DOPING AND PHARMACOLOGY IN SPORTS AND SOCIETY

Assist. Prof. Lovro Žiberna, PhD MPharm
Doping is a social phenomenon. It is not only a problem of sport, but rather a problem of society.
DRUGS - SUBSTANCES

CLASSICAL MUSICIANS

ATHLETES

SOLDIERS

MOVIE ACTORS

MANAGERS

STUDENTS

PERFORMANCE ENHANCING
DRUGS - SUBSTANCES

CLASSICAL MUSICIANS

SOLDIERS

MOBILE ACTORS

MANAGERS

STUDENTS

Doping control

PERFORMANCE ENHANCING
DOPING IN MUSIC?

Can we use certain substances to improve our music performance?
Beta-blockers (reduce the effects of adrenaline and noradrenaline as the consequence of fear, performance anxiety)
- increased heart rate
- tremor
- sweating
- vibrating voice
- dizziness, vertigo

Example of doping protocol for the musicians:
5-20 mg propranolol/ performance; 60-90 min before (start protocol)

The Musician’s Steroid: The Controversy Surrounding Beta Blockers

"Some of my teachers in conservatory days would gladly carry around a flask of Scotch and take it before they went on stage," she said. "But I don’t see that in any of the orchestras that I’ve played in recently."

Instead, Mulcahy and other orchestra musicians increasingly turn to beta blockers. According to Mulcahy and other musicians who spoke with WQXR, in some backstage areas, they’re passed around like chewing gum or mints. Mulcahy recalls panicked colleagues calling “Oh my God, does anybody have any Inderal?”

URL: http://www.wqxr.org/#!/story/312920-musicians-use-beta-blockers-relieve-stage-fright/
DOPING IN ART – PSYCHODELIC SUBSTANCES FOR IMPROVED CREATIVITY
Can we increase our creativity and thinking?
FRANCIS CRICK – discovery of DNA. Nobel Prize in Medicine awarded in 1962. Used LSD with researcher at University of Cambridge – also during the discovery.

STEVE JOBS – founder of Apple. In years 1972-1974 used LSD.

BILL GATES – founder of Microsoft. Used LSD in the age <25 years.

KARY MULLIS – developed PCR. Nobel prize in chemistry in 1993. LSD

“What if I had not taken LSD ever; would I have still invented PCR? I don’t know. I doubt it. I seriously doubt it.”

RICHARD FEYNMAN, USA physicist, Nobel prize in physics in 1965. LSD, marijuana, ketamine.
MICRODOSE DOPING TO INCREASE PRODUCTIVITY AS „CREATIVITY ENHANCERS“

Protocol 1:
10-15 µg LSD (10% „normal dose“)

Protocol 2:
taking sub-perceptual doses (6-25 microgram LSD, 0.2-0.5 gram dried mushrooms, 50-75 microgram mescaline HCL

Purpose: to improve „out-of-the-box-thinking“
1400 researchers from 60 countries

3 substances as academic doping:
- modafinil: 62 %
- methylphenidate: 44 %
- beta-blockers: 15 %

All 3 are prohibited in sports (by WADA).

Taking substances to improve cognitive performance?

STUDENT DOPING AT UNIVERSITY?
# PREVALENCE - MEDICAL STUDENTS IN CANADA

## TABLE 2
Prevalence Data

<table>
<thead>
<tr>
<th>Substance group</th>
<th>Lifetime use</th>
<th>Use within the last year (recent use)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee, tea, cola</td>
<td>300 (92%, *CI: 89%–95%)</td>
<td>271 (83%, CI: 79%–87%)</td>
</tr>
<tr>
<td>High-caffeine energy beverages</td>
<td>169 (52%, CI: 47%–57%)</td>
<td>82 (25%, CI: 20%–30%)</td>
</tr>
<tr>
<td>Natural supplements (i.e., gingko biloba, omega 3 fatty acids, B vitamins, melatonin, choline)</td>
<td>97 (30%, CI: 25%–35%)</td>
<td>62 (19%, CI: 15%–23%)</td>
</tr>
<tr>
<td>Tobacco, decongestants</td>
<td>39 (12%, CI: 8%–15%)</td>
<td>8 (2%, CI: 0.2%–4%)</td>
</tr>
<tr>
<td>Stimulant pharmaceuticals (i.e., methylphenidate, modafinil, dextroamphetamine, dextro/levoamphetamine, adrafanil, piracetam)</td>
<td>49 (15%, CI: 11%–19%)</td>
<td>14 (4%, CI: 2%–6%)</td>
</tr>
</tbody>
</table>

*All 95% CI.

UNIVERSITY STUDENTS in GERMANY

amphetamines

methylphenidate

final exams: 8-10x increase in sewage water collected at college campus

NEW DRUG SUBSTANCES

Therapeutic usage vs. abuse by health individuals as PED
THE ORIGIN OF NOVEL DOPING SUBSTANCES

DRUG DISCOVERY
- PHARMA INDUSTRY
- ACADEMIC RESEARCH
- NON-REGISTERED LABS

SCREENING PROCESS
- ANTI-DOPING

FROM BENCH TO BEDSIDE
- DOING SOCIETY

DRUG USERS / ABUSERS
- PATIENTS
- ATHLETES
- RECREATIONAL USERS / DRUG ADDICTS
COLLABORATION WITH PHARMA INDUSTRY

23rd July 2012 – start of Protecting the Integrity of Science and Sport

1 - International Federation of Pharmaceutical Manufacturers & Associations
2 - Biotechnology Industry Organization (BIO)
3 - World Anti-Doping Agency (WADA)

FIRST COLLABORATION started in 2004 – Roche Holding AG and WADA. EPO 3rd.gen. - CERA – in 2007 arrival on the market → in 2008 many athletes tested positive
DOPING IN SPORT
What is doping? Why we fight against doping?
GOLDMAN DILEMMA

“Would you take an illegal performance enhancing drug that was undetectable
Condition 1: “and guaranteed you would win an Olympic gold medal, if it would kill you in five years?” (n = 125, 64.8% male, mean age

Elite athletes (1984): 52 % YES

General population (2009): 0.8 % YES

Figure 2. Development of the arithmetical mean of the time of the top 20 athletes on the men’s 5000 m from 1985 to 2010 (o) connected through a polynomial spline (—−) and further described with the corresponding moving average (−).
Figure 2. Development of the arithmetical mean of the time of the top 20 athletes on the men’s 5000 m from 1985 to 2010 (o) connected through a polynomial spline (— —) and further described with the corresponding moving average (—).
WHY ARE (SHALL/MUST BE) SUBSTANCES PROHIBITED?

