Central European Journal of Sport Sciences and Medicine | Vol. 41, No. 1/2023: 69–80
ISSN (print): 2300-9705 | ISSN (online): 2353-2807 | DOI: 10.18276/cej.2023.1-07

THE POPULAR ERGOGENIC SUBSTANCES IN SPORT AND PHYSICAL ACTIVITY

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Abstract Few supplements have a scientifically proven ergogenic effects of improving exercise capacity and/or physical performance in sport. The athletes require specialised nutrition, including precisely good quality supplementation, i.e. scientifically tested. Nowadays, more and more athletes use nutritional supplementation to improve their sporting performance both at the elite and non-elite levels. In this review, ergogenic substances such as the β-alanine, caffeine, creatine monohydrate, creatine malate, sodium bicarbonate were analysed among athletes/active people from an exercise and health capacity perspective. The aim of this review is to analyse the efficacy, mechanisms of action, dosage, side effects of the selected ergogenic substances, among athletes involved in physical effort/specific sport disciplines. Furthermore, the article will show the benefits of using these supplements in terms of health as well as improvement of exercise capacity among athletes.

Key words: β-alanine, caffeine, creatine monohydrate, creatine malate, sodium bicarbonate

Introduction

Dietary supplements are called ergogenic substances/aids which are commonly and/or increasingly used by athletes at both competitive elite-levels and amateur/non-elite levels. The definition of a food supplement is a foodstuff, the purpose of which is to supplement a normal diet, having a nutritional or other physiological effect, marketed in a dosage form like capsules, tablets, beverage etc. (Kerksick et al., 2018). Ergogenic dietary supplements are used in order to enhance exercise performance capacity by improving strength, endurance, training adaptations, increase lean body mass (LBM) and other significant physiological parameters (Stecker et al., 2019). However, the amount of supplements on the market far exceeds the number whose effectiveness has been properly researched and described (Maughan et al., 2018). It is widely known that interest in supplementation in sport is growing. According to the studies it is suggested that between 64% and 89% of college athletes regularly use at least one dietary supplement (Osterman et al., 2020). Moreover, it is reported that the rate of supplement consumption among US athletes is higher when it comes to elite athletes compared with non-elite athletes (Knapik et al., 2016). American trends in nutrition/supplementation often overlap with European trends in sport. Athletes require more energy in order to have an adequate capacity for training, performance and effective recovery. In order to meet these specialised supplements and/or ergogenic aids requirements, a few organisations have developed scientifically proper and tested supplementation. The European Food Safety Authority provides independent scientific advice on nutrition/supplementation-related risks (European Food Safety Authority [EFSA], 2015). EFSA's opinions form the basis of European regulations, rules and policy-making and thus they help to protect consumers/sportspeople/athletes from food risks. The Australian Institute of Sport has the ABCD classification of sports supplements that determine whether a product/supplement is safe, permitted and effective in improving sports performance. The first group (Group A) consists of supplements with proven performance and safety in specific sporting situations and these are the β-alanine, caffeine, creatine, dietary nitrate/beetroot juice, sodium bicarbonate, glycerol (Australian Institute of Sport [AIS], 2022). International Society of Sports Nutrition (ISSN) has also created recommendations for athletes regarding the use of supplementation based on scientific research as well as practical knowledge (Kerksick et al., 2018). What is more, the International Olympic Committee (IOC) has issued a position statement on the selection of supplements in sport with a scientifically proven effect, placing caffeine, creatine, dietary nitrates, β-alanine and sodium bicarbonate (SB) among the supplements that directly improve exercise capacity (Maughan et al., 2018). This article reviews the most researched/scientifically proven ergogenic substances used in both elite and non-elite levels such as: β-alanine, coffeine, creatine monochydrate (CrM), creatine malate (CrML), sodium bicarbonate (SB). This review describes the efficacy, mechanism of action, dosage, side effects of ergogenic substances in exercise among athletes and active people who may benefit from their use in sport and health

Beta-alanine (β-alanine)

β-alanine is a non-proteogenic amino acid that is produced endogenously in the human liver, alternative synthesis pathways in the gut (Sadikali et al.1975). The ergogenic potential of β-alanine comes from the fact that it combines with histidine within organs with high energy requirements: skeletal muscle, brain and heart forming carnosine. The higher the concentration of carnosine in the tissues, the better the exercise capacity (Sale et al., 2013). Gulewitsch was the first to identify carnosine in 1900 (Gulewitsch & Amiradzhibi, 1900). Eleven years later, he discovered and identified its constituent amino acids, β-alanine and histidine (Guney et al., 2006).

