

RESEARCH MONOGRAPH . COMPOUND PROFILE

L-Arginine

L-arginine; the direct substrate for nitric oxide synthase and a urea cycle intermediate; used as a pre-workout supplement and in cardiovascular research.

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COMPOUND CLASS	Conditionally essential amino acid / nitric oxide precursor

ABSTRACT

L-arginine ((S)-2-amino-5-guanidinopentanoic acid; CAS 74-79-3; molecular formula C₆H₁₄N₄O₂; molecular weight 174.20) is a conditionally essential alpha-amino acid that serves as the direct substrate for nitric oxide synthase (NOS), producing NO and citrulline; arginine is also the rate-limiting urea cycle intermediate for ammonia clearance. Despite the direct NOS substrate role, oral arginine supplementation has limited efficacy at increasing systemic NO production because intestinal and hepatic arginase metabolizes arginine to ornithine before it reaches systemic circulation; citrulline, which is converted to arginine in the kidney bypassing arginase, is paradoxically more effective at raising plasma arginine. Clinical research has investigated arginine for cardiovascular conditions (endothelial dysfunction, peripheral artery disease, erectile dysfunction) with mixed results. Plasma half-life is approximately 1 to 2 hours. Used as the canonical NOS substrate amino acid in research.

1. Compound Identification

L-Arginine is described as conditionally essential amino acid / nitric oxide precursor. L-arginine; the direct substrate for nitric oxide synthase and a urea cycle intermediate; used as a pre-workout supplement and in cardiovascular research.

1.1 Class summary

Conditionally essential amino acid / nitric oxide precursor

1.2 Subtitle

L-arginine; the direct substrate for nitric oxide synthase and a urea cycle intermediate; used as a pre-workout supplement and in cardiovascular research.

2. Abstract

L-arginine ((S)-2-amino-5-guanidinopentanoic acid; CAS 74-79-3; molecular formula C₆H₁₄N₄O₂; molecular weight 174.20) is a conditionally essential alpha-amino acid that serves as the direct substrate for nitric oxide synthase (NOS), producing NO and citrulline; arginine is also the rate-limiting urea cycle intermediate for ammonia clearance. Despite the direct NOS substrate role, oral arginine supplementation has limited efficacy at increasing systemic NO production because intestinal and hepatic arginase metabolizes arginine to ornithine before it reaches systemic circulation; citrulline, which is converted to arginine in the kidney bypassing arginase, is paradoxically more effective at raising plasma arginine. Clinical research has investigated arginine for cardiovascular conditions (endothelial dysfunction, peripheral artery disease, erectile dysfunction) with mixed results. Plasma half-life is approximately 1 to 2 hours. Used as the canonical NOS substrate amino acid in research.

3. Mechanism of Action

Direct nitric oxide synthase substrate; urea cycle intermediate. Intestinal arginase limits oral bioavailability for systemic NO 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

Supplement 3 to 9 g per oral administration daily.

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. Bode-Boger SM, et al. L-arginine and the cardiovascular system. Pharmacol Ther 2007.
2. Wu G, et al. Arginine metabolism and nutrition in growth, health and disease. Amino Acids 2009.
3. Schwedhelm E, et al. Pharmacokinetic and pharmacodynamic properties of oral L-citrulline and L-arginine. Br J Clin Pharmacol 2008.

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