3.2 Ergogenic Aids with Chronic Effect

We end this course by looking at ergogenic aids subject to chronic use. This ensures that throughout the course we will have covered all sports foods and ergogenic aids whose effectiveness is backed by solid evidence, pointing out doses, how and when to use them, and in what situations.

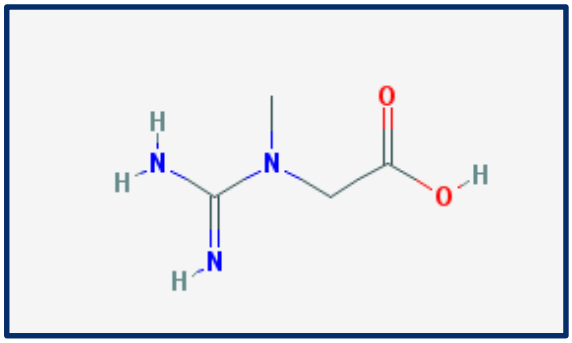
3.2.1 Creatine

Like caffeine, creatine is one of the most widely researched supplements and has a strong evidence base. **Creatine or methylguanidine-acetic acid** (figure 6) is a naturally occurring compound found in abundance in human skeletal muscle. Its most widely studied commercial form is monohydrate.

Creatine is a guanidine compound that is synthesized in the liver and kidneys from the amino acids arginine, glycine and methionine. From a dietary perspective, the predominant sources for creatine are fish and red meat; for example, 1 kg [2.2 lbs] of steak contains around 5 g [0.18 oz] of creatine (Maughan et al., 2011). The largest creatine store in the body is found in skeletal muscles (Wyss & Kaddurah-Daouk 2000), which store approximately 60-70% in phosphorylated form known as **phosphocreatine (PCr)**. There is a broad body of research dedicated to this substance. Worth pointing out are the findings put forward in a recent review by the ISSN [International Society of Sports Nutrition].

Despite persistent myths surrounding exercise-associated supplementation with creatine, creatine monohydrate continues to be one of the most effective and widely studied ergogenic aids available to athletes. Hundreds of studies have demonstrated the effectiveness of creatine monohydrate supplementation for increasing anaerobic capacity, strength and lean body mass in conjunction with training. (Bufford, 2007, p. 1).

Figure 6: Chemical Structure of Creatine Monohydrate



Source: Pubchem https://pubchem.ncbi.nlm.nih.gov/compound/586

Supplementation with creatine in the context of intermittent high-intensity team sports is of particular interest, as PCr stores show significant drops during soccer matches (Krustrup et al., 2006). In this sense, supplementation with creatine improves repeated sprint performance during short burst and dynamic, long duration intermittent exercises (Mujika et al., 2000), most likely due to an increase in resting muscle PCr stores, as well as improvements in PCr resynthesis rates during recovery periods between repeated sprints (Casey et al., 1996). In both of the studies cited here, the improvements in sprint performance after using creatine (compared to the placebo) were between 1-4%. In addition to enhancing performance in repeated sprints, players may also want to consume creatine in order to boost the improvements derived from training for muscle mass, strength and energy (Branch 2003).

Composition and Dose

The Cr transporter is called CRT1. CRT1 is used by muscle cells in Cr uptake (Mesa et al., 2002). Type II muscle fibers show greater expression of the CRT1 transporter than type I. The normal blood concentration interval of creatine is from 50-100 μM, and an acute intake of 5 g [0.18 oz] of Cr raises this concentration to 600-800 μM in approximately one hour. Taking into account that the Km value of the CRT1 transporter is 15-30 μM, the increase in Cr concentration in the blood caused by such a dose would enable muscles to reach their maximum rate of Cr uptake.

It is important to point out that when 20 g [0.71 oz] of Cr is administered per day over several days, almost 30% of the Cr administered is retained during the first two days of supplementation, although this percentage drops to just 15% from days two to four (Mesa et al., 2002). Thus, much of the Cr ingested is retained by the body (primarily by the muscle tissue) in the first few days of supplementation, whereas a large portion (85 to 90%) is excreted in the urine as Cr and creatinine during subsequent days of supplementation. Therefore, a loading phase is

proposed (four doses of approximately 5 g [0.18 oz] per day) for just two days followed by a maintenance phase of 3 to 5 g [0.11-0.18 oz] doses of Cr per day for just three or four days a week; for example, only after days where exercise is performed. Given the limitations of having players follow such a protocol, it should be pointed out that daily consumption of low doses over longer periods of time (in other words, 3-5 g [0.11-0.18 oz] per day for 30 days) would, over time, increase muscle creatine to levels similar to those observed in classic loading protocols (Hultman et al., 1996). Ingesting lower quantities of creatine monohydrate (such as 5 g [0.18 oz] per day) will increase muscle creatine stores over a period of three to four weeks. These elevated muscle creatine stores tend to return to basal levels five to eight weeks after ceasing supplementation. Considering that it takes weeks to return to basal levels after ceasing supplement ingestion (which means that the ergogenic effects should remain), athletes might find it prudent to "stage" creatine supplementation at certain times during a season (for example, during preseason, at set times) and/or take them for training objectives (for example, strength/hypertrophy) (Morton 2014).

