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DHEA supplementation: The claims in perspective

ABSTRACT

Deficiency of dehydroepiandrosterone (DHEA) is associated with lupus erythematosus, diabetes mellitus, Alzheimer disease, and some cancers, but we are not yet ready to conclude that prescribing supplemental DHEA is helpful in these or any other conditions. DHEA shows some promise in observational clinical studies and laboratory experiments, but we still need large-scale human studies to answer key questions. For now, we do not have enough evidence to recommend routine treatment with DHEA. As with other supplements, quality control is always a concern, and different brands may contain different amounts of active ingredient.

KEY POINTS

Despite some evidence that DHEA may protect against cancer, its potential adverse effects on some cancers must be considered for patients at risk for these kinds of tumors.

Controlled trials have shown that taking oral DHEA sulfate increases bone mineral density in elderly women with low pretreatment DHEA levels, but oral DHEA has not been found to affect bone turnover in middle-aged to elderly men.

Use of DHEA to prevent cardiovascular disease is not supported by the evidence so far.

The actual amount of DHEA in over-the-counter dietary supplements may differ greatly from the amount listed on the label. The supplements may contain as little as no DHEA or as much as 150% of the amount listed on the label. DHEA should be obtained from a compounding pharmacy instead of through over-the-counter products.

LOW CIRCULATING LEVELS of dehydroepiandrosterone (DHEA) are seen in conditions as diverse as lupus erythematosus, diabetes mellitus, Alzheimer disease, and some cancers (**TABLE 1**). But does this mean that DHEA supplements could be used in their treatment?

Incidental findings and lay press reports claim DHEA is an "energy booster," an aphrodisiac, or an antiaging medication, and DHEA supplementation has been proposed for a wide variety of problems, from chronic fatigue to sexual dysfunction. However, normal circulating DHEA levels vary widely by age, sex, and ethnicity and are affected by day-to-day changes in corticosteroid production, alcohol intake, smoking, body mass index, medications, and thyroid function,[1–3] all of which profoundly complicate the way we interpret clinical data regarding DHEA levels. In addition, DHEA converts into a number of active metabolites, further confounding the assessment of its net effects when considered as a treatment in heterogenous populations.

So it is not surprising that reports of efficacy of DHEA supplementation have been inconsistent and controversial, thus hampering confirmation of its clinical usefulness. Still, some data suggest that DHEA may be a promising treatment for common disorders arising in the context of chronic illnesses. So what are clinicians to think about DHEA supplementation, and what should we tell our curious patients?

In this article we examine the physiologic roles of DHEA and evaluate the evidence to

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TABLE 1

Conditions considered for DHEA supplementation

Adrenal insufficiency
Aging
Alzheimer disease
Anorexia nervosa
Cardiovascular disease
Chronic fatigue
Crohn disease
Depression
Diabetes, insulin resistance
Heart failure
Obesity
Osteoporosis
Perimenopause
Sexual dysfunction
Sleep disorders
Systemic lupus erythematosus
Well-being

date in order to put the claims and facts in perspective for practicing internists.

PHARMACOLOGY OF DHEA

DHEA levels and their significance vary widely among people

Endogenous DHEA

DHEA is a weak androgen that is a critical precursor in the pathway of sex hormone metabolism, and it may have direct effects on sex steroid receptors.[4,5] DHEA and its main metabolite DHEA sulfate (DHEAS) are the most prevalent circulating hormones in the body. Because these steroids are primarily synthesized in the zona reticularis of the adrenal gland, they have become known as adrenal androgens, but they are also produced by the gonads, the gastrointestinal tract, and the brain, where local effects on neurotransmitters have been observed.[4,6]

The degree and the rate of synthesis of androgens are regulated by a number of factors, including pituitary corticotropin, immune cells, cytokines, and neuroendocrine factors. As the biochemistry of interactions among the immune, endocrine, and neurologic systems has become better understood, it has become apparent that there are multiple genetic influences on the regulation of these metabolic pathways.[7–9] Thus, the amount and the significance of DHEA concentrations in the bloodstream vary widely among individuals for many reasons (TABLE 2).