Fair-play violation – cheating.  

Danger to health.
Sevilla's Puerta dies in hospital

Spain international Antonio Puerta has died after suffering a heart attack in his club side Sevilla's 4-1 win against Getafe on Saturday.

Defender Puerta, 22, collapsed in the first-half and medics prevented him from swallowing his tongue.

But he collapsed again after going off and was given cardiac resuscitation before being taken to hospital.

He was placed in intensive care and doctors said on Tuesday his condition had deteriorated before his death.

Puerta helped Sevilla win the Uefa Cup last season.

Belgian rider Sermon dies in sleep

BRUSSELS, Feb 15 - Belgian cyclist Johan Sermon has died in his sleep at the age of 21, news agency Belga reported.

Sermon, of the Daikin team, appeared to have died of natural causes, Belga quoted team manager Ernest De Vuyst as saying.

"An autopsy has been carried out and we are now awaiting the results. But I can already say with certainty it was a natural death," said De Vuyst, who added that he believed Sermon had died of heart failure.

Former Tour de France winner Marco Pantani was found dead in a hotel room in Italy at the weekend.

Belga quoted former French Minister of Youth and Sports Marie-George Buffet as saying: "I am devastated by the announcement of the deaths of Marco Pantani and Johan Sermon."
What is doping in sports?

Doping is defined as the occurrence of one or more of the anti-doping rule violations.

The current official definition of doping is given based on the World Anti-Doping Code.
1) Presence of a prohibited substance or its metabolites or markers in an athlete’s sample

- substances and methods which have been included on the Prohibited List
2) Use or Attempted Use by an Athlete of a Prohibited Substance or a Prohibited Method

- it is each athlete’s personal duty to ensure that no prohibited substance enters his or her body and that no prohibited method is used
- the success or failure of the use or attempted use of a prohibited substance or prohibited method is not important
3) Evading, Refusing or Failing to Submit to Sample Collection

- evading sample collection, or without compelling justification, refusing or failing to submit to sample collection after notification as authorized in applicable anti-doping rules
4) Whereabouts Failures

• Any combination of three missed tests and/or filing failures, as defined in the International Standard for Testing and Investigations, within a 12-month period by an Athlete in a Registered Testing Pool.
5) Tampering or Attempted Tampering with any part of Doping Control

- intentionally interfering or attempting to interfere with a Doping Control official,
- providing fraudulent information to an Anti-Doping Organization,
- intimidating or attempting to intimidate a potential witness

- Including: altering identification numbers on a Doping Control form during Testing, breaking the B bottle at the time of B Sample analysis, or altering a Sample by the addition of a foreign substance
6) Possession of a Prohibited Substance or a Prohibited Method

• possession by an athlete of any prohibited substance or any prohibited method on both in-competition and out-of-competition period

• exceptions are substances, which are used for therapeutic purposes

• valid for both athletes and athlete support person
7) Trafficking or Attempted Trafficking in any Prohibited Substance or Prohibited Method
8) Administration or Attempted Administration to any Athlete of any Prohibited Substance or Prohibited Method

- In-competition, and out-of-competition
- help, advisory role, induction, covering up, ...
- national Crime laws

e.g. in SLOVENIA: 
*Kazenski zakonik (KZ-1) – 186. člen in 187.člen (od 1.novembra 2008)*
9) Complicity

• assisting, encouraging, aiding, abetting, conspiring, covering up or any other type of intentional complicity involving an anti-doping rule violation,
10) Prohibited Association

Association by an Athlete to any personnel, which is:

- serving a period of Ineligibility
- convicted or found in a criminal, disciplinary or professional proceeding to have engaged in conduct which would have constituted a violation of anti-doping rules if Code-compliant rules had been applicable to such Person
- serving as a front or intermediary for an individual described above (intermediary person)
- suspension from competition
- results are erased
- (UCI – financial penalty)

- prison
- captured material
- financial penalty (depending on national laws)

WADA CODE

KAZENSKI ZAKONIK

SPORT PENALTY

- WADA
- national anti-doping organizations (e.g. SLOADO)
- International sports organization (UCI, FIFA, UEFA, FIBA, IAAF, itd.)

CRIMINAL LAW

- police
- criminal investigation
DOPING CONTROLS IN SPORT

Prevalence: only cca. 1% of all athletes underwent doping controls
Doping for seniors

