

RESEARCH MONOGRAPH . COMPOUND PROFILE

Alpha-Ketoglutarate (AKG)

A TCA cycle intermediate sold as calcium alpha-ketoglutarate (Ca-AKG) for longevity applications based on extension of lifespan in mice and worms.

DOCUMENT	KDC-MN-105
ISSUED	2026-05-09
REVISION	1.0
AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	TCA cycle intermediate / 2-oxoglutarate

RESEARCH USE ONLY

ABSTRACT

Alpha-Ketoglutarate (AKG, 2-oxoglutarate; CAS 328-50-7; molecular formula C₅H₆O₅; molecular weight 146.10) is a tricarboxylic acid cycle intermediate that declines with age in plasma and tissues. The compound is a substrate for the 2-oxoglutarate-dependent dioxygenase family of enzymes (including DNA and histone demethylases, prolyl hydroxylases, and TET enzymes), placing it at a hub of cellular regulation. AKG supplementation extends lifespan in *C. elegans* (up to 50 percent) and in mice when given as the calcium salt at 2 percent in chow. The mechanism in mice is incompletely characterized but appears to involve reduced cellular senescence, improved metabolic flexibility, and reduced inflammaging markers. Sold as calcium alpha-ketoglutarate (Ca-AKG, Rejuvant) for supplemental use. Doses are typically 500 to 2000 mg per day.

1. Compound Identification

Alpha-Ketoglutarate (AKG) is described as tca cycle intermediate / 2-oxoglutarate. A TCA cycle intermediate sold as calcium alpha-ketoglutarate (Ca-AKG) for longevity applications based on extension of lifespan in mice and worms.

1.1 Class summary

TCA cycle intermediate / 2-oxoglutarate

1.2 Subtitle

A TCA cycle intermediate sold as calcium alpha-ketoglutarate (Ca-AKG) for longevity applications based on extension of lifespan in mice and worms.

2. Abstract

Alpha-Ketoglutarate (AKG, 2-oxoglutarate; CAS 328-50-7; molecular formula $C_5H_6O_5$; molecular weight 146.10) is a tricarboxylic acid cycle intermediate that declines with age in plasma and tissues. The compound is a substrate for the 2-oxoglutarate-dependent dioxygenase family of enzymes (including DNA and histone demethylases, prolyl hydroxylases, and TET enzymes), placing it at a hub of cellular regulation. AKG supplementation extends lifespan in *C. elegans* (up to 50 percent) and in mice when given as the calcium salt at 2 percent in chow. The mechanism in mice is incompletely characterized but appears to involve reduced cellular senescence, improved metabolic flexibility, and reduced inflammaging markers. Sold as calcium alpha-ketoglutarate (Ca-AKG, Rejuvant) for supplemental use. Doses are typically 500 to 2000 mg per day.

3. Mechanism of Action

TCA cycle intermediate and substrate for 2-oxoglutarate-dependent dioxygenases. Reduces senescence and inflammaging in aged mice.

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

500 to 2000 mg per day.

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. Asadi Shahmirzadi A, et al. Alpha-ketoglutarate, an endogenous metabolite, extends lifespan and compresses morbidity in aging mice. Cell Metab 2020.

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.