Carnosine is a physicochemical buffer in a muscle and is the first line of defence against local pH changes. Therefore, any measures that increase the ability of muscles to buffer the H+ produced during high-intensity exercise can be significant for many athletes, since β-alanine is a rate-limiting precursor to carnosine synthesis in muscle fibres (Ng & Marshall, 1978). When it comes to the mechanism of action: β-alanine is a substrate of carnosine – a major contributor to H+ buffering during high-intensity exercise, β-alanine combines with histidine, the pKa of the imidazole ring of the histidine residue is increased to 6.83, enabling it to act as a highly effective intracellular pH buffer (Kendrick, et al., 2009). The rate limiting factor to muscle carnosine synthesis is the availability of β-alanine from the daily intake of food such as red or white meat and fish (Dunnett & Harris, 1999; Harris et al., 2006;) so, an additional supply of this amino acid is the most effective way to achieve an optimal carnosine concentration in the human body. Moreover, other roles of carnosine have also been suggested, such as protection against oxidative damage, glycation and regulation of calcium sensitivity (Boldyrev et al., 2013) which are important for maintaining health among athletes and active people.

It is reported that the efficacy of β-alanine supplementation concerns high-intensity exercise performance, with optimum benefit demonstrated for physical activity lasting between 30 s and 10 min (Saunders et al., 2017). Moreover, the result of β-alanine on trained individuals showed smaller effect sizes than on non-trained individuals, while isolated limb and whole body exercise were shown to equally benefit from β-alanine. Additionally, co-supplementation of β-alanine and sodium bicarbonate (SB), to increase or improve both intracellular and extracellular buffering capacity, was demonstrated to result in additional improvements above β-alanine alone (Saunders et al., 2017).

When it comes to dosage of beta-alanine among individual athletes, the daily intake of β-alanine is for a minimum of 2–4 weeks at a dose of 3.2–6.4 g/day ingested at several time points throughout the day (0.8–1.6 g every 3– 4 hour) to avoid acute side effects (Saunders et al., 2017). According to the study, the small amount of supplementation such as 1.6 g/day for as little as 2 weeks has been shown to increase muscle carnosine (Stellingwerff et al., 2012).

The peak of β-alanine concentration in blood-plasma occurs between 30 and 40 min after ingesting 10 mg of that substance per 1kg/body weight. On the other hand, the half-life of β-alanine (time when there is a 50% reduction of the peak concentration) amounts to 25 minutes but remains in the circulation for about 3 hours following ingestion. (Harris et al., 2006). When it comes to the positive interaction of supplementation, it is reported that supplementation of β-alanine and caffeine in higher doses (≥ 6 mg·kg^{-1}) has an ergogenic effect to enhance ergometer during long distance performance (2000-m) in trained rowers (Turnes et al., 2019).

In the context of long-term beta-alanine supplementation, it is suggested that twenty-four weeks of β-alanine supplementation increased muscle carnosine content and improved high-intensity cycling capacity but it is also supposed that there are other determinants such as genetic aspects which may have an impact on muscle carnosine content (Saunders et al., 2017). In this study twenty-five active males were supplemented with 6.4 g·d−1 of sustained release β-alanine or placebo for a 24 week period. Undoubtedly, further scientific research is needed in the aspect of the long-term consumption of this substance and its impact on exercise capacity and health.

According to the research, a positive ergogenic effect occurs while combining, for example, two supplements. For instance the combination of β-alanine and creatine in resistance training has influenced on greater increases in strength, training volume, and LBM, compared with using creatine only or placebo conditions (Hoffman et al., 2006). With regard to the endurance exercise/training and aerobic capacity, it is also proved that the combination of β-alanine and CrM has an improved ergogenic effect, for example on increasing maximal aerobic capacity (VO_2max) at ventilatory threshold (Zoeller et al., 2007).

The positive interaction of supplementation, for example, among bodybuilders during the off-season phase occurs in combining the following substances: CrM (3–5 g/day), caffeine (5–6 mg/kg), β-alanine (3–5 g/day) and citrulline malate (8 g/day). This interaction allows to have ergogenic effects for bodybuilders, for example, in the context of building LBM which increases strength and power of muscles. This study had also specific dietary recommendation on meal composition that had an influence on the ergogenic effect in this case (Iraki et al., 2019).

