MK-3207 Hydrochloride

Cat. No.: HY-10302

CAS No.: 957116-20-0

Molecular Formula: $C_{31}H_{30}ClF_2N_5O_3$

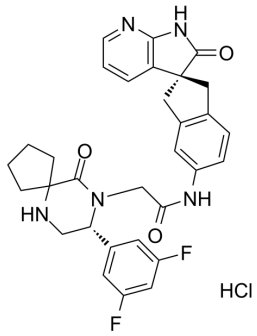
Molecular Weight: 594.05

Target: CGRP Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (168.34 mM)

H_2O : 50 mg/mL (84.17 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.6834 mL	8.4168 mL	16.8336 mL
	5 mM	0.3367 mL	1.6834 mL	3.3667 mL
	10 mM	0.1683 mL	0.8417 mL	1.6834 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MK-3207 (Hydrochloride) is a potent and orally bioavailable CGRP receptor antagonist with IC_{50} of 0.12 nM and K_i of 0.024 nM, and is highly selective versus human AM1, AM2, CTR, and AMY3.

IC_{50} & Target

IC50: 0.12 nM (CGRP receptor)

In Vitro

MK-3207 displays a similar affinity (K_i) for the rhesus monkey receptor (0.024±0.001 nM; n=14) as for human, but it displays >400-fold lower affinity for the canine and rat receptors, with values of 10 nM and 10±1.2 nM, respectively. MK-3207 is highly

	selective versus the human AM1 (CLR/RAMP2) and AM2 (CLR/RAMP3) receptors, with K_i values of 16,500 nM and 156±17 nM, respectively. MK-3207 maintains a high degree of selectivity versus human CTR, with a K_i value of 1.9±0.58 μM. MK-3207 also displays good selectivity versus the AMY3 (CTR/RAMP3) receptor, with a K_i value of 128±25 nM, but it is less selective versus the AMY1 (CTR/RAMP1) receptor, with a K_i value of 0.75±0.13 nM. MK-3207 potently blocks human α-CGRP-stimulated cAMP responses in human CGRP receptor-expressing HEK293 cells, with an IC_{50} value of 0.12±0.02 nM. MK-3207 displays significantly lower potency for the rat CGRP receptor, with a pIC_{50}=7.31±0.09[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	MK-3207 is CNS-penetrant and therefore significantly engaging central receptors. After an oral dose of 10 mg/kg MK-3207, the CSF/plasma ratio is 2 to 3%[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Amylin binding assays are conducted by combining MK-3207 and 40 pM ^{125}I-rat amylin, followed by 25 μg of CTR/RAMP1 or 25 μg of CTR/RAMP3 membranes and incubated for 3 h at room temperature in binding buffer (10 mM HEPES, 5 mM $MgCl_2$, and 0.2% bovine serum albumin) in a total volume of 1 mL. Calcitonin binding assays are with 25 μg of CTR membranes and 30 pM ^{125}I-human calcitonin as the radioligand. Incubations are terminated by filtration through GF/B 96-well filter plates that has been blocked with 0.5% polyethylenimine. Data are analyzed using Prism, and the K_i value is determined using the equation $K_i=IC_{50}/1 + ([ligand]/K_D)$. The K_D value for each receptor is determined by saturation binding experiments. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	A customized flexible silicone catheter is freely suspended in the cisterna magna, anchored firmly on both sides of the atlanto-occipital membrane, and tunneled subcutaneously to the midscapular region where it is fed into a surgically implanted port body. CSF is accessed by aseptically inserting a needle through the skin and membrane covering the port into the reservoir of the port body; blood samples are collected by peripheral venipuncture. After oral administration of MK-3207 at 10 mg/kg (0.5% methylcellulose, with an adjusted pH appr 3) to cisterna magna catheter and port-implanted rhesus monkeys, CSF and plasma samples are collected at 0.5, 1, 2, 4, 8, and 24 h and analyzed for compound levels. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Vascul Pharmacol. 2017 Mar;90:36-43.
- Eur J Pharmacol. 2018 Jun 15;829:85-92.
- Pharmacology. 2019;104(5-6):332-341.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Salvatore CA, et al. Pharmacological properties of MK-3207, a potent and orally active calcitonin gene-related peptide receptor antagonist. J Pharmacol Exp Ther. 2010 Apr;333(1):152-60.

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA