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L-Citrulline Supplementation in Exercise: Effects on Blood Flow, Muscular Performance, and Post-Exercise Recovery — A Narrative Review

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Abstract

Background. L-citrulline increases L-arginine availability and may enhance nitric oxide synthesis, vascular function, exercise performance, and recovery.

Aim. To evaluate the effects of L-citrulline and citrulline malate supplementation on blood flow, muscular performance, fatigue, and post-exercise recovery.

Methods. A structured narrative review was conducted using PubMed/MEDLINE, supplemented by reference-list screening and citation tracking.

Results. L-citrulline increases circulating L-arginine concentrations, but its effects on exercise performance remain inconsistent. Citrulline malate may modestly improve muscular endurance during high-volume resistance exercise, whereas evidence concerning maximal strength,

power, and aerobic performance is inconclusive. Supplementation may reduce muscle soreness, but evidence for accelerated functional recovery remains limited.

Conclusions. L-citrulline is generally well tolerated, but its ergogenic effects appear modest and dependent on the exercise context. Further studies using verified formulations and standardized protocols are required.

Keywords: L-citrulline; citrulline malate; nitric oxide; blood flow; exercise performance; muscle recovery; dietary supplements

1. Introduction

Dietary supplements are widely used by both competitive athletes and recreationally active individuals seeking to improve exercise capacity, delay fatigue, and accelerate post-exercise recovery. However, only a limited number of supplements demonstrate consistent ergogenic effects supported by high-quality scientific evidence, while the effectiveness of many products remains uncertain because of small study populations, methodological heterogeneity, and differences in supplementation protocols [1, 2]. In recent years, increasing attention has been paid to supplements that may enhance nitric oxide bioavailability and consequently improve vascular function, skeletal muscle perfusion, and exercise performance. One such compound is L-citrulline, a non-protein amino acid available either as a standalone supplement or combined with malate in the form of citrulline malate. Its proposed physiological effects and growing popularity among physically active individuals have stimulated research into its potential influence on blood flow, muscular performance, exercise-induced fatigue, and post-exercise recovery [3].

L-citrulline is a non-essential, non-protein amino acid that plays an important role in the urea cycle and in the endogenous synthesis of L-arginine. Following oral administration, L-citrulline largely escapes intestinal and hepatic first-pass metabolism and is transported to the kidneys, where it is converted into L-arginine through successive reactions catalyzed by argininosuccinate synthase and argininosuccinate lyase [4, 5]. This metabolic pathway allows L-citrulline to increase circulating L-arginine concentrations more effectively than equivalent amounts of orally administered L-arginine, which undergoes substantial presystemic degradation by intestinal and hepatic arginase [5, 6]. L-arginine subsequently serves as a substrate for nitric oxide synthase, which produces nitric oxide and L-citrulline. Nitric oxide activates soluble guanylate cyclase in vascular smooth muscle cells, increasing cyclic guanosine monophosphate concentrations and promoting vasodilation. Consequently, L-citrulline supplementation may enhance endothelial function and muscle perfusion, potentially facilitating oxygen delivery, nutrient transport, and metabolite removal during and after exercise [4–6].

The exercise-related rationale for L-citrulline supplementation extends beyond vasodilation alone. Increased nitric oxide availability may improve the matching of oxygen delivery to metabolic demand, whereas the involvement of citrulline in the urea cycle may facilitate ammonia clearance and reduce the accumulation of metabolites associated with muscular fatigue. Citrulline malate has additionally been proposed to support aerobic energy production through the participation of malate in the tricarboxylic acid cycle, although the independent contribution of malate to exercise performance remains insufficiently established. Despite these plausible mechanisms, the available clinical evidence is inconsistent. Meta-analyses suggest that acute citrulline malate supplementation may produce a small improvement in repetition performance during high-volume resistance exercise, but it does not appear to meaningfully

increase maximal muscle strength [7, 8]. Similarly, pooled evidence has not demonstrated a significant overall improvement in aerobic performance, oxygen uptake kinetics, blood lactate concentrations, or perceived exertion [9]. These discrepancies indicate that physiological changes in arginine and nitric oxide availability do not necessarily result in clinically or athletically meaningful improvements in performance.

Several factors may explain the inconsistent findings reported in the literature, including differences in supplement formulation, dosage, timing of ingestion, duration of supplementation, participants' training status, and the exercise protocols used to evaluate performance. Interpretation is further complicated by the frequent use of the terms L-citrulline and citrulline malate interchangeably, despite differences in their composition and the possible contribution of malate. Moreover, many available studies have included small and predominantly male samples, limiting the generalizability of their findings. The most recent meta-analytic evidence indicates that citrulline malate may provide small and context-dependent performance benefits; however, the certainty of this evidence remains low or very low [10]. Therefore, the aim of this narrative review is to critically evaluate the current evidence regarding the effects of L-citrulline and citrulline malate supplementation on nitric oxide bioavailability, vascular function, muscle blood flow, resistance and endurance exercise performance, exercise-induced fatigue, and post-exercise recovery. Particular attention is given to the differences between supplement formulations, practical dosing strategies, safety, and the methodological limitations of the available research.

