Evidence Based Approach to the Use of Dietary Supplements as Ergogenic Aids in Athletes.

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Declaration of Conflict of Interest:

- No Conflict: Elizabeth Tenison
  - The views presented in these slides and in today's discussion are mine.
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  - The views presented in these slides and in today's discussion are mine.
  - My views may not be the same as the views of my company's clients or those of my colleagues.
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Symposium Session Agenda:

- Fill the knowledge gap regarding efficacy of ergogenic dietary supplements with the goal of helping athletic trainers to remain current and up-to-date.
- Provide an evidence based review of the emerging ergogenic dietary supplements in comparison with a "food first" approach.
- Provide guidance on how to evaluate supplements in order to provide sound recommendations to athletes.

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Learning Objectives:

1. Recognize emerging dietary supplements in the field of performance nutrition.
2. Demonstrate how to evaluate ergogenic dietary supplements for efficacy.
3. Select ergogenic dietary supplements with evidence based efficacy regarding athletic performance and muscle soreness.

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What is Sports Nutrition/ Performance Nutrition?

Specialized branch of nutrition that studies food with relevance to athletic performance.

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Signs An Athlete May Need to Improve Their Nutrition

- Training hard but not improving performance.
- Feeling tired or "run down" all the time.
- Early fatigue during games or intense practices.
- Excessive cramping and/or soreness of muscles.
- Frequent injuries.
- Lengthy recovery time from injury or simply from one game to the next.
- Frequent illnesses such as always seeming to have a cold.
- Frequent headaches.
- Legs feel heavy or weak during exercise.

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Healthy Eating Snapshot for Athletes

1. Follow a healthy eating pattern and appropriate distribution of calories from the macronutrients ("MACROS").
2. Aim for 3 balanced meals and 2-3 snacks per day. Don't skip breakfast!!
3. Focus on whole grains, fruits, vegetables ["eat the rainbow"], lean protein and healthy fats!
4. Limit processed foods and foods high in calories from added sugars, trans-fats and saturated fats.
5. Stay hydrated! Drink water throughout the day and leave the sports drinks to before, during and/or after training, events, and games.

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Helpful Resources on Sports Nutrition To Provide Guidance to Athletes and Professionals Working with Athletes

Recommendations and Guidelines on Sports Nutrition Topics

- Academy of Nutrition and Dietetic's Practice Group Sports, Cardiovascular and Wellness Nutrition[SCAN]
  - www.scandpg.org/
  - Resources and Fact Sheets
- Collegiate and Professional Sports Dietitians Association [CPSDA]
  - www.sportsrd.org/
  - Resources and Fact Sheets
- United States Olympic Committee [USOC]
  - www.teamusa.org
  - Resources and Fact Sheets
- National Athletic Trainers Association [NATA]
  - www.nata.org
  - Resources and Fact Sheets

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Practice Application: Why Should Athletic Trainers Care About Sports Nutrition and Dietary Supplements?

- Value of optimal nutrition in sports performance has been acknowledged within the field of athletic training evidenced by the incorporation of a general nutrition content area to the Athletic Training Education Competencies.
- NATA's Position Statement: "Evaluation of Dietary Supplements for Performance Nutrition" further emphasizes the value of optimal nutrition and a "food first" approach[1].
- ATs are often the ones with the most frequent contact with the athletes.
- Athletes are susceptible to supplement marketing due to the desire to gain a competitive edge and most athletes are not well informed on this issue.
- Any nutrition information disseminated to the athletes must be accurate especially regarding questions about ergogenic dietary supplements.

[1]Buell ,JL., et al. (2013). National Athletic Trainers' Association Position Statement: Evaluation of Dietary Supplements for Performance Nutrition. Journal of Athletic Training, 48(1), 124-136.

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Current Status of Dietary Supplement Intake Among Competitive Athletes

- According to a recent systematic review and meta-analysis by Knapik et al (2016[1]) which reviewed 159 studies internationally with sample sizes ranging from 12-2297:
  - Overall prevalence= ~60% of any dietary supplement [range 4-100%].
  - Vitamin and Mineral= 42%.
  - Specific vitamin or mineral= 40%.
  - Amino acids or protein= 52%.
  - Creatine= 31%.
  - Herbal=17%.
  - Sports drinks= 21%.
  - Sports bars= 11%.
  - Omega 3 fatty acids=7%.
  - Caffeine= 5%.
  - Energy drink= 4%.
- In comparison to NHANES[2] (U.S. general population):
  - Overall prevalence= 42-54%.
    - Mainly from vitamin and mineral supplements with only 1% attributed to amino acids.

[1]Knapik JJ., et al. (2016). Prevalence of Dietary Supplement Use by Athletes: Systematic Review and Meta-Analysis. Sports Med, 46, 103-123.
[2]Timbo BB, et al. (2006). Dietary supplements in a national survey: prevalence of use and reports of adverse events. J Am Diet Assoc. 2006;106:1966-74.

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Definition of Dietary Supplement[1]

- The law defines dietary supplements in part as products taken by mouth that contain a "dietary ingredient." Dietary ingredients include vitamins, minerals, amino acids, and herbs or botanicals, as well as other substances that can be used to supplement the diet.
- Dietary supplements come in many forms, including tablets, capsules, powders, energy bars, and liquids.
  - Note: an ergogenic aid refers to anything other than actual training that purports to enhance or improve athletic performance.

[1]www.fda.gov

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Regulation of Dietary Supplements[1]

- Dietary Supplement Health and Education Act of 1994 [DSHEA].
- 1994 statute of United States Federal legislation which defines and regulates dietary supplements.
- Regulated by the Act under the FDA for Good Manufacturing Practices (21 CFR Part 111).
- Defines supplements as “food” and not “drugs”; different than other countries.