It is important to remember that people do not always respond to creatine supplementation in the same way, insofar as increased muscle creatine stores and subsequent improvements in performance are concerned. In fact, the extent to which muscle creatine increases following a dose of creatine varies widely and seems to be largely subject to the initial concentration level of muscle creatine prior to supplementation, the latter likely determined by dietary habits (Hultman et al., 1996). Consequently, creatine-induced performance improvements in intermittent exercise are greater in those individuals who showed higher increases in muscle creatine (particularly type II fibers) and PCr (Casey et al., 1996).

Nearly all studies indicate that proper Cr supplementation increases body mass by approximately 1-2 kg [2.2-4.4 lbs] during the first week of loading (Bufford, 2007). This could prove detrimental to performance in sports involving body mass transfer such as running and cycling (particularly in the mountains). These increases in body mass are limited to fat-free body mass and are probably due to increased intracellular accumulation of water. This is why not all players are able to use creatine supplementation, given the sensation of feeling heavier and slower. This can particularly affect those athletes who rely on physical speed and agility as key attributes (such as forwards and midfielders in soccer).

In order to maximize creatine storage, it is also recommended that creatine be consumed after exercise and in conjunction with carbohydrates and/or proteins, given that muscle concentration and elevated insulin are known to increase the absorption of muscle

creatine (Robinson et al., 1999). It has been demonstrated that Cr intake together with carbohydrates helps produce a 60% greater increase in total muscle Cr content than when Cr is ingested on its own. Also of interest, some findings suggest that Cr intake combined with carbohydrates reduces variation in Cr accumulation among individuals.

It is worth mentioning that glycogen supercompensation tends to be greater if carbohydrate and creatine loading are performed simultaneously, given that creatine loading increases muscle volume, which in turn improves glycogen supercompensation. This suggests some possible practical applications for different sports with respect to optimizing glycogen levels, regardless of the other effects associated with this supplement. A previous creatine load may also improve the resynthesis rate of muscle glycogen after exercise (Robinson et al., 1999). Taking into account the difficulty of refilling muscle glycogen stores after games, even with sufficient amounts of carbohydrates and proteins, players may find this strategy particularly relevant during specific, intensive periods when they play more than one game with little recovery time in between games.

Also noteworthy, it has been reported that Cr intake after one hour of submaximal physical exercise increases accumulation of muscle creatine by 10%, although marked variations have been observed among individuals. Nevertheless, it should also be kept in mind that the extent of muscle creatine accumulation is reduced when Cr is ingested with carbohydrates after exercising to exhaustion.

Applications

The proposed mechanism through which Cr acts as an ergogenic aid involves increasing the total muscle creatine content [creatine + phosphocreatine (PCr)] (Mesa et al., 2002). Muscle creatine increases by approximately 50% while phosphocreatine increases by 12.5% (Mesa et al., 2002).

Taking into account that ATP is resynthesized from PCr during the first few seconds of maximum-intensity, short-duration workouts, the increased concentration of muscle phosphocreatine enables resynthesis of ATP to be sustained at a higher rate for longer periods of time. Thus, a large portion of double-blind and cross-linking studies have shown that administering Cr does in fact have an ergogenic effect on power production during high-intensity, short-duration activities.

Thus, there is evidence of enhanced strength and power, and therefore, enhanced performance in single and repeated sprints in running and cycling, as is there evidence of enhanced strength and muscle mass when used in overload training processes. The application of Cr in

endurance sports (without a loading phase) are not only related to improvements in sprint capacity, but also to increases in glycogen stores.

Timing

Before and after exercise, and during other parts of the day when a loading phase is carried out, always accompanied by carbohydrates (for example 1 g/kg [0.04 oz/lb]).

