

RESEARCH MONOGRAPH . COMPOUND PROFILE

Selegiline

A propargyl phenethylamine MAO-B inhibitor used in Parkinson disease and at higher doses in depression via MAO-A engagement.

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AUTHOR	Kodiac biolabs Research
COMPOUND CLASS	Selective irreversible MAO-B inhibitor

ABSTRACT

Selegiline ((R)-N-methyl-N-(1-phenylpropan-2-yl)prop-2-yn-1-amine; CAS 14611-51-9; molecular formula C₁₃H₁₇N; molecular weight 187.28) is an irreversible propargyl-substituted MAO-B inhibitor developed by Joseph Knoll in Hungary in the 1960s. At low oral doses (5 to 10 mg daily) the compound is selective for MAO-B (selectivity ratio approximately 100:1 over MAO-A), preventing dopamine catabolism in the basal ganglia and providing modest symptomatic benefit and possibly disease-modifying effect in Parkinson disease (DATATOP trial). At higher doses (above 20 mg daily) selectivity is lost and MAO-A inhibition contributes, producing classical MAOI antidepressant pharmacology with the corresponding tyramine cheese-effect risk. The transdermal patch (6 to 12 mg/24 h, Emsam) achieves antidepressant plasma levels while bypassing first-pass GI MAO-A inhibition, mitigating the tyramine restriction at the low-dose patch (6 mg). Metabolites include amphetamine and methamphetamine, contributing to subjective alertness and complicating drug screening. Used as a reference MAO-B selective inhibitor in Parkinson research and as a transdermal MAOI in depression studies.

1. Compound Identification

Selegiline is described as selective irreversible mao-b inhibitor. A propargyl phenethylamine MAO-B inhibitor used in Parkinson disease and at higher doses in depression via MAO-A engagement.

1.1 Class summary

Selective irreversible MAO-B inhibitor

1.2 Subtitle

A propargyl phenethylamine MAO-B inhibitor used in Parkinson disease and at higher doses in depression via MAO-A engagement.

2. Abstract

Selegiline ((R)-N-methyl-N-(1-phenylpropan-2-yl)prop-2-yn-1-amine; CAS 14611-51-9; molecular formula C₁₃H₁₇N; molecular weight 187.28) is an irreversible propargyl-substituted MAO-B inhibitor developed by Joseph Knoll in Hungary in the 1960s. At low oral doses (5 to 10 mg daily) the compound is selective for MAO-B (selectivity ratio approximately 100:1 over MAO-A), preventing dopamine catabolism in the basal ganglia and providing modest symptomatic benefit and possibly disease-modifying effect in Parkinson disease (DATATOP trial). At higher doses (above 20 mg daily) selectivity is lost and MAO-A inhibition contributes, producing classical MAOI antidepressant pharmacology with the corresponding tyramine cheese-effect risk. The transdermal patch (6 to 12 mg/24 h, Emsam) achieves antidepressant plasma levels while bypassing first-pass GI MAO-A inhibition, mitigating the tyramine restriction at the low-dose patch (6 mg). Metabolites include amphetamine and methamphetamine, contributing to subjective alertness and complicating drug screening. Used as a reference MAO-B selective inhibitor in Parkinson research and as a transdermal MAOI in depression studies.

3. Mechanism of Action

Irreversible MAO-B inhibition (selective at low dose, both A and B at higher dose). Metabolites include amphetamine and methamphetamine. Patch form bypasses GI MAO-A.

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 5 to 10 mg per oral administration daily for Parkinson; 6 to 12 mg/24 h transdermal for depression. Rodent studies 0.25 to 5 mg/kg/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. Knoll J. The pharmacological profile of selegiline. Mech Ageing Dev 2003.
2. Parkinson Study Group. Effect of deprenyl on the progression of disability in early Parkinson's disease. N Engl J Med 1989.
3. Patkar AA, et al. Selegiline transdermal system: a novel treatment option for major depressive disorder. Expert Opin Pharmacother 2007.

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