[1]https://www.congress.gov/bill/103rd-congress/senate-bill/784/text

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Regulation of Dietary Supplements
KEY POINTS

- No evaluations of effectiveness or safety prior to a product entering the market.
- Law does not include a requirement for a manufacturer to provide evidence of effectiveness or safety.
- Only way to remove a product from the market, is AFTER it is proven unsafe.
- The question of purity is of upmost importance to athletes in which contamination with regulated and/or banned substances can jeopardize their eligibility.
  - Can happen intentionally by a manufacturer or can happen inadvertently through the manufacturing process.
  - Common occurrence with supplements designed for weight loss and the building of muscle.

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Need to Ask Specific Questions For Each Supplement

START HERE! ➡ Is the athlete's diet currently adequate, well balanced and optimized for performance within their sport and training regimen? If yes, then consider questions 1-3.

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Helpful Resources Provide Guidance to Athletes and Professionals Working with Athletes

Supplement Certification, Purity, Safety

- National Sanitation Foundation [NSF] Certified for Sport® – considered the "gold standard"
  - http://nsfsport.com
  - New Certified for Sport® App
  - Available on the website-White paper illustrating just how common it is for supplements to be contaminated with potentially harmful substances and the need for Good Manufacturing Practices.
- Informed Choice
  - http://www.informed-choice.org
- Consumer Lab
  - www.consumerlab.com
- US Pharmacopeia
  - www.usp.org
- FDA
  - www.fda.gov
  - Adverse event reporting, recalled products, regulatory after-market action against companies etc.

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Helpful Resources Provide Guidance to Athletes and Professionals Working with Athletes

Regulations and Banned Substances

- National Collegiate Athletic Association [NCAA]
  - www.ncaa.com
  - Permissable and Non-permissible Lists
  - Banned Substances List
  - https://dfsaxis.com [Drug Free Sport Axis]
- International Olympic Committee [IOC]
  - https://www.olympic.org/the-ioc
- World Anti-Doping Agency [WADA] and US Anti-Doping Agency [USADA]
  - www.wada.org
  - www. usada.org
  - Banned/Prohibited Substances List
- Professional Sports
  - Each Pro sport league will have its own list of banned/regulated substances.
- High School Sports
  - Information is more varied but a good starting point is each state's interscholastic athletic website.

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Examples Of Additional Questions To Ask Related to Safety and Effectiveness

- Is the claim physiologically/biologically plausible? What is the purported mechanism?
- Is there research/scientific evidence to support the claim? Quality & Quantity Matter!
- Was the research performed in the target population you are looking for?
- Where and when was it published (peer reviewed journal)? and how was it funded (potential bias)?
- Has the study been replicated by other groups?
- Was the research hypothesis driven with clear objectives?
- What was the study design?
  - Gold standard: double blind, randomized, control trial!
- What was the number of subjects? [ie. Required power to detect statistical significance]
- Are the results significant not just statistically but with physiologic/biologic relevance?
- Dose response study with adequate length of time?
- Were the proper controls and valid variables/outcomes used?
  - E.g. was dietary intake controlled for? Biomarkers vs direct measurement? Pre-supplement baseline testing vs just post-supplementation? Actual use of a sport-specific, relevant, "real world" performance test or was it lab engineered, lab controlled?

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Steps in the Evidence Analysis Process

Formulate	Formulate PICO question
Gather	Gather Research through a Review of the Literature
Appraise/Evaluate	Critically Appraise/Evaluate the Studies
Summarize	Summarize the evidence and provide conclusion.
Grade	**Assign a Strength of Evidence Grade [grading system adapted from the Academy of Nutrition and Dietetics' Evidence Analysis ToolKit[1]]**

[1]https://www.andeal.org/vault/2440/web/files/QCC_3.pdf

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PICO question

Among competitive athletes (P), what is the effect of ergogenic dietary supplements (I) versus no ergogenic dietary supplements (C) on athletic performance and muscle soreness (O)?

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Ergogenic Dietary Supplements that will be evaluated:

- Branched Chain Amino Acids
- Creatine
- Citrulline
- Anti-oxidants
- Collagen/ Vitamin C
- Omega-3 Fatty Acids
- Vitamin D

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Outcomes:

- Athletic Performance
- Muscle Soreness

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Methodology Used To Evaluate the Evidence

- National Library of Medicine's PubMed database was searched using the terms from the PICO question with specific use of the terms related to the supplements of interest in this presentation and "human", "English", "athlete", "trained", "muscle*". ^
- Also, consulted references of resulting articles^.
- All study designs except for case reports.
- Critiquing the Studies to obtain a Strength of Evidence Grade
  - SOURCE FOR QUALITY CRITERIA CHECKLIST USED IN PRIMARY RESEARCH: Academy of Nutrition and Dietetics, Evidence Analysis Library[1]
  - Individual study ratings have been combined to determine the overall strength of evidence.

^The Presenters attempted to find all available studies meeting the parameters of the PICO question but can not guarantee with 100% certainty that all studies were located/identified.

[1]https://www.andeal.org/vault/2440/web/files/QCC_3.pdf

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Symbols Used in the Academy's Quality Checklist[1]
[corresponding terminology used here that is more recognizable to other disciplines]

Grade	Description
(+), POSITIVE [GOOD]	**AND/EAL Positive:** Indicates that the report has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis.
(∅), NEUTRAL [FAIR]	**AND/EAL NEUTRAL:** Indicates that the report is neither exceptionally strong nor exceptionally weak.
(-), NEGATIVE [Weak]	**AND/EAL NEGATIVE:** Indicates that these issues have not been adequately addressed.

[1]https://www.andeal.org/vault/2440/web/files/QCC_3.pdf

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Challenges We Faced In Reviewing Dietary Supplement Research

- Limited Human Studies.
  - Most are not in a relevant population: ie. Post-menopausal women, or "untrained" individuals or "recreational" athletes [not competitive athletes].
- Limited randomization, blinding, proper controls and small sample size.
  - No placebo group. Did not controlled for current dietary intake.
  - NONE compared the amount being provided in a supplement to an equivalent amount provided by a controlled diet.
- Very few dose response studies, highly variable doses among studies and very few measured supplement compliance.
- Many only looked at whether a supplement could correct a deficient/insufficient blood level rather than whether that correction led to any performance or recovery benefits.
- Some of the studies may have revealed a benefit but maybe they looked at the wrong period of time: ie. Training vs competition day.
- Few incorporated a pre-supplement baseline testing to compare to post-supplementation.
  - In addition, few used a "real world", sport specific performance indicator [many used lab engineered or lab controlled scenarios].
- *The following slides are the summaries of studies done in competitive athletes only:*
  - *Note: references for the individual supplements can be found grouped together at the end of the slide set.*

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What is the Evidence Regarding BCAA Supplements and effects on Athletic Performance and Muscle Soreness?

