Effect of oral DHEA on serum testosterone and adaptations to resistance training in young men

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Brown, Gregory A., Matthew D. Vukovich, Rick L. Sharp, Tracy A. Reifenrath, Kerry A. Parsons, and Douglas S. King. Effect of oral DHEA on serum testosterone and adaptations to resistance training in young men. *J. Appl. Physiol.* 87(6): 2274–2283, 1999.—This study examined the effects of acute dehydroepiandrosterone (DHEA) ingestion on serum steroid hormones and the effect of chronic DHEA intake on the adaptations to resistance training. In 10 young men (23 ± 4 yr old), ingestion of 50 mg of DHEA increased serum androstenedione concentrations 150% within 60 min ($P < 0.05$) but did not affect serum testosterone and estrogen concentrations. An additional 19 men (23 ± 1 yr old) participated in an 8-wk whole body resistance-training program and ingested DHEA (150 mg/day, $n = 9$) or placebo ($n = 10$) during *weeks 1, 2, 4, 5, 7,* and *8*. Serum androstenedione concentrations were significantly ($P < 0.05$) increased in the DHEA-treated group after 2 and 5 wk. Serum concentrations of free and total testosterone, estrone, estradiol, estriol, lipids, and liver transaminases were unaffected by supplementation and training, while strength and lean body mass increased significantly and similarly ($P < 0.05$) in the men treated with placebo and DHEA. These results suggest that DHEA ingestion does not enhance serum testosterone concentrations or adaptations associated with resistance training in young men.

insulin; liver transaminases; serum lipids; serum estrogens; strength training

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DEHYDROEPIANDROSTERONE (DHEA; 3β-hydroxy-5-andro-sten-17-one) and its conjugate sulfate (DHEA-S) are the steroid hormones of greatest abundance in the blood. Although the physiological role(s) of DHEA and DHEA-S is unclear, abnormal levels of blood DHEA and DHEA-S may be related to obesity (16) and insulin resistance (2, 16). Furthermore, blood concentrations of DHEA and DHEA-S decrease in men after 25 yr of age (31).

Blood-borne DHEA can be converted to androstenedione or androstenediol, which in turn can be converted to testosterone. However, DHEA, testosterone, androstenediol, and androstenedione can also be aromatized to estrogens or reduced to dihydrotestosterone (DHT) by 5α-reductase in peripheral tissues (24), which may mitigate any increase in the serum testosterone concentration after DHEA intake. Although ingestion of DHEA has been shown to increase blood androstenedione (27–30, 39), DHEA (27–29, 39), and DHEA-S levels (25,

27–30, 38, 39), it is not clear whether oral administration of DHEA increases blood testosterone levels in men (25, 27–30, 39). In addition, artificially increased blood testosterone concentrations have been shown to suppress testosterone production through negative feedback of the hypothalamic-pituitary-adrenal loop (5, 22). Therefore, one purpose of this study was to determine the effect of a single ingestion of 50 mg of DHEA and ingestion of 150 mg DHEA/day on serum steroid hormone concentrations.

Resistance training produces hypertrophy of skeletal muscle fibers, particularly type II fibers (36). It is recognized that the use of exogenous testosterone and anabolic steroids in conjunction with resistance training increases the gains in muscle mass and strength associated with resistance training (5, 22). Although muscle mass may also be augmented with DHEA supplementation alone (27, 30, 39), the impact of DHEA supplementation during resistance training on muscle mass and strength is unknown. Percent body fat is decreased with anabolic steroid use (5, 22) and has been reported to be unchanged (27, 28, 38) or decreased (10, 13, 14, 27, 30, 39) in response to chronic ingestion of DHEA. There are no available data on the effect of DHEA supplementation during resistance training on body composition. Therefore, another purpose of this study was to explore the effects of DHEA ingestion during resistance training on muscle mass, muscle fiber diameter, muscle strength, and body fat.

Reduced blood levels of DHEA have been associated with hyperglycemia and insulin resistance (2, 16). Some authors have observed no change in insulin sensitivity in response to chronic DHEA ingestion (27, 28, 30, 39), while others have observed an increased (29) or reduced (7, 10, 13) insulin response to a glucose challenge after DHEA supplementation. In contrast, recent reports suggest that DHEA may improve insulin action by increasing phosphatidylinositol 3-kinase (13) and protein kinase C activity (35). Although glucose tolerance is unchanged or improved after resistance training, the observed reduction in the plasma insulin response to oral glucose indicates an improved insulin sensitivity (9, 26, 34). Anabolic-androgenic steroids are known to increase the risk of cardiovascular disease as a result of decreased serum high-density-lipoprotein cholesterol (HDL-C) concentrations and increased serum concentrations of low-density-lipoprotein cholesterol (LDL-C). Liver function may also be adversely affected by elevated blood testosterone concentrations (19, 22, 23). Chronic DHEA ingestion has been shown to reduce (28, 29) or have no effect (30, 38) on blood HDL-C concentrations. The effect of chronic DHEA ingestion

on liver function in young men is also unknown. Therefore, the final purpose of this study was to determine the effect of DHEA ingestion in conjunction with resistance training on glucose tolerance and insulin sensitivity, blood lipid profiles, and tests of liver function.

METHODS

Subjects. A total of 30 healthy young (19- to 29-yr-old) men were recruited for the study, which was approved by the Iowa State University Human Subjects Committee. All participants completed a written questionnaire regarding the use of nutritional supplements or participation in a resistance-training program before enrollment in the study. Subjects did not report any present or previous supplement use or resistance training. All subjects were free of cardiovascular or orthopedic conditions that would contraindicate exercise.

Acute administration of DHEA. The effects of acute ingestion of DHEA on the serum concentrations of androstenedione, free testosterone, total testosterone, estradiol (E_2), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were studied in 10 of the men (23 ± 4 yr old). On two separate occasions separated by ≥ 1 wk and after an overnight fast, 50 mg of DHEA (one-third of the daily dose given during the resistance training) or placebo (PL, 83 mg of rice flour) were administered in a randomly assigned double-blind manner. Blood samples were obtained before and every 30 min for 6 h after ingestion. Serum hormone concentrations were determined as described below.