TABLE 2

Variables affecting circulating levels of DHEA and DHEAS

Age
Alcohol intake
Body mass index
Corticosteroid production
Ethnicity
Nutritional status
Other medications
Sex
Smoking
Thyroid function

Age-related changes in endogenous DHEAS levels

Fetal DHEAS levels are high due to synthesis by the fetal adrenal gland, but secretion falls soon after birth.[10] Serum levels start to rise again during puberty, reaching a peak in early adulthood.[11,12] Subsequently, levels gradually decline with age at a rate of about 10% per decade until approximately age 70, when they are only 10% to 20% of their peak value.[11] This age-related decline in DHEAS seems associated with the involution of the zona reticularis.[12]

Metabolic pathways of endogenous DHEA

DHEA and DHEAS are 19-carbon steroids that are easily converted to either androgens or estrogens. The principle metabolite of DHEA is androstenedione, which is converted to various metabolites in a tissue-dependent manner.[9]

DHEA has the potential to be converted into a large number of metabolites, although their in vivo functions are not well understood. In one series of biochemical assessments, 19 different metabolites of DHEA were confirmed, and 12 additional metabolites were also reported as a preliminary observation.[13]

Optimizing the bioavailability of exogenous DHEA

DHEA has low oral bioavailability in its natural form, losing up to 90% of its potency

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when taken orally.[14] However, most orally administered DHEA is converted to DHEAS by intestinal cells and is thus absorbed primarily in that form, which then acts as an inactive reservoir[15,16] from which the body can make more DHEA. Intravenously administered DHEA is subject to rapid hepatic clearance, whereas DHEAS is resistant to first-pass metabolism.[15,16]

A transdermal form of supplemental DHEA has been proposed as an alternative.[14,17,18] Assuming that 100% of DHEA is bioavailable when given subcutaneously, it was estimated that the potencies of DHEA by the percutaneous and oral routes were approximately 33% and 3%, respectively.[17] Daily application for 2 weeks of 10 mL 20% DHEA solution on the skin of healthy male volunteers and postmenopausal women ages 60 to 70 caused increases in serum DHEA of 175% to 200% over basal values.[18] In one study, DHEA permeation was improved using a gel formulation and an alpha-cyclodextrin complex.[19]

Binding and clearance of DHEA vs DHEAS

Close to 90% of DHEA is bound to albumin, with minor binding to the steroid receptors cortisol-binding globulin and sex hormone binding globulin.[20,21] DHEAS exhibits very strong binding to albumin and is reabsorbed by renal tubules, leading to a very slow metabolic clearance rate, up to 100 times that of DHEA.[21] The half-life for disappearance of DHEAS may be up to 14 hours, about 48 times that of DHEA.[15,16,22,23]

Drug interactions and hormonal pathway changes due to DHEA supplements are not yet known

In a study of the pharmacokinetics of daily oral dosing of the Genelabs formulation of DHEA (Prasterone),[22] in healthy people taking 200 mg/day, DHEA concentrations of about 1 µg/dL and DHEAS concentrations greater than 400 µg/dL were achieved by 1 week and were maintained for as long as 1 month,[22] while corticosteroids were given concomitantly.

It is apparent that DHEAS can serve as a stable reservoir for DHEA, providing a ready supply of substrate for sulfatases that can convert it to the active parent hormone as needed. Therefore, although the oral form of DHEA has low potency and DHEA itself is short-lived in the bloodstream, its rapid interconversion with DHEAS means that appropriate dosing might lead to acceptable pharmacokinetics.

Drug interactions with supplemental DHEA

Very little is known about the potential for drug interactions or alterations in hormonal pathways caused by DHEA given exogenously. In the Genelabs study,[22] 200 mg/day of DHEA did not seem to alter the pharmacokinetics of prednisolone or its effects on endogenous cortisol secretion.[22]

Other drugs that patients might be taking could affect circulating concentrations of adrenal androgens. Dexamethasone might inhibit corticotropin and decrease endogenous DHEA and DHEAS.[23] Drugs that induce P450 enzymes would increase the metabolism of DHEA and DHEAS, decreasing circulating concentrations of these hormones and altering the ratio of their various metabolites.[23] Danazol, sometimes used in steroid-sparing therapy for lupus patients with thrombocytopenia, is a sulfatase inhibitor and so may decrease the conversion of DHEAS to DHEA.[23]

Targeting exogenous DHEA

The pharmacokinetics and metabolism of supplemental DHEA also depend on the target organ in question, since its fate is highly dependent on local metabolic conditions, which can vary greatly within the same individual.

