Oral Andro-Related Prohormone Supplementation: Do the Potential Risks Outweigh the Benefits?

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Abstract/Résumé

Androstenedione, 4-androstenediol, 5-androstenediol, 19-norandrostenediol and 19-norandrostenedione are commonly referred to as “Andro” prohormones. Over the last few years, supplementation using these prohormones has been aggressively marketed to the general public. Supplement manufacturers often claim that Andro use improves serum testosterone concentrations, increases muscular strength and muscle mass, helps to reduce body fatness, enhances mood, and improves sexual performance. However, to date, most studies contradict these claims. In contrast, several studies using oral Andro related prohormones show that Andro use can abnormally elevate estrogen related hormones as well as alterations in hormonal markers (i.e., abnormal elevations in serum estrogen) thought to increase a person’s risk for developing prostate or pancreatic cancers. In addition, most studies also indicate that significant declines in high-density lipoproteins occur leading to an increased cardiovascular disease risk. Thus, to date, the current research base suggests that Andro prohormone use does not support manufacturer claims. But it does suggest there should be strong concerns regarding long-term oral Andro prohormone use, especially regarding its effects on blood lipids and estrogen hormone profiles.

L’androstènedione, le 4-androstènediol, le 5-androstènediol, le 19-norandrostènediol et le 19-norandrostènedione sont appelées des prohormones “Andro.” Au cours des dernières années, il y a eu beaucoup de promotion auprès du public en général concernant les suppléments de prohormones. Les fabricants de ces suppléments prétendent généralement...
que les Andro augmentent la concentration sérique de testostérone, la masse et la force musculaires, contribuent à la réduction des graisses corporelles, améliorent l’humour et la performance sexuelle. Pourtant, la majorité des études contredisent ces effets. Des études rapportent même que la consommation per os de ces prohormones augmente anormalement la concentration des hormones reliées aux estrogènes et modifie les marqueurs hormonaux (i.e. augmentation anormale de la concentration sérique des estrogènes) ; selon des études, ces modifications sont associées à l’augmentation du risque de développer le cancer de la prostate ou du pancréas. De plus, la plupart des études observent une diminution importante de la concentration des HDL, ce qui accroît le risque de maladie cardiovasculaire. Jusqu’à ce jour, les études scientifiques ne confirment pas les allégations des fabricants de prohormones du type Andro ; les études indiquent les risques d’une consommation à long terme, notamment à propos des effets sur les lipides sanguins et les oestrogènes.

Introduction

Over the last few years, prohormone supplementation, using dehydroepiandrosterone (DHEA), 4-androstenediol, 5-androstenediol, 19-norandrostenediol, 19-norandrostenedione and androstenedione, has been marketed to the general public. Androstenedione, 4-androstenediol, 5-androstenediol, 19-norandrostenediol, and 19-norandrostenedione are commonly referred to as “Andro” prohormones. Some supplement manufacturers claim that Andro use improves serum testosterone concentrations, increases muscular strength and muscle mass, helps to reduce body fatness, enhances mood and improves sexual performance. However, to date, most studies contradict these claims, raising strong concerns regarding orally supplemented Andro prohormones (Broeder et al., 2000; Brown and Vukovich, 2000; King et al., 1999; Leder et al., 2000; Lee et al., 1999; Rasmussen et al., 2000; Wallace et al., 1999).

The introduction of prohormones in the United States market place is the direct result of The Dietary Supplement Health and Education Act (DSHEA) passed by congress (1994). This act’s initial intent was to allow consumers access to nutrition-based supplements such as vitamins, minerals and herbal supplements. Since this act was passed, manufacturers regularly introduce hormone based or chemically developed supplements that are not commonly found in our diets. The purpose of this review will be to highlight what is currently known about Andro-related prohormones with special emphasis on oral androstenedione and androstenediol. Data will be presented highlighting both the acute and chronic effects of Andro supplementation in young (18–35 yr old), middle-aged (36–50 yr old), and older (51–65 yr old) men. Finally, potential risk factors and concerns will be noted from the current data available.

