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Review

The Physiological Effects of Amino Acids Arginine and Citrulline: Is There a Basis for Development of a Beverage to Promote Endurance Performance? A Narrative Review of Orally Administered Supplements

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Abstract: Nutritional and ergogenic aid supplementation is prevalent within athletic or general fitness populations, and is only continuing to gain momentum. Taken in isolation or as a combination, amino acid (AA) supplementation has the potential to increase endurance performance among other benefits. L-Arginine (L-Arg) and L-Citrulline (L-Cit) are two AAs proposed to increase endothelial nitric oxide (NO) synthesis, with potential additional physiological benefits, and therefore may contribute to enhanced performance outcomes such as increased power output, or time to exhaustion. However, the appropriate dose for promoting physiological and performance benefits of these AAs, and their potential synergistic effects remains to be determined. Therefore, the aim of this review was to evaluate the varied concentrations used in the current literature, assess the effects of L-Arg and L-Cit in combination on physiological responses and endurance performance, and consider if there is a fundamental basis for providing these supplements in the form of a beverage. A total of six studies were considered eligible for the review which utilized a range of 3–8 g of the AA constituents. The findings support the notion that supplementing with a combination of L-Arg and L-Cit may increase NO production, enhance vasodilation, and therefore increase performance capacity in athletes. A beverage as a carrier for the two AAs is worth considering; however, there remains limited research assessing these outcomes across a consistent range of concentrations in order to see their full potential.

Keywords: L-Arginine; L-Citrulline; performance; exercise; vasodilation; functional beverage

1. Introduction

Supplementation and athletic performance share a long history [1,2]. There is a continual search for the latest supplements for enhancing athletic performance, reducing fatigue and recovery time, and providing a 'competitive edge' [1]. However, due to the relatively easy addition of supplements to a diet or training regime, they are often misused or used in the absence of evidence supporting their claims [3,4]. Amino acids (AAs) are the basic building blocks of proteins, which play an essential role in the body for cellular signaling and transport [5]. These signaling and transport proteins affect basic

physiological functioning through mediating the bioavailability of nutrients and gene expression and are, therefore imperative constituents to overall health [5,6]. The categorization of AAs as a whole fall into two pools: non-essential, which can be synthesized solely within the body, and essential, which cannot, and therefore are required to be consumed and obtained from the diet [5,6]. The consumption of different AAs as supplements are proposed to enhance athletic performance, predominately by increasing blood flow to skeletal muscle, and in turn, improving performance capacity [4,7]. Two AAs in particular, Arginine (L-Arg) and Citrulline (L-Cit), are commonly used as sporting supplements and have been studied for their inhibition of exercise-induced fatigue and vasodilatory effects which can subsequently result in enhanced performance including increased power output, reduced energy expenditure, and improved time to exhaustion [8–10]. Over the last few decades, numerous members of the AA family have been studied, some at great length, for their potential to modify these physiological attributes [4]. L-Arg and L-Cit are relatively recent AAs of interest due to their potential synergistic and potent vasodilatory effects [11,12], and in addition are also easily accessible and readily available to consumers in today's supplement market [4,13]. While studies have assessed the benefit of these AAs in human and animal trials, there is some degree of variance in concentrations administered, commonly between 3 and 6 g of L-Arg and 3 and 8 g of L-Cit. As such, it remains difficult to assess the presence or magnitude of any performance benefits that are elicited, due to such varied dose ranges.

As an essential AA in adults, the main dietary sources of L-Arg are lean meats, nuts, seeds, and legumes [14]. While playing a major role in protein synthesis, L-Arg has also demonstrated improvements to endothelial and immune function, reduced oxidative stress and vasodilation through increasing the generation of nitric oxide (NO) [14,15]. The development and production of NO is considered one of the most important factors associated with vasodilation of the cardiovascular system [16]. Furthermore, vasodilation is an integral component of the maintenance of vascular health, where the endothelium (cells that line the interior surface of blood and lymphatic vessels) produces several vascular responses that are important in the regulation of vascular tone [16,17]. The increase and maintenance of NO levels proposed from L-Arg supplementation can have additional, potentially beneficial effects during exercise and the compensatory vasodilation may result in improved exercise capacity, as well as possibly reducing oxygen (O_2) cost of moderate intensity exercise [11,14].