2. Methodology

2.1 Review design and literature search strategy

This manuscript was designed as a narrative literature review evaluating the effects of L-citrulline and citrulline malate supplementation on vascular function, exercise performance, and post-exercise recovery. A structured, non-exhaustive search was conducted in PubMed/MEDLINE, supplemented by reference-list screening and citation tracking. The search covered publications available up to September 2026. Search terms included “L-citrulline”, “citrulline malate”, “nitric oxide”, “blood flow”, “vascular function”, “exercise performance”, “resistance exercise”, “muscular endurance”, “strength”, “aerobic exercise”, “high-intensity exercise”, “fatigue”, “muscle soreness”, and “recovery”. Terms were combined using the Boolean operators “AND” and “OR”. Recent systematic reviews and meta-analyses were used to identify additional relevant primary studies.

2.2 Eligibility criteria

Eligible publications included randomized controlled trials, placebo-controlled crossover studies, prospective intervention studies, systematic reviews, and meta-analyses evaluating acute or chronic supplementation with pure L-citrulline or citrulline malate. Studies were considered relevant when they involved healthy adults, physically active individuals, or trained athletes and assessed vascular, performance-related, metabolic, or recovery outcomes. Publications investigating multi-ingredient supplements were excluded when the independent effects of citrulline could not be determined. Animal and in vitro studies, conference abstracts, editorials, commentaries, and non-peer-reviewed sources were excluded from the principal synthesis. Selected mechanistic publications were used to explain citrulline metabolism and nitric oxide-related pathways.

2.3 Study selection and evidence synthesis

Titles and abstracts were screened for relevance to the aims of the review, followed by an assessment of the full texts of potentially eligible publications. Extracted information included study design, participant characteristics, training status, supplementation formulation, dose, timing and duration, comparator, exercise protocol, measured outcomes, and principal findings. Because of substantial heterogeneity among the available studies, the findings were synthesized narratively rather than pooled quantitatively. Greater interpretative weight was assigned to randomized placebo-controlled trials, systematic reviews, and meta-analyses. Evidence was organized into thematic categories covering metabolism, vascular function, resistance and aerobic exercise performance, post-exercise recovery, dosage, and safety.

3. Results and thematic review

3.1 Physiological Characteristics and Metabolism of L-Citrulline

L-citrulline is synthesized endogenously, primarily in enterocytes of the small intestine, from precursor amino acids such as glutamine, glutamate, and proline. In contrast to most amino acids absorbed from the gastrointestinal tract, citrulline is not substantially incorporated into intestinal proteins and largely bypasses hepatic uptake. It is therefore released into the portal and systemic circulation and transported mainly to the kidneys [4, 5]. Within renal proximal tubular cells, citrulline is sequentially converted into argininosuccinate by argininosuccinate synthase and subsequently into L-arginine by argininosuccinate lyase. The resulting L-arginine is released into the circulation and becomes available to peripheral tissues. This intestinal–renal axis represents an important endogenous source of L-arginine and helps maintain whole-body arginine homeostasis, particularly when dietary arginine availability is limited or metabolic demand is increased [4, 5].

Oral L-citrulline appears to be an efficient nutritional strategy for increasing systemic L-arginine availability. Unlike orally administered L-arginine, citrulline is not a substrate for intestinal or hepatic arginase and consequently undergoes limited presystemic degradation. After absorption, it reaches the systemic circulation and is converted into L-arginine in the kidneys, producing a dose-dependent increase in plasma citrulline and arginine concentrations [6]. Pharmacokinetic evidence indicates that oral L-citrulline may increase circulating arginine more effectively and with better gastrointestinal tolerance than an equivalent amount of L-arginine. This apparent paradox results from the extensive first-pass metabolism of dietary L-arginine and the ability of citrulline to bypass this metabolic barrier [5, 6]. Increased systemic arginine availability may subsequently provide more substrate for nitric oxide synthesis, although changes in plasma amino acid concentrations do not necessarily indicate a proportional increase in endothelial nitric oxide production or exercise performance.

L-arginine serves as the principal nitrogen-containing substrate for nitric oxide synthesis. In vascular endothelial cells, endothelial nitric oxide synthase catalyzes the oxidation of L-arginine to nitric oxide and L-citrulline in a reaction requiring molecular oxygen, nicotinamide adenine dinucleotide phosphate, tetrahydrobiopterin, flavin cofactors, and calcium-bound calmodulin [11]. Once produced, nitric oxide diffuses from the endothelium into adjacent vascular smooth muscle cells, where it activates soluble guanylate cyclase. This enzyme increases the formation of cyclic guanosine monophosphate, which activates protein kinase G and reduces intracellular calcium availability, ultimately promoting smooth muscle relaxation and vasodilation. During exercise, this pathway contributes to the regulation of vascular tone

and blood flow distribution according to the metabolic requirements of active tissues. Therefore, increasing L-arginine availability through L-citrulline supplementation could theoretically enhance nitric oxide-dependent vascular responses; however, nitric oxide production is also regulated by enzyme activity, cofactor availability, oxidative stress, and baseline endothelial function [11].