Testosterone and Andro Related Prohormones

Testosterone is an important androgenic hormone regulating tissue repair, secondary sex characteristics and various growth functions (Maas et al., 1997; Villareal and Morley, 1994). Testosterone is a steroid-based hormone synthesized from cholesterol. Intermediate synthesis by-products between cholesterol and testosterone include several compounds, including androstenedione, androstenediol, and
dehydroepiandrosterone (DHEA), promoted as key prohormones. Manufacturers promote these prohormones as testosterone boosting substances and ultimately claim they enhance anabolic androgenic related performance factors. The most common Andro prohormones marketed today include 4-androstenediol (4-androsten-3β,17β-diol), 5-androstenediol (5-androsten-3β,17β-diol), 19-norandrostenediol (19-nor-4-androsten-3,17-diol), 19–nor-4-androsten-3,17-dione) and androstenedione (4-androsten-3,17-dione).

Prohormones are required precursors in the development of functional hormones such as testosterone. Theoretically, the fewer interconversion steps a prohormone must complete in the synthesis pathway to the active hormone, the greater potential for enhancing active hormone production. For example, androstenedione converts to testosterone more readily than DHEA (Mahesh and Greenblatt, 1962). In Figure 1, testosterone production is synthesized through either the Δ-4 or Δ-5 pathways (Williams, 1998). However, in vitro data suggests that androstenedione is also converted into 4-androstenediol within the Δ4 pathway (Blaquier et al., 1967). As a result, 4-androstenediol is often thought to be a more potent testosterone producing prohormone compared to androstenedione (Blaquier et al., 1967). In vivo research indicates, however, that oral androstenedione conversion to testosterone by 17β-OH-steroid dehydrogenase of the delta-4 pathway is more predominant compared to the delta-5 pathway using the 3β-OH-steroid dehydrogenase-isomerase conversion of androstenediol to testosterone (Broeder et al., 2000; Earnest et al., 2000).

**Figure 1.** Pathway for testosterone synthesis (Williams RH, 1998).
Acute or Short-Term Andro Supplementation Responses

The first study to examine the acute effects of oral androstenedione supplementation was performed in two women by Mahesh and Greenblatt in 1962 (Mahesh and Greenblatt, 1962). In this study, 100 mg of androstenedione or DHEA were ingested. Compared to DHEA, androstenedione supplementation produced a more acute testosterone elevation (4 to 7 fold increase) a result expected of the pathways involved. More recently, several studies in men have failed to show any significant acute increases in endogenous serum testosterone concentrations following 100 mg of oral androstenedione ingestion (Ballantyne et al., 2000; Brown and Vukovich, 2000; King et al., 1999; Leder et al., 2000). The difference in responses between the studies may be dose or gender related. In women, normal resting testosterone values range from 0.7 nmol/L to 2.8 nmol/L while normal values for men are 10.0 nmol/L to 42.0 nmol/L (Leavell, 1994). Thus, for an acute dose of androstenedione to have a stimulating effect on serum testosterone concentrations, greater concentrations are required to over-come local tissue incorporation (i.e., muscle and fat tissue both contain the enzyme complexes required to convert androstenedione and testosterone to estrone and estradiol) (Forney et al., 1981; Horton and Tait, 1966; Longcope et al., 1978; Matsumine et al., 1986). In fact, in a study from our group, a single 200 mg dose of oral androstenedione supplementation produced a significant 23% rise in the area-under-the-curve (AUC) for serum total testosterone ($p = 0.05$) while free-testosterone AUC neared significance ($p = 0.06$) for 90 minutes post ingestion. (Earnest et al., 2000) Correspondingly, Leder et al. (2000) found that 300 mg/day of androstenedione for 7 days significantly increased serum total testosterone concentrations 34% in men with similar pretreatment resting testosterone concentrations as in our study. They also found no significant testosterone enhancement effects with 100 mg/day in this same population of men. In combination, these results indicate that, following oral androstenedione supplementation, acute testosterone synthesis increases in a dose-response relationship above 100 mg/day and up to 300 mg/day in men.

