

RESEARCH MONOGRAPH . COMPOUND PROFILE

Amphetamine

*The prototype phenethylamine stimulant;
a monoamine releaser used in ADHD and
narcolepsy and the foundation of an entire
pharmacological class.*

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COMPOUND CLASS	Phenethylamine monoamine releaser

ABSTRACT

Amphetamine ((R/S)-1-phenylpropan-2-amine; CAS 300-62-9; molecular formula C₉H₁₃N; molecular weight 135.21) is the prototype phenethylamine stimulant, first synthesized in 1887 by Edeleanu and clinically developed in the 1930s as Benzedrine. Mechanism: reversal of vesicular monoamine transporter 2 (VMAT2) and plasma membrane dopamine, norepinephrine, and serotonin transporters (DAT, NET, SERT), producing transporter-mediated efflux (release) rather than reuptake inhibition; the result is increased synaptic dopamine and norepinephrine concentrations. Secondary effects include MAO inhibition and TAAR1 agonism. The two enantiomers have differing pharmacology: d-amphetamine is more dopaminergic; l-amphetamine has greater peripheral noradrenergic activity. Approved indications: ADHD, narcolepsy, exogenous obesity (rare). Marketed as Adderall (mixed salts), Dexedrine (d-amphetamine), Evekeo (racemic). Plasma half-life is 9 to 14 hours. Schedule II in the US under the CSA. Used as the canonical monoamine releaser in pharmacology and the foundation for the broader phenethylamine class.

1. Compound Identification

Amphetamine is described as phenethylamine monoamine releaser. The prototype phenethylamine stimulant; a monoamine releaser used in ADHD and narcolepsy and the foundation of an entire pharmacological class.

1.1 Class summary

Phenethylamine monoamine releaser

1.2 Subtitle

The prototype phenethylamine stimulant; a monoamine releaser used in ADHD and narcolepsy and the foundation of an entire pharmacological class.

2. Abstract

Amphetamine ((R/S)-1-phenylpropan-2-amine; CAS 300-62-9; molecular formula C₉H₁₃N; molecular weight 135.21) is the prototype phenethylamine stimulant, first synthesized in 1887 by Edeleanu and clinically developed in the 1930s as Benzedrine. Mechanism: reversal of vesicular monoamine transporter 2 (VMAT2) and plasma membrane dopamine, norepinephrine, and serotonin transporters (DAT, NET, SERT), producing transporter-mediated efflux (release) rather than re-uptake inhibition; the result is increased synaptic dopamine and norepinephrine concentrations. Secondary effects include MAO inhibition and TAAR1 agonism. The two enantiomers have differing pharmacology: d-amphetamine is more dopaminergic; l-amphetamine has greater peripheral noradrenergic activity. Approved indications: ADHD, narcolepsy, exogenous obesity (rare). Marketed as Adderall (mixed salts), Dexedrine (d-amphetamine), Evekeo (racemic). Plasma half-life is 9 to 14 hours. Schedule II in the US under the CSA. Used as the canonical monoamine releaser in pharmacology and the foundation for the broader phenethylamine class.

3. Mechanism of Action

Reverses VMAT2, DAT, NET, SERT to produce transporter-mediated monoamine release. Secondary MAO inhibition and TAAR1 agonism. d-enantiomer more dopaminergic; l-enantiomer more noradrenergic.

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 60 mg per oral administration daily, in divided doses or ER. Rodent research 0.5 to 5 mg/kg.

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. Sulzer D, et al. Mechanisms of neurotransmitter release by amphetamines: a review. Prog Neurobiol 2005.
2. Heal DJ, et al. Amphetamine, past and present - a pharmacological and clinical perspective. J Psychopharmacol 2013.
3. Wilens TE, et al. ADHD treatment with once-daily OROS methylphenidate vs amphetamine salts. J Atten Disord 2006.

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