In Italy a 55-year-old was caught for doping in an amateur race. The rider for Team Marlis won a race in the category for 55 to 59-year-olds, but CONI, the Italian Olympic committee, announced that the amateur racer was caught for using stimulants, according to La Gazzetta dello sport. He is facing a suspension until he turns 57 as well as a revoking of his title.
<table>
<thead>
<tr>
<th>Sports</th>
<th>Disciplines</th>
<th>Sub</th>
<th>Total Samples</th>
<th>Total AAFs</th>
<th>% AAF</th>
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<tbody>
<tr>
<td><strong>PARACYCLING</strong></td>
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<tr>
<td>Cycling</td>
<td>Para-Cycling**</td>
<td>108</td>
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<td>114</td>
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<td>Para-Cycling Track Sprint**</td>
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<td>Para-Cycling Track Endurance**</td>
<td>37</td>
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<td>CISS Cycling</td>
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<td></td>
<td>Mountain Bike</td>
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<td>33</td>
<td>354</td>
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<td></td>
<td>Track</td>
<td>908</td>
<td>3</td>
<td>12</td>
<td>384</td>
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<td></td>
<td>Cyclo-Cross</td>
<td>687</td>
<td>-</td>
<td>11</td>
<td>60</td>
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<td>Track Endurance</td>
<td>374</td>
<td>2</td>
<td>2</td>
<td>172</td>
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<td></td>
<td>Track Sprint</td>
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<td></td>
<td>BMX</td>
<td>256</td>
<td>-</td>
<td>-</td>
<td>119</td>
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<td></td>
<td>Trials</td>
<td>103</td>
<td>5</td>
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<td>-</td>
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<td></td>
<td>Indoor (Artistic, Cycle Ball) (R)</td>
<td>14</td>
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<td>-</td>
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<tr>
<td></td>
<td>Artistic</td>
<td>4</td>
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<td>Cycle-Ball</td>
<td>7</td>
<td>-</td>
<td>2</td>
<td>-</td>
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<td><strong>AMATEUR CYCLING</strong></td>
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<tr>
<td>Cycling</td>
<td>Amateur (R)</td>
<td>115</td>
<td>4</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td>Military Cycling</td>
<td>12</td>
<td>-</td>
<td>-</td>
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</table>
LIST OF PROHIBITED SUBSTANCES AND METHODS
ADVERSE ANALYTICAL FINDINGS

Table 1: Total Samples Analyzed (All Sports)

<table>
<thead>
<tr>
<th>Sport</th>
<th>Analyzed</th>
<th>AAFs 1 (%)</th>
<th>ATFs 2 (%)</th>
<th>Total Findings 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olympic Sports 4</td>
<td>195,581</td>
<td>1,634</td>
<td>1,585</td>
<td>3,219</td>
</tr>
<tr>
<td>Non-Olympic Sports 3</td>
<td>32,831</td>
<td>888</td>
<td>320</td>
<td>1,208</td>
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<tr>
<td>Non-ADAMS Data 6</td>
<td>73,957</td>
<td>1,287</td>
<td>198</td>
<td>1,485</td>
</tr>
<tr>
<td>TOTAL</td>
<td>303,369</td>
<td>3,809</td>
<td>2,108</td>
<td>5,912</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Substance Group</th>
<th>Occurrences</th>
<th>% of all ADAMS reported findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1. Anabolic Agents</td>
<td>1728</td>
<td>50%</td>
</tr>
<tr>
<td>S6. Stimulants</td>
<td>528</td>
<td>15%</td>
</tr>
<tr>
<td>S5. Diuretics and Other Masking Agents</td>
<td>428</td>
<td>12%</td>
</tr>
<tr>
<td>S9. Glucocorticosteroids</td>
<td>215</td>
<td>6%</td>
</tr>
<tr>
<td>S4. Hormone and Metabolic Modulators</td>
<td>152</td>
<td>4%</td>
</tr>
<tr>
<td>S8. Cannabinoids</td>
<td>127</td>
<td>4%</td>
</tr>
<tr>
<td>S3. Beta-2 Agonists</td>
<td>115</td>
<td>3%</td>
</tr>
<tr>
<td>S2. Peptide Hormones, Growth Factors and Related Substances</td>
<td>98</td>
<td>3%</td>
</tr>
<tr>
<td>S7. Narcotics</td>
<td>21</td>
<td>1%</td>
</tr>
<tr>
<td>P2. Beta-Blockers</td>
<td>19</td>
<td>1%</td>
</tr>
<tr>
<td>M2. Chemical and Physical Manipulation</td>
<td>1</td>
<td>0.03%</td>
</tr>
<tr>
<td>P1. Alcohol</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>M1. Enhancement of Oxygen Transfer</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>TOTAL*</td>
<td>3432</td>
<td></td>
</tr>
</tbody>
</table>
Is there a high-risk sport?
MENTAL (MATH) EXPERIMENT

Sport A
Prevalence=1%
Testing program = 50,000 samples/year
AAF = 500 samples (athletes)

Sport B
Prevalence=1%
Testing program = 1,000 samples/year
AAF = 10 samples (athletes)

Which sport is more risky? Which sport has higher prevalence of doping?

MEDIA: Sport A. There are 500 athletes positive each year.

Relative value ≠ Absolute value
## 2010 Adverse Analytical Findings and Atypical Findings
Reported by Accredited Laboratories