Australian Institute of Sport Protocol

- The most researched dietary creatine supplement is creatine monohydrate, which has a variety of established loading protocols:
  - Rapid loading can be achieved with 5 days of repeated doses (for example, four doses of 5 g [0.18 oz]) of creatine.
  - Slow loading is performed over a longer period (28 days with daily doses of 3 g [0.11 oz]).
  - The maintenance dose of 3 g/day [0.11 oz/day] allows high levels of creatine to be maintained.
  - Unloading: Once muscle creatine content has reached saturation, at least four weeks are required for it to return to resting levels.
- Consumption of the creatine dose with a substantial amount of carbohydrates (50-100 g [1.8-3.5 oz]) (Green et al., 1996) increases incorporation and storage of creatine in the muscles. Consuming the creatine dose together with a carbohydrate-rich meal or snack will help individuals to respond to creatine supplementation and reach muscle creatine storage threshold.
- Acute loading generally produces a weight increase of 600-1000 g [21.2-35.2 oz], which may indicate liquid retention. Although it has been suggested that a slow loading protocol can prevent this weight gain, this theory is yet to be adequately studied. It is possible that any change in weight associated with slow loading is masked by normal fluctuations in body mass or the results of training and longer-term dietary interventions.
- Creatine monohydrate is a common source of creatine found in supplements available for purchase, and the combined experience of 20 years of research and use of this product in accordance with established protocols all suggests that it is safe and effective. Other forms of creatine have been included in new supplements with the argument that they represent a better source of creatine. These new formulas include creatine serum, creatine malate and creatine ethyl ester. The effectiveness, safety and regulations surrounding the majority of these new forms of creatine found in

dietary supplements have not been properly established. Moreover, there is little or no evidence that supports the marketing claims that these alternative sources of creatine are more stable, more easily digestible, and more effective at increasing creatine levels in the muscles and achieving results in performance or are associated with less side effects (Jager et al., 2011).

- There is a strong body of evidence that supplementation with creatine can improve the physical performance involved in repeated sprints or series of high-intensity workouts separated by short recovery periods. Improved performance during competitions can be seen as a result of acute loading or chronic use. On this point, we might mention the following cases:
  - A well-trained athlete performs strength training to increase lean body mass.
  - Interval training sessions with sprints in which the athlete must repeat maximal explosive strength exercises with brief recovery intervals.
  - Sports with intermittent work patterns (for example, soccer, basketball, American football, racket sports).
- The use of creatine loading to increase glycogen storage or cerebral creatine stores has not been sufficiently investigated so as to make clear recommendations, but conducting detailed studies into this topic would be highly worthwhile.
- It would also be important to perform additional research into creatine supplementation that involves sport-specific applications and with highly trained or elite athletes.

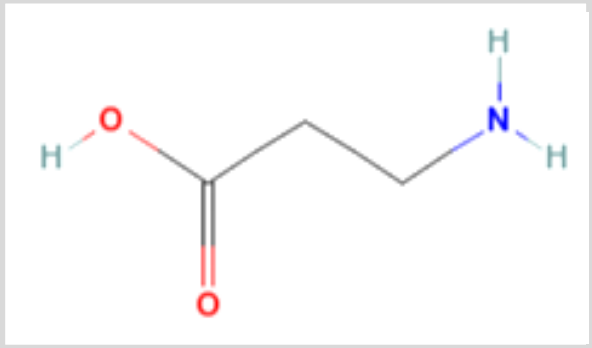
3.2.2 Beta-Alanine

This amino acid (figure 7) together with L-histidine forms a dipeptide (figure 8) called **carnosine** that is found in high concentrations in skeletal muscle, particularly in type II fibers (Van Thienen, 2009). Carnosine has been identified as involved in a series of cellular functions, including the regulation of calcium sensitivity, glycosylation inhibition and protein cross-linking, as well as the destruction of free radicals and enzyme activity regulation. To date, the only physiological role of carnosine that has been corroborated by human observation is intracellular pH buffering.

The imidazole ring (the ring that appears to the left of figure 8) of carnosine has a pKa = 6.83, close to intracellular pH during exercise (~6.5), which converts the carnosine into a powerful molecular buffer for protons and hydrogen ions (H+). Currently, thinking is that carnosine accounts for approximately 10% of total buffer capacity in skeletal muscle cells. It is interesting to note that while the cellular mechanisms involved in fatigue onset are still up for debate, it is believed that the intracellular accumulation of protons is related with fatigue during high-intensity muscle contractions.

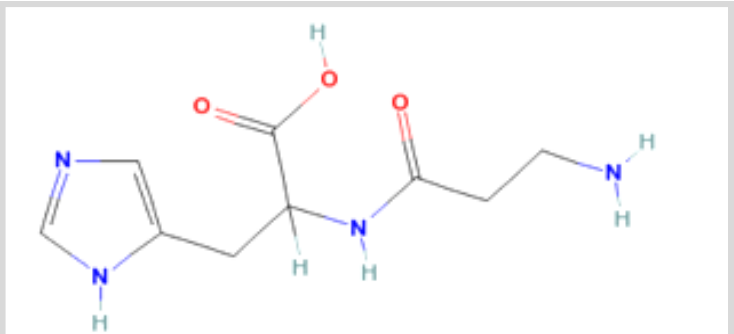
As such, it has become common practice among soccer players to take daily β-alanine supplements to increase the carnosine stores in the muscles, thereby potentially increasing performance in high-intensity exercises. Unfortunately, research evaluating the effects of β-alanine in field sports such as soccer, where high-intensity intermittent exercise takes place, remains limited and controversial.