In addition to its involvement in nitric oxide metabolism, citrulline participates in the urea cycle, which converts potentially toxic ammonia into urea. Ammonia production increases during intense exercise as a consequence of amino acid catabolism and the deamination of adenosine monophosphate. Its accumulation has been proposed to contribute to both peripheral and central fatigue by interfering with cellular metabolism and neurotransmission. By supporting urea-cycle flux, citrulline supplementation could theoretically facilitate ammonia clearance and delay exercise-induced fatigue, although this mechanism has not been consistently confirmed in human performance studies. Citrulline malate may exert an additional metabolic effect because malate is an intermediate of the tricarboxylic acid cycle and may support oxidative adenosine triphosphate production. An early human study reported that citrulline malate supplementation influenced oxidative energy production during exercise and phosphocreatine recovery after exercise [12]. Nevertheless, the independent contribution of malate remains uncertain because most trials have not compared citrulline malate directly with an equivalent dose of pure L-citrulline or malate alone.

3.2 Effects on Vascular Function and Muscle Blood Flow

By increasing circulating L-arginine availability, L-citrulline supplementation may support endothelial nitric oxide production and improve endothelium-dependent vasodilation. Vascular effects have commonly been evaluated using flow-mediated dilation, pulse-wave analysis, arterial stiffness indices, and resting or stress-induced blood pressure measurements. Some clinical studies have demonstrated improvements in endothelial function and modest reductions in systolic blood pressure following L-citrulline supplementation, particularly in individuals with elevated blood pressure, impaired vascular function, or increased cardiometabolic risk. A systematic review and meta-analysis reported a reduction in systolic blood pressure, while the effect on diastolic blood pressure was less consistent and appeared to depend on dose, intervention duration, and participant characteristics [13]. In contrast, studies involving young, healthy, physically active participants have frequently demonstrated smaller or absent vascular effects. This may reflect an upper physiological limit because individuals with preserved endothelial function and high baseline nitric oxide availability have less potential for measurable improvement.

During exercise, blood flow to active skeletal muscles increases through the integrated effects of central hemodynamic responses and local vasodilatory mechanisms. Nitric oxide contributes to this response by reducing vascular resistance and supporting the distribution of oxygenated blood within the muscle microcirculation. Consequently, L-citrulline supplementation has been proposed to improve muscle oxygen delivery, accelerate oxygen uptake kinetics, and facilitate the removal of metabolites generated during muscular contraction. Some experimental studies have reported improvements in muscle oxygenation or oxygen uptake responses following citrulline supplementation, particularly during high-intensity exercise [14]. However, other trials have found no meaningful changes in limb blood flow, muscle oxygenation, or exercise hyperemia despite clear increases in plasma L-arginine concentrations. These findings suggest that substrate availability is only one of several factors regulating exercise-induced vasodilation. Functional redundancy among nitric oxide, prostaglandins, adenosine, potassium

ions, and other local mediators may limit the measurable contribution of supplemental citrulline, especially in healthy individuals with normal endothelial function.

The vascular response to L-citrulline supplementation is likely influenced by the baseline physiological characteristics of the studied population. Individuals with hypertension, arterial stiffness, metabolic disorders, aging-related endothelial dysfunction, or reduced nitric oxide availability may have greater potential to benefit than young and healthy athletes with preserved vascular function [13]. Supplement dose and duration may also be relevant, as an acute increase in plasma arginine does not necessarily produce the same vascular adaptations as repeated supplementation. Furthermore, differences in the methods used to assess vascular function complicate comparisons among studies. Resting blood pressure, flow-mediated dilation, pulse-wave velocity, near-infrared spectroscopy, and Doppler-derived limb blood flow reflect related but distinct aspects of vascular physiology. Overall, the evidence supports the ability of L-citrulline to increase arginine availability, but its effects on exercise-induced muscle perfusion remain variable. Improvements in vascular biomarkers should therefore not be interpreted automatically as evidence of enhanced physical performance [6, 13, 14].

3.3 Effects on Resistance Exercise Performance

Resistance exercise, particularly when performed with moderate loads, multiple sets, and repetitions to muscular failure, creates substantial metabolic demand and progressively reduces the capacity to maintain force production. L-citrulline and citrulline malate have been proposed to delay this decline through several complementary mechanisms. Increased nitric oxide availability may enhance muscle perfusion and oxygen delivery, whereas improved removal of exercise-related metabolites could support contractile function during repeated sets. Citrulline participation in the urea cycle may facilitate ammonia clearance, while malate has been suggested to support oxidative adenosine triphosphate production and phosphocreatine recovery [12, 14]. Together, these effects could increase the number of repetitions completed before muscular failure and help maintain performance across successive sets. Nevertheless, these mechanisms remain partly theoretical, and the ergogenic response may be more apparent during high-volume protocols that generate considerable metabolic fatigue than during brief tests of maximal strength or power [7].

