"Muscle Building" Nutritional Supplements: Is Androstenedione An Anabolic Steroid?

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Roger Maris
61 Home Runs in a Season
1961

Mark McGwire
70 Home Runs in a Season
1998
Serum androgen levels after intake of 100 mg Androstenedione in Two Women

Androstenedione

Total Testosterone

(Mahesh & Greenblatt, 1962)
Does acute androstenedione intake alter serum hormone concentrations in young men?
Time After Intake (min)

[0 60 120 180 240 300 360]

Serum Androstenedione (nM)

[10 15 20 25 30 35 40]

* vs baseline (P<0.05)

King et al, 1999

PL

ASD

100 mg Andro.

King et al, 1999
King et al, 1999
Does Chronic Androstenedione Intake Enhance The Gains In Muscle Size and Strength During Resistance Training?

King et al, 1999
• 20 untrained subjects
  – Male (~23 y)
  – No current/previous supplement or steroid use
• 8 weeks full body resistance training
  • 3 days/week
  • 80-85% 1 RM
• Random, double blind
  – PL (rice flour)
  – Androstenedione (100 mg t.i.d)
Supplementation

Blood Chemistry

Body Composition

Sex Hormones

Muscle Biopsy

1 RM Testing

King et al, 1999
King et al., 1999

Lower Body Strength

Knee Ex + R. Leg Flexion + L. Leg Flexion (N)

Placebo

<table>
<thead>
<tr>
<th>Before Training</th>
<th>After Training</th>
<th>*</th>
</tr>
</thead>
</table>

Androstenedione

<table>
<thead>
<tr>
<th>Before Training</th>
<th>After Training</th>
<th>*</th>
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</table>
Lean Body Mass (kg)

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Androstenedione</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Training</td>
<td>Before Training</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>40</td>
</tr>
</tbody>
</table>

King et al, 1999
King et al, 1999
Weeks of Supplementation

Androstenedione (nM)

0 2 4 6 8

Placebo
Androstenedione

King et al, 1999
Free Testosterone (pM)

Total Testosterone (nM)

0  2  4  6  8

Weeks of Supplementation

King et al, 1999

Placebo
Androstenedione
Is Androstenedione Intake Safe?
Before Training | After Training
--- | ---
Placebo | Androstenedione
King et al, 1999

HDL-Cholesterol (mg/dL)
King et al, 1999
Other Notable Findings
Effect of 100 mg androstenedione/day on Muscle Protein Fractional Synthetic Rate

Rasmussen et al, 2000
Testosterone (ng/dL)

Baseline

Peak

Baseline

Peak

No Change

P=0.001

Leder et al, 2000

100 mg
Androstenedione

300 mg
Androstenedione

Leder et al, 2000
Effect of 100 mg androstenedione t.i.d. in different ages

Serum Free Testosterone (pM)

30 year olds

40 year olds

50 year olds

Brown et al, 2000

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Brown et al, 2000
Effect of 100 mg androstenedione t.i.d. in different ages

Brown et al, 2000

Dihydrotestosterone (pM)

30 year olds

40 year olds

50 year olds

Effect of 100 mg androstenedione t.i.d. in different ages

Brown et al, 2000
To Summarize

- Chronic androstenedione intake in doses up to 100 mg t.i.d. does not enhance
  - The increase in muscle mass and strength associated with resistance training
  - Serum testosterone
  - Muscle protein synthesis
To Summarize

- Chronic androstenedione intake in doses up to 100 mg t.i.d. **does**
  - Increase Serum Dihydrotestosterone
  - Increase Serum Estrogens
  - Decrease Serum HDL-C
Possible Adverse Health Consequences

Lowered HDL-C

• Increased CV disease risk by 10-15%

Elevated Estrogens Have been linked to...

• Increased CV disease risk
• Pancreatic Cancer
• Gynecomastia
Possible Adverse Health Consequences

Elevated Androstenedione may be associated with...
- Prostate Cancer
- Pancreatic Cancer
- Neural/Behavioral

Elevated Dihydrotestosterone has been linked to...
- Benign Prostate Hypertrophy
- Baldness
<table>
<thead>
<tr>
<th>Compound</th>
<th>Daily Dose</th>
<th>Purpose</th>
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<tbody>
<tr>
<td>Saw Palmetto</td>
<td>480 mg</td>
<td>Reduce DHT metabolism/binding Inhibit 5α reductase</td>
</tr>
<tr>
<td>Indole-3-Carbinol</td>
<td>450 mg</td>
<td>Inhibit formation of estrogens</td>
</tr>
<tr>
<td>Tribulus Terristris</td>
<td>1,350 mg</td>
<td>Increase LH, FSH, Testosterone</td>
</tr>
<tr>
<td>γ-Linolenic Acid</td>
<td>1,500 mg</td>
<td>Inhibit 5α reductase</td>
</tr>
<tr>
<td>Chrysin</td>
<td>300 mg</td>
<td>Inhibit aromatization</td>
</tr>
</tbody>
</table>

Brown et al, 2000 and 2001
Addition of These Herbal Extracts

- Does not prevent formation of estrogens from androstenedione, and
- Does not increase serum testosterone levels.