### Olympic Sport Sample Analysis

<table>
<thead>
<tr>
<th>Sport</th>
<th>Total Samples per Sport</th>
<th>A Sample Adverse Analytical Findings</th>
<th>A Sample Atypical Findings</th>
<th>A Sample Total Findings</th>
<th>% Adverse Analytical Findings</th>
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<tbody>
<tr>
<td>Aquatics</td>
<td>13,138</td>
<td>90</td>
<td>65</td>
<td>155</td>
<td>0.69%</td>
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<tr>
<td>Archery</td>
<td>1,156</td>
<td>17</td>
<td>4</td>
<td>21</td>
<td>1.47%</td>
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<td>Athletics</td>
<td>25,013</td>
<td>196</td>
<td>242</td>
<td>438</td>
<td>0.78%</td>
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<td>Badminton</td>
<td>1,250</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>0.24%</td>
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<tr>
<td>Basketball</td>
<td>9,575</td>
<td>139</td>
<td>62</td>
<td>201</td>
<td>1.45%</td>
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<tr>
<td>Biathlon</td>
<td>1,967</td>
<td>-</td>
<td>18</td>
<td>18</td>
<td>0.00%</td>
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<tr>
<td>Bobsleigh</td>
<td>1,214</td>
<td>2</td>
<td>17</td>
<td>19</td>
<td>0.16%</td>
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<tr>
<td>Boxing</td>
<td>3,874</td>
<td>75</td>
<td>35</td>
<td>110</td>
<td>1.94%</td>
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<tr>
<td>Canoe / Kayak</td>
<td>3,726</td>
<td>15</td>
<td>35</td>
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<td>Curling</td>
<td>477</td>
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<td>5</td>
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<td>Cycling</td>
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<td>254</td>
<td>359</td>
<td>613</td>
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<td>Equestrian</td>
<td>723</td>
<td>12</td>
<td>5</td>
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<td>Fencing</td>
<td>1,916</td>
<td>8</td>
<td>20</td>
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<td>Football</td>
<td>30,398</td>
<td>146</td>
<td>257</td>
<td>403</td>
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<td>Gymnastics</td>
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<td>Handball</td>
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<td>Ice Hockey</td>
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<td>Judo</td>
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<td>Sport</td>
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<td>Gold</td>
<td>Silver</td>
<td>Bronze</td>
<td>Total Athletes</td>
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<td>------------------------</td>
<td>------</td>
<td>-----</td>
<td>-------</td>
<td>-------</td>
<td>----------------</td>
</tr>
<tr>
<td>Air Sports</td>
<td>97</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>3</td>
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<tr>
<td>Bandy</td>
<td>199</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>0.50%</td>
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<td>Baseball</td>
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<td>89</td>
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<td>Baseball/Softball</td>
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<td>Boules</td>
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<td>21</td>
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<td>347</td>
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<td>2</td>
<td>4</td>
<td>0.58%</td>
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<tr>
<td>Bridge</td>
<td>50</td>
<td>3</td>
<td>-</td>
<td>3</td>
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<td>Chess</td>
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<td>2</td>
<td>2</td>
<td>4</td>
<td>1.26%</td>
</tr>
<tr>
<td>Cricket</td>
<td>943</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>0.21%</td>
</tr>
<tr>
<td>Dance Sport</td>
<td>405</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>0.74%</td>
</tr>
<tr>
<td>Floorball</td>
<td>523</td>
<td>5</td>
<td>5</td>
<td>10</td>
<td>0.96%</td>
</tr>
<tr>
<td>Golf</td>
<td>1,619</td>
<td>33</td>
<td>12</td>
<td>45</td>
<td>2.04%</td>
</tr>
<tr>
<td>Karate</td>
<td>1,078</td>
<td>10</td>
<td>7</td>
<td>17</td>
<td>0.93%</td>
</tr>
<tr>
<td>Korfball</td>
<td>86</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>0.00%</td>
</tr>
<tr>
<td>Life Saving</td>
<td>331</td>
<td>3</td>
<td>-</td>
<td>3</td>
<td>0.91%</td>
</tr>
<tr>
<td>Motorcycle Racing</td>
<td>482</td>
<td>20</td>
<td>5</td>
<td>25</td>
<td>4.15%</td>
</tr>
</tbody>
</table>
Table 3  Period prevalence of doping in various target groups using randomised response technique questionnaires

<table>
<thead>
<tr>
<th>Publication</th>
<th>Target group</th>
<th>n</th>
<th>Prevalence of doping (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitsch et al. [79]</td>
<td>Adult elite</td>
<td>448</td>
<td>26–48 Ever; 20–39 Last year</td>
</tr>
<tr>
<td>Striegel et al. [72]</td>
<td>Junior elite</td>
<td>480</td>
<td>3–11 Ever</td>
</tr>
<tr>
<td>Simon et al. [81]</td>
<td>Fitness centre visitors</td>
<td>500</td>
<td>8–17 Ever</td>
</tr>
<tr>
<td>Stubbe et al. [80]</td>
<td>Fitness centre visitors</td>
<td>447</td>
<td>5–23 Last year</td>
</tr>
</tbody>
</table>

Table 4  Overview of estimates of the period prevalence of doping amongst elite athletes based on different analysis techniques

<table>
<thead>
<tr>
<th>Analysis techniques</th>
<th>Estimated prevalence</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doping control test results</td>
<td>1–2 % Last year [15]</td>
<td>Stable figure for the last 25 years. Not likely to reflect true intentional doping (see Sect. 2.1)</td>
</tr>
<tr>
<td>Population estimates based on biological value parameters</td>
<td>14 % Over 10 years [36]</td>
<td>Blood manipulations in elite athletes in athletics; data on other sorts of doping or sports modalities as yet unavailable (see Sect. 2.2)</td>
</tr>
<tr>
<td>Standard questionnaires</td>
<td>1–15 % [4, 45–59]</td>
<td>Mostly performed on adolescents and/or students; little research in elite sports (see Sect. 3.1)</td>
</tr>
<tr>
<td>Randomised response questionnaires</td>
<td>20–39 % Last year (adult) [79]</td>
<td>German athletes; data on other nationalities or sports modalities as yet unavailable (see Sect. 3.2)</td>
</tr>
<tr>
<td></td>
<td>3–11 % Lifetime (junior) [72]</td>
<td>Popular input for doping-related discussions but impossible to reflect prevalence of doping (see Sects. 4.1, 4.2)</td>
</tr>
<tr>
<td>Inferences from athletic performances</td>
<td>–</td>
<td>Give some insight into the sociological background of doping and perceived prevalence, but not true prevalence (see Sect. 5)</td>
</tr>
</tbody>
</table>

LIST OF PROHIBITED SUBSTANCES AND METHODS

2015
List of Prohibited Substances and Methods

PROHIBITED AT ALL TIMES
PROHIBITED IN-COMPETITION
PROHIBITED IN PARTICULAR SPORTS
By Substance
By Method

LINKS
2015 List Information
Monitoring Program (PDF)
Prohibited List (PDF)

WADA – http://www.wada-ama.org
SLOADO – http://www.sloado.si
How does a substance become prohibited?

What are the criteria for adding a substance to the List?

Must meet any 2 of the following 3 criteria:

- It has the potential to enhance or enhances sport performance;
- It represents an actual or potential health risk to the athlete;
- It violates the Spirit of Sport.
One example: AAS

Most widely abused doping substances
S1. ANABOLIC AGENTS

Anabolic agents are prohibited.

