AIS SPORTS SUPPLEMENT FRAMEWORK
ß-ALANINE

What is it?

> The current interest in ß-alanine was initiated by research from Professor Roger Harris (who also lead the original studies into creatine supplementation) and colleagues who found that chronic supplementation with ß-alanine leads to an increase in muscle carnosine content[1] and subsequently improves high-intensity cycling capacity.[2]

> Carnosine is a L-histidine-containing dipeptide found in several human tissues but displays its highest concentration in skeletal muscle and is formed from the amino acids ß-alanine and L-histidine. Carnosine can be found in red meat, white meat and fish but is rapidly broken down to ß-alanine and L-histidine following ingestion. Thus, carnosine supplementation does not augment muscle carnosine content.

> Carnosine plays several key physiological roles including:

1. Proton buffering
2. Regulating calcium
3. Preventing antiglycation
4. Acting as an antioxidant

> Carnosine is an extremely stable muscle metabolite but it does have a large between individual variability which may be moderated by:

1. Muscle fibre type composition (carnosine is ~two-fold higher in type II muscle fibres)
2. Sex (carnosine is lower in women compared to men)
3. Specific Muscle Group (carnosine concentration varies across different muscles; for example, carnosine is lower in the soleus compared to gastrocnemius)
4. Age (carnosine increases following puberty in males and tends to increase in females and then gradually decreases with age)
5. Athlete type (highest in sprint/explosive athletes compared to endurance athletes)
6. Diet (ß-alanine increases muscle carnosine and one cross-sectional study[3] has shown lower levels of carnosine in vegans but a 6-month vegetarian diet in omnivorous women did not decrease muscle carnosine content[4])

> Numerous studies have demonstrated substantial increases in muscle carnosine in responses to a variety of ß-alanine supplementation protocols (~3.2- 6.4g·day^{-1}, for periods ranging from 4 to 24 weeks) and supplementation protocols of this duration appear to be safe.[5,6]

> Although L-histidine is an essential amino acid in humans, it is found in sufficient supply in the body, whereas ß-alanine is not. As such, ß-alanine is considered to be the rate limiting amino acid to carnosine synthesis (Harris et al., 2006). It should be noted that although L-histidine is not rate limiting, its availability is not unlimited and may decline upon chronic ß-alanine supplementation.[7]

> The increase in muscle carnosine has been shown to improve high-intensity endurance performance in both trained and untrained individuals across a range of exercise capacity tests, fixed duration and intermittent exercise tasks that are typically within a range 30s-10min in duration.[8] There are specific examples of when exercise performance may be augmented outside of this duration, whereby more prolonged exercise tasks could be enhanced by an improvement in sprint performance following prolonged exercise.[9] Furthermore, one study has also shown that ß-alanine supplementation can increase training intensity during a 5-week mesocycle of sprint-interval training in well-trained cyclists.[10]

> Increasing muscle carnosine content with chronic ß-alanine supplementation may offer an alternative to acute sodium bicarbonate loading for high-intensity exercise given that the latter may be associated with gastrointestinal upset in some athletes. Theoretically, ß-alanine loading may also offer an additive effect to bicarbonate supplementation given that muscle carnosine is an intracellular buffer, while bicarbonate facilitates extracellular buffering. The weight of evidence suggests that co-supplementation may result in a small effect size improvement compared to ß-alanine supplementation alone.[8]

> Despite ß-alanine being a common ingredient in “pre-exercise” supplement formulas (i.e., acute supplementation) used by athletes there is no evidence that acute supplementation is advantageous to performance.[11]

ASC36194

What does it look like?

> ß-alanine supplements include instant release powders and capsules as well as sustained release preparations.

> Although the sustained and rapid release formulations result in similar increases in muscle carnosine when matched for the amount of ß-alanine ingested[12,13], sustained release ß-alanine would be advisable given that a larger single dose can be ingested with improved whole body retention and sensory side-effects that are not discernible from consuming a placebo.[13,14] As such, a greater daily intake of sustained release ß-alanine could be tolerated given that paraesthesia symptoms would be mitigated using this formula.

> Efficacy of ß-alanine supplementation is not dependant on baseline muscle carnosine levels or sex and there does not appear to be any non-responders, although the increase in muscle carnosine content between individuals can vary.

