

RESEARCH MONOGRAPH . COMPOUND PROFILE

HGH Fragment 191-203

A 13-residue C-terminal fragment of human growth hormone (residues 191 through 203), studied as a research tool for the lipolytic activity of GH separated from somatogenic and insulin-like effects.

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COMPOUND CLASS	C-terminal fragment of human growth hormone with lipolytic activity

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ABSTRACT

HGH Fragment 191-203 (Tyr-Leu-Arg-Ile-Val-Gln-Cys-Arg-Ser-Val-Glu-Gly-Ser; molecular weight 1495.78) is a 13-residue C-terminal fragment of human growth hormone (residues 191 through 203 of the mature 191-residue hGH polypeptide) developed as a research tool for separating the lipolytic activity of growth hormone from the somatogenic (growth-promoting) and insulinotropic activities. The full-length 191-residue hGH produces both lipolytic effects (acute fatty acid mobilization, chronic reduction of fat mass with a delay) and somatogenic and insulin-like effects (longitudinal bone growth in pediatric populations, insulin resistance in chronic exposure). Carboxypeptidase digestion of hGH produces fragments that retain selective subsets of these activities; the 191-203 fragment was characterized in the 1990s as a lipolytic-selective fragment in rodent adipocyte models and at the obese rodent in vivo level. The shorter fragment AOD9604 (KDC-MN; aod-9604), a tyrosine-conjugated 16-residue C-terminal fragment, was developed by Metabolic Pharmaceuticals (now Lateral) as a clinical agent in the same activity class and reached Phase 2 in obesity before discontinuation owing to insufficient effect size. Fragment 191-203 is the simpler underlying research tool from which AOD9604 was derived. The principal pharmacological signature is direct activation of beta-3 adrenergic receptor or downstream lipolytic signaling at the adipocyte level (the precise mechanism remains debated), increased fatty acid oxidation, and reduced de novo lipogenesis, without engagement of the GH receptor and without IGF-1 elevation. Plasma half-life is short (minutes) and the compound is administered subcutaneously. The compound is not

approved by any regulatory authority and is sold only as a research-grade peptide; the principal published evidence base is from the 1990s and early 2000s and the clinical translation through AOD9604 did not produce a marketed agent.

1. Compound Identification

HGH Fragment 191-203 is described as c-terminal fragment of human growth hormone with lipolytic activity. A 13-residue C-terminal fragment of human growth hormone (residues 191 through 203), studied as a research tool for the lipolytic activity of GH separated from somatogenic and insulin-like effects.

1.1 Class summary

C-terminal fragment of human growth hormone with lipolytic activity

1.2 Subtitle

A 13-residue C-terminal fragment of human growth hormone (residues 191 through 203), studied as a research tool for the lipolytic activity of GH separated from somatogenic and insulin-like effects.

2. Abstract

HGH Fragment 191-203 (Tyr-Leu-Arg-Ile-Val-Gln-Cys-Arg-Ser-Val-Glu-Gly-Ser; molecular weight 1495.78) is a 13-residue C-terminal fragment of human growth hormone (residues 191 through 203 of the mature 191-residue hGH polypeptide) developed as a research tool for separating the lipolytic activity of growth hormone from the somatogenic (growth-promoting) and insulinotropic activities. The full-length 191-residue hGH produces both lipolytic effects (acute fatty acid mobilization, chronic reduction of fat mass with a delay) and somatogenic and insulin-like effects (longitudinal bone growth in pediatric populations, insulin resistance in chronic exposure). Carboxypeptidase digestion of hGH produces fragments that retain selective subsets of these activities; the 191-203 fragment was characterized in the 1990s as a lipolytic-selective fragment in rodent adipocyte models and at the obese rodent in vivo level. The shorter fragment AOD9604 (KDC-MN; aod-9604), a tyrosine-conjugated 16-residue C-terminal fragment, was developed by Metabolic Pharmaceuticals (now Lateral) as a clinical agent in the same activity class and reached Phase 2 in obesity before discontinuation owing to insufficient effect size. Fragment 191-203 is the simpler underlying research tool from which AOD9604 was derived. The principal pharmacological signature is direct activation of beta-3 adrenergic receptor or downstream lipolytic signaling at the adipocyte level (the precise mechanism remains debated), increased fatty acid oxidation, and reduced de novo lipogenesis, without engagement of the GH receptor and without IGF-1 elevation. Plasma half-life is short (minutes) and the compound is administered subcutaneously. The compound is not approved by any regulatory authority and is sold only as a research-grade peptide; the principal published evidence base is from the 1990s and early 2000s and the clinical translation through AOD9604 did not produce a marketed agent.

3. Mechanism of Action

Selective lipolytic activity at the adipocyte level without GH receptor engagement; proposed beta-3 adrenergic or downstream signaling. Increased fatty acid oxidation and reduced de novo lipogenesis. No IGF-1 elevation.

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

Research-grade dosing 250 to 500 mcg subcutaneous daily, on the AOD9604 dosing pattern. No human clinical record specific to fragment 191-203.

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. Ng FM, et al. The lipolytic effect of a synthetic hexadecapeptide hGH 177-191. Horm Metab Res 1994.
2. Heffernan M, et al. AOD9604, a synthetic analog of human growth hormone fragment 177-191. J Endocrinol 2001.
3. Wu Z, et al. Lipolytic effects of hGH fragments. Mol Cell Endocrinol 2003.

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.