DHEA supplementation during resistance training. After they were screened, 20 of the men were randomly assigned in a double-blind manner to groups that ingested 150 mg DHEA/day or PL (250 mg of rice flour) during *weeks 1–2, 4–5, and 7–8* of the 8 wk of resistance training (Fig. 1). This dose of DHEA was one that exceeded the dose recommended (50–100 mg/day) by many suppliers of DHEA. Supplementation was administered in a cyclic pattern of 2 wk on supplements followed by 1 wk off supplements to simulate the supplementation regimen recommended by many suppliers of bodybuilding supplements. This cyclical pattern is thought to allow for a washout period, reducing the likelihood of negative side effects, such as gynecomastia and cholesterol abnormalities
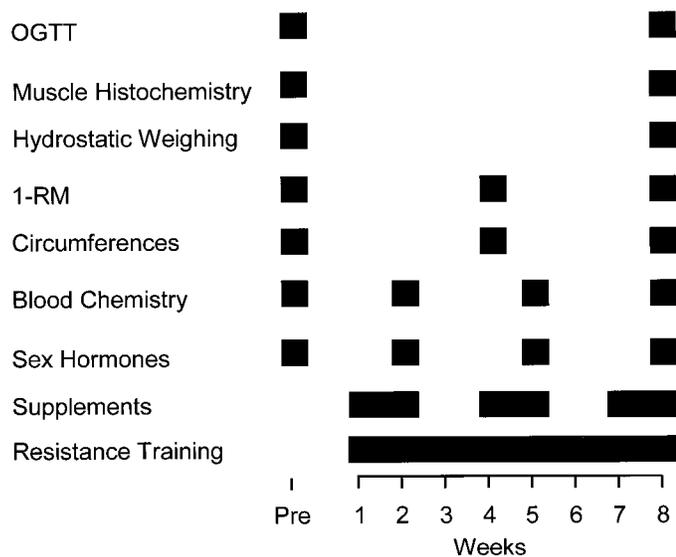
associated with androgenic supplement use. Supplements were taken in three equal doses before 9:00 AM, at 3:00 PM, and at bedtime. The DHEA (Experimental and Applied Sciences, Golden, CO) is a commercially available product derived from wild yams and was assayed to be 98 and 99% pure by HPLC by two independent laboratories (Biomedical Laboratories, Petaluma, CA, and Integrated Biomolecule, Tucson, AZ, respectively). To encourage compliance, subjects maintained a record of supplement ingestion and were required to return unused supplements at the completion of the study.

Resistance training. Subjects performed resistance training 3 days/wk on nonconsecutive days using bench press, shoulder press, knee extension, right and left knee flexion, vertical butterfly, leg press, calf press, biceps curl, triceps curl, and latissimus dorsi pulldown. Subjects were instructed on proper lifting technique and supervised during all lifting sessions. The resistance-training program was designed to increase muscle strength in all major muscle groups of the body. Subjects performed 3 sets of 10 repetitions for the first 2 wk of resistance training. For the final 6 wk of training, subjects performed three sets of eight repetitions. Resistance was established at 80–85% of the untrained one repetition maximum (1 RM). After the determination of 1 RM after 4 wk of training, the training intensity was adjusted to 80–85% of the new 1 RM. The amount of weight lifted, number of sets, and repetitions performed were recorded for each training session. Subjects were instructed to limit exercise to the prescribed training regimen throughout the study.

Strength testing. Before training and after 4 and 8 wk, subjects were tested for 1 RM. Subjects were allowed a brief light-resistance warm-up, and then they were encouraged to meet their 1 RM within five trials of increasing resistance (1). One repetition maximum was assessed on bench press, shoulder press, knee extension, right and left knee flexion, biceps curl, triceps extension, latissimus dorsi pulldown, and vertical butterfly. All resistance training and 1-RM testing were performed on multistation isotonic resistance equipment (model FTX, Paramount Fitness Equipment, Los Angeles, CA).

Body composition. Height, weight, and body circumferences were determined before training and after *weeks 4* and *8.* Circumferences were measured by the same investigator at the shoulders, biceps, chest, abdomen, waist, hips, gluteus, thigh, and calf with use of methods specified by the American College of Sports Medicine (1). Body composition was determined through hydrostatic weighing by use of a computer-interfaced load cell and custom computer program before training and after 8 wk of training and supplementation. The computer program utilizes the Siri equation for body fat (33) and the Goldman-Becklake equation for residual lung volume (12).

Clinical blood chemistry and hormone analyses. Blood samples were obtained after an overnight fast for standard blood chemistry and hormone analyses before training and after 2, 5, and 8 wk of training and supplementation. Blood was withdrawn without stasis from a catheter inserted into an antecubital vein. A commercial laboratory (Labcorp, Kansas City, MO) performed all clinical blood chemistry analyses. Another blood sample was centrifuged, and serum was frozen at $-80°C$ until analysis. Serum concentrations of free and total testosterone, androstenedione, estrone (E_1), E_2, and estriol (E_3) were measured with RIA by using commercially available kits (Diagnostic Products, Los Angeles, CA, and Diagnostic Systems Laboratories, Webster, TX). Serum concentrations of LH and FSH were measured using commercially available immunoradiometric assay kits (Diagnostic

Fig. 1. Experimental design. OGTT, oral glucose tolerance test; RM, repetition maximum; Pre; prexercise.

Products). All samples for each subject were assayed in the same run. The intra-assay coefficients of variation were 7.3, 7.7, 6.7, 4.7, 3.9, 8.2, 6.0, and 7.3% for free testosterone, total testosterone, androstenedione, LH, FSH, E_1, E_2, and E_3, respectively.

Oral glucose tolerance test. Before training and again within 3 days (48 ± 1 h) after the last training session, the subjects underwent a 2-h 75-g oral glucose tolerance test (OGTT) between 5 and 10 AM after an 8- to 12-h fast. Blood samples (~10 ml) were obtained at 0, 30, 60, 90, and 120 min from a flexible catheter inserted into an antecubital vein. Plasma was separated and stored at $-80°$C until analysis for glucose and insulin concentrations. Plasma glucose concentrations were measured spectrophotometrically using the hexokinase method (Sigma Chemical, St. Louis, MO). Plasma insulin concentrations were determined by RIA (Diagnostic Products). The intra-assay coefficient of variation for insulin was 7.1%.

Subjects were given written instructions for a 150 g/day carbohydrate diet and instructed to otherwise maintain their regular diet. Diet records were maintained for 3 days before the initial OGTT, and subjects were provided copies of the initial diet record and asked to repeat the same diet for the posttraining OGTT. Dietary records were assessed for composition by use of a computer food analysis program (Food Comp, Iowa State University). Subjects were also instructed to maintain their usual dietary regimen throughout the study.

