

RESEARCH MONOGRAPH . COMPOUND PROFILE

Pentoxifylline

A methylxanthine non-selective phosphodiesterase inhibitor that improves erythrocyte deformability and microcirculation; used for intermittent claudication.

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ABSTRACT

Pentoxifylline (1-(5-oxohexyl)-3,7-dimethylxanthine; CAS 6493-05-6; molecular formula C₁₃H₁₈N₄O₃; molecular weight 278.31) is a methylxanthine non-selective phosphodiesterase inhibitor developed at Hoechst (now Sanofi) and approved by the FDA in 1984 under the trade name Trental. Mechanism: weak non-selective PDE inhibition (PDE3, PDE4, PDE5) increases intracellular cAMP and cGMP. The principal clinically meaningful effect is improvement in erythrocyte deformability and reduced platelet aggregation, producing improved microcirculatory blood flow. Approved for intermittent claudication. Off-label use in chronic cognitive impairment from small-vessel cerebrovascular disease, peripheral neuropathy, and tinnitus. Plasma half-life is approximately 0.4 to 0.8 hours; metabolism is hepatic. Used as a reference hemorheologic agent and weak non-selective PDE inhibitor.

1. Compound Identification

Pentoxifylline is described as methylxanthine pde inhibitor / hemorheologic agent. A methylxanthine non-selective phosphodiesterase inhibitor that improves erythrocyte deformability and microcirculation; used for intermittent claudication.

1.1 Class summary

Methylxanthine PDE inhibitor / hemorheologic agent

1.2 Subtitle

A methylxanthine non-selective phosphodiesterase inhibitor that improves erythrocyte deformability and microcirculation; used for intermittent claudication.

2. Abstract

Pentoxifylline (1-(5-oxohexyl)-3,7-dimethylxanthine; CAS 6493-05-6; molecular formula $C_{13}H_{18}N_4O_3$; molecular weight 278.31) is a methylxanthine non-selective phosphodiesterase inhibitor developed at Hoechst (now Sanofi) and approved by the FDA in 1984 under the trade name Trental. Mechanism: weak non-selective PDE inhibition (PDE3, PDE4, PDE5) increases intracellular cAMP and cGMP. The principal clinically meaningful effect is improvement in erythrocyte deformability and reduced platelet aggregation, producing improved microcirculatory blood flow. Approved for intermittent claudication. Off-label use in chronic cognitive impairment from small-vessel cerebrovascular disease, peripheral neuropathy, and tinnitus. Plasma half-life is approximately 0.4 to 0.8 hours; metabolism is hepatic. Used as a reference hemorheologic agent and weak non-selective PDE inhibitor.

3. Mechanism of Action

Weak non-selective phosphodiesterase inhibition (PDE3-5); increases erythrocyte deformability and reduces platelet aggregation.

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 400 mg per oral administration three times daily.

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. Frampton JE, Brogden RN. Pentoxifylline (oxpentifylline). A review of its therapeutic efficacy in the management of peripheral vascular and cerebrovascular disorders. Drugs Aging 1995.
2. Salhiyyah K, et al. Pentoxifylline for intermittent claudication. Cochrane Database Syst Rev 2015.
3. Gordon MN, et al. Pentoxifylline in dementia. Drugs Aging 1992.

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