Aromatase and 17-beta-hydroxylase activity has been found to be high in breast tissue and other adipose tissue, suggesting that obesity might increase the conversion of DHEA to estrogens.[24] Selective expression of 17-beta-hydroxylase genes in various organs suggests that the liver, ovary, endometrium, and testis are prominent sites for estrogen synthesis and that the placenta, liver, testis, endometrium, prostate, adrenal, and skin are areas of androgen synthesis.[9] Thus, the skin has a high expression of enzymes required to transform DHEA into dihydrotestosterone, whereas conversion of DHEA in the vagina would be mainly to estrogens.[9,25]

Therefore, understanding the net effects of DHEA supplementation is essential, since the effects could be estrogenic or androgenic and

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either conducive or inhibitory to health or disease, depending on the hormonal and metabolic conditions and the responsiveness of the targeted condition to hormonal or intracrine effects. In line with this concept, low levels of DHEA have been associated with breast cancer risk in premenopausal patients, whereas high levels have been associated with breast cancer risk in postmenopausal patients.[13]

POTENTIAL USES IN CANCER

Complexity of DHEA with regard to cancer

It may be that DHEA has chemopreventive and antiproliferative actions on some tumors.[6,26–28] DHEA treatment in a model of colon carcinogenesis in mice decreased the number of cancer precursors, although it did not affect malignant potential.[27] A nested case-control study failed to prove that serum levels of DHEA and DHEAS are associated with the likelihood of developing colon cancer.[29] Among men in this study, however, DHEAS was minimally associated with a decreased risk of colon cancer, but this was within the bounds of chance.[29] A case-control study examining the association between serum levels of DHEAS and melanoma and squamous cell carcinoma of the skin found no statistically significant trend toward either protection or risk.[30]

In adrenal insufficiency, taking DHEA improved mood, well-being, and sexuality

However, adrenal androgens have also been shown to increase cancer risk for several types of tumors, most notably breast and prostate cancers.[5,13,31] The steroid sulfatase enzyme that converts estrone sulfate to estrone also controls the formation of DHEA from DHEAS. The sulfatase pathway is thought to be an important target for blockade in estrogen-sensitive breast cancer patients. It may be that the DHEA conversion is as much a candidate for this blockade as the estrogen conversion, given recent findings of its ability to directly and indirectly stimulate the growth of breast cancer cells in vitro and in vivo.[13,31]

Fluid from human breast cysts contains a high concentration of DHEAS.[32] Aromatases are also expressed in significant levels in breast cancer cell lines, and in vitro studies suggest that aromatization of DHEA stimulates the growth of breast cancer cells.[5,33] In patients with late-stage breast cancer treated with aromatase inhibitors, DHEAS was found to be lower during responsive phases than during disease progression.[31] Thus, despite some evidence that DHEA may protect against cancer, its potential adverse effects on some cancers must be considered for patients at risk for these kinds of tumors.

EFFECTS OF DHEA ON THE BRAIN

Effects on cognition

In vitro and animal studies have suggested that DHEA might regulate neuronal function by effects on norepinephrine and serotonin transmission.[34–37] DHEA has also been implicated in modulating the deleterious effects of corticosteroids on neuron survival.[38] Circumstantial data suggest that DHEA levels might be related to cognition in the elderly, although potentially confounding variables have not been consistently assessed. In a large nursing home study, an inverse relationship between circulating DHEA and formal cognition scores was observed.[39] In a different study, women with Alzheimer disease had significantly increased levels of androstenedione and DHEA after adjustment for age and body mass index.[40] Several reviews of data on DHEA supplementation in the elderly have found little or no support for significant cognitive effects when it is used as a general supplement.[34,41,42] In the only study so far of DHEA in Alzheimer disease, 58 Alzheimer patients received 100 mg/day of DHEA or placebo for 6 months and showed only transient minor improvements, which were not statistically significant.[43]

Effect on general mood, well-being, sexuality in the elderly

Studies assessing the effects of DHEA replacement on physiologic well-being have been performed in patients with adrenal insufficiency and in the elderly. DHEA supplementation (25 to 50 mg/day orally) in adrenal insufficiency has consistently been found to restore circulating DHEAS levels to the normal range for healthy young adults, with a single morning dose being sufficient to maintain normal DHEAS levels for 24 hours.[44–48] In most studies in patients with adrenal insufficiency, DHEA has been observed to improve mood,