The side effect of β-alanine supplementation is paraesthesia (i.e., tingling) which appears due to the fact that it activates nerve receptors located under the skin. However, studies demonstrate this might be attenuated by using divided lower doses (1.6 g) or using a sustained-release formula (Trexler et al., 2015).

Caffeine

Caffeine is an active food, one of the most commonly worldwide used ingredients which athletes frequently use as an ergogenic aid. Even though more people drink tea than coffee, the concentration of caffeine in coffee is so high that it has become the greatest source of ingested caffeine worldwide. (Bailey et al., 2014; Graham et al., 1998; Harland, 2000). From a chemical point of view this is a purine alkaloid, which was discovered by a German chemist Friedrich Ferdinand Runge in 1819 (Runge, 1820). This organic chemical compound has more than 250 different common names, for instance: guaranine, thein, methyltheobromine, caffeina, mateina etc. Caffeine sources can be divided into two groups: those of natural origin, and those products to which caffeine has been added as a separate ingredient at the technological process stage. This natural substance is found in the seeds, leaves, fruit of coffee, tea, cocoa, maté, guarana, kola nuts, yerba maté, and more than 60 other plants native to Africa, East Asia and South America (Andrews et al., 2007; Caballero et al., 2005). This substance is also added to a lot of products for its known stimulant effects: energy drinks, sport gels, alcoholic beverages, chewing gums, caffeinated water, protein bars, dark/milk chocolate.

Caffeine is a central nervous system (CNS) stimulant of the methylxanthine class/grup (1,3,7-trimethylxanthine) that includes theophylline, paraxanthine, and theobromine. Caffeine is mainly metabolized in the human liver by hepatic cytochrome P450 1A2, and paraxanthine states more than 80% of the metabolites. Furthermore, caffeine's metabolites have similar activities to caffeine itself which can lead to the systemic effects (Graham & Spriet, 1995; Nehlig et al., 1992).There are several known mechanisms of action to explain the effects of this substance. The most prominent is that it reversibly blocks the action of adenosine on its receptors. Caffeine has a chemical structure similar to adenosine which has an affinity to the same receptor as adenosine and competes with it. It works by blocking the site for adenosine on the receptor, hence the adenosine-receptor complex does not form. The signal of tiredness does not reach the brain, and stimulatory neurotransmitters are continuously released, resulting in stimulation (Camfield et al., 2014). After oral ingestion, caffeine enters the human blood and is absorbed by body tissues. It enters all human tissues, crosses with ease the blood-brain barrier and reaches peak concentrations up 30 to 60 minutes after intake. Thanks to this feature, it has stimulating properties. Moreover, the physiological effects of caffeine include: increase in urine production, decrease in peripheral vascular resistance, increase in gastric secretions, activation of cardiac muscle, and relaxation of smooth muscle (Graham et al., 1998; Graham & Spriet, 1995; Kalmar, Cafarelli, 1999). The peak urinary caffeine concentration lasts about two and a half hours. The half-life of caffeine is quite variable, ranging from 2.7–9.9 hours, however, after 3–6 hours, the concentration of caffeine decreases by 50–75% (Blanchard & Sawers 1983; Kaplan et al., 1997).

Caffeine has been a legal substance in sport since 1 January 2004, when the World Anti-Doping Agency (WADA) removed caffeine from the list of banned substances. However, this substance is on the monitored list by the WADA (Goldstein et al., 2010). When it comes to the elite-athletes, there are some limitations. The IOC and the National Collegiate Athletic Association (NCAA) settled some limits regarding urine levels of caffeine - up to 12 μg/mL by the former and up to 15 μg/mL by the latter (Goldstein et al., 2010).

In order to achieve the ergogenic effects, it is advisable to use/dose 3–9 mg/kg of caffeine about 60 min before exercise/physical activity/competition (Brooks et al., 2016). This supplement/substance is commonly used among endurance athletes. Caffeine supplementation improves muscle endurance and performance as well as contributes to a reduction in the perception of pain and fatigue. It has been shown to increase endurance and power, especially during a prolonged physical activity. The positive ergogenic effects among triathlon athletes are shown with relatively low habitual caffeine intake if they ingest 6 mg/kg body weight caffeine, 45–60 min before the start of Olympic-distance triathlon in order to enhance their performance (Potgieter et al., 2018). The research is inconclusive when it comes to the results in strength and sprint performance, therefore further research is needed. It is observed that sprint cycling performance was influenced by torque factor and sprint duration but it was only when torque factor and sprint duration were optimized to allow participants to express their highest peak power output. When it comes to the sprint cycling performance, the effect of caffeine supplementation was visible only after such optimizing. In this study athletes were given a gelatin capsule containing 5mg/kg body weight of caffeine, 45 minutes before the sprint test (Glaister et al., 2018). On the other hand, in another study, in the strength training when it was tested one repetition maximum for the back squat and bench press exercises (during the first session), the caffeine, with dose 6mg/kg body weight ingestion, enhanced lower-body strength performance and this enhancement in performance was accompanied by reduced exercise fatigue. There were no effects for the upper-body strength and for the muscular endurance (Grgic & Mikulic, 2017).

