associated with youthful and healthy functioning across a range of physiological systems.
- Levels of DHEA decline steadily with age, and low DHEA levels are associated with increased cardiovascular risk, diabetes, obesity, loss of vigor and sexual energy, depression, and even visible skin aging.
- The most up-to-date scientific research indicates that DHEA can protect brain cells involved in memory function, alleviate depression and enhance mood, strengthen bone health, bolster immunity, lower blood glucose, limit the complications of obesity and diabetes, support healthy cardiovascular function, and enhance sexuality at both the psychological and physical levels.
- As little as **50 mg of DHEA per day** may favorably alter gene expression to inhibit multiple factors implicated in metabolic syndrome; boost bone strength; enhance cognitive function and memory; and ward off osteoarthritis.
- DHEA is also available in topical crèmes that has been shown to dramatically enhance the youthful appearance of skin.
- Individuals who have been diagnosed with any type of hormone-related cancer should not supplement with DHEA.



Optimal Immune Strength and Anti-Viral Protection

The precipitous age-related decline in DHEA/DHEA-S levels results in the immune deficiency we call *immunosenescence*.³² Supplementation with DHEA may beneficially modulate immunity^{33,34} to help combat debilitating age-related conditions through multiple, complementary pathways.

DHEA has boosted immune function in blood cells taken from patients after major abdominal surgery.³⁵ This action may help to prevent serious infections and promote healing. In the setting of dangerous infections and trauma in laboratory animals, DHEA and its metabolites markedly upregulate host immune responses, modulate inflammation, and improve survival.³⁶⁻³⁸ In animal models, DHEA's ability to raise sex hormone concentrations to youthful levels also promoted wound healing.³⁹

DHEA also possesses significant antiviral properties. It has blocked replication of several different, potentially deadly virus families in the laboratory—more effectively and more selectively than the drug **gibavirin**!^{40,41}

A 2008 study showed that DHEA also increases natural resistance to certain lethal parasites, including *Trypanosoma cruzi* (the cause of **Chagas disease**),⁴² a microorganism that causes death from heart disease and brain damage, particularly in immunocompromised patients. Subsequent research conducted in 2009 found that DHEA supplementation *reduced* parasite levels, raised levels of defensive macrophage white blood cells, and increased levels of immune signalling *interferons*.^{43,44}

Among individuals stricken with autoimmune disorders such as rheumatoid arthritis or lupus, treatment with conventional corticosteroids not only *over-suppresses* the immune system, it can also promote bone resorption and catastrophic fractures. DHEA has been shown to reduce expression of **cytokines** and other factors that lead to bone resorption in steroid-treated tissue, while still suppressing inflammation effectively.⁴⁵

There's good news for asthma and allergy patients who respond poorly to regular steroid usage as well. DHEA is now known to suppress **allergy-induced inflammatory cytokines** in reactive airway cells while increasing the ratio of beneficial interferon to inflammatory cytokines—highly significant advances in the management of this troubling condition.⁴⁶

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Combat Metabolic Disorders

We've known for over a decade that DHEA protects against obesity and its consequences in aging and diabetic animals.^{47,48} In 2009, scientists confirmed that **low DHEA levels in men** were linked to **diabetes** and **coronary heart disease**.⁴⁹ DHEA powerfully *modulates* gene expression to shift the metabolic balance in favor of energy utilization and away from storage as fat.⁵⁰

DHEA also activates gene expression of cellular machinery that affects a cell's consumption of fats and sugars to remove them from circulation.^{51,52} These molecules help correct harmful lipid abnormalities and unhealthy body fat distribution—a possible mechanism by which DHEA decreases total body fat.^{53,54}

In 2007, researchers demonstrated in aged rats fed a high-fat diet that DHEA increased body protein, while decreasing total caloric intake, body weight, body fat, and total size and number of fat cells.⁵⁵ In a related experiment, researchers discovered that DHEA could change the composition of adipose tissue, boosting levels of beneficial **omega-3 fatty acids** while reducing harmful omega-6 fatty acids.⁵⁶



A human study showed how powerfully these DHEA effects can modify body composition.⁴ When 52 elderly men and women took **50 mg per day** of DHEA or placebo for 6 months, it reduced stubborn abdominal and subcutaneous body fat. Insulin levels dropped significantly in supplemented patients as well, indicating enhanced insulin sensitivity. The researchers concluded appropriately that “*DHEA replacement could play a role in prevention and treatment of the metabolic syndrome associated with abdominal obesity.*”

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DHEA is highly protective against diabetes and its complications. In diabetic rats, DHEA prevented increases in oxidant stress and oxidative damage related to the disease. It also significantly improved blood vessel relaxation, improving blood flow.⁵⁷ DHEA induces genes in muscle tissue that increase uptake and utilization of blood glucose as energy, significantly lowering blood sugar in diabetic animals.⁵⁸ In humans with **type 2 diabetes**, DHEA counteracts oxidative imbalance and the formation of deadly **advanced glycation end products** (AGEs), and downregulates the inflammatory TNF-alpha system—effects that may prevent the onset and slow the progression of deadly diabetes.⁵⁹

Cardiovascular Disease Defense

The past several years have witnessed extraordinary advances in our understanding of DHEA’s cardioprotective power—and its relationship to cardiovascular disease.

A 2009 study of 153 diabetic men with stable coronary heart disease (CHD) found that **77%** were DHEA-S deficient, significantly more than in healthy peers.⁶⁰ Over the next 19 months of follow-up, **43** of those men died of CHD; the data showed that **low DHEA-S** and low testosterone levels were two of the four most *significant* predictors of death.

