

Nitric Oxide — L-Citrulline & L-Arginine

Amino acid nitric oxide precursors — L-citrulline, citrulline malate and L-arginine

Nitric oxide is not a supplement; it is a signaling gas with a half-life measured in seconds. What is actually sold are precursors, and the two that matter are L-citrulline and L-arginine. The counterintuitive finding shaping this category: citrulline raises blood arginine more effectively than arginine itself does, making most of the arginine on the market the inferior product.

SUMMARY TABLE

Attribute	Summary
Primary uses	Vasodilation/endothelial function and blood flow; lowering blood pressure; exercise tolerance and muscular endurance; adjunct in erectile dysfunction (arginine).
Evidence strength	Moderate for L-citrulline and blood pressure. Low/unstable for citrulline malate and performance (2026 meta-analysis: small effect, low-to-very-low GRADE certainty). Moderate for arginine in erectile dysfunction, especially with PDE5 inhibitors.
Effective dose	L-citrulline: 3–6 g/day (BP/vascular); 6–8 g (performance). Citrulline malate: 8 g is the most-studied dose. L-arginine: 3–6 g/day, up to 5 g twice daily for ED.
How to take	Dissolve powder in water; citrulline malate 40–120 minutes pre-exercise. L-citrulline is preferred for most purposes — it bypasses intestinal/hepatic arginase that degrades oral arginine.
Time to effect	Acute vasodilation within 1–2 hours; BP changes over days to weeks; erectile-function benefit generally required 4–12 weeks.
Serious risks	L-arginine is not recommended after a heart attack (mortality signal in post-MI patients) and can worsen asthma/airway inflammation. Both can cause meaningful hypotension when stacked with BP medication.
Who should avoid it	Recent heart attack (arginine specifically); asthma prone to arginine-triggered inflammation; nitrate medication users; anyone with hypotension.
Quality markers	Grams of actual citrulline or arginine stated per serving, not blend weight; citrulline-to-malate ratio disclosed; third-party testing (NSF, Informed Sport, USP); no proprietary blends.

WHY THE PRECURSOR MATTERS MORE THAN THE MOLECULE

Oral arginine is heavily degraded by arginase in the gut wall and liver before reaching circulation. L-citrulline is not an arginase substrate; it passes through intact and converts to arginine in the kidneys. A 2025 comprehensive review states plainly that L-citrulline demonstrated superior bioavailability compared with L-arginine at raising plasma arginine — a single fact that reorganizes the category toward citrulline as the default purchase.

BLOOD PRESSURE AND PERFORMANCE

An 11-trial meta-analysis (224 participants) found citrulline reduced systolic BP by 3.74 mmHg and diastolic by 2.00 mmHg — real but smaller than dietary nitrate's effect in hypertensive populations. A June 2026 three-level meta-analysis of citrulline malate for exercise (30 RCTs, 644 participants) found a small overall improvement (effect size 0.16, $p=0.01$), concentrated in muscular endurance, with GRADE certainty low to very low and statistical power across included studies estimated at only 8–9%.

WHERE ARGININE STILL HAS A ROLE — AND WHERE IT IS DANGEROUS

Arginine retains a legitimate niche in erectile dysfunction, alone and more consistently combined with PDE5 inhibitors. But it is advised against after a heart attack, can worsen asthma, and causes dose-dependent GI distress more often than citrulline. Its interaction list includes anticoagulants, antihypertensives, diabetes medication, nitrates, sildenafil and potassium-sparing diuretics.

BOTTOM LINE

For nearly every use case, L-citrulline is the correct choice — better absorbed, better tolerated, and free of arginine's post-infarction and asthma cautions. Three to six grams daily is defensible for vascular purposes; six to eight grams 40–120 minutes pre-training is the performance protocol, with modest expectations warranted. L-arginine is worth considering only for erectile dysfunction alongside a prescribed PDE5 inhibitor and that prescriber's knowledge.

SOURCES

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4. Mayo Clinic. "L-arginine — uses, safety, side effects and interactions."
5. "Daily oral L-arginine and PDE5 inhibitors for erectile dysfunction: systematic review." 2021.

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