2 β-Alanine and Carnosine: The science and its application

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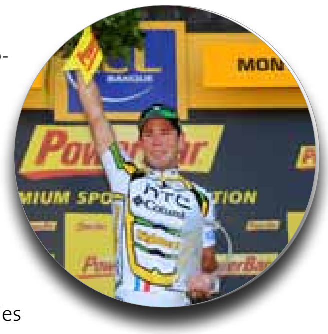

Intense exercise is primarily fuelled by anaerobic glycolysis with large lactate and hydrogen ion (H+) production. These large increases in H+ can cause significant decreases in muscle pH, from resting values of ~7.1 down to pH values of 6.3 to 6.5. The primary causes of fatigue during intense exercise lasting from ~1 to 10 min involves both limitations imposed by anaerobic glycolysis, as well as negative consequences resulting from the associated muscular acidosis caused by declining muscle pH. This drop in muscular pH (not lactate) has been shown to negatively affect metabolic processes, including disturbances of the creatine-phosphorylcreatine equilibrium limiting the re-synthesis of phosphorylcreatine, as well as the inhibition of glycolysis and the muscle contraction processes itself (for reviews see: (5)).

During high-intensity exercise many different innate metabolic processes and physio-chemical properties contribute to muscular buffering capacity in attempts to maintain intramuscular pH, including muscle histidine and carnosine (5). A buffer has the ability to retain a nearly constant pH when either a small amount of an acid or base is added to a solution. Accordingly, a higher innate buffering capacity between different athletes has been directly associated with improved high-intensity performance, with sprinters and rowers having higher measured muscle carnosine, buffering capacity, and high-intensity performance as compared to marathon runners (6). Therefore, the further enhancement of intra-muscular buffering capacity within a given athlete should lead to a further increase in performance during high-intensity exercise situations where metabolic acidosis is a limiting factor. Accordingly, a recent and novel nutritional supplement that athletes can utilise to augment intra-muscular buffering capacity is via the prolonged supplementation of ß-alanine to increase muscle carnosine contents. As of 2010, ß-alanine supplementation is not on the World Anti-Doping Agencies (WADA) prohibited substances list.

Role of Carnosine to Intra-Muscular Buffering

Carnosine (ß-alanyl-L-histidine) is a cytoplasmic dipeptide found at high concentrations in skeletal muscle, and in particular type II (fast twitch) muscle (for review see: (3)), and there are higher concentrations in sprinters and rowers, as compared to marathon runners (6). Carnosine has been described since the 1930's as a potent intra-muscular buffer due to its nitrogen containing side imidazole ring, which can directly accept and buffer H+ ions, thus slowing the decline in pH during intense exercise. Supporting this mechanism, is recent evidence showing that 4 weeks of β-alanine supplementation, with assumed increased muscle carnosine contents, directly reduced muscle acidosis, through an attenuation of the decline in normal exercise associated decrease in blood pH (1). The contribution of normal muscle carnosine levels to total intracellular muscle buffering capacity has been suggested to reach ~6 to 7%. However, when increased via β-alanine supplementation can reach ~15% (4).

Prolonged β-alanine supplementation leads to increased muscle carnosine contents

Prof. Roger Harris was the first to show increases in muscle carnosine with prolonged β-alanine supplementation (4). All studies to date that have measured muscle carnosine following β-alanine supplementation (minimum 2 wks) have shown a significant increase (~40 to 50%) in muscle carnosine levels utilising ~3 to 6 g of β-alanine /day over 4 to 8 wks. On average, this has lead to a significant ~40% increase in muscle carnosine (or approximately an increase of ~10 -15 mmol/kg dw of muscle carnosine (Fig. 1). Even 1.6g β-alanine/day can lead to a ~30% increase in muscle carnosine in 8wks of supplementation (7). Figure 1 highlights all the studies that have directly measure muscle carnosine after β-alanine supplementation.

