Survodutide TFA

Cat. No.: HY-P4146A

Molecular Formula: $C_{192}H_{289}N_{47}O_{61}.xC_2HF_3OC_2$

Sequence Shortening: H-{1-amino-1-cyclobutanecarboxylic acid}-QGTFTSDYSKYLDERAAKDFIK-{GGSGSG-γE-C18 di-acid)}-WLESA-NH2

Survodutide (TFA)

Target: GLP Receptor; GCGR

Pathway: GPCR/G Protein

Storage: Sealed storage, away from moisture and light

Powder -80°C 2 years

-20°C 1 year

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture and light)

SOLVENT & SOLUBILITY

In Vitro

H_2O : ≥ 100 mg/mL

* "≥" means soluble, but saturation unknown.

BIOLOGICAL ACTIVITY

Description

Survodutide (BI 456906) TFA is a potent, selective glucagon receptor/GLP-1 receptor (GCGR/GLP-1R) dual agonist with EC_{50}s of 0.52 nM and 0.33 nM in CHO-K1 cells, respectively. Survodutide TFA, a 29-amino-acid peptide, is a potent acylated peptide containing a C18 fatty acid. Survodutide TFA has robust anti-obesity efficacy achieved by increasing energy expenditure and decreasing food intake[1].

In Vitro

The EC_{50} is 0.36 nM for Survodutide (BI 456906) TFA in the endogenous mouse GLP-1R in the insulinoma cell line MIN6, and the EC_{50} is 60 pM for GLP-1. In 0.5% human and mouse plasma, Survodutide TFA shows a similar potency to that of endogenous GLP-1. For the GCGR, in 0.5% human and mouse plasma, Survodutide TFA is 6-fold less potent (0.29 and 0.17 nM, respectively) in relation to endogenous glucagon (47 and 30 pM, respectively)[1].

Proteolytic stability of Survodutide TFA is helped by C-terminal amidation and the introduction of a non-coded amino acid 1-aminocyclobutane-1-carboxylic acid (Ac4c) in position 2, well established as the site of proteolytic activity for dipeptidyl peptidase-4. The desired extended terminal half-life of Survodutide TFA is achieved by the introduction of a glycine–serine linker in position 24, carrying a C18 di-acid[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Survodutide (BI 456906; 3, 10, 20, 30 nmol/kg; SC; daily; 30 days) TFA achieves a greater bodyweight-lowering efficacy in diet-induced obese mice compared with maximally effective doses of Semaglutide (HY-114118; 20, 100 nmol/kg). Survodutide TFA dose-dependently reduces plasma glucagon[1].

Survodutide (1, 3, 10, 30, 100 nmol/kg; SC; single dose) TFA dose-dependently reducesacute food intake in WT but not in GLP-1R KO mice (Three-week-old, male, lean NMRI outbred mice)[1].

Survodutide (1, 3, 10, 30, 100 nmol/kg; SC; single dose) TFA engages the glucagon receptor in vivo upon single dosing, increases liver nicotinamide N-methyltransferase mRNA, and reduces plasma serine and glutamine[1].

Survodutide (SC injection) TFA causes mean residence times of 44 and 140 h and T_{max} values of 7 and 51 h obtained in mice and dogs, respectively[1].

Pharmacokinetic Parameters of Survodutide (BI 456906) in mice and dogs[1].

	Mice (20 nmol/kg; SC)	Dogs (10 nmol/kg; SC)
T_{max} (h)	7	50.7
C_{max} (nM)	84.9	62.0
$AUC_{0-\infty}$ (nM·h)	4640	9540

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Animal Model:	Male C57BL6/J mice pre-fed with a 60% HFD (22 weeks)[1]
Dosage:	3, 10, 20, 30 nmol/kg
Administration:	SC; daily; 30 days
Result:	Dose-dependently reduced bodyweight from baseline by up to 32% at Day 28 at a dose of 30 nmol/kg.

REFERENCES

[1]. Tina Zimmermann, et al. BI 456906: Discovery and preclinical pharmacology of a novel GCGR/GLP-1R dual agonist with robust anti-obesity efficacy. Mol Metab. 2022 Dec:66:101633.

Caution: Product has not been fully validated for medical applications. For research use only.

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