It is important to point out however, that simply producing an acute elevation in a particular hormone concentration (i.e., testosterone) does not necessarily result in increases in muscle mass, strength or sexual performance as promoted by supplement manufacturers. In fact, as described below, the chronic use of oral Andro supplements do not appear to have functional benefits when taken in daily concentrations up to 300 mg per day in young, (Ballantyne et al., 2000; King et al., 1999) middle-aged, (Broeder et al., 2000; Wallace et al., 1999) or older men (Broeder et al., 2000).

Chronic Andro Supplementation On Hormonal Blood Profiles and Physiological Responses to Resistance Training

In 1999, King et al. (1999) published the first well-controlled chronic use study examining the effects of androstenedione supplementation. In this study, 20 healthy, untrained and normotestosteronegenic men ages 19 to 29 participated in 8 weeks of whole-body resistance training and supplemented either 300 mg/day of oral androstenedione or placebo. Supplementation occurred on weeks 1, 2, 4, 5, 7, and 8. Weeks 3 and 6 were non-supplemental weeks. This supplementation approach is
similar to how anabolic steroids are often administered to enhance performance gains while minimizing feedback-induced down-regulation of endogenous testosterone. Despite a 100% increase in serum androstenedione concentrations at weeks 2, 5 ($p < .05$) and 8 weeks ($p = 0.07$), both free- and total-testosterone concentrations were not significantly elevated during the study. When statistical effect size was considered, 160 subjects would have been required for the reported free- and total-testosterone concentrations to reach significance. This study highlights either the weak androgenic effects of androstenedione or an inadequate oral dosage for elevating serum testosterone concentrations (Leder et al., 2000; Orth and Kovacs, 1998). In contrast, both estradiol and estrone were significantly elevated by the second week ($p < .05$). With regard to the physiological response to resistance training, no significant benefits beyond the training and placebo group were observed for muscular strength, body composition, muscle fiber distribution or cross-sectional fiber area.

In follow-up letters sent to the Journal of The American Medical Association (JAMA), some researchers suggested that because subjects were untrained and normotestosterogenic, that any potential benefits of oral androstenedione supplementation were confounded by the study’s population characteristics (O’Gara, 2000). However, additional studies by Wallace et al. (1999), Brown and Vukovich (2000) and Broeder et al. (2000), clearly reconfirmed the results of King et al. (1999). In the study by Wallace et al. (1999), resistance-trained middle-aged men consumed either 100 mg of DHEA or androstenedione over a 12-week intervention period in a double-blind study. The results indicated there were no significant differences in lean body mass, strength or testosterone concentrations in either the DHEA or androstenedione supplement groups. In the study by Brown et al. (2000) from the same Iowa State group as King et al. (1999), 300 mg of androstenedione were taken over 8 weeks (supplements were again taken on weeks 1, 2, 4, 5, 7, and 8 with weeks 3 and 6 as supplement off weeks) in combination with 150 mg DHEA, 750 mg tribulus terretris, 625 mg Chrysin, 300 mg Indole-3-carbinol, and 540 mg saw palmetto. As in this group’s previous study, serum testosterone concentrations and strength were unaffected by supplementation. Interestingly, even with the addition of compounds purported to enhance testosterone production or prevent estrogenic aromatization of androstenedione and testosterone, no ergogenic benefits were observed. In addition, there was also no blunting in the development of steroid-based aromatization by-products estradiol and estrone.

In our first study from “The Andro Project,” (Broeder et al., 2000) we investigated the physiological and hormonal responses to 200 mg/day orally administered androstenedione (4-androstene-3,17-androstenedione) or androstenediol (4-androstene-3β,17-androstenediol) in men ages 35 to 65 participating in a 12-week high-intensity resistance program. Middle-aged to older men were selected for this study because compared to younger men; the older population would most likely be able to benefit from the supplementation protocol. In addition, both trained and untrained men were also recruited for this study. Two hundred milligrams per day, a dosage often recommended by manufacturers, was chosen based on our initial study (Earnest et al., 2000) which showed that an acute rise in total- and free-testosterone occurred in younger men. As previously shown, neither androstenediol nor androstenedione enhanced muscular strength development or produced positive body composition changes compared to the resistance-training
program under placebo conditions (Broeder et al., 2000). In this study, even when initial training status and muscle strength were accounted for using ANCOVA procedures, there still were no significant differences in strength and body composition between the three treatment groups. However, unlike the studies of King (1999) and Wallace (1999), both free and total serum testosterone concentrations were significantly elevated by the 4-week measurement period ($p < .05$). These results were similar to another study by Brown et al. (2000) in men ages 30–56 that consumed 300 mg/day of oral androstenedione for 4 weeks. Interestingly in contrast to previous studies (Brown et al., 2000; King et al., 1999; Wallace et al., 1999) data from The Andro Project showed a significant reduction in serum luteinizing hormone (LH) concentrations by 33% at week 4 in the androstenedione group.

