

The background is a dark, textured surface resembling a chalkboard. It is covered with various light-colored chalk sketches. In the upper left, there's a large 'V' and a globe. Below the globe is a detailed drawing of a microscope. To the right of the microscope is a large, stylized number '1'. In the lower left, there's a drawing of a stack of books. In the lower right, there are several mathematical symbols including a percentage sign, an exclamation mark, and a less-than sign. The overall theme is scientific and academic.

Sports Performance Supplements

Michael Osterholt, MD, CAQSM

Disclosures

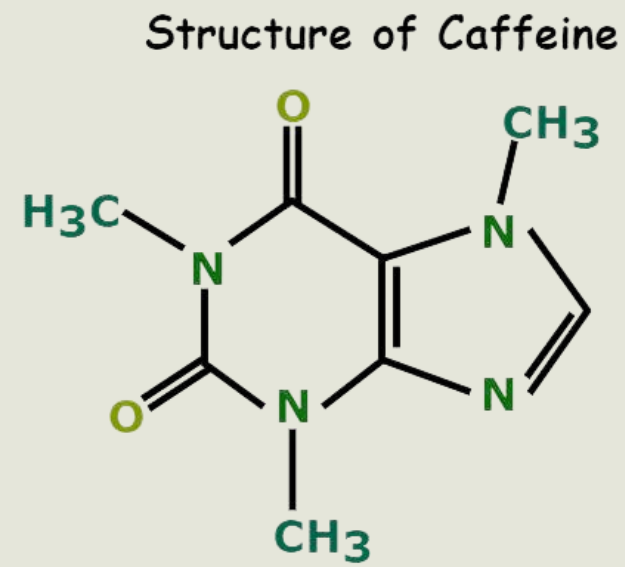
- None of the faculty for this educational activity have relevant financial relationships with ineligible companies to disclose.

Caffeine



Caffeine

- Caffeine is the world's most widely consumed psychoactive substance
- Naturally occurring in more than 60 plant species.
 - 95% of ingestion coming in the form of coffee, tea, and soft drinks.
- 75% of elite athletes may use caffeine as an ergogenic aid prior to or during event/sport based on WADA/IOC data
- Caffeine is easily and rapidly absorbed.
 - Peak concentration within 45 minutes
 - Half life of about 4-5 hours



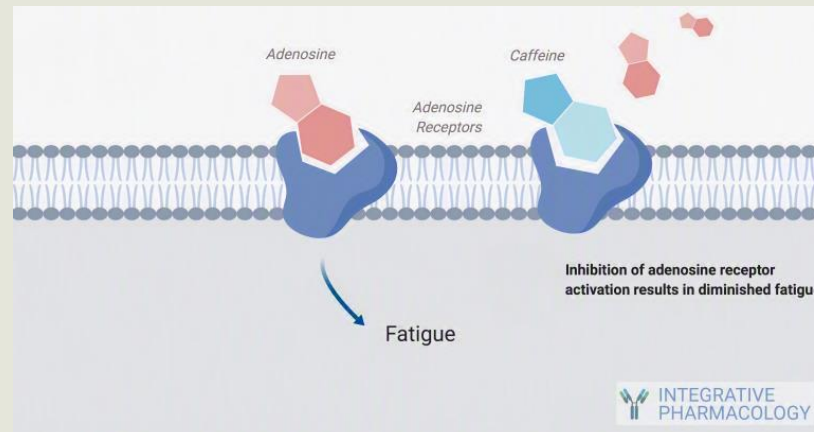
How does it improve physical performance?

- Ergogenic Effects
 - Performance
 - Stamina
 - Recovery
- Proposed mechanisms of action
 - First thought that an increase in free fatty acid oxidation with possible glycogen sparing
 - Subsequently dismissed.
 - Direct effect on muscle
 - Increased mobilization of intracellular calcium facilitating force production.
 - Reduces fatigue caused by gradual reduction of Ca^{2+}
 - Increased $\text{Na}^{+}/\text{K}^{+}$ activity to enhance excitation/contraction coupling

How does it improve physical performance?

- CNS Effects

- Evidence suggests this is the primary mechanism by which caffeine changes mental/physical performance.
- Caffeine binds to adenosine receptors, blocking its effects.
 - Adenosine is involved in numerous processes and pathways
 - Decreases serotonin, dopamine, acetylcholine, norepinephrine, and glutamate
 - Caffeine binding results in positive effects on mood, vigilance, focus, alertness



Caffeine and Endurance Exercise

- Caffeine has consistently shown to improve endurance performance by 2-4% across studies using 3-6mg/kg body mass dose.

Caffeine and Endurance Exercise

EFFECT OF CAFFEINE ON SPORT-SPECIFIC ENDURANCE PERFORMANCE: A SYSTEMATIC REVIEW

**MATTHEW S. GANIO, JENNIFER F. KLAU, DOUGLAS J. CASA, LAWRENCE E. ARMSTRONG,
AND CARL M. MARESH**

Human Performance Laboratory, Department of Kinesiology, University of Connecticut, Storrs, Connecticut

- Critically reviewed studies that examined effect of caffeine on time trial endurance (>5 minutes)
- 33 trials across 21 studies all high quality data
- Mean improvement in performance of 3.2% was statistically significant with caffeine ingestion compared to placebo

Caffeine and Endurance Exercise

Meta-Analysis

> Sports Med. 2018 Aug;48(8):1913-1928. doi: 10.1007/s40279-018-0939-8.

