Androstenedione
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- An anabolic-androgenic steroid hormone produced by the gonads, adrenal glands, or by peripheral transformation.
- An immediate precursor to testosterone and estrogen.
- Marketed as increasing blood testosterone concentrations for the purposes of increased strength, lean mass, and sexual performance.
- Recommended daily dosages for oral preparations range from 100 to 1,200+ mg/day.
- Little is known about children’s or adults’ frequency of use of androstenedione.
- Studies of healthy men taking oral androstenedione have mixed outcomes regarding the effects on serum testosterone levels. However, two long-term studies of androstenedione supplementation in strength-trained men failed to show significant increases in serum testosterone concentrations, strength, or muscle mass.
- Acute adverse effects in men include increased estrogen levels and decreased HDL-C levels. There is a significant probability of virilization of women.
- Long-term health effects are unknown.
- Androstenedione is classified as a dietary supplement.
- Androstenedione is specifically banned by the NCAA, USOC, and IOC.

Name
Androstenedione (Androstenedione. Other substances that are chemically and pharmacologically related to androstenedione are also available: 5-androstenedione, 4-androstenediol, 5-androstenediol, 19-norandrost-4-enedione, 19-norandrost-5-enediol, and 19-norandrost-4-enediol. Along with DHEA, androstenedione is often described as a prohormone or hormone precursor. Whereas Andro is the most popular “street name,” numerous brands of supplements containing androstenedione are available such as: Nitrobolic 300, Androteston, Andro Tri-plex 650, Androbolic 300, AndrosteDerm, and Andro Spray.)
Description
Androstenedione is an anabolic-androgenic steroid hormone produced by the gonads (testes/ovaries), adrenal glands, or emanating from dehydroepiandrosterone (DHEA) by peripheral transformation. By itself, androstenedione is a relatively weak steroid whose anabolic-androgenic activity is one-fifth to one-tenth that of testosterone. Women’s production of androstenedione is approximately one-third greater than men’s production of androstenedione. In both men and women, androstenedione is an immediate precursor to testosterone as well as estradiol and estrone (estrogens). Consequently, it makes sense that increased levels of androstenedione could be accompanied not only by increased testosterone levels, but also by increased production of estrogens. Aromatase, the enzyme that converts androstenedione to estrone and estradiol, is found in various cells, including skeletal muscle and fat. The conversion of androstenedione to testosterone is accomplished by means of the enzyme 17-dehydrogenase, which is also found in most cells in the body. This enzymatic process, like others in the hormonal pathways, is regulated by the thermostatic-like feedback mechanisms that maintain homeostasis. Thus, if a male with normal testosterone levels ingested large amounts of androstenedione, one would predict, based on this feedback loop, that the body would produce only enough 17-dehydrogenase to result in a modest increase in testosterone production. The rest of the androstenedione would be metabolized and excreted. If, however, androstenedione does significantly increase serum testosterone levels, one would expect, in conjunction with strength training and conditioning, significant increases in anabolism and anticatabolism commonly associated with testosterone administration.

Usage
Androstenedione is marketed as increasing blood testosterone concentrations for the purposes of increased strength, lean mass, and sexual performance. Recommended daily dosages for oral preparations range from 100 to 1,200+ mg/day. Androstenedione and its analogs are also available as a sublingual spray or percutaneous gel.

Prevalence
There is a lack of national-level epidemiologic data on the incidence of use of androstenedione (or other supplements) by either children or adults. However, the illicit use of anabolic steroids (a scheduled substance) among adolescents is well documented (lifetime use of 4 to 6% for males and 1 to 2% for females). It is logical to conclude that even a larger percentage of adolescents would use a purported anabolic steroid, such as androstenedione, that could be purchased legally. This conclusion is supported, in part, by claims by the Office of National Drug Control Policy that androstenedione use by youngsters increased fivefold since Mark McGwire’s 1998 admission of use, as well as by manufacturer estimates that sales of androstenedione have skyrocketed as a result of the publicity surrounding McGwire’s use.

Chemical Mechanism
See Description Section
Clinical Evidence
Androstenedione does not have any known clinical applications.

