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METABOLISM AND SUPPLEMENTATION: A SYSTEMATIC REVIEW ON ANAEROBIC ENERGY METABOLISM AND SUPPLEMENTATION TO IMPROVE PERFORMANCE BY LIMITING THE NEGATIVE EFFECTS OF BLOOD LACTATE

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ABSTRACT

Our knowledge on preparing the athlete for competition has increased dramatically over the years, especially in the field of sports nutrition. The foundation of any dietary regimen is centered on appropriate and healthy whole foods; however, certain athletes may wish to complement their diet with additional supplements to gain a performance advantage over their competition. The purpose of this article is to review anaerobic metabolism and lactate production, and discuss certain supplements that can improve performance by limiting the detrimental effects of lactate accumulation. More specifically, this article first describes the properties of anaerobic metabolism (phosphagen and glycolytic systems) and how creatine, β-alanine, sodium phosphate, and sodium citrate improve subsequent performance by limiting the negative effects of lactate that ultimately disturb the sarcomere of the muscle.

Keywords: Phosphocreatine, Creatine, Creatine Monohydrate, Beta-Alanine, Sodium Citrate, Sodium Bicarbonate, Lactate, Lactic Acid, Alkalotic, Energy Systems, Aerobic, Anaerobic, Performance, Supplementation

INTRODUCTION

Sports such as of football, basketball, and hockey rely heavily on the anaerobic energy system to create energy rapidly (1-5); whereas, sports such as soccer, field hockey, and distance running rely primarily upon the aerobic energy system to provide ATP throughout the matches (6, 7). The anaerobic energy systems are comprised of the phosphagen and the glycolytic system (as well

as the adenylate kinase system). Due to the repetitive nature of the previously mentioned anaerobic sports, as well as the short rest periods between plays, the athletes' phosphocreatine stores become depleted, thus a greater reliance on anaerobic glycolysis is necessary for force production (8). Anaerobic athletes primarily recruit their type IIx and IIa muscle fibers when they need to produce substantial force in their sport. These muscle fibers create the largest amount of power of all the various isoforms of skeletal muscle fibers. However, the more developed the type IIx muscle fibers of an individual, the greater formation of blood lactate accumulates in that person. This occurs because of increased glycogen stores, increased motivation, increased glycolytic enzymes (specifically phosphofructose kinase), increased work rate, and high levels of lactate dehydrogenase (LDH) (9). Anaerobic sprint athletes typically achieve 20-30% higher blood lactate levels than non-anaerobic athletes (9).

Sports such as soccer, field hockey, and long distance running rely heavily upon aerobic metabolism; however, glycolysis is necessary for aerobic metabolism. Although the aerobic energy system can utilize substrates such as proteins, pyruvate, fats, and carbohydrates to create ATP, the glycolytic system can only utilize carbohydrates (i.e. glucose from blood glucose or from stored intramuscular glycogen). Glycolysis produces necessary intermediates for the Krebs cycle which allows the electron transport chain to be able to utilize the previously mentioned substrates (proteins, pyruvate, fats and carbohydrates) in order to produce ATPs oxidatively. It should be noted that glycolysis always produces pyruvate which has the capability and probability of transforming into lactate. In fact, the ratio of lactate to pyruvate in resting skeletal muscle is around or greater than 10:1. Under resting conditions, the lactate is oxidized via oxidative metabolism in the mitochondria, a theory referred to as the "intracellular lactate shuttle concept" (10, 11). At rest and during submaximal exercise, the clearance of lactate limits the accumulation of lactate; however, during intense exercise, when high threshold motor units are recruited, lactate formation exceeds the clearance of lactate, thus an accumulation of lactate occurs. Since high threshold motor units also referred to as glycolytic, fast twitch, and/or white fibers contain low amount of mitochondria, pyruvate does not have the capability to further be metabolized via oxidative metabolism. Therefore, recruitment of fast twitch fibers dramatically elevates lactate concentrations (11).

Since the formation of lactate is probable (even under resting conditions), both aerobic and anaerobic athletes who seek to minimize the accumulation of lactate should seek ergogenic aids to avoid the accumulation of lactate such as proper training to improve the athletes buffering systems and/ or the possibility of supplementation (i.e. Creatine, β-Alanine, Sodium Citrate, and/or Sodium Bicarbonate). The purpose of this article is to review anaerobic energy metabolism and discuss the how, why, and results of lactate production, as well as review supplements capable of improving performance by either limiting lactate production or by decreasing lactate's effect on the sarcomere by maintaining an optimal pH.

THE PHOSPHAGEN ENERGY SYSTEM

The body has three immediate energy sources which are as follows: 1.) Utilizing stored ATP; 2.) Employing the adenylate kinase system; and 3.) Engaging the phosphocreatine system. ATP is a heavy molecule, thus the body only stores a finite amount of ATP in the body; therefore, ATP is depleted rapidly with the onset of exercise. However, the body has mechanisms to maintain ATP homeostasis. During heavy/

intense exercise, ATP homeostasis must be maintained; therefore, the body must rephosphorylate ADP to ATP rapidly by using either the adenylate kinase system and/or the phosphocreatine system. Although the adenylate kinase system (also referred to as the myokinase system) is a powerful stimulus of energy metabolism because of its production of AMP, this paper will focus on the phosphagen system because it can be enhanced through supplementation of creatine.