Muscle histochemistry. Muscle biopsies were obtained before and after resistance training for determination of skeletal muscle fiber type distribution and mean cross-sectional area. Muscle samples (~100 mg) were obtained from the lateral aspect of the vastus lateralis muscle of the subjects by use of the needle-biopsy technique described by Bergstrom (4). Muscle specimens were placed in mounting medium and frozen in isopentane cooled to the temperature of liquid nitrogen for later sectioning and staining. Frozen transverse sections (~10 μm) were cut on a histostat (Histostat Microtome, AO Scientific Instruments) at $-20°$C. The percentage of type I and type II muscle fibers was determined in sections stained for ATPase activity at pH 9.4 after a preincubation at pH 4.3. In addition, the samples were counterstained with an eosin Y stain for color enhancement to aid in the image analysis of the different muscle fiber types. Muscle fiber type distribution and muscle fiber areas were determined using a computer-operated image analysis system (Neosis Visilog Image Analysis Software, SGI-Computer; model DXC-3000A camera, Sony). The system captures the light-microscopic image, thresholds the images, traces the muscle fiber boundaries, counts the light and dark muscle fibers, and measures the cross-sectional areas of all muscle fibers. To determine the percent distribution of type I and type II fibers, all viable fibers were used. The mean cross-sectional fiber areas were determined on 20 randomly selected fibers from each fiber type. For determination of mean cross-sectional area of type I and type II fibers, groupings of clearly delineated fibers were highlighted, and a technician blinded to the treatments randomly selected 20 fibers of each type.

Calculations and statistics. Incremental areas under the curve for insulin and glucose were calculated using the trapezoidal model with a custom computer program. Statistical analysis was performed using a two-way repeated-measure ANOVA. When significant interactions were observed, specific mean differences were located with a Newman-Keuls multiple-comparison test. All statistical tests were performed with commercial software (Sigma Stat 1.0, Jandel Scientific, San Rafael, CA) and were evaluated at $P < 0.05$.

RESULTS

Subjects. Of the 30 subjects who started the project, 1 subject from the DHEA group participating in resistance training withdrew. This study was part of a larger investigation involving various supplements, and the data from the subjects given PL have been reported elsewhere (20). There was no difference between the treatment groups in terms of fitness, age, or exercise experience.

Acute hormone response to DHEA administration. Ingestion of 50 mg of DHEA resulted in increased serum androstenedione concentrations within 30 min (Fig. 2; $P < 0.05$) that peaked at 150% above baseline by 60 min after ingestion. Serum androstenedione concentrations tended to decline after 60 min but remained significantly elevated for 360 min after ingestion of DHEA ($P < 0.05$). Ingestion of PL resulted in no change in serum androstenedione concentrations. Serum concentrations of LH and FSH were also not altered during the 360 min after ingestion of DHEA or PL. Ingestion of DHEA or PL did not alter the serum concentrations of
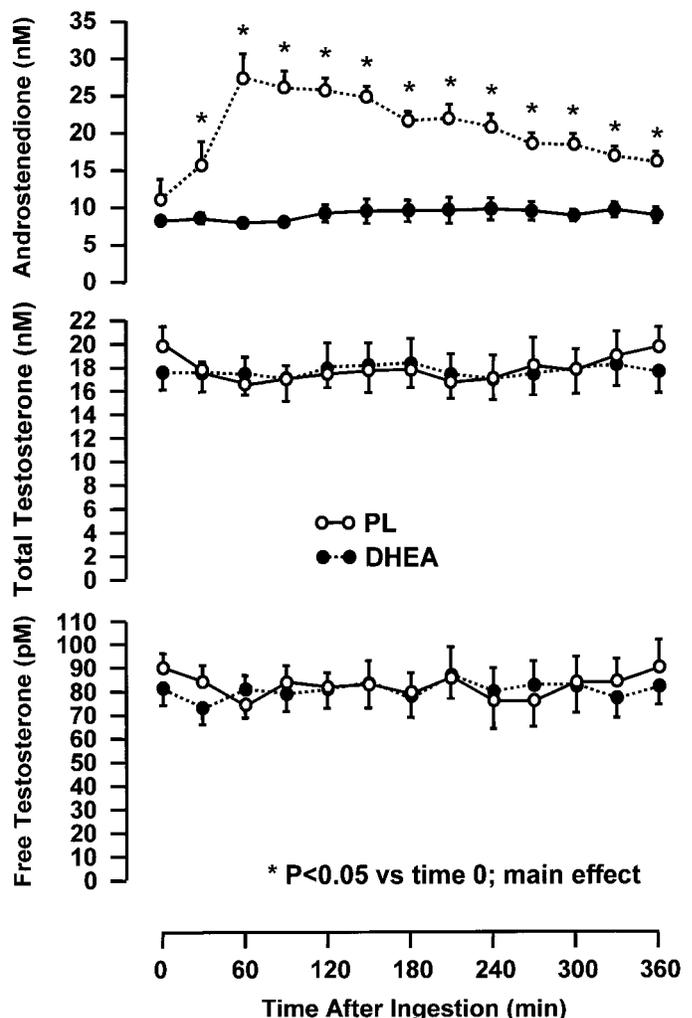

Fig. 2. Serum androstenedione and free and total testosterone concentrations after ingestion of 50 mg of dehydroepiandrosterone (DHEA) or placebo (PL). Values are means $\pm$ SE ($n = 10$). *Significantly different from *time 0* for DHEA ($P < 0.05$).

free testosterone or total testosterone. Serum E_2 concentrations increased significantly 60 min after ingestion of PL and DHEA (main effect for time, $P < 0.05$) and were not different between the two groups.

Resistance training. There were no significant differences between PL and DHEA supplementation in the number of sets or repetitions performed per exercise session or the relative intensity of each exercise session. When the data from all exercises are combined, subjects exercised at an intensity of $81 \pm 2\%$ of 1 RM during the first 4 wk of training and at $83 \pm 1\%$ of 1 RM for the final 4 wk of training. The total mean force produced per subject each day was 46 ± 1 kN during the first 4 wk of training and 43 ± 1 kN during the final 4 wk of training, with no differences observed between groups. The lower amount of force produced during *weeks 4–8* was due to the lower number of repetitions performed during each exercise session.

Hormone response to DHEA administration during resistance training. Because of a loss of power to the laboratory freezer and thawing of serum samples, we were unable to measure serum concentrations of DHEA or DHEA-S. Serum androstenedione concentrations (Fig. 3) were significantly increased in subjects treated with DHEA at *week 2* (13 ± 1 nM) and *week 5* (17 ± 2 nM) compared with *week 0* (10 ± 1 nM, $P < 0.05$). At *week 8*, serum androstenedione concentrations were not significantly different from those at *week 0*. Serum androstenedione concentrations were unaffected by training and supplementation in the subjects given PL. The calculated effect size for the comparison of the androstenedione concentrations was very large (1.1). This calculation highlights the effect of DHEA in increasing serum androstenedione concentrations.