The Effect of Acute Caffeine Ingestion on Endurance Performance: A Systematic Review and Meta-Analysis

Kyle Southward¹, Kay J Rutherford-Markwick^{2 3}, Ajmol Ali^{4 5}

- 57 trials from 45 studies with a total of 1001 participants (639 participating in studies that reported time outcomes and 362 that reported power output)
- Mean age 27.7
- Mean caffeine dose 4.9 +/- 1.3 mg/kg varying from 3mg/kg-6mg/kg
- Overall time trials were faster compared to placebo by 2.22%. Power output was greater compared to placebo by 2.9%

Safety

- High doses of caffeine (500 mg/day or more)
 - Jittery, anxious, over arousal
 - Side effects increase linearly
- Other adverse effects
 - Insomnia, restlessness, nausea, vomiting, headaches, tachycardia, arrhythmia, anxiousness.
 - FDA states doses below 400mg/day typically do not incur dangerous effects
- AMA recommends <500 mg/day
- Pure powdered caffeine
 - One tablespoon can contain 10g
 - 10-14g can be fatal



Is it a banned substance?

- Oddly enough, yes. Kind of.
- IOC banned caffeine from 1984-2004, and WADA from 2000-2004
 - Cutoff of 12 ug/ml
 - Athletes still recommended to stay below 12 ug/ml
 - ~10 mg/kg body mass
 - 3x the amount to improve performance
- NCAA still classifies caffeine as a banned stimulant
 - Positive test if urinary concentration is 15 ug/ml
 - Consumption 500-600 mg a few hours prior to competition

Final statement

- Safe and effective supplement to improve sport performance
- Recommend 3-6mg/kg 30-60 minutes prior to activity
- Endorsed by
 - Academy of Nutrition and Dietetics
 - Dieticians of Canada
 - American College of Sports Medicine
 - International Society of Sports Nutrition
- Endorsed as being
 - Effective in improving sports performance
 - Reducing perceived fatigue
 - Enabling users to sustain exercise at desired intensity longer