Figure 7: Chemical Structure of β-Alanine



Source: National Institutes of Health, 2004. Retrieved from https://goo.gl/SFiPdy

Figure 8: Chemical Structure of Carnosine



Source: National Institutes of Health, 2004. Retrieved from https://goo.gl/24tnNX

Composition and Dose

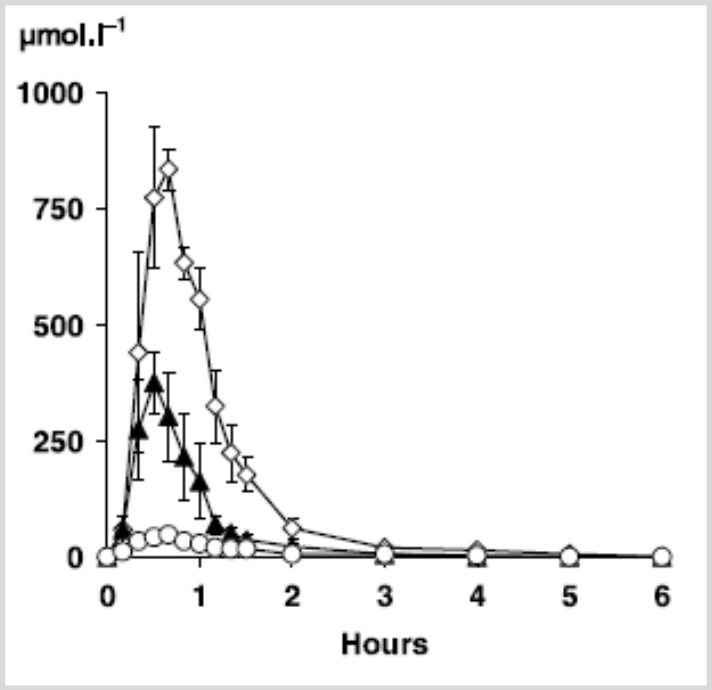
Harris et al. (2006) studied acute and chronic responses to the ingestion of different amounts of β-alanine. Figure 9 shows the blood concentration of β-alanine over time following the ingestion of different doses. Peak blood levels of β-alanine were reached in less than one hour with doses of 10 to 40 mg/kg^{-1} [4.5 to 18.2 mg/lb^{-1}] of body mass, returning to resting levels within three hours. Doses of 10, 20 and 40 mg/kg^{-1} [4.5, 9.1 and 18.2 mg/lb^{-1}] increased blood concentrations of β-alanine from a value below 0.5 μM to values of 50-100 μM, approximately 400 μM and 800 μM, respectively.

Taking into account the Km of the β-alanine (40 μM) transporter, the blood values attained after taking the aforementioned doses meant that 67%, 91% and 95% of the maximum transportation speed of β-alanine to the muscle is reached. Based on these results, the most appropriate dose would be 40 mg/kg^{-1} [18.2 mg/lb^{-1}]; nevertheless, this dose characteristically brought about a tingling sensation (or paresthesia), a side effect of β-alanine ingestion that has been previously reported in the literature and in anecdotal reports by athletes. To reduce these symptoms, sustained release formulas have been developed in which two 800 mg doses are ingested simultaneously without presenting any symptoms whatsoever (Decombaz et al., 2012). While the optimal dose and delivery strategy for β-alanine is not currently known, it is worth highlighting that there is a linear relation between total ingestion of β-alanine (between 1.6 - 6.4 g/day [0.06 - 0.23 oz/day]), and absolute and relative increases in muscle carnosine (Stellingwerff et al., 2012).

On the other hand, it is also important to keep in mind the losses via urine that occur following ingestion of the different doses. Researchers (Harris et al., 2006) discovered losses of 0.60±0.09, 1.50±0.40, and 3.64±0.47% of the ingested dose in acute doses of 10, 20 and 40 mg/kg^{-1} [4.5, 9.1 and 18.2 mg/lb^{-1}], respectively. Thus, it is not recommended to exceed 20 mg/kg [9.1 mg/lb] or approximately 1.6-2 g [0.027 - 0.032

oz/lb] of β-alanine per dose. These same authors studied the effect of ingesting 3.2 or 6.4 g [0.11 or 0.23 oz] of β-alanine/day^{-1}, with ingestion divided into different doses; for example, 4 doses of 800 mg, or 400 and 800 mg doses distributed throughout the day over four weeks. What they observed was a 42.1% and 64.2% increase in β-alanine concentration in the muscles after four weeks of supplementation.

