THE CHRONIC EFFECTS OF ANDROST-4-ENE-3,6,17-TRIONE ON ENDOCRINE RESPONSES IN RESISTANCE-TRAINED MEN

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Abstract

A naturally occurring compound, androst-4-ene-3,6,17-trione (also known as 3,6,17-androstenetrione or 6-keto-androstenedione), hereafter referred to as 6-OXO, is believed to have aromatase inhibition properties. The application of such a compound would be to help address abnormalities of estrogen metabolism. This initial investigation will test the effects of 6-OXO in healthy men. The research hypothesis is that 6-OXO will attenuate aromatase activity resulting in an increase in serum androgens. Six male subjects, ages 32-40 years of age, were prescreened via a medical doctor for endocrine abnormalities. The subjects' physical characteristics were: height 177.38 ± 8.57 cm, weight 88.8 ± 13.65 kg, body fat percentage 14.9 ±3.5%. Subjects ingested 300 mg bid for three weeks as part of an open label design. Resting AM blood draws were taken at 0, 1, 2, and 3 weeks of supplementation. The table below indicates the changes in endocrine markers over the time evaluated. Results were analyzed using a Repeated Measures-ANOVA design with paired samples t-tests as appropriate. The results support the notion that 6-OXO can increase testosterone levels under the conditions of this study design. Future research should investigate the effects of 6-OXO in clinical populations.

This study was funded by LPJ Research.

Hypothesis

A naturally occurring compound, androst-4-ene-3,6,17-trione (also known as 3,6,17-androstenetrione or 6-keto-androstenedione), hereafter referred to as 6-OXO, is believed to have aromatase inhibition properties. Research studies in isolated cells and animals support this contention [1-3]. The application of such a compound would be to help address abnormalities of estrogen metabolism induced by excess body fat [4-6], aging [6-14], androgen abuse [15-17], gynecomastia associated with prescribed use of DHT inhibitors [18-20], and other clinical conditions.

It is my hypothesis that 6-OXO will cause a reduction of serum estrogens and an increase in serum androgens.

Methods

Subjects

Six healthy, resistance-trained men, 32-40 years of age, were recruited to participate in this study. The subjects were and had previous weight-training experience. They were prescreened via a medical doctor for endocrine abnormalities. The subjects' physical characteristics were: height 177.38 ± 8.57 cm, weight 88.8 ± 13.65 kg, body fat percentage 14.9 ± 3.5%. Each subject was completely informed of the potential risks and possible benefits associated with participation in the study before signing an informed consent document.

Methods

Design

- Open label trial
- 6 participants

Duration

- Three weeks

Inclusion Criteria

- Healthy adult males from 25-35 years of age
- > 3 years weight training experience

Exclusion Criteria

- Any personal history of heart disease, high blood pressure, renal or hepatic impairment/disease, Type I or II diabetes, psychiatric disorders, cancer, benign prostatic hypertrophy, use of any monoamine oxidase inhibitor medication, unstable thyroid disease, or any condition deemed exclusionary by the medical staff
- Recent weight loss or gain greater than 5 kilograms (past month)
- History of heavy alcohol use (ie > 3 drinks per day) or binge drinking (> 1 day per week)
- Anabolic-androgenic steroid use within the past year
- Prohormone use within the past year
- Creatine supplementation within the past 2 months
- Dietary supplements, except for a multiple vitamin mineral pill, with nutrients not to exceed 150% of the RDIs

Diet

- Free living

Exercise

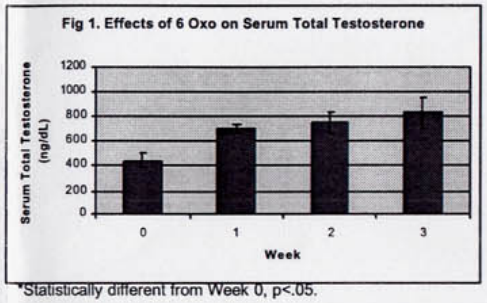
- All subjects will follow a specified resistance training program consisting of 4 days per week
- The exercise protocol has been previously published in the scientific literature and established as effective in promoting gains in lean body mass and strength

Product Dosage

- Subjects will take the supplement according to the following guidelines:
- One serving in AM and one serving in PM

Testing Protocol

Test: Weeks	0	1	2	3
Physical	Y	N	N	N
Blood work	Y	N	N	Y
Body weight	Y	N	N	Y
Percent body fat	Y	N	N	Y
Lean body mass	Y	N	N	Y
Endocrine testing	Y	Y	Y	Y
Heart rate	Y	Y	Y	Y
Blood pressure	Y	Y	Y	Y



*Statistically different from Week 0, p<.05.

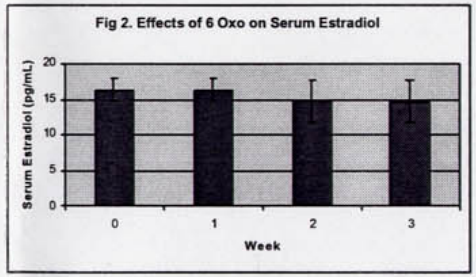


Table 1. Endocrine Values

Endocrine Marker	Week 0	Week 1	Week 2	Week 3
Total testosterone (ng/dL)	443.67 ± 59.07	701.17 ± 36.85*	752.17 ± 78.11*	835.33 ± 124.74*
Free testosterone (nmol/L)	126.67 ± 31.99	216.67 ± 33.64*	252.33 ± 53.48*	285.67 ± 69.22*
Sex hormone binding globulin (SHBG) (nmol/L)	21.83 ± 4.36	20.5 ± 3.83	19.5 ± 5.54	18.83 ± 6.18
Estradiol (pg/mL)	16.5 ± 1.38	16.5 ± 2.93	14.8 ± 2.93	14.67 ± 2.94
Estrone (pg/mL)	31 ±6.26	56.67 ± 29.41	84.8 ± 50.86	81.33 ± 36.08
Estriol (ng/mL)	< 0.25	< 0.25	< 0.25	< 0.25
Dihydrotestosterone (ng/dL)	33.33 ± 3.56	39.83 ± 7.88	45.83 ± 14.72	47.5 ± 8.17*

*Statistically different from Week 0, p<.05.

Results/Discussion

The research hypothesis for this study was that serum levels of estradiol (E2) would decrease and serum levels of testosterone (T) would increase after ingesting the supplement. Table 1 presents the results for all hormones measured. Total testosterone and free testosterone were significantly increased each week of the study. Serum estradiol did not change significantly. DHT levels increased towards the end of the study and reached significance at Week 4. Serum estrone levels increased however they did not reach statistical significance. The mechanisms hypothesized to account for these effects revolve the actions of an irreversible suicide inhibitor, androst-4-ene-3,6,17-trione in brief, the molecule binds to aromatase irreversibly. The reduction in E2 leads to an increase in T, which in turn makes more T available to interact with aromatase. This changes the "set point" resulting in a higher serum T while maintaining normal E2 levels. There appears to be a trend toward an increase in DHT and estrone levels in some men. The results from this acute study warrant further investigation utilizing larger numbers of subjects.

Conclusion

This study investigated the chronic effects of a dietary supplement on serum estrogen and androgens. Significant effects were found indicating the potential for this dietary supplement to modulate hormone levels. Further study is warranted.

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