Creatine

**BEFORE
CREATINE**



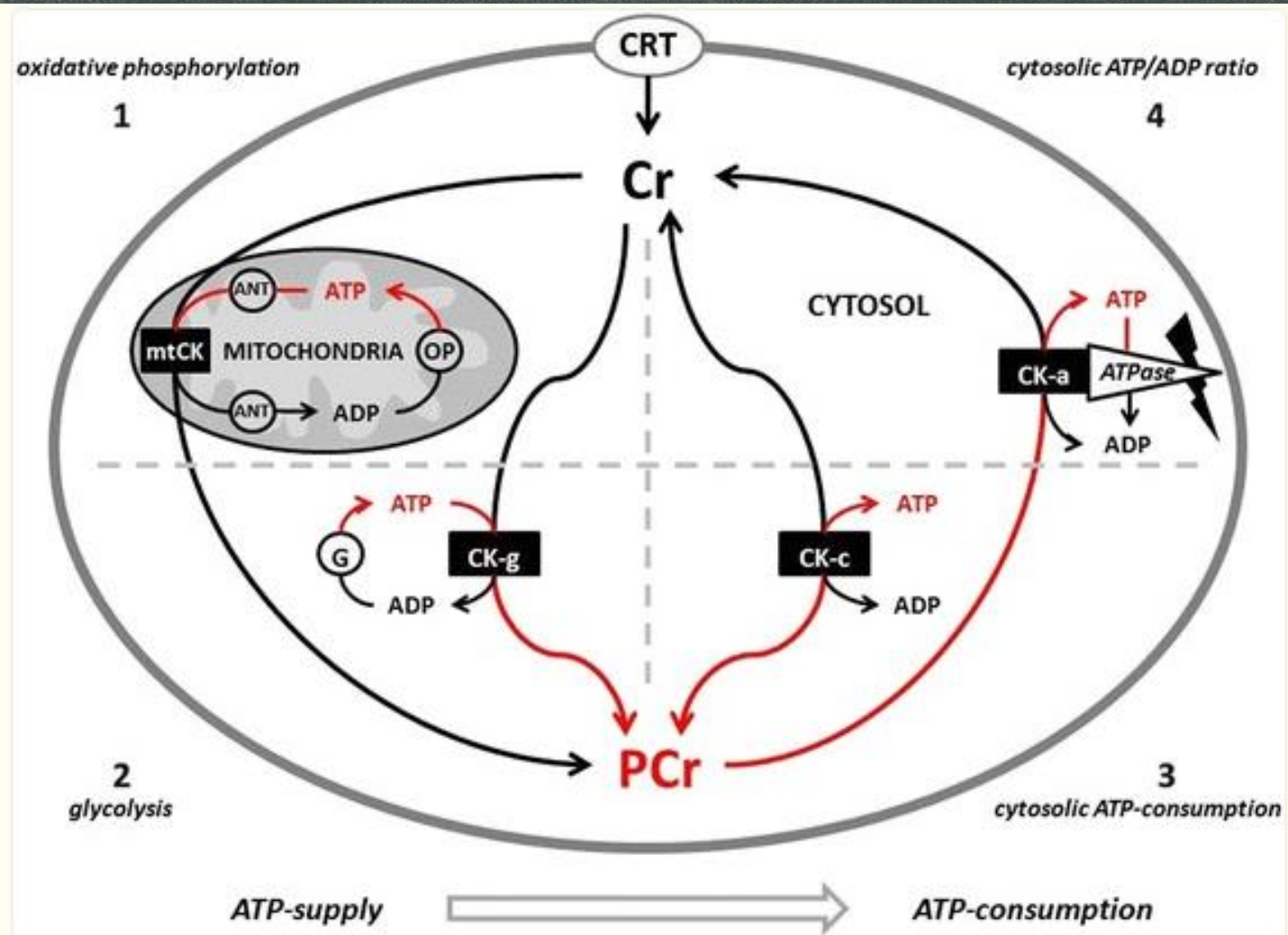
**AFTER
CREATINE**



Creatine

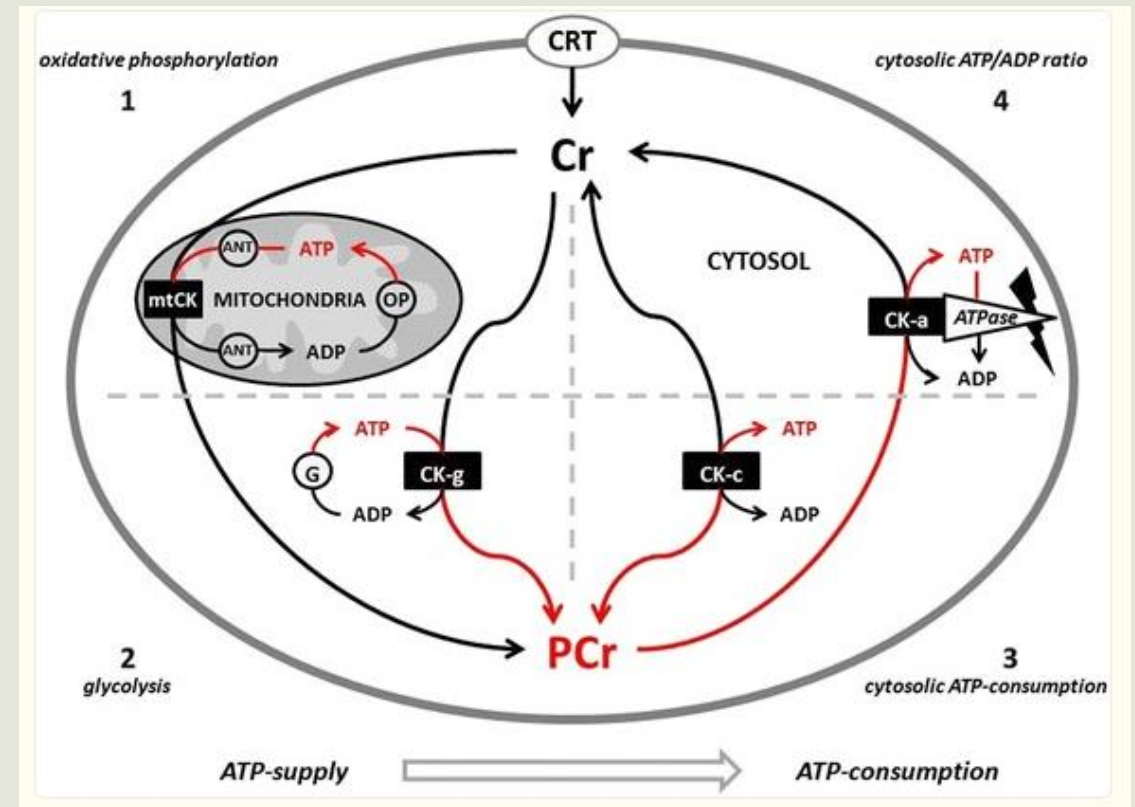
- One of the most popular and widely researched natural supplements
- Single nitrogenous non-protein amino acid compound
 - Arginine, Glycine, Methionine
- 95% found in skeletal muscle
 - 2/3rds phosphocreatine (PCr)
 - Remaining is free creatine
- About 1 g/day produced endogenously
 - Liver, kidneys
 - Lesser extent in pancreas
- Remainder of creatine obtained through diet
 - 1 g/day in omnivorous diet
- Individual with a mass of 70kg has total store ~120-140g
 - 1-2% is degraded and excreted in urine daily
 - 1-3 g of creatine needs to be replenished daily