Phospahgen or ATP-PC System

Adenylate or Myokinase Reaction:

$$ADP + PCr \xrightarrow[Creatine\ Kinase]{} ATP + Cr$$

$$ADP + ADP \xrightarrow[Adenylate\ Kinase]{} ATP + AMP$$

`The two primary determinants of which energy system is used are intensity and duration with intensity being more important. As intensity increases, the body has to use anaerobic means to yield ATP due to the necessity to produce ATP rapidly. High intensity- all out events lasting from 10-15 seconds rely mostly on the phosphagen system to rephosphorylate ADP to ATP (12). After this time span, phosphocreatine (PCr) stores deplete, thus glycolysis must take over to maintain ATP homeostasis.

PCr rephosphorylates using oxidative metabolism. Harris et al. (13) determined that the rephosphorylation of PCr is biphasic, meaning it consists of a fast phase and a slow phase. During the fast phase (21-22 seconds), most of the degraded phosphocreatine is replenished; whereas, during the slow phase (>170 seconds), the remaining phosphocreatine is replenished. If an athlete engages in a singular event that relies heavily on the phosphagen system (i.e. 200 meter sprint), or if an athlete participates in an activity that has repeated bouts of effort (i.e. hockey), supplementation with creatine can be implemented to reduce the amount of resulting lactate produced from limiting the necessity for glycolysis.

As mentioned, the two primary determinants of which energy systems are utilized are intensity and duration. The phosphagen system is only capable of producing ATP for 10-15 seconds during high intensity exercise (12). As PCr becomes depleted during exercise, the body relies on anaerobic glycolysis to yield ATP. Glycolysis occurs in the cytosol and consists of 10 steps which do not require oxygen (14). Increased exertion leads to an increase in sympathetic nervous activity which stimulates the release of glucagon from the α-cells of the pancreas which causes glycogenolysis (the breakdown of stored glycogen) of liver glycogen (15). In addition to this, increased exertion stimulates the release of epinephrine from the adrenal medulla which causes glycogenolysis in skeletal muscle (15). The breakdown of liver glucose increases blood glucose levels which is then transported via circulation to the active skeletal muscle where the glucose is converted to glucose 6 phosphate (G6P) via hexokinase. Muscular glycogen is broken down to glucose then converted to G6P via the activated enzyme phosphorylase (15). The G6P stimulates glycolysis which ultimately leads to the formation of pyruvate. If the rate of glycolysis exceeds the capacity of the Krebs cycle to further breakdown and oxidize the substrates of glycolysis, then pyruvate is converted to lactate via the enzyme lactate dehydrogenase.

$$Pyruvate + NADH + H^{+} \xleftrightarrow[Lactate\ Dehydrogenase]{} Lactate + NAD^{+}$$

Lactic acid is continually being produced and removed, even during resting conditions. This is known as lactate turnover. During submaximal exercise, lactate turnover is greatly elevated, yet there is no rise in blood

lactate concentration due to the fact that the amount of lactate being cleared is equal to the amount of lactate being produced. During aerobic exercise, oxygen consumption rises almost linearly with an increase in intensity; whereas, blood lactate during exercise does not rise until approximately 50-60% of an untrained individual's VO_2 max and 70-80% of a trained athletes VO_2 max (16, 17). The point where blood lactate dramatically rises in a non-linear fashion because its production exceeds its rate of removal is termed lactate threshold and/ or the lactate inflection point (15, 18). A second point of inflection of lactate concentration is termed onset of blood lactate accumulation (OBLA). OBLA occurs at 4 mmol/L (19, 20). OBLA is believed to be associated when athletes begin to recruit their high threshold motor units. High threshold motor units produce lactic acid when recruited (compared to low threshold motor units) because of their activity of M-type LDH (which favors the formation of lactate) found in the cytosol, as well as their low mitochondrial density; whereas, low threshold motor units favor lactate oxidation (15).

All out exercising lasting 1-4 minutes will elicit the highest concentration of hydrogen ions (H^+), thus producing the lowest pH (21). Research conducted by Noonan indicates that ice hockey players blood lactate values range from 4.4 – 13.7 $mmol \cdot L^{-1}$ throughout a game (22), while various research has shown that basketball players achieve average blood lactate values between 5.5 – 6.8 $mmol \cdot L^{-1}$ (2, 23, 24). The concentration of blood lactate is the relationship between the production and the removal of lactate (25). Blood lactate forms when pyruvate, an end product of glycolysis, combines with H^+ by the enzyme LDH. An increase in H^+ produces negative effects on exercise performance (26), as well as increases their rate of perceived exertion (27). These negative effects are a direct result of the decrease in pH resulting in the decrease and inhibition glycolytic enzymes, the depletion of PCr, changes in myosin ATPase, ionic imbalances of Na^+, Ca^{++}, K^+, inhibition of the interactions between myosin and actin, and the disturbance in the T-tubules (8, 28-34). In addition to this, the decline in pH from lactic acidosis inhibits lipolysis and free fatty acid uptake by the mitochondria (35). As a result of the previously mentioned intracellular disturbances, the individual must apply more effort and have more motivation to continue to exercise at the same work rate, thus increasing their rate of perceived exertion.