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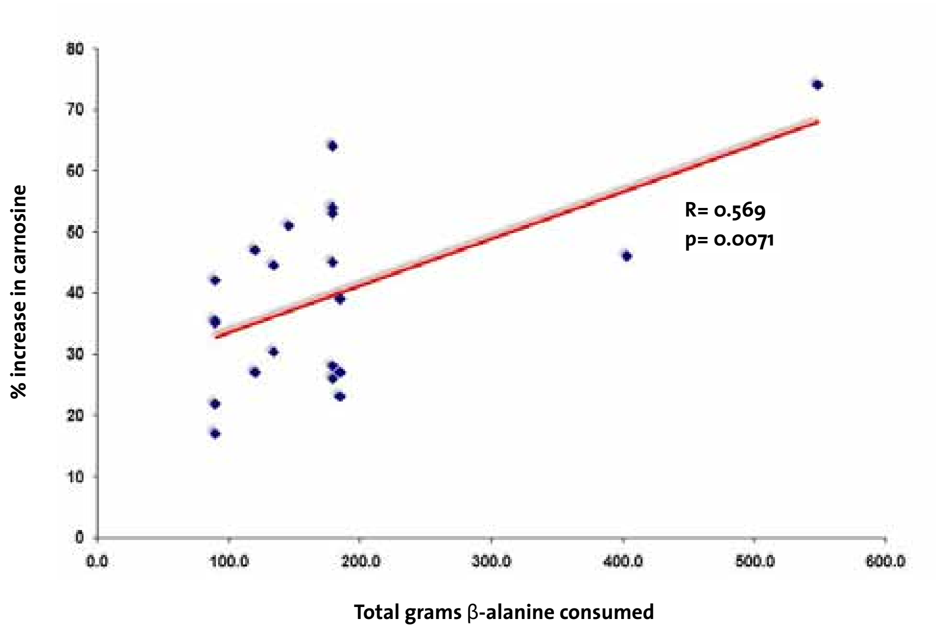
Figure 1:
Corrleation between the percent increase in muscle carnosine with the total grams of §-alanine consumed across 9 different studies utiizing different §-alanine dosing protocols and measured in different muscle groups.



The variability of % increase with similar total β-alanine consumed (~120 to 200g) is most likely due to different dosing protocols, different carnosine measurement methods, different muscle groups measured, and individual subject responsiveness. However, despite this variability, there appears to be a direct liner correlation between the amount of β-alanine consumed and the % increase in muscle carnosine. In fact, the continued apparent linearity (or the non-saturation) of the data points suggests that maximal muscle carnosine levels levels that are potentially attainable remains to be identified.

Figure 2 below is adapted from Baguet et al. (2), but includes recent un-published data also examine carnosine washout (7). Unlike creatine, the washout of augmented skeletal muscle carnosine after the termination of β-alanine supplementation is very slow, with an estimated washout time of ~10 to 15 weeks after a ~50% increase in muscle carnosine (2, 7). Practically speaking, once muscle carnosine is increased, athletes can expect potential performance benefits up to even 1-month post-supplementation due to the stability of muscle carnosine and the slow washout profile.