Scientific Research
It is yet to be determined whether androstenedione significantly increases strength and lean mass by way of increasing blood testosterone levels. There are two studies lasting 8 and 12 weeks, respectively, that used healthy males (age 19 to 60) who were administered oral androstenedione in doses of 100 mg or 300 mg per day in conjunction with strength-training regimens. These studies failed to detect significant increases in blood testosterone levels, strength, or muscle mass. There have been several studies that have administered oral androstenedione for 1 to 7 days primarily to assess the effect on serum testosterone levels. A study using healthy young males administered a single 100 mg or 300 mg dose each day of androstenedione for 7 days. Significant, although transitory, increases in serum testosterone concentrations with the single 300 mg/day dose were observed. No effect was observed with the single 100 mg/day dose. Another study confirmed that oral administration of androstenedione at 100 mg/day did not significantly increase plasma testosterone concentrations and had no anabolic effect on muscle protein metabolism. Conversely, another study demonstrated a transitory increase in urinary testosterone concentrations with a one-time administration of 50 mg of androstenedione or 100 mg of androstenediol. The testosterone (T) concentrations increased faster than that of epitestosterone (E), causing the T/E ratio in some of the androstenedione recipients to exceed the IOC-imposed 6:1 limit. This same study also administered a single oral dose of norandrostenedione to other volunteers and high concentrations of the metabolites of the anabolic steroid nandrolone were found in the urine. A similar study evaluated the effect of a one-time administration of 100 mg of androstenedione or 100 mg of androstenediol and found significant increases in serum testosterone concentrations with both preparations. Thus, while some studies show significant increases in serum testosterone levels with oral androstenedione, others do not. More importantly, to date, no study has demonstrated an association between oral androstenedione and significant increases in strength and muscle mass. Yet even more questions remain to be answered. Undoubtedly there are a number of androstenedione users who are taking daily oral doses substantially higher than those used in the studies reviewed here. Therefore, what would be the effect of a 1 g or more daily dose of oral androstenedione or one of its analogs for a prolonged period? Likewise, the effects of injecting an oil-based version of androstenedione have yet to be articulated. In addition, the performance effects of androstenedione in adolescents, elderly males, or among different races have yet to be examined. There is only one study of the effects of androstenedione on women. This study administered 100 mg per day to two women and found a significant increase in blood testosterone levels.

Administration
Recommended daily dosages for oral preparations range from 100 to 1,200 mg/day. Androstenedione and its analogs are also available as a sublingual spray or percutaneous gel.
Dosage
Recommended daily dosages for oral preparations range from 100 to 1,200+ mg/day.

Contraindications
Women should avoid using androstenedione, given the possibility of significant increases in blood testosterone levels and the attendant risk of virilization. Sustained elevated testosterone levels in children have been associated with precocious puberty and premature epiphyseal closure leading to diminished adult height.

Precautions/Warnings
The long-term health effects of prolonged androstenedione supplementation are unknown. However, recent studies have noted acute adverse effects. At least three studies have reported a significant increase in blood estrogen levels (estrone and estradiol) in healthy males with oral androstenedione supplementation. Elevated estrogen levels in males are associated with gynecomastia and other feminizing effects as well as an increased risk of cardiovascular disease. One study also examined the impact of oral androstenedione on blood lipid levels and found a significant reduction (12%) in HDL-C that was sustained during the 8 weeks of the study. This reduction in HDL-C is highly consistent with the findings of numerous studies of the effects oral anabolic steroids on blood lipid levels. If these decreased HDL-C levels were maintained, an increased risk of cardiovascular disease would result. The literature clearly supports the hepatotoxicity of many oral anabolic steroids. Since the oral androstenedione-related decrease in HDL-C is likely the result of an increase in hepatic triglycerol lipase activity, it is prudent to assume that prolonged use at high doses could adversely affect other aspects of liver structure and function. If oral androstenedione did substantially increase testosterone levels in males, then one would expect to observe testicular atrophy and infertility.

Banned/Permitted
Androstenedione is specifically banned by name by the NCAA, USOC, and IOC. However, the chemical analogs of androstenedione, such as norandrostenedione, share metabolites with certain anabolic steroids (e.g., nandrolone decanoate) that are banned by virtually all sport federations that drug test.

Legality
Androstenedione is classified by the Food and Drug Administration as a dietary supplement. As such it can be sold legally without restriction in the United States. However, in 1999 the Federal Trade Commission successfully challenged the lack of substantiation of the claims of two major marketers of androstenedione regarding the safety and lack of side effects of their products. They agreed to disclose the potential health risks of the supplements in all future advertising.
References

Degree of Confidence
1.0

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