For example, sprinting is a common component of many sports. The greater the intensity, acceleration, and speed of the sprint, the greater the reliance on fast glycolysis, which results in the accumulation H^+ within the individual causing a decrease in performance and acceleration (36-38). The ability to perform sprints repeatedly is dependent upon the individual' capacity to buffer the accumulation of lactate, as well as their glycogen content (39, 40). When performing repeated bouts of exercise, lactate levels dramatically increase as a result of "lactate stacking." It should be noted that performing low intensity exercise between intervals (active recovery) increases subsequent performance through the removal of lactate, as well as the facilitation of glycogenesis in the fast switch fibers if the intensity is low enough (29, 41-50). The removal of lactate is due to the increase in circulation in the active musculature due to the muscular contractions involved in the recovery. However, in certain sports, such as hockey and football, the athletes do not engage in an active recovery. Any process that increases the buffering of lactate or limits it production (i.e. supplementation) will therefore lead to subsequent improvements in performance (25, 51-54).

However, the reader should note the following: 1.) Lactate is not a waste product and 2.) Lactate formation is necessary for rapid energy metabolism. Lactate is not a waste product due to the fact that it is necessary to continue glycolysis during high intensity exercise (14) and it can be converted to useable forms of energy during and post workout (15). During intense exercise, lactate allows glycolysis to continue at a high rate because it frees up NAD^+. Without the combination of H^+ and pyruvate via LDH, glycolysis would cease because glycolysis is regulated by NAD^+ readiness (14). Post workout, lactate can be 1.) Oxidized; 2.) Be a gluconeogenic precursor; and/ or 3.) Be used to form amino acids and proteins. If post exercise glycogen levels are depleted and the body is in a state of hypoglycemia, then lactate favors gluconeogenic pathways; whereas, if post exercise the body's glycogen and blood glucose levels are maintained, lactate favors oxidation by transforming into pyruvate which allows it to proceed to the Krebs cycle (15).

To further demonstrate that lactic acid is not a dead end product, the authors will briefly describe the "Glucose Paradox" and the "Intracellular Lactate Shuttle." According to the "Glucose Paradox," the liver may actually prefer to build up its glycogen stores from lactate than glucose. In the "Glucose Paradox", following a meal containing carbohydrates, the glucose bypasses the liver and stores in the muscle as glycogen. Through glycolysis, lactate is produced and circulated to the liver. Once at the liver, the lactate is then converted and stored as liver glycogen (11). The "Intracellular Shuttle" refers to the process of where lactate is transported to the mitochondria during exercise and is oxidized into pyruvate via mitochondrial LDH. The newly formed pyruvate then enters the Krebs cycle to produce more ATPs (11). Therefore, during intense exercise where lactate is formed yet aerobic metabolism is still operating, lactate directly serves as a fuel source for skeletal muscle. Within the following sections, the science and ingestion protocols for select nutritional supplements that decrease lactate accumulation are discussed.

CREATINE

Creatine, with over 1,000 published articles, is probably the most researched supplement, perhaps second only to caffeine. The International Society of Sports Nutrition states that, "the most effective nutritional supplement available to athletes to increase high intensity exercise capacity and muscle mass during training is creatine monohydrate (55)" Although creatine has been blamed in the past, as well as currently, in the media for causing severe physiological distortions such as compartment syndrome, there is no scientific data to support supplementation of creatine to elicit any real side effects (56-58) other than weight gain (56, 59, 60). It is often said that any weight gain from supplementing with creatine is due to water retention; however, the increase in total body water is proportional to the increase in muscle mass (61). Since skeletal muscle is 75% water, 5% inorganic salts, and 20% protein (62), any increase in muscle mass (regardless of supplementation) will increase total body water (61).