CLAIM
Increase muscle mass.
Increase endurance and power.
Attenuate muscle damage associated with exercise.

WHOLE FOOD SOURCES
meat, chicken, fish, dairy products and eggs
DOSE
~ 2-3 g of leucine daily

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Author year Study design Class Rating	Purpose	Study Population	Intervention	Outcomes
Kephart et al 2016 Randomized Controlled Trial Class A Rating +	The aim of this study is to explore the long term effects of BCAA supplementation on markers of endurance in elite cyclists in a 10 week training session	18 well trained cyclists volunteered for the study and training schedules were maintained during the 10 weeks.	Volunteers were randomized into BCAA group (n=9) and Control Group (n=9). The BCAA group took 12gms/day of BCAA over a 10 week training period. Pre and post training, the participants were tested for 4 hour fast blood glucose, body composition, Wingate Peak power tests and 4 km time trials	Significant increase in peak power test (p =0.01), mean power (p =0.01)in the BCAA group compared to the control group and, total neutrophil number was significantly different between groups (p=0.01). No significant difference was found between the two groups for time to complete the 4km time trial. **Performance**
Knectle et al 2012 Randomized Controlled Trial Class A Rating +	The aim of the study was to explore the impact of BCAA supplementation before and after 100km ultra marathon on attenuation of muscle damage and renal function	27 male ultra- marathoners volunteered for the study. All participants maintained a rigorous training schedule prior to the race.	Volunteers were randomized into BCAA group (n=14) and Control Group (n=13). The BCAA group took 12 BCAA tablets one hour prior to the start of the race and 4 tablet at 17 fueling stations during the event. Urine and blood samples were collected pre and post- race. Anthropometric measurements were collected pre- race only	Mean difference in finish time was significantly faster in the BCAA group (p= 0.033). Perceived muscle soreness pre to post race was not significantly different between the groups. The blood and urinary parameters collected pre to post race were not significantly different between the groups. BCAA attenuated lactic acid production post race. **Performance** **Muscle Soreness**
Areces et al 2014 Randomized Controlled Trial Class A Rating +	The aim of the study was to determine the impact of a 7 days oral supplementation with BCAA to prevent muscle damage during a marathon	50 marathon runners volunteered for the study and were matched into two groups by age, training and running experience. 43 males and 7 females	Volunteers were randomized in BCAA group (n=25) and Control Group (n=25). The BCAA group received 35grams of supplement for 7 days prior to the race.(5gms per day) The Control group received cellulose. Prior to the race, all participants performed a vertical jump test, handgrip strength and urine samples were collected. Three minutes post completion of the race, participants performed a vertical jump test and handgrip strength. Leg soreness was assessed. Urine was collected 30 to 60 minutes post-race.	No significant difference found in running pace during the race between the groups. No significant difference found in vertical jump post-race between the groups. No significant difference found in perceived muscle soreness between the groups. The pH of the urine was significantly lower in the BCAA group as compared to the control group ($p<0.05$) and the leukocyte count was significantly lower in the BCAA group as compared to the control group. ($p<0.05$) **Performance** **Muscle Soreness**
Matsumoto et al 2009 Randomized Controlled double blind placebo controlled crossover trial Class A Rating +	The aim of the study was to explore the impact of BCAA supplementation prior to an incremental loading exercise test post 7 days of BCAA on the level of lactic acid as an indicator of endurance capacity among trained athletes	8 male well trained male athletes participated in both supplemented and control trials separated by one week.	Volunteers consumed 2.0gms BCAA three times a day (6.0gms) during the training period. The training was maintained at a specific time and intensity in both trials. On the 7th day, the athletes underwent an incremental loading test. Respiratory exchange ratios were calculated every 30secs. Blood samples (BCAA and lactate) were obtained pre and immediately post loading test.	The VO2 and workload levels at endurance capacity were higher in the BCAA group as compared to the Control group ($p<0.05$) VO2 max was higher in the BCAA group as compared to the control group ($p<0.05$) **Performance** **Muscle Soreness**
Wisnik et al 2011 Randomized Controlled double blind placebo controlled trial Class A Rating +	The aim of the study was to determine changes in the multiple-choice reaction time (MRT) and the effect of BCAA on performance during treadmill running test which simulated a soccer game in male players	10 male professional soccer players volunteered for the study. Training schedules were maintained during the study.	Volunteers performed a treadmill running test twice in a 2 week time frame. One hour before the test blood samples were obtained and 7 grams of BCAA (n=5) or placebo ingested (n= 5). The test consisted of two 45 minutes of running separated by 15 minutes of sitting rest and a 20 minute recovery post second 45 minutes of running. Running speeds were adjusted periodically on the treadmill. At regular intervals runners reacted to a colored light signals flashed on a board. BCAA and lactate levels were collected during the walking phase of the tests.	BCAA significantly improved performance on the MRT ($p<0.01$) No significant differences were found in blood lactate between groups. **Performance**

BCAA Conclusion Statement

- Muscle glycogen is depleted; BCAA are used as a fuel source leading to an increased level of serotonin as a by product of metabolism. Serotonin is associated with fatigue. BCAA supplements may mitigate serotonin formation [Foure, 2017; Kreider, 2010; Williams, 2005].
- Bottom Line: Safe, possibly effective for minimizing skeletal muscle damage and offering ergogenic benefits and, in certain circumstances, BCAA may minimize skeletal muscle damage.

