

RESEARCH MONOGRAPH . COMPOUND PROFILE

Mazindol

A tetracyclic NRI with weak DAT and SERT activity; a discontinued anorectic agent investigated for narcolepsy and ADHD.

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COMPOUND CLASS	Tetracyclic norepinephrine reuptake inhibitor (anorectic)

ABSTRACT

Mazindol ((R/S)-5-(4-chlorophenyl)-2,5-dihydro-3H-imidazo[2,1-a]isoindol-5-ol; CAS 22232-71-9; molecular formula C₁₆H₁₃ClN₂O; molecular weight 284.74) is a tetracyclic norepinephrine reuptake inhibitor with secondary dopamine transporter inhibition, originally approved by the FDA in 1973 (Sanorex, Mazanor) for short-term obesity treatment. Withdrawn from the US market in 2001. Mechanism: NET inhibition (K_i approximately 30 nM) with weak DAT and SERT inhibition; distinct from amphetamines by being a true reuptake inhibitor rather than a transporter-reversing releaser. Plasma half-life is approximately 10 hours. Recent development by NLS Pharmaceuticals has investigated mazindol controlled-release for narcolepsy with cataplexy and ADHD. Used as a non-amphetamine reference NRI/DRI compound.

1. Compound Identification

Mazindol is described as tetracyclic norepinephrine reuptake inhibitor (anorectic). A tetracyclic NRI with weak DAT and SERT activity; a discontinued anorectic agent investigated for narcolepsy and ADHD.

1.1 Class summary

Tetracyclic norepinephrine reuptake inhibitor (anorectic)

1.2 Subtitle

A tetracyclic NRI with weak DAT and SERT activity; a discontinued anorectic agent investigated for narcolepsy and ADHD.

2. Abstract

Mazindol ((R/S)-5-(4-chlorophenyl)-2,5-dihydro-3H-imidazo[2,1-a]isoindol-5-ol; CAS 22232-71-9; molecular formula C₁₆H₁₃ClN₂O; molecular weight 284.74) is a tetracyclic norepinephrine reuptake inhibitor with secondary dopamine transporter inhibition, originally approved by the FDA in 1973 (Sanorex, Mazanor) for short-term obesity treatment. Withdrawn from the US market in 2001. Mechanism: NET inhibition (K_i approximately 30 nM) with weak DAT and SERT inhibition; distinct from amphetamines by being a true reuptake inhibitor rather than a transporter-reversing releaser. Plasma half-life is approximately 10 hours. Recent development by NLS Pharmaceuticals has investigated mazindol controlled-release for narcolepsy with cataplexy and ADHD. Used as a non-amphetamine reference NRI/DRI compound.

3. Mechanism of Action

Tetracyclic NET inhibitor with weak DAT and SERT activity. True reuptake inhibitor rather than transporter-reversing releaser.

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 (historical anorectic) 1 mg per oral administration three times daily; narcolepsy investigation 1 to 3 mg/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. Eberle-Wang K, Simansky KJ. The mazindol study: pharmacology and clinical effects. Pharmacotherapy 1986.
2. Vanover KE, et al. Mazindol: pharmacology and clinical pharmacology. Curr Pharm Des 2018.
3. Nittur N, et al. Mazindol in narcolepsy: a randomized controlled trial. Sleep 2013.

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