Creatine supplementation has been shown to: increase intramuscular stores of free creatine and phosphocreatine, increase protein synthesis, increase power, facilitate hydration of muscle cells, reduce the need for glycolysis, lower the accumulation of H^+ ions thus preserving intracellular pH, improve training capacity, increase phosphocreatine resynthesis, delay phosphocreatine depletion, facilitate ATP turnover, increase training intensity, improve short term muscular performance, enlarge the diameter of type IA, IIA, and IIX fibers, increase bone mineral density (possibly due to the increase in external load while

resistant training), and increase lean body mass, as well as the possibility of improving ATP shuttle in the mitochondria thus enhancing aerobic respiration (55, 61, 63-68). In addition to this, creatine ingestion may actually decrease the injury rate for athletes (69-74), as well as improve cognitive function, sleep, and mood (65). It is beyond the scope of this article to provide a comprehensive review of creatine; however, if the reader wishes to further their knowledge on creatine, the authors recommend the following sources (55, 61, 75). The purpose of this section on creatine is to provide the basic fundamentals on creatine, explain how the ingestion of creatine can decrease the formation of lactate, and discuss how to ingest creatine, as well as what type of creatine to ingest.

Creatine is synthesized from methionine, glycine, and arginine which are three amino acids. Since creatine is formed from amino acids, the body will synthesize creatine without the need from supplementation. Without supplementation, a person will increase their creatine stores through their diet by ingestion of creatine in meat products such as chicken and fish, as well as the formation of creatine in the liver form methionine, glycine, and arginine. It should be noted that raw foods such as sushi will contain more creatine than cooked fish since the heat from cooking will denature creatine. Kreider (61) suggests that approximately half of a person's daily creatine needs can be ingested through a normal diet. When ingested, creatine passes through the gastrointestinal tract unaltered and is transported primarily to skeletal muscle for storage (63). Vegetarians usually benefit more from creatine ingestion because they typically have less creatine stores because their diet lacks meat sources. Creatine supplementation has been shown to provide the most ergogenic aid for individuals who initially have the lowest amount of stored creatine (61).

As mentioned, anaerobic athletes typically achieve 20-30% higher blood lactate levels than non-anaerobic athletes due to their: increased glycogen stores, increased motivation, increased glycolytic enzymes (specifically phosphofructose kinase), increased work rate, and high levels of lactate dehydrogenase (9). As an athlete begins to recruit their Type II fibers during high intensity exercise, their lactate concentrations will rise. Since Type II fibers have the capability to store around four to six times more phosphocreatine than ATP, supplementation with exogenous creatine can help reduce the accumulation of lactate by reducing the need for glycolysis (63). To gain the most benefits from supplementing with creatine, the authors recommend the following suggestions found in Table 1:

TABLE 1: Summary- Creatine

Purchase creatine in the form of creatine monohydrate over other forms such as: creatine citrate, creatine phosphate, and creatine ester because creatine monohydrate is the most effective form of creatine researched thus far. In addition to this, creatine monohydrate is usually less expensive than other forms of creatine that claim to be more effective.
When purchasing creatine monohydrate, purchase a high quality form of creatine monohydrate, preferably from Germany or the United States and be cautious of creatine supplements from China.
When buying any supplement, attempt to buy supplements that have been tested by a third party (i.e. NSF Certified Products, etc…) to ensure its safety and effectiveness.
Ingesting creatine monohydrate with carbohydrates, especially high glycemic carbohydrates will increase storage perhaps as much as 60% due to the elevation in insulin levels. This is because creatine storage is facilitated by insulin. Ingestion of creatine alone does not stimulate insulin levels to rise.

Ingesting a creatine-high glycemic carbohydrate beverage with Whey protein may further facilitate the storage of intramuscular creatine. This beverage could be ingested immediately post workout to enhance recovery, increase substrate storage, blunt cortisol, elevate insulin levels, and bolster the immune system.
Various loading protocols for creatine have been proposed. Loading protocols quickly saturate intramuscular creatine stores; whereas non-loading protocols will eventually and gradually saturate intramuscular storage sites. If the athlete wishes to load rapidly, it has been suggested to ingest ~0.3 grams creatine monohydrate per kilogram of body mass for at least 3 days followed by a maintenance phase of 3-5 grams per day. Research has shown most of supplemental creatine to be stored during the first 2-3 days of a loading phase.
After supplementation, an athlete can maintain intramuscular creatine levels for around 3 weeks. Therefore, an athlete can cycle on and off creatine if he or she wishes. If an athlete does cycle on and off creatine, they should plan so according to their level of training intensity- providing the substrate during the highest workloads in their training cycle. However, there is no research indicating that cycling on and off creatine is more or less effective. Since creatine monohydrate is not that expensive, an athlete can continually ingest creatine in low doses (i.e. 3-5 grams per day) to continually saturate their intramuscular creatine stores if he or she wishes. Any excess creatine ingested will be excreted through their urine.
Research has shown that creatine monohydrate can possibly reduce injuries while not causing any physiological distortion or abnormalities. Therefore, continual supplementation with creatine could potentially reduce the likelihood of injury, while providing a higher training intensity for the athlete with low risk of any complications from the supplement itself.

