The Science of Energy Drink Efficacy, Safety, and Mechanisms of Action

J. Mark Davis, Ph.D.
Professor
Department of Exercise Science
Arnold School of Public Health
University of South Carolina
Columbia, SC
markd@mailbox.sc.edu

OBJECTIVES

- At the end of this session, the participant will:
  - Be able to identify the ingredients of most energy drinks/shots and recognize the few that are likely to produce most of the benefits and/or negative side-effects.
  - Appreciate what little is available with respect to the science of Energy Drinks.
  - Understand the underlying mechanisms for the “energy” produced by energy drinks and how this translates into possible benefits to mental and physical performance.
  - Learn about an exciting new ingredient for use in energy drinks that appears to enhance energy in a different way with much less side effects than caffeine.
  - Translate information learned in this session to advise clients, parents and active people on the positive and negative effects of caffeine and energy drinks.

Common Ingredients in Energy Drinks
(Campbell, et al., 2013)

Common Ingredients in Energy Shots
(Campbell, et al., 2013)

Ingredients in Energy Drinks – CNS Stimulants
(Campbell et al., 2013)

DISCLOSURE

J. Mark Davis, Ph.D.

- Past Board Member/Advisory Panel
  - American College of Sports Medicine Board of Trustees
  - Gatorade Sports Science Institute Science Advisory Board
- Consultant
  - Scientific Advisor, The FRS Company
- Present and Past Research Support
  - American College of Sports Medicine Foundation
  - National Institutes of Health (NIH)/National Cancer Institute (NCI)
  - Defense Advanced Research Projects Agency (DARPA)
  - Department of Defense – Army (DoD)
  - Gatorade Sports Science Institute (GSSI)
Ingredients in Energy Drinks – Cognitive Enhancers (Campbell, et al., 2013)

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Potential ergogenic value</th>
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<tbody>
<tr>
<td>Taurine</td>
<td>Improved mental focus, concentration, serve as antioxidant, glucose homoeostasis (21-24)</td>
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<tr>
<td>Gingsko Biloba</td>
<td>Improve memory and mental concentration</td>
</tr>
<tr>
<td>L-Tyrosine</td>
<td>Prevents depletion of catecholamines, may attenuate decline in cognition with acute stress (40-47)</td>
</tr>
<tr>
<td>Citrulline</td>
<td>Intermediate in the generation of phosphadialcholine from choline.</td>
</tr>
<tr>
<td>S-Hydroxy-L-Tryptophan (S-HTP)</td>
<td></td>
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<tr>
<td>St. John’s Wort</td>
<td>Anti-depressant (56-58)</td>
</tr>
</tbody>
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Summary of Physical Performance Studies

- MacRae & Mefferd, 2006. FRS 30 km cycling time trial
- Del Cosa, et al., 2012. Red Bull sprint speed, distance covered & jump height in simulated soccer game
- Gwacham & Wagner, 2012. AdvoCare Spark sprint performance & anaerobic power
- Astorino, et al., 2012. Red Bull repeated sprinting
- Candow, et al., 2009. SF Red Bull run time to exhaustion

Summary of Cognitive Function Studies

- Overwhelming lack of evidence to substantiate claims that components of Energy Drinks, other than caffeine, contribute to the enhancement of physical and/or cognitive performance (Campbell, et al., 2013; McLellan & Leiberman, 2012; Higgins, et al. 2010).

Unresolved Issue/Future Directions

- Experimental Design
  - Sample size
  - Cross-section/Cross-over
- Inconsistent Methodologies
  - Dose/timing/acute/chronic
  - Test compound/mixtures/delivery vehicle (bioavailability)
  - Environmental factors
  - Performance tests
  - Other parameters measured (sensitivity/specificity)
- Subject Characteristics
  - Human/rodent (individual variability in bioavailability)
  - Trained/untrained
  - Old/young
  - Male/female
  - Healthy/disease

CAFFEINE

- Dates back 4700 y
- Most widely consumed, behaviorally active food component/drug in the world.
- 80% of US adults use (~200-300 mg/d)
- Scandinavians highest per person: 400 mg/d
- Ergogenic dose 3-6 mg/kg (~200-500 mg), 30-60 min before event (Higher Doses can be Dangerous)
- Side effects: dizziness, nausea, tremor, anxiety, death
- Former IOC ban: > 12 µg/mL urine (~6-9 cups coffee = 700-900 mg)
- Half-life = 3-6 h; Effect time: 2-4 h

Caffeine Effects in Elite Athletes


<table>
<thead>
<tr>
<th>Time to Exhaustion (min)</th>
<th>Placebo</th>
<th>Caffeine (9 mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Run</td>
<td>50</td>
<td>60</td>
</tr>
<tr>
<td>Cycle</td>
<td>50</td>
<td>60</td>
</tr>
</tbody>
</table>

Caffeine Effects in Elite Athletes

Time to Exhaustion (min)

Placebo vs Caffeine (9 mg/kg)
Caffeine and Mental Function - Summary

- Caffeine has stimulant-like effects on mood and cognitive performance
- Caffeine also can decrease pain perception, force sensation and perceived exertion
- Beneficial effects are well documented
  - in rested and sleep-deprived individuals in doses found in single servings of foods (approx 100 mg)
  - during exercise higher doses are typically used, but benefits are still observed at low doses (150 – 300 mg)
  - however, there can be large individual differences in optimal doses
- At high doses, side effects can be detrimental to mental performance and health

