Allopurinol does not reduce exercise induced muscle damage in ultra-marathon runners.

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Exercise induced muscle damage.

- novel or unaccustomed exercise
- soreness and swelling
- reduced power
- reduces ability to perform subsequent bouts of exercise
Mechanisms of exercise induced muscle damage.

- Mechanical
  - muscle contraction
  - shock impulses

- Reactive oxygen species
  - unbalanced valence shell
  - oxidise amino acids
  - oxidise cell membrane
  - damage of DNA / RNA
Biopsy findings in exercise induced muscle damage.

- Structural changes
- Cell necrosis
Serology of exercise induced muscle damage.

- released intra-cellular elements
  - Creatine Kinase
  - Lactate Dehydrogenase
  - Aspartate Aminotransferase

- oxidised cell membranes
  - Lipid peroxidation
  - Produces malondialdehyde
Production of reactive oxygen species (1/2)

- ~2% of oxygen in ETC forms ROS
- by-product of oxygen metabolism
Production of reactive oxygen species (2/2)

- Xanthine oxidase activity
- Purine metabolism
- Produces ROS
- Found in many tissues
  - liver
  - intestines
  - endothelium
  - lungs
- relative hypoxia increases activity
Allopurinol

Active metabolite
oxypurinol

- Inhibits xanthine oxidase
- Half life 23.3 +/- 6.0 hours
- Reduces ROS production

![Chemical Reaction Diagram]
APO-ALLOPURINOL

IN COMPETITION
Route of administration: all routes
Status: 

OUT OF COMPETITION
Route of administration: all routes
Status: 

STATUS DEFINITIONS
- Permitted for use
- Prohibited
- Permitted in females only
- Subject to certain conditions
Past research
Allopurinol and Markers of Muscle Damage Among Participants in the Tour de France

Significant differences (placebo vs allopurinol)

- CK (P=0.03)
- AST (P=0.02)
- Malondialdehyde (P=0.009)

Allopurinol prevents cardiac and skeletal muscle damage in professional soccer players.

- Significant differences (placebo vs allopurinol)
  - CK (P<0.05)
  - LDH (P<0.05)
  - AST (P<0.05)
  - Myoglobin (P<0.05)
  - Malondialdehyde (P<0.05)

Oxidative stress in marathon runners: interest of antioxidant supplementation.

- Placebo: increase in malondialdehyde (P<0.05)
- Allopurinol: no significant change in malondialdehyde
- Between group: no significant difference

Hypothesis

- Prophylactic allopurinol may lead to reduced exercise induced muscle damage by reducing oxidative stress in ultra-marathon runners.
Ultra-marathons

- >42km
- Often extreme conditions
- >3,000 ultra-marathons annually globally
Great North Walk 100’s

- 103.7 km
  - 3,800m ascent/descent
  - 22 hour limit
- 175.3 km
  - 6,200m ascent/descent
  - 36 hour limit
- Check points ~25km apart (eat, drink and rest)
Methodology

- Recruitment via email
- 13 runners (8 male, 5 female)
- Pre-event blood test
  - baseline renal/hepatic function
  - baseline uric acid levels
- Test dose 300mg allopurinol/placebo
- Dose night before event (300mg)
- Dose on morning of event (300mg)
- Post event blood test 48 hours post event
### Results (1/2)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Distance (km)</th>
<th>Time</th>
<th>Group</th>
<th>CK (pre)</th>
<th>CK (post)</th>
<th>LDH (pre)</th>
<th>LDH (post)</th>
<th>AST (pre)</th>
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Results (2/2)

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<th>Allopurinol vs. Control</th>
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Discussion

- Shock impulses vs muscle contraction
  - Running vs. skiing

- Event duration vs oxypurinol half life
  - 4 runners >30 hours
  - Re-analysis did not change results
Conclusion

- Premature to discount benefits of prophylactic allopurinol in reducing oxidative stress
- Malondialdehyde useful to assess oxidative stress directly
- Future research should focus on
  - Low impact activities
  - Event duration <17 hours
Questions.