Overall caffeine is a legal substance, which has a positive influence on people's health: especially recommended for its cognitive functions including alertness, attention, concentration, mood stimulation, increase of energy, improvement of performance, and reduction of tiredness (Andrews et al., 2007; Applegate, 1999; Graham, 2001; Nehlig et al., 1992; Tarnopolsky & Cupido, 2000). These health factors are important for elite/non-elite athletes in order to achieve their sporting success.

According to the study, positive effects on the cardiovascular system occur with a daily caffeine intake of the range 100–600 mg., whereas above 600mg per day is toxic to the human body. Moreover, excessive caffeine consumption is associated with the appearance of the side effects such us: high blood pressure, high heart rate, high cholesterol, bone mineral density, osteoporosis, anxiety, depression, anger/confusion, headache, insomnia, reproductive and developmental problems (Wikoff et. al., 2017).

Creatine monohydrate (CrM)

The creatine (Cr) was discovered by a French scientist Michael Eugen Chevereul in 1832 as a component of the skeletal muscle and named as a creatine monohydrate (CrM). Its name comes from the Greek word „kreas", meaning meat, as it is in meat products that its content is the highest (Salomons & Wyss, 2007). The EFSA, the AIS and the American College of Sports Medicine have categorized creatine as an evidence-based performance enhancing dietary supplement (AIS 2022; EFSA 2011; Thomas et al., 2016).

CrM is an organic compound (methylguanidine-acetic acid) that stimulate phosphocreatine (PCr) synthesis, increase PCr concentration and enhance the effectiveness of adenosine triphosphate (ATP) resynthesis in a muscle tissue (Cooper et al., , 2022; Kreider et al., 2017). The basic substrates for the CrM, synthesized in the kidneys and liver are semi-essential amino-acids L-arginine, glycine and methionine (Brosnan et al., 2011). CrM can be acquired from meat and fish (Persky & Brazeau, 2001). Vegetarians have lower total creatine levels in comparison with non-vegetarians (Burke et al., 2003).

CrM is quite well tolerated by human body, but mostly/only at recommended dosages i.e. 3–5 g/per day or 0.1 g/kg of body mass/per day (Antonio et al., 2021). International Society of Sports Nutrition (ISSN) proved that both short and long-term supplementation (up to 30 g/day for 5 years) is secure and very well tolerated among healthy individuals starting from infants to elderly. This is important in the context of physically active people at all ages. Furthermore, important health benefits may be provided by habitual, low dietary creatine ingestion (e.g., 3 g/day) throughout the lifespan (Fazio et al., 2022; Kreider et al., 2017). This is a crucial health factor for physically active people.

The ergogenic effect of CrM supplementation has been recommended to improve power/strength among elite-athletes (sprint) and to optimize/enhance training adaptations such us intermittent sprint as well as to recover during competition, for example, football, basketball, tennis etc. (Kreider, 2003). It has been proved many times that CrM improves high-intensity exercise capacity and increases LBM and muscle performance in resistance training. The effect of CrM upon LBM may be greater in men in comparison with women. (Kreider et al., 2017; Mihic et al., 2000). The ergogenic effect of creatine supplementation before such as training include enhanced force output, augmented power output; increased strength, anaerobic threshold and work capacity (Antonio et al., 2021; Kerksick et al., 2018).

In the context of athlete health it is common to observe depression and injuries among physically active people (Łuszczyńska & Abraham, 2012; Reng, 2015). From the point of view of health, CrM supplementation may have a significant antidepressant effect (in depressive disorders). In the aspect of the rehabilitation and treatment of post-operative conditions, CrM supplements appear to speed up recovery time (Hespel et al., 2001; Mihic et al., 2000).

