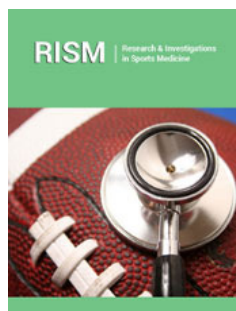


Single Ingredient Pre-Workout Supplements for Muscle Strength and Hypertrophy

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Summary

Currently, the supplement market has gained a large dimension, promising products that can increase performance and muscle hypertrophy. This review aimed to address which are the main single-component products suggested and how effective they are without intending to cover the entire subject. For that, we use our previous work and what is in the field. As main results, we observed that some supplements, such as caffeine and creatine, have a robust body of evidence regarding their effectiveness. Other products, such as beta alanine, BCAA, sodium bicarbonate, arginine, present several favorable results for their use, however, with some studies not proving this effectiveness. Thus, future well-controlled studies are suggested to clarify some controversies observed.

Introduction

The use of supplements as a pre-workout ergogenic aid is a vast subject and has been addressed by our group for more than two decades. We have some publications in book form and book chapters, addressing pharmac nutrients to maximize performance [1-4]. This work aims to make a brief review of the main pre-workout products. Didactically, supplements can be primarily intended to act on the Central Nervous System (CNS) or peripheral systems. They can be single or multi-ingredient pre-workout supplement. Some products, such as BCAAs and multi-nutrients, are often used with central and peripheral application. Furthermore, the systems are integrated and do not work in isolation. In the case of carbohydrates, for example, it is intended to supply energy to the muscle, but its depletion increases the subjective perception of fatigue by the CNS [1,5]. Here we will only cover single nutrient products.

Central nervous system stimulants (mental alert)

We observed that supplementation of 6mg/kg of caffeine improved strength performance and fatigue tolerance of young women who frequented a strength training gym, especially in lower limb exercises, submitted to a 4-moment crossover system [6] (Figure 1). Corroborating what we found, a more recent meta-analysis concluded that caffeine supplementation has an ergogenic effect for women performing endurance and strength exercises [7]. Another mechanism observed with caffeine supplementation was the reduction of urea in soccer players. The authors suggest that caffeine may reduce systemic urea, due to the decrease in serum glutamine, which in turn decreases the amounts of transported ammonia, which is fatigue factor for the CNS [8]. Arginine also has the potential to reduce ammonia, therefore it can delay CNS fatigue from strenuous exercise. In addition to this amino acid, tyrosine has also been used to delay central fatigue. Tyrosine competes with tryptophan, increasing the production of norepinephrine and reducing that of serotonin, providing mental alertness [2,9].

