Safety and pharmacokinetic study with escalating doses of 3-acetyl-7-oxo-dehydroepiandrosterone in healthy male volunteers

Michael Davidson, MD
Ashok Marwah, PhD
Ronald J. Sawchuk, PhD
Kevin Maki, PhD
Padma Marwah, PhD
Charles Weeks, PhD
Henry Lardy, PhD

Abstract

Objectives: To evaluate the safety and pharmacokinetics of 3-acetyl-7-oxo-DHEA (3ß-acetoxyandrost-5-ene-7,17-dione) given orally.

Design: A randomized, double blind, placebo-controlled, escalating dose study.

Setting: The Chicago Center for Clinical Research.

Participants: Twenty-two healthy men.

Study method: The participants received placebo (n = 6) or 3-acetyl-7-oxo-DHEA (n = 16) at 50 mg/d for 7 days followed by a 7-day washout; 100 mg/d for 7 days followed by a 7-day washout; and 200 mg/d for 28 days.

Outcome measures: Safety parameters, evaluated at each dose level, included measurement of total testosterone, free testosterone, dihydrotestosterone, estradiol, cortisol, thyroxin and insulin levels. Analyses for 7-oxo-DHEA-3ß-sulfate (DHEA-S), the only detectable metabolic product of the administered steroid, were conducted on plasma drawn from all subjects at 0.25, 0.5, 1, 2, 4, 6 and 12 hours after the final 100 mg dose of 3ß-acetyl-7-oxo-DHEA.

Results: There were no differences in the clinical laboratory values or in reported minor adverse experiences, between treatment and placebo groups. In general, blood hormone concentrations were unaffected by the treatment with 3ß-acetyl-7-oxo-DHEA and remained within the normal range. No changes in vital signs, blood chemistry or urinalysis occurred during treatment with 3ß-acetyl-7-oxo-DHEA compared to placebo. The administered steroid was not detected in the blood but was rapidly converted to 7-oxo-DHEA-S, the concentrations of which were proportional to dose. This steroid sulfate did not accumulate; plasma concentrations 12 hours after the 3ß-acetyl-7-oxo-DHEA dose at 7 and 28 days on the 200 mg/d dose were 15.8 and 16.3 µg/L respectively. The mean time to peak plasma level of 7-oxo-DHEA-S was 2.2 hours; the mean half life was 2.17 hours. The apparent clearance averaged 172 L/h, and the apparent mean volume of distribution was 540 L.

Conclusion: These results indicate that 3ß-acetyl-7-oxo-DHEA is safe and well tolerated in normal healthy men at doses up to 200 mg/d for 4 weeks.

Résumé

Objectifs : Évaluer l’innocuité et la pharmacocinétique de la 3-acétyl-7-oxo-DHEA (3ß-acétoxyandrost-5-ène-7,17-dione) administrée par voie orale.

Conception : Étude randomisée, à double insu, contrôlée par placebo et à dose croissante.

Contexte : Le Chicago Center for Clinical Research.

Participants : Vingt-deux hommes en bonne santé.
**Introduction**

Dehydroepiandrosterone (DHEA) is a steroid produced by the adrenal cortex in response to stimulation by adrenocorticotropic (ACTH) and in the brain by pathways still to be elucidated. Most of the circulating DHEA is in its conjugated form, dehydroepiandrosterone sulfate (DHEA-S), the most abundant steroid in human blood. Normal levels of DHEA-S vary with age; levels are high in the developing fetus, nearly undetectable shortly after birth, rise at adrenarch, peak at about age 25 years and then gradually decline. On average, by age 75 years, circulating DHEA-S levels are only about 10% of their peak concentration.

Until the late 1970s, DHEA was considered a relatively inert compound whose main function was as an intermediate in the bioconversion of cholesterol to androgens and estrogens. Pioneering studies stimulated research, which indicated that DHEA has potential benefits in treating a number of conditions, including systemic lupus erythematosus, cancer, insulin resistance, cardiovascular disease, viral infections, osteoporosis and depression. Because levels of DHEA and general health decline with age, it has been postulated that DHEA replacement may help to maintain a more youthful state. Overall wellbeing, particularly in the aged, is suggested to improve with DHEA supplementation, with possible benefits in muscle strength, mood ratings and memory performance.