THEORETICAL CAFFEINE MECHANISMS

- ↑ ADRENALINE?
- ↑ USE OF FAT/↓ USE OF GLYCOGEN?
- ↑ Ca++ SUPPLY TO MUSCLES?
- ↑ CNS STIMULATION (block adenosine receptors)

CNS Effects of Caffeine and Adenosine on Fatigue During Prolonged Treadmill Running

Results Involving Brain Injections

Run Time to Fatigue With i.c.v Injection (n = 10)

P<0.001

Common Caffeine Products

- Energy Drinks
- Energy Bars
- Gum
- Supplements (pills or powder)- often with other stimulants

Safety

Caffeine/Ephedrine/Amphetamine/Cocaine Side-Effects

LOW

- Insomnia
- Tremors
- Anxiety
- Irritability
- Headaches
- GI distress/nausea

HIGH

- Diuresis
- Tachycardia
- Arrhythmia
- Hypertension
- Dependence
- Seizures, coma, death

Caffeine, Electrolyte Balance in Body Fluids, and Exercise Performance

- Recommendation to entirely avoid caffeinated beverages during exercise is unsupported (AT LOW - MODERATE doses)
  - Moderate daily intake of caffeine stimulates a mild diuresis similar to water, with no evidence of fluid-electrolyte imbalances detrimental to exercise performance and health
  - Caffeinated beverages are similar to water in terms of retention of volume consumed (at rest or during and after exercise)
  - No evidence of detriments in CV or thermoregulatory function with caffeine consumption during exercise in hot environments


GENERAL ADVICE ON USE OF CAFFEINE

- BE CAREFUL
  - Don’t expect miracles
  - Effects are highly variable among individuals
  - Avoid excessive doses that will do no good and are likely to be harmful, ESPECIALLY WHEN TAKEN WITH OTHER STIMULANTS
  - Avoid during multiple practice/competition days, especially when it’s hot (i.e., two-a-days in football)
  - Maintain hydration

Effects of caffeine, ephedrine and their combination on time to exhaustion during high-intensity exercise

Be careful of dangerous side-effects when mixing caffeine and other stimulants like ephedrine


Caffeine/Ephedrine Substitutes

- Bitter Orange - Green Orange, Kitjitsu, Citrus Aurantium, synephrine
- Tea - English Tea, Chinese Tea, EGCG
- Cola Nut - Bissy Nut, Cola Nut, Guru Nut, Kola Nut
- Ginseng - American Ginseng, Panax Ginseng
- Guarana - Brazilian Cocoa, Paullinia, Zoom
- Mate - Yerba Mate, Jesuit’s tea, Nervea
- Ephedra - MaHuang, Sida cordifolia

Quercetin

- Flavonol consumption by U.S. adults is approximately 20-50 mg/day (quercetin 3/4s this amount)
- Apples, onions, berries, red grapes, black tea, and other fruits and vegetables are sources of quercetin. One large red apple has ~10 mg quercetin.
- Quercetin is absorbed with reported plasma half-lives of 6 to 12 hours.
- It’s SAFE (Food Additive in Japan, Supplement in US (GRAS); FDA-notified GRAS approval)

Quercetin Can Increase Mitochondria in Muscle and Brain in rodents

- Ingestion of as little as 12.5 mg/kg in mice and rats (~875mg in humans) of quercetin for 7 days can increase mitochondrial mass/enzymes 25 - 100% in skeletal MUSCLE, LIVER, and BRAIN.
- Effects are lost after 7 days without Q.

Davis, Am J Physiol. 2008
Quercetin Can Increase VO$_2$max and Endurance Performance in Mice and humans

- 7d of Quercetin feeding was associated with
  - Increased endurance performance during force treadmill running and voluntary wheel running in sedentary mice
  - Increased VO$_2$max and endurance cycling in young healthy, but untrained, humans.

Davis, Am J Physiol. 2008
7-day Quercetin (1000mg/d) Increased Maximal Aerobic Power (~3.9% in Humans)

7-day Quercetin (1000mg/d) Increased Endurance Cycling Capacity (~13% in Humans)

Summary of Human Quercetin Studies
- MacRae & Mefferd, Int J Sports Nutr Exerc Metab 2006 (30 km cycling time trial)
- Davis, et al., Am J Physiol. 2009 (run time to fatigue & voluntary activity)
- Cheuvront, et al., Am J Physiol. 2009 (15 min cycle time trial after 30 min submaximal exercise in the heat)
- Cureton, et al. J Appl Physiol. 2009 (10-min time trial & VO2max)
- Neiman, et al. Med Sci Sports Exerc. 2010 (10-min run time trial after 60 min submaximal run)

fMRI study of the effects of quercetin and caffeine on brain activation during exercise in a fatigued state

Global Effects of Quercetin and Caffeine
- Caffeine > Placebo & Quercetin > Placebo
- Caffeine = Red
- Quercetin = Green
- Overlap = Yellow

PRACTICE APPLICATIONS
- Be aware that of the many ingredients in energy drinks/shots it's the caffeine and caffeine-like ingredients that are providing the energy (primarily mental energy). The other ingredients provide at best trivial benefits.
- Make a point to advise others of the ingredients that have caffeine-like effects that can easily add to the side effects of caffeine.
- Low to moderate doses of caffeine (100 – 500 mg) are generally safe and can lead to increased mental and physical performance in healthy, relatively fit individuals. Higher doses can impair performance and are dangerous.
- The dietary flavonoid Quercetin is a newcomer to energy drinks and is gaining a lot of attention in the scientific community for its ability to increase mental and physical energy differently than caffeine and is safe.