Figure 9: Average Concentration of Blood β-Alanine (µmol.L-1) after Ingestion of 10 (○), 20 (▲), or 40 (◊) mg/kg-1 [4.5 (○), 9.1 (▲), or 18.1 (◊) mg/lb-1] of β-Alanine.



Source: Harris et al., 2006, p. 282.
For the sake of clarity, the standard deviations of the mean values are only shown for measurements following 20 and 40 mg/kg [9.1 and 18.2 mg/lb] ingestions.

Applications

Regarding the application of β-alanine to endurance sports, the recent findings of Jeffrey R. Stout et al. (2006) are of particular interest. The authors conducted research over a 28-day period, studying the effects of β-alanine and Cr supplementation (administering them jointly or separately) on the onset of neuromuscular fatigue as measured via a test previously validated with untrained men (a test evaluating the capacity for physical exertion at fatigue threshold). The trial subjects were randomly assigned to one of four treatment conditions using a double-blind design: (a) placebo (PLA, 34 g [1.2 oz] of dextrose; n=13), (b) creatine (CrM, 5.25 g [0.19 oz] of creatine monohydrate (CrM) plus 34 g [1.2 oz] of dextrose, n=12), (c) β-alanine, (1.6 g [0.06 oz] of β-Ala plus 34 g [1.2 oz] of dextrose, n=12) or (d) β-alanine plus CrM (CrBA, 5.25 g [0.19 oz] of creatine monohydrate, plus 1.6 g [0.06 oz] of β-alanine plus

34 g [1.2 oz] of dextrose, n=14). The supplements were identical in flavor and appearance and were dissolved in approximately 450 ml [15.9 fl oz] of water, to be ingested four times a day for six consecutive days. Following the six day period, the supplements were ingested twice a day for 22 days before performing the second physical aptitude assessment (the first was performed before the start of the supplementation period). The only supplement groups in which a significant increase in power production was observed relative to that produced at the onset of neuromuscular fatigue were β-Ala and CrBA groups.

Therefore, CrM did not have any effect on neuromuscular fatigue threshold, where the entire effect could be attributed to β-alanine. As such, the primary result of this study suggests that supplementation with β-alanine (3.2 g/day [0.11 oz/day]) during 28 days may delay the onset of neuromuscular fatigue and improve the capacity for physical exertion during exercise using a stationary bicycle. Although recommendations should only be made following clinical tests, these findings may be useful to nutritionists, professionals that specialize in strength and fitness, and athletes considering using β-alanine. These findings also lay the foundations for future studies aimed at testing the hypothesis that β-alanine is capable of increasing muscle carnosine concentrations, with subsequent improvements in the buffering capacity of protons (H+) in skeletal muscle.

Studies performed recently on humans have consistently shown that supplementation with β-alanine (4 to 6 g [0.14 to 0.21 oz] per day) over a period of four to ten weeks can substantially increase (> 50%) carnosine content in type I and II muscle fibers, implying an improvement in performance of 1 to 2 minute maximal exercise series. Taking into account that creatine has the capacity to increase maximum power production in short-duration exercises and to increase performance in repeated sprints, and that β-alanine and sodium bicarbonate can increase intracellular buffering capacity, the combination of all three supplements may be ideal in some athlete populations, such as sprint athletes and cyclists. Thus, the combined effect of all three supplements may be beneficial to strength training.

In a recent study, Van Thienen et al. (2009) looked at the effect of β-alanine supplementation (eight weeks of 2 to 4 g [0.07 to 0.14 oz] doses per day administered in 500 mg capsules throughout the day) in 21 young, moderate to highly-trained cyclists in a 10 minute time trial and a 30 minute sprint. Supplementation with β-alanine increased both sprint capacity and average power production during the time trial. As mentioned earlier, the tingling sensation following ingestion of β-alanine may appear when the dose exceeds 20 mg/kg^{-1} [9.1 mg/lb^{-1}]. In Van Thienen et al.'s study, (2009), subjects ingested the supplement in several doses throughout the day, where doses of 7 mg/kg^{-1} [3.2 mg/lb^{-1}]

did not produce any side effects. It is worth mentioning that the minimum effective dose was reported at 65-86 mg/kg^{-1}/day^{-1} [29.5-39.1 mg/lb^{-1}/day^{-1}]; nevertheless, this study identified an ergogenic effect with a lower dose (55 mg/kg^{-1}/day^{-1} [25 mg/lb^{-1}/day^{-1}]).