Several adverse experiences have been reported from the use of DHEA. Some involve alterations of sex hormone levels, resulting from transformation of DHEA to testosterone and estrogen. These steroid transformations may lead to acne, hair loss, facial hirsutism, mood changes, deepening of the voice and other signs of masculinization. DHEA may also affect the growth of prostate cancer in men and breast cancer in women; the National Institute of Aging has issued a public service announcement warning consumers about the use of DHEA because of its sex steroid-associated side effects.

There is need for a DHEA-like compound capable of similar health maintenance benefits without the adverse effects. Fluasterone, a fluorinated form of DHEA, avoids the androgen-producing effects of DHEA and is being developed as a drug. Another candidate is the natural metabolite, 7-oxo-DHEA which is produced from DHEA via the 7α-hydroxy derivative followed by its oxidation. 7-oxo-DHEA does not activate the androgen receptor, is not converted to androgen and because of its carbonyl function on the 7 position is not a substrate for the estrogen-forming
Dehydroepiandrosterone (DHEA) and its sulfate ester (DHEA-S) are produced in human adrenal glands beginning at about 7 years of age (adrenarche). DHEA-S is the most abundant steroid (14 mg/L) in the blood plasma of humans at age 20 to 30 years and decreases steadily to about one-tenth that concentration at age 70 to 80 years. DHEA is an intermediate in the biologic conversion of cholesterol to androgens and estrogens. It can be hydroxylated in tissues to produce both 7α- and 7β-hydroxy-DHEA, which in turn can be oxidized at the 7 position. 7-oxo-DHEA has no androgenic activity, is not converted to androgen and, because substitution at the 7 position prevents aromatization, it cannot be converted to estrogen.

Until 1977, DHEA was not known to have other functions, but at that time T. Yen of Eli Lilly Laboratories found that including DHEA in the diet of mice genetically predisposed to obesity caused them to remain lean despite consuming as much feed as their obese litter mates. Yen’s finding stimulated considerable research, and various provocative metabolic and other effects have since been attributed to DHEA. In animals, enhanced metabolism and thermogenesis decreased blood cholesterol, decreased blood sugars in diabetic animals, enhanced activity of the immune system, inhibition of tumour development and improved memory have all been reported. More limited effects of DHEA have been found in human subjects.

The safety of DHEA as a potential therapeutic agent in humans has been questioned because it increases blood testosterone when given to women, even at the limited dose of 50 mg daily. It appears not to increase plasma testosterone concentration in men.

The effects on animals already mentioned were generally obtained with large doses (e.g., 0.5% w/w in the diet). These, and the fact that no receptor for DHEA has been isolated, suggest that, in systems that respond, DHEA may be acting as a precursor of a more active steroid just as it is a precursor of androgens and estrogens. We therefore initiated a search for possible metabolites of DHEA in the hope of finding an active steroid with more selectivity in its metabolic effects and independent of conversion to sex steroids.

When we found that DHEA induced the synthesis of hepatic thermogenic enzymes in rats in a similar fashion to thyroid hormone, we were able to use this response as an assay in the search for active derivatives or metabolites of DHEA. In this assay, 7-oxo-DHEA is more active than either DHEA or 7α-hydroxy-DHEA, and we have postulated that the 7-hydroxy and 7-oxo derivatives of DHEA are intermediates in the conversion of DHEA to more active and possibly more specific hormones. Because of its high activity and because it is relatively easy to prepare, we have tested 7-oxo-DHEA for tolerance and metabolic effects in the hope that it might be useful clinically.

We have compared the effects of DHEA and 7-oxo-DHEA on retention of spatial memory in aged mice using a Morris water maze: 7-oxo-DHEA was much more effective than DHEA in this model. In collaboration with Professor David Pauza, we have tested 500 mg 7-oxo-DHEA daily in a simian model of the wasting seen in humans with HIV. The CD4+ cell counts of the monkeys increased from approximately 200/mm³ to 800 to 1200/mm³ over 5 months. These results, together with the earlier effects reported on metabolism, suggest various therapeutic possibilities in humans, but safety must first be established.

In animal studies of safety, 7-oxo-DHEA fed as the acetyl ester was not toxic to rats in doses up to 2000 mg/kg. It had no effect on blood chemistry, blood cell counts or histologic structure in 42 different tissues. Monkeys were given 1000 mg/kg without affecting these same parameters. This paper demonstrates that 7-oxo-DHEA is well tolerated by humans and should encourage further research into possible therapeutically useful actions.
It is approximately 2.5 times as active as DHEA as an inducer of the thermogenic enzymes — mitochondrial glycerophosphate dehydrogenase and cytosolic malic enzyme. It enhances interleukin-2 production by human mononuclear leukocytes and is more effective than DHEA in improving memory in old mice.