Strength of evidence =Grade 1; Good
Five Randomized Controlled Trials

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What is the Evidence Regarding Creatine Supplements and effects on Athletic Performance and Muscle Soreness?

CLAIM
Increased sprint performance.
Increased work and exercise capacity.
Enhanced recovery.

WHOLE FOOD SOURCES
Red meat, white fish and milk
DOSE
~0.07 g/kg/day to 5 g/day

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Author year Study design Class Rating	Purpose	Study Population	Intervention	Outcomes
Lamontagne-Lacasse et al 2011 Parallel randomized double blinded trial Class A Rating +	The aim of this study was to explore the impact of Creatine supplementation vs placebo on SJ and BJ among highly trained university elite level volleyball players	12 male volleyball players from Sherbrooke University volleyball team with a consistent training regime throughout the study period of 28 days.	The randomized volleyball players were supplemented with Creatine monohydrate powder or a placebo for 28 days. Pre and post intervention, all volunteers were tested in a no step vertical jump(BJ) and a three- step vertical jump (SJ) for executed height.	Due to attrition, 8 participant results were reported (n=4 creatine; n=4 placebo) Pre to post intervention, the BJ performance was statistically greater in the creatine group (p=0.03) SJ performance was not significantly different between groups. **Performance**
Deminice et al 2013 Randomized Controlled double blinded trial Class A Rating +	The aim of this investigation was to explore the impact of creatine on oxidative stress and inflammatory markers post -acute repeated sprints in soccer players	25 well trained soccer players from an under 20- year old soccer team in Brazil. Men trained 5 days a week for 2 hours at time using a repeated sprint type training technique.	The volunteers were randomly assigned to receive Creatine (n=13) (0.3g/kg/day) or a placebo (n=12) for 7 consecutive days. Pre and post supplementation, athletes ran two Running based Anaerobic Sprint tests (RAST) with power parameters were determined Blood samples were collected pretest, immediately posttest and 1- hour posttest for plasma tumor necrosis factor (TNF) and C-reactive protein (CRP), lactate, malondiadehyde, lactate dehyrodgenase (LDH), catalase, and superoxide dismutase enzymes.	Average, maximum and minimum power values were significantly greater in the Creatine supplemented group (p <0.05). Creatine supplementation did not change the blood lactate levels or oxidative markers in either group post exercise. LDH was increased by 28% in the placebo group. Creatine supplementation did not change enzymes levels in either group post exercise. Creatine supplementation significantly lowered the TNF and CRP levels (p <0.05) compared to the placebo group post exercise. **Performance** **Muscle Soreness**
Azizi et al 2011 Randomized Controlled double blinded trial Class A Rating +	The aim of this study was to examine the impact of creatine supplementation on anaerobic performance and sprint swimming records.	20 elite female swimmers volunteered. Participants maintained training schedule, activity level and normal dietary intake during the investigation.	The volunteers were randomly assigned to the creatine group (n=10) or the placebo groups (n=10) The creatine group consumed 5 grams of creatine monohydrate 4 times a day for 7 days during a swimming and conditioning program. Pre and post intervention the volunteers were tested for maximum bench press, vertical jump, 60 yard dash and swimming 25 and 50 meters.	The results indicated that the creatine supplemented group increased bench press capacity (p=0.019), vertical jump (p=0.027) and anaerobic power (sprint test), (p=0.021), however no significant changes in timed swimming events 25m or 50m. **Performance**
Yanez-Silva et al 2017 Randomized Controlled double blinded trial Class A Rating +	The aim of this study was to explore the impact of low dose short-term creatine supplementation on muscle power output in elite male soccer players	19 elite male soccer players from Brazil who played internationally for the same team. Players trained 5 days a week for 2 hours. During the intervention period the volunteers practiced two days a week with no competitive games.	The volunteers were randomly assigned to receive the creatine supplementation (0.03gm/kg/day for 14 days) or a placebo. Pre and post intervention subjects were evaluated for oxygen uptake, ventilatory threshold and a Wingate Aerobic Test. (WAnT) MPO is mean power output; PPO is peak power output during the WAnT	Creatine supplementation increased the PPO significantly (P <0.05) when compared to the placebo group and increased the MPO significantly (P<0.05) when compared to the placebo group. **Performance**
Rahimi et al 2015 Parallel randomized double blinded trial Class A Rating +	The aim of this study was to determine if creatine supplementation would act as an antioxidant and prevent apoptosis in male athletes	31 Male elite wrestlers ranked in the top ten of national championships	Participants were randomly assigned to the creatine supplementation group 20 grams of creatine, n = 15 or placebo group n=16. Supplementation was taken for 7 days with pre and post testing of VO2 Max after cycling to exhaustion Blood was collected pre and posttest for p53 and Insulin like growth factor-1 (INF-1)	Serum p53 levels were significantly higher (p 0.05) in the Creatine group as compared to the placebo group. No differences were found between the groups for levels of INF-1 **Muscle Soreness**

Creatine Conclusion Statement

- Powerful antioxidants that work with glutathione to reduce oxidative stress; Aerobic exercise increases production of free radicals. Creatine is part of phosphocreatine which is needed to produce ATP. [Kreider, 2017 & Butts, 2018].
- Bottom Line: Safe, effective for reducing oxidative stress, offering ergogenic benefits and, large doses are not beneficial.

Strength of evidence =Grade 1; Good
Five Randomized Controlled Double Blinded Placebo Trial

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What is the Evidence Regarding Citrulline Supplements and effects on Athletic Performance and Muscle Soreness?

CLAIM

Improve athletic performance.

Relieves muscle soreness.