> Muscle carnosine increases are most pronounced during the initial weeks of ß-alanine supplementation, whereby the increase in muscle carnosine content is greater during the first compared to subsequent 12 days of supplementation[7], and the first 4 weeks compared to the remaining 20 weeks of supplementation.[6]

> The initial review conducted by Stellingwerff et al.[15] detailing the ß-alanine prescriptive application to augment muscle carnosine highlighted a linear relationship between the total amount of ß-alanine ingested and the subsequent relative increase in muscle carnosine (%) and suggested that for a desired ~50% increase in muscle carnosine, a total of ~230 g of ß-alanine must be taken (within a daily consumption range of 1.6–6.4 g·day^{-1}). However, a more recent review[16] has indicated that the muscle carnosine increase in response to ß-alanine supplementation is non-linear, and that the greatest increases occur in the earlier stages of supplementation. One long term supplementation study (24 weeks) did demonstrate substantial further increases in muscle carnosine in the final 4 weeks of supplementation but there was no clear evidence of further improvements in high-intensity cycling capacity.[17]

> Once muscle carnosine is augmented, the washout is very slow (~2%·wk-1).[15]

> The efficiency of carnosine loading is significantly higher when ß-alanine is co-ingested with a meal (+64%) compared with in between meals (+41%), suggesting that insulin stimulates muscle carnosine loading.[12]

> Carnosine loading is more pronounced in the trained vs. untrained muscles of athletes, whereby the increase in carnosine is greater in arm (deltoid) vs. leg (soleus + gastrocnemius) muscles in kayakers, whereas the reverse pattern is observed in cyclists. Swimmers observe significantly higher increases in carnosine in both deltoid and gastrocnemius muscle compared with nonathletes. These findings suggest that training status and/or exercise training itself is a possible determinant of carnosine loading, but it remains to be determined whether these effects are due to the acute exercise effects and/or to chronic adaptations of training.

How and when do I use it?

> The most practical supplementation regimen entails athlete's consuming a 1600 mg dose of ß-alanine with their 3 main daily meals and largest snack each day (i.e., 6400 mg of ß-alanine per day spread evenly over four eating times). This is likely to reduce the incidence and severity of paraesthesia, maximise carnosine loading by co-ingesting ß-alanine with meals and promote compliance for athletes.

> While the time-to-maximal carnosine content is variable (mean 18 wk with 6.4 g·d^{-1}; range 4 to 24 wk), a minimum supplementation period of 4 weeks would be advisable in order to obtain an ergogenic benefit for specific exercise tasks (see below). However, it is not clear whether further increases in muscle carnosine (beyond those achieved with 6.4 g·d^{-1} for 4 wk) result in additional improvements in exercise performance.[17]

> A maintenance dose of ~1.2 g·d^{-1} ß-alanine seems to be sufficient to maintain muscle carnosine content elevated at 30%-50% above baseline for a prolonged period.

> Supplementation with ß-alanine in the weeks preceding a period of training where training intensity is prioritized and/or prior to periods of competition when it is desirable to maximize performance.

> There is good evidence to support the use of ß-alanine by athletes undertaking high-intensity endurance events whereby:

- Sustained competitive events last 30 seconds to 10 minutes (e.g. rowing, swimming, track cycling, middle distance running):
- Repeated bouts of high-intensity efforts are performed including:
  - High intensity interval and resistance training.
  - Team and racquet sports.
- High-intensity effort(s) are undertaken within or at the end of prolonged exercise (e.g. road cycling and distance running).

> The chronic increase in muscle carnosine may increase muscle buffering capacity or improve other mechanisms within the muscle e.g. antioxidant activity) that could enhance training adaptations by increasing training capacity.

AIS ACTAS ACT ACADEMY OF SPORT nswis NSW INSTITUTE OF SPORT NTIS Queensland Government
SASI South Australian Sports Institute FTIS VICTORIAN INSTITUTE OF SPORT wais
ASC36194

Are there any concerns or considerations?

> Acute doses of instant release ß-alanine exceeding 800-1600 mg result in paraesthesia which is an uncomfortable tingling sensation on the skin that can last up to an hour. Although the exact cause of paraesthesia is unknown, it is thought to be due to ß-alanine activated strychnine-sensitive glycine receptor sites in the brain and central nervous system and the mas-related gene family of G protein coupled receptors[18], which are triggered by interactions with ß-alanine.[19] Sustained release formulations directly reduce the symptoms of paraesthesia.

> Human skeletal muscle has an extremely large capacity for carnosine loading and commonly used supplementation protocols (e.g., 4 weeks at 6.4 g·day^{-1}) may not come close to saturating muscle carnosine. Further research is required to better understand the efficacy of longer supplementation protocols in order to maximise muscle carnosine.