The purpose of this study was to examine the safety and pharmacokinetic characteristics of 3β-acetyl-7-oxo-DHEA in healthy adult men. Women were not included in the 8-week trial because of the influence of menstrual cycles on blood steroid concentrations. A separate trial with women as the subjects is underway. Because the acetyl ester is the form in which the 7-oxo group is introduced in the chemical synthesis currently used, it is the more economical choice for therapy. The acetyl derivative of 7-oxo-DHEA is readily hydrolyzed by tissue esterases to liberate free 7-oxo-DHEA. Because it is not converted to sex hormones, 7-oxo-DHEA may be a safer alternative to DHEA for supplementation.

Subjects and methods

Subjects

The subjects ranged in age from 21 to 47 years and had a mean body mass index of 25 kg/m². In the steroid-treated group there were 10 Caucasians, 6 Afro-Americans and 1 Hispanic; in the placebo group were 3 Caucasians, 1 Afro-American, 1 Hispanic and 1 Asian. The treated and placebo groups did not differ in baseline demographic characteristics.

Study design

This was a randomized, double-blind, placebo-controlled, escalating dose study conducted at a single clinical site. The study protocol was approved by the Schulman Associates Institutional Review Board (Cincinnati) and each subject gave written consent before participation. Confidentiality of study data was assured, particularly with regard to HIV test results (tests had to be negative for study participation). Twenty-four healthy, nonsmoking men who met entrance criteria (as determined at a screening clinic visit from the medical history, vital signs, physical examination, electrocardiography, hematologic tests, and clinical laboratory blood and urine chemical evaluations) were invited to return to the clinic for enrollment within 3 weeks after screening. At baseline, subjects were assigned randomly either to placebo (n = 6) or 3β-acetyl-7-oxo-DHEA (n = 17) groups. One of the qualified subjects did not report to the clinic for randomization. Baseline vital signs and blood concentrations of total and free testosterone, dihydrotestosterone (DHT), estradiol, thyroxin (T4), cortisol, insulin, 7-oxo-DHEA and its acetyl and sulfate esters were determined. Concomitant medications were reviewed and subjects were instructed on the first dosing schedule, including completion of dose diaries and the procedures for missed doses. Dose amounts were 50 mg/d (25 mg twice daily) for 7 days followed by a 7-day washout period; 100 mg/d (50 mg twice daily) for 7 days followed by a 7-day washout period; and finally, 28 days of 200 mg/d (100 mg twice daily).

Steroid

3β-acetyl-7-oxo-DHEA (3β-acetoxyandrost-5-ene-7,17-dione), prepared as described under GMP (good medical practice) conditions, was supplied in capsules by Humanetics Corp., Chanhassen, Minn.

Safety evaluations

Safety assessments, including vital signs, hematologic measurements, results of serum chemistry, and urinalysis were completed after each dose sequence and weekly during the administration of the 200 mg/d dose. Adverse experiences, concomitant medications and compliance (dose diary and pill count) were reviewed at the end of each dosing period (week 1 and week 3) and weekly during the 28-day period of dosing at 200 mg/d. In addition, at day 42 and day 56 (days 14 and 28, respectively, of the 200 mg/d dosing) subjects had a physical examination and electrocardiography. On day 56, blood was collected for an endocrine panel (see study design) and pharmacokinetic assessment. The serum samples were analysed by ARUP Laboratories (Salt Lake City) except for measurement of DHT (radioimmunoassay by Endocrine Sciences, Calabasas Hills, Calif.) and 7-

At screening and at each clinic visit (days 7, 21, 35, 42, 49 and 56), fasting blood was analysed for electrolytes (sodium, potassium, chloride, carbon dioxide, calcium and phosphate), uric acid, urea nitrogen, creatinine, glucose, enzymes (alkaline phosphatase, lactic dehydrogenase, serum glutamic-oxaloacetic transaminase [aspartate aminotransferase], alanine aminotransferase, γ-glutamyltranspeptidase), total protein, albumin, total and direct bilirubin, and cholesterol. Total and differential blood cell counts, hemoglobin and hematocrit levels were measured. Urinalysis evaluated urine colour, appearance, specific gravity, pH, protein, glucose, ketones, bilirubin, blood, leukocytes, nitrite and urobilinogen.