1. **Anabolic Androgenic Steroids (AAS)**

   a. *Exogenous* AAS, including:

   - 1-androstenediol (5α-androst-1-ene-3β,17β-diol);
   - 1-androstenedione (5α-androst-1-ene-3,17-dione);
   - bolandiol (estr-4-ene-3β,17β-diol);
   - bolasterone;
   - boldione (androsta-1,4-diene-3,17-dione);
   - calusterone;
   - clomestane;
   - danazol [(1,2)oxazol][4',5':2,3]pregna-4-en-20-yn-17α-ol);
   - dehydrochloromethyltestosterone (4-chloro-17β-hydroxy-17α-methylandrosta-1,4-dien-3-one);
   - desoxymethyltestosterone (17α-methyl-5α-androst-2-en-17β-ol);
   - drostanolone;
   - ethylestrenol (19-norpregna-4-en-17α-ol);
   - fluoxymesterone;
   - formebolone;
   - furazabol (17α-methyl[1,2,5]oxadiazolo[3',4':2,3]-5α-androstan-17β-ol);
   - gestrinone;
   - 4-hydroxytestosterone (4,17β-dihydroxyandrost-4-en-3-one);
   - mesterolone;
   - metandienone (17β-hydroxy-17α-methylandrosta-1,4-dien-3-one);
   - metenolone;
   - methandriol;
   - methasterone (17β-hydroxy-2α,17α-dimethyl-5α-androstan-3-one);
   - methylidenolone (17β-hydroxy-17α-methylene-4,9-dien-3-one);
   - methyl-1-testosterone (17β-hydroxy-17α-methyl-5α-androst-1-en-3-one);
   - methyltestosterone (17β-hydroxy-17α-methylene-4-en-3-one);
   - metribolone (methyltrienolone, 17β-hydroxy-17α-methylene-4,9,11-trien-3-one);
   - nandrolone;
   - 19-norandrostenedione (estr-4-ene-3,17-dione);
   - norboleton; nortestobol; norethandrolone; oxabolone; oxandrolone; oxymesterone; oxymetholone; prostanolol (17β-{[(tetrahydroxyran-2-yl)oxy]-1'Hpyrazolo[3,4:2,3]-5α-androstane; quinbolone; stanozolol; stenbolone; 1-testosterone (17β-hydroxy-5α-androst-1-en-3-one); tetrahydrogestrinone (17β-hydroxy-18α-homo-19-nor-17α-pregna-4,9,11-trien-3-one); trenbolone (17β-hydroxyestr-4,9,11-trien-3-one);

and other substances with a similar chemical structure or similar biological effect(s).

- “exogenous” refers to a substance which is not ordinarily produced by the body naturally.
- “endogenous” refers to a substance which is ordinarily produced by the body naturally.
Mode of action I

Steroids abuse: orally or intravenously

Target cells with specific receptors

Vascular system

Mode of action II

DNA

mRNA

Protein Synthesis

Steroid hormone

Steroid hormone response
Harmonising the Knowledge about Biomedical Side Effects of Doping

Biomedical side effects of anabolic androgenic steroids...

...on the skin

Anabolic androgenic steroids (AAS)

→ Hypertrophy of sebaceous glands

→ Sebum excretion ↑

→ Skin surface lipids ↑

→ Propionibacterium acnes ↑

Acne by AAS abuse


Get further information: www.doping-prevention.sp.tum.de

www.doping-prevention.com
Biomedical side effects of anabolic androgenic steroids…

...on the skin

Intake of Anabolic androgenic steroids

Striae distensae developing at places of strong skin stretching (e.g. shoulder, upper limb, breast or back)


Get further information: www.doping-prevention.sp.tum.de
General side effects:

- Psychological dependence
- Increased aggression
- Mood swings
- Increased risk of liver disease
- Increased risk of cardiovascular disease
- High blood pressure
### Side effects by an abuse on semen parameters

#### The Reversibility of Androgen-Induced Hypogonadism in a Bodybuilder [Case Report]

<table>
<thead>
<tr>
<th>Semen parameters</th>
<th>After 10 months abuse</th>
<th>5 months post cessation</th>
<th>10 months post cessation</th>
<th>Normal ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (mL)</td>
<td>1.5</td>
<td>1.5</td>
<td>2.0</td>
<td>1.5 - 5.0</td>
</tr>
<tr>
<td>Sperm count (millions per mL)</td>
<td>0</td>
<td>3</td>
<td>20</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Motility (%)</td>
<td>0</td>
<td>6</td>
<td>30</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Normal morphology fraction (%)</td>
<td>0</td>
<td>13</td>
<td>42</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Testosterone (nmol-L⁻¹)</td>
<td>0.54</td>
<td>1.25</td>
<td>20.58</td>
<td>8.7 - 33</td>
</tr>
</tbody>
</table>


$^{18}$F-FDG PET/CT

40-years old bodybuilder with chronic application of AAS

- mild abdominal aortic atherosclerosis
- inferolateral infaction (occlusion of R coronary art.)
Long-term Adverse Effects:

Cardiovascular toxicity:

• left ventricular hypertrophy, diastolic heart failure,
• arrhythmias,
• hypertension,
• endothelial dysfunction, atherogenic lipid blood profile, increased development of atherosclerosis
• higher risk of acute myocardial infarction and acute heart failure (acute heart arrest)
Long-term Adverse Effects:

Higher incidence of cancer:
• primary liver neoplasms
• renal carcinoma
• testicular cancer
• prostate cancer.

RISK OF DEATH is for AAS users 4.6 x higher in comparison to the control group.
HEIDI KRIEGER (20/7/1966) since the age of 16 included in systematic AAS doping program

1986 – Gold medal on EC

ANDREAS KRIEGER, since 1997
- shorter life span
- long-term consequences due to AAS use when "young"
- 6-months of AAS use on mice - cca 20% of average mouse life span

*Figure 23.4* Life-shortening effects of exogenous anabolic steroid use in mice. (Modified from Bronson FH, Matherne CM. Exposure to anabolic–androgenic steroids shortens life span of male mice. Med Sci Sports Exerc 1997;29:615.)
INADVERTENT DOPING

Non-intentional / Accidental / Mistake vs. On Purpose?
• in 2003 tested positive due to the contaminated nutritional supplement: multivitamins contained traces of 19-norandrosterone.