Mechanism



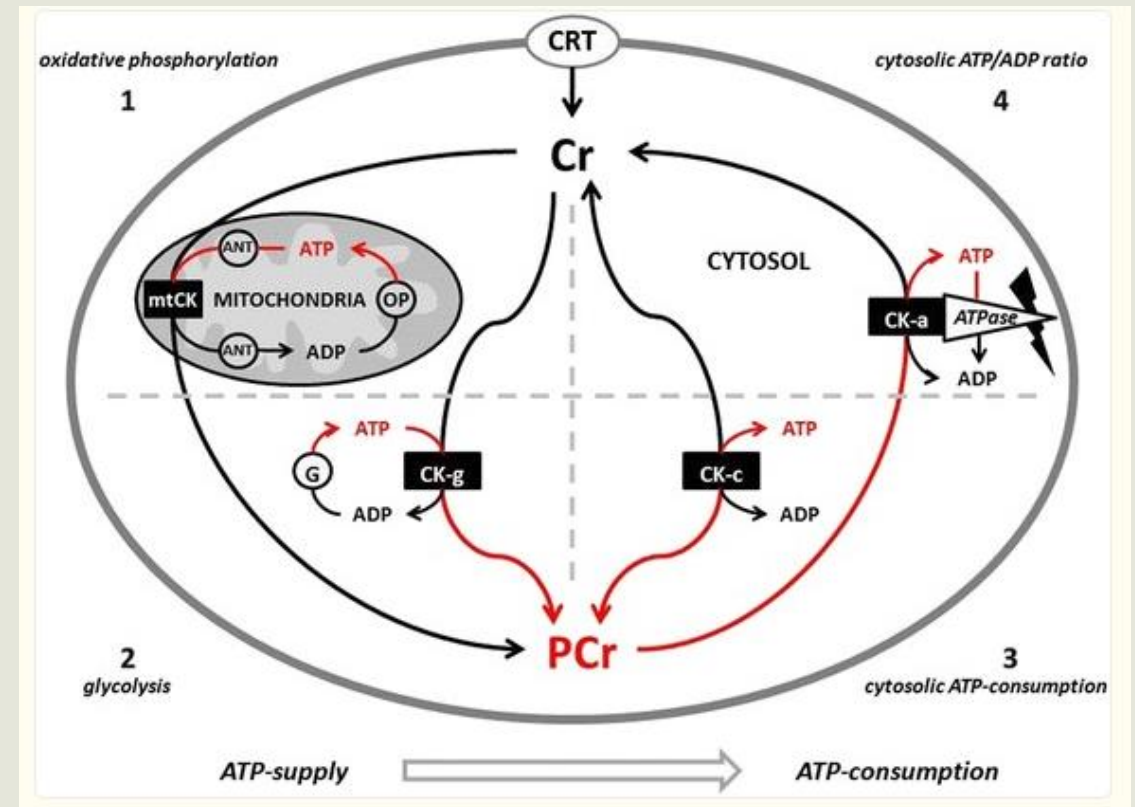
Mechanism

- Primary metabolic role
 - Creatine combines with a phosphoryl group (Pi) to form Phosphocreatine (PCr)
 - Enzymatic reaction of Creatine Kinase (CK)
 - CK/PCr system
- Buffer
 - Hydrolysis of PCr into Cr + Pi acts as buffer to resynthesize ATP
 - Maintains ATP availability during maximum effort
- CK/PCr system shuttles intracellular energy from mitochondria to cytosol
 - Leads to improved exercise capacity and training adaptations



Mechanism

- Primary metabolic role
 - PCr stores become depleted during intense exercise
 - Inability to resynthesize the ATP required
 - Energy available diminishes
 - Hypothesized that increasing muscle creatine may increase available PCr



Dosing

- Typical dosing strategy:
 - 20g of creatine monohydrate per day (0.3g/kg/d)
 - Split into 5g four times daily for one week
 - Followed by 5g daily
- This strategy saturates creatine and produces effects faster.
 - Reported to increase total creatine and phosphocreatine by 15-40%
- Some protocols recommend 3-6g daily (0.3-0.1g/kg/d) but takes 21-28 days for ergogenic effect.

Potential Ergogenic Benefits

Table 1.

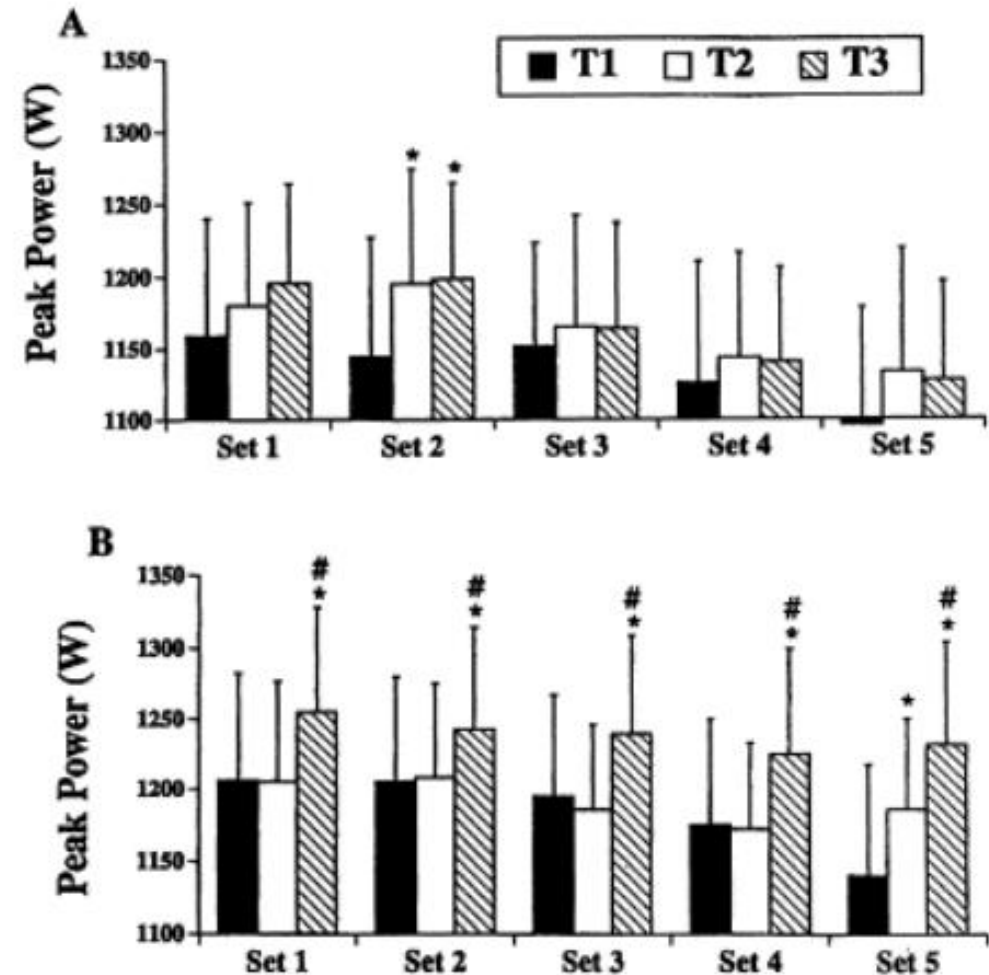
Potential ergogenic benefits of creatine supplementation