Traditionally, a non-essential AA, L-Cit can be found in some fruits such as watermelon, melons, and pomegranates [18]. Synthesized from several overlapping pathways, L-Cit acts as a pivotal point in the central reaction of the urea cycle, mediating the removal of ammonia in the body [18,19]. L-Cit also acts as a precursor to L-Arg, as it becomes actively converted into L-Arg via enzymatic hydrolysis [17,19,20]. Increased plasma levels of L-Cit have been associated with a protective role in oxidative damage and supporting the maintenance of 'normal' functioning of the cardiovascular system due to its role in NO metabolism [21,22]. Relatively recent studies have indicated that supplementing with a combination of L-Arg and L-Cit could potentially increase plasma L-Arg concentration and rapidly enhance NO bioavailability [13,21]. However, the use of these two AA reports a mixed consensus on their effects as nutritional ergogenic aids, both individually and in combination, likely due to a lack of consistency in concentrations tested (mainly <6 g each) as acute supplements [9,23].

Among other things, endurance performance depends on the interaction between a number of central and peripheral physiological factors [24]. A major factor differentiating endurance performance is running economy (RE), defined as the energy demand for a given velocity of submaximal running, and can be determined by measuring steady-state consumption of oxygen [25]. Cardiovascular responses, oxygen delivery to, and utilization by the tissues during exercise, play a fundamental role in determining RE and overall performance [24]. In addition, NO bioavailability has the potential to modify endurance performance with a specific focus on cardiovascular responses (via vasodilation), and supplementation with L-Arg and/or L-Cit may be an underlining driver to potentially optimize these processes.

Despite the associated physiological benefits of L-Cit and L-Arg in concentrations ranging from 3 to 8 g, few studies have investigated the effectiveness of these AAs in athletic, recreational,

and non-recreational individuals [13,26,27]. Generally, studies using either AAs or both in combination, have investigated predominantly physical and perceived parameters of exercise such as blood pressure (BP), sprinting time, jump height or Rating of Perceived Exhaustion (RPE) [9,12,28]. However, to date, an assessment of these outcomes against the diverse range of concentrations administered has not been performed. Therefore, the purpose of this review is to evaluate the range of L-Arg and L-Cit concentrations used in eligible studies, assess the effects of both AAs (individually or in combination) relating to performance outcomes, and to consider if there is a fundamental basis for providing these supplements in the form of a beverage.

2. Methods

Literature searches were performed in a non-systematic manner to assess the effectiveness of two commonly used AA, L-Arg and L-Cit as a combined supplement, on performance outcomes. Four electronic databases were searched (PubMed, Cochrane Library, Web of Science, and SCOPUS) using the terms "L-Arginine" OR "L-Citrulline" AND "athletes" AND "performance", (human and animal trials) in addition to manual searches of the identified article reference lists. Only peer-reviewed, randomized control trials published in the English language were of interest to the review. In particular, studies that used greater than 3 g of each supplement constituent in humans (or 0.05 g/kg of body mass) and at least 1.43 mmol·kg^{-1} of animal body mass were considered, based on inclusion criteria from previously published systematic reviews and meta-analyses [12,29]. Studies with a sample population considered 'healthy', placebo group as a comparator, and performance variables resulting from an exercise intervention in a trained population were of interest. All evidence was synthesized under the themes of AA bioavailability, vasodilation and NO biomarkers, physiological response, and performance outcomes as well as potential synergistic effects of both AAs. Results of the studies have been synthesized in Table 1.