Table 1 References: (55-58, 61, 65, 69-78)

BETA ALANINE

Supplementation with β-alanine has been shown to improve an individual's anaerobic capacity (79-82). When ingested, β-alanine (a nonessential amino acid) has the ability to combine with another amino acid, histidine. When β-alanine and histidine combine, they form a dipeptide molecule known as carnosine. Carnosine has been implicated in several physiological mechanisms such as Ca^{++} release from the sarcoplasmic reticulum (83) and/ or increased Ca^{++} sensitivity (84), as well as a combatant of free radicals (85). Skeletal muscle, especially fast-twitch fibers, naturally contain carnosine (86). Skeletal muscle has greater concentrations of carnosine compared to other tissues because skeletal muscle lacks the enzyme carnosinase, which breaks down carnosine (87). Due to its pKa (88), intramuscular carnosine is a powerful lactate buffer; therefore, increasing intramuscular carnosine is beneficial for certain athletes (89). As mentioned earlier, when pyruvate combines with H^+, lactate forms. Carnosine buffers the accumulation of H^+, thus preventing the decline in muscle pH (89). Thus, by buffering the accumulation of H^+, β-alanine prevents the decline in muscle pH; thereby not only promoting an optimal environment for the sarcomere, but possibly also decreasing the RPE for the athlete (27).

β-alanine is the rate limiting factor in the formation of carnosine because of the abundance of histidine in the muscle. Supplementation with β-alanine has been shown to increase intramuscular stores of carnosine (90-94). Note that ingestion of carnosine provides no extra benefit than ingesting β-alanine by itself because during the digestive process, carnosine is broken down into histidine and β-alanine.

A recent article in 2012 (95) showed that 12 weeks of β–alanine supplementation to

improve scores for intermittent YoYo test for English football players throughout a competitive season. Previous research (96) has shown exhaustion from the intermittent YoYo test to be a result of muscle pH and lactate. The experimental group ingested 3.2 grams of β–alanine per day; whereas the placebo group ingested maltodextrin. There was no difference in the YoYo scores prior to the supplementation protocol; however, after 12 weeks, the β–alanine group increased their scores (+34.3%; $p \leq 0.001$); whereas the placebo groups' performance decreased (-7.3%; $p = 0.24$). We as the authors showed to highlight this particular article because in this study, the subjects were engaged in a competitive season. Many studies on β–alanine are either during a training season or in a training study. The authors suggested that β–alanine supplementation can potentially increase anaerobic performance over a competitive season, which is usually associated with a decrease in performance.

A recent meta-analysis written on β–alanine in 2012 (97) revealed that β–alanine is most effective for intense exercise lasting 60-240 seconds. This would make sense considering the highest H^+ concentration occurs during intense exercise lasting 1-4 minutes (21). Although β–alanine is still effective at durations greater than 240 seconds, its ergogenic effect is less pronounced. Furthermore, activities lasting less than 60 seconds do not appear to be significantly affected by ingestion of β–alanine (97). The authors' result of the previously referenced meta-analysis (97) revealed that supplementation with β–alanine will result in a median improvement of 2.85% compared to the placebo. According to the authors, this would theoretically improve an elite athlete's 1,500 meters run time by ~6 seconds, which would bring the last place men's finalist at the 2008 Beijing Olympic Games to the bronze medal. In addition to this, the authors stated that β–alanine appears more effective on exercise capacity rather than exercise performance. The authors hypothesize that this is due to the fact that the measures used to test exercise performance required the ability of the subjects to pace themselves; whereas during the studies involving exercise capacity tests, the subjects were asked to go all out.

β-alanine supplementation is known to increase intramuscular carnosine levels (90-94). Athletes, who wish to increase their carnosine levels rapidly, should employ a supplementation protocol with higher dosages, whereas athletes who are not in a rush to increase their intramuscular carnosine levels can use a less aggressive supplementation protocol. Stellingwerff et al. (94) showed that four weeks of supplementing with 3.2 grams of β–alanine increased the carnosine stores for the tibialis-anterior and gastrocnemius by approximately two-fold compared to the group who only supplemented 1.6 grams per day. The meta-analysis (97) suggested that β–alanine supplementation will improve exercise outcome by 2.85% when supplemented with 179 grams of β–alanine. The need to supplement with approximately 179 grams of β–alanine to see an improvement in performance provides an explanation on why some studies do not show β–alanine to be effective at improving performance. For example, Kraemer et al. (98) saw no benefit for subjects performing four- 30 second Wingate tests while supplementing with only 185 mg of carnosine. (The reader should note that in this study (98) other ingredients were used that could theoretically alter the acid-base balance of the participants).