Brown et al, 2000 and 2001
Future Directions

- To what extent do greater (>300 mg/d) doses of androstenedione affect serum testosterone, muscle strength and size?
Future Directions

• What are the long term health consequences of prolonged androstenedione intake?
  • Cardiovascular Risk
  • Fertility
Future Directions

- What are the effects of age and gender on modifying the response to androstenedione?
- What are the effects of alternative modes of delivery?
Future Directions

- What are the effects of other andro compounds?
- What are the effects of combining various forms of andro?
We are grateful to

For their support.
Extra Slides
Mr. McGwire on A New Study Says: 

ANDRO. 

The Steroid Andro. 

A new study says, Mr. McGwire, the steroid doesn’t build muscle and may cause enlarge ment of breast tissue. 

Comment: Unavailable for shoot, was Victorias Secret.
Extra Summary of Other Clinical Findings

- Chronic androstenedione intake in doses up to 100 mg t.i.d. does not alter serum concentrations of
  - Low Density Lipoprotein
  - Very Low Density Lipoprotein
  - Gamma-glutamyltransferase
  - Aspartate aminotransferase
  - Alanine aminotransferase
  - Globulins
  - Proteins
  - Prostate Specific Antigen

King et al, 1999 and Brown et al, 2000
A single 100-200 mg dose of androstenedione does not increase serum concentrations of testosterone in young men.

A single 300 mg dose of androstenedione may slightly increase serum concentrations of testosterone.
Extra Summary

- Chronic androstenedione intake in doses up to 100 mg t.i.d. **does not** enhance
  - Serum testosterone
  - Muscle protein synthesis
  - Adaptations to resistance training
    - lean mass
    - fat mass
    - muscle fiber size
    - muscle strength

King et al, 1999
Extra training data

Weeks of Supplementation

LH (mIU/ml) vs Weeks of Supplementation

- **LH (mIU/ml):**
  - Y-axis: 0 to 7
  - Data points at weeks 0, 2, 4, 6, 8

- **FSH (mIU/ml):**
  - Y-axis: 0 to 6
  - Data points at weeks 0, 2, 4, 6, 8

- **Lines and Symbols:**
  - **PL** (Blue Circles)
  - **ASD** (Yellow Circles)

- **Legend:**
  - "PL" for Placebo
  - "ASD" for ASD Supplementation
Weeks of Supplementation

24 68 0

10

20

30

40

50

Serum HDL (mg/dL)

Placebo

Androstenedione

Extra training data

*
Weeks of Supplementation

Serum LDL (mg/dL)

Extra training data

PL

ASD

0 2 4 6 8

Weeks of Supplementation
<table>
<thead>
<tr>
<th>Exercise</th>
<th>ASD (n=9) Wk 0</th>
<th>ASD (n=9) Wk 8</th>
<th>PL (n=10) Wk 0</th>
<th>PL (n=10) Wk 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bench Press *</td>
<td>647 ± 68</td>
<td>840 ± 73</td>
<td>851 ± 95</td>
<td>1,047 ± 119</td>
</tr>
<tr>
<td>Biceps Curl *</td>
<td>287 ± 19</td>
<td>331 ± 22</td>
<td>351 ± 21</td>
<td>391 ± 25</td>
</tr>
<tr>
<td>Knee Extension *</td>
<td>717 ± 46</td>
<td>1,024 ± 57</td>
<td>770 ± 45</td>
<td>1,095 ± 52</td>
</tr>
<tr>
<td>Lat Pulldown *</td>
<td>657 ± 25</td>
<td>787 ± 44</td>
<td>672 ± 35</td>
<td>876 ± 50</td>
</tr>
<tr>
<td>Left Leg Flexion *</td>
<td>277 ± 17</td>
<td>415 ± 22</td>
<td>307 ± 11</td>
<td>440 ± 18</td>
</tr>
<tr>
<td>Right Leg Flexion *</td>
<td>292 ± 14</td>
<td>430 ± 28</td>
<td>311 ± 10</td>
<td>445 ± 16</td>
</tr>
<tr>
<td>Shoulder Press *</td>
<td>420 ± 28</td>
<td>463 ± 27</td>
<td>494 ± 51</td>
<td>569 ± 50</td>
</tr>
<tr>
<td>Triceps Extension *</td>
<td>311 ± 24</td>
<td>390 ± 19</td>
<td>329 ± 31</td>
<td>454 ± 30</td>
</tr>
<tr>
<td>Vertical Butterfly *</td>
<td>774 ± 107</td>
<td>1,081 ± 94</td>
<td>927 ± 99</td>
<td>1,268 ± 89</td>
</tr>
</tbody>
</table>

