

RESEARCH MONOGRAPH . COMPOUND PROFILE

Berberine

An isoquinoline alkaloid from Berberis and other plants, characterized by AMPK activation with metabolic effects comparable to metformin in some contexts.

DOCUMENT	KDC-MN-178
ISSUED	2026-05-09
REVISION	1.0
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COMPOUND CLASS	Isoquinoline alkaloid / AMPK activator

ABSTRACT

Berberine (CAS 2086-83-1; molecular formula $C_{20}H_{18}NO_4^+$; molecular weight 336.36) is an isoquinoline alkaloid present in *Berberis* species, *Coptis chinensis* (goldthread), and *Hydrastis canadensis* (goldenseal). The compound activates AMPK through complex I inhibition (similar mechanism to metformin) with downstream metabolic effects: improved insulin sensitivity, reduced hepatic glucose output, modest LDL cholesterol reduction. Clinical trials in T2DM show glycemic improvements comparable to metformin in some studies. The compound is also used for gut dysbiosis and SIBO based on antimicrobial activity. Bioavailability is poor (~5 percent oral); dihydroberberine has improved bioavailability. Doses are typically 500 mg to 1.5 grams per day in divided doses.

1. Compound Identification

Berberine is described as isoquinoline alkaloid / ampk activator. An isoquinoline alkaloid from Berberis and other plants, characterized by AMPK activation with metabolic effects comparable to metformin in some contexts.

1.1 Class summary

Isoquinoline alkaloid / AMPK activator

1.2 Subtitle

An isoquinoline alkaloid from Berberis and other plants, characterized by AMPK activation with metabolic effects comparable to metformin in some contexts.

2. Abstract

Berberine (CAS 2086-83-1; molecular formula $C_{20}H_{18}NO_4^+$; molecular weight 336.36) is an isoquinoline alkaloid present in *Berberis* species, *Coptis chinensis* (goldthread), and *Hydrastis canadensis* (goldenseal). The compound activates AMPK through complex I inhibition (similar mechanism to metformin) with downstream metabolic effects: improved insulin sensitivity, reduced hepatic glucose output, modest LDL cholesterol reduction. Clinical trials in T2DM show glycemic improvements comparable to metformin in some studies. The compound is also used for gut dysbiosis and SIBO based on antimicrobial activity. Bioavailability is poor (~5 percent oral); dihydroberberine has improved bioavailability. Doses are typically 500 mg to 1.5 grams per day in divided doses.

3. Mechanism of Action

AMPK activator through complex I inhibition. Anti-microbial activity. Multiple metabolic and gut effects.

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 mg to 1.5 g per day in divided doses.

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. Yin J, et al. Efficacy of berberine in patients with type 2 diabetes mellitus. Metabolism 2008.

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