

RESEARCH MONOGRAPH . COMPOUND PROFILE

Trimipramine

A sedating tertiary amine TCA with weak SERT and NET activity; the principal effect is dopaminergic and antihistaminergic.

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COMPOUND CLASS	Tricyclic antidepressant (sedating tertiary amine)

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ABSTRACT

Trimipramine (3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N,2-trimethylpropan-1-amine; CAS 739-71-9; molecular formula C₂₀H₂₆N₂; molecular weight 294.43) is a 2-methylated dibenzazepine TCA approved by the FDA in 1979 under the trade name Surmontil. The methyl substitution at the propanamine's beta carbon disrupts transporter binding: SERT Ki approximately 150 nM, NET Ki approximately 2400 nM, both several orders of magnitude weaker than amitriptyline or imipramine. The therapeutic effect is therefore primarily attributed to potent H₁ (Ki approximately 0.27 nM, comparable to first-generation antihistamines), 5-HT_{2A}, alpha-1, and D₂ antagonism. The compound is among the most sedating TCAs in clinical use and is used preferentially in depression with severe insomnia. Plasma half-life is 16 to 40 hours; metabolism is via CYP2D6, CYP2C19, CYP3A4. Used as a reference compound for non-transporter TCA mechanism research; the H₁ and dopaminergic profiles distinguish it from typical TCA pharmacology.

1. 1. Compound Identification

Trimipramine is described as tricyclic antidepressant (sedating tertiary amine). A sedating tertiary amine TCA with weak SERT and NET activity; the principal effect is dopaminergic and antihistaminergic.

1.1. 1.1 Class summary

Tricyclic antidepressant (sedating tertiary amine)

1.2. 1.2 Subtitle

A sedating tertiary amine TCA with weak SERT and NET activity; the principal effect is dopaminergic and antihistaminergic.

2. Abstract

Trimipramine (3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N,2-trimethylpropan-1-amine; CAS 739-71-9; molecular formula C₂₀H₂₆N₂; molecular weight 294.43) is a 2-methylated dibenzazepine TCA approved by the FDA in 1979 under the trade name Surmontil. The methyl substitution at the propanamine's beta carbon disrupts transporter binding: SERT Ki approximately 150 nM, NET Ki approximately 2400 nM, both several orders of magnitude weaker than amitriptyline or imipramine. The therapeutic effect is therefore primarily attributed to potent H₁ (Ki approximately 0.27 nM, comparable to first-generation antihistamines), 5-HT_{2A}, alpha-1, and D₂ antagonism. The compound is among the most sedating TCAs in clinical use and is used preferentially in depression with severe insomnia. Plasma half-life is 16 to 40 hours; metabolism is via CYP2D6, CYP2C19, CYP3A4. Used as a reference compound for non-transporter TCA mechanism research; the H₁ and dopaminergic profiles distinguish it from typical TCA pharmacology.

3. Mechanism of Action

Weak SERT/NET activity; primary therapeutic effect via potent H1 antagonism and 5-HT2A, alpha-1, D2 receptor antagonism. Distinct from typical TCA 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. 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. 5. Reported Research Dose Ranges

Clinical 50 to 300 mg per oral administration nightly. Rodent studies 5 to 30 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. 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. 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. 9. References

1. Settle EC, Ayd FJ. Trimipramine: twenty years' worldwide clinical experience. J Clin Psychiatry 1980.
2. Eckert A, et al. Trimipramine and monoamine receptor binding. J Neural Transm 1996.
3. Riemann D, et al. Trimipramine in primary insomnia. Pharmacopsychiatry 2002.

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