SUPPLEMENT SAFETY AND REGULATION

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OVERVIEW

• Supplement safety is an issue for any athlete

• A dietary supplement with illegal or harmful ingredients can cause serious health issues

• Dietary supplements are not well regulated within the US although steps are being taken to improve regulation

• There are scenarios when dietary supplementation may be beneficial for athlete
PRACTICAL ISSUES IN EVIDENCE-BASED USE OF PERFORMANCE SUPPLEMENTS: SUPPLEMENT INTERACTIONS AND REPEATED USES

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- Current sports nutrition guidelines recommend that athletes consume supplements following an evidence-based analysis of their use in supporting training outcomes or competition performance in their specific event.
- While there is sound evidence to support the use of certain performance supplements under specific scenarios (e.g., creatine, caffeine, β-alanine, β-hydroxy β-methyl butyrate, and perhaps, phosphatidylcholine), more research is needed around several challenges, including their real-world use in competitive sport.
- There is limited knowledge around the synergistic and antagonistic effects of several supplements in events in which performance benefits are seen with each product in isolation. Supplement combinations have the potential to produce additive, multiplicative, or subtractive outcomes.
- The repeated use of the same supplement in sports involving two or more events within 24 h is usually allowed in most regulations, but has been met with less enthusiasm in theory, protocols for subsequent use may need to be adjusted to account for effects arising from their recent activity from the first dose or a desensitization effect.

INTRODUCTION

Although there is concern about the indiscriminate use of performance supplementation by athletes, many expert groups now take a pragmatic approach to the use of products and protocols which have passed a validation analysis of being safe, effective, and legal, while also being associated with the athletes' age and maturation in their sport (NSP Sports Nutrition Framework). Indeed, a number of supplements have received various labels from sports scientists to produce substantial evidence of the scenarios in which they can enhance sports performance. These include caffeine (Burke et al., 2013), creatine monohydrate (Burke et al., 2007), carbohydrates (Carre et al., 2011b), beta-alanine (Burke et al., 2010), and beetroot (Juiz et al., 2014). This work was reviewed by a recent consensus conference and the accompanying published statement as it applies to the high-performance athlete (Burke et al., 2017).

Although there is general support for the limited uses of these performance supplements, several issues related to their real-life use is competitive sport remain unclear or ignored. These include the additive and interactive effects of combining the use of several performance supplements for a single event as well as the repeated use of performance supplement in sports which require several events or events within 24 h. The Sports Science Exchange article will examine the current state of knowledge around these issues, with focus on the performance supplements which were previously identified as having support for their benefits to performance or a single competitive event.

POTENTIAL OUTCOMES FROM COMBINING THE USE OF SEVERAL SUPPLEMENTS

Supplements can enhance performance of specific events by mechanisms including increased substrate availability, reduced perception of pain or effort, buffering of metabolites to muscle pH, increased efficiency of muscle contraction. Some sports events can benefit from several of these effects and studies may show that different supplements can improve performance when used in isolation. Therefore, there is some logic to taking the use of these supplements in combination, in some events, in fact, it is possible that at least four identified performance supplements exhibit additive - for example, in iron, a 2000 m running event might benefit from beetroot juice, caffeine, β-alanine, and creatine supplementation. It would take enormous organization to conduct a study in which the separate and combined effects of each of these products could be investigated. Therefore, it is not surprising that the existing branches of research have only tackled independent and additive effects of two supplements to date. A range of possible outcomes could be expected:

- The supplements work by different mechanisms and the combination effects are additive.
- The supplements work by different mechanisms and the combined effects cancel each other out to have an additive effect.
- The supplements work by different mechanisms but the combination interacts in a negative way to reduce the benefit.
- The supplements work by the same mechanisms and the combination can be additive, neutral or counterproductive.

The available literature on the single and additive effects of well-known performance supplements is predominantly intuitive. Competitive sports is summarized in table 1 (supplements which have similar mechanisms of action) and Table 2 (supplements which have different mechanisms of action). Beta-alanine (monohydrate and b-carnitine-acetyl-glutamate protocol) are on obvious combinations, providing a potential benefit to events that are limited by excessive hydrogen ion production.
What is a supplement?

