

RESEARCH MONOGRAPH . COMPOUND PROFILE

Kisspeptin

*An endogenous neuropeptide encoded by the **KISS1** gene, master regulator of GnRH neuron firing and reproductive function.*

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COMPOUND CLASS	Hypothalamic neuropeptide / KISS1R agonist

ABSTRACT

Kisspeptin (kisspeptin-54 and shorter active fragments including kisspeptin-10; encoded by the KISS1 gene) is an endogenous peptide identified in 2003 as the master regulator of GnRH neuron firing in the hypothalamus, controlling reproductive function and pubertal onset. Loss-of-function mutations in KISS1 or its receptor KISS1R produce hypogonadotropic hypogonadism. Exogenous kisspeptin administration stimulates LH and FSH release through GnRH neuron activation. The compound has been studied as a fertility therapeutic (induction of ovulation in functional hypothalamic amenorrhea) and as a research probe for reproductive neuroendocrine function. Pharmacokinetics: plasma half-life of kisspeptin-54 is ~30 minutes; kisspeptin-10 has shorter half-life. Research doses are highly variable; clinical trial doses range 0.01 to 6.4 nmol/kg IV.

1. Compound Identification

Kisspeptin is described as hypothalamic neuropeptide / kiss1r agonist. An endogenous neuropeptide encoded by the KISS1 gene, master regulator of GnRH neuron firing and reproductive function.

1.1 Class summary

Hypothalamic neuropeptide / KISS1R agonist

1.2 Subtitle

An endogenous neuropeptide encoded by the KISS1 gene, master regulator of GnRH neuron firing and reproductive function.

2. Abstract

Kisspeptin (kisspeptin-54 and shorter active fragments including kisspeptin-10; encoded by the KISS1 gene) is an endogenous peptide identified in 2003 as the master regulator of GnRH neuron firing in the hypothalamus, controlling reproductive function and pubertal onset. Loss-of-function mutations in KISS1 or its receptor KISS1R produce hypogonadotropic hypogonadism. Exogenous kisspeptin administration stimulates LH and FSH release through GnRH neuron activation. The compound has been studied as a fertility therapeutic (induction of ovulation in functional hypothalamic amenorrhea) and as a research probe for reproductive neuroendocrine function. Pharmacokinetics: plasma half-life of kisspeptin-54 is ~30 minutes; kisspeptin-10 has shorter half-life. Research doses are highly variable; clinical trial doses range 0.01 to 6.4 nmol/kg IV.

3. Mechanism of Action

KISS1R receptor agonist; activates GnRH neurons. Master regulator of reproductive endocrine axis.

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

0.01 to 6.4 nmol/kg IV in clinical trials.

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. Seminara SB, et al. The GPR54 gene as a regulator of puberty. N Engl J Med 2003.

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