The reader should be cautioned that ingesting too much β–alanine at once is associated with paraesthesia- a condition where the individual has tingling and numbness in their skin and extremities. Paraesthesia typically occurs with β–alanine

doses greater than 10 mg/kg (82). To avoid this, the user can either: 1.) Take smaller doses of β–alanine throughout the day and/or 2.) Use timed release capsules to provide a sustain release of β–alanine over a given time period to reach the 179 gram threshold proposed by Hobson's et al. meta-analysis (97). To the authors' knowledge, there are currently no known scientifically suggested protocols for loading β–alanine. Research on β–alanine have used daily doses ranging from 1.6 – 6.4 grams per day, as well as durations varying from four weeks to 90 days (79, 80, 90, 99-101). Several studies have started with a lower dose per day and increased the amount of β–alanine ingested throughout the study (79, 90); while other studies start with higher doses and decrease the amount ingested throughout the study (100, 101); whereas other studies maintained the same dose per day throughout the study (99). Certain studies only evaluated muscle carnosine concentrations (90, 93); while others studies solely investigated performance measurements from the supplementation protocol (80, 99-101). In some studies, the researchers have included other ingredients besides β– alanine such as creatine (80, 102). In addition to this, the mode of testing and/ or training have all varied in the literature. Therefore, determining an exact dosing protocol can be confusing, especially if we take into account confounding factors such as age, training status, and gender.

Further research is needed for β–alanine to establish sound protocols and scientific recommendations for the loading process. As mentioned, to the authors' knowledge, there are currently no known recommendations for β–alanine supplementation/ loading. We suggest that if an athlete wishes to increase the intramuscular carnosine levels rapidly, higher dosing protocols such as 3.2 grams per day compared to 1.6 grams per day (94) should be implemented as long as paraesthesia does not occur. Supplementing several times throughout the day, using time-release capsules, and avoiding doses greater 10 mg/ kg per day should help avoid paraesthesia. Since the washout period for β–alanine is approximately 15 weeks or longer (90, 94), this factor makes repeated measures research difficult due to the adaptations that can occur over this time period (97). Finally, it should be noted that although β-alanine supplementation increases intramuscular carnosine, an athlete who does not want to supplement with β-alanine can still increase intramuscular carnosine through proper intense training (89, 103-105).

TABLE 2: Summary- β-alanine

β-alanine has been shown to increase intramuscular carnosine levels. Carnosine, which naturally occurs in skeletal muscle fibers (especially fast twitch fibers), is a powerful lactate buffer.
When supplementing to increase intramuscular carnosine stores, the user should use β–alanine since it is the limiting factor in carnosine and not histidine. Furthermore, supplementing with carnosine is not beneficial since the digestive process will break down carnosine into histidine and β–alanine.
It appears supplementing 179 grams of β–alanine will improve exercise outcome by 2.85%. The user can either obtain this amount by two methods: 1.) Supplementing with lower dosages over a longer time, or 2.) Supplementing with higher dosages over a shorter period.
If the athlete wishes to increase their intramuscular carnosine stores rapidly, they should ingest higher dosages of β–alanine initially. However, the reader should be cautioned that high ingestions of β–alanine may elicit paraesthesia- a condition where the individual has tingling and numbness in their skin and extremities.
To avoid paraesthesia, the athlete can use time

released capsules, supplement several times throughout the day, and should avoid doses higher than 10 mg/kg day.
The lowest muscle pH occurs at all out activities lasting 1-4 minutes; therefore, β-alanine is most effective for high intensity activities lasting 60-240 seconds. β–alanine is still effective at durations >240 seconds, but its effects are not as pronounced during activities lasting 60-240 seconds. β–alanine does not appear to be ergogenic for durations <60 seconds.
When buying any supplement, attempt to buy supplements that have been tested by a third party (i.e. NSF Certified Products, etc…) to ensure its safety and effectiveness.
Further research is needed on β–alanine to determine an efficient loading and maintenance protocol. It is unknown whether or not there is a limit on intramuscular carnosine levels. However, since the washout period of β–alanine is 15 weeks or longer, the athlete should not fear losing its ergogenic effects if temporarily abstaining from supplementation (whether intentionally or unintentionally).

Table 2 References: (21, 82, 90-94, 97)

SODIUM BICARBONATE

Whereas creatine decreases lactate formation by reducing the need for glycolysis, and β-alanine reduces lactate concentration by scavenging H^+, sodium bicarbonate and sodium citrate do not decrease the concentration of lactate formed from intense exercise. In fact, sodium bicarbonate and sodium citrate have been shown to lead to greater lactate concentrations following an intense exercise bout (106-109). Sodium citrate and sodium bicarbonate work by raising the pH in the blood prior to exercise. Thus, these supplements delay the decrease in pH from intense exercise by producing a more alkalotic state during exercise. Recall that 1.) Lactate decreases performance and disturbs the sarcomere because of the drop in pH (8, 28-34), and 2.) The production of lactate is necessary in order for glycolysis to continue to operate at a high rate by increasing NAD^+ readiness (14). Therefore, ingestion of products such as sodium bicarbonate and sodium citrate has the potential to improve performance by maintaining an optimal pH for the sarcomere.