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well-being, and sexuality.[4,42–55] The only study that failed to detect the benefits of DHEA in primary adrenal insufficiency was a 9-month randomized, parallel-group clinical trial using 25 mg of DHEA,[48] and the reviewers of this work felt that the study was grossly underpowered to detect significant changes.[56]

In view of the age-related decline in circulating DHEAS, a number of randomized trials assessed the effect of oral DHEA in otherwise healthy elderly subjects.[42–55] Most of the studies used only nonvalidated personal interviews to assess general and psychological well-being.[42,52–54] The largest double-blind, placebo-controlled study was performed using a wide range of validated tools.[49] This trial of 280 healthy individuals given 50 mg of DHEA or placebo daily for 1 year showed that DHEA improved neither well-being nor cognition. Furthermore, no potentially harmful accumulation of DHEAS or active steroids was recorded. Bone turnover improved only in women over age 70, as assessed by the dual-energy x-ray absorptiometry and the decrease of osteoclastic activity. A significant increase in most indicators of libido was also found in these older women. Skin improvements were also observed, particularly in women, in terms of hydration, epidermal thickness, sebum production, and pigmentation.[49]

Clearly, based on the reported studies, no consensus has been reached. Taking together all of the studies on DHEA supplementation in the elderly, the results show only very limited effects of DHEA vs placebo. The reason for this lack of efficacy may be related to selection bias. Almost all studies included only healthy people with excellent performance status at baseline, thereby limiting the possibility of further improvement.[56] The data so far offer no evidence of improvement in memory or other aspects of cognitive function with DHEA treatment in normal older people.

In view of the growing public enthusiasm for DHEA supplementation, particularly in the United States, and of the possibility that any neuroprotective effect of DHEAS may be evident only in the long term, high-quality trials are needed to study DHEA treatment for at least 1 year, and the number of participants must be large enough to detect effects if they exist.[41]

Depression

Since elevated basal cortisol levels are found in depressive illness, and since DHEA is known to have glucocorticoid-opposing effects, it was surprising that one study observed a decrease in DHEA and DHEAS in patients as depression improved on antidepressant treatment.[57] Another study found that low DHEAS levels correlated with elevated depressive symptoms in older women with an opposite effect in younger women.[58] Beneficial effects of DHEA were found in randomized double-blind studies in patients with major depression.[50,51] In a recent double-blind trial in schizophrenic patients with predominant negative symptoms, 100 mg of DHEA daily led to significant improvement in negative symptoms of schizophrenia (eg, avolition, anhedonia, amotivation, alogia), as well as in depressive symptoms and anxiety.[59] It is possible that DHEA can have some mood-altering effects, but many variables, still poorly understood, might contribute to the net effect of DHEA supplementation on brain functions.

DHEA AND METABOLISM

The role of DHEA supplements in obesity, diabetes, and dyslipidemia is still unknown

DHEA appears to have the potential for significant metabolic effects as well. One study in healthy men suggested a positive correlation between DHEAS levels and levels of the cholesterol-regulating apolipoprotein A1.[60] In a long-term treatment study in postmenopausal women, DHEA also improved the lipid pattern,[61] even though its androgenic effects should tend to produce the opposite effect.

DHEA has been found to improve insulin sensitivity without affecting glucose tolerance[61] and may affect weight in complex ways. It has been suggested that this hormone may cause weight loss by effects on adipocytes.[62] However, hyperthyroid patients have been found to have low DHEA, which reversed with supplementation.[63] Patients with anorexia nervosa have also been observed to have low DHEA.[64] In that study, 61 young women with anorexia nervosa were randomly assigned to receive oral DHEA (50 mg/day) or hormone replacement therapy (20 µg ethinyl estradiol with 0.1 mg levonorgestrel). The results suggest that DHEA

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has both anabolic and antiresorptive effects on bone. DHEA resulted also in improvements in psychological variables, implying that it may help to reverse some of the emotional disturbances associated with this disease.[64]

Again, numerous potential metabolic effects of DHEA are possible, given various in vitro studies of the isolated effects of this hormone. DHEA supplementation may be a complex and unpredictable issue in people with obesity, diabetes, or adverse lipid profiles. Beneficial or harmful results from DHEA therapy might depend on complex clinical and metabolic variables.