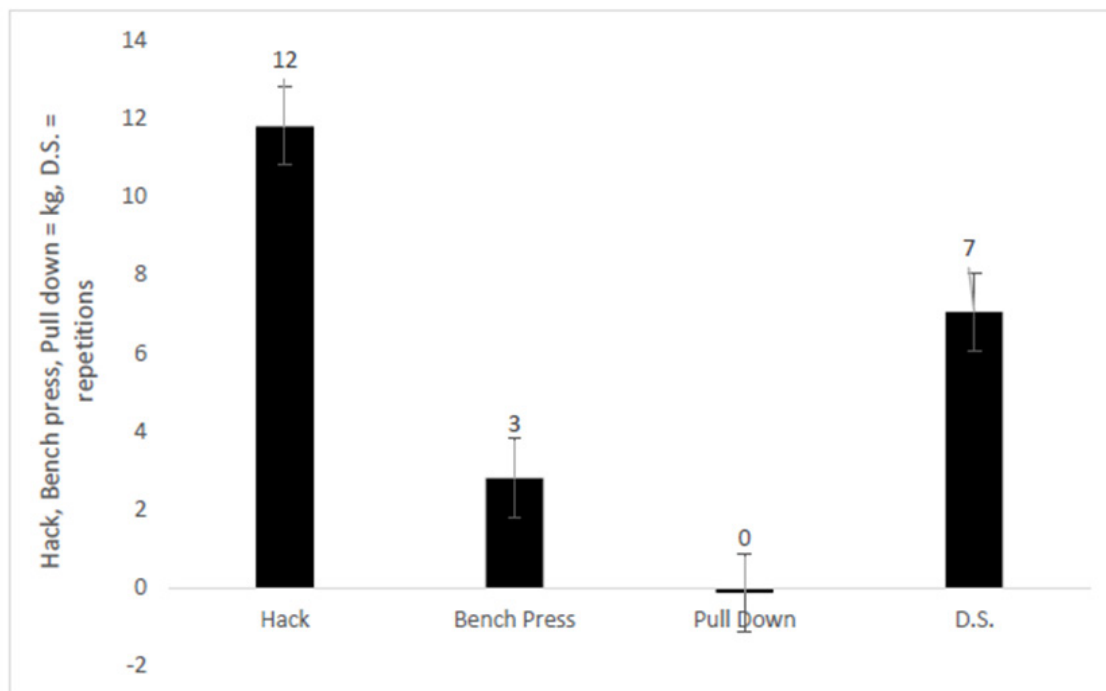


Figure 1: Delta of caffeine effect (mean of the caffeine moments less the mean of the basal and placebo) to 1-RM of Hack Squat, Bench Press, Pull Down and Drop Set (DS) to the knee extension starting with 100kg and drop to 80kg and 60kg without resting, in the following conditions: moment 1: basal (B) without supplements; moment 2: caffeine supplement; moment 3: placebo (P) with starch capsule, and; moment 4: caffeine supplement 6mg/kg 30 min before tests, apart one week one each other intervention. Statistics: Paired t-test between the mean of basal and placebo $([B+P]/2)$ vs. the caffeine 1 and caffeine 2 $([C1+C2]/2)$. Pull Down $P=0.8$; Hack $P=0.004$; Bench Press $P=0.007$; Drop Set $P=0.001$ [6].

In another crossover, double-blind, randomized study, we observed that 6mg/kg of caffeine improved oxidative stress in active youth undergoing an incremental treadmill test. The reduction in IL-6 suggests that caffeine may contribute to muscle hypertrophy, as it has a myokine effect, but this still needs to be further investigated [10]. The authors of a very comprehensive review article that included 21 meta-analyses on caffeine suggested that caffeine improves performance in a broad spectrum of physical exercise. However, due to the lack of some evidence, the authors recommended that more primary studies be done with women, middle-aged individuals, and strength exercises [11]. In this sense, a more recent meta-analysis has already responded to this last suggestion, concluding that caffeine is highly effective in improving speed in resistance exercises. This effect was observed at low, medium and high loads for both upper and lower limbs [12]. In an opinion article commissioned by a fight magazine, we discussed the benefits of using caffeine for fighters, associating its use with improving the performance of these athletes [13]. Confirming our recommendations, a recent meta-analysis concluded that caffeine supplementation is beneficial for a variety of aspects involving combat sports including isometric strength, anaerobic power, reaction time, and anaerobic metabolism [14].

Peripheral Mechanisms

The use of carbohydrate supplements is the simplest in terms of quick energy replacement. However, the use of medium-chain fatty

acids has shown promise for energy production during physical exercise since they produce twice as much energy per g and have an absorption rate similar to that of carbohydrate. Omega-3 has also shown promise in increasing strength, not so much for the extra energy provided, but for acting in a similar way to a hormone. We observed that both MCT and W-3 supplementation, at a dose of 4g/d for one month, favored strength performance and fatigue tolerance [15]. Another supplement widely used to improve strength, by directly activating ATP regeneration, is creatine. In our chapter we present a table with five meta-analyses on creatine carried out in the last 10 years, covering various populations, athletes, elderly, and women. Creatine has been shown to be an efficient ergogenic for improving muscle mass, strength performance, and power in these different populations [1]. Regarding safety, the authors of a meta-analysis performed with women and creatine supplementation, covering 29 studies and 951 participants, concluded that supplementation in different dose regimens is safe, like what has already been observed in men [16]. The buffering system to reduce the pH drop is sodium bicarbonate, to transform lactic acid into carbonic acid and then into carbon dioxide and water [1]. A meta-analysis of bicarbonate supplementation concluded that acute sodium bicarbonate supplementation improved peak anaerobic power, anaerobic capacity, endurance performance in events from ~45s to 8min, muscular endurance, performance in 2000m rowing and high-intensity intermittent running. However, further studies are needed to generalize these findings to women [17].

