Super Ergogenic Aids

Content
Ergogenic Aids
Defined
When to take an Ergogenic Aid
Ergogenic Aids for Aerobic Exercise
Caffeine
Dietary Nitrates
High Intensity Exercise - β-alanine
Ergogenic Aids for Resistance Exercise
Leucine
β-hydroxy-β-methylbuturate

Ergogenic Aid
Anything that will improve or enhance physical performance

Ergogenic or Ergolytic?
Sometimes a supplement, drug or product can be both ergogenic and ergolytic

When to use an Ergogenic Aid
Purported Ergogenic Effect
Safety
Safe ✗Unsafe (Do not use)
Legality
Legal ✗Illegal (Do not use)
Effectiveness
Effective ✗Ineffective (Do not use)
Side Effects
No Side Effect ✗Side Effects (Do not use)
Timing
Know Effect Time ✗Don’t know Effect Timing (Do not use)

If answers to the questions are all on left, then it is appropriate to use.

Ergogenic Aids for Aerobic Exercise
Caffeine Content in Food

<table>
<thead>
<tr>
<th>Food</th>
<th>Content (mg/oz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tea (hot)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>8.4 – 10.7</td>
</tr>
<tr>
<td>Green</td>
<td>5.6 – 7.7</td>
</tr>
<tr>
<td>Coffee</td>
<td></td>
</tr>
<tr>
<td>Instant</td>
<td>13.1 – 15.0</td>
</tr>
<tr>
<td>Percolated</td>
<td>20.8 – 26.8</td>
</tr>
<tr>
<td>Carbonated Beverage</td>
<td></td>
</tr>
<tr>
<td>Cola</td>
<td>2.5 – 5.4</td>
</tr>
<tr>
<td>Energy Drink</td>
<td>9.0 – 12.0</td>
</tr>
<tr>
<td>Chocolate</td>
<td></td>
</tr>
<tr>
<td>Syrup</td>
<td>10.0 – 17.0</td>
</tr>
<tr>
<td>Milk Chocolate</td>
<td>6.0 – 7.0</td>
</tr>
</tbody>
</table>

Experimental Protocol

N = 9 trained cyclists (2 females and 7 males)

Treatments:
1) Ingestion of 250 mg of CAF 60 min prior to the ride was followed by ingestion of an additional 250 mg fed at 15 min during the first 90 min of exercise
2) Placebo provided at same times.

Performance was determined by the amount of work production (kpm) during two hours of isokinetic cycling exercise (80 rpm).


Caffeine as an Ergogenic Aid for Aerobic Endurance

Mean Rating of Perceived Exertion

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Caffeine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>13.3</td>
<td>12.3</td>
</tr>
<tr>
<td>±</td>
<td>0.20</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Experimental Protocol

N = 8 trained cyclist

Exercise: 2 randomized and double-blind cycling trials at approximately 80% VO2 max

Treatments:
- a. placebo (PL, 9 mg/kg dextrose)
- b. caffeine (CAF, 9 mg/kg) 1 h before exercise

Muscle biopsies taken before exercise, 15 min after start of exercise and at exhaustion

More Contemporary Caffeine Research


Other Possible Mechanisms of Action of Caffeine

- Reduce perception of pain by elevating β-endorphins.
- Adenosine receptor binding
- Increase facilitation of muscle recruitment reducing the mental drive necessary for a given exercise intensity

The Effective Amount of Caffeine

Experimental Protocol

N = 8, well-trained runners
Treatments: Placebo, 3 mg/kg body wt, 6 mg/kg body wt, and 9 mg/kg body wt
Supplements were provided 1 hour before exercise
Exercise: Run to exhaustion at 85% VO₂ max

Effect of Regular Caffeine Use on Caffeine Supplement Response

Low and High Caffeine Users


Caffeine and Energy Expenditure

Subject (n = 14) received either a placebo or caffeine supplement (2 x 3 mg/kg) 90 min before and 30 min after 1 h of cycling at 65% VO2 max.

Results:
1. During exercise and a 2 h recovery period, caffeine increased energy expenditure and fatty acid oxidation about that of placebo.
2. Caffeine lowered hunger during recovery exercise and made exercise more enjoyable.