Several placebo-controlled studies have reported improvements in repetition performance following acute citrulline malate supplementation. In a frequently cited randomized crossover trial, resistance-trained men consumed 8 g of citrulline malate or placebo one hour before performing a high-volume bench-press protocol. Citrulline malate increased the number of repetitions completed during the later sets and reduced self-reported muscle soreness during the subsequent recovery period [15]. Improvements have also been observed during multi-exercise protocols involving large muscle groups, suggesting that the potential benefit may become more apparent as fatigue accumulates across repeated sets [16]. These findings support the hypothesis that citrulline malate may enhance local muscular endurance rather than maximal force production. However, the reported improvements should be interpreted cautiously because the studies involved relatively small samples, were conducted predominantly in resistance-trained men, and used protocols based on repetitions to failure, which may be influenced by motivation, pacing, and participants' familiarity with the testing procedure.

In contrast to the positive findings, several randomized trials have failed to demonstrate improvements in total repetitions, peak torque, mean power, or resistance-exercise volume after acute citrulline malate ingestion. Pooled evidence reflects this inconsistency. A meta-analysis

of repetition-to-failure studies identified only a small ergogenic effect, corresponding on average to approximately three additional repetitions across an entire exercise protocol [7]. Subgroup analysis suggested a possible benefit for lower-body exercise, whereas the effect for upper-body protocols was not statistically significant. Furthermore, a separate meta-analysis found no significant improvement in maximal muscle strength among resistance-trained adults [8]. The heterogeneity of these findings may result from differences in exercise selection, training volume, rest intervals, participant experience, supplement dose, ingestion timing, and the actual citrulline content of commercial products. Individual responsiveness may also be relevant, as participants with high baseline nitric oxide availability or well-developed exercise tolerance may obtain little additional benefit. Thus, the available evidence suggests a possible but small improvement in muscular endurance, without convincing evidence of increased maximal strength or power [7, 8, 10].

Interpretation of resistance-exercise studies is further complicated by differences between pure L-citrulline and citrulline malate. Citrulline malate is generally described as a combination of citrulline and malate in a 1:1 or 2:1 molar ratio; however, these formulations do not provide equivalent amounts of active citrulline. For example, 8 g of a theoretical 2:1 preparation contains substantially less than 8 g of L-citrulline, making direct dose comparisons inappropriate. In addition, independent analyses have raised concerns that some commercial products may not match the ratios declared by manufacturers. Many exercise trials did not chemically verify supplement composition or report the precise quantity of each component. It therefore remains uncertain whether differences among studies reflect the physiological response to citrulline, a possible contribution of malate, or variability in the actual dose administered. Future trials should independently verify supplement composition and report both the total mass of citrulline malate and the amount of elemental L-citrulline [6, 10].

From a practical perspective, acute citrulline malate supplementation may provide a small benefit during resistance-training sessions involving multiple sets, moderate loads, short-to-moderate recovery intervals, and repetitions performed close to muscular failure. The effect appears less likely during isolated maximal-strength tests, low-volume training, or brief assessments of peak power. Even when statistically significant, the average improvement remains modest and demonstrates substantial variability among individuals [6, 10]. It is also unclear whether completing a small number of additional repetitions during a single session produces meaningful long-term improvements in strength or muscle hypertrophy, as chronic training studies remain limited. Therefore, citrulline should not be considered a substitute for appropriate training design, adequate energy and protein intake, sleep, or recovery. Current evidence supports describing it as a potentially useful but nonessential ergogenic aid for muscular endurance, while claims regarding major improvements in strength, power, or muscle growth are not sufficiently supported [7, 8, 10].

3.4 Effects on Aerobic and High-Intensity Exercise Performance

Aerobic and high-intensity exercise performance depends on the coordinated delivery and utilization of oxygen, regulation of vascular tone, mitochondrial adenosine triphosphate production, and the capacity to tolerate progressive metabolic disturbance. By increasing L-arginine availability and supporting nitric oxide synthesis, L-citrulline may enhance vasodilation and improve the distribution of blood flow to active skeletal muscles. Greater oxygen delivery could theoretically accelerate pulmonary and muscular oxygen uptake kinetics, reduce the oxygen deficit at the onset of exercise, and delay the development of fatigue [14]. Citrulline participation in ammonia metabolism and the potential contribution of malate to the

tricarboxylic acid cycle provide additional theoretical mechanisms, particularly during intense exercise involving a substantial anaerobic contribution. However, improved vascular or metabolic biomarkers do not necessarily translate into faster time-trial performance, greater maximal oxygen uptake, or a longer time to exhaustion. The practical effect depends on whether oxygen delivery or nitric oxide availability represents a limiting factor under the specific exercise conditions [9, 14].