* Week 8 vs week 0 (main effect; P<0.05)
### Extra training data

#### Body Composition - * Wk 8 significantly different from Wk 0 (main effect, P<0.05)

<table>
<thead>
<tr>
<th></th>
<th>ASD (n=9)</th>
<th></th>
<th>PL (n=10)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wk 0</td>
<td>Wk 8</td>
<td>Wk0</td>
<td>Wk 8</td>
</tr>
<tr>
<td>Height, cm</td>
<td>176.8 ± 2.7</td>
<td>178.0 ± 1.5</td>
<td>81.1 ± 5.2</td>
<td>83.2 ± 4.9</td>
</tr>
<tr>
<td>Body Mass, kg</td>
<td>80.6 ± 4.1</td>
<td>81.2 ± 4.2</td>
<td>81.1 ± 5.2</td>
<td>83.2 ± 4.9</td>
</tr>
<tr>
<td>Lean Body Mass, kg*</td>
<td>61.2 ± 2.5</td>
<td>64.1 ± 2.4</td>
<td>63.1 ± 2.6</td>
<td>66.0 ± 2.5</td>
</tr>
<tr>
<td>Fat Mass, kg</td>
<td>19.3 ± 2.9</td>
<td>17.1 ± 3.4</td>
<td>18.0 ± 2.9</td>
<td>17.2 ± 2.9</td>
</tr>
<tr>
<td>Body Fat, %</td>
<td>23.5 ± 2.4</td>
<td>20.3 ± 3.0</td>
<td>21.3 ± 1.9</td>
<td>19.9 ± 2.1</td>
</tr>
</tbody>
</table>

#### Circumferences, cm

<table>
<thead>
<tr>
<th></th>
<th>ASD (n=9)</th>
<th></th>
<th>PL (n=10)</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Wk 0</td>
<td>Wk 8</td>
<td>Wk0</td>
<td>Wk 8</td>
</tr>
<tr>
<td>Biceps</td>
<td>31.9 ± 0.8</td>
<td>32.4 ± 0.8</td>
<td>32.6 ± 1.4</td>
<td>33.4 ± 1.3</td>
</tr>
<tr>
<td>Shoulder</td>
<td>119.3 ± 1.3</td>
<td>121.1 ± 1.4</td>
<td>120.3 ± 3.4</td>
<td>120.7 ± 3.3</td>
</tr>
<tr>
<td>Chest</td>
<td>99.6 ± 2.0</td>
<td>99.2 ± 1.9</td>
<td>98.0 ± 3.8</td>
<td>100.9 ± 3.4</td>
</tr>
<tr>
<td>Abdomen</td>
<td>89.5 ± 5.2</td>
<td>87.7 ± 5.1</td>
<td>87.2 ± 3.8</td>
<td>85.9 ± 3.6</td>
</tr>
<tr>
<td>Waist</td>
<td>86.6 ± 4.2</td>
<td>83.7 ± 3.6</td>
<td>84.9 ± 3.9</td>
<td>83.7 ± 3.7</td>
</tr>
<tr>
<td>Hips</td>
<td>91.3 ± 3.5</td>
<td>88.1 ± 3.7</td>
<td>89.2 ± 2.5</td>
<td>85.7 ± 2.3</td>
</tr>
<tr>
<td>Gluteal</td>
<td>101.7 ± 3.1</td>
<td>98.2 ± 3.1</td>
<td>100.4 ± 2.5</td>
<td>97.4 ± 2.3</td>
</tr>
<tr>
<td>Thigh</td>
<td>54.2 ± 1.3</td>
<td>54.4 ± 1.8</td>
<td>54.7 ± 1.2</td>
<td>55.1 ± 1.5</td>
</tr>
<tr>
<td>Calf</td>
<td>37.8 ± 0.7</td>
<td>37.6 ± 0.8</td>
<td>37.4 ± 1.7</td>
<td>38.6 ± 0.9</td>
</tr>
</tbody>
</table>
Time After Ingestion (min) | Serum DHT (pmol/L)
--- | ---
0 | 1200
60 | 1600
120 | 2000
180 | 2400
240 | 2800
300 | 3200
360 | 3600
420 | 4000