Timing

Before and after exercise, and at other times of the day with meals to facilitate beta-alanine absorption.

Australian Institute of Sport Protocol

- β-alanine supplements include rapid absorption powders and capsules, as well as other sustained release formulations.
- The protocols for optimizing carnosine content have yet to be explored in detail, but some basic principles are clear.
- The rapid increase of β-alanine levels in the blood is associated with the side effect of paresthesia (the tingling sensation on the skin), which certain individuals may find uncomfortable.
- This generally occurs at doses of >10 mg/kg [>4.5 mg/lb] of body mass and can equal the amount provided by dietary sources, such as a large chicken breast.
- The levels of β-alanine in the blood rise and fall within two hours of supplementation; therefore, doses sequenced or divided into small quantities (<10 mg/kg [>4.5 mg/lb]) throughout the day, enabling continuous maintenance of blood concentrations, can be an effective strategy for maximizing muscle consumption while minimizing side effects.
- Sustained release formulations of β-alanine can achieve the same effect as divided doses of a rapid absorption formula (Harris et al., 2008).
- Protocols that have proven effective at increasing carnosine concentration in muscles include doses of 3.2-6.4 g/day [0.11-0.23 oz/day] during six to ten weeks.
- To date, there is no clear guideline for the maximum value of muscle carnosine content, nor which dose protocols should be followed in order to keep a muscle loaded with carnosine.
- All individuals appear to respond to β-alanine supplementation regardless of the initial carnosine content in the muscles.
- The period for cleansing muscle carnosine following interruption of supplementation is slow and it can take approximately 15 weeks for concentrations to return to their initial state (Baguet et al. 2009).
- β-alanine supplementation is not associated with weight gain.
- There is a sizable body of new evidence supporting the use of β-alanine by athletes who participate in events affected by decreased pH levels (increase in H+ ions) in the muscles generally associated with high-intensity exercises.

    - Competitive events lasting one to seven minutes (for example, rowing, swimming, track cycling, middle-distance running).
    - Repeated series of high-intensity exercises (sprints, weightlifting) that cause an increase in H+ ions over time. We can include among these:
        - Interval training and strength training.
        - Team and racket sports.
        - High-intensity exercises performed during or at the end of prolonged exercises that are mainly performed at intensities lower than those associated with the reduction of pH levels (for example, road cycling and long-distance running).
- In these situations, supplementation with β-alanine provides a chronic strategy for increasing muscle buffer capacity. This can increase performance in single or repeated competition events.
- A chronic increase in muscle buffer capacity can also help to increase adaptations to training by either increasing the capacity for strenuous training or by reducing damage associated with high levels of muscle acidity.
- β-alanine can potentially provide a strategic or additional alternative to bicarbonate/citrate loading.
- Increased muscle carnosine concentration can offer, in addition to training and competition adaptations, other advantages that arise from the other roles performed by the muscle (for example, antioxidant activity).

3.2.3 Periodization of Ergogenic Aids

Having analyzed the available ergogenic aids and protocols, it is very important for the prescribing professional to schedule their use according to the athlete's objectives and competition calendar.

We have found that the washout period for these ergogenic aids is around 8 to 12 weeks, which may coincide with the athlete's transition or recovery period. It is important to keep in mind that, in the case of beta-alanine, 4 to 8 weeks of continuous supplementation are required to obtain the greatest benefits. This obviously needs to be taken into account in order to coincide with those periods when the athlete wishes to be in top physical shape for achieving maximum performance.

3.2.4 Ineffective or Dangerous Substances

In module two we have highlighted some ineffective or dangerous substances. Below is a list of some ergogenic aids available for purchase that are ineffective or dangerous:

- Ephedrine.
- Pseudoephedrine.
- Tribulus Terrestris.
- DHEA.
- ATP.
- Ginseng.
- Cytochrome C.
- Nitric oxide.

Bibliography

Beelen, M., J. Kranenburg, J. M. Senden, H. Kuipers and L. J. Loon. (2012). Impact of Caffeine and Protein on Post-Exercise Muscle Glycogen Synthesis. Med Sci Sports Exerc 44(4): 692-700.

Branch, J. D. (2003). Effect of Creatine Supplementation on Body Composition and Performance: a Meta-Analysis. Int J Sport Nutr Exerc Metab 13(2): 198-226.

Buford T. W., Kreider, R.B., Stout, J.R., Greenwood, M., Campbell, B., Spano, M., Ziegenfuss, T., Lopez, H., Landis, J., and Antonio, J. (2007). International Society of Sports Nutrition Position Stand: Creatine Supplementation and Exercise. *Journal of the International Society of Sports Nutrition*.