Some controlled studies have reported favorable effects of L-citrulline on oxygen utilization and exercise tolerance. Bailey et al. observed that short-term L-citrulline supplementation accelerated pulmonary oxygen uptake kinetics and improved tolerance during severe-intensity cycling exercise [14]. In another randomized, double-blind crossover study, trained men consumed an L-citrulline-containing beverage before a cycling time trial. Supplementation was associated with a modest improvement in completion time and a lower subjective perception of muscle fatigue after exercise [17]. These findings suggest that citrulline may be more effective during high-intensity exercise in which rapid adjustment of oxidative metabolism and local blood flow is important. Nevertheless, the observed changes were small, and the studies involved limited numbers of predominantly young male participants. Differences in supplementation duration, exercise protocol, nutritional control, and participant training status restrict the extent to which these findings can be generalized to other sports or populations.

Despite positive findings from individual experiments, the overall evidence does not demonstrate a consistent improvement in aerobic performance. A systematic review and meta-analysis examining citrulline supplementation found no statistically significant effects on aerobic performance, oxygen uptake kinetics, blood lactate concentrations, or ratings of perceived exertion [9]. Similarly, a subsequent meta-analysis focused on young healthy adults did not identify a meaningful improvement in endurance performance after either acute or short-term supplementation [18]. The most recent broader analysis reported a small overall effect on exercise performance, but the estimate was accompanied by wide prediction intervals and low-to-very-low certainty of evidence [10]. The apparent discrepancy between isolated positive trials and pooled results may reflect small sample sizes, publication bias, different exercise tests, and variation in citrulline formulation and dosing. Accordingly, current findings do not support a reliable ergogenic effect on maximal oxygen uptake, time-trial performance, or prolonged endurance exercise, although small benefits under selected high-intensity conditions cannot be excluded.

The effects of citrulline supplementation on sprinting, repeated high-intensity efforts, and interval exercise remain insufficiently established. These activities rely heavily on phosphocreatine availability, anaerobic glycolysis, rapid metabolite handling, and the recovery of force or power between consecutive efforts. Improved perfusion and faster phosphocreatine resynthesis could theoretically help maintain performance during repeated bouts, whereas enhanced ammonia clearance might delay fatigue during longer high-intensity protocols. Nevertheless, studies have produced inconsistent findings, with some reporting small improvements in time to exhaustion or repeated-effort performance and others showing no changes in peak power, mean power, sprint time, or fatigue index. The most recent meta-analysis suggested a possible benefit during some short anaerobic tasks, but this result was based on exploratory subgroup analyses and was not robust across all sensitivity analyses [10]. Thus, the current evidence is insufficient to recommend citrulline specifically for sprint or interval performance, and further trials using standardized repeated-sprint protocols are required.

3.5 Effects on Post-Exercise Recovery

Post-exercise recovery involves the restoration of cellular energy stores, normalization of muscle function, removal or reutilization of exercise-related metabolites, and repair of exercise-induced tissue disruption. L-citrulline may theoretically support these processes by increasing nitric oxide availability and improving post-exercise muscle perfusion. Enhanced blood flow could facilitate oxygen and nutrient delivery while supporting the transport of metabolites away from previously active tissues. Citrulline involvement in the urea cycle may additionally promote ammonia clearance, whereas malate has been proposed to support oxidative metabolism and phosphocreatine resynthesis [12]. These mechanisms could potentially reduce fatigue and accelerate the recovery of contractile performance between training sessions. Citrulline supplementation has also been investigated in relation to delayed-onset muscle soreness, although the biological basis for a possible analgesic or muscle-protective effect remains unclear. Improvements in perceived soreness may reflect altered metabolite handling or subjective recovery rather than a direct reduction in structural muscle damage [15].

The effect of citrulline supplementation on delayed-onset muscle soreness has been investigated primarily after high-volume resistance exercise. Pérez-Guisado and Jakeman reported lower perceived muscle soreness at 24 and 48 hours after a bench-press protocol following the acute ingestion of 8 g of citrulline malate [15]. However, subsequent studies have not consistently reproduced this effect. A systematic review and meta-analysis found that citrulline supplementation may reduce muscle soreness during the first 24–48 hours after exercise, but the magnitude and reliability of this effect were limited by small samples and substantial methodological heterogeneity [19]. Importantly, muscle soreness is a subjective outcome and may not correspond directly to the extent of structural muscle damage or the recovery of physical performance. Differences in training experience, exercise selection, soreness-assessment scales, and the presence or absence of a familiarization session may also affect the results. Thus, current evidence suggests a possible modest reduction in perceived soreness, but it does not establish a consistent muscle-protective effect.

Biochemical outcomes used to evaluate recovery have included blood lactate, creatine kinase, lactate dehydrogenase, ammonia, and inflammatory markers. Although improved muscle perfusion could theoretically accelerate lactate transport and reutilization, pooled evidence has not demonstrated a consistent reduction in post-exercise blood lactate following citrulline supplementation [9, 19]. Moreover, lactate should not be regarded as a direct cause of delayed-onset muscle soreness, because it is rapidly cleared after exercise and also serves as an important metabolic substrate. Findings concerning creatine kinase and other markers of muscle membrane disruption are similarly inconsistent. Some studies have reported lower post-exercise concentrations, whereas others have found no difference compared with placebo. Interpretation is difficult because these biomarkers demonstrate substantial interindividual variability and may not correspond closely with soreness or functional recovery. Therefore, the available evidence does not establish that L-citrulline or citrulline malate meaningfully reduces exercise-induced muscle damage, even when participants report lower subjective soreness.