> The carnosine loading efficiency following chronic orally ingested ß–alanine is very low (~3%)[12] so further strategies could be developed to increase carnosine loading efficiency.

> Although ß-alanine is considered the rate-limiting precursor for carnosine synthesis, one recent study[7] demonstrated that L-histidine levels were significantly decreased in blood plasma (-30.6%) and muscle (-31.6%) in subjects who supplemented with ß-alanine alone (6.0 g·d^{-1} for 23 d), while the decrease in L-histidine was prevented when ß-alanine and L-histidine (3.5 g·d^{-1}) were supplemented simultaneously. Furthermore, despite not being statistically significant, Varanoske et al.[13] observed an ~18.0% decrease in muscle L-histidine following 28 d of ß-alanine supplementation (6.0 g·d^{-1}). However, more research is required to determine the significance of the decline in L-histidine observed in some studies and whether the co-supplementation of L-histidine and ß-alanine is advantageous compared to ß-alanine supplementation alone.

> Given the chronic nature of the ß-alanine supplementation protocol required for carnosine loading, ß-alanine products may be expensive and require a substantial financial commitment. Therefore, the athlete should be assured that they are using a sound supplementation protocol and applying it to a situation in which there is evidence or a strong hypothesis of performance enhancement.

> Given that ß-alanine supplementation may enhance training capacity during sprint-interval training, athletes should consider the possibility of an increased risk of injury, illness, or overreaching/fatigue.

Where can I find more information?

Sports Dietitians Australia

www.sportsdietitians.com.au/factsheets/supplements/beta-alanine-%ce%b2-alanine

Gatorade Sports Science Institute

www.gssiweb.org/docs/default-source/sse-docs/stellingwerff_sse_208_a03.pdf?sfvrsn=2

Supplement safety information

www.sportintegrity.gov.au/what-we-do/anti-doping/supplements-sport

References

1. Harris, R. C., Tallon, M. J., Dunnett, M., Boobis, L., Coakley, J., Kim, H. J., Fallowfield, J. L., Hill, C. A., Sale, C., & Wise, J. A. (2006). The absorption of orally supplied ß-alanine and its effect on muscle carnosine synthesis in human vastus lateralis. AA, 30(3), 279-289.
2. Hill, C. A., Harris, R. C., Kim, H. J., Harris, B. D., Sale, C., Boobis, L. H., Kim, C. K., & Wise, J. A. (2007). Influence of ß-alanine supplementation on skeletal muscle carnosine concentrations and high intensity cycling capacity. AA, 32(2), 225-233.
3. Everaert, I., Mooyaart, A., Baguet, A., Zutinic, A., Baelde, H., Achten, E., Taes, Y., De Heer, E., & Derave, W. (2011). Vegetarianism, female gender and increasing age, but not CNDP1 genotype, are associated with reduced muscle carnosine levels in humans. AA, 40(4), 1221-1229.
4. Blancquaert, L., Baguet, A., Bex, T., Volkaert, A., Everaert, I., Delanghe, J., Petrovic, M., Vervaet, C., De Henauw, S., Constantin-Teodosiu, D., Greenhaff, P., & Derave, W. (2018). Changing to a vegetarian diet reduces the body creatine pool in omnivorous women, but appears not to affect carnitine and carnosine homeostasis: a randomised trial. BJN, 119(7), 759-770.
5. Dolan, E., Swinton, P. A., Painelli, V. d. S., Stephens Hemingway, B., Mazzolani, B., Infante Smaira, F., Saunders, B., Artioli, G. G., & Gualano, B. (2019). A Systematic Risk Assessment and Meta-Analysis on the Use of Oral ß-Alanine Supplementation. AN, 10(3), 452-463.
6. Saunders, B., Franchi, M., de Oliveira, L. F., da Eira Silva, V., da Silva, R. P., de Salles Painelli, V., Costa, L. A. R., Sale, C., Harris, R. C., Roschel, H., Artioli, G. G., & Gualano, B. (2020). 24-Week ß-alanine ingestion does not affect muscle taurine or clinical blood parameters in healthy males. EJN, 59(1), 57-65.
7. Blancquaert, L., Everaert, I., Missinne, M., Baguet, A., Stegen, S., Volkaert, A., Petrovic, M., Vervaet, C., Achten, E., & De Maeyer, M. (2017). Effects of histidine and ß-alanine supplementation on human muscle carnosine storage. MSSE, 49(3), 602-609.
8. Saunders, B., Elliott-Sale, K., Artioli, G. G., Swinton, P. A., Dolan, E., Roschel, H., Sale, C., & Gualano, B. (2017). ß-alanine supplementation to improve exercise capacity and performance: a systematic review and meta-analysis. BJSM, 51(8), 658-669.