![Figure 2](image.png)

**Figure 2.** Effects of chronic oral andro supplementation on total and free testosterone (Broeder et al., 2000).
Serum LH concentrations remained suppressed 18% at week 12 the final measurement period. The end results were free- and total-testosterone returned to baseline concentrations with free-testosterone serum concentrations also being significantly lower on week 12 compared to peak serum concentrations measured at week 4 ($p = .04$) (Figures 2 and 3). Step-wise multiple regression analyses showed that 67.4% of the decline in total-testosterone from the pre- to post-treatment period was accounted for by the changes in androstenedione, free-testosterone and luteinizing serum hormone concentrations.

The lack of additional training adaptations beyond placebo and resistance training is not surprising with androstenedione and androstenediol supplementation. These compounds are considered weak androgens and appear highly prone to aromatization conversions in muscle and fat tissue. Longcope et al. (1978) showed that 35% to 45% of the total extragonadal aromatization of androstenedione to estrogens can be accounted for by muscle and fat tissue. King et al. (1999) showed that the 47-pmol/L increase in serum estrone concentrations in their study between weeks 0 to 2 could be accounted for solely by their subjects 19.3 kg of fat-mass content. Thus, when one considers other tissue conversions, one can understand, especially in men with normal serum testosterone concentrations, why long-term serum total- and free-testosterone concentrations are difficult to increase with oral Andro supplementation between 100 and 300 mg/day. In addition, Rasmussen et al. (2000) have shown, using a three-compartment model involving infusion of L-[ring H5]phenylalanine, blood sampling from femoral artery and vein sites and muscle biopsies, that 100 mg of oral androstenedione supplementation did not enhance muscle protein synthesis. Instead, androstenedione supplementation enhanced protein breakdown. Based on previous research, elevations in estradiol

Figure 3. Effects of oral andro supplementation on total testosterone and luteinizing hormone over time (Broeder et al., 2000).
may have caused the increased protein breakdown as well since in rats, long-term exposure to estrogens decreases muscle fiber size (Suzuki and Yamamuro, 1985).

Relative to mood and sexual performance claims, two published studies have shown that 100 to 300 mg/day of androstenedione use does not significantly enhance either sexual arousal states or markers of mood compared to placebo (Brown et al., 2000; Wallace et al., 1999). Initial analyses from The Andro Project’s standardized mood and sexual survey results confirm these findings (Earnest et al., 2001a, 2001b). However, androstenediol did increase overall sexual function and orgasm score as delineated by the Derogatis Inventory of Sexual Function test (Earnest et al., 2001a, 2001b).

In summary, oral androstenedione and androstenediol supplementation in men ranging in age from 19 to 65 appears to have no ergogenic benefits when combined with a high-quality, resistance-training program. In men under the age of 30, Andro dosages = 300 mg/day produces no long-term enhancement in either total- or free-testosterone concentrations but does produce a significant rise in serum estrogen related compounds. In middle-aged to older men (30–65 years of age), low dosage oral Andro supplementation (100 mg/day) has no benefits on serum testosterone concentrations. In contrast, higher dosages of Andro supplementation (200 to 300 mg/day) can temporarily produce a significant increase in both total- and free testosterone serum concentrations after 4 weeks of use. However, in men whom have intact hypothalamic, pituitary and gonadal axis function, down-regulation of endogenous testosterone production appears to be occurring via a lowering of luteinizing hormone secretion. This potential down-regulation of endogenous testosterone production in combination with a rapid and strong tendency for oral Andro related compounds to aromatize, may lead to less biologically active free-testosterone with chronic oral Andro use.