3. Background

3.1. Prevalence of Supplementation in Athletic and Recreational Populations

Supplementation for competitive or recreational use is widespread in today's society, and it has become increasingly popular in recent years [1]. Results of a survey in 2016, indicated around 50% of athletes are taking supplements regularly, although this does not capture the 'irregular' supplement users, or what a particular individual might define as a 'supplement' [30,31]. While the prevalence of supplementation has not necessarily increased over the period of a few years, a study by Shaw et al. (2016) observed a greater amount of supplements being used within the same populations [30]. In general, a number of different supplementation products are becoming increasingly available and predominately sold as food supplements such as gels, bars, protein powders, or beverages. These products also contain a plethora of caffeine, different sugars and other ingredients (e.g., herbal extracts) that might be more attributable to an increased performance outcome than the *'active'* ingredient itself [2]. In addition, these beverages are also sources of an arbitrary combination of vitamins, minerals, and herbs; mixed with ergogenic aids such as nitrates (beetroot juice), and creatine, with the majority having limited or no scientific support behind their consumption [32]. Several institutions, such as the Australian Institute of Sport (AIS), provide a framework of supplement classifications, which includes an educational tool to rank sports foods and supplements (and their 'functional' ingredients) according to their scientific evidence and safety, allowing a practical contribution to an individual's performance goals [32]. In 2018, the International Olympic Committee (IOC) released a consensus statement on supplements and the high-performance athlete, indicating supplement use varied between different sports or activities [31]. This also increased with age, the level of training or performance, and was strongly influenced by perceived cultural and social norms [31]. Overall, an individual's motivation for supplement use is mainly attributable to the proposed health benefits, such as preventing nutrient deficiencies that may hinder performance or impair health, while supplementing for the purpose of a

direct performance outcome was only secondary [30,31]. This further iterates the importance of using supplements that are evidence-based, and designed with the individual in mind. With supplements being increasingly consumed by active individuals, could the burden of handfuls of capsules, tablets or powders be alleviated through convenient and specifically developed beverages?

3.2. L-Arginine

One of the popular nutritional supplements is L-Arg, which is reported to have potentially beneficial effects on athletic performance and health in general [16]. It has been previously established that L-Arg's key roles in the health and upkeep of cardiac and skeletal muscles are important in the regulation of homeostasis and hemodynamics of the body [16,33], including its mediation of creatine synthesis and growth hormone release [34]. These parameters, in addition to the requirement of L-Arg for NO production, outline the integral role of L-Arg in vascular function, and skeletal muscle maintenance [34]. In endothelial cells, NO is synthesized from L-Arg by eNOS and induces smooth muscle relaxation through guanylate cyclase activation [35,36]. For this reason, it has been proposed circulating L-Arg in the blood produced by oral administration, may represent a possible therapeutic mechanism to increase the synthesis and bioavailability of NO [13].

3.3. L-Citrulline

The consumption of L-Cit, known for its vasodilatory and NO production properties, has been postulated to increase muscular repair and accelerate wound healing. In addition, many of the health-related applications of L-Cit supplementation are primarily centered on the capacity for L-Cit to increase the availability of L-Arg for NO production [22]. Unlike L-Arg, L-Cit is transported directly to the kidneys after ingestion, where it is then catabolized into L-Arg by arginosuccinate enzymes (synthase and lyase) [37]. Due to the suggested vasodilation activity, supplementation with L-Cit is thought to affect exercise performance positively, gaining increased interest in the sporting and nutrition fields [28]. However, currently, ambiguity surrounding the effects of acute vs. chronic L-Cit supplementation, the method of delivery, and particular considerations in terms of the bioavailability of the supplement, all remain to be confirmed [28].

