

RESEARCH MONOGRAPH . COMPOUND PROFILE

Thyrotropin-Releasing Hormone (TRH)

A hypothalamic tripeptide that triggers pituitary TSH release; used as a pharmacological probe for pituitary function and investigated for cognitive enhancement.

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COMPOUND CLASS	Hypothalamic tripeptide (thyrotropin-releasing hormone)

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ABSTRACT

TRH (thyrotropin-releasing hormone; pyroglutamyl-histidyl-prolinamide; CAS 24305-27-9; molecular formula C₁₆H₂₂N₆O₄; molecular weight 362.39) is a hypothalamic tripeptide that activates pituitary TRH receptors to trigger TSH release. Discovered independently by Schally and Guillemin in the late 1960s (Nobel Prize 1977). The compound is the smallest peptide hormone of the hypothalamic-pituitary axis. Pharmacologically, exogenous TRH has been used as a clinical probe of pituitary thyrotroph function (the TRH stimulation test, now largely supplanted by sensitive TSH assays). Beyond TSH release, TRH receptors are distributed throughout the CNS and TRH has direct effects on arousal, mood, and cognitive function; clinical trials in depression, ALS, and spinocerebellar ataxia have been mixed. Plasma half-life is approximately 5 minutes, severely limiting clinical use; analog development has produced taltirelin (approved in Japan for spinocerebellar degeneration) and other TRH receptor agonists with extended pharmacokinetics. Used as the canonical hypothalamic peptide for pituitary axis research.

1. 1. Compound Identification

Thyrotropin-Releasing Hormone (TRH) is described as hypothalamic tripeptide (thyrotropin-releasing hormone). A hypothalamic tripeptide that triggers pituitary TSH release; used as a pharmacological probe for pituitary function and investigated for cognitive enhancement.

1.1. 1.1 Class summary

Hypothalamic tripeptide (thyrotropin-releasing hormone)

1.2. 1.2 Subtitle

A hypothalamic tripeptide that triggers pituitary TSH release; used as a pharmacological probe for pituitary function and investigated for cognitive enhancement.

2. 2. Abstract

TRH (thyrotropin-releasing hormone; pyroglutamyl-histidyl-prolinamide; CAS 24305-27-9; molecular formula C₁₆H₂₂N₆O₄; molecular weight 362.39) is a hypothalamic tripeptide that activates pituitary TRH receptors to trigger TSH release. Discovered independently by Schally and Guillemin in the late 1960s (Nobel Prize 1977). The compound is the smallest peptide hormone of the hypothalamic-pituitary axis. Pharmacologically, exogenous TRH has been used as a clinical probe of pituitary thyrotroph function (the TRH stimulation test, now largely supplanted by sensitive TSH assays). Beyond TSH release, TRH receptors are distributed throughout the CNS and TRH has direct effects on arousal, mood, and cognitive function; clinical trials in depression, ALS, and spinocerebellar ataxia have been mixed. Plasma half-life is approximately 5 minutes, severely limiting clinical use; analog development has produced taltirelin (approved in Japan for spinocerebellar degeneration) and other TRH receptor agonists with extended pharmacokinetics. Used as the canonical hypothalamic peptide for pituitary axis research.

3. Mechanism of Action

Tripeptide TRH receptor agonist; triggers pituitary TSH release. Direct CNS effects on arousal, mood, and cognition through widely distributed TRH receptors.

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

Research 200 to 500 mcg intravenous (TSH stimulation test); intranasal research applications 1 to 5 mg.

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. Reichlin S. Neuroendocrinology of TRH. N Engl J Med 1989.
2. Gary KA, et al. The thyrotropin-releasing hormone (TRH) hypothesis of homeostatic regulation. CNS Spectr 2003.
3. Yarbrough GG, et al. Thyrotropin-releasing hormone: structure-activity relationships. CNS Drug Rev 2007.

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