Serum concentrations of LH were not altered by supplementation and training in subjects treated with DHEA (3.5 ± 0.7 vs. 3.4 ± 0.8 mIU/ml) or those given PL (2.5 ± 0.6 vs. 2.9 ± 0.6 mIU/ml). Supplementation and training also did not alter serum FSH concentrations in subjects treated with DHEA (2.9 ± 1.1 vs. 3.1 ± 1.2 mIU/ml) or those given PL (2.6 ± 0.6 vs. 3.0 ± 0.6 mIU/ml).

Serum free and total testosterone concentrations (Fig. 3) were not altered by 8 wk of resistance training and supplementation in subjects given PL or those treated with DHEA.

Because one subject in the PL group had very high initial serum E_2 concentrations (0.46 nM), his data were excluded from the statistical analysis of serum E_2 concentrations. Serum E_1, E_2, and E_3 concentrations were not significantly altered during the 8-wk resistance-training and supplementation period in the subjects given PL or those treated with DHEA (Fig. 4).

Muscle strength. Muscle strength was not significantly different between the subjects given PL and those treated with DHEA before training or after 4 or 8 wk of training. To facilitate data presentation (Fig. 5), upper body strength was calculated as the sum of 1 RM for bench press, shoulder press, and latissimus dorsi pulldown. Upper body strength was increased similarly in the subjects given PL and those treated with DHEA
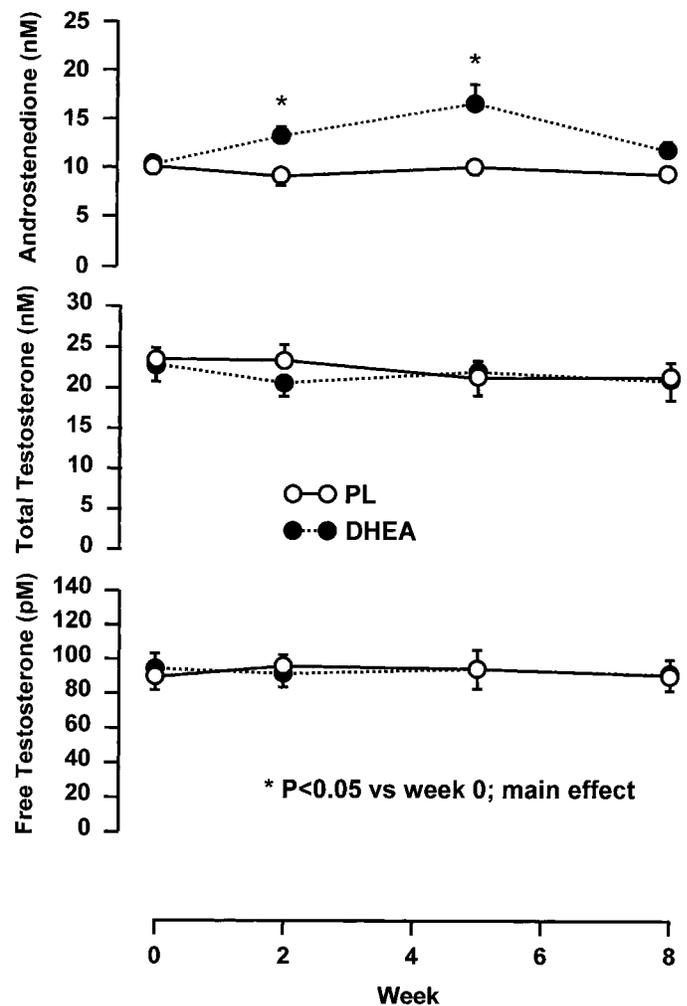

Fig. 3. Serum androstenedione and free and total testosterone concentrations before and during resistance training combined with 150 mg DHEA/day ($n = 9$) and PL ($n = 10$) supplementation. Supplements were administered during *weeks 1–2, 4–5,* and *7–8.* Values are means $\pm$ SE. *Significantly different from *week 0* for DHEA ($P < 0.05$).

after 4 wk of resistance training and supplementation (main effect, $P < 0.05$). Upper body strength was further increased in all groups during the final 4 wk of resistance training and supplementation (main effect, $P < 0.05$). The overall increase in upper body strength from *week 0* to *week 8* was not different in subjects given PL ($2,016 \pm 170$ vs. $2,492 \pm 203$ N) and those treated with DHEA ($1,815 \pm 187$ vs. $2,242 \pm 279$ N). Calculating the effect size for the upper body strength data reveals an effect size of 0.18. With the assumption of a power of 80% and $P = 0.05$, a sample size of 475 would have been required to determine an effect of this size. These calculations emphasize the lack of effect of DHEA on muscle strength during resistance training. Lower body strength was calculated as the sum of knee extension and right and left knee flexion. Lower body strength increased similarly during the first 4 wk of resistance training and supplementation in subjects given PL and those treated with DHEA (main effect, $P < 0.05$). The final 4 wk of resistance training and
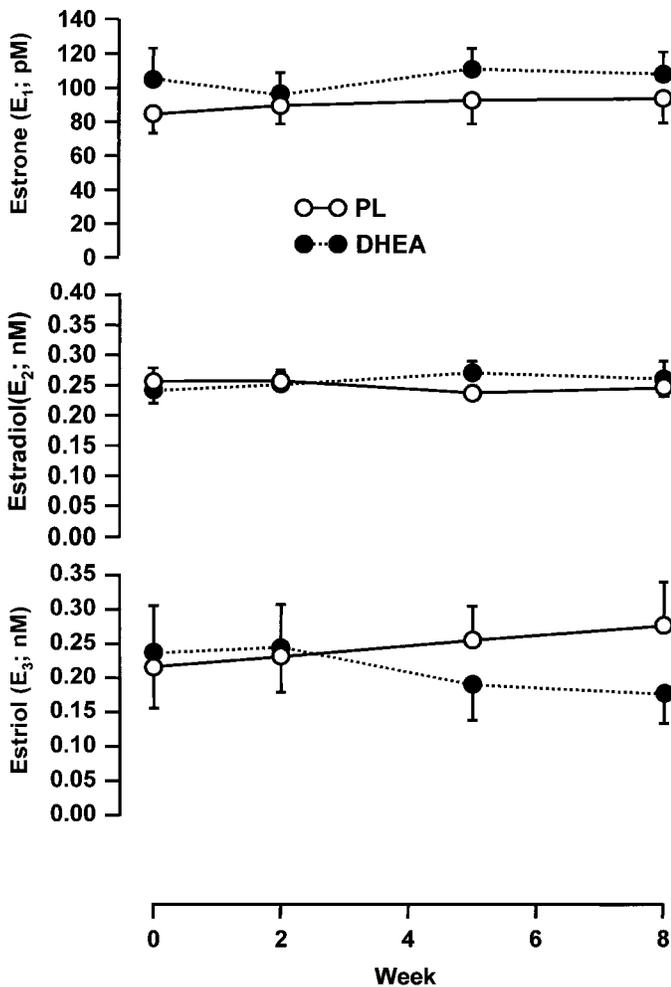
Fig. 4. Serum estrone, estradiol, and estriol concentrations before and during resistance training combined with 150 mg DHEA/day (n = 9) and PL (n = 10) supplementation. Supplements were administered during *weeks 1–2, 4–5,* and *7–8.* Values are means ± SE.