Vital signs (pulse, respiratory rate, temperature, and blood pressure) and body weight were measured at screening, baseline and at each clinic visit. Also at each visit, adverse experiences were assessed and documented by the investigators. Statistical analyses compared the changes in blood pressure, heart rate, and body weight between groups (analysis of variance [ANOVA] and Mann–Whitney U tests) and within groups (1 sample t-test) from baseline (average of screening day and day 0) to each post randomization visit.

**Pharmacokinetic study methods**

An extraction procedure and an HPLC analytical method were developed for quantitation of 7-oxo-DHEA and for 7-oxo-DHEA-S in human plasma, utilizing calibration curves in the range of 10 to 500 µg/L.

Trough levels of blood plasma steroid were measured after each dose sequence. The pharmacokinetic study was conducted on all subjects during day 56 at the end of the 200 mg/d or placebo dosing period. The first blood sample was drawn 12 hours after the second placebo of the previous day or prior 100-mg dose of 3β-acetyl-7-oxo-DHEA. All subjects were then given 100 mg of 3β-acetyl-7-oxo-DHEA (t = 0), and blood was drawn by venipuncture at 0.25, 0.5, 1, 2, 4, 6 and 12 hours from the t = 0 time point. Subjects fasted from t = 0 to t = 4 hours for measurement of plasma levels of parent compound and metabolites.

**Noncompartmental pharmacokinetic analysis**

The parameters of maximum concentration (C_{max}), time to reach maximum concentration (t_{max}), elimination rate constant, half-life (t_{1/2}), and area under the plasma concentration-time curve (AUC) were estimated for each subject with the use of standard non-compartmental methods.²⁴

**Estimation of apparent clearance and volume distribution of 7-oxo-DHEA-S**

It was assumed that subjects who were receiving active compound for 4 weeks exhibited steady state plasma concentrations of 7-oxo-DHEA-S. Apparent clearances of 7-oxo-DHEA-S (CL/F) for these subjects were calculated from the data as the dose divided by AUC to 12 hours: CL/F = dose / AUC_{0–12h}.

Conversely, for placebo subjects who were receiving their first dose of 3β-acetyl-7-oxo-DHEA as the pharmacokinetic test dose, apparent clearances of 7-oxo-DHEA-S were calculated from the data as the dose divided by AUC_{infinity}.

It should be noted that since 7-oxo-DHEA-S is a metabolite of the administered steroid, F is interpreted as the product of systemic bioavailability of the parent compound and the fraction of the amount of absorbed parent compound that is metabolized to 7-oxo-DHEA-S. Thus, the amount of 7-oxo-DHEA-S that gains access to systemic circulation through absorption and metabolism is FDose.

The apparent volume of distribution (V/F) of 7-oxo-DHEA-S in the terminal elimination phase was calculated as: V/F = 1.44(t_{1/2})Dose / AUC.

Here, AUC is the area under the plasma concentration-time curve over 12 hours for subjects receiving steroid, and it is the area under the plasma concentration-time curve to infinity for subjects in the placebo group, for whom this dose was their first.

**Simulations of plasma concentrations of 7-oxo-DHEA-S**

These were performed to represent the regimens employed in the dose-escalation study. Nine hypothetical subjects were used in the simulations employing 3 levels of the apparent clearance and 3
levels of the apparent volume of distribution, resulting in a $3 \times 3$ array. A 1-compartment model was assumed with first-order absorption and no lag phase. The typical subject exhibited apparent clearance and volume of distribution of 172 L/h (range simulated was from 105 to 239 L/h) and 540 L, (range from 330 to 750 L/h) respectively. It was assumed that conversion of parent compound to the 7-oxo-DHEA-S metabolite was so rapid that the metabolite profile followed closely that of the parent compound: it was biexponential. The dosing regimens in the simulations were identical to those employed in the escalation-dose study.

**Statistical analysis**

Descriptive statistics were used to characterize baseline and post-randomization data. Comparability of the baseline characteristics of the 2 treatment groups was evaluated with ANOVA and Fisher’s exact test for continuous and categorical variables, respectively. One-way ANOVA models were generated to assess possible differences between treatment groups in responses for endocrine parameters (percent changes from baseline). Single-sample $t$-tests were used to evaluate within-group changes in these parameters from the baseline. Because of the small sample size in the placebo group, it was not possible to confirm that the assumptions necessary for use of parametric statistical procedures had been met. Accordingly, additional non-parametric tests were run (Mann–Whitney U test and sign test) to confirm results produced with parametric procedures.