ASC36194

9. Van Thienen, R., Van Proeyen, K., Vanden Eynde, B., Puype, J., Lefere, T., & Hespel, P. (2009). Beta-alanine improves sprint performance in endurance cycling. MSSE, 41(4), 898-903.

10. Bellinger, P. M., & Minahan, C. L. (2016). Performance effects of acute ß-alanine induced paresthesia in competitive cyclists. EJSS, 16(1), 88-95.

11. Bellinger, P. M., & Minahan, C. L. (2016). Additive benefits of beta-alanine supplementation and sprint-interval training. MSSE, 48(12), 2417-2425.

12. Stegen, S., Blancquaert, L., Everaert, I., Bex, T., Taes, Y., Calders, P., Achten, E., & Derave, W. (2013). Meal and beta-alanine coingestion enhances muscle carnosine loading. MSSE, 45(8), 1478-1485.

13. Varanoske, A. N., Hoffman, J. R., Church, D. D., Coker, N. A., Baker, K. M., Dodd, S. J., Harris, R. C., Oliveira, L. P., Dawson, V. L., Wang, R., Fukuda, D. H., & Stout, J. R. (2019). Comparison of sustained-release and rapid-release ß-alanine formulations on changes in skeletal muscle carnosine and histidine content and isometric performance following a muscle-damaging protocol. AA, 51(1), 49-60.

14. Décombaz, J., Beaumont, M., Vuichoud, J., Bouisset, F., & Stellingwerff, T. (2012). Effect of slow-release ß-alanine tablets on absorption kinetics and paresthesia. AA, 43(1), 67-76.

15. Stellingwerff, T., Decombaz, J., Harris, R. C., & Boesch, C. (2012). Optimizing human in vivo dosing and delivery of ß-alanine supplements for muscle carnosine synthesis. Amino Acids, 43(1), 57-65.

16. Rezende, N. S., Swinton, P., de Oliveira, L. F., da Silva, R. P., da Eira Silva, V., Nemezio, K., Yamaguchi, G., Artioli, G. G., Gualano, B., Saunders, B., & Dolan, E. (2020). The Muscle Carnosine Response to Beta-Alanine Supplementation: A Systematic Review With Bayesian Individual and Aggregate Data E-Max Model and Meta-Analysis. FP, 11(913).

17. Saunders, B., de Salles Painelli, V., De Oliveira, L. F., da Eira Silva, V., Da Silva, R. P., Riani, L., Franchi, M., de Souza Gonçalves, L., Harris, R. C., & Roschel, H. (2017). Twenty-four weeks of ß-alanine supplementation on carnosine content, related genes, and exercise. MSSE, 49(5), 896-906.

18. Liu, Q., Sikand, P., Ma, C., Tang, Z., Han, L., Li, Z., Sun, S., LaMotte, R. H., & Dong, X. (2012). Mechanisms of itch evoked by ß-alanine. JN, 32(42), 14532-14537.

19. MacPhee, S., Weaver, I. N., & Weaver, D. F. (2013). An evaluation of interindividual responses to the orally administered neurotransmitter ß-alanine. JAA, 2013.

The Australian Institute of Sport (AIS) Supplement Framework is an initiative of the Australian High Performance Sport System. The AIS acknowledges the support of members of the National Institute Network (NIN) and National Sporting Organisations (NSO) and their staff in delivering content expertise. This information is intended to help athletes, coaches and scientists make evidence-based decisions about the use of supplements and sports foods. Before engaging in supplement use, we recommend that each individual refer to the specific supplement policies of their sporting organisation, sports institute or parent body, and seek appropriate professional advice from an accredited sports dietitian (**www.sportsdietitians.com.au**).

Athletes should be aware that the use of supplements may have doping implications. Athletes are reminded that they are responsible for all substances that enter their body under the 'strict liability' rules of the World Anti-Doping Code. Some supplements are riskier than others. The Sport Integrity Australia (SIA) app is a useful resource to help mitigate the risk of inadvertent doping by helping to identify supplements that have been batch-tested. The SIA App provides a list of more than 11,000 batch-tested products. We recommend that all athletes consult the educational resources of SIA regarding the risks associated with supplements and sports foods.. While batch-tested products have the lowest risk of a product containing prohibited substances, they cannot offer you a guarantee that they are not contaminated (**www.sportintegrity.gov.au/what-we-do/supplements-sport**).

Last updated March 2021

ASC36194