mentation in subjects given PL (3,980 ± 411 vs. 4,102 ± 604 μm²) or those treated with DHEA (4,054 ± 369 vs. 4,285 ± 356 μm²). The mean cross-sectional area of type II fibers increased (significant main effect, $P < 0.05$) in subjects given PL (5,271 ± 485 vs. 5,728 ± 451 μm²) and those treated with DHEA (5,724 ± 456 vs. 5,829 ± 354 μm²).

Anthropometric data. There were no significant differences between subjects treated with DHEA and those given PL in the changes in body composition observed as a consequence of resistance training (Table 1). Significant increases in circumferences occurred for the biceps, shoulder, and chest sites (main effect, $P < 0.05$), whereas the abdominal, waist, hip, and gluteal circumferences decreased during resistance training in subjects treated with DHEA and those given PL (main effect, $P < 0.05$). Additionally, the resistance-training program significantly (main effect, $P < 0.05$) reduced the percent body fat in both groups.

Clinical blood chemistry. The 8-wk period of training and supplementation did not affect serum concentra-
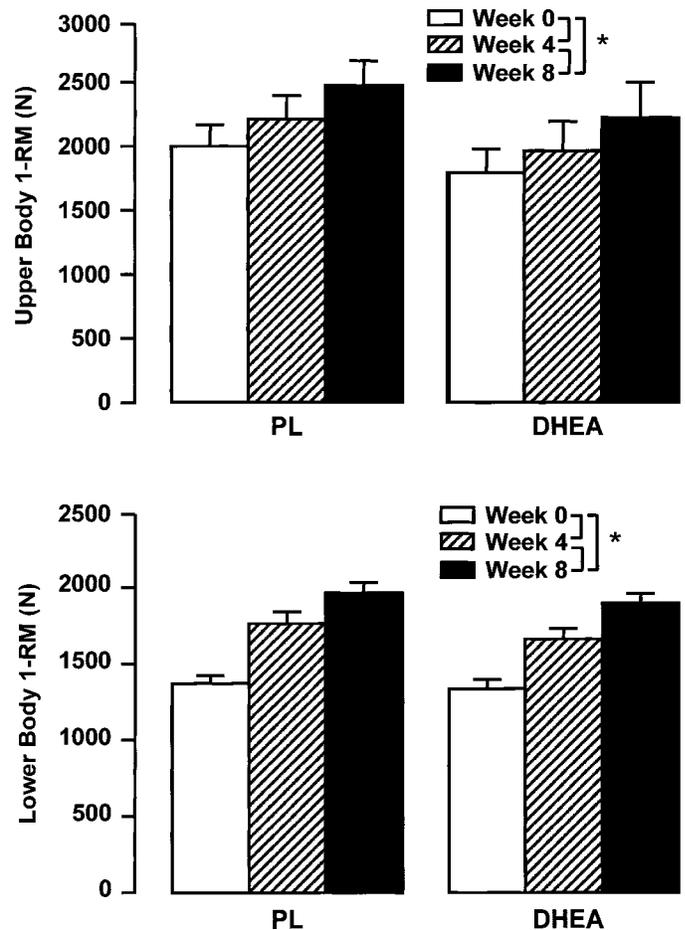

Fig. 5. Upper and lower body strength before and after resistance training combined with 150 mg DHEA/day (n = 9) or PL (n = 10) supplementation. Supplements were administered during *weeks 1–2, 4–5,* and *7–8.* Upper body strength was calculated as sum of 1 RM for bench press, shoulder press, and latissimus dorsi pulldown. Lower body strength was calculated as sum of knee extension and right and left knee flexion. Values are means ± SE. *Significantly different from before resistance training (significant main effect, $P < 0.05$).

supplementation resulted in additional increases in lower body strength in both groups (main effect, $P < 0.05$). The overall increase in lower body strength from *week 0* to *week 8* was not different in subjects given PL (1,387 ± 55 vs. 1,980 ± 70 N) or those treated with DHEA (1,349 ± 61 vs. 1,912 ± 62 N). When the data for both groups and all exercises are combined, the mean gain in whole body muscle strength for the first 4 wk of training was 17 ± 2%, whereas the final 4 wk of resistance training resulted in an additional increase in muscle strength of 11 ± 2%.

