

RESEARCH MONOGRAPH . COMPOUND PROFILE

Citrulline Malate

L-citrulline complexed with malic acid; a nitric oxide precursor (via arginine) and TCA cycle substrate used in pre-workout supplements.

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COMPOUND CLASS	Amino acid + organic acid (NO precursor / TCA cycle support)

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ABSTRACT

Citrulline malate (L-citrulline DL-malate, CAS 70796-17-7; complex of L-citrulline (CAS 372-75-8, $C_6H_{13}N_3O_3$, MW 175.19) and malic acid (CAS 6915-15-7, $C_4H_6O_5$, MW 134.09); commercial 2:1 or 1:1 ratios) is a complex of the amino acid L-citrulline with malic acid. L-citrulline is converted in the kidneys to L-arginine, the substrate for nitric oxide synthase; circulating arginine produced from citrulline supplementation is paradoxically more effective than direct arginine supplementation owing to the bypass of intestinal arginase. The malic acid portion is a TCA cycle intermediate supporting aerobic ATP production. Combined, the compound improves exercise performance through vasodilation (nitric oxide-mediated), reduced ammonia accumulation (urea cycle support), and ATP production. Plasma half-life of citrulline is approximately 1 hour. Used widely in pre-workout supplements (8 to 10 g doses, 60 to 90 minutes pre-exercise) with documented effects on resistance training volume and reduced post-exercise soreness.

1. Compound Identification

Citrulline Malate is described as amino acid + organic acid (no precursor / tca cycle support). L-citrulline complexed with malic acid; a nitric oxide precursor (via arginine) and TCA cycle substrate used in pre-workout supplements.

1.1 Class summary

Amino acid + organic acid (NO precursor / TCA cycle support)

1.2 Subtitle

L-citrulline complexed with malic acid; a nitric oxide precursor (via arginine) and TCA cycle substrate used in pre-workout supplements.

2. Abstract

Citrulline malate (L-citrulline DL-malate, CAS 70796-17-7; complex of L-citrulline (CAS 372-75-8, C₆H₁₃N₃O₃, MW 175.19) and malic acid (CAS 6915-15-7, C₄H₆O₅, MW 134.09); commercial 2:1 or 1:1 ratios) is a complex of the amino acid L-citrulline with malic acid. L-citrulline is converted in the kidneys to L-arginine, the substrate for nitric oxide synthase; circulating arginine produced from citrulline supplementation is paradoxically more effective than direct arginine supplementation owing to the bypass of intestinal arginase. The malic acid portion is a TCA cycle intermediate supporting aerobic ATP production. Combined, the compound improves exercise performance through vasodilation (nitric oxide-mediated), reduced ammonia accumulation (urea cycle support), and ATP production. Plasma half-life of citrulline is approximately 1 hour. Used widely in pre-workout supplements (8 to 10 g doses, 60 to 90 minutes pre-exercise) with documented effects on resistance training volume and reduced post-exercise soreness.

3. Mechanism of Action

L-citrulline converted to L-arginine in kidney; supports nitric oxide synthesis (vasodilation) and urea cycle ammonia clearance. Malate supports TCA cycle ATP production.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

6 to 10 g per oral administration 60 to 90 minutes pre-exercise.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Perez-Guisado J, Jakeman PM. Citrulline malate enhances athletic anaerobic performance and relieves muscle soreness. J Strength Cond Res 2010.
2. Bailey SJ, et al. L-Citrulline supplementation improves O2 uptake kinetics and high-intensity exercise performance in humans. J Appl Physiol 2015.
3. Glenn JM, et al. Acute citrulline malate supplementation improves upper-body resistance exercise performance. Eur J Sport Sci 2017.

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