* vs. 0, P<0.05

Extra Acute Data

King et al, unpublished data
**Extra Acute Data**

**Serum Total Testosterone (nmol/L)**

- **Time After Ingestion (min)**: 0 60 120 180 240 300 360

- **-100 mg ASD**
  - PL
  - ASD

- **Y-axis**: Serum Total Testosterone (nmol/L)
  - 0 2 4 6 8 10 12 14 16 18 20 22 24

- **X-axis**: Time After Ingestion (min)
  - 0 60 120 180 240 300 360
Rasmussen et al, 2000

**Extra Supporting Acute Data**

**Androstenedione**

**Testosterone**

Minutes After Androstenedione Intake (100 mg)

Rasmussen et al, 2000
Extra 100 mg androstenedione t.i.d. in different ages

Brown et al, 2000
Extra 100 mg androstenedione t.i.d. in different ages

Brown et al, 2000

30 year olds

40 year olds

50 year olds
Extra 100 mg androstenedione t.i.d. in different ages

Estradiol (nM)

30 year olds

40 year olds

50 year olds

Brown et al, 2000

Brown et al, 2000
Weeks of Supplementation

Prostate Specific Antigen (ng/ml)

Extra 100 mg androstenedione t.i.d. in different ages

PL (n=13; 44 y)

ASD (n=13; 41 y)

Brown et al, 2000
**Extra 20mg sublingual cyclodextrin androstenediol administration**

Serum Androstenedione (nmol/L)

- SL-Androstenediol
- Placebo

Brown et al, 2002
Extra 20mg sublingual cyclodextrin androstenediol administration

Brown et al, 2002
Extra 20mg sublingual cyclodextrin androstenediol administration

Brown et al, 2002
Michaelis Constants for Enzymes Catalyzing Conversion of Androstenedione to Other Steroids

Androstenedione

- **165 nM**
- **1500 nM**
- **25 nM**

DHT

Testosterone

Estrone (E2)

- **5α-Reductase**
- **17β-Hydroxysteroid DH**
- **Aromatase**
A: T Conversions by Testicular Microsomes

17 β-HSD Activity (pmol/h/mg)

Blomquist, 1995
Evidence that Oral Androstenedione Increases Serum Testosterone

<table>
<thead>
<tr>
<th>Authors</th>
<th>Subjects</th>
<th>Dose</th>
<th>[Testosterone]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mahesh &amp; Greenblatt</td>
<td>2 Women</td>
<td>100 mg</td>
<td>↑ 500%</td>
</tr>
<tr>
<td>Hacker &amp; Mattern</td>
<td>???</td>
<td>???</td>
<td>↑ 237%</td>
</tr>
<tr>
<td>Earnest et al, 1999</td>
<td>8 men, 24 y</td>
<td>200 mg</td>
<td>↑ 15-20%</td>
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</tbody>
</table>
### Evidence that Oral Androstenedione Does Not Increase Serum Testosterone

<table>
<thead>
<tr>
<th>Authors</th>
<th>Subjects</th>
<th>Dose</th>
<th>[Testosterone]</th>
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<tbody>
<tr>
<td>King et al, 1999</td>
<td>10 men, 23 y</td>
<td>100 mg</td>
<td>↔</td>
</tr>
<tr>
<td></td>
<td></td>
<td>300 mg/day</td>
<td>↔</td>
</tr>
<tr>
<td></td>
<td></td>
<td>for 8 wk</td>
<td>↔</td>
</tr>
<tr>
<td>Rassmussen et al, 1999</td>
<td>6 men</td>
<td>100 mg</td>
<td>↔</td>
</tr>
<tr>
<td>Spratt et al, 1999</td>
<td>6 men</td>
<td>1 wk: 100 mg/d</td>
<td>↓ 26%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 wk: 200 mg/d</td>
<td>↔</td>
</tr>
<tr>
<td>Ziegenfuss et al, 1998</td>
<td>7 men, 28 y</td>
<td>100 mg</td>
<td>↔</td>
</tr>
</tbody>
</table>
Effect of 100- and 200 mg Androstenedione in 6 Healthy men

Androgenic 17β-HSD Activity in Human Tissue

<table>
<thead>
<tr>
<th>T Formation</th>
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<tbody>
<tr>
<td>Adipose</td>
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<tr>
<td>Adrenal</td>
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<td>Breast</td>
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<td>Endometrium</td>
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<td>Myometrium</td>
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<td>Ovary</td>
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<td>Placenta</td>
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<td>Skin</td>
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<td>Spleen</td>
<td></td>
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<tr>
<td>Testis</td>
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</table>

pmol/mg protein/min

0.01 0.1 1 10 100 1000
Figure 1. Human Steroidogenic Enzymes in Peripheral Intraocular Tissues.