

RESEARCH MONOGRAPH . COMPOUND PROFILE

Creatine Monohydrate

A nitrogenous organic acid; the most thoroughly studied ergogenic supplement; phosphocreatine pool expansion supports rapid ATP regeneration during high-intensity exercise.

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ABSTRACT

Creatine monohydrate (N-(aminoiminomethyl)-N-methylglycine; CAS 6020-87-7; molecular formula $C_4H_9N_3O_2$ (anhydrous); molecular weight 131.13) is a nitrogenous organic acid biosynthesized in the liver and kidneys from arginine, glycine, and methionine and stored in skeletal muscle (95 percent of body creatine pool). Mechanism: phosphocreatine, the phosphorylated storage form, donates phosphate to ADP via creatine kinase to rapidly regenerate ATP during high-intensity exercise; supplementation expands the muscle phosphocreatine pool by approximately 20 to 40 percent, supporting longer high-intensity efforts. The most thoroughly studied ergogenic supplement, with hundreds of trials demonstrating consistent ~5 to 10 percent improvement in strength and power output and meaningful effects on lean body mass. Emerging interest in cognitive enhancement, neurodegenerative disease (creatine kinase activity in brain), and depression. The 5-day loading protocol (20 g/day) versus daily maintenance (3 to 5 g/day) produces equivalent muscle saturation with maintenance over 3 to 4 weeks. Plasma half-life is approximately 3 hours; muscle storage is the relevant pharmacokinetic measure. Used as the canonical ergogenic supplement in sport science and exercise physiology research.

1. Compound Identification

Creatine Monohydrate is described as endogenous metabolite / ergogenic supplement. A nitrogenous organic acid; the most thoroughly studied ergogenic supplement; phosphocreatine pool expansion supports rapid ATP regeneration during high-intensity exercise.

1.1 Class summary

Endogenous metabolite / ergogenic supplement

1.2 Subtitle

A nitrogenous organic acid; the most thoroughly studied ergogenic supplement; phosphocreatine pool expansion supports rapid ATP regeneration during high-intensity exercise.

2. Abstract

Creatine monohydrate (N-(aminoiminomethyl)-N-methylglycine; CAS 6020-87-7; molecular formula $C_4H_9N_3O_2$ (anhydrous); molecular weight 131.13) is a nitrogenous organic acid biosynthesized in the liver and kidneys from arginine, glycine, and methionine and stored in skeletal muscle (95 percent of body creatine pool). Mechanism: phosphocreatine, the phosphorylated storage form, donates phosphate to ADP via creatine kinase to rapidly regenerate ATP during high-intensity exercise; supplementation expands the muscle phosphocreatine pool by approximately 20 to 40 percent, supporting longer high-intensity efforts. The most thoroughly studied ergogenic supplement, with hundreds of trials demonstrating consistent ~5 to 10 percent improvement in strength and power output and meaningful effects on lean body mass. Emerging interest in cognitive enhancement, neurodegenerative disease (creatine kinase activity in brain), and depression. The 5-day loading protocol (20 g/day) versus daily maintenance (3 to 5 g/day) produces equivalent muscle saturation with maintenance over 3 to 4 weeks. Plasma half-life is approximately 3 hours; muscle storage is the relevant pharmacokinetic measure. Used as the canonical ergogenic supplement in sport science and exercise physiology research.

3. Mechanism of Action

Phosphocreatine pool expansion supports rapid ATP regeneration via creatine kinase during high-intensity exercise. Cognitive effects through similar bioenergetic mechanism in brain.

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

Loading 20 g per oral administration daily for 5 days; maintenance 3 to 5 g 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. Kreider RB, et al. International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine. J Int Soc Sports Nutr 2017.
2. Avgerinos KI, et al. Effects of creatine supplementation on cognitive function of healthy individuals. Exp Gerontol 2018.
3. Rae C, et al. Oral creatine monohydrate supplementation improves brain performance: a double-blind, placebo-controlled, cross-over trial. Proc Biol Sci 2003.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.