DHEA AND BONE DENSITY

DHEAS has been found to stimulate osteoblasts.[65] A positive clinical correlation between bone mineral density and DHEAS was reported in postmenopausal women,[66] and it was speculated that osteoblast aromatases might play an important role in maintaining bone density in the elderly by converting DHEA to estrone.[66] Controlled trials have shown that taking oral DHEAS increases bone mineral density,[67,68] particularly in elderly women with low pretreatment DHEA levels. Oral DHEA has not been found to affect bone turnover in middle-aged to elderly men.[69] A proposed explanation is that elderly men maintain production of testosterone in the testes, so that DHEA treatment might have relatively minor impact on that population.[68] Dosing might also be an issue. Interestingly, it has been reported that adrenal androgen synthesis is suppressed in men with steroid-induced osteoporosis,[70] thus suggesting a subgroup of men who might benefit from DHEA supplementation.

DHEA AND THE CARDIOVASCULAR SYSTEM

Data on the relationship of DHEA and cardiovascular disease are conflicting.[71–78] Animal studies have shown that giving DHEA reduces the buildup of atherosclerotic plaque in animals fed high-fat diets.[71,72] DHEA also has been observed to reduce platelet adhesion in vivo.[73] Thus, an increase in plaque formation may explain the increase in cardiovascular events in persons with low DHEA.[74,75] Barrett-Conner et al[74] reported a protective role of DHEA in a trial of 250 men over age 50, with a 48% reduction in the death rate from cardiovascular disease in these men. Later, the same group followed more than 1,000 men for 19 years and found only a mild reduction of cardiovascular events in men with higher DHEAS levels.[76] In the Massachusetts Male Aging Study of 1,167 men, those with serum DHEAS levels in the lowest quartile at baseline were shown to be more likely to develop ischemic heart disease over a 9-year period.[77]

Data for women are more uniform than for men. Most studies suggest that the DHEAS level does not affect cardiovascular risk in postmenopausal women.[76] A case-control study of 942 postmenopausal women who were part of the Rancho Bernardo cohort revealed no association between DHEAS levels and cardiovascular death.[76] One prospective observational study did suggest that low levels of DHEAS predicted death from ischemic heart disease in postmenopausal women with diabetes.[78] However, this observation cannot be used as a basis for therapy in light of the adverse metabolic consequences.

Data on DHEA and cardiovascular disease are conflicting

In summary, appropriately randomized trials evaluating the efficacy of DHEA supplementation and reduction of cardiovascular events are lacking. For this reason, the use of DHEA to prevent cardiovascular disease cannot be supported, even for men in whom beneficial effects could be assumed on the basis of some data.

DHEA AND SYSTEMIC LUPUS

Since estrogens are known to enhance autoantibody production, and since androgens are known to suppress it, DHEA has also been studied as a treatment in systemic lupus erythematosus. In studies of lupus in mice, DHEA has been found to be low in association with the characteristic adverse immune profiles seen.[79] DHEA has been observed to promote a shift in both murine and human lupus immune disorders.[80–82] How might this occur? Early gene array studies have compared the effects of DHEA and glucocorticoids on human peripheral blood leukocytes and have

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TABLE 3

Potential adverse effects of DHEA supplementation

Acne
Hirsutism
Metabolic (complex effects on lipids)
Antiglucocorticoid effects
Effects on hormone-dependent malignancies (eg, breast and prostate cancer)

shown that DHEA and corticosteroids may have opposing effects on immune-cell gene expression.[83] Since corticosteroids are a mainstay of treatment for sudden lupus flares but have numerous adverse effects, these opposing actions could potentially be beneficial, mutually stabilizing, or harmful, depending on the clinical situation.

A number of phase I, II, and III trials have tested the effects of DHEA on human lupus.[84–91] Although outcome data using global scores of lupus disease activity have been controversial, these studies suggest the possibility that 200 mg of DHEA a day can decrease the corticosteroid requirement in patients with clinically active lupus,[85–89] increase their perception of improvement,[85,88] decrease the number of flares[88] and increase bone mineral density.[90,91]

Adverse effects of DHEA include acne, hirsutism, and perhaps unfavorable lipid effects

ADVERSE EFFECTS OF DHEA

The most common side effects of DHEA (TABLE 3) are linked to its androgenic effects and include acne, hirsutism, and the potential for unfavorable effects on lipid metabolism. As mentioned previously, some studies have confirmed androgenic effects on lipids, in particular that DHEA lowers high-density lipoprotein cholesterol (HDL-C).[92]

Most of the expected side effects from DHEA were borne out in the lupus studies,[85–92] suggesting that adverse effects in humans were generally mild and self-limiting. In considering the long-term use of this agent in patients with lupus, however, the possible growth-stimulating effects on hormone-dependent malignancies, particularly of the prostate or breast, should be kept in mind, as well as the theoretical potential for DHEA to exacerbate lupus via its immunostimulating and antiglucocorticoid effects.[93] This might be a relevant issue in patients with more severe lupus, which may be more likely to involve a complex, mixed immune disorder, or in patients who rely on glucocorticoids for clinical stability.