3.4. The Bioavailability of L-Arg and L-Cit

A number of different factors are associated with affecting the bioavailability of AA, including their chirality (L- or D- forms), concentrations provided, site of absorption, gastrointestinal health, transit time through the gastrointestinal tract and food matrix in which they are consumed [38,39]. Therefore, the mode of delivery has a strong potential to influence AA absorption, potentially making them more readily available in the body, as it may interact with several different factors resulting in a difference in the speed of the absorption or in some cases, even impaired absorption [39]. As most of the essential AA are usually consumed as dietary sources in the form of protein-containing foods, after ingestion they are absorbed relatively slowly and undergo extensive systemic and pre-systemic elimination [21,39,40]. In contrast, non-essential AA can be readily absorbed (specifically the L-forms) relatively quickly, and can also further contribute to the synthesis of essential AA in most cases [21]. Orally available AA supplements are often consumed as a pressed tablet, capsule, or powder, and often other ingredients are added to lessen an unfavorable taste if provided in liquid form [41]. However, the physiologically relevant responses may exceed consumption of the several grams range, and consequently, providing capsules might not necessarily be the most effective and convenient way of supplementation [42]. The combination of AA in beverage supplements, other liquid forms and in some pre-prepared food products can also affect the bioavailability of the AA. Hence, subsequent effects cannot be solely attributed to the particular compound being marketed [42,43]. Interestingly, a pharmacokinetic study [21] assessing doses of both L-Arg and L-Cit ranging from 5 to 10 g, demonstrated L-Cit is more readily absorbed and bioavailable compared with L-Arg. Although from a performance perspective, Ermolao et al. (2017), observed no significant in sprint time when supplementing with 3 g of L-Arg in a

500 mL carbohydrate (CHO) beverage (Total CHO 26.7 g) [44]. However, the effect that this may have had on the binding of the AA with the CHO matrix was not considered [44]. Unfortunately, there is a lack of recent pharmacokinetic studies on L-Cit and L-Arg despite the need to determine an effective dose range or upper limit, nor how ingesting food before or alongside supplementation may interact with its metabolism in the body. This reiterates the need to explore the effects of these AA and their combination in potentially higher doses (6 g and greater) as they are reported to be relatively safe and are currently largely unexamined [40,44]. Moreover, there is growing interest to support the potential health properties of these AA surrounding their performance enhancing, and general beneficial health properties, including vasoactivity [40,44].

4. Discussion of Results

4.1. L-Arg and L-Cit on Vasodilation and NO Biomarkers

The endothelial-derived vasoactive factor, NO, is a potent signaling molecule that plays a major role in vasodilatory capacity and thereby increasing oxygen uptake in skeletal muscle [45]. L-Arg is a substrate for vascular NO (Figure 1), and endothelial NO synthase (eNOS)–dependent NO formation [14]. It has also been proposed that endogenous NO production is dependent on extracellular L-Arg concentration, and therefore, by increasing extracellular L-Arg levels, NO-dependent vasodilation will also be enhanced [27,46]. A study by Bailey et al. (2016), reported a significant increase ($p < 0.05$) in NO production when supplementing with standalone L-Arg (6 g) and tended to increase with standalone L-Cit ($p = 0.08$) at concentrations of 6 g when compared with placebo [46]. In an animal study by Morita et al. (2014), rats and New Zealand white rabbits received either 2.85 mmol/kg of L-Cit, 2.85 mmol·kg^{-1} of L-Arg or 1.43 mmol·kg^{-1} of each in combination, to assess the acute effects on NO and blood flow [13]. This L-Arg/L-Cit combination caused NO bioavailability and blood flow (measured in the central ear artery) to increase more rapidly when compared with the other treatment groups ($p < 0.05$) [13]. While promising, a caveat for future studies was that the dosage used was relevant to the weight of the animal; however, it is stated in the article that relatively large dosages (5–15 g daily) would be required to improve endothelial function in humans [13].

4.2. L-Arg and L-Cit on Physiological Response and Exercise Performance Outcomes

Relatively recent studies have investigated the effects of both L-Arg and L-Cit supplementation on physiological responses and improving exercise performance [9,10,26,27,35,44,46–48]. Exercise intensity (i.e., velocity or power output) refers to the amount of work that can be accomplished to perform a given activity, often expressed as a percentage of an individual's VO_{2max}, or maximal power output, both typically measured using incremental exercise testing [49]. Exercise capacity refers to the ability of an individual to perform at a specific workload intensity [50].