The incidence of laboratory abnormalities and adverse experiences in the 2 treatment groups was compared with Fisher’s exact test.

**Results and discussion**

**Safety of 3β-acetyl-7-oxo-DHEA**

Mean compliance was generally similar between treatment and placebo groups, ranging from 92% to 98% for the placebo group and 96% to 99% for the 3β-acetyl-7-oxo-DHEA group.

Endocrine parameters including total and free testosterone, dihydrotestosterone, estradiol, cortisol, thyroxin and insulin, measured at baseline and at the end of the study and analysed using parametric and nonparametric statistical procedures, were not statistically different between treated and placebo subjects ($p > 0.10$) (Table 1). However, within the treatment group, small but statistically significant changes were noted. Despite an 8% decrease in total testosterone in the blood of 7-oxo-DHEA-treated subjects ($p < 0.01$), both statistical methods disclosed that there was a significant (14.4%, $p < 0.01$) increase of free testosterone from day 0 (26.7 [1.3] pg/mL, mean [and standard deviation]) to day 56 (30.8 [1.9] pg/mL) in subjects treated with 3β-acetyl-7-oxo-DHEA. A slight increase in DHT(2.5%) and a decrease of 7.5%...
in estradiol levels in these treated subjects were not significant; thyroxine declined by 5.8% (p < 0.05). All of these hormone concentrations remained well within normal clinical ranges.

Potentially serious negative side effects of DHEA replacement therapy can stem from its conversion to estrogens and androgens. Several studies of DHEA supplementation have reported elevations of blood testosterone concentrations ranging from 50% to 20-fold. In light of this, the small changes in steroid hormone levels found in this trial are minor and of doubtful clinical importance. Adding support to this statement is the lack of any differences in endocrine parameters between placebo and treated subjects and the fact that all hormone levels remained within normal ranges. Thus, in terms of its hormone-affected activity, 3β-acetyl-7-oxo-DHEA may be a safer alternative to DHEA.

Results of serum chemistry, hematologic tests and urinalysis throughout the study were used to determine the safety of escalating subjects to the next higher level of steroid dosage. Although these laboratory values shifted in some subjects from high-normal to low and low-normal to high, there was no difference between the placebo and treated groups in the number of such occurrences. In general, the shifts in laboratory values were not deemed serious, and all subjects, with the exception of one, were allowed to escalate to the next higher dose. This subject was withdrawn from the study after 7 days on the 50 mg/d dose of 3β-acetyl-7-oxo-DHEA because of decreased hemoglobin and hematocrit levels.

Table 2 summarizes the effects of 3β-acetyl-7-oxo-DHEA on systolic and diastolic blood pressure, heart rate and body weight, which were measured at each weekly clinic visit. The only difference found between treated and placebo groups was in diastolic blood pressure at day 35 compared with baseline. The decrease in diastolic pressure was significantly greater in the steroid-treated group (p < 0.05). There were multiple significant effects on blood pressure within the steroid-treated group: compared with baseline values, systolic blood pressure was decreased at day 35 and diastolic blood pressure was significantly lower at days 21, 35, 49 and 56. There were no detrimental effects of treatment with 3β-acetyl-7-oxo-DHEA on vital signs, but further research beyond the scope of this trial would be needed to determine possible cardiovascular benefits of 3β-acetyl-7-oxo-DHEA.

Body weights throughout the treatment periods are also reported in Table 2. There were significant differences between placebo and treated subjects from screening and baseline to days 7, 21, 49 and 56. These differences result from an increase in mean body weight in placebo-treated subjects and relatively stable weight in the steroid-treated subjects. Although some investigators have reported that DHEA affects body composition, others have reported no effect. Our study was not designed to evaluate the effects of 7-oxo-DHEA on body weight except as it related to the safety issues.

Adverse experiences were evaluated at each clinic visit as another safety indicator. There were no statistically significant differences in adverse experiences between the 2 groups. Overall 82% of the subjects receiving the steroid and 100% of those receiving placebo reported mild adverse effects. Gastro-
intestinal upset was the most common adverse event, reported by 18% of the steroid-treated subjects and 33% of the placebo subjects. Headaches were reported by 4 of the steroid-treated subjects. There were 2 adverse experiences deemed as possibly related to the study product. These were the decreased hemoglobin and hematocrit levels (n = 1) and the heightened sensitivity to mosquito bites (itching) (n = 1).

