

RESEARCH MONOGRAPH . COMPOUND PROFILE

Pindolol

A non-selective beta-blocker with intrinsic 5-HT1A partial agonism; investigated as an SSRI augmenting agent.

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AUTHOR	Kodiac bioLabs Research
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RESEARCH USE ONLY

ABSTRACT

Pindolol (1-(1H-indol-4-yloxy)-3-(propan-2-ylamino)propan-2-ol; CAS 13523-86-9; molecular formula C₁₄H₂₀N₂O₂; molecular weight 248.32) is a non-selective beta-adrenergic antagonist with intrinsic sympathomimetic activity (partial agonism) and 5-HT_{1A} partial agonism, approved by the FDA in 1982. The compound's distinguishing pharmacological feature in psychiatric research is high-affinity 5-HT_{1A} binding (K_i approximately 50 nM) with partial agonist activity at presynaptic autoreceptors; concurrent administration with an SSRI desensitizes the autoreceptor more rapidly than the SSRI alone, hypothetically accelerating the antidepressant response. Multiple placebo-controlled trials in the 1990s and 2000s reported faster onset (1 to 2 weeks shorter latency) but inconsistent overall efficacy improvement. Plasma half-life is 3 to 4 hours; metabolism is hepatic. Approved indications in cardiology include hypertension and angina; the SSRI augmentation use remains off-label. Used as the canonical 5-HT_{1A} binding beta-blocker in mechanism studies.

1. Compound Identification

Pindolol is described as non-selective beta-adrenergic antagonist with 5-HT_{1A} partial agonism. A non-selective beta-blocker with intrinsic 5-HT_{1A} partial agonism; investigated as an SSRI augmenting agent.

1.1 Class summary

Non-selective beta-adrenergic antagonist with 5-HT_{1A} partial agonism

1.2 Subtitle

A non-selective beta-blocker with intrinsic 5-HT_{1A} partial agonism; investigated as an SSRI augmenting agent.

2. Abstract

Pindolol (1-(1H-indol-4-yloxy)-3-(propan-2-ylamino)propan-2-ol; CAS 13523-86-9; molecular formula C₁₄H₂₀N₂O₂; molecular weight 248.32) is a non-selective beta-adrenergic antagonist with intrinsic sympathomimetic activity (partial agonism) and 5-HT_{1A} partial agonism, approved by the FDA in 1982. The compound's distinguishing pharmacological feature in psychiatric research is high-affinity 5-HT_{1A} binding (K_i approximately 50 nM) with partial agonist activity at presynaptic autoreceptors; concurrent administration with an SSRI desensitizes the autoreceptor more rapidly than the SSRI alone, hypothetically accelerating the antidepressant response. Multiple placebo-controlled trials in the 1990s and 2000s reported faster onset (1 to 2 weeks shorter latency) but inconsistent overall efficacy improvement. Plasma half-life is 3 to 4 hours; metabolism is hepatic. Approved indications in cardiology include hypertension and angina; the SSRI augmentation use remains off-label. Used as the canonical 5-HT_{1A} binding beta-blocker in mechanism studies.

3. Mechanism of Action

Non-selective beta-adrenergic antagonism plus 5-HT_{1A} partial agonism (K_i approximately 50 nM). Used to accelerate SSRI antidepressant onset by autoreceptor desensitization.

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 30 mg per oral administration daily; SSRI augmentation 2.5 to 7.5 mg twice daily. Rodent studies 1 to 10 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. Artigas F, et al. Acceleration of the effect of selected antidepressant drugs in major depression by 5-HT_{1A} antagonists. Trends Neurosci 1996.
2. Perez V, et al. Randomised, double-blind, placebo-controlled trial of pindolol in combination with fluoxetine antidepressant treatment. Lancet 1997.
3. Tome MB, et al. Paroxetine and pindolol: a randomized trial of serotonergic autoreceptor blockade in the reduction of antidepressant latency. Int Clin Psychopharmacol 1997.

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