Muscle histochemistry. Because of the loss of power to the laboratory freezer and thawing of some of the muscle samples, viable sections were obtained for only nine subjects given PL and five subjects treated with DHEA. The percentage of type I fibers before resistance training and supplementation was similar in subjects given PL (44 ± 6%) and those treated with DHEA (53 ± 5%) and did not change after resistance training in those given PL (45 ± 5%) or treated with DHEA (52 ± 4%). The mean cross-sectional area of type I fibers (Fig. 6) was not altered with resistance training and supple-
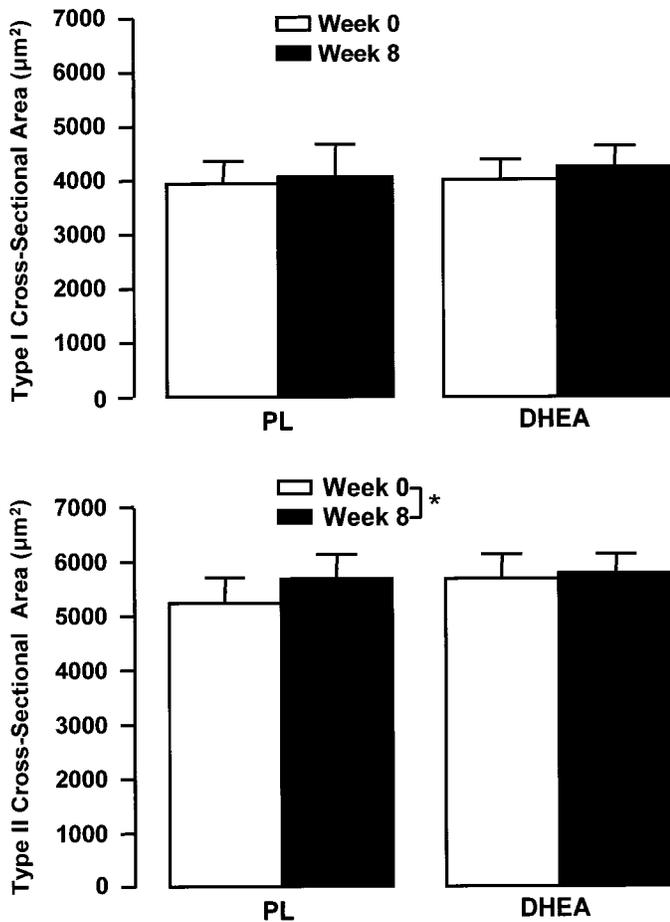
Fig. 6. Mean change in cross-sectional areas of type I and type II muscle fibers from vastus lateralis muscle before and after resistance training combined with 150 mg DHEA/day ($n = 5$) or PL ($n = 9$) supplementation. Supplements were administered during *weeks 1–2, 4–5,* and *7–8.* Values are means ± SE. *Significantly different from before resistance training for both treatment groups (significant main effect, $P < 0.05$).

tions of total cholesterol, HDL-C, LDL-C, very-low-density-lipoprotein cholesterol, or triglycerides (Table 2). Serum concentrations of liver function enzymes were unaltered by training or supplementation. Total iron, hematocrit, and Hb concentrations were also not significantly altered by 8 wk of resistance training or supplementation.

Dietary control. Total dietary energy (9,547 ± 179 vs. 9,983 ± 214 kJ/day), carbohydrate (229 ± 5 vs. 246 ± 7 g/day), or protein (89 ± 6 vs. 83 ± 5 g/day) intake was not different for subjects treated with DHEA and those given PL before each OGTT. The total dietary energy intake was somewhat lower than expected, possibly because of underreporting by the subjects. However, comparison of the glucose and insulin responses in subjects treated with DHEA and those given PL is appropriate, since subjects reproduced the diet before the OGTT in the trained state. In addition, subjects were instructed throughout the study to maintain their typical dietary regimen, and all indicated that their dietary practices did not change during the course of the study.

Glucose tolerance and plasma insulin response. The 8 wk of resistance training and supplementation resulted in no significant alteration in the incremental area under the glucose curve (Fig. 7) for the subjects given PL or those treated with DHEA. Eight weeks of resistance training and supplementation resulted in significant attenuation in the insulin area under the curve for subjects given PL and those treated with DHEA, which was independent of treatment (main effect, $P < 0.05$). To provide information regarding the effect of training and supplementation on insulin sensitivity, the product of the incremental glucose and insulin areas (IG index) was calculated. The IG index (mM·min·pM·min·10^6) was reduced significantly by resistance training (main effect, $P < 0.05$) and was not different in subjects treated with DHEA and those given PL before (8.6 ± 5.7 and 12.9 ± 2.5 for subjects treated with DHEA and

Table 1. *Anthropometric data during resistance training and supplementation with DHEA or PL*

	PL ($n = 10$)			DHEA ($n = 9$)		
	Week 0	*Week 4*	*Week 8*	*Week 0*	*Week 4*	*Week 8*
Age, yr	23.3 ± 1.1			23.2 ± 0.8		
Height, cm	178.0 ± 1.5			179.3 ± 1.6		
Body mass,*† kg	81.1 ± 5.2	83.3 ± 5.1	83.2 ± 4.9	85.9 ± 7.2	88.2 ± 7.2	88.4 ± 7.2
Lean body mass,† kg	63.1 ± 2.6		66.0 ± 2.5	64.5 ± 3.9		68.4 ± 3.7
Fat mass,† kg	18.0 ± 2.9		17.2 ± 2.9	21.4 ± 4.2		19.9 ± 4.6
Body fat,† %	21.3 ± 1.9		19.9 ± 2.1	23.7 ± 3.1		21.2 ± 3.5
Circumferences, cm						
Biceps*†	32.6 ± 1.4	33.2 ± 1.4	33.4 ± 1.3	32.4 ± 1.5	32.9 ± 1.5	33.3 ± 1.5
Shoulder†‡	120.3 ± 3.4	120.2 ± 3.5	120.7 ± 3.3	122.9 ± 4.5	123.6 ± 4.4	123.9 ± 4.4
Chest†‡	98.0 ± 3.8	99.9 ± 3.8	100.9 ± 3.4	103.8 ± 5.2	102.6 ± 4.8	103.0 ± 4.8
Abdomen*†‡	87.2 ± 3.8	86.5 ± 4.0	85.9 ± 3.6	92.3 ± 5.8	90.8 ± 6.1	90.6 ± 6.1
Waist*†	84.9 ± 3.9	83.6 ± 3.9	83.7 ± 3.7	88.9 ± 5.8	87.8 ± 5.8	87.8 ± 5.7
Hips*†‡	89.2 ± 2.5	87.7 ± 2.1	85.7 ± 2.3	93.3 ± 3.7	90.2 ± 3.4	88.8 ± 3.2
Gluteal*†‡	100.4 ± 2.5	98.6 ± 2.5	97.4 ± 2.3	103.2 ± 3.5	100.2 ± 3.7	99.3 ± 3.4
Thigh	54.7 ± 1.2	55.1 ± 1.4	55.1 ± 1.5	55.8 ± 1.9	55.5 ± 2.2	56.4 ± 2.1
Calf	37.4 ± 1.7	38.4 ± 0.9	38.6 ± 0.9	39.2 ± 1.1	38.7 ± 1.1	38.9 ± 1.1

Values are means ± SE of all data for dehydroepiandrosterone (DHEA, 150 mg/day) and placebo (PL); *n*, no. of subjects. Subjects performed resistance training for 8 wk and ingested PL or DHEA. * *Week 4* significantly different from *week 0* (main effect, $P < 0.05$). † *Week 8* significantly different from *week 0* (main effect, $P < 0.05$). ‡ *Week 8* significantly different from *week 4* (main effect, $P < 0.05$).