WHOLE FOOD SOURCES

Salmon, red meat, watermelon and leafy greens

DOSE

6-8 gms of L-Citrulline per day

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uthor ear tudy design lass ating	Purpose	Study Population	Intervention	Outcomes
uzuki et al 16 andomized Controlled Double inded Placebo Crossover Trial ass A ating +	The aim of the study was to explore the impact of oral supplementation of L-Citrulline on a cycling trial in well trained male athletes	22 trained male athletes volunteered for this study and maintained their usual training schedules	The participants were randomized into two groups. Group one received 2.4 gms of L-Citrulline. Group two received the placebo for seven consecutive days. Baseline blood pressure and heartrate measurements were obtained. One hour post ingestion of L-Citrulline or placebo the volunteers were tested using a 4km timed cycling test. Post-test blood samples were drawn. After a three week washout the groups switched interventions	Levels of L-Citrulline (p<0.05), arginine (p<0.05) and BCAA (p<0.001) were significantly higher in the Citrulline group vs the Control group. Completion time in the cycling test was significantly faster than the control group (p < 0.05). No significant difference noted between groups for perceived muscle fatigue. **Performance** **Muscle soreness**
enn et al 16 andomized Controlled Double inded Placebo Crossover Trial ass A ating +	The aim of the study was to investigate the impact of acute L-Citrulline supplementation on hand grip strength, vertical power and anaerobic Wingate cycling performance in female masters level tennis players	17 female masters level tennis players volunteered for this study. The volunteers played a minimum of twice a week and competed in competitive tennis events for past 2 years	The participants reported to the laboratory for three visits. Visit one included anthropometric assessment of body fat and lean mass. At visit two and three, the participants consumed 8 grams of L-Citrulline or a placebo prior to completion of the Wingate cycling exercise tests. One week wash-out period between testing.	Hand grip strength was significantly improved for maximal (p=0.042) and average measurements (p=0.045). No significant difference were found between the groups for the vertical jump tests. During the Wingate cycling test, explosive (p<0.001) and peak power (p<0.001) were significantly higher with L-Citrulline than placebo. **Performance**
ax et 15 andomized Controlled Double inded Placebo Crossover Trial ass A ating +	The aim of the study was to investigate the impact of acute L-Citrulline supplementation on exercise performance, blood lactate, heart rate and blood pressure during lower body dynamic performance in 12 advanced resistance trained males	12 advanced resistance trained males who participated in high stress weight training 4 times a week for longer than one year volunteered for the study. Volunteers maintained nutrition logs and typical weight training during the study with the exception of refraining from lower level training 72 hours and upper level training 48 hours prior to each test day.	The participants reported to the laboratory for three visits. Visit one included anthropometric assessment of body fat and baseline exercise testing. At visit two and three, the participants consumed 8 grams of L-Citrulline or a placebo one hour prior to completion of the exercise tests. Participants warmed up on a stationary bike followed by leg press, squats and extension until exhaustion. Blood parameters were obtained per and post exercise test. One-week wash-out period between testing.	Participants performed lower body weight repetitions to exhaustion; the L-Citrulline group performed more repetitions than the control group (p<0.05). There were no significant difference between the L-Citrulline group and the control group for blood lactate, blood pressure or heart rate. **Performance**
erez-Guisado et al 10 andomized Controlled Double inded Placebo Crossover Trial ass A ating +	The aim of the study was to investigate the impact of acute L-Citrulline supplementation on performance of flat barbell bench presses in well trained males in an eight week study period.	41 males who trained > 3 hours a week with a program using a bench press volunteered for the study. Participants maintained a consistent training program during the eight week study period	The participants reported to the laboratory for three visits. Visit one included baseline strength testing with barbells. At visit two and three, the participants consumed 8 grams of L-Citrulline or a placebo one hour prior to completion of the 8 sets of flat barbell bench presses. The muscle soreness at 24 and 48 hours was assess per self- evaluations. Two weeks of training followed by testing with one week wash-out period between testing.	The number of repetitions for bench press was significantly greater with supplementation than the placebo group (p<0.001). Self-reported muscle soreness was significantly lower with supplementation than the placebo group (p<0.001) at 24 and 48 hours. **Performance** **Muscle soreness**
unniffe et al 16 andomized ontrolled Double Blinded Placebo rossover Trial ass A ating +	The aim of the study was to investigate the impact of acute L-Citrulline supplementation on acid base balance and high intensity exercise.	10 well trained males (8 endurance athletes, 1 semi-professional soccer player and 1 mix martial artist) All athletes trained 5 days/12 hours a week	The participants reported to the laboratory for three visits. Visit one included baseline of VO2 max while on a calibrated cycle. At visit two and three, baseline blood parameters were collected pre-test. The participants consumed 12 grams of L-Citrulline or a placebo one hour prior to completion of the sprint cycling tests. The volunteers cycled until exhaustion. Mean power, speed, distance, work, and time to exhaustion were recorded. Blood parameters were collected post-test.	No significant difference were noted in acid base balance, perceived exertion and speed, cadence, distance or work achieved between the L-Citrulline group and the placebo group. **Performance**

Citrulline Conclusion Statement

- L-Citrulline is an amino acid that is a precursor for L-Arginine, which is a substrate for Nitric Oxide(NO). Nitric oxide enhances blood flow, muscle energy metabolism and mitochondrial respiration during physical activity. [Cunniffe, 2016 & Wax 2015]
- Bottom Line: Safe, possibly effective for reducing delayed onset muscle soreness and offering ergogenic benefits. Appropriate dose unknown.

Strength of evidence =Grade 1; Good

Five Randomized Controlled Double Blinded Placebo Trial

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What is the Evidence Regarding Omega-3 Fatty Acid Supplements and effects on Athletic Performance and Muscle Soreness?

CLAIM

Reduce Inflammation.

Support Immune Function.

Support Muscle Repair and Remodeling.