The most practically relevant indicator of recovery is the restoration of the capacity to perform subsequent exercise. However, relatively few studies have assessed whether citrulline supplementation accelerates the recovery of strength, power, or exercise volume in the hours or days after a demanding training session. Evidence of faster phosphocreatine recovery provides a plausible metabolic mechanism [12], but this does not yet translate into consistent improvements in repeated-session performance. Studies reporting reduced muscle soreness

have not always demonstrated corresponding improvements in force production or functional performance [19]. This distinction is important because a participant may perceive less discomfort while neuromuscular function remains impaired. At present, the evidence is therefore insufficient to conclude that L-citrulline meaningfully shortens the recovery period between training sessions. Future studies should combine subjective soreness ratings with objective measures such as maximal voluntary contraction, countermovement-jump performance, repeated-sprint ability, and training volume completed during a subsequent standardized session.

3.6 L-Citrulline Versus Citrulline Malate

Pure L-citrulline and citrulline malate should be considered related but distinct supplementation strategies. Pure L-citrulline contains a defined amount of the amino acid responsible for increasing circulating citrulline and L-arginine concentrations. Citrulline malate combines citrulline with malate, most commonly in a nominal 1:1 or 2:1 ratio, although the actual proportions may vary between products. The citrulline component is expected to increase L-arginine availability and support nitric oxide synthesis, whereas malate has been proposed to facilitate oxidative metabolism through its participation in the tricarboxylic acid cycle [6, 12]. This has led to the hypothesis that citrulline malate may influence both vascular function and cellular energy production. However, direct evidence for an independent ergogenic effect of malate is limited, and few trials have compared pure L-citrulline, citrulline malate, malate alone, and placebo within the same experimental design. It is therefore uncertain whether any apparent advantage of citrulline malate results from synergy between its components or simply from the delivered citrulline dose [10].

Dose comparisons between pure L-citrulline and citrulline malate require particular caution. An 8 g dose of pure L-citrulline provides 8 g of citrulline, whereas an 8 g dose of a citrulline-malate mixture contains both citrulline and malate. If the declared 2:1 ratio refers to relative mass, 8 g of the mixture would theoretically provide approximately 5.3 g of citrulline and 2.7 g of malate. A 1:1 mixture would provide an even smaller amount of citrulline. However, some publications and commercial labels do not specify whether the declared ratio is based on mass or molar proportions, and the composition is rarely confirmed through independent chemical analysis. Consequently, reporting only the total dose of citrulline malate may obscure the actual amount of citrulline administered and contribute to heterogeneity between studies. Future research should report the precise mass of both components, define how the ratio was calculated, and verify the composition analytically before evaluating efficacy [6, 10].

The two formulations have also been studied in different research contexts. Pure L-citrulline has been used more frequently in pharmacokinetic and vascular studies because it permits precise evaluation of citrulline exposure, L-arginine availability, nitric oxide metabolism, and endothelial responses [6, 13]. In contrast, citrulline malate has been used predominantly in studies of resistance exercise, repetition performance, fatigue, and muscle soreness [7, 15, 16]. This separation limits direct comparisons and prevents firm conclusions regarding which formulation is more effective for exercise performance. Pure L-citrulline offers greater dosing precision and a clearer mechanistic interpretation, whereas citrulline malate has a larger body of performance-oriented research but greater uncertainty regarding composition. Until direct comparative trials become available, conclusions obtained with one formulation should not be automatically extrapolated to the other.

3.7 Dosage, Timing and Safety

Supplementation protocols vary considerably across the literature, and an optimal dose has not been conclusively established. Studies investigating pure L-citrulline have commonly administered approximately 3–6 g per day, either as a single pre-exercise dose or for several consecutive days. Resistance-exercise studies have more frequently used 6–8 g of citrulline malate approximately 40–60 minutes before exercise [7]. This timing broadly corresponds to pharmacokinetic evidence demonstrating that plasma citrulline and arginine concentrations increase within the first hours following oral ingestion [6]. Nevertheless, comparisons based solely on total supplement mass are problematic because citrulline-malate products provide less citrulline than an equivalent amount of the pure amino acid. Moreover, the most recent meta-analysis did not identify statistically significant differences according to dose or ingestion timing, indicating that the available evidence is insufficient to define a universally effective protocol [10]. These ranges should therefore be understood as doses investigated experimentally rather than definitive evidence-based recommendations.