• He lost his spot at US national team for Olympic Games in 2004 in Athens

• in 2005 he won $578,635 suit against the nutritional supplement producer: Ultimate Nutrition of Farmington, Conn.

NEVER TESTED POSITIVE ON DOPING

7 – times winner of Tour de France, world champion, Olympic medal winner

EPO, testosteron, cortikosteroids, hGH, blood doping

Assessment 20 m$/year -> 83.333 $/day
Source: http://www.best-reviewer.com
Gateway to doping? Supplement use in the context of preferred competitive situations, doping attitude, beliefs, and norms

S. H. Backhouse¹, L. Whitaker¹, A. Petróczí²,³

¹Carnegie Research Institute, Leeds Metropolitan University, Leeds, United Kingdom, ²Faculty of Life Sciences, Kingston University, Kingston, UK, ³Sheffield University, Sheffield, UK

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Accepted for publication 20 June 2011

Nutritional supplement (NS) use is widespread in sport. This study applied an integrated social cognitive approach to examine doping attitudes, beliefs, and self-reported doping use behavior across NS users (n = 96) and nonusers (n = 116). Following ethical approval, 212 competitive athletes (age mean = 21.4, s = 4.5; 137 males) completed self-reported measures of doping-related social cognitions and behaviors, presented in an online format where completion implied consent. Significantly more NS users (22.9%) reported doping compared with nonusers (6.0%; U = 4628.0, P < 0.05). NS users presented significantly more positive attitudes toward doping (U = 3152.0, P < 0.05) and expressed a significantly greater belief that doping is effective (U = 3152.0, P < 0.05). When presented with the scenario that performance-enhancing substances are effective and increase the possibility of winning, NS users were significantly more in favor of competing in situations that allow doping (U = 3504.5, P < 0.05).

In sum, doping use is three-and-a-half times more prevalent in NS users compared with nonusers. This finding is accompanied by significant differences in doping attitudes, norms, and beliefs. Thus, this article offers support for the gateway hypothesis; athletes who engage in legal performance enhancement practices appear to embody an “at-risk” group for transition toward doping. Education should be appropriately targeted.
Table 2: Prevalence of multiple supplements use in the full sample (n = 874) and among supplement users (n = 520)

<table>
<thead>
<tr>
<th>Number of supplements reported</th>
<th>% of all athletes</th>
<th>% of all supplement users</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>40.2</td>
<td>17.4</td>
</tr>
<tr>
<td>1 supplement</td>
<td>10.4</td>
<td>14.2</td>
</tr>
<tr>
<td>2 supplements</td>
<td>14.2</td>
<td>23.7</td>
</tr>
<tr>
<td>3 supplements</td>
<td>12.9</td>
<td>21.6</td>
</tr>
<tr>
<td>4 supplements</td>
<td>9.8</td>
<td>16.4</td>
</tr>
<tr>
<td>5 supplements</td>
<td>9.8</td>
<td>9.4</td>
</tr>
<tr>
<td>6 supplements</td>
<td>6.4</td>
<td>5.4</td>
</tr>
<tr>
<td>7 supplements</td>
<td>3.2</td>
<td>3.1</td>
</tr>
<tr>
<td>8 supplements</td>
<td>1.8</td>
<td>1.7</td>
</tr>
<tr>
<td>9 supplements</td>
<td>1.0</td>
<td>1.3</td>
</tr>
</tbody>
</table>

around 60% of athletes are using NS

RISK FOR INADVERTENT DOPING

• strict-liability of the athletes in accordance with WADA (World Anti-Doping Agency) code:

“athletes remain responsible for substances detected in their biofluids, irrespective of their origin”
REGULATIVE CHALLENGES

• A dietary supplement is not reviewed pre-market and does not have to be proven safe in order to be sold on the shelves of a store.”

• In USA: in 2004 – 2012 FDA removed 237 nutritional supplements from the market

Nutritional supplement can come to the market without being tested for SAFETY or EFFICACY.
Recall -- Firm Press Release

FDA posts press releases and other notices of recalls and market withdrawals from the firms involved as a service to consumers, the media, and other interested parties. FDA does not endorse either the product or the company.

SmartLipo365 Issues Voluntary Nationwide Recall of Smart Lipo Due to Undeclared Sibutramine, Desmethylysibutramine, and Phenolphthalein

Contact:
Consumer:
1-(800)-547-6365

FOR IMMEDIATE RELEASE — June 3, 2015 — Dallas, TX, SmartLipo365 is voluntarily recalling 122 lots of Smart Lipo (800, 900, 950 mg) capsules, to the consumer level. FDA received samples of 800 and 900mg capsules of Smart Lipo and the lab
Problems of contaminated NS

1. producers don’t specify ingredients properly

2. cross-contamination with prohibited substances (company working with other substances using same equipment)

3. Intentional addition of pharmacologically-effective substances to get better results
Table 1. Nutritional supplements cross-contaminated with anabolic-androgenic steroids (prohormones) in different countries in 2001/2002\textsuperscript{23,24}

<table>
<thead>
<tr>
<th>Country</th>
<th>No. of analyzed products</th>
<th>No. of cross-contaminated products</th>
<th>Percentage of cross-contaminated products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherlands</td>
<td>31</td>
<td>8</td>
<td>25.8</td>
</tr>
<tr>
<td>Austria</td>
<td>22</td>
<td>5</td>
<td>22.7</td>
</tr>
<tr>
<td>UK</td>
<td>37</td>
<td>7</td>
<td>18.9</td>
</tr>
<tr>
<td>USA</td>
<td>240</td>
<td>45</td>
<td>18.8</td>
</tr>
<tr>
<td>Italy</td>
<td>35</td>
<td>5</td>
<td>14.3</td>
</tr>
<tr>
<td>Spain</td>
<td>29</td>
<td>4</td>
<td>13.8</td>
</tr>
<tr>
<td>Germany</td>
<td>129</td>
<td>15</td>
<td>11.6</td>
</tr>
<tr>
<td>Belgium</td>
<td>30</td>
<td>2</td>
<td>6.7</td>
</tr>
<tr>
<td>France</td>
<td>30</td>
<td>2</td>
<td>6.7</td>
</tr>
<tr>
<td>Norway</td>
<td>30</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>Switzerland</td>
<td>13</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sweden</td>
<td>6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Hungary</td>
<td>2</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
WHICH PROHIBITED SUBSTANCES?