WHOLE FOOD SOURCES

Cold water fatty fish (tuna, salmon), fish oils, krill oil

DOSE

~0.2-2.4 g/day EPA/DHA [DRI/AI=1.1-1.6g/day]

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Author (year) Class Rating	Purpose	Study Population	Intervention	Outcomes
Raastad et al (1997) Class: A, RCT Rating: +	Study the effect of n-3 supplementation on maximal aerobic power, anaerobic threshold and running performance	N=28 Soccer players	n-3 1.6g/day EPA 1.04g/day DHA Placebo=corn oil 10 week trial [diet controlled] Testing 1-7 days prior to start of supplementation and again on the last day of supplementation.	Aerobic power and running performance: no difference. **Performance.**
Buckley et al (2009) Class: A, RCT Rating: Ø	Examined the effects of n-3 on endurance performance, recovery and CV risk factors in elite Australian Rules football players	N= 25 Australian Rules Football	Fish oil 6g/day [0.36g/day EPA 1.56g/day DHA] Placebo=sunflower oil Tested at baseline then 5 weeks later. Supplementation started after baseline testing. 5 week trial	Endurance performance, recovery: no difference Serum fatty acids and TG: no difference RBC n-3 PUFA content: doubled **Performance.**
Nieman et al (2009) Class: A, RCT Rating: +	Test the influence of n-3 PUFA on exercise performance, inflammation, and immune measures before and after a 3-d period of intense exercise	N=23 trained cyclists	n-3 2.4g/day EPA 0.4g/day DHA Placebo=soy bean oil Supplemented before and after a 3-day intense exercise trial 6 week trial [diet controlled]	10-km time trial (~65% max power output):no difference. Inflammatory serum markers: no difference Plasma EPA and DHA: increased levels **Performance.**
Mingley et al (2017) Class: A, RCT Rating: Ø	Determine if DHA-rich fish oil can improve Wingate and cycling time trial performance.	N=26 trained cyclists	Fish oil 2g/day [140mgEPA 560mg DHA] Placebo=soy bean oil Testing at baseline then 8 weeks later Supplementation started after baseline testing. 8 week trial	Wingate: no difference. Max cycle power: no difference 5-min Cycling Time Trial: no difference Quad iso strength: no difference **Performance.**
Lewis et al (2015) Class: A, RCT Rating: Ø	Determine effect of short-term n-3 on neuromuscular function and physical performance.	N=30 mixed sports	n-3 (seal oil) 375mg EPA 510mg DHA Placebo=olive oil Testing at baseline then 21 days later Supplementation started after baseline testing. 21 day trial	Iso contractions:unclear Wingate:unclear 250 kj time trial:unclear **Performance.**

Omega-3 FA Conclusion Statement

- N-3 fatty acids are essential fatty acids that serve as precursors to eicosanoids with anti-inflammatory properties. Supplementation of n-3FA has been purported to be beneficial to athletes by decreasing inflammation, supporting immune function and supporting muscle repair and remodeling.
- Bottom Line: Limited human studies in competitive athletes; evidence does not support the hypothesis that omega 3 PUFA supplementation is effective in enhancing athletic performance.
  - Not all used proper dietary controls, did not select an appropriate placebo (needs to be one that will not alter the n-6:n-3 ratio) and most did not measure supplement compliance during the study.

Strength of evidence=fair-weak

Number of relevant human studies in competitive athletes=5 RCTs

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What is the Evidence Regarding Vitamin C Supplements and effects on Athletic Performance and Muscle Soreness?

CLAIM

Act in an antioxidant capacity to reduce inflammation(see antioxidant section).

In combination with collagen/gelatin, promote collagen synthesis.

WHOLE FOOD SOURCES

Gelatin, vitamin C rich foods such as oranges, berries, grapefruit

DOSE

≥15g collagen hydrolysate with ≥50mg Vit C 1 hr before training [RDA=75-90mg/day]

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Author Year Class Rating	Purpose	Study Population	Intervention	Outcomes
Shaw et al 2017 Class: A , RCT Rating Ø	To determine whether gelatin+vit C supplementation combined with exercise could increase collagen synthesis.	8 healthy male subjects	5g or 15g of vitamin C-enriched gelatin or placebo. Blood sample taken every 30 minutes post-consumption of gelatin or placebo for amino acid content. Blood samples also obtained before and 1 hour after for use with engineered ligaments. Blood was added to engineered collagen for 6 days to measure effect on collagen content and mechanics. One hour after initial supplement, subjects completed 6 min of jumping rope in order to stimulate collagen synthesis. Procedure repeated 3 times per day with at least 6h in between X 3 days. Additional blood samples collected at 4, 24, 48 and 72 hours post first bout of exercise to measure amino-terminal propeptide of collagen I content.	Circulating levels of glycine, proline, hydroxyproline, hydroxylysine significantly increased after both doses of gelatin with a peak at 1 hr post supplementation as well as increased levels of amino-terminal propeptide of collagen I in the blood. Doses of gelatin also resulted in significantly increased collagen content and enhanced mechanics in the engineered ligaments **"Performance"** **"Muscle Soreness"**

Vitamin C + Gelatin Conclusion Statement

- Vitamin C is required for collagen synthesis and in combination with gelatin, is purported to be beneficial in reducing injuries and enhancing tissue repair during intermittent exercise.
- Bottom Line: Encouraging and interesting results yet too preliminary to provide conclusive and overwhelming evidence. Future larger scale, well-designed RCTs in competitive athletes are needed.

Strength of evidence=fair-weak

Number of relevant human studies in competitive athletes=1

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What is the Evidence Regarding Vitamin E/Antioxidant Supplements and effects on Athletic Performance and Muscle Soreness?

CLAIM

Act in an antioxidant capacity to reduce inflammation and subsequent delayed onset muscle soreness with the ultimate goal of enhancing performance.

WHOLE FOOD SOURCES

Vegetable oil, whole grains, nuts, seeds, (vitamin E)

Fruit and vegetables (general antioxidants)

DOSE

Varies but doses as high as 32-1000mg/day [RDA=15mg/day 10-30IU].