Together with physiological responses associated with the autonomic nervous system (ANS) such as heart rate, heart rate variability and blood pressure, sub-maximal and maximal oxygen consumption (VO_2) and exercise economy, to name a few, are factors directly affecting the performance of an individual [51]. A study by Bailey et al. (2015), compared L-Arg and L-Cit individual supplementation on running economy and exercise performance in active males [46]. After acute supplementation with 6 g of L-Arg and 6 g of L-Cit, the authors reported no significant effects ($p > 0.05$) on either running economy or overall exercise performance after a moderate intensity cycle compared with placebo. This study, however, did not assess the potential effects of the AA in combination. In contrast, Chen et al. [10] assessed running economy in 12 athletes using L-Arg and L-Cit in combination using an oral tablet. The treatment group, who received 0.05 g/kg of body weight of L-Arg/L-Cit, improved performance over two consecutive days compared with PL ($p = 0.002$) [10]. Similarly, Hsueh et al. (2018) reported male swimmers improved high-intensity interval training performance after a 50-m swim when supplementing with an average of 3.2 g for both L-Arg and L-Cit (average based on AA 0.05 g/kg body weight). [27]. While the studies assessing both L-Arg and L-Cit in combination

had relatively small sample sizes (n = 10–24), overall, enhancing cardiorespiratory efficiency through NO modulation with a combination of L-Arg and L-Cit was seen to more efficiently enhance VO_2 kinetics (pulmonary O_2 uptake)—a valuable outcome in endurance athletes by positively affecting power output and metabolic responses. It is for these reasons that L-Arg and L-Cit require further investigation, specifically given their potential to enhance physiological responses, either as standalone supplements or in combination.

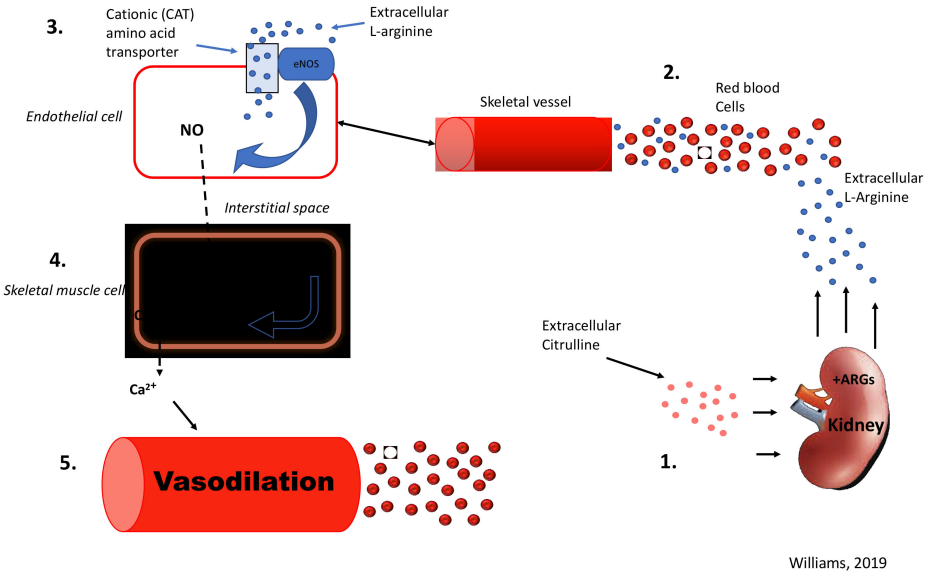

Figure 1. L-Arg, L-Cit and their role in vasodilation. Step **1.** Citrulline in systemic circulation is metabolized in the kidneys by ARGs to form L-arginine. Step **2.** L-arginine is released systemically into blood vessels. Step **3.** L-arginine is transported into endothelial cells via CAT transporters and eNOS to produce nitric oxide (NO). Step **4.** NO diffuses from endothelial cells into skeletal cells. Step **5.** NO presence and activation of GC and GTP produces cGMP causing cellular calcium efflux, leading to vasodilation. **Abbreviations;** ARGs = arginosuccinate synthase; CAT = cationic amino acid transporter; eNOS = extracellular nitric oxide synthase; NO = nitric oxide; GTP = guanosine triphosphate; GC = guanylyl cyclase; cGMP = cyclic guanosine monophosphate. Figure 1 was provided as a courtesy by Mr. Jackson Williams.

4.3. Potential Synergistic Effects of L-Arg and L-Cit

The effects of L-Arg are known to be hampered by its absorption due to intestinal arginase activity [39]. While L-Cit is made available rather quickly, it can also be metabolically converted into L-Arg, thus showing potential for a synergistic relationship between the two [14,52]. While only four known studies [10,13,26,27], to our knowledge, have assessed both AA in combination, it cannot be ruled out that their combined consumption has the potential to be more efficient in achieving improved performance outcomes. Three human trials [10,26,27] identified in this review, while having relatively small sample sizes (12–16 participants), still found enhanced responses for their collective outcome measures of fatigue modification and exercise performance. Previous human pharmacokinetic studies [21,40] have demonstrated the 'recycling' mechanism of L-Arg through the involvement of L-Cit in the urea cycle, and have focused on the suggestion that increasing L-Cit would result in increased plasma L-Arg [40]. From the studies assessed in this review, it can be speculated that due to their synergistic effects, supplementing with a combination of L-Arg and L-Cit may be more effective than supplementing with the individual AA, due to the potential for increased bioavailability and the reuptake of L-Arg [13,40]. However, there is no consensus on the appropriate concentration of each AA when used in combination, and if it is possible to achieve the expected results with a lesser dose but with chronic supplementation, compared with acute supplementation with a higher dose.

Table 1. Summary of studies which tested L-Arginine and L-Citrulline in combination in humans and animal studies.

Author, Year	Participants (n)	Objective	Outcomes	Concentration of Supplement	Strengths	Limitations
Bailey et al., 2015 [53]	$n = 10$	To compare the effects of L-Cit and L-Arg supplementation on NO biomarkers, $\dot{V}O_2$ kinetics, and exercise performance.	Plasma NO concentration was increased with L-Arg supplementation ($p < 0.05$) and tended to increase with L-Cit supplementation ($p = 0.08$) compared with PL. $\dot{V}O_2$ during moderate-intensity cycle exercise was not significantly different ($p > 0.05$).	6 g (of each)	Due to the short study design, a familiarization and baseline testing session was conducted to discount a 'learning effect' in exercise testing.	Short study duration (seven days) and small sample size ($n = 10$).
Chen et al., 2016 [10]	$n = 12$	To investigate the effect of the combination L-Arg and L-Cit on central fatigue.	Significantly better response time measured in AA group compared with PL.	0.05 g/kg of body weight (of each)	Previously tested the point after supplementation when plasma L-Arg would peak, and began testing protocol 1-h after supplementation.	Small sample size ($n = 12$).
Cheng et al., 2016 [26]	$n = 13$	To investigate the combination of L-Arg and L-Cit on endurance performance.	AA group significantly better in two endurance running distances on both days.	0.05 g/kg of body weight (of each)	Testing protocol was repeated a day later to validate outcomes.	Assessed acute effect of supplementation with one day washout period—potential accumulation of plasma AA not discussed?
Hsueh et al., 2018 [27]	$n = 16$	To examine the effect of co-ingestion of L-Arg and L-Cit on high-intensity interval swim performance in trained young swimmers.	Average swim time was shorter in treatment group when compared with PL. RPE was similar between the two groups.	0.05 g/kg of body weight (of each)	Testing protocol began one hour after supplementation to allow for peak plasma levels.	Relatively small sample size ($n = 16$).
Morita et al., 2014 [13]	[animal] $n = 24$	To investigate the acute effects of a combination of oral L-Cit and L-Arg on plasma L-Arg and NO levels, as well as on blood circulation.	L-Arg and L-Cit combined caused a more rapid increase and enhancement of NO bioavailability compared with single individual AA.	2.85 mmol·kg^{-1} (of each) animal body weight, and 1.43 mmol/kg of combined L-Arg/L-Cit	Strong study design, highlights future direction for human studies.	Animal trial—not directly transferrable?
Silva et al., 2017 [8]	[animal] $n = 40$	To evaluate the effects of supplementing with L-Arg and L-Cit on performance and oxidative stress in trained and untrained rats	Supplementation improved physical performance in both control and trained groups.	300 mg/kg animal body weight	Strong study design, highlights future direction for human studies.	Animal trial—not directly transferrable?

Key: L-Arg = Arginine; L-Cit = Citrulline; PL = placebo; RPE = Rating of Perceived Exhaustion; NO = Nitric Oxide; AA = Amino Acids; BMI = Body Mass Index; CM = Citrulline Malate; RSA = Repeated Sprint Ability.

While there is relatively strong evidence related to improved sports performance, vasodilation and NO production after supplementation with L-Arg and L-Cit individually, trials assessing a combination of L-Arg and L-Cit are still relatively scarce. There is conflicting evidence relating to the most appropriate and effective concentration of both AA, and larger trials are needed in order to assess the true potential of L-Arg and L-Cit as a combined nutritional ergogenic aid.

5. Summary of Key Findings and Future Directions

Despite the consistent yet still emerging use of sporting supplements, there remains a lack of consensus underlying their effectiveness. Supplementation with L-Arg and L-Cit still requires further investigation using larger sample sizes, a consistent range of AA concentrations and timing of administration, to determine the optimal effect on physiological parameters. There also lies a general acceptance that the ratio at which L-Arg and L-Cit should be consumed in combination, typically a 2:1 L-Cit to L-Arg, as opposed to a 1:1 ratio, which may alter the effectiveness of functional beverages which contain both AAs. However, further research is needed to determine the optimal quantities of each AA required to be consumed in order to potentially exhibit beneficial effects in performance. Additionally, by providing supplementation in the form of a functional beverage, there is potential for more natural consumption of the product during various types of athletic events (i.e., running, weight lifting, and swimming), and whether the timing of supplementation could be spaced out and delivered at the most critical time points to promote improved performance.

Taking into account that sports beverages are primarily developed and formulated to be effective in improving performance, and to provide hydration and a cooling effect when required, traditionally, there are no universal agreements for the most efficacious formulations. The main reason for this could be seen in the versatility and convenience in the use of sports drinks. For example, regardless of formulation, a particular beverage could be used in several different sports or physical activities and more recently, their availability on the market has provided opportunities for use in general populations too. This requires a level of likeness or acceptability of a particular product in order to be selected by everyday individuals or recreational athletes—which in the case of L-Arg and L-Cit, in addition to the competitive nature of product development, can be a difficult obstacle. Although the flavor modulation in beverages is achieved with the use of sweeteners (carbohydrates, artificial and semi-artificial sweeteners), salts and encapsulation, it is important to select ingredients that will not interfere with the stability or in some cases the absorbability of the active compounds. Some of the potential avenues could include pH-sensitive encapsulation of the active ingredients targeting specific sites of absorption in the small intestine while masking the potential undesirable flavor of the active ingredients. Additionally, many of the commercially available L-Cit supplements currently on the market today are commonly prepared with citrulline malate, and future studies should look to investigate any differences in effectiveness between the salt and isolated compounds.

6. Conclusions

A beverage that provides the potential ergogenic benefits of L-Arg and L-Cit supplementation in the convenience of a sports drink with the tested stability of the active ingredients and flavor adaptation to make it more palatable is worth considering. Overall, there remains a relatively mixed consensus surrounding the quantities of L-Arg and L-Cit that need to be consumed to elicit the most beneficial effects in humans, while animal studies have highlighted a path for future human studies and potential mechanisms of action. Further research should assess these outcomes across a range of concentrations in order to see the full potential in the delivery of these AA on endurance performance for immediate use pre-, during- and post-event within the athletic, recreational sport, and general populations.

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