Summary
Caffeine may improve aerobic performance by several mechanisms, including:
1. Increasing fat oxidation and sparing muscle glycogen
2. Reducing sensation of effort (perceived exertion)
3. Maintaining high CNS drive by blocking adenosine receptors
4. Increasing muscle fiber recruitment

An effective dose of caffeine is 1.5 to 2 mg/kg body wt.

Dietary Nitrate and Nitric Oxide Production

What is Nitric Oxide?
- NO is a gaseous, inorganic, uncharged, diatomic molecule and a free radical with one unpaired electron in its external orbital. It is one of the most important signaling molecules in the body.
- Considered a major mediator of end-organ function, NO is synthesized on demand with specific biological effects.
- NO should not be confused with nitrous oxide (N2O), which is a poisonous air pollutant.

Effect of caffeine on cycling time trial performance in low and high caffeine users.

<table>
<thead>
<tr>
<th>Time to Finish (SEC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4500</td>
</tr>
<tr>
<td>4000</td>
</tr>
<tr>
<td>3500</td>
</tr>
<tr>
<td>3000</td>
</tr>
<tr>
<td>2500</td>
</tr>
<tr>
<td>2000</td>
</tr>
<tr>
<td>0</td>
</tr>
</tbody>
</table>

*Significant treatment effect
†Significant time effect

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Nitric oxide plays a key role in the regulation of numerous vital biological functions:

- Cardiovascular system
- Respiratory tract
- Immunology
- Cell proliferation
- Central nervous system
- Peripheral nervous system
- Gastrointestinal/urogenital tract
- Myocardial contractility
- Microvascular permeability
- Vasorelaxation
- Blood cell regulation
- Neuronal control
- Microscopic blood flow
- Learning and memory
- Pain sensitization
- Epilepsy
- Neurodegeneration
- Control of BP
- Central BP control
- Apoptosis
- Angiogenesis
- Tumor cell growth
- Unspecific immunity
- Inhibition of viral replication
- Transplant rejection
- Penile erection
- Birth control
- Pre-term labour
- Regeneration
- Mobilization of resident stem cells
- Targeted differentiation
- Skeletal muscle
- Mitochondrial efficiency
- Contractile properties
- Gastrointestinal/urogenital tract
- Fluid entry
- Permeability
- Respiratory tract
- Airflow resistance
- Immunologic
- Mucosal resistance
- Nitric oxide synthase

Limitations:
- Depends on a very complex enzyme that requires many co-factors that can be deficient in the diet.
- Enzyme requires adequate oxygen and is not very functional when oxygen tension declines to low levels such during exercise or at altitude.
- Enzyme does not function well at low pH.
- There is loss of enzyme function with age, i.e. reduced expression and uncoupling.
- *L-arginine Km for NOS is 5µM and plasma has 100µM. Usually L-arginine is not a limitation and supplementing with L-arginine has little effect.

Why would so important a process as generating a key ubiquitous signaling molecule like N-O be left up to such a fragile and complex reaction?
The reduction of nitrite to nitric oxide by reduced hemoglobin and reductase enzymes is most effective under low pH and hypoxic conditions making this NO pathway most effective during high intensity exercise and at altitude.

Dietary Sources of Nitrate and Nitrite

<table>
<thead>
<tr>
<th>Nitrate content (mg/100 g fresh weight)</th>
<th>Vegetable varieties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low, &lt;20</td>
<td>Artichoke, spinach, broad bean, eggplant, garlic, onion, green beans, mushroom, pea, pepper, potato, summer squash, sweet potato, zucchini, watermelon</td>
</tr>
</tbody>
</table>
The body converts dietary nitrate and nitrite to nitric oxide (NO), which supports the increasing blood flow to the active muscles. The effect during exercise is seen primarily in fast twitch – glycolytic fibers. This helps the body boost delivery of oxygen and nutrient to less oxidative muscle fibers, facilitating mitochondrial ATP production, which supports more intense workouts and increased stamina without excessive fatigue. Increased muscle blood flow also helps the body support a faster rate of recovery by increasing removal of metabolic waste products such as lactic acid and carbon dioxide and replenishing depleted fuel stores.

Nitric Oxide and Blood Flow

N-O Increases O₂ Efficiency

Nitric Oxide Increases Oxygen Efficiency. This means aerobic energy production in the mitochondria of the muscle is more efficient, i.e. the ATP production per unit of oxygen converted to H₂O is reduced. Reducing the O₂ cost of exercise is associated with greater endurance.