The side effect of this supplement is the risk of diarrhea, that can be increased, but following intake of 10 grams of creatine per single serving. Study in top-level athletes showed that the most frequent gastrointestinal distress complaints were diarrhea, stomach upset and belching (Ostojic & Ahmetovic, 2007). What is more, CrM supplements should not be used in people with chronic renal disease or using potentially nephrotoxic medications, because clinical laboratories report the estimated glomerular filtration rate based on serum Cr, which elevation can lead to overdiagnosis of chronic renal failure, with the inherent health consequences (Vega & Huidobro, 2019).

Creatine malate (CrML)

New forms of creatine have been discovered in order to improve its physical, chemical and physiological properties in comparison to CrM. Creatine malate (CrML) known as a tri-creatine malate is a compound made from one molecule of malic acid with three molecules of CrM through the use of an ester bond. Every 4 g of CrML contains 3 g of CrM and 1 g of malic acid. CrML is a compound of three particles of creatine connected through an ester bond with one particle of malate. Even though it has two weak bonds which are susceptible to esterase, there is one strong bond which is secure enough to prevent the creatine particle from its conversion into creatinine.

When it comes to the creatine absorption and digestion as a CrML , it is much more efficient in comparison to other forms of creatine. CrML supplementation does not result in water retention in the muscle cells and gastrointestinal discomfort due to better solubility in water (in comparison with the monohydrate creatine). On the other hand, in this study there was no information about adverse effects; the study was investigating an intake of 5 g tricreatine malate per day for six weeks in young men during judo training (Sterkowicz et al., 2012).

Furthemore, when it comes to the ergogenic effect of CrML, there is much more evidence among sprinters than long distance runners (Tyka et al., 2015). In this study, scientists have observed that a six-week supplementation with CrML (Olimp Labs capsules, Poland) along with physical training (Wingate Test) has higher ergogenic effect among sprinters than long-distance runners. It resulted in increases in anaerobic power, total work in Wingate test and changes in body composition. The preparation was dosed of 0.07 g×kg–1 lean body mass (LBM) which corresponded to 5 g of the preparation for a person with LBM of 70 kg. The second group took placebo capsules. In this study, ergogenic supplementation effect in sprinters also resulted in a relevant increase in growth hormone in comparison with other groups. What is more, supplementation of CrML intensified the secretion of such a hormone, increasing the ergogenic effect. The higher the concentration of growth hormone after physical exercise, the more favourable the release of free fatty acids and thus the more effective the increase in LBM. On the other hand, in this study the significant rise in the running distance observed in the supplemented long-distance runners did not coincide with significant changes in maximal oxygen uptake, relative peak anaerobic power and relative total work, which may suggest positive effect of supplementation of CrML on aerobic endurance development.

CrML can support high-intensity physical exercise and regulate anabolic signals provided by exercise stimuli. Moreover, it supports increase of LBM, the development of muscle strength and power, as well as exercise capacity in single and repeated sprints (Kerksick et al., 2018). In this aspect, CrML is highly significant for strength and speed–strength sport disciplines, therefore this is a strong anabolic substance used among elite/non-elite athletes.

Based on the available studies on athletes, it can be concluded that short-term supplementation of CrML among athletes is a safe practice while administered within recommended criteria. Therefore, this form of creatine can stay a safe practice to human health (EFSA, 2011; EFSA 2006). The results of current research are promising, however, more research is needed on the effectiveness, regeneration, and health aspect of a long use of creatine malate among different groups of athletes or physically active people at different ages. As far as side effects are concerned, further research is also necessary.