These results further support the concept that 3β-acetyl-7-oxo-DHEA is safe and well tolerated. In future testing, it will be important to monitor hematologic parameters.

**Pharmacokinetic findings**

Neither free 7-oxo-DHEA nor 3β-acetyl-7-oxo-DHEA were detected in the blood of subjects receiving 3β-acetyl-7-oxo-DHEA (limit of detection = 3 µg/L).²² The circulating product of the administered steroid was identified as 7-oxo-DHEA-3β-sulfate. Predose (trough) plasma concentrations of the sulfate ester in the placebo group were close to the limit of detection (2 to 3 µg/L) (Fig. 1). Trough (12 hours after the previous dose) plasma concentrations in the 3β-acetyl-7-oxo-DHEA group (n = 16) increased proportionally to the daily dose (Table 3). Mean trough levels (15.8 µg/L) in the treated subjects after 1 week of dosing at 200 mg/d were similar to those determined after 4 weeks of dosing (16.3 µg/L). This indicated that the ratio of the formation rate to clearance is constant during multiple dosing.

The blood plasma concentrations of 7-oxo-DHEA-3β-sulfate after the ingestion of 200 mg of the steroid acetyl ester are shown in Fig. 1. The elimination rate
constants, $t_{d}$, $t_{max}$, $C_{max}$ and AUCs for 7-oxo-DHEA-3β-sulfate were determined by noncompartmental analysis (Table 4). The average $t_{d}$ (harmonic mean) for 7-oxo-DHEA-S was 2.17 hours. The mean $t_{max}$ was 2.2 hours, indicating rapid absorption of the parent compound and conversion to the 3β-sulfate ester.

The mean $C_{max}$ of sulfate ester achieved by the placebo group after the 100-mg dose of the acetyl ester was 158 µg/L. The mean AUC$_{0-12h}$ was 665 µg·h/L.
and the mean AUC\textsubscript{\text{\infty}} was 724 \mu g-h/L. The ratio of AUC\textsubscript{0-12h} to AUC\textsubscript{\text{\infty}} averaged 96%, reflecting the short \( t_{\text{\infty}} \) relative to the sampling period.

The apparent clearance, CL/F, for 7-oxo-DHEA-3\beta-sulfate averaged 172 L/h \((n = 22)\). No physiological interpretation of this parameter is possible because the bioavailability of the parent compound and the fraction of its disposition which results in the generation of the 7-oxo-DHEA-S metabolite is unknown. The apparent volume of distribution (V/F) averaged 540 L.

Simulations of 7-oxo-DHEA-3-sulfate plasma concentrations in 9 hypothetical subjects were performed to reflect the regimens used in the escalating-dose study. Nine sets of apparent clearances and volumes of distribution (a \( 3 \times 3 \) array) were used in the simulations, with values based on the observed means and standard deviations of the parameters determined by noncompartmental analysis. The typical subject exhibited apparent clearance and volume of distribution of 172 L/h (range simulated was from 105 to 239 L/h) and 540 L (range from 330 to 750 L/h) respectively. There was good agreement between simulated and measured means of the trough plasma levels in the escalating-dose study. Plasma concentrations of 7-oxo-DHEA-S were also simulated over 1 dosing interval following a 100-mg dose in the pharmacokinetic study, using the same parameters. Agreement between mean measured and simulated plasma concentrations of 7-oxo-DHEA-S over 1 interval was also reasonable, as illustrated in Fig. 2.

Conclusions

The acetylated derivative of 7-oxo-DHEA, which is devoid of androgenic activity and is not metabolically convertible to estrogens or androgens, was found to be safe and well tolerated in normal healthy adult men at doses up to 200 mg/d for 28 days. 3\beta-acetyl-7-oxo-DHEA was found to lack any of the clinically significant sex-hormone elevating actions that have been reported with DHEA supplementation. Safety laboratory determinations also indicated that treatment with 3\beta-acetyl-7-oxo-DHEA does not affect hematologic, serum chemical or urine values differently from placebo. Vital signs were another indicator of the safety of this steroid. Thus, the results of this clinical trial support the view that 3\beta-acetyl-7-oxo-DHEA is a safe and well-tolerated DHEA metabolite that has potential clinical utility in several medical conditions for which DHEAs is currently being used.

Acknowledgement

This work was supported by Humanetics Corp. Chanhassen, Minn.

References


Reprint requests to: Dr. Henry Lardy, Institute for Enzyme Research, 1710 University Ave., Madison, WI 53705, USA