Casey, A., D. Constantin-Teodosiu, S. Howell, E. Hultman and P. L. Greenhaff (1996). Creatine Ingestion Favorably Affects Performance and Muscle Metabolism During Maximal Exercise in Humans. Am J Physiol 271(1 Pt 1): E31-37.

Davis, J. M., Z. Zhao, H. S. Stock, K. A. Mehl, J. Buggy and G. A. Hand (2003). Central Nervous System Effects of Caffeine and Adenosine on Fatigue. Am J Physiol Regul Integr Comp Physiol 284(2): R399-404.

Decombaz, J., M. Beaumont, J. Vuichoud, F. Bouisset and T. Stellingwerff (2012). Effect of Slow-Release Beta-Alanine Tablets on Absorption Kinetics and Paresthesia. Amino Acids 43(1): 67-76.

Duvnjak-Zaknich, D. M., B. T. Dawson, K. E. Wallman and G. Henry (2011). Effect of Caffeine on Reactive Agility Time when Fresh and Fatigued. Med Sci Sports Exerc 43(8): 1523-1530.

Foskett, A., A. Ali and N. Gant (2009). Caffeine Enhances Cognitive Function and Skill Performance During Simulated Soccer Activity. Int J Sport Nutr Exerc Metab 19(4): 410-423.

Fredholm, B. B. (1995). [Should Coffee be Classified as a Doping Agent? Caffeine is Definitely Effective when it Comes to Performance Capacity]. Lakartidningen 92(44): 4079-4080.

Gant, N., A. Ali and A. Foskett (2010). The Influence of Caffeine and Carbohydrate Coingestion on Simulated Soccer Performance. Int J Sport Nutr Exerc Metab 20(3): 191-197.

Graham, T. E. and L. L. Spriet (1995). Metabolic, Catecholamine, and Exercise Performance Responses to Various Doses of Caffeine. J Appl Physiol (1985) 78(3): 867-874.

Haider, G. and J. P. Folland (2014). Nitrate Supplementation Enhances the Contractile Properties of Human Skeletal Muscle. Med Sci Sports Exerc.
Harris, R., Tallon, M., Dunnett, M., Boobis, L., Coakley, J., Kim, H., Fallowfield, J., Hill, C., Sale, C., and Wise, J. (2006). The Absorption of Orally Supplied β-Alanine and Its Effect on Muscle Arnosine Synthesis in Human Vastus Lateralis. Amino Acids.

Hodgson, A. B., R. K. Randell and A. E. Jeukendrup (2013). The Metabolic and Performance Effects of Caffeine Compared to Coffee During Endurance Exercise. PLoS One 8(4): e59561.

Hoffman Jay R., Jie Kang, Nicholas A. Ratamess, Stefanie L. Rashti, Christopher P. Tranchina and Avery D. Faigenbaum (2009). Thermogenic Effect of an Acute Ingestion of a Weight Loss Supplement. Journal of the International Society of Sports Nutrition, 6:1.

Hultman, E., K. Soderlund, J. A. Timmons, G. Cederblad and P. L. Greenhaff (1996). Muscle Creatine Loading in Men. J Appl Physiol (1985) 81(1): 232-237.

International Endurance Work Group. (2014). AIS Protocol on the Use of Caffeine. Retrieved on 03/6/2016 from http://goo.gl/D3zMxN

International Endurance Work Group. (2014). AIS Protocol on the Use of Bicarbonate. Retrieved on 03/6/2016 from http://goo.gl/vVg8rx

International Endurance Work Group. (2014). AIS Protocol on the Use of Beet Juice. Retrieved on 03/6/2016 from http://goo.gl/pctXeo

International Endurance Work Group. (2015). AIS Protocol on the Use of Creatine. Retrieved on 03/6/2016 from http://goo.gl/9qJGUJ

International Endurance Work Group. (2014). AIS Protocol on the Use of Beta-Alanine. Retrieved on 6/3/2016 from http://goo.gl/jSy3uC

Jones A. M., Satoshi Haramizu, Mayur Ranchordas, Louise Burke, Samantha Stear, and Linda M. Castell. (2011). BJSM Reviews: A-Z of Nutritional Supplements: Dietary Supplements, Sports Nutrition Foods and Ergogenic Aids for Health and Performance. Part 27. Br J Sports Med, 45: 1246-1248.

Jones, A. M. (2014). Dietary Nitrate Supplementation and Exercise Performance. Sports Med 44 Suppl 1: S35-45.

