

RESEARCH MONOGRAPH . COMPOUND PROFILE

Metformin

A first-line type 2 diabetes biguanide derived from French lilac (Galega officinalis), increasingly investigated for longevity and cancer prevention applications.

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COMPOUND CLASS	Biguanide / AMPK activator

ABSTRACT

Metformin (Glucophage; 1,1-dimethylbiguanide; CAS 657-24-9; molecular formula $C_4H_{11}N_5$; molecular weight 129.16) is a biguanide derived from guanidine, originally identified in the 1920s from the French lilac (*Galega officinalis*) and approved in Europe in 1957 and the United States in 1995 for type 2 diabetes. The compound is the most prescribed oral antihyperglycemic globally. Primary mechanism is mild inhibition of mitochondrial complex I producing AMPK activation, with downstream reduction in hepatic gluconeogenesis, improved insulin sensitivity in skeletal muscle, and reduced gut glucose absorption. Beyond diabetes management, metformin has accumulated evidence in cancer prevention (reduced incidence in diabetics), cardiovascular outcomes (UKPDS, in obese diabetics), and possible longevity effects. The TAME trial (Targeting Aging with Metformin) is investigating longevity endpoints in non-diabetic populations. Pharmacokinetics: plasma half-life 4 to 9 hours; oral bioavailability 50 to 60 percent; renally excreted unchanged. Approved doses are 500 to 2550 mg per day in divided administrations. Lactic acidosis is the principal serious adverse event but is rare with appropriate renal function monitoring.

1. Compound Identification

Metformin is described as biguanide / ampk activator. A first-line type 2 diabetes biguanide derived from French lilac (*Galega officinalis*), increasingly investigated for longevity and cancer prevention applications.

1.1 Class summary

Biguanide / AMPK activator

1.2 Subtitle

A first-line type 2 diabetes biguanide derived from French lilac (*Galega officinalis*), increasingly investigated for longevity and cancer prevention applications.

2. Abstract

Metformin (Glucophage; 1,1-dimethylbiguanide; CAS 657-24-9; molecular formula $C_4H_{11}N_5$; molecular weight 129.16) is a biguanide derived from guanidine, originally identified in the 1920s from the French lilac (*Galega officinalis*) and approved in Europe in 1957 and the United States in 1995 for type 2 diabetes. The compound is the most prescribed oral antihyperglycemic globally. Primary mechanism is mild inhibition of mitochondrial complex I producing AMPK activation, with downstream reduction in hepatic gluconeogenesis, improved insulin sensitivity in skeletal muscle, and reduced gut glucose absorption. Beyond diabetes management, metformin has accumulated evidence in cancer prevention (reduced incidence in diabetics), cardiovascular outcomes (UKPDS, in obese diabetics), and possible longevity effects. The TAME trial (Targeting Aging with Metformin) is investigating longevity endpoints in non-diabetic populations. Pharmacokinetics: plasma half-life 4 to 9 hours; oral bioavailability 50 to 60 percent; renally excreted unchanged. Approved doses are 500 to 2550 mg per day in divided administrations. Lactic acidosis is the principal serious adverse event but is rare with appropriate renal function monitoring.

3. Mechanism of Action

Mild complex I inhibition with AMPK activation. Reduces hepatic gluconeogenesis, improves muscle insulin sensitivity, reduces gut glucose absorption.

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 2550 mg 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. UKPDS 34: Effect of intensive blood-glucose control with metformin. Lancet 1998.
2. Barzilai N, et al. Metformin as a tool to target aging. Cell Metab 2016.

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