Sodium bicarbonate

Sodium bicarbonate (SB) is an inorganic chemical compound of the bicarbonate group that is being researched since the 1930 on the ergogenic effect of the exercise performance (Dennig et al., 1931). In accordance with studies, SB has been reported as a performance enhancing aid/substance by reducing acidosis during exercise. During high-intensity exercise, acid and carbon dioxide build up in the muscles and blood. SB increases buffering capacity, potentially benefiting high performance during exercise. It supports intracellular pH regulation by increasing pH and bicarbonate concentration (Carr et al., 2011; Mueller et al., 2013). The pH gradient created between the two environments leads to an efflux of H+ and La- ions (lactate) from muscles subjected to work during a training unit (Bishopet al., 2004). SB increases athletes' exercise capacity during exercise. It improves performance by around 2% for short sprints of considerable intensity, the duration of which is max. 60 seconds but when the duration of exercise exceeds 10 minutes, SB is no longer of such use (Maughan et al., 2018) . SB also enhances the performance of those doing high-intensity, repetitive strength exercises such as CrossFit. SB allows 2–6% more repetitions in this type of training. Research confirms that it can improve the performance of trained swimmers in 200m freestyle distance, as well as the exercise capacity during a short-distance 400–800m run or a 2/3km bike ride (Carr et al., 2011; Mero et al., 2013; Mueller et al., 2013). On the other hand, another study showed that SB supplementation significantly enhances muscular endurance of small and large muscle groups but without any visible ergogenic effect on muscular strength (Grgic et al., 2020). According to the study, doses of SB from 0.2 to 0.5 g/per 1 kg body mass can enhance performance in muscular-endurance exercises, martial arts (boxing, judo, karate, taekwondo), and in high-intensity cycling, running, swimming, rowing (Grgic et al., 2021). The optimum dose of SB for ergogenic effects seems to be 0.3 g/per 1 kg body mass. Moreover, the ergogenic effects are highly documented for physical activity of high-intensity between 30 s and 12 min of time. According to studies, recommended intake of SB ingestion is between 60 and 180 min before physical activity in order to notice ergogenic effects. Long-term use of SB, for example, before every exercise can improve training adaptations such as increased time to fatigue and increase power output (Grgic et al., 2021).

Side effects of SB supplementation may cause gastrointestinal distress. Scientists proved that rowers' performance in 2,000-m efforts can enhance by ~2% with 6 mg/kg body mass with caffeine supplementation but when caffeine is combined with SB, gastrointestinal symptoms can contribute to reduce performance (Carr et al., 2011). The side-effects of SB are generally rare. The main side effects include bloating, nausea, vomiting, and abdominal pain. In order to reduce the risk of SB-induced side-effects on the day of competition or exercise it is recommended to use smaller doses e.g., 0.1 to 0.2 g/kg of SB consumed with the main meals for 3–7 days (Grgic et al., 2021). Furthermore, there is a positive interaction between supplementation of SB, CrM and beta-alanine on exercise performance (Saunders et al., 2017).

Results

To conclude, the ergogenic substances such us β-alanine, caffeine, CrM, CrML, SB are scientifically proven aids to enhance physical performance, recommended by the worldwide institutions such as EFSA, AIS, IOC, ISSN (EFSA 2015; Kerksick et al., 2018; Maugham 2018). These substances are associated with several mechanisms that affect the metabolism and adaptation of the human body to physical exercise. Substances such as β-alanine and carnitine are obtained endogenously in the human body but in the case of elite athletes there is a greater need to increase exercise capacity. According to the studies, a daily diet is insufficient to improve exercise capacity in elite-level sport. Therefore, supplementation, especially for elite athletes, is necessary. There are many forms of creatine, but CrM is the most researched substance. Nevertheless, CrML, according to current studies, is just as effective as CrM but better absorbed.

There is usually a positive interaction of supplements (for example β-alanine/caffeine/CrM) in order to get positive ergogenic effect in sport. Nevertheless, the ergogenic effect of the selected substances depends on the type of exercise or sporting discipline. In some cases there is a negative interaction when it comes to the ergogenic effect, for example, combining caffeine supplementation with SB.

Side effects often depend on the body's individual tolerance to the supplement or perhaps on the condition of a person's digestive tract (absorption, sensitivity, etc.). In the context of the adverse effects of supplementation with substances that improve exercise ergogenicity, the condition of the gastrointestinal tract should be noted as an additional variable in the study. Ergogenic supplements should be safe for human health for both amateur and competitive trainers. Therefore, these ergogenic substances should be investigated during long-term use, in the context of health effects.

Newest trends in sports genetics also include ergogenic substances, for example, caffeine which is already being investigated in terms of selected genetic variants that improve exercise capacity in sport (Grgic et al., 2020; Kot & Daniel, 2008). From a genetic point of view, it is widely known that genetic variation influences caffeine responses, but the cause(s) of this variability are unknown (Loy et al., 2015; Womack et al., 2012). Nevertheless, further research in this science area is needed as caffeine supplementation improves performance but the ergogenic effect is variable.

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Cite this article as: Świtała, K. (2023). The Popular Ergogenic Substances in Sport and Physical Activity. *Central European Journal of Sport Sciences and Medicine*, *1*(41), 69–80. https://doi.org/10.18276/cej.2023.1-07.