

RESEARCH MONOGRAPH . COMPOUND PROFILE

Galantamine

A natural alkaloid from Galanthus and Narcissus species, FDA-approved as Razadyne for Alzheimer disease, distinguished by dual AChE inhibition and nicotinic receptor allosteric modulation.

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RESEARCH USE ONLY

ABSTRACT

Galantamine (Razadyne, Reminyl; CAS 357-70-0; molecular formula $C_{17}H_{21}NO_3$; molecular weight 287.36) is a tertiary amine alkaloid extracted originally from *Galanthus nivalis* (snowdrop) and *Narcissus* species, approved by the FDA in 2001 for mild-to-moderate Alzheimer disease and now produced synthetically. The compound is a selective reversible acetylcholinesterase inhibitor (K_i approximately 360 nM) with substantially weaker AChE inhibition than donepezil, but with a distinctive secondary mechanism that distinguishes it from other AChE inhibitors used clinically: galantamine is a positive allosteric modulator (PAM) of nicotinic acetylcholine receptors, particularly the α -7 and α -4- β -2 subtypes most relevant to cognition. The dual mechanism produces a clinical profile considered slightly different from donepezil; some investigators report better effects on attention and behavioral symptoms. Pharmacokinetics: plasma half-life 7 hours; oral bioavailability essentially complete; metabolism is hepatic via CYP2D6 and CYP3A4. Approved doses are 16 to 24 mg per day in two divided administrations; lower starting doses minimize gastrointestinal adverse events. Schedule status: prescription-only but not federally scheduled.

1. Compound Identification

Galantamine is described as selective acetylcholinesterase inhibitor + alpha-7 nachr pam. A natural alkaloid from Galanthus and Narcissus species, FDA-approved as Razadyne for Alzheimer disease, distinguished by dual AChE inhibition and nicotinic receptor allosteric modulation.

1.1 Class summary

Selective acetylcholinesterase inhibitor + alpha-7 nAChR PAM

1.2 Subtitle

A natural alkaloid from Galanthus and Narcissus species, FDA-approved as Razadyne for Alzheimer disease, distinguished by dual AChE inhibition and nicotinic receptor allosteric modulation.

2. Abstract

Galantamine (Razadyne, Reminyl; CAS 357-70-0; molecular formula $C_{17}H_{21}NO_3$; molecular weight 287.36) is a tertiary amine alkaloid extracted originally from *Galanthus nivalis* (snowdrop) and *Narcissus* species, approved by the FDA in 2001 for mild-to-moderate Alzheimer disease and now produced synthetically. The compound is a selective reversible acetylcholinesterase inhibitor (K_i approximately 360 nM) with substantially weaker AChE inhibition than donepezil, but with a distinctive secondary mechanism that distinguishes it from other AChE inhibitors used clinically: galantamine is a positive allosteric modulator (PAM) of nicotinic acetylcholine receptors, particularly the α -7 and α -4- β -2 subtypes most relevant to cognition. The dual mechanism produces a clinical profile considered slightly different from donepezil; some investigators report better effects on attention and behavioral symptoms. Pharmacokinetics: plasma half-life 7 hours; oral bioavailability essentially complete; metabolism is hepatic via CYP2D6 and CYP3A4. Approved doses are 16 to 24 mg per day in two divided administrations; lower starting doses minimize gastrointestinal adverse events. Schedule status: prescription-only but not federally scheduled.

3. Mechanism of Action

Reversible AChE inhibitor ($K_i \sim 360$ nM) plus positive allosteric modulator of α -7 and α -4- β -2 nicotinic receptors. Dual mechanism.

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

16 to 24 mg per day in two divided doses (clinical use).

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. Maelicke A, et al. Allosterically potentiating ligands of nicotinic receptors as a treatment strategy for Alzheimer's disease. Biol Psychiatry 2001.
2. Loy C, Schneider L. Galantamine for Alzheimer's disease and mild cognitive impairment. Cochrane Database Syst Rev 2006.

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