ATP Turnover Rate

N-O AND MUSCLE CONTRACTION

N-O improves energy efficiency. Improvement in exercise performance is related to the ability of NO to reduce the amount of ATP utilized per force generated by the muscles during exercise. This effect is seen at all exercise intensities and is the reason dietary nitrates have been found to improve exercise performance in all different types of sports such as cycling, running, rowing, swimming, team sports, resistance exercise, etc.
Acute Physiological Effects of N-O

- Increases vasodilation, thereby facilitating blood flow to the working muscles. This increases \( \text{O}_2 \) and nutrient delivery to the muscles and the rapid removal of metabolic waste products.
- Increases the efficiency of the mitochondria to use \( \text{O}_2 \) for energy production decreasing the \( \text{O}_2 \) cost of exercise.
- Increases the energy efficiency of the muscle to generate force, i.e., less ATP per unit of force generated.

Pharmacodynamics and dose-response to dietary nitrate

Conclusions

- Nitric oxide can be produced by conversion of L-arginine to L-citrulline via NOS, and the conversion of nitrate to nitric oxide.
- Dietary nitrate can improve exercise performance at all exercise intensities.
- Acutely, dietary nitrates provided before exercise increase blood flow to fast twitch-glycolytic muscle, increase \( \text{O}_2 \) efficiency and decrease the energy cost of exercise.
- Consumption of approximately 8 mmol of nitrate about 2.5 h before exercise are required to see an enhancement in exercise performance.
- The effect is most prominent in less fit and older individuals.

Nitric Oxide Products

- Citrulline are not effective N-O boosters, particularly during exercise.
- Not all beet products (vegetable products) have sufficient nitrate to increase N-O.
- Where and when the beets are grown and how they are cultivated will affect the nitrate levels.
- The manufacturing process will also affect nitrate levels (nitrate is heat sensitive).
Ergogenic Aid for High Intensity Exercise

**β-alanine**

**Metabolic Buffers**

Physico-chemical H⁺ buffers: Carnosine

A dipeptide of histidine with β-alanine. Bonding β-alanine raises the pKa of the imidazole ring from 6.1 to 6.83.

β-alanine is a non-proteogenic amino acid and renders the HIS inert to further involvement in protein building or to the action of cellular proteases. Therefore cells can accumulate high concentrations without affecting other processes.

Carnosine: Variation With Chronic Training


<table>
<thead>
<tr>
<th></th>
<th>Untrained</th>
<th>Body Builders</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>26 ± 4</td>
<td>31 ± 3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>178 ± 8</td>
<td>181 ± 3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78 ± 12</td>
<td>106 ± 2</td>
</tr>
<tr>
<td>In training</td>
<td>6</td>
<td>13.7 ± 7</td>
</tr>
<tr>
<td>Carnosine</td>
<td>19.8 ± 3.3</td>
<td>43.0 ± 8.3</td>
</tr>
</tbody>
</table>

Mean Lowest Highest 14.9 38.1 24.2 50.9

P < 0.001

Influence of β-alanine supplementation on skeletal muscle carnosine concentrations and high intensity cycling capacity

**Purpose**

- Study the effects of β-supplementation on muscle carnosine levels
- Determine if β-alanine supplementation improve high intensity cycling performance

**Methods**

- 25 physically active male subjects
- Treatments
  - β vs PLA
  - Supplement for 4 or 10 wks
- Muscle biopsies
  - Pre, 4 wks and 10 wks post
- Cycle performance test at 110% Wmax
  - Pre, 4 wks and 10 wks post

**Meta-Analysis on β-Alanine and Exercise Capacity and Performance**

- Evaluated 15 studies
- The analysis was limited to human studies using a placebo control, double blinded trials, published in English in a peer reviewed journal, and β-alanine was the only supplementation group.
- Analysis was divided into exercise lasting <60 s, between 60 – 240 s, and >240 s
- * Overall 2.85% improvement in exercise response was found