Table 2. *Serum lipid data during resistance training and supplementation with DHEA or PL*

	PL ($n=10$)				DHEA ($n=9$)			
	Week 0	*Week 2*	*Week 5*	*Week 8*	*Week 0*	*Week 2*	*Week 5*	*Week 8*
Blood lipids, mg/dl								
Total cholesterol	156 ± 10	158 ± 12	168 ± 9	160 ± 9	166 ± 17	166 ± 14	167 ± 16	167 ± 16
HDL cholesterol	39 ± 2	38 ± 3	39 ± 3	39 ± 3	39 ± 1	41 ± 2	39 ± 2	42 ± 2
LDL cholesterol	94 ± 7	94 ± 8	105 ± 8	101 ± 8	101 ± 14	99 ± 12	105 ± 13	106 ± 14
VLDL cholesterol	22 ± 5	22 ± 5	23 ± 5	19 ± 5	25 ± 4	26 ± 5	23 ± 4	18 ± 3
Triglycerides	111 ± 28	111 ± 26	119 ± 23	97 ± 23	126 ± 19	131 ± 23	115 ± 18	91 ± 17
Liver function enzymes, IU/l								
GGT	19 ± 4	19 ± 5	25 ± 9	20 ± 5	23 ± 3	23 ± 3	25 ± 4	22 ± 3
SGOT	19 ± 2	25 ± 4	27 ± 5	24 ± 3	15 ± 1	17 ± 2	16 ± 1	20 ± 1
SGPT	21 ± 5	27 ± 7	34 ± 15	24 ± 7	18 ± 2	21 ± 4	18 ± 3	28 ± 10

Values are means $\pm$ SE; *n*, no. of subjects. Subjects performed resistance training for 8 wk and ingested PL or DHEA (150 mg/day). HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; GGT, γ-glutamyl transpeptidase; SGOT, glutamate-oxaloacetate transaminase; SGPT, glutamate-pyruvate transaminase.

those given PL, respectively) or after (10.3 $\pm$ 2.8 and 11.9 $\pm$ 5.4 for subjects treated with DHEA and those given PL, respectively) training and supplementation. Although the incremental area under the insulin curve and the IG index before training and supplementation
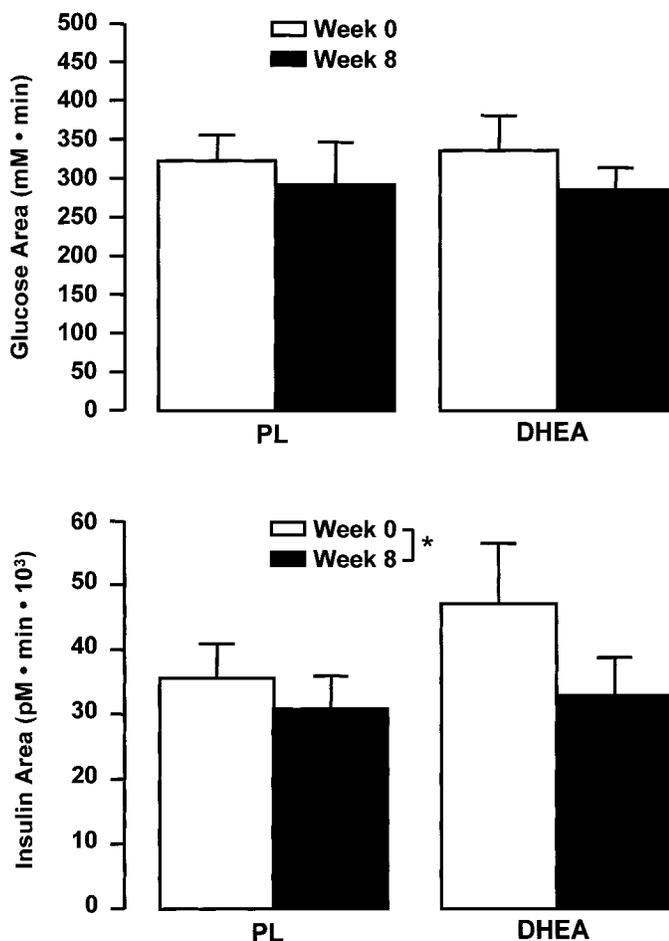

Fig. 7. Incremental area above baseline under glucose and insulin response curve during 75-g OGTTs before and after resistance training combined with 150 mg DHEA/day (n = 9) or PL (n = 10) supplementation. Supplements were administered during *weeks 1–2, 4–5,* and *7–8.* Values are means $\pm$ SE. *Significantly different from before resistance training for both treatment groups (significant main effect, $P < 0.05$).

tended to be higher in subjects treated with DHEA than in those given PL, this was the result of the extremely high incremental insulin area of one subject (99.2 pM·min·10^3), and the mean difference between groups did not approach significance. Removal of this subject's data from the statistical analysis did not affect the results; therefore, these data are included in Fig. 7.

DISCUSSION

Acute administration of 50 mg of DHEA and chronic administration of 150 mg DHEA/day did not increase serum testosterone concentrations in young men. Increases in serum testosterone concentrations after DHEA administration have been observed in women (21, 25, 27–29, 39) but not in normotestosterogenic men (21, 27, 28, 30, 39). For example, Morales et al. (28) observed a 203% increase in serum testosterone concentrations after ingestion of 50 mg of DHEA in middle-aged women, whereas serum testosterone concentrations were unaffected in men. Furthermore, daily doses of 1,600 mg of DHEA have not increased serum testosterone concentrations in healthy young men (30). Taken together with the present results, these data suggest that oral DHEA supplementation may increase serum testosterone concentrations only in postmenopausal women.

In older men, daily ingestion of 50 and 100 mg of DHEA has been reported to increase the serum androstenedione concentrations by 20 and 100%, respectively (27, 28). In the only published report on the serum androstenedione response to DHEA supplementation in young men, ingestion of 1,600 mg DHEA/day produced a 100% increase in serum androstenedione concentration (30). We recently reported a 100% increase in serum androstenedione in young men in response to daily ingestion of 300 mg of androstenedione (20). These data, along with the 61% increase in serum androstenedione after ingestion of 150 mg DHEA/day in the present study, indicate that DHEA and androstenedione ingestion increase the concentrations of serum androstenedione without a resultant increase in serum testosterone. These findings are consistent with the results of Horton and Tait (18) showing that blood

androstenedione does not contribute significantly to blood-borne testosterone in men.

