

RESEARCH MONOGRAPH . COMPOUND PROFILE

Gaboxadol (THIP)

A 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol agonist selective for extrasynaptic GABA-A receptors containing the delta subunit; investigated as a hypnotic.

DOCUMENT	KDC-MN-255
ISSUED	2026-05-09
REVISION	1.0
AUTHOR	Kodiac biolabs Research
COMPOUND CLASS	Selective extrasynaptic GABA-A delta-subunit agonist

RESEARCH USE ONLY

ABSTRACT

Gaboxadol (THIP; 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol; CAS 64603-91-4; molecular formula C₆H₈N₂O₂; molecular weight 140.14) is a selective extrasynaptic GABA-A receptor agonist developed at Lundbeck and Merck through the 1990s and 2000s. Distinct from benzodiazepines and barbiturates by selective binding to GABA-A receptor isoforms containing the delta subunit (alpha4-beta3-delta and alpha6-beta3-delta), which are predominantly extrasynaptic and mediate tonic (continuous, low-amplitude) inhibition rather than the phasic (high-amplitude, transient) inhibition mediated by synaptic alpha1/2/3-beta-gamma2 receptors. The compound is a superagonist at delta-containing receptors (efficacy greater than that of GABA itself). Phase 3 trials in primary insomnia (2007) were halted following adverse psychiatric events including disorientation and hallucinations; development was abandoned. The compound retains research utility as the canonical extrasynaptic delta-GABA-A agonist for academic GABA pharmacology and sleep architecture studies. Plasma half-life is approximately 1.5 to 2 hours.

1. Compound Identification

Gaboxadol (THIP) is described as selective extrasynaptic gaba-a delta-subunit agonist. A 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol agonist selective for extrasynaptic GABA-A receptors containing the delta subunit; investigated as a hypnotic.

1.1 Class summary

Selective extrasynaptic GABA-A delta-subunit agonist

1.2 Subtitle

A 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol agonist selective for extrasynaptic GABA-A receptors containing the delta subunit; investigated as a hypnotic.

2. Abstract

Gaboxadol (THIP; 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol; CAS 64603-91-4; molecular formula C₆H₈N₂O₂; molecular weight 140.14) is a selective extrasynaptic GABA-A receptor agonist developed at Lundbeck and Merck through the 1990s and 2000s. Distinct from benzodiazepines and barbiturates by selective binding to GABA-A receptor isoforms containing the delta subunit (alpha4-beta3-delta and alpha6-beta3-delta), which are predominantly extrasynaptic and mediate tonic (continuous, low-amplitude) inhibition rather than the phasic (high-amplitude, transient) inhibition mediated by synaptic alpha1/2/3-beta-gamma2 receptors. The compound is a superagonist at delta-containing receptors (efficacy greater than that of GABA itself). Phase 3 trials in primary insomnia (2007) were halted following adverse psychiatric events including disorientation and hallucinations; development was abandoned. The compound retains research utility as the canonical extrasynaptic delta-GABA-A agonist for academic GABA pharmacology and sleep architecture studies. Plasma half-life is approximately 1.5 to 2 hours.

3. Mechanism of Action

Selective superagonist at extrasynaptic GABA-A receptors containing the delta subunit. Distinct from benzodiazepine pharmacology by extrasynaptic localization.

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

Investigational; trial doses 5 to 20 mg per oral administration as a hypnotic. Rodent research 3 to 30 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. Krogsgaard-Larsen P, et al. GABAA agonists and partial agonists: THIP (gaboxadol) as a non-opioid analgesic and a novel type of hypnotic. *Biochem Pharmacol* 2004.
2. Wafford KA, Ebert B. Gaboxadol - a new awakening in sleep. *Curr Opin Pharmacol* 2006.
3. Mathias S, et al. The GABA uptake inhibitor tiagabine versus gaboxadol on slow wave sleep. *Sleep* 2005.

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.