Classified by the US Food and Drug Administration

- Vitamins
- Minerals
- Herbs or other botanicals
- Amino acids
- Other dietary substances
- Any concentrate, metabolite, constituent, extract, or combination of these ingredients
~$40 Billion Industry in the United States
Top Supplements Used

- Multivitamins
- Vitamin C
- Protein Products
- Sports Drinks
- Sports Bars
- Energy Drinks

58-62% of athletes use some variety of dietary supplement

Positive Drug Tests can result in:

- Loss of scholarship
- Ban from play
- Stripping of medals
- Monetary fines
1994: Dietary Supplement Health and Education Act Passed
Supplements do not need to be proven safe or effective before entering the market.

Good manufacturing practices are difficult to enforce.

Supplement must be proven unsafe before the FDA can require its removal from the market.
Dietary Supplement Recalls – Top 3 Categories

Muscle Building → steroids

Weight loss → prescription appetite suppressants, stimulants & laxatives

Sexual Enhancement → active ingredients in several commonly prescribed medications

[Source: https://www.accessdata.fda.gov/scripts/sdra/sdnavigation.cfm?sd=tainted_supplements_cder]

Class I recalls

Class I: there is reasonable probability that the use or exposure to a product will cause serious adverse health consequences or death.

HEALTH CONCERNS
Cardiovascular issues

- Hypertension, cardiac issues and death have all been reported with dietary supplement use.

Renal Issues

- Kidney damage can occur, especially with supplements that contain herbs.

Hepatic Issues

- ~20% of drug induced liver injuries are from dietary supplements.

Seizures

- Acute neurotoxicity can occur after ingestion of dietary supplements with sympathomimetic properties.

Medication Interactions

- Athletes are not always truthful with healthcare providers when discussing supplements. There can be potential interactions between supplemental ingredients and medications.
Tolerable Upper Limits (UL) are the highest level of nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals in the general population.

As intake increases above the UL, the risk of adverse effects increases.
Excess intake of the water-soluble vitamins is less of a concern because generally excess is excreted in the urine.

In some instances, supplementation with certain water-soluble vitamins can be toxic.

Fat soluble vitamins as well as minerals are not as easily cleared by the body and can become toxic at high levels.

Symptoms of toxicity include but are not limited to: changes to vision, bone and joint pain, skin changes, muscle weakness, diarrhea, increased risk of bleeding, skin flushing, heart arrythmias.

<table>
<thead>
<tr>
<th>Water-Soluble Vitamins</th>
<th>Fat-Soluble Vitamins</th>
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<tbody>
<tr>
<td>Vitamin C</td>
<td>Vitamin A</td>
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<tr>
<td>Thiamin (B1)</td>
<td>Vitamin D</td>
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<tr>
<td>Riboflavin (B2)</td>
<td>Vitamin E</td>
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<td>Niacin (B3)</td>
<td>Vitamin K</td>
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<td>Pantothenic Acid (B5)</td>
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<td>Vitamin B6</td>
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<td>Biotin</td>
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<td>Vitamin B12</td>
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<td>Folic Acid</td>
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• Communicate more quickly when unlawful or potentially dangerous products are marketed as dietary supplements
• Balance Safety and Innovation in the regulatory framework
• Work closely with industry partners to protect public health and safety and support evaluation of new products
• Take action to protect public health and develop new enforcement strategies
• Engage in public dialogue around additional steps to modernize DSHEA are necessary
WHICH SUBSTANCES ARE BANNED?
THE WORLD ANTI-DOPING CODE
INTERNATIONAL STANDARD

PROHIBITED LIST
JANUARY 2020

https://www.wada-ama.org/en/content/what-is-prohibited
• **Anabolic Agents**
  - Anabolic androgenic steroids
  - Other anabolic agents

• **Peptide hormones, growth factors, related substances or mimetics**
  - Erythropoietins (EPO) & agents affecting erythropoiesis
  - Peptide hormones & releasing factors
  - Growth factors & growth factor modulators

• **Beta-2 agonists**

• **Hormone and metabolic modulators**
  - Aromatase inhibitors
  - Selective estrogen receptor modulators
  - Anti-estrogenic substances
  - Agents preventing activin receptor IIB activation
  - Metabolic modulators