The mechanism(s) for the significantly increased serum androstenedione concentrations after DHEA ingestion at *weeks 2* and *5*, but not at *week 8*, is unknown. Mortola and Yen (29) found a similar pattern in the serum androstenedione response to ingestion of 1,600 mg DHEA/day and speculated that the reduced concentrations of androstenedione with continued supplementation may be due to an increased metabolic clearance rate or decreased entry of DHEA into the circulation. A third possibility for the decline in serum androstenedione at *week 8* may be decreased 3β-hydroxysteroid dehydrogenase activity, since DHEA has been observed to directly inhibit 3β-hydroxysteroid dehydrogenase activity in placenta (37) and adrenal microsomes (6).

Although blood-borne androstenedione can be converted to testosterone in men and women, it appears that androstenedione in the blood is a quantitatively more important precursor to testosterone in women, since only 1.8% of blood androstenedione is converted to testosterone in men compared with 60% in women (18). Recent research from this laboratory found that although androstenedione ingestion in young men did not affect serum testosterone concentrations, serum estrogen concentrations were significantly elevated, indicating that a significant portion of the ingested androstenedione underwent aromatization (20). The finding that DHEA supplementation does not affect serum estrogen concentrations, despite significantly increased serum androstenedione concentrations (present study; 21, 28, 30, 39), is somewhat surprising and difficult to explain. It is possible that the increased serum androstenedione after DHEA ingestion is converted to DHT by 5α-reductase and, subsequently, to DHT metabolites. However, increased serum DHT concentrations after DHEA ingestion have been observed in women, but not in men (27–29, 39). Labrie et al. (21) found that percutaneous DHEA administration in men increased serum concentrations of androsterone glucuronide, androstane-3α,17β-diol-glucuronide, androstane-3β,17β-diol-glucuronide, and androsterone sulfate, but not DHT, suggesting that DHEA administration results in the formation of only inactive steroid metabolites.

The use of anabolic steroids or exogenous testosterone causes depressed serum LH and FSH concentrations as a result of negative feedback of the hypothalamic-pituitary-adrenal loop (5, 22). The findings of the present study are similar to those of Mortola and Yen (29), demonstrating that DHEA ingestion has no effect on serum FSH or LH concentrations and suggesting that the hypothalamic-pituitary-adrenal regulation of testosterone production is not altered by DHEA intake.

The increases in muscle strength found in the present study demonstrate the effectiveness of the resistance-training protocol used. The finding of increased strength with no differences between treatment groups in the present study indicates that ingestion of DHEA is not effective in promoting muscle strength during resis-tance training in young men. The present findings of no effect of DHEA supplementation on muscle strength also indicate that increased serum androstenedione does not enhance muscle strength gains, possibly because of the weakness of androstenedione as an anabolic-androgenic steroid (32).

Whereas DHEA ingestion may protect against adiposity in animals (10, 13, 14), the effect of DHEA on body composition in humans is equivocal (27–30, 38, 39). Morales et al. (27) found that intake of 100 mg DHEA/day for 6 mo increased muscle mass and muscle strength in older men without resistance training. Nestler et al. (30) observed that consumption of 1,600 mg DHEA/day for 28 days decreased body fat and increased muscle mass in young men. In contrast, Welle et al. (38) observed that intake of 1,600 mg DHEA/day for 4 wk did not alter energy or protein metabolism, body weight, or two indexes of lean body mass (total body water and total body potassium). In the present study the decreased body fat and increased lean body mass observed with resistance training were unaffected by daily supplementation with 150 mg of DHEA. Although the effect of higher doses of DHEA on body composition is still unclear, these data indicate that ingestion of 150 mg DHEA/day is insufficient to promote changes in body composition and strength beyond those normally associated with resistance training in healthy young men.

The reduced plasma insulin response during the OGTT, despite normal or improved glucose tolerance after resistance training, indicates that the resistance-training program improved insulin action, as has been previously reported (9, 26, 34). Although the mechanism(s) responsible for the improved insulin action observed after exercise remains unknown, it is likely that changes in glucose transporter number and/or translocation (17) and changes in intracellular signaling (15) are important. In rats, DHEA does not increase muscle GLUT-4 content (13) but may improve whole body insulin action by increasing phosphatidylinositol 3-kinase (13) and protein kinase C activity (35). In contrast, the improved whole body insulin action observed with resistance training in the present study was not augmented by the daily intake of 150 mg of DHEA. This finding is consistent with previous reports that chronic ingestion of DHEA by humans in daily doses of 50 mg (28) and 100 mg (27) does not alter whole body insulin action. Furthermore, it is unlikely that daily doses of DHEA higher than those used in the present study would result in improved insulin action, since previous research has shown that 1,600 mg DHEA/day does not improve insulin action in young men (30) and may reduce insulin sensitivity in postmenopausal women (29). Although the finding that insulin action is improved by DHEA intake in rats (13, 35) but not humans (present study; 27–30) is difficult to explain, the failure of DHEA to augment the improved insulin action observed with resistance training in the present study suggests that any effect of DHEA on insulin action in humans might be obscured by the

improved insulin action concomitant with resistance training.

The use of anabolic steroids has been shown to cause insulin resistance (8, 11), and elevated levels of blood testosterone have been correlated to reduced insulin sensitivity (2). The present research found reduced plasma insulin levels during an OGTT after resistance training in both groups, despite increased levels of serum androstenedione with DHEA supplementation. Because androstenedione is a weaker androgenic hormone than testosterone (32), it is likely that the improved insulin action brought about by resistance training more than compensated for any deleterious effect of androstenedione on insulin action.

Anabolic-androgenic steroids have been shown to decrease HDL-C concentrations and increase serum concentrations of LDL-C (19, 22, 23). Although at least one previous study has reported that DHEA lowers serum LDL-C concentrations (30), more recent reports (28, 38), as well as the present study, suggest that DHEA does not affect serum LDL-C concentrations. The finding of no change in the serum HDL-C concentration with DHEA supplementation in the present study is also in agreement with previous reports (28, 30, 38). These results suggest that DHEA supplementation does not significantly alter the blood lipid profile.

Previous research on anabolic steroid use has found increased activity of liver transaminases (19, 23). It has been reported that plasma transaminase levels in guinea pigs are not altered by exogenous DHEA-S (3). The present findings extend these results and demonstrate that DHEA ingestion does not affect liver transaminase activity in young men.

In summary, oral supplementation with DHEA resulted in increased serum concentrations of androstenedione but did not affect serum free or total testosterone concentrations or serum estrogen concentrations. DHEA supplementation did not enhance the effects of resistance training on glucose tolerance, insulin sensitivity, muscle strength, or body composition. Finally, DHEA supplementation during resistance training did not affect serum lipid profiles or markers of liver function in healthy young men.

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