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Author (year) Class Rating	Purpose	Study Population	Intervention	Outcomes
Nieman et al. (2002) Class: A, RCT Rating:+	Measure the influence of vitamin C on oxidative and immune changes in runners competing in an ultramarathon race.	29 male and female ultramarathoners	Vit C=1500mg in a carb-beverage [diet controlled], placebo Double blind, 7-day supplementation prior to and on race day.	PI. Vit C levels and blood markers of oxidative and immune changes; no actual measure of performance. No difference in levels found except for an increase in Vit C. **No Actual Performance Measure.**
Paulsen et al. (2014) Class: A, RCT Rating:+	Investigate the effects of vit C and E supplementation on endurance training adaptations in humans.	54 trained and untrained men and women placed on an endurance training program.	Vit C=1000mg Vitamin E=235mg 11 week trial [diet controlled], placebo Double blind, testing before and after supplementation.	VO2 max and 20-m shuttle run test Both increased, not significant **Performance.**
Tatli et al. (2009) Class:A, RCT Rating:Ø	Study the effects of alpha-tocopherol supplementation on the cardiopulmonary fitness in endurance athletes (cyclists) and non-athletes	40 cyclists	Vitamin E=200mg 21 day trial, placebo Testing before and after supplementation.	VO2 max and Physical Fitness Index No difference. **Performance.**
Louis et al. (2010) Class:A, RCT Rating:Ø	Influence of vitamin and mineral complex supplementation on muscular activity and cycling efficiency	16 elderly endurance athletes	Vit A=5.7mg as beta carotene Vit C=104mg Vitamin E=16mg 21 day trial, placebo Double blind, testing before and after supplementation.	Max voluntary contraction of knee extensor followed by 10-min cycle No difference in MVC but small improvement in cycle efficiency. **Performance.**
Teixiera et al. (2009) Class:A, RCT Rating:+	Determine the effects of antioxidant supplements on exercise-induced lipid peroxidation, muscle damage and inflammation.	20 trained kayakers	Vit A=30mg as beta carotene Vit C=400mg Vitamin E=272mg 30 day trial [diet controlled], placebo Double blind, testing before and after supplementation.	Time to complete a 1,000-m kayak race Race time increased, not significant Also noted evidence of increased muscle damage in trt group(p=0.049) **Performance. Muscle Soreness**

Vitamin E/Antioxidant Conclusion Statement

- One additional relevant study performed at high altitude: Simon-Schnass and Pabst (1998) performed controlled trials in trained males at high altitude investigating the effects of 363mg Vit E for 4 weeks on anaerobic threshold power during an incremental cycle test; statistically significant increase of 18% .
- Vitamin E and other antioxidant nutrients such as vitamin C and beta carotene/vitamin A may act in an antioxidant capacity to reduce inflammation and subsequent delayed onset muscle soreness with the ultimate goal of enhancing athletic performance.
- Bottom Line: Inconclusive evidence to support the use of non-physiologic doses of antioxidant supplements to improve athletic performance and enhance recovery through decreased muscle soreness except at high altitude; some evidence to support the opposite (a detrimental effect by interfering with the necessary adaptive and recovery process).
  - Some lack proper dietary controls and did not measure supplement compliance during the study.
  - Future larger scale, well-designed RCTs in competitive athletes are needed that focuses on periodization investigating the differences in antioxidant supplementation during the training period versus competition day. Further, studies comparing equivalent levels of the antioxidants found naturally in foods vs supplementation should be performed.

Strength of evidence=fair-weak

Number of relevant human studies in competitive athletes=5 [~17 performed in competitive athletes including the 1 study from this slide performed at high altitude but only the 5 most recent were included in the table since all results were similar in that there was no significant benefit detected].

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What is the Evidence Regarding Vitamin D Supplements and effects on Athletic Performance and Muscle Soreness?

CLAIM

Reduce Inflammation.
Support Immune Function.
Support Muscle Repair and Remodeling
High prevalence of vitamin D deficiency among athletes.

WHOLE FOOD SOURCES

*from sunlight, egg yolks, fortified foods

DOSE

0.75-3.75ug[RDA=15ug/day 600IU/day]

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Author (year) Class Rating	Purpose	Study Population	Intervention	Outcomes
Close et al, (2013) Class: A, RCT Rating ⌀	Examine effect of vit D supplementation on serum levels and physical performance.	N= 30 club level competitive athletes	53°N, winter 20,000IU(500ug), 40,000(1000ug) D3 capsules/day cholecalciferol 12 week trial, placebo Double blind, testing performed before, at 6 & 12 weeks of suppl.	1-RM bench pull, weighted reverse grip chin-up, bench press 10-m and 30-m sprint time Serum 25(OH)D: increased **Performance:** no difference
Hastrzeboska et al 2016) Class: A, RCT Rating +	Investigate the effect of vitamin D supplementation in response to HIIT.	N=36 football(soccer)	5000IU(125ug) D3 capsules/day cholecalciferol 8 week trial [diet controlled] placebo Double blind, testing performed before and after supplementation.	Wingate test Squat jump height Sprint times Serum 25(OH)D: increased **Performance:** no difference
Todd et al, (2017) Class: A, RCT Rating +	Investigate the effect of vitamin D supplementation on VO2 max, skeletal muscle and lung function.	N=42 Gaelic Footballers	55°N, fall/winter, 3000IU(75ug) D3 spray/day cholecalciferol 12 week trial [diet controlled] placebo Double blind, testing performed before and after supplementation.	VO2 max Vertical jump height (cm) Hand grip strength (kg) Serum 25(OH)D: increased **Performance:** no difference.
Hyon et al (2016) Class: A, RCT Rating ⌀	Examine the acute effects of vitamin D supplementation on muscle function using isokinetic dynamometry.	N=22 judo	52.3°N, winter, 150,000IU(3750ug) one time dose, D3 tablets cholecalciferol 8 day trial, placebo Double blind, testing performed before and after supplementation.	Quadriceps (30°/s) (N m) Quadriceps (200°/s) (N m) Hamstrings (30°/s) (N m) Hamstrings (200°/s) (N m) Serum 25(OH)D: increased **Performance:** significant increase in all
Fairbairn et al (2018) Class: A, RCT Rating ⌀	Examine effect of vit D supplementation on athletic performance.	N=57 professional rugby.	45°S, fall, 50,000IU(1.25mg) one dose every two weeks, D3 tablet cholecalciferol 11-12 week trial, placebo Double blind, testing performed before, at 6 & 12 weeks of suppl	10-m and 30-m sprint time 1-RM bench pull, weighted reverse grip chin-up, bench press. Serum 25(OH)D: increased **Performance:** no difference. except for 1-RM chin-up (inc. 5.8kg)

