

RESEARCH MONOGRAPH . COMPOUND PROFILE

# Hydergine (Ergoloid Mesylates)

*A mixture of dihydrogenated ergoloid alkaloids; used historically for cognitive decline and as a senescence-associated nootropic.*

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|----------------|---------------------------------------------------------------------------------|
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| COMPOUND CLASS | Ergoloid mixture (dihydroergocornine, dihydroergocristine, dihydroergocryptine) |

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## ABSTRACT

Hydergine (codergocrine mesylate; CAS 8067-24-1; mixture of dihydroergocornine, dihydroergocristine, and dihydroergocryptine alpha and beta isomers in 3:3:2:1 ratio; molecular weight approximately 660 to 700 Da) is a mixture of dihydrogenated ergoloid alkaloids developed at Sandoz (now Novartis) by Albert Hofmann in the 1940s. The compound was approved for senescence and senile mental status in many countries from the 1950s onward; it was once among the most prescribed drugs globally. Mechanism is multifactorial and incompletely characterized: alpha-adrenergic antagonism, dopaminergic and serotonergic effects, modulation of neuronal energy metabolism, and weak antioxidant activity. Modern systematic reviews have produced inconsistent evidence of cognitive benefit; the compound is largely supplanted in clinical practice by cholinesterase inhibitors and memantine for dementia. Plasma half-life is approximately 5 hours. Used as a historical nootropic and ergoloid reference compound.

# 1. Compound Identification

**Hydergine (Ergoloid Mesylates)** is described as ergoloid mixture (dihydroergocornine, dihydroergocristine, dihydroergocryptine). A mixture of dihydrogenated ergoloid alkaloids; used historically for cognitive decline and as a senescence-associated nootropic.

## 1.1 Class summary

Ergoloid mixture (dihydroergocornine, dihydroergocristine, dihydroergocryptine)

## 1.2 Subtitle

A mixture of dihydrogenated ergoloid alkaloids; used historically for cognitive decline and as a senescence-associated nootropic.

## 2. Abstract

Hydergine (codergocrine mesylate; CAS 8067-24-1; mixture of dihydroergocornine, dihydroergocristine, and dihydroergocryptine alpha and beta isomers in 3:3:2:1 ratio; molecular weight approximately 660 to 700 Da) is a mixture of dihydrogenated ergoloid alkaloids developed at Sandoz (now Novartis) by Albert Hofmann in the 1940s. The compound was approved for senescence and senile mental status in many countries from the 1950s onward; it was once among the most prescribed drugs globally. Mechanism is multifactorial and incompletely characterized: alpha-adrenergic antagonism, dopaminergic and serotonergic effects, modulation of neuronal energy metabolism, and weak antioxidant activity. Modern systematic reviews have produced inconsistent evidence of cognitive benefit; the compound is largely supplanted in clinical practice by cholinesterase inhibitors and memantine for dementia. Plasma half-life is approximately 5 hours. Used as a historical nootropic and ergoloid reference compound.

### 3. Mechanism of Action

Multifactorial: alpha-adrenergic antagonism, dopaminergic/serotonergic modulation, neuronal energy effects. Mixture of dihydrogenated ergoloid alkaloids.

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

Clinical 4.5 to 9 mg per oral administration daily, 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. Schneider LS, Olin JT. Overview of clinical trials of hydergine in dementia. Arch Neurol 1994.
2. Olin J, Schneider L, et al. Hydergine for dementia. Cochrane Database Syst Rev 2001.
3. Crook T. The pharmacotherapy of memory disorders. Drugs Aging 1990.

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