• **Diuretics or masking agents**

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WADA PROHIBITED AT ALL TIMES

• Stimulants
  • Specified and non-specified ingredients

• Narcotics

• Cannabinoids
  • All natural and synthetic cannabinoids except cannabidiol

• Glucocorticoids
PROHIBITED IN PARTICULAR SPORTS

Beta-Blockers – 19 substances

• Acebutolol, alprenolol, atenolol
• Betaxolol, bisoprolol, bunolol
• Carteolol, carvedilol, celiprolol
• Esmolol, labetalol, metipranolol
• Metoprolol, nadolol, oxprenolol
• Pindolol, propranolol
• Sotalol, timolol

Sports

Archery
Automobile
Billiards
Darts
Golf
Shooting
Skiing/Snowboarding
Underwater sports

https://www.wada-ama.org/en/content/what-is-prohibited/prohibited-in-particular-sports
Drug Free Sport International

Drug testing  Education  300

https://www.drugfreesport.com/
• Drug testing
• Supplement 411
• Education
  • Testing policies, procedures & exemptions
  • Bringing attention to the impact inadequate drug testing and/or punishment for doping has on clean athletes

https://www.usada.org/
NIH Office of Dietary Supplements
https://ods.od.nih.gov/

Medline Plus for Herbs and Supplements
https://medlineplus.gov/druginfo/herb_All.html

Natural Medicines Database
https://naturalmedicines.therapeuticresearch.com/
SUPPLEMENT EFFICACY
Athlete goals vs. Demands of the athletes’ sport
Generally, a well-balanced diet that meets caloric needs allows the athlete to get adequate macro and micro-nutrients from whole foods.
Is the athlete meeting basic needs?

- What does the overall diet looks like?
- Can the training program be optimized further to meet goals?
- Is the athlete getting adequate sleep to support recovery?
POTENTIAL BENEFITS
Micronutrient Deficiencies

Supplementation is recommended when the athlete has or is attempting to prevent a diagnosed micronutrient deficiency.
The International Olympic Committee has identified a group of supplements that have evidence to support a performance benefit.

- Caffeine
- Creatine monohydrate
- Nitrate
- Sodium bicarbonate
- Beta-alanine


• Be aware of the FDA’s dietary supplement labeling laws
• Watch out for “proprietary blends”
• Check serving size
• Examine amount per serving of desired ingredient(s)
• “Filler” or cheaper ingredients may be used

IDENTIFYING SAFER SUPPLEMENTS
- Big claims
- Promise quick and unrealistic results
- “Alternatives” to prescription drugs
- Proprietary blends
Recommendations for 3rd party supplement testing

- Certifying program and labs accredited to ISO 17065
- Certifying program controls their certification mark
- Impartiality and written conflict of interest policies
- Methods to revoke certification and inform consumers
- Complaint and appeals process for clients
- Program certifies against NSF/ANSI 173
- Testing programs that certify ingredients, batches of products, and/or manufacturing facilities
- Athletes or athletic staff can send samples to independent labs for testing
NSF Certified for Sport

- Products do not contain any of approximately 270+ substances banned by major athletic organizations.
- The contents of the supplement actually match what is printed on the label.
- There are no unsafe levels of contaminants in the tested products.
- The product is manufactured at a facility that is GMP registered and audited twice annually for quality and safety by NSF International.
Example 2: Informed Choice

- Certified finished products – full manufacturing audit and regularly tested for a wide variety of WADA banned substances.
- Certified raw ingredients – full manufacturing audit and every batch is pre-market tested for a wide variety of WADA banned substances.
- Certified sites – assurance that facilities are equipped with adequate critical control procedures.

https://www.informed-choice.org/
Supplement safety is a huge issue for any athlete.

- A positive drug test can have serious consequences on an athlete’s health and career.
- A dietary supplement with illegal or harmful ingredients can cause serious health issues.

Dietary supplements are not well regulated within the US although steps are being taken to improve regulation.

There are scenarios when dietary supplementation may be beneficial for athletes from either a health or performance standpoint.

There are 3rd party testing organizations that help practitioners and athletes identify supplements that meet strict quality-controlled standards.