• stimulants
• precursors of anabolic steroid hormones
• anabolic-androgenic steroids
• β2-agonists
Case study: NS product CREATINE

Contaminated creatine product contained 7 steroid precursors and testosterone

Fig. 1. Urinary concentrations of 19-norandrosterone in 5 male volunteers after administration of a contaminated nutritional supplement.


List of Prohibited Substances:
S1 – Anabolic Steroids

19-norandrosterone above the detection limit for 36 h after consumption

WADA detection limit for adverse analytical finding
Chinese herbal tea for weight loss contaminated with sibutramine

Lista of prohibited substances:
S6 - STIMULANTS

Supplements
Understand the issues
Learn to reduce risk
Make an informed decision

Start Tutorial Here

NEWS
10/4/2012
Dozens of dietary supplements are illegally labeled
Associated Press

10/2/2012
Questioning the Superpowers of Omega-3 in Diets
Wall Street Journal

10/1/2012
To supplement or not, that is the question
Macon Telegraph

ADDITIONAL RESOURCES
Supplement Bottle
In this section, viewers will get an in-depth look at a hypothetical dietary supplement bottle and explore the real-life issues associated with dietary supplement packaging.

High Risk Dietary Supplement List
By submitting this form the user agrees to receive the USADA High risk dietary supplement list as well as follow-up correspondence regarding the list.
Products that have been tested and shown to contain prohibited substances.

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Company</th>
<th>What the label says</th>
<th>Prohibited List Classification</th>
<th>Test Results show</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-OXO (Lot EL40)</td>
<td>ErgoPharm</td>
<td>Label lists a variety of herbs including tribulus terrestris, maca extract, saw palmetto berry, and others.</td>
<td>S1. Anabolic Agents</td>
<td>Contains 4-androstenedione and turinabol</td>
</tr>
<tr>
<td>3 Test OXO (Lot # PB0079712)</td>
<td>Complete Nutrition</td>
<td></td>
<td>S1. Anabolic Agents and S6. Stimulants</td>
<td>Contains dehydroepiandrosterone, progesterone, cathine, ephedrine, methylhexanamine, octopamine, pseudoephedrine</td>
</tr>
<tr>
<td>Andro-XS (Lot not specified)</td>
<td>Sports One Nutrition</td>
<td>4-chloro-17a-methyl-andro-4-ene-3β,17β-diol</td>
<td>S1. Anabolic Agents</td>
<td>Contains turinabol</td>
</tr>
<tr>
<td>Craze (Lot 1202487)</td>
<td>Driven Sports</td>
<td>N,N-Dimethyl-B-Phenylethylamine</td>
<td>S6. Stimulants</td>
<td>Contains amphetamine; N-methylphenethylamine, beta-methylphenethylamine, ethylamphetamine</td>
</tr>
<tr>
<td>Decabolen (Lot 0906162)</td>
<td>CTD Labs</td>
<td>4-chloro-17a-methyl-andro-4-ene-3β,17β-diol; 2α17α-dimethyl-5α-androstan-3-one</td>
<td>S1. Anabolic Agents</td>
<td>Contains 4-chloro-17α-methyl-andro-4-ene-3β,17β-diol - was not detected in the product but methasterone (2α17α-dimethyl-5α-androstan-3-one) and its isomer</td>
</tr>
<tr>
<td>DR1 (Lot# PB0079412)</td>
<td>Complete Nutrition</td>
<td></td>
<td>S1. Anabolic Agents and S6. Stimulants</td>
<td>Contains 4-Androsten-3,6,17-trione, formestane, 4-Androstenedione, drostanolone, 4-Androstene-3β-17β-diol, cindol, ephedrine, methylphenethylamine, N-methylphenethylamine, pseudoephedrine.</td>
</tr>
<tr>
<td>Dual Action Grow Tabs (Lot CW-68)</td>
<td>IDS</td>
<td></td>
<td>S1. Anabolic Agents</td>
<td>Contains 1- androstenedione, 4-androstenedione, methandione, turinabol.</td>
</tr>
<tr>
<td>E-911 (Lot #9164)</td>
<td>LG Sciences</td>
<td></td>
<td>S6. Stimulants</td>
<td>Contains methylxynephrine, octopamine.</td>
</tr>
</tbody>
</table>
The Cologne List supports the assessment of a certain nutritional supplement by athletes, coaches and sport medicine specialists. The Cologne List and respectively the Olympic Centre Rheinland do not take on any responsibility using a product published on the Cologne List. The ultimate responsibility remains with each athlete.

Please note:
Neither the fact that a product is published on the Cologne List nor a negative laboratory analysis is a warranty that the product does not contain any prohormones, anabolic substances, or stimulants. The Cologne List only ascertains that listed products are associated with a minimized risk of doping.