-
- Increased single and repetitive sprint performance
 - Increased work performed during sets of maximal effort muscle contractions
 - Increased muscle mass & strength adaptations during training
 - Enhanced glycogen synthesis
 - Increased anaerobic threshold
 - Possible enhancement of aerobic capacity via greater shuttling of ATP from mitochondria
 - Increased work capacity
 - Enhanced recovery
 - Greater training tolerance
-

Creatine supplementation enhances muscular performance during high-intensity resistance exercise

J S Volek¹, W J Kraemer, J A Bush, M Boetes, T Incledon, K L Clark, J M Lynch

- 14 men randomly assigned in a double blind controlled fashion to creatine group (N=7) or placebo group (n=7)
- Each group performed bench press protocol and jump squat protocol on 3 separate occasions. T1 no supplementation. T2 both placebo supplementation. T3 one group 25g creatine monohydrate daily the other placebo.
- Total repetitions for each set of bench press and peak power output measure.
- Creatine resulted in significant increase in peak power output during all 5 jump squat sets and increased repetitions in all 5 bench press sets.



Creatine supplementation improves sprint performance in male sprinters

O C Skare¹, Skadberg, A R Wisnes

- 18 male competitive sprinters average age of 21.1. Main distances 100m, 200m, 400m, and 110/400m hurdles
- Completed 100m sprint and 6 intermittent 60m sprints all electronically timed. Pre-test baseline values were obtained.
- Sprinters assigned to placebo (n=9) or creatine (n=9)
- Placebo group consumed 10g of glucose 4x daily for 5 days creatine group consumed 5gcr/glucose 4x daily for 5 days. 5 days of supplementation was completed prior to repeat test

Skare et al.

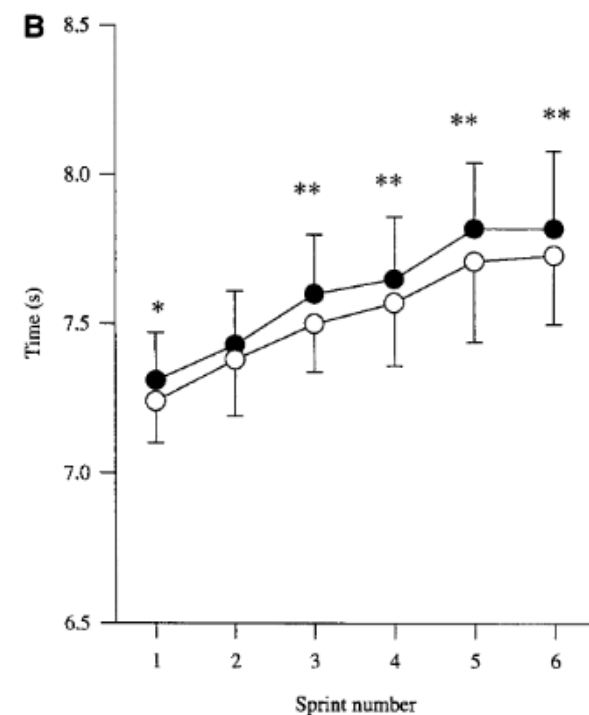
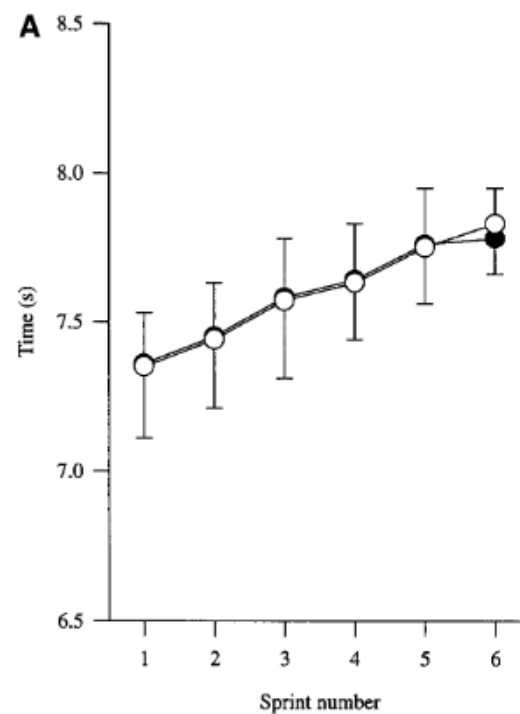


Fig. 1. The sprint time (s) for each 60 m, during 6 intermittent 60 m sprints. A) Sprint times prior to (black) and after (white) placebo supplementation. B) Sprint times prior to (black) and after (white) Cr supplementation. Significant * $P < 0.02$, ** $P < 0.01$ treatment effect with Cr supplementation.

Table 1

	Placebo (n=9)		Creatine (n=9)	
	Pre-test ¹	Post-test ²	Pre-test ¹	Post-test ²
Body weight (kg)	72.5 (6.0) 61.4–79.2	72.0 (5.7) 60.7–78.3	73.6 (5.0) 63.9–79.0	74.2 (5.0)* 64.8–80.5
Plasma creatine (μmol/l)	11.9 (3.2) 8.5–13.5	12.7 (3.2) 9.1–17.4	12.8 (2.1) 10.3–14.3	167.3 (84.0)*** 82.6–318.4
Sprint, 100 m (s)	11.74 (0.35) 11.41–12.32	11.76 (0.35) 11.41–12.35	11.68 (0.27) 11.25–12.08	11.59 (0.31)** 11.12–12.05
Total sprint time (6×60 m) (s)	45.58 (0.92) 44.13–47.09	45.57 (1.21) 44.06–47.69	45.63 (1.11) 44.02–47.12	45.12 (1.1)*** 43.57–46.74
Plasma/serum constituents 5 min after the 6th intermittent 60 m sprint				
Lactate (mmol/l)	18.7 (2.2) 16.6–21.6	18.7 (3.2) 15.8–21.7	17.9 (2.5) 17.2–21.6	19.4 (2.5)** 17.0–22.1
Ammonia (μmol/l)	179.8 (36.7) 158–233	168.5 (95.0) 139–221	155.8 (62.7) 89–220	137.1 (64.0) 65–174
Creatinine (μmol/l)	126.2 (7.7) 121–135	129.3 (6.4) 125–134	125.8 (7.1) 118–134	146.8 (10.5)*** 137–159

* $P<0.05$, ** $P<0.02$, *** $P<0.01$ (after compared to before).