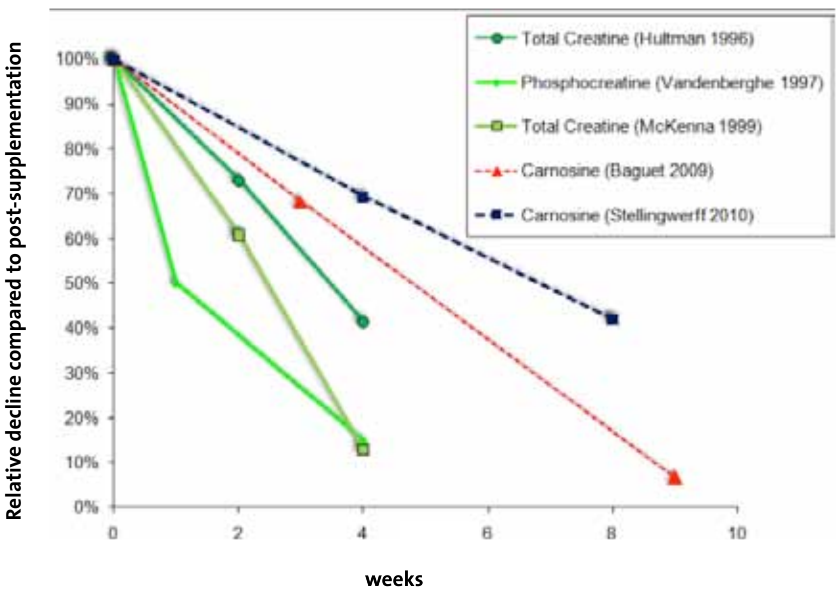


Figure 2:
Comparison of the relative washout of muscle creatine with carnosine post-supplementation.

Study	**Subjects**	**BA Supple. Protocol**	**Total BA Supple.**	**Performance Test**	**Performance Benefit?**	**Comments**
Baguet et al., JAP, 2010	n = 9 trained male rowers per group	5g/day for 7 wks	245g	2000m rowing ergometer test	NO: 4.3 sec faster than Placebo (p=0.07); YES: correlation between inc. muscle carnosine and performance	Pre-supple. muscle carnosine and inc. in carnosine correlated to rowing performance
Derave et al., JAP, 2007	n = 7 or 8 trained male 400m runners per group	2.4 to 4.8g/day for 4 wks	120g	5 bouts of 30 maximal isokinetic knee extensions; Isometric knee extension until exhaust.; 400m race	Isokinetic extension: YES; Isometric extension: NO; 400m race: NO	400m race too short and not anaerobic enough? (~51 sec)
Hill et al., Amino Acids, 2007	n= 12 to 13 un-trained males per group	6.4g/day for 4 to 10 wks	4wks:145.6g; 10wks:548.8g	Cycling capacity test at 110% Wmax until exhaust. (~2.5min)	Total cycling work done: YES	Clear dose-response demonstrated between muscle carnosine levels and performance

Study	Subjects	BA Supple. Protocol	Total BA Supple.	Performance Test	Performance Benefit?	Comments
Hoffman et al., Int. J. Sports Med., 2008	n=8 resistance trained males	4.8g/day for 30 days	144g	1-RM squat test	Squat test: NO	cross-over design with too short of a washout (4 wks), and test not anaerobic enough
Kendrick et al., Amino Acids, 2008	n=13 untrained males per group	6.4g/day for 4 wks	179.2g	Whole body strength; Isokinetic force production; Arm-curl performance test	NO differences in any test	Were performance measures too short and explosive, and thus, not anaerobic enough?
Stout et al., J. Strength & Cond. Res., 2006	n= 12 to 13 untrained males per group	6.4g/day for 6 days followed by 3.2g/day for 22 days	108.8g	Physical working capacity at fatigue threshold	YES: for BA pre to post supple.; NO for between group analysis	Enough BA supplemented?
Stout et al., Amino Acids, 2007	n=11 untrained females per group	3.2g/day for 1 wk followed by 6.4g/day for 3 wks	156.8g	Continuous incremental cycling TTE (~18min); Physical working capacity at fatigue threshold; VO2max	TTE: YES; Physical working capacity: YES; VO2max: NO	Most studies showing no changes on VO2max, including this study.
Stout et al., J. Int. Soc. Sports Nutr., 2008	n= 12 elderly males & females (~73 yrs) per group	2.4g/day for 90 days	216g	Physical working capacity at fatigue threshold	Physical working capacity: YES	Only study thus far in elderly.
Van Thienen et al., JAP, 2009	n=8 well-trained male cyclists per group	2 to 4g/day (average of 3g/day)	168g	30 sec all out cycling at end of 110 min of cycling; 10min TT at end of 110 min of cycling	30 sec sprint: YES; 10min TT: NO	Under-powered for TT test? (as post-test TT wattage in BA was > pre-test but not against placebo)
Zoeller et al., Amino Acids, 2006	n=12 to 13 untrained males per group	6.4g/day for 6 days followed by 3.2g/day for 22 days	108.8g	Ventilatory threshold; Lactate threshold; VO2max; 15min TTE	NO differences in any test	Enough BA supplemented? 15min TTE too long?