<table>
<thead>
<tr>
<th>Product</th>
<th>Product category</th>
<th>Company</th>
<th>Last analysis Prohormones</th>
<th>Last Analysis Stimulants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitals Langzeitvitaltablette A-Z Balance</td>
<td>Other (miscellaneous) products</td>
<td>PHARCONA GmbH</td>
<td>20.08.2012</td>
<td>20.08.2012</td>
</tr>
<tr>
<td>Vitals Langzeitvitaltablette A-Z Generation 50+</td>
<td>Other (miscellaneous) products</td>
<td>PHARCONA GmbH</td>
<td>20.08.2012</td>
<td>20.08.2012</td>
</tr>
<tr>
<td>Vitals Magnesium 250 mg + Vitamin E-Sticks</td>
<td>Mineral nutrients and trace elements</td>
<td>ALDI Einkauf GmbH &amp; Co. OHG</td>
<td>29.08.2012</td>
<td>29.08.2012</td>
</tr>
<tr>
<td>Vitals Magnesium 350mg + Vitamin C Brausetablette</td>
<td>Other (miscellaneous) products</td>
<td>ALDI Einkauf GmbH &amp; Co. OHG</td>
<td>20.03.2012</td>
<td>20.03.2012</td>
</tr>
<tr>
<td>Vitals Magnesium Tabletten</td>
<td>Other (miscellaneous) products</td>
<td>PHARCONA GmbH</td>
<td>20.08.2012</td>
<td>20.08.2012</td>
</tr>
<tr>
<td>Vitals Multivitamin Brausetablette</td>
<td>Other (miscellaneous) products</td>
<td>ALDI Einkauf GmbH &amp; Co. OHG</td>
<td>20.03.2012</td>
<td>20.03.2012</td>
</tr>
</tbody>
</table>
The Most Powerful Pre-Workout Powder Ever

Neurocore MuscleTech Geranium Extract (Geranium robertianum, aerial parts)

Methylhexanamine, S6. Stimulants
MUSCLE

NeuroCore contains 3200mg of beta-alanine – the exact dose scientifically shown to help enhance the muscle- and strength-building process.

STRENGTH

A highly potent and unique creatine known as creatine HCl has been infused into the formula. Creatine is clinically validated to amplify gains in size and strength.

PUMP

NeuroCore™ is formulated with a research-tested dose of pure L-citrulline instead of L-arginine or L-arginine AKG for intense, long-lasting muscle pumps. L-citrulline has actually been shown in research on nitric oxide metabolism to reach superior peak plasma arginine levels compared to a larger dose of L-arginine.

ENHANCED SENSORY EXPERIENCE

A potent yohimbe bark extract has been added to NeuroCore™. This extract supplies rauvoscine and yohimbine, which are categorized as selective alpha-2 receptor antagonists. Human research indicates that blocking alpha-2 receptors may play a significant role in supporting blood flow.

The Facts Don't Lie

Many pre-workout concentrates do not disclose the ingredient amounts in their formulas, so we tested their formulas and discovered that they’re underdosed when it comes to the latest scientific research – and we have the third-party lab tests to back it up.

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<th>NeuroCore</th>
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<th>What You Should Know</th>
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<tr>
<td>Ingredient Amounts Fully Disclosed</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
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**Frequently Asked Questions**

**What can I expect to feel on NeuroCore?**

NeuroCore is a super-concentrated pre-workout performance-enhancing stimulant formulated to deliver intense energy, mental focus, increased muscle and strength and awesome muscle pumps for an outstanding training experience.
CARDIOTOXICITY – ACUTE MYOCARDIAL INFARCTION

DMAA supplement linked to marathon runner's death is still on sale online
Stimulant taken by Claire Squires before she died during marathon is legally available in UK through overseas websites

Case Report

Cardiac Arrest in a 21-Year-Old Man After Ingestion of 1,3-DMAA–Containing Workout Supplement
Lioudmila V. Karnaiovskaya, MD,* Juan C. Leoni, MD,† and Michelle L. Freeman, MD*
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News

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Loudmila V. Karnasovskaya, MD,* Juan C. Leoni, MD,† and Michelle L. Freeman, MD*
Acute Myocardial Infarction Associated with Dietary Supplements Containing 1,3-Dimethylamylamine and *Citrus aurantium*

We describe the case of a previously healthy 22-year-old man who presented with anginal chest pain and was diagnosed with a non-ST-elevation myocardial infarction. For 3 weeks, he had been ingesting the dietary supplements Jack3d® (principal ingredient, 1,3-dimethylamylamine) and Phenorex™ (principal ingredient, *Citrus aurantium*) daily, before undertaking physical activity. Coronary angiograms revealed a proximal left anterior descending coronary artery thrombus with distal embolization. A combined medical regimen led to resolution of the thrombus. Three months later, the patient was asymptomatic with no evidence of ischemia.

The primary ingredients in the sympathomimetic supplements taken by our patient are controversial in the medical community and have been individually associated with adverse cardiac events. There are no safety data on their simultaneous use. We discuss other reports of adverse effects associated with these supplements and recommend that the relevant safety guidelines be revised. *(Tex Heart Inst J 2014;41(1):70-2)*

contaminant 1,3-dimethylamylamine (DMAA) – sympaticomimetic activity
HEPATOTOXICITY – ACUTE LIVER FAILURE

- Hawaii Department of Health (HDOH) in period May – October 2013 evaluated 29 acute hepatitis (acute liver failures) related to the use of OxyElitePro
  - 1 athlete died
  - 2 athletes needed liver transplantation
  - 2 athletes with long hospital stay
  - aegelin, DMAA

Notes from the Field: Acute Hepatitis and Liver Failure Following the Use of a Dietary Supplement Intended for Weight Loss or Muscle Building – May-October 2013

Weekly
October 11, 2013 / 62(40):817-819

Guidelines: “Clinicians evaluating patients with acute hepatitis should ask about consumption of dietary supplements as part of a comprehensive evaluation. “
Fat burner–induced acute liver injury: Case series of four patients

Aleksandar Gavrić M.D.  a, Marija Ribnikar M.D.  a, Lojze Šmid M.D., Ph.D.  a, Boštjan Luzar M.D., Ph.D. b, Borut Štabuc M.D., Ph.D. a


University Medical Center Ljubljana, in Slovenia, from May 2010 to July 2015

Healthy women using “fat-burners”
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Thank you for your attention!