Clozapine (N-oxide)

Cat. No.: HY-17366
CAS No.: 34233-69-7
Molecular Formula: C