Finally, DHEA or its metabolites may have protean effects on intracellular signaling pathways[6,26,62] that are as yet largely unexplored, posing a risk for as yet unforeseen side effects.

DHEA SUPPLEMENTATION: PRACTICAL CONSIDERATIONS

At present, DHEA has no established indications and no generally accepted pharmacological preparation.

Evidence supports the benefit of DHEA replacement in a substantial percentage of patients with adrenal insufficiency. Treatment usually starts with 25 mg/day, aiming at serum DHEAS concentrations within the respective sex-specific reference range.[56] In women, additional monitoring of serum androgens is recommended. It is important to know that significant improvements in mood and health-related quality of life may occur only after 3 to 4 months of treatment, possibly as a result of gradual adjustment of the neurosteroidal equilibrium.[56]

By contrast, the physiologic, age-associated decline in circulating DHEAS in healthy elderly people per se does not justify DHEA supplementation. Evidence so far indicates no benefit of DHEA supplementation in this population. This does not exclude the possibility that certain elderly people may benefit from DHEA supplementation, but these groups need to be defined.[56] In particular, to date there is little evidence that DHEA supplementation reverses relevant aspects of aging. If patients opt for DHEA supplementation, they should be informed of the experimental nature of such treatment—specifically, the possible risks of androgenic side effects and the potential promotion of sex-steroid-dependent tumor growth need to be addressed.[56]

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Physiologic replacement dosages of oral DHEA in healthy people over age 40 are in the range of 20 to 50 mg/day for men and 10 to 30 mg/day for women.[94] These dosages are usually adequate to increase serum DHEAS to levels found in adults 20 to 30 years of age and to bestow the reported benefits of a heightened sense of well-being in both sexes, increased bone mineral density in postmenopausal women, and amelioration of erectile dysfunction in men. Higher dosages may be necessary for increasing suppressed DHEA and DHEAS levels secondary to chronic disease, adrenal exhaustion, and corticosteroid therapy. Pharmacologic dosages of 200 mg/day have been successfully used in patients with systemic lupus erythematosus.[85–90]

We recommend measuring the serum DHEAS concentration before starting DHEA supplementation,[95] and subsequently checking serum levels of DHEAS and its androgenic and estrogenic metabolites at least annually to ensure that they are within the normal range. Patients should also undergo mammography or prostate-specific antigen testing according to current guidelines. To minimize adverse effects and maximize benefits, dosages in healthy adults should be adjusted to maintain serum levels of DHEAS in the second or third quartile of ranges for young adults according to sex.[95]

Several steroidal hormone DHEA products are commercially available in the United States as so-called dietary supplements, which means they do not require evaluation for safety and efficacy by the US Food and Drug Administration. These products do not have to be manufactured in compliance with that agency's Good Manufacturing Practices, nor do they have to meet quality control standards expected of approved drugs.[96] Synthetic DHEA is available as an oral formulation, an intra-oral spray, and a transdermal cream or gel.

Independent analysis of commercial DHEA preparations found that the actual amount of DHEA differed significantly from the amount listed on the label.[97] In the worst cases, the product contained no DHEA or, as in one case, contained 150% of the amount claimed. This wide range of variation of actual DHEA content vs label claims has important safety implications for this steroid, which is why DHEA should be obtained from a compounding pharmacy instead of through over-the-counter products.

CURRENT RECOMMENDATIONS

DHEA and DHEAS are intriguing hormones. However, we do not have enough evidence to recommend routine treatment with DHEA. Furthermore, patients with a family or personal history of a tumor responsive to hormones should be dissuaded from taking DHEA. If the patient opts for DHEA supplementation, medical supervision is recommended.

The lack of quality control of the substances currently marketed is also a concern. Nevertheless, some data suggest that DHEA may be a promising treatment for common disorders arising in the context of chronic illnesses. Large-scale human studies are needed to address these intriguing issues.

DHEA still has no established indications, no standard pharmacologic preparation

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