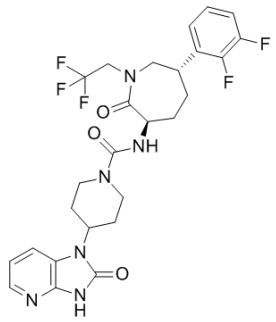
Telcagepant

Cat. No.:	HY-32709
CAS No.:	781649-09-0
Molecular Formula:	$C_{26}H_{27}F_5N_6O_3$
Molecular Weight:	566.52
Target:	CGRP Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (88.26 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7652 mL	8.8258 mL	17.6516 mL
5 mM	0.3530 mL	1.7652 mL	3.5303 mL
10 mM	0.1765 mL	0.8826 mL	1.7652 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: ≥ 3 mg/mL (5.30 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 3 mg/mL (5.30 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3 mg/mL (5.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Telcagepant (MK-0974) is an orally active calcitonin gene-related peptide (CGRP) receptor antagonist with K_is of 0.77 nM and 1.2 nM for human and rhesus CGRP receptors, respectively.
IC_{50} & Target	Ki: 0.77 nM (human CGRP), 1.2 nM (rhesus CGRP)
In Vitro	Telcagepant (MK-0974) displays affinity (K_i) for the canine and rat receptors, with values of 1204 nM and 1192 nM (n=10),

	respectively. Telcagepant (MK-0974) potently blocks human α-CGRP-stimulated cAMP responses in human CGRP receptor expressing HEK293 cells with an IC_{50} of 2.2 nM[1]. Telcagepant (MK-0974) displays saturable binding to SK-N-MC membranes with a K_D of 1.9 nM and B_{max} of 479 fmol/mg protein. Telcagepant (MK-0974) also displays saturable binding to rhesus cerebellum homogenate with a K_D of 1.3 nM and B_{max} of 20 fmol/mg[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Telcagepant (MK-0974) (i.v. bolus, 1 mg/kg) demonstrates that the efficacy of this antagonist is time-dependent and correlated with plasma levels[1]. The pharmacokinetics of Telcagepant (MK-0974) remains linear across 0.5-10 mg/kg intravenous dose in monkeys, but the oral area under the plasma concentration-time curve (AUC) increase (5-30 mg/kg) is 15-fold over dose-proportional[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	HEK293 cells stably transfected with CLR/RAMP1 are plated in complete growth medium at 85,000 cells/well in 96-well poly-D-lysine-coated plates and cultured for 19 h before assay. Cells are washed with PBS and then incubated with inhibitor in the presence or absence of 50% human serum for 30 min at 37°C and 95% humidity in Cellgro Complete Serum-Free/Low-Protein medium with L-glutamine and 1 g/L bovine serum albumin. Isobutylmethylxanthine is added to the cells at a concentration of 300 μM and incubated for 30 min at 37°C. Human α-CGRP is added to the cells at a concentration of 0.3 nM and allowed to incubate at 37°C for 5 min. After α-CGRP stimulation, the cells are washed with PBS and processed for cAMP determination using the two-stage assay procedure according to the manufacturer's recommended protocol. Dose-response curves are plotted, and IC_{50} values are determined. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Monkeys: Rhesus monkeys (male and female) weighing between 4 and 10 kg are used. The right saphenous vein is cannulated for intravenous drug delivery, and blood samples are obtained from the left saphenous artery. Four rubber O-rings (8 mm inner diameter) are placed on the ventral side of the forearm without directly being positioned over a visible vessel. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Vascul Pharmacol. 2017 Mar;90:36-43.

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REFERENCES

[1]. Salvatore CA, et al. Pharmacological characterization of MK-0974 [N-[(3R,6S)-6-(2,3-difluorophenyl)-2-oxo-1-(2,2,2-trifluoroethyl)azepan-3-yl]-4-(2-oxo-2,3-dihydro-1H-imidazo[4,5-b]pyridin-1-yl)piperidine-1-carboxamide], a potent and orally active calcitonin gene-related peptide receptor antagonist for the treatment of migraine. J Pharmacol Exp Ther. 2008 Feb;324(2):416-21. Epub 2007 Nov 26.

[2]. Moore EL, et al. Examining the binding properties of MK-0974: a CGRP receptor antagonist for the acute treatment of migraine. Eur J Pharmacol. 2009 Jan 14;602(2-3):250-4.

[3]. Roller S, et al. Preclinical pharmacokinetics of MK-0974, an orally active calcitonin-gene related peptide (CGRP)-receptor antagonist, mechanism of dose dependency and species differences. Xenobiotica. 2009 Jan;39(1):33-45.

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

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