

RESEARCH MONOGRAPH . COMPOUND PROFILE

Imipramine

The first synthetic antidepressant; the parent compound of the TCA class and the historical reference for monoamine theory of depression.

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COMPOUND CLASS	Tricyclic antidepressant (tertiary amine; first synthetic antidepressant)

ABSTRACT

Imipramine (3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine; CAS 50-49-7; molecular formula C₁₉H₂₄N₂; molecular weight 280.41) is a dibenzazepine tertiary amine TCA developed at Geigy by Roland Kuhn in 1958, the first synthetic compound demonstrated to relieve depressive symptoms in clinical trial. The historical observation underpinned the catecholamine hypothesis of depression and launched modern psychopharmacology. SERT and NET affinities are balanced (SERT K_i approximately 1 nM, NET K_i approximately 21 nM); the active metabolite desipramine is a NET-preferring secondary amine. Off-target activity parallels amitriptyline: muscarinic, H₁, alpha-1, and sodium channel block. Plasma half-life is 11 to 25 hours; metabolism is via CYP2D6 and CYP2C19. Approved for major depressive disorder; clinical use today focuses on enuresis (bedwetting) in children (low-dose for anticholinergic and alpha-1 effects on bladder) and panic disorder. The TCA cardiotoxicity profile is the principal limitation. Used as the historical reference TCA and the prototype monoamine reuptake inhibitor in pharmacology.

1. Compound Identification

Imipramine is described as tricyclic antidepressant (tertiary amine; first synthetic antidepressant). The first synthetic antidepressant; the parent compound of the TCA class and the historical reference for monoamine theory of depression.

1.1 Class summary

Tricyclic antidepressant (tertiary amine; first synthetic antidepressant)

1.2 Subtitle

The first synthetic antidepressant; the parent compound of the TCA class and the historical reference for monoamine theory of depression.

2. Abstract

Imipramine (3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine; CAS 50-49-7; molecular formula C₁₉H₂₄N₂; molecular weight 280.41) is a dibenzazepine tertiary amine TCA developed at Geigy by Roland Kuhn in 1958, the first synthetic compound demonstrated to relieve depressive symptoms in clinical trial. The historical observation underpinned the catecholamine hypothesis of depression and launched modern psychopharmacology. SERT and NET affinities are balanced (SERT K_i approximately 1 nM, NET K_i approximately 21 nM); the active metabolite desipramine is a NET-preferring secondary amine. Off-target activity parallels amitriptyline: muscarinic, H₁, α-1, and sodium channel block. Plasma half-life is 11 to 25 hours; metabolism is via CYP2D6 and CYP2C19. Approved for major depressive disorder; clinical use today focuses on enuresis (bedwetting) in children (low-dose for anticholinergic and α-1 effects on bladder) and panic disorder. The TCA cardiotoxicity profile is the principal limitation. Used as the historical reference TCA and the prototype monoamine reuptake inhibitor in pharmacology.

3. Mechanism of Action

Balanced SERT/NET inhibition with anticholinergic, antihistaminergic, alpha-1, and sodium channel block. Historical reference compound for monoamine theory of depression.

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 25 to 300 mg per oral administration daily. 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. 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. Kuhn R. The treatment of depressive states with G 22355 (imipramine hydrochloride). Am J Psychiatry 1958.
2. Bryson HM, Wilde MI, et al. Imipramine. A review of its pharmacological properties and therapeutic use. Drugs 1996.
3. Owens MJ, et al. Second-generation SSRIs: human monoamine transporter binding profile. Biol Psychiatry 2001.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.