**Known And Potential Risks Associated With Oral Andro Supplementation**

Researchers have suggested a number of potential risk factors associated with Andro use similar to those observed with anabolic steroids (Broeder et al., 2000; King et al., 1999; Leder et al., 2000). These risk factors include an increased risk for cardiovascular disease, prostate cancer, pancreatic cancer, breast cancer, gynecomastia and premature epiphyses closures compromising final adult height if taken by children (Alén et al., 1985, 1987; Broeder et al., 2000; King et al., 1999; Leder et al., 2000; Peterson and Fahey, 1984). To date, there are no long-term prospective epidemiological studies regarding Andro supplementation on any of these proposed risks. However, to say there is no evidence supporting the potential for these risks would be incorrect from a professional standpoint.

One of the hallmarks of preventive medicine is to identify and reduce the environmental risks associated with developing a particular disease. In the case of oral Andro supplementation, the single most consistent finding among all studies investigating chronic oral use is an elevation in estrogen-based hormones beyond the upper-concentration normally observed in males. In addition, Brown et al. (2000) recently found that dihydrotestosterone (DHT) is also significantly elevated with chronic use. Both abnormal concentrations of estrogen and DHT have been identified as key risk factors for breast and prostate cancer, respectively (Baer, 2000;
Strum and Mc Dermed, 2000). In a more detailed analysis of the hormone data from “The Andro Project” (Miller, 2000; Quindry et al., 2000), we evaluated the relative risk ratio (RR) effects and how oral Andro compounds altered hormonal profiles as predictors of gynecomastia, prostate (Barrett-Conner et al., 1990) and pancreatic cancer (Fernandez-del Castillo et al., 1990). For gynecomastia, the estradiol/total-testosterone ratio is generally considered a key risk factor (Braunstein, 1993; Lewin, 1941; McFadyen et al., 1980). With oral androstenedione use, the estradiol/total-testosterone ratio increased 83% from baseline by week 4 and remained significant throughout the study (Week 4, \( p = .01 \); Week 12, \( p = .05 \)). In contrast, androstenediol use did not significantly alter the estradiol/total-testosterone ratio after 12 weeks of oral use.

Barrett-Conner et al. (1990) examined the role of androgens and estrogens in prostate cancer development. Baseline hormone concentrations were measured in 1,008 men ages 40 to 79 in regards to prostatic cancer incidence. These authors concluded that the age adjusted relative risk for prostate cancer increased 0.26 units for every 1.1 nmol/L increase in serum androstenedione concentrations. In addition, for every 40 pmol/L increase in estradiol and 70 pmol/L increase in estrone concentration, relative risk increased 0.10 and 0.09 units, respectively. Using these criteria with data from The Andro Project, the relative risk for prostate cancer based on the changes in serum androstenedione concentrations significantly increased after 12 weeks of 300 mg/day of both androstenedione and androstenediol use. After correcting for age as in the Barrett-Connor et al. study (1990), both the androstenediol and androstenedione group showed significant relative risk increases of 43% and 103%, respectively. However, it is important to note, that prostate specific antigen did not significantly changed during the 12-week intervention.

One of the most remarkable findings of our follow-up analysis was the effect androstenedione supplementation had on the hormone related risks (androstenedione to total-testosterone ratio) for pancreatic cancer. In the androstenediol group, the relative risk for pancreatic cancer significantly increased 8.9% while the androstenedione group increased a dramatic 172% from baseline in just over 12-weeks of use (Pre RR: \( .39 \pm .15 \); Post RR: 1.06 \( .65, p \text{ < .01} \)). Effect size (ES) determinations for these results further demonstrated the importance of this finding. Effect size displays the degree of significance between pre- and post-test measures as displayed in the following formula: Effect Size = \( \frac{\text{Pre-mean} - \text{Post-mean}}{\text{standard deviation of the pre-mean}} \). As a result, the differences between the means are then expressed in standard deviation units. These units are defined as follows: 0.2 or less is a small effect; 0.5 is a moderate effect; and 0.8 or greater is a large effect (Cohen, 1969). Thus, for the significant increases observed in pancreatic cancer risk highlighted above, the ES was 0.13 (low value) in the androstenediol group and 4.47 (very large effect size) for androstenedione group. Since all studies of chronic Andro-related prohormone use have shown nearly identical alterations in hormonal profiles, it would be most prudent to suggest that chronic Andro supplementation places a person at an increased risk for developing gynecomastia, prostate, pancreatic and, possibly breast cancer; especially if a person’s genetic make-up (i.e., family history) already predisposes them to higher risk.

