**Telcagepant**

Cat. No.: HY-32709  
CAS No.: 781649-09-0  
Molecular Formula: C_{26}H_{27}F_{5}N_{6}O_{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: $\geq 50$ mg/mL (88.26 mM)  
*"$\geq$" means soluble, but saturation unknown.*

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>1.7652 mL</td>
<td>8.8258 mL</td>
<td>17.6516 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3530 mL</td>
<td>1.7652 mL</td>
<td>3.5303 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1765 mL</td>
<td>0.8826 mL</td>
<td>1.7652 mL</td>
</tr>
</tbody>
</table>

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

**In Vivo**  
1. Add each solvent one by one: 10% DMSO $\gg$ 40% PEG300 $\gg$ 5% Tween-80 $\gg$ 45% saline  
   Solubility: $\geq 3$ mg/mL (5.30 mM); Clear solution
2. Add each solvent one by one: 10% DMSO $\gg$ 90% (20% SBE-β-CD in saline)  
   Solubility: $\geq 3$ mg/mL (5.30 mM); Clear solution
3. Add each solvent one by one: 10% DMSO $\gg$ 90% corn oil  
   Solubility: $\geq 3$ mg/mL (5.30 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**  
Telcagepant (MK-0974) is a *calcitonin gene-related peptide (CGRP)* receptor antagonist with $K_i$ of 0.77 nM and 1.2 nM for human and rhesus CGRP receptors, respectively.

**IC_{50} & Target**  
$K_i$: 0.77 nM (human CGRP), 1.2 nM (rhesus CGRP)
**In Vitro**

Telcagepant (MK-0974) displays affinity (Kᵢ) 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 IC₅₀ of 2.2 nM[1]. Telcagepant (MK-0974) displays saturable binding to SK-N-MC membranes with a Kᵦ of 1.9 nM and Bₘₐₓ of 479 fmol/mg protein. Telcagepant (MK-0974) also displays saturable binding to rhesus cerebellum homogenate with a Kᵦ of 1.3 nM and Bₘₐₓ of 20 fmol/mg[2].

**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].

**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 IC₅₀ 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 anesthetized initially with ketamine (0.1 mL/kg i.m.) and then placed in the supine position on a temperature-controlled water circulating blanket and intubated with a 3-mm tracheal tube connected to 1-liter oxygen/1 to 2% isoflurane gas anesthesia. 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.

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**REFERENCES**