Another 2009 study of 247 men with a mean age of 76 years revealed that those with **low DHEA-S** had a **96%** increased risk of **diabetes** and a **48%** increased risk of **coronary heart disease**.⁴⁹

A 2009 study from the University of Pennsylvania discovered a surprisingly close relationship between **mortality** and the trajectory of **DHEA-S decline** in older adults.⁶¹ Specifically, a rapid or *erratic* decline in DHEA-S predicted earlier death, and both together increased the death rate by nearly **threefold!** Regular blood testing for healthy DHEA-S levels are the only way to detect these lethal changes in DHEA levels early. It is of *paramount* importance that you have your DHEA-S levels checked at least once a year.

A Mayo Clinic study found that DHEA supplementation (**50 mg per day**) in women with low DHEA levels and low adrenal function improved plasma DHEA content, significantly lowered total cholesterol, and tended to reduce triglyceride and low-density lipoprotein (LDL) levels.⁶² But supplemented patients also had reductions in their beneficial high-density lipoprotein (HDL) levels. This study suggests that long-term studies are needed to determine the impact of DHEA supplementation on cardiovascular risk in women with low adrenal function.

Additional support for DHEA’s benefits in patients suffering from vascular disease came in two remarkable 2009 studies.^{63,64} The first examined vascular remodeling, a dangerous process that occurs when vessels are injured by atherosclerosis.⁶³ Vascular remodeling can impede blood flow and ultimately worsen cardiovascular disease.⁶⁵

DHEA significantly *inhibited* vascular remodeling in a rabbit model of carotid artery injury and limited deadly buildup of smooth muscle in vessel walls.⁶³ Another study of rabbits fed a high-fat diet showed that DHEA supplements restored oxidative balance, lowered lipid levels and inflammatory damage, and prevented heart muscle tissue death and dysfunction,



Enhanced Well-Being and Libido Even in *Challenged* Populations

Studies as early as 2000 demonstrated how DHEA improved well-being and could help to manage menopause without deleterious effects.^{28,66} In 2006 it was revealed that **50 mg per day** of DHEA could improve psychological well-being even in challenging populations such as those with decreased pituitary function.⁶⁷

DHEA exerted a remarkably positive effect on health-related quality of life in women taking long-term steroids for **lupus** (chronic steroid therapy can produce powerful depression and reduction in quality of life measures).⁶⁸ Of particular importance, the DHEA-supplemented groups also reported improvement in sexuality.

Additional research supports an excitatory effect for DHEA on **sexuality**—especially in women. In one study, sixteen sexually functional postmenopausal women were randomly given either placebo or a single DHEA supplement of **300 mg**, 60 minutes before presentation of an erotic video.⁶⁹ Women in the supplement group showed significantly greater mental and physical sexual arousal during the video than did the control women. The supplemented women also reported a greater increase in positive affect (generally feeling good) compared to placebo recipients.

A 2009 animal study may shed light on some of the physical causes behind these benefits: DHEA applied to the smooth muscle of rabbit clitoris resulted in significant relaxation,⁷⁰ allowing the increased blood flow and engorgement that results in enhanced sensitivity during **sexual arousal**.

Favorable Gene Expression for Youthful, Glowing Skin

A growing body of scientific evidence suggests that DHEA has *especially* favorable effects on skin health and appearance. In a 2000 laboratory study, DHEA was shown to increase production of **collagen**—the protein that gives youthful skin its suppleness—while decreasing production of the collagenase enzymes that destroy it.⁷¹

It wasn't until 2008, however, that Canadian scientists discovered more than 50 **DHEA-responsive genes** in the skin of women using a topical DHEA crème.⁷² DHEA “switched on” multiple **collagen-producing genes** and reduced expression of genes associated with production and cornification (hardening) of the tough keratinocytes that form **calluses** and rough skin. The researchers concluded, “*DHEA could exert an anti-aging effect in the skin through stimulation of collagen biosynthesis, improved structural organization of the dermis while modulating keratinocyte metabolism.*”



Other unexpected benefits of topical DHEA on aging skin are emerging. DHEA treatment increases production of sebum, or skin oil.⁷³ Sebum not only contributes to smooth, supple skin; it also contains myriad antimicrobial components that prevent infection and irritation. Topical DHEA also improves skin “brightness” and counteracts the “papery” appearance of aging skin, combating the epidermal thinning that is a visible hallmark of aging.⁷³ The study authors note that these are “beneficial effects on skin characteristics that are rarely provided by topical treatments.”

Summary

In the past few years alone, significant scientific substantiation of DHEA's anti-aging effects has emerged. Its neuroprotective effects are now recognized as being vital in protecting memory and reducing depressive symptoms in older adults. DHEA enhances bone health by improving mineralization to reduce fracture risk. DHEA modulates immunity in a coordinated fashion, boosting resistance to infection while quelling dangerous inflammation. DHEA supports cardiovascular health and activates genes that prevent cardiovascular risk factors, including diabetes and obesity. DHEA is intimately

involved in improving quality of life and bolstering sexual arousal, while dramatically improving the appearance of healthy, youthful skin. As little as **50 mg of DHEA per day** may favorably alter gene expression to inhibit multiple factors implicated in metabolic syndrome; boost bone strength; enhance cognitive function and memory; and ward off osteoarthritis. DHEA topical crèmes allow ready application of DHEA to the site of action.

Note: Individuals who have been diagnosed with a hormone-dependent cancer should not supplement with DHEA until their cancer is cured.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

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