Heart disease is one of the leading causes of death in both men and women in North America today. Thus, it is important to determine if Andro supplementation increases a person’s risk for coronary heart disease as anabolic steroids
reportedly does (Bhasin et al., 1996; Kantor et al., 1984; Peterson and Fahey, 1984). In three of the four chronic use studies, negative effects were observed regarding lipid profiles after Andro use (Broeder et al., 2000; Brown et al., 2000; King et al., 1999; Wallace et al., 1999). In one study, androstenedione was administered at a relatively low dose (100 mg/d), which did not show negative lipid effects. In the three studies showing negative lipid effects, androstenedione or androstenediol were administered in 200 mg/day and 300 mg/day dosages. These findings highlight that the potential for negative consequences rises with increases in oral Andro concentration levels similar to anabolic steroid use (Bhasin et al., 1996; Kantor et al., 1984; Peterson and Fahey, 1984).

In the study by King et al. (1999) serum high-density lipoprotein (HDL) concentration was significantly reduced by the second week and remained low throughout the study ($p < .05$). Because cardiovascular disease risk (CVD) increases 2% to 3% with each 0.03-mmol/L (1-mg/dL) decline in HDL concentration, the small change observed in HDL resulted in a 10.3% increase in CVD risk (Gordon et al., 1989). Correspondingly, Brown et al. (2000) showed HDL decreased 10% in just 4 weeks of oral androstenedione use in men ages 30 to 56. In the Andro project, both androstenedione and androstenediol use produced a 6.5% increase in HDL-related CVD risk while the placebo resistance trained group showed a 6.9% decline in CVD risk (Broeder et al., 2000). These results agree well with previous studies. In addition, when we examined the changes in the low-density lipoproteins/high-density lipoproteins ratio divided by the apolipoprotein-A/apolipoprotein-B ratio, the placebo group showed a significant 12.3% decline in the lipid risk ratio while the androstenedione group’s lipid risk ratio increased 10.5%. Even more striking was the fact that when each group was divided into low- versus high-responders regarding changes in pre-to-post testosterone concentrations. The high-responders in the placebo group, observed natural increases in total testosterone concentrations after training, showed a significant 26.2% improvement in their lipid risk profiles ($p < .001$) while no negative changes were observed in the placebo group non-responders, no change in total testosterone concentrations after training. In sharp contrast, the androstenedione group members who were high-responders, showing artificially enhanced testosterone concentrations with oral androstenedione use, had no improvement in their lipid risk profiles while the low-responders showed a 20.3% unfavorable change ($p = .001$) (Figure 4). These results suggest that positive lifestyle changes that enhance a male’s testosterone concentrations can improve CVD risk profiles. But, when artificial enhancements of male hormonal profiles are attempted, dramatic increases in CVD risk profiles can occur despite positive lifestyle behaviors like exercise, especially in non-responders to oral androstenedione supplement.