¹Before placebo or creatine supplementation respectively.

²After placebo or creatine supplementation respectively.

- Cr Supplementation resulted in statistically significant improvement in sprint time
 - 11.68 (0.27) 11.59 (0.31)** $P<0.02$ 100m sprint
 - 45.63 (1.11) 45.12 (1.1)*** $P<0.01$ Total time 6x60m

Clinical Trial > Med Sci Sports Exerc. 1999 Aug;31(8):1147-56.

doi: 10.1097/00005768-199908000-00011.

Performance and muscle fiber adaptations to creatine supplementation and heavy resistance training

J S Volek¹, N D Duncan, S A Mazzetti, R S Staron, M Putukian, A L Gómez, D R Pearson, W J Fink, W J Kraemer

- 19 healthy men randomly assigned to 12 weeks of placebo or creatine (25g for 1 week followed by 5g daily)
- Body mass, fat-free mass, bench press, squat, and creatine values measure
- Significant increase in body mass and fat free mass (6.3 % and 6.3% compared to 3.6/3.1%)
- Significant increase in bench press and squat (24% and 32% compared to 16%/24%)
- Significant increase in muscle creatine concentration
- No side effects

Long-term creatine intake is beneficial to muscle performance during resistance training

K Vandenberghe ¹, M Goris, P Van Hecke, M Van Leemputte, L Vangerven, P Hespel

- 19 females randomly assigned to placebo (n=9) or creatine (n=10)
- Cr group received 5g of Cr Monohydrate 4x/day for 4 days then 5g/day
- Placebo group received placebo 5g maltodextrine 4x/day for 4 days then one tablet daily
- They were followed for 10 weeks
- At 5 and 10 week intervals, significant
 - Increase in PCr by 6% (P<0.05) maintained throughout trial
 - Increase in fat free mass
 - Increase in arm flexion torque

	Pre	5 wk	10 wk
Leg press			
Placebo group	231 ± 18	272 ± 25	288 ± 24
Creatine group	244 ± 20	292 ± 20	348 ± 304-150
Bench press			
Placebo group	48 ± 3	54 ± 4	66 ± 4
Creatine group	47 ± 2	59 ± 3	68 ± 4
Leg curl			
Placebo group	28 ± 2	32 ± 2	39 ± 4
Creatine group	27 ± 2	36 ± 3	44 ± 2
Leg extension			
Placebo group	51 ± 4	71 ± 4	80 ± 6
Creatine group	54 ± 4	85 ± 7	100 ± 84-150
Squat			
Placebo group	57 ± 4	68 ± 4	71 ± 6
Creatine group	57 ± 3	80 ± 6	83 ± 54-150
Shoulder press			
Placebo group	50 ± 2	56 ± 3	62 ± 2
Creatine group	52 ± 3	60 ± 3	68 ± 3

Safety

- 1,000s of studies have been performed on creatine.
 - Only consistently reported side effect is weight gain
- Short and long term data ranging from children to elderly with doses ranging from 0.3-0.8 g/kg/day up to 5 years have consistently shown creatine supplementation poses no adverse health risks.
- Numerous well controlled studies have shown that creatine does not increase MSK injuries, cause dehydration, muscle cramps, GI upset, renal dysfunction, or long-term detrimental effects.
 - Kreider RB, et al. Long-term creatine supplementation does not significantly affect clinical markers of health in athletes. Mol Cell Biochem. 2003
 - Greenwood M, et al. Creatine supplementation during college football training does not increase the incidence of cramping or injury
 - Watson G, et al. Creatine use and exercise heat tolerance in dehydrated men. J Athl Train. 2006
 - Lopez RM, et al. Does creatine supplementation hinder exercise heat tolerance or hydration status? a systematic review with meta-analyses
 - Dalbo VJ, et al. Putting to rest the myth of creatine supplementation leading to muscle cramps and dehydration. Br J Sports Med. 2008
 - Santos RV, et al. The effect of creatine supplementation upon inflammatory and muscle soreness markers after a 30 km race
 - Schroder H, Terrados N, Tramullas A. Risk assessment of the potential side effects of long-term creatine supplementation in team sport athletes

Is it banned?