Research on sodium bicarbonate is conflicting. Sodium bicarbonate has shown to be beneficial (110-114), as well as not beneficial (115-119) to measured outcomes. Therefore, the reader should determine if and how their methods of the research differed, and whether or not sodium bicarbonate would benefit their sport and/ or event. For example, even though research on a supplement(s) and their ergogenic effects may use the same mode of exercise (i.e. 400 meter sprint), they can have conflicting results. The conflict in research can often stem from differing loading protocols, sample size, study design, and subjects (trained versus untrained). For example, Kindermann et al. (115) found no ergogenic effects in the 400 meter's time for their subjects (N=10) when supplementing with sodium bicarbonate, whereas Pouzash et al. (110) saw an ergogenic effect from sodium bicarbonate ingestion in their subjects (N=16) when running 400 meters. The conflicting results could stem from various sources. In Kindermann's et al. (115) study, there were only 10 subjects and only six subjects ingested sodium bicarbonate with the remaining four subjects ingesting Tris-buffer. In addition to this, Kindermann et al. (115) infused the subjects when these supplements until their pH reached 7.5, had the subjects warm-up for 15 minutes, and then perform the 400 meter sprint. (Note that one subject had venous spasms and the infusion stopped early). Whereas Pouzash's et al. (110) study not only had more subjects (16 verses 10), but the researchers also used a counter balanced repeated measures design and had the subjects

ingest sodium bicarbonate (0.3 grams per kilogram) one hour prior to the 400 meter sprint. Pouzash et al. (110) noted a significant improvement from the supplemental protocol (57.41 ± 0.11 seconds) compared to the placebo (59.01 ± 0.78 seconds).

By ingesting sodium bicarbonate 1-3 hours prior to competition, there is an elevation the pH of the blood (112, 120) and not an elevation of pH intramuscularly (121). The alkalotic state should theoretically provide a benefit to its users since the sarcomere optimally functions at a specific pH. However, research on sodium bicarbonate is often times conflicting. For example, discrepancies in sodium bicarbonate effects have been found in: exercise lasting less than 120 seconds (110, 111, 115, 116), repeated exercise bouts (112, 113, 117, 118), and exercise lasting over 120 seconds (114, 119). As mentioned, the conflict in research can often stem from differing loading protocols, sample size, study design, and subjects (trained versus untrained). Since intense exercise lasting 1-4 minutes produces the highest concentration in lactate (21), it would appear the most ergogenic effect from sodium bicarbonate would last in this time span. It should be noted that some people experience gastrointestinal distress when ingesting sodium bicarbonate (122). Therefore, it is prudent that athletes experiment with sodium bicarbonate prior to competition. Furthermore, it has been suggested for athletes experimenting with sodium bicarbonate to slowly increase the amount of sodium bicarbonate ingested to accommodate. According to Potteiger et al. (123), athletes should ingest sodium bicarbonate approximately 120 minutes prior to exercise in a dose of 0.3 grams per kilogram of body weight. Furthermore, research has shown that chronic intake of sodium bicarbonate (6 days) can provide an ergogenic effect ($p < 0.001$) on cycling ergometry (124). In this study (124), the authors noted an improvement following both acute ($p<0.05$) and chronic ($p<0.001$) ingestion of sodium bicarbonate in a dose of 0.5 grams per kilogram compared to the placebo trial. The authors concluded that sodium bicarbonate loading prior to competition may be beneficial in order to avoid any possible gastrointestinal disturbances.

SODIUM CITRATE

Unlike sodium bicarbonate, sodium citrate appears not to cause gastrointestinal problems, although not all research has shown this to be true (106). As mentioned, by inducing an alkalotic state prior to competitions, an athlete should increase performance because muscular contractions (125) and glycolysis (126, 127) are pH sensitive. Upon ingestion, sodium citrate dissociates into $sodium^{+}$ and $citrate^{-}$, which, through a cascade of events, produces an alkalotic environment (128). The alkalotic environment helps prevent the decline in pH associated with intense exercise, thus allowing for optimal performance. Some research (106-109, 122) has shown sodium citrate to be beneficial on improving subsequent performance, while other research (125, 127, 129) has shown sodium citrate to be non-advantageous to performance. It appears that the duration of the event, the amount of sodium citrate ingested, as well the time of ingestion prior to exercise will determine sodium citrate ability to increase performance. Requena et al. (128) state that sodium citrate is most effective as an ergogenic aid when the partaker consumes the product at 0.5 grams per kilogram of body mass 120 minutes before engaging in the activity and the event lasts over a minute.

Research on sodium citrate on activities less than 120 seconds appears to be not advantages. For example, Ibañez et al. (129) showed no positive effects for elite 400

meter sprinters (N=6) while sprinting 300 meters. Recall that typically the highest lactate levels occur when exercising at high intensities for 1-4 minutes (21). In this study (129), the subjects only exercised between 30-40 seconds; therefore, activities lasting less than one minute may not benefit from sodium citrate supplementation due to the lack of lactate accumulation. This is similar to the meta-analysis on β–alanine (97) that showed the most ergogenic effect of β–alanine is during activities lasting 60-240 seconds.