Kreider R. B, A. L Almada, J. Antonio, C. Broeder, C. Earnest, M. Greenwood, T. Incledon, D. S. Kalman, S. M. Kleiner, B. Leutholtz, L. M. Lowery, R. Mendel, J. R. Scout, D. S. Willoughby, T. N. Ziegenfuss (2004). ISSN Exercise & Sport Nutrition Review: Research & Recommendations. Sports Nutrition Review Journal; 1 (1), pp. 1–44.

Krustrup, P., M. Mohr, A. Steensberg, J. Bencke, M. Kjaer and J. Bangsbo (2006). Muscle and Blood Metabolites During a Soccer Game: Implications for Sprint Performance. Med Sci Sports Exerc 38(6): 1165-1174.

Larsen, F. J., T. A. Schiffer, S. Borniquel, K. Sahlin, B. Ekblom, J. O. Lundberg and E. Weitzberg. (2011). Dietary Inorganic Nitrate Improves Mitochondrial Efficiency in Humans. Cell Metab 13(2): 149-159.

Maridakis, V., M. P. Herring and P. J. O'Connor (2009). Sensitivity to Change in Cognitive Performance and Mood Measures of Energy and Fatigue in Response to Differing Doses of Caffeine or Breakfast. Int J Neurosci 119(7): 975-994.

Maughan, R. J., P. L. Greenhaff and P. Hespel. (2011). Dietary Supplements for Athletes: Emerging Trends and Recurring Themes. J Sports Sci 29 Suppl 1: S57-66.

Meeusen, R. (2014). Exercise, Nutrition and the Brain. Sports Med 44 Suppl 1: S47-56.

Mesa, L., Ruiz, J., González-Gross, M., Gutiérrez Sáinz, A., and Castillo Garzón, and M. Oral. (2002). Creatine Supplementation and Skeletal Muscle Metabolism in Physical Exercise. Sports Med.

Morton, J. P. (2014). Supplements for Consideration in Football. Sports Science Exchange 27(130): 1-8.

Mujika, I., S. Padilla, J. Ibanez, M. Izquierdo and E. Gorostiaga (2000). Creatine Supplementation and Sprint Performance in Soccer Players. Med Sci Sports Exerc 32(2): 518-525.

Pedersen, D. J., S. J. Lessard, V. G. Coffey, E. G. Churchley, A. M. Wootton, T. Ng, M. J. Watt and J. A. Hawley. (2008). High Rates of Muscle Glycogen Resynthesis after Exhaustive Exercise when Carbohydrate is Coingested with Caffeine. J Appl Physiol (1985) 105(1): 7-13.

Robinson, T. M., D. A. Sewell, E. Hultman and P. L. Greenhaff (1999). Role of Submaximal Exercise in Promoting Creatine and Glycogen Accumulation in Human Skeletal Muscle. J Appl Physiol (1985) 87(2): 598-604.

Stear J., L.M. Castell, L.M. Burke, L. L. Spriet. (2010). BJSM Reviews: A–Z of Nutritional Supplements: Dietary Supplements, Sports Nutrition Foods and Ergogenic Aids for Health and Performance Part 6. Br. J. Sports. Med. 44: 297-298

Stellingwerff, T., H. Anwander, A. Egger, T. Buehler, R. Kreis, J. Decombaz and C. Boesch (2012). Effect of Two Beta-Alanine Dosing Protocols on Muscle Carnosine Synthesis and Washout. Amino Acids 42(6): 2461-2472.

Stout, J., Cramer, J., Mielke, M., O'Kroy, J., Torok, D., and Zoeller, R.F. are of particular interest. Effects of Twenty-eight Days of Beta-Alanine and Creatine Monohydrate Supplementation on the Physical Working Capacity at Neuromuscular Fatigue Threshold. The Journal of Strength & Conditioning Research.

Van Montfoort BM, Van Dieren L, Hopkins WG, Shearman JP. (2004). Effects of Ingestion of Bicarbonate, Citrate, Lactate, and Chloride on Sprint Running. Med Sci Sports Exerc. 2004; 36 (7): 1239-43.

Van Thienen, R., Van Proeyen, K., Vanden Eynde, B., Puype, J., Lefere, T., and Hespel, P. (2009) B-Alanine Improves Sprint Performance in Endurance Cycling. Medicine & Science in Sports & Exercise.

Wylie, L. J., M. Mohr, P. Krustrup, S. R. Jackman, G. Ermiotadis, J. Kelly, M. I. Black, S. J. Bailey, A. Vanhatalo and A. M. Jones (2013). Dietary Nitrate Supplementation Improves Team Sport-Specific Intense Intermittent Exercise Performance. Eur J Appl Physiol 113(7): 1673-1684.
Wyss, M. and R. Kaddurah-Daouk (2000). Creatine and Creatinine Metabolism. Physiol Rev 80(3): 1107-1213.