- NCAA
 - Not banned
 - Does not allow institutions to provide creatine to athletes or any other “muscle building” supplements. (protein, amino acids, etc.)
- WADA or IOC
 - Not banned

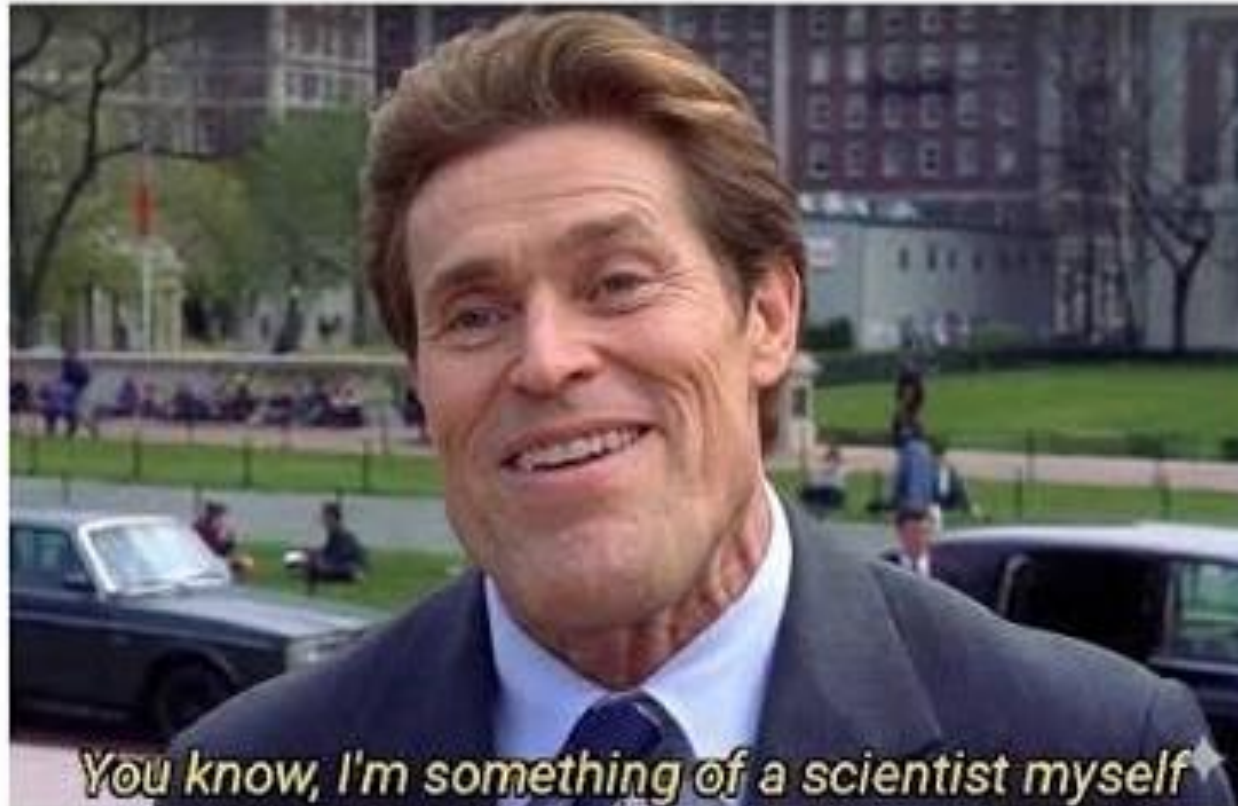
Final Thoughts

- Position Statement from International Society of Sports Nutrition
 - “Creatine monohydrate is the most effective ergogenic nutritional supplement currently available to athletes with the intent of increasing high-intensity exercise capacity and lean body mass during training”
 - “Creatine monohydrate supplementation is not only safe, but has been reported to have a number of therapeutic benefits in healthy and diseased populations ranging from infants to the elderly. There is no compelling scientific evidence that the short- or long-term use of creatine monohydrate (up to 30 g/day for 5 years) has any detrimental effects on otherwise healthy individuals or among clinical populations who may benefit from creatine supplementation”

Peptides

"Research purposes only, not for human consumption"

Peptide users:



What are peptides?

- BPC-157 and TB -500 are two peptides with massive uprise in public interest across social media and within the athletic/orthopedic community.
- Short chains of amino acids
 - Typically <50
 - Often lack 3-dimensional folding
 - Simpler structure results in more limited functional/regulatory abilities
- Function as signaling molecules
- Synthetic peptides have played a massive role in modern medicine
 - Insulin, vasopressin, oxytocin, GLP-1
- Emerging as a trending topic
 - Recovery, Metabolism, Tissue Repair, Injury
 - 26 new peptides approved by FDA from 2016-2022

Advantages and Limitations

- Advantages

- To date very minimal identified side effects
- Efficient metabolism to non-toxic products
- High affinity for specific molecular targets resulting in high efficacy and low relative dosing
- Absence of accumulation in the body