**Effective Dosage**

- 6.4 g/d for 28 days maximizes the carnosine concentration in skeletal muscle
- Must be provided in divided dosages (≤800mg) because of paraesthesia around the face, back of neck and arms and hands
- Time-released β-alanine (CarnosynSR™) allows the dosage to be doubled and total daily volume reduced to 3.2 g/d.
- A maintenance dosage of 1.6 g/d will keep carnosine levels elevated in the muscle.
Conclusions

• β-alanine can improve high intensity exercise by 2.85%
• The effect is more related to an increase in exercise capacity rather than performance
• It is most effective for exercises lasting between 60-240 sec

Ergogenic Aids to Increase Muscle Fitness and Mass

Effect of Protein + Leucine


Experimental Protocol

- N = 40. Randomly divided into treatment groups
- Preformed unilateral knee-extension exercise
- Received treatments before exercise while fasted and following resistance exercise
- Treatments:
  - Placebo
  - 6 g whey protein
  - 6 g whey protein + low Leucine (total 3 g)
  - 25 g whey protein
  - 6 g whey protein + BCAA (total Leucine 5 g)
  - 6 g whey protein + high Leucine (total Leucine 5 g)

Effect of β-hydroxy-β-methylbutyrate (HMB) on Protein Synthesis and Degradation

Leucine Metabolism

Leucine is a branch chain amino acid

HMB is a downstream metabolite of L-leucine

Nissen et al. JAP 81: 2095-2104, 1996

- and protein levels were 117g/d or 175 g/d. Subjects lifted for 1.5 h/d, 3d/wk for 3 wk.
- Study 2 – HMB given 0 or 3.0 g/d. Subjects lifted 2-3 h/d, 6 d/wk for 7 wk.
Study 1 Total Strength

![Study 1 Total Strength Graph]

Fat Free Mass in Study 2

![Fat Free Mass Graph]

Studies that Support the Use of HMB

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Design/Duration</th>
<th>Performance</th>
<th>Body Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nissen et al. (34)</td>
<td>0.5 or 3 g/day for 7 weeks.</td>
<td>Greater total weight lifted, dose-dependent.</td>
<td>Greater LBM, dose-dependent II.</td>
</tr>
<tr>
<td>Van Someren et al. (91-93)</td>
<td>3 grams of HMB and 0 grams of BC, 1 tablet 3 times daily, for 12 weeks.</td>
<td>Greater I-RM bench press and squat, lower DOMS.</td>
<td>NR</td>
</tr>
<tr>
<td>Gallagher et al. (94)</td>
<td>50 mg or 75 mg/day for 4 weeks.</td>
<td>Greater muscle mass &amp; endurance, dose-dependent, independent of dose.</td>
<td>NR, no effect on FMI, independent of dose.</td>
</tr>
<tr>
<td>Neissen et al. (28)</td>
<td>0.625 or 3 g/day for 4 weeks.</td>
<td>Greater bench press II-RM.</td>
<td>Increase in LBM &amp; FMI.</td>
</tr>
<tr>
<td>Neissen et al. (63)</td>
<td>0.625 or 3 g/day for 4 weeks.</td>
<td>Greater leg extension strength.</td>
<td>NR</td>
</tr>
<tr>
<td>Neissen et al. (41)</td>
<td>0.625 or 3 g/day for 4 weeks.</td>
<td>Greater leg extension strength.</td>
<td>NR</td>
</tr>
<tr>
<td>Neissen et al. (32,37)</td>
<td>3 grams of HMB and 0.3 grams of KIC, prior to a single bout of eccentric exercise.</td>
<td>Greater I-RM bicep curl and ROM, lower DOMS.</td>
<td>Greater I-RM bicep curl and ROM, lower DOMS.</td>
</tr>
</tbody>
</table>

Interaction of Leucine and HMB on Signaling Proteins Controlling Protein Synthesis and Degradation

![mTOR Signaling Pathway Diagram]
Summary for Leucine and HMB

- Leucine can increase muscle protein synthesis post resistance exercise and possibly work additively with protein.
- 3 to 4 grams of leucine are required to turn on protein synthesis.
- HBM, a metabolite of leucine, can enhance muscle mass development and strength during resistance training.
- 3 grams per day appears optimal.
- The mechanism of action is to reduce the rate of protein degradation and not an increase in protein synthesis.
- Protein or leucine supplementation with HMB should have an additive effect on protein accretion during resistance training.