Shave et al. (106) showed that sodium citrate at 0.5 grams per kilogram significantly ($p < 0.05$) improved 3,000 meter trials for their subjects (N=9) by reducing their run time by 10.7 seconds on average. In addition to this, the authors (106) noted an significant increase in post workout lactate concentration following supplementation compared to the placebo trials, which is in accordance with prior research (107-109). There are two proposed theories for why sodium citrate ingestion allows for greater lactate accumulation: 1.) Anaerobic glycolysis can be maintained for a longer period of time because of the pre-exercise alkalotic state (106), and/ or 2.) An enhanced efflux caused by the increase in the transport rate thought the monocarboxylate transporter (109), which is pH sensitive (130).

Some studies have investigated and compared the effects of sodium bicarbonate verses sodium citrate. There appears to be no significant difference between sodium citrate and sodium bicarbonate in regards to measured outcomes (116, 123, 131). However, it is generally agreed upon that sodium citrate produces less gastrointestinal distress compared to sodium bicarbonate; however, some people react poorly to sodium citrate. Therefore, experimentation with these supplements prior to competition is a must. The reader should note that future studies on both sodium bicarbonate and sodium citrate should be performed. This is because of the conflicting results, which often seem to stem from a small sample size, methodology, exercise task, subjects (trained or untrained), and/ or loading protocols. For further readings on sodium bicarbonate and sodium citrate, the reader should read the detailed review article by Requena et al. (128) that deals specifically with sodium bicarbonate and sodium citrate. Table 3 provides a summary and considerations when supplementing with sodium bicarbonate and/or sodium citrate.

TABLE 3: Summary- Sodium Bicarbonate and Sodium Citrate

Although there have been several studies on both sodium bicarbonate and sodium citrate, many studies are conflicting. This is often a result of sample size, methodology, exercise task, subjects training status, and/ or loading protocols.
Although many of the studies vary on sodium bicarbonate and sodium citrate's ergogenic effect, similar to β–alanine, these alkalotic agents appear to be most beneficial for intense exercise greater than 60 seconds. This is because the greatest lactate concentration occurs from 1-4 minutes of all out exercise.
Sodium bicarbonate in large doses causes severe gastrointestinal distress in many people. Although sodium citrate appears not to cause as much gastrointestinal distress in individuals, sodium citrate has still been associated with gastrointestinal distress. Therefore, athletes should experiment with these alkalotic agents prior to competitions in regards to timing and dose.
Loading with sodium bicarbonate may be beneficial to athletes because it has potential to improve subsequent performance without the possibility of producing gastrointestinal disturbances during competitions.
Athletes should ingest sodium bicarbonate approximately 120 minutes prior to exercise in

a dose of 0.3 to 0.5 grams per kilogram of body weight. Doses less than 0.3 grams per kilogram of body weight appear to have no effect on performance.
Sodium citrate is most effective as an ergogenic aid when the athlete consumes the product at 0.5 grams per kilogram of body mass 120 minutes before engaging in the activity and the event lasts over a minute.
When buying any supplement, attempt to buy supplements that have been tested by a third party (i.e. NSF Certified Products, etc…) to ensure its safety and effectiveness.
Further research is needed to confirm or dispute findings that could have resulted from certain methodologies.

References: (21, 106-119, 122, 125, 127, 129)

CONCLUSIONS

It is important to note that in order to determine the true ergogenic effect of a self-reported supplement, the methods should be sport specific with subjects who participate in the particular sport (132). The International Society of Sports Nutrition recommends that athletes experiment with supplementation during the training sessions and practices prior to game situations in order to avoid complications. Throughout the paper, the authors demonstrated how creatine (more specifically creatine monohydrate), β-alanine, sodium bicarbonate, and sodium citrate can help reduce the detriments to performance from lactate formation. However, the authors do not recommend all athletes engage in supplementation to improve performance. Prior to supplementation usage, the athlete should focus on implementing a proper diet by consuming the appropriate proportion and amounts of macronutrients and micronutrients, as well as consume ample amounts of water. Any athlete and/or coach who are unsure of their own or their athlete's current dietary regimen's worth, should either become educated on sports nutrition, or seek a registered dietician and/or a sports nutritionist. If an athlete does not wish to ingest supplements, they can still rely on properly designed training programs to offstage the accumulation of lactate formation. For example, conditioned anaerobic athletes will naturally have greater intramuscular carnosine levels without the supplementation of β–alanine (89, 103-105). It should be noted that although carnosine is known to buffer lactate, anaerobic athletes will have a greater production of lactate (9). However, this increase in lactate is associated with an increase in short term power production; therefore, the ability to generate high levels of lactate is a consequence of their ability to perform activities at intense levels. In addition to this, aerobically trained athletes have greater lactate clearance rates than untrained or lesser trained athletes (15). However, anaerobic athletes should be cautioned before engaging in an aerobic training program because it is known that concurrent training for strength and endurance reduces both power and strength. Lastly, it should be noted that unlike creatine (which has over 1,000 published articles), further research is needed on β–alanine, sodium bicarbonate, and sodium citrate to determine the best ingestion protocols and its true ergogenic effects.

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