- Limitations

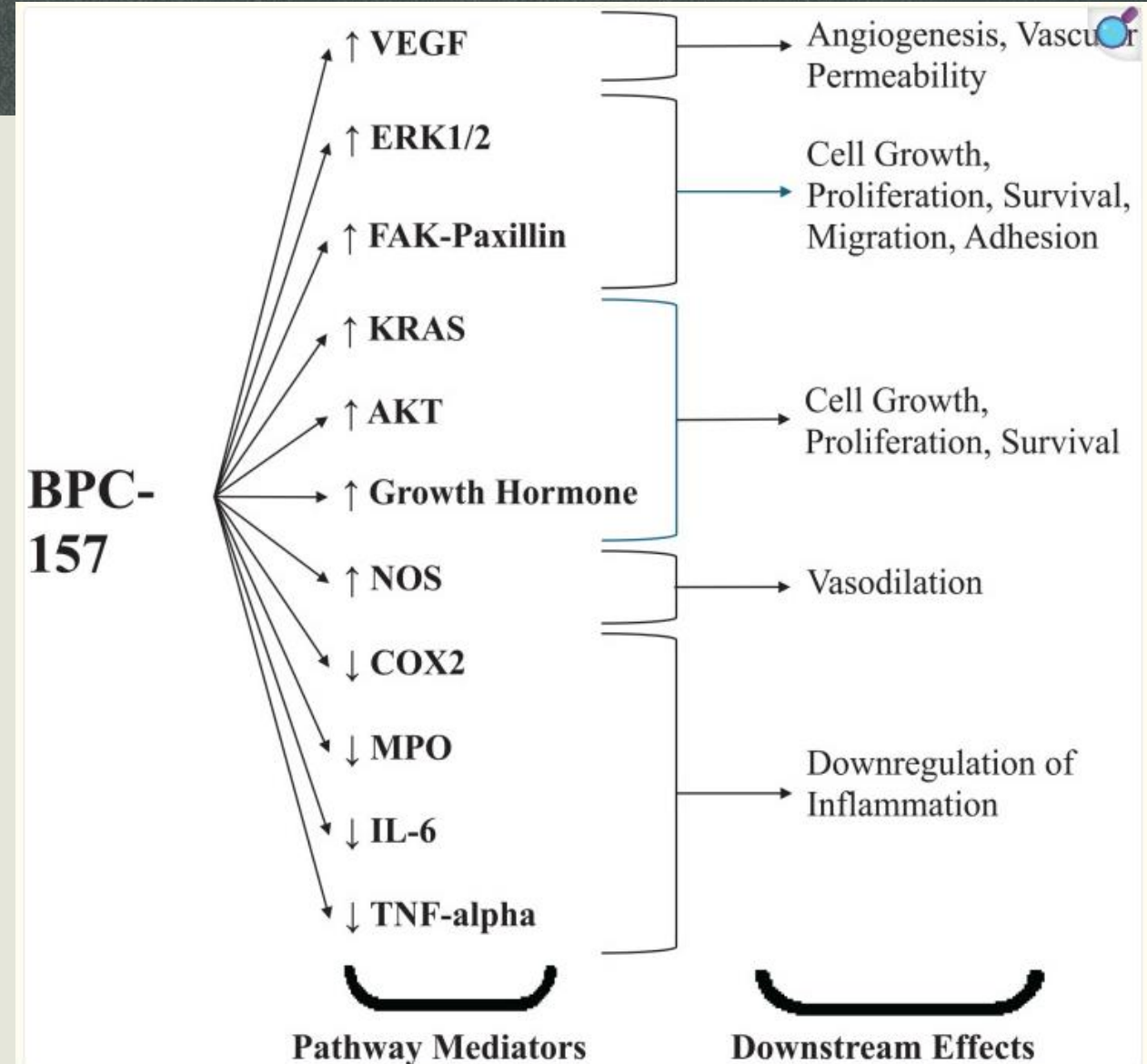
- Short duration of action
- Insufficient penetration BBB
- Rapid hepatic and renal clearance
- Administration orally can be difficult due to breakdown by GI proteolytic enzymes

Recent news

- July 23rd the FDA compounding advisory committee voted narrowly to recommend adding 6 peptides to the 503A Bulks List
 - Would allow compounding pharmacies to produce and sell directly to consumers
 - This went against FDA staff's written recommendation
 - The 6 compounds are
 - BPC-157
 - KPV
 - TB-500
 - MOTS-c
 - Epitalon
 - Semax
- Not officially added to the list, nor are they FDA approved
- Concerns include:
 - Difficulty compounding some substances
 - Possible drug impurities
- BPC-157 and TB-500 classified as doping substances by international sports committees
 - Often mentioned as sports performance aids

BPC-157

- 15 amino acid synthetic peptide
- Derived from human gastric juice
- Studied for its pro healing effects in tendons, ligaments, bones
 - Initially studied for its benefits in ulcer healing, colonic fistula healing, and treatment in IBD
- Cellular Pathways
 - Activates Vascular endothelial growth factor (VEGF) receptor pathway to promote angiogenesis
 - Promotes tenocyte migration/survival.
 - Growth hormone receptor upregulation in tendon fibroblasts.
 - Interacts with nitric oxide system increasing expression of several antioxidants



BPC-157

- Animal studies
 - Improved collagen architecture and increased load to failure in both Achilles and MCL transection recovery
 - Improved histological appearance and load tolerance of damaged muscle
 - Augmented fracture healing with similar outcomes to autologous bone marrow grafting
- Significant limitations in sample sizes, dosing/route of administration, and safety data.
- Human evidence extremely limited

TB-500 or TB-4?

- Structure

- 7-amino acid peptide derived from thymosin beta-4 (TB-4)
- Naturally present in all human cells

- Functions

- TB-4 plays a role in numerous biological processes
- Most peer reviewed data regarding TB-500 is extrapolated from TB-4 data.
 - Cell migration via TB-500 binding site
 - Promotes angiogenesis via VEGF
 - Inhibits apoptosis and slows senescence
 - Reduces inflammation
- Widespread claims of tissue repair and increased muscle growth
 - Limited evidence to support
 - Rat studies failed to demonstrate significant benefit compared to placebo
 - No peer-reviewed human trials have examined TB-500 for MSK indications
 - Multiple chronic wound healing trials have demonstrated some clinical efficacy with accelerated wound healing.

BPC-157 and TB-500 Safety

- No clear human dosing established
- Heavily controlled under athletic doping rules banned by most professional athletic organizations including by WADA/IOC
- No safety data in animals past 6 weeks and no safety data in humans at all
- Product quality and purity raise massive concerns

Final thoughts

- While short term animal model data is reassuring for BPC-157, there is mixed data for TB-500
- No significant human trials to date
- No long term (>6 weeks) animal safety data and no human safety data
- There is increased public interest across social media surrounding BPC-157 and TB-500. However, it would be premature to recommend to any patient or athletes until further clinical data regarding efficacy/safety is available.

Resources

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