Acute supplementation is intended to increase circulating citrulline and arginine concentrations during a specific exercise session and has been used predominantly in studies of resistance exercise and time-trial performance. In contrast, repeated supplementation over several days or weeks may maintain greater arginine availability and potentially produce more stable effects on endothelial function or oxygen uptake kinetics [14, 17]. However, the distinction between acute and chronic protocols remains unclear because relatively few studies have compared them directly using the same dose, formulation, and exercise test. The latest meta-analysis suggested that evidence may be more consistent for acute citrulline-malate supplementation than for chronic use, but the difference between protocol subgroups was uncertain [10]. Furthermore, improvements observed after repeated intake cannot necessarily be attributed to cumulative physiological adaptation, as the final dose is usually consumed shortly before testing. Well-controlled studies comparing an isolated dose, chronic supplementation with an acute final dose, and chronic supplementation without pre-exercise ingestion are needed to establish whether repeated administration provides an independent benefit.

L-citrulline is generally well tolerated in short-term human studies, including investigations using single doses higher than those commonly evaluated for exercise performance [20]. Reported adverse effects have usually been mild and infrequent, with gastrointestinal discomfort, nausea, abdominal bloating, or diarrhea occurring in some participants. L-citrulline may be better tolerated than high doses of oral L-arginine because it avoids extensive intestinal arginase metabolism and causes a smaller gastrointestinal osmotic burden. Nevertheless, evidence regarding long-term daily use remains limited, particularly in adolescents, pregnant or breastfeeding individuals, older adults with multiple diseases, and patients with renal, hepatic, or cardiovascular disorders. Because citrulline may influence vascular tone and blood pressure, caution is warranted when it is combined with antihypertensive agents, organic nitrates, or phosphodiesterase type 5 inhibitors. The safety of multi-ingredient pre-exercise products cannot be inferred from studies of isolated L-citrulline, as their effects may depend on additional stimulants and other active compounds.

The quality of commercially available citrulline supplements represents an additional safety and research concern. Dietary supplements may differ from pharmaceutical products in the extent of mandatory pre-market verification, and the quantity of an active ingredient may not always correspond precisely to the value declared on the label. This issue is particularly relevant to citrulline malate because uncertainty regarding its component ratio may lead to inaccurate

estimation of the delivered citrulline dose. Multi-ingredient pre-exercise products may also contain undeclared pharmacologically active substances or compounds prohibited in competitive sport. Athletes are personally responsible for substances detected during anti-doping testing, including those consumed unintentionally through contaminated supplements [1]. When supplementation is considered in a competitive-sport context, products subjected to independent batch testing provide greater quality assurance, although certification cannot completely eliminate risk. Research studies should similarly use independently analyzed preparations to ensure that observed outcomes can be attributed to a known dose and formulation.

The principal findings of the systematic reviews and meta-analyses included in this narrative synthesis are summarized in Table 1.

Table 1. Summary of systematic reviews and meta-analyses evaluating citrulline supplementation

Study	Type of evidence	Outcomes	Main findings
Vårvik et al. [7]	Systematic review and meta-analysis	Resistance-exercise repetitions	Citrulline malate produced a small increase in total repetitions, with inconsistent effects between upper- and lower-body exercise.
Aguiar and Casonatto [8]	Systematic review and meta-analysis	Maximal muscle strength	No significant improvement in upper- or lower-body muscle strength was demonstrated.
Viribay et al. [9]	Systematic review and meta-analysis	Aerobic performance, oxygen uptake, lactate and perceived exertion	No significant overall effects on aerobic performance or related physiological outcomes were observed.
Wang et al. [10]	Systematic review and three-level meta-analysis	Overall exercise performance and perceived exertion	A small, context-dependent improvement in exercise performance was reported, but certainty of evidence was low or very low.

Study	Type of evidence	Outcomes	Main findings
Barkhidarian et al. [13]	Systematic review and meta-analysis	Blood pressure	A possible reduction in systolic blood pressure was observed, while findings for diastolic pressure were less consistent.
Rhim et al. [19]	Systematic review and meta-analysis	Muscle soreness, perceived exertion and blood lactate	Supplementation may modestly reduce post-exercise soreness, but effects on lactate and perceived exertion were inconsistent.

Source: authors' own elaboration based on the cited publications.

4. Discussion

4.1 Limitations of the Available Evidence

The available evidence is limited by the small and demographically homogeneous samples used in many studies. Trials have frequently included fewer than 20–30 participants and have predominantly recruited young, healthy, resistance-trained men [7–10]. Small samples reduce statistical power, increase the influence of individual responders, and may generate unstable effect estimates. Women remain substantially underrepresented, and few studies have considered potential differences related to hormonal status, menstrual-cycle phase, or hormonal contraception. Evidence is also limited in older adults, adolescents, highly trained endurance athletes, and individuals with cardiometabolic disorders. As baseline nitric oxide availability, endothelial function, muscle mass, training status, and metabolic health may modify the response to supplementation, findings obtained in young men cannot be generalized reliably to all physically active populations. Future trials should recruit larger and more diverse samples and report sex-specific results whenever possible.