Curiously, one would suspect that because estrogen concentrations were elevated as a result of androstenedione and androstenediol use that positive effects might be incurred regarding a person’s blood lipid profiles. Estrogen is considered protective for CVD and is correlated with increased HDL concentrations in men and women (Giri et al., 1998). However, one must keep in mind how most of the estrogen increases occurred in the supplemental groups. For example, in The Andro Project by Broeder et al. (2000), under placebo conditions, estradiol concentrations increased 17% from baseline values. Thus, one could consider this change to be the appropriate hormonal adaptation required for meeting the physiological
needs of the current resistance-training program (i.e., an increase in positive bone turnover) (Falahati-Nini et al., 2000; Khosla et al., 2001; Orwoll, 2001). In the androstenedione and androstenediol groups however, estradiol concentrations increased 92.1% and 57.4%, respectively. Thus, above the normal training-induced response in estradiol, androstenedione and androstenediol use dramatically increased estradiol concentrations beyond each group’s physiological adaptive needs. When one considers that a primary function of endogenous cholesterol synthesis is steroid hormone production, it is easy to understand how artificial enhancement of testosterone concentrations could deteriorate blood lipid profiles observed in most studies (Tyagi et al., 1999). With artificial increases in testosterone precursors during oral Andro prohormone use (i.e., androstenedione or androstenediol), feedback controls would lead to a down-regulation in endogenous testosterone production. In turn, conversion of serum cholesterol towards testosterone synthesis is attenuated and would have negative effects on blood lipid profiles (i.e., reductions in serum HDL concentrations) as anabolic steroid use has been reported to cause (Alén et al., 1985, 1987; Peterson and Fahey, 1984).  

In addition to the health risks proposed with oral Andro supplementation, studies suggest that over-the-counter oral Andro prohormone use may produce positive urine test results for nandrolone metabolites (Catlin et al., 2000; Uralets and Gillette, 2000). In a study by Catlin et al. (2000) nine products were tested for purity and androstenedione content. In addition, the effects that 7 days of oral consumption of 100 mg/day or 300 mg/day of androstenedione supplementation had on urinary concentrations of 19-norandrosterone concentrations were also investigated. Regarding purity and concentration, 3 brands showed androstenedione concentrations ± 10% of the stated label values. Three brands showed androstenedione concentrations less than 90% of what was stated on their labels while one

Figure 4. Responder effects on the low density lipoprotein/high density lipoprotein ratio/apolipoprotein-A/apolipoprotein-B ratio profiles (low responders = No change or a decline in total testosterone post treatment; High Responders = An increase in total-testosterone post treatment).
brand had no androstenedione at all (labeled 50 mg). Only two androstenedione supplement brands were considered 99.9% pure. These findings highlight one major concern in the supplement market in general. Due to a lack of regulations regarding the manufacturing of supplement products, it is often likely that consumers do not receive what is advertised. In some cases, when consuming Andro related supplements, consumers can ingest significant impurities or even illegal substances for over-the-counter sales. This was also evident from the Catlin et al. (2000) study. One supplement product contained 10 mg of pure testosterone. Finally, the results of this study showed that trace contamination with 19-norandrostenedione was sufficient to cause positive urine test results for 19-norandrosterone, the standard marker for the anabolic steroid nandrolone. In a similar study by Uralets and Gillette (2000) they also showed that Andro supplements containing androstenedione produced high urine concentrations of norandrosterone and noretiocholanolone for up 7 to 10 days after a single 50 mg dose.

Thus, preliminary data supports a need for concern regarding the potential risks of Andro-related prohormone use. The data shows that disease related risk factors can worsen as oral Andro concentrations increase (i.e., a lowering of serum HDL concentrations). In addition, because of a clear lack of manufacturer quality controls appear evident; additional concerns must be raised pertaining to the quality and purity of Andro supplements.

Summary

In summary, much of the hype from manufacturers regarding the effectiveness of oral Andro related supplements is unwarranted when consumed in the common dosages recommended. To date, longitudinal research does not support the hypotheses that oral Andro use enhances body composition profiles, strength, mood or sexual arousal in young, middle-aged and older-men. When one also considers the negative effects oral Andro use has on lipid risk profiles and hormonal markers of pancreatic and prostate cancers, it is prudent to suggest that Andro use is inappropriate. In the unregulated world of supplement use, where the norm among supplement users is to consume more than the recommended amount, (Yesalis, 1999) the negative risks associated with abnormal estrogenic concentrations are likely to be magnified with increased oral Andro prohormone dosages. This is especially true in men who have normal resting free-testosterone concentrations and feedback control function. Coupled with the fact that research clearly demonstrates that consumers do not get what they pay for in many supplement brands, this author believes that if an individual chooses to use prohormone supplementation, it is essential that regular monitoring (i.e., monthly) of serum hormone concentrations, blood lipid profiles, urine profiles and hormonal cancer markers be performed.

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