In the book *Aminoacids* we discuss BCAAs, which are used as pre and post workouts with the aim of better recovery and muscle hypertrophy [2]. One of the main purposes that they are used is to recover the delayed pain of training caused by micro-injuries in the muscles. A review paper concluded that there is a large reduction in delayed pain in the groups that supplemented with BCAA compared to placebo [18]. Glutamine was addressed by us in two books and the main indications at the time were related to strengthening the immune system and decreasing muscle catabolism for athletes, however, there was no consensus in the literature [2,4].

A more recent meta-analysis showed that glutamine supplementation was associated with weight and neutrophil reduction, with no impact on the immune system [19]. However, another aspect that glutamine has been indicated is to reduce intestinal dysbiosis from the ischemia/reperfusion process caused by intense exercise. The authors of a study with rats that had ulcerative colitis demonstrated that there was a reduction in inflammation caused by both strength and endurance physical exercise and glutamine supplementation [20]. More recently, a double-blind, randomized, control-group human study investigated the influence of supplementation of cystine (0.23g), glutamine (1.00g) and maltodextrin (1.23g), or maltodextrin placebo (2.46g) per 5 days three times a day (10:00, 15:00 and before bed). Supplementation reduced intestinal permeability and inflammation markers [21]. A study of 30 healthy men randomized to glutamine supplementation (0.3g/kg + 25g of sugar) and placebo (25g of sugar) for 14 days. Participants performed a strenuous exercise session and blood samples were taken for markers of atherosclerosis. The authors concluded that glutamine supplementation is beneficial for athletes undergoing strenuous exercise and that it was able to reduce markers of atherosclerosis and could be a preventive supplementation for this disease [22]. Regarding intestinal permeability, the use of bovine colostrum, glutamine, carbohydrate supplementation and maintaining euhydration were associated with reduced endothelial injury induction by intense physical exercise [23].

In a meta-analysis of beta alanine supplementation for athletes performing a level 2 Yo-Yo test variant, pointed to the direction of improved performance with this supplementation. It is important to note that the effect appears only in studies that used supplementation chronically for 6 to 12 weeks [24]. Yet another meta-analysis with beta alanine, despite two studies using up to 12g/d, concluded that at a dosage of up to 6.4g/d it is safe, having been used for up to 24 weeks [25]. In our recent work on bioenergetics, we addressed pyruvate supplementation [1]. Pyruvate is a limiting factor to produce aerobic energy in the Krebs cycle and its precursor is glucose, which after 10 metabolic reactions forms pyruvate. Speculation is that if pyruvate is supplemented, it could increase the oxidative process even under low glycemic conditions and would favor performance and fat oxidation [1]. Some studies have presented data on body fat reduction in overweight individuals [26], improvement in intermittent handgrip strength [27], increase in strength and power and improvement in body

composition of soccer players. football [28], in insulin resistant rats, reduced weight gain, improved insulin sensitivity, reduced plasma cholesterol, blood pressure and heart rate, improved aerobic capacity [29]. However, a meta-analysis on the use of pyruvate for weight loss concluded that there is no convincing data showing the effectiveness of this supplementation [30]. Due to the limited evidence on the safety of pyruvate and the lack of consistency of studies that unexplainedly stopped in the year 2005, we suggest further studies with greater rigor to conclude on the ergogenic effect of its supplementation [31].

Conclusion

Muscle hypertrophy depends on a complex integrated system of stimulation and recovery. In addition to training of adequate quality and intensity, nutrition is a limiting factor for the optimal performance of muscle response. Several foods and pharmac nutrients can help in the performance of sports training and in their adequate recovery. A variety of studies have suggested that caffeine-based ergogenic, herbal products, sodium bicarbonate, nitrates, and amino acids such as BCAAs, arginine, tyrosine, creatine, and beta alanine may play a favorable role in this scenario. More studies are needed to clarify some discrepant results found in the literature.

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