Vitamin D Conclusion Statement

- Vitamin D is a fat soluble vitamin that may have beneficial effects on athletic performance and muscle soreness through a reduction in inflammation, supporting the immune system and muscle repair and remodeling. Further, there is believed to be a high prevalence of Vitamin D deficiency among athletes[Owens, 2018].
- Studies included measured an effect on performance or muscle; not just whether supplementation could increase (correct) vit D blood levels.
- Bottom Line: Inconclusive evidence to support a recommendation to supplement vitamin D in competitive athletes. All but one study showed an increase in serum 25(OH)D levels but no statistically significant differences in the performance measure. If athletes undergo screening of Vit D levels, supplementation should be based on the need for overall health and not as an attempt to enhance athletic performance until supported by evidence.
  - Most lacked proper dietary controls and did not measure supplement compliance during the study.

Strength of evidence=fair

Number of relevant human studies in competitive athletes=5 RCTs

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Conclusion

- Since so few human studies in competitive athletes exist, our focus shifted from simply compiling this presentation to more of a "call to action". MORE WELL-DESIGNED, RELEVANT, AND VALID RESEARCH IS NEEDED!
- Until well-designed studies are done in the human athletic population clearly showing a dietary supplement to be superior to an adequate, well-balanced, whole-food diet, optimized for performance, then we must continue to recommend "food first".
  - Consider that "whole food" contains many different nutrients and compounds in more physiological amounts that provide less risk of harmful effects and toxicity.
  - One particular nutrient in isolation may not be beneficial and may in fact, have detrimental effects.
  - Synergy amongst these nutrients and compounds may be the key factor.
  - A compound that has not yet been identified may actually be the critical factor.

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Clinical Bottom Line[1-4]:

- Evidence does not support supplementation of omega-3 PUFA, vitamin D, vitamin C or antioxidant combinations for enhanced athletic performance and muscle soreness, with some possible benefits for citrulline.
- Evidence to show that supplementation with branched chain amino acids and creatine has positive benefits on athletic performance and muscle recovery. Of importance, is that the same benefits can be found with sufficient intake of high protein food sources such as meat, dairy, nuts and legumes[1].
- A food-first approach with a well-balanced diet that includes high protein food sources and antioxidant-rich foods provide the benefit of a more balanced profile of the nutrients and is less costly compared with supplemental form.
- Athletic Trainers should recommend a food first approach to nutrition to promote highest athletic performance. Avoiding commercialized supplements is best because the contents are not FDA approved, products are not regulated, may be contaminated or contain banned substances[2]. In the absence of strong scientific evidence of efficacy and safety regarding a supplement, the recommendation for a food first approach is best practice.

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[2]Knapik JJ., et al. (2016). Prevalence of Dietary Supplement Use by Athletes: Systematic Review and Meta-Analysis. Sports Med, 46, 103-123.
[3]Heaton LE., et al. (2017). Selected In-Season Nutritional Strategies to Enhance Recovery for Team Sport Athletes: A Practical Overview. Sports Med, 47, 2201-2218.
[4]Tipton KD. (2015). Nutritional Support for Exercise-Induced Injuries. Sports Med, 45(Suppl), S93-S104.

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Case Study

YOUR ATHLETE

20 year old collegiate football player with the goal of increasing explosive power and speed; asking about Supplement X4 recommended by a friend from the gym back home.

Supplement X4

Claim: Explosive energy, increased focus and speed during workouts and quicker recovery.

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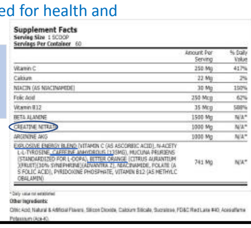
WHAT ARE THE STEPS YOU SHOULD TAKE?

- ***START HERE!*** Is the athlete's diet currently adequate, well balanced and optimized for performance within their sport and training regimen?
- Let's assume the diet is already optimized for health and performance. What's next?

SAFE? | EFFECTIVE? | LEGAL WITHIN THE SPORT?

RECOMMENDATION TO ATHLETE:
SKIP THIS SUPPLEMENT!


Supplement Facts
Serving Size 1 SCOOP
Servings Per Container 60

	Amount Per Serving	% Daily Value
Vitamin C	250 Mg	417%
Calcium	22 Mg	2%
NIACIN (AS NIACINAMIDE)	30 Mg	150%
Folic Acid	250 Mcg	62%
Vitamin B12	35 Mcg	588%
BETA ALANINE	1500 Mg	N/A*
CREATINE NITRATE	1000 Mg	N/A*
ARGININE AKG	1000 Mg	N/A*
EXPLOSIVE ENERGY BLEND (VITAMIN C (AS ASCORBIC ACID), N-ACETY L-L-TYROSINE, CAFFEINE ANHYDROUS (125MG), MUCUNA PRURIENS (STANDARDIZED FOR L-DOPA), BITTER ORANGE (CITRUS AURANTIUM)(FRUIT)(30% SYNEPHRINE)(ADVANTRA Z), NIACINAMIDE, FOLATE (A S FOLIC ACID), PYRIDOXINE PHOSPHATE, VITAMIN B12 (AS METHYLC OBALAMIN)	741 Mg	N/A*

*Daily value not established
Other Ingredients:
Citric Acid, Natural & Artificial Flavors, Silicon Dioxide, Calcium Silicate, Sucralose, FD&C Red Lake #40, Acesulfame Potassium (Ace-K).

"Some nutritional supplements help some athletes in some sports some of the time, but no supplement helps all athletes all of the time, causing recommendations for nutritional supplement use to be difficult to make on a team or program basis"[1].

QUESTIONS?

[1]Schwenk T and Costley C. When food becomes a drug: nonanabolic nutritional supplement use in athletes. *Am J Sports Med*. 2002;30(6):907-916.

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