Considerable methodological heterogeneity further limits the interpretation of the literature. Studies have used pure L-citrulline or citrulline malate in different doses, ratios, and supplementation durations, ranging from a single pre-exercise dose to several weeks of daily intake. The timing of ingestion, nutritional status, background diet, and use of additional supplements have not always been standardized. Exercise protocols have included single-joint and multi-joint resistance exercises, repetitions to failure, cycling time trials, incremental tests, constant-load exercise, and repeated sprints, each representing a different physiological demand. Outcome measures have also varied substantially and have included total repetitions, maximal strength, peak power, oxygen uptake, blood lactate, perceived exertion, soreness, and vascular biomarkers. This diversity increases clinical heterogeneity and makes pooled estimates difficult to interpret. A benefit observed in one specific protocol should not therefore be assumed to apply to another exercise modality or sporting context [7, 9, 10, 18].

Several sources of bias may also affect the reported results. Although many trials have been described as randomized and double-blind, the effectiveness of blinding has rarely been

formally assessed. Citrulline-malate products have a characteristic acidic taste, which may allow participants to distinguish the supplement from an inadequately matched placebo and influence effort-dependent outcomes such as repetitions to failure or perceived soreness. Small studies may additionally be vulnerable to selective outcome reporting and publication bias, particularly when multiple exercises, time points, or performance variables are analyzed. Positive findings from individual secondary outcomes may consequently receive greater attention than neutral primary results. Another important limitation is the lack of independent chemical verification of supplement composition. If the administered product contains a different citrulline-to-malate ratio than declared, the true dose and causal interpretation become uncertain. Recent evidence assessments have therefore rated the certainty of conclusions regarding exercise performance as low or very low [10].

Future research should use adequately powered, preregistered randomized controlled trials with standardized supplementation and exercise protocols. The chemical composition of both pure L-citrulline and citrulline-malate preparations should be independently verified, and doses should be reported according to the actual amount of each component. Direct comparisons among pure L-citrulline, citrulline malate, malate alone, and placebo would help determine whether malate provides an independent or synergistic effect. Studies should include more women, older adults, athletes from different sporting disciplines, and participants with varying baseline vascular function. Both acute and chronic protocols should be evaluated, with outcomes extending beyond subjective fatigue or soreness to include muscle blood flow, oxygenation, standardized performance tests, and the recovery of subsequent exercise capacity. Longer training interventions are particularly needed to determine whether small acute increases in repetition performance translate into meaningful adaptations in strength, endurance, or muscle hypertrophy.

4.2 Practical Implications

Current evidence suggests that L-citrulline supplementation should be viewed as a potentially useful but nonessential ergogenic strategy. The most plausible application is the acute support of muscular endurance during high-volume resistance exercise, where citrulline malate may allow a small increase in the total number of repetitions performed [6, 10]. In contrast, evidence does not support a consistent improvement in maximal strength, peak power, maximal oxygen uptake, or prolonged endurance performance [8, 9, 18]. A possible reduction in post-exercise soreness has been reported, but it remains uncertain whether this corresponds to faster recovery of muscle function [19]. Therefore, expectations should remain realistic: any benefit is likely to be modest, task-specific, and variable between individuals. Citrulline supplementation cannot compensate for inadequate training programming, insufficient recovery, sleep deprivation, or poor nutritional intake, which remain the principal determinants of performance and adaptation.

When citrulline supplementation is evaluated in practice, the formulation and verified ingredient content are important considerations. Pure L-citrulline provides clearer dose standardization, whereas citrulline malate has been investigated more frequently in resistance-exercise protocols but may vary in its actual citrulline-to-malate ratio. Independently batch-tested products are preferable in competitive sport because they reduce, although do not eliminate, the risk of inaccurate labeling or contamination [1]. Individual response should be evaluated using reproducible outcomes relevant to the athlete's discipline, such as total training volume, standardized time-trial performance, or recovery of performance during a subsequent session, rather than transient sensations of muscle "pump." Because the average ergogenic

effect is small, normal day-to-day variation may easily be mistaken for a supplement benefit. Individuals using medications or living with cardiovascular, renal, or hepatic disease should seek professional medical advice before supplementation.

5. Conclusions

L-citrulline is an effective precursor of L-arginine and can increase substrate availability for nitric oxide synthesis, providing a biologically plausible mechanism for improved vascular function, muscle perfusion, and exercise tolerance. Nevertheless, these physiological effects do not consistently translate into meaningful improvements in physical performance. The strongest evidence indicates that acute citrulline malate supplementation may produce a small increase in muscular endurance during high-volume resistance exercise, whereas effects on maximal strength, power, aerobic performance, and perceived exertion remain inconsistent. Citrulline may also modestly reduce post-exercise muscle soreness, but evidence that it accelerates the recovery of muscle function or reduces structural muscle damage is insufficient. Interpretation is limited by small, predominantly male samples, heterogeneous protocols, variable supplement composition, and low-to-very-low certainty of evidence. Overall, L-citrulline should be regarded as a generally well-tolerated but context-dependent ergogenic aid whose benefits are likely to be modest. Larger, independently replicated trials using verified formulations and standardized outcomes are required to establish optimal dosing strategies and identify populations most likely to benefit.

Disclosure

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