Short forms: BA = beta-alanine; exhaust.= exhaustion; Supple. = Supplemented; TT = time-trial; Wmax = wattage maximum

Increased muscle carnosine increases anaerobic performance

Table 1 highlights the published studies thave have exclusively used ß-alanine supplemetnation. Several well-done studies have shown that prolonged ß-alanine supplementation can result in significant anaerobic performance benefits (for review see: (3)). The studies not demonstrating positive performance effects are most likely due to either inadequate total β-alanine dosing, studies not using well-trained and motived subjects, being under-powered and/or inappropriately designed performance tests. Taken together, the emerging data is starting to reveal that when subjects consume ~3 to 6g ß-alanine/day over 4 to 8 weeks (for a total ß-alanine intake of >120g) this will result in an increase of muscle carnosine of about 40 to 50%, and this will lead to positive anaerobic performance outcomes. At this point, whether prolonged ß-alanine supplementation can also lead to significantly enhanced weight training, or single-sprints (<15 sec) and endurance (>20min) performance, remains to be further established.

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Paraesthesia symptoms with β-alanine supplementation

When pure β-alanine is supplemented at levels greater than 800mg/dose it results in mild paraesthesia in most subjects (paraesthesia: minor "pins and needles", skin vasodilation, flushing, over ~ 60 to 120min). Given this, most published studies and commercial products have implemented and recommended small repeated daily doses of ffi 800mg doses, to circumvent and minimise paraesthesia symptoms. Recently a commercialised slow-release tablet of β-alanine has been produced and demonstrated that a 1.6g dose resulted in a blunting of the peak plasma curve, but the same total area under the curve, and none of the subjects reported any paraesthesia symptoms, as compared to a pure β-alanine reference (8). This slow-release β-alanine also showed significantly less urinary spill-over when measured 6 hrs after supplementation. Other than acute paraesthesia, no other side effects (including no changes in body weight) have been demonstrated with β-alanine supplementation.

The pros and cons of supplement use

There are many pros and cons that need to be considered with the use of any supplement. Table 2 below highlights some practical advice that athletes, coaches and practitioners need to consider when evaluating the use of a new supplement.

Table 2:
General practical recommendations for the use of any new supplement.

Items to consider with supplement use in athletes
"Supplements do not compensate for poor food choices. Some supplements may benefit performance, but athletes are cautioned against the use of these products without first conducting an individual risk-benefit analysis" (2007 IAAF Consensus Statement).
Only consider supplement(s) if the athlete has already nearly maximized progress and quality in training, everyday wholesome nutrition, sleep, and proactive recovery approaches and healthcare support.
Get advice on supplements from several reputable sources, and cross-reference that advice with published papers/reviews - do your homework!
Only a handful of supplements have strong scientific support for ergogenic benefit, there is a moderate list with emerging potential, and even a longer list with no proven benefits.
Many supplements will add no further benefit over what a wholesome well-balanced diet will provide, except extra expenses.
A previous study has shown that ~15% of supplements (out of 634 supplements tested) contained WADA prohibited substances.
Only obtain supplements from reputable sources and/or check with: Informed Choice, NSF Company or Global Drug Reference Online for companies that batch test supplements for quality and purity.
Athletes may improve performance on supplements due to either: 1) direct ergogenic (performance-enhancing) effect or 2) placebo effect or 3) allowance of a higher training load or 4) all of the above.
Understand the physiology and metabolism behind the supplement, and therefore, whether it is relevant for a certain type of athlete. Periodize the supplement in accordance to the individual athletes training and competition schedule.
Know the specific efficacious dosing regimen and protocol, and stick to it.
Pilot test any new supplement very early in the competitive or training season (during the less important time of the year).
Try to collect as much data from both the athlete and coach (give them a log) during this period (e.g. body comp, physiological testing, competition testing, psychological outcomes, side-effects etc.) to ascertain whether the individual athlete is having a positive, neutral or negative impact from the supplement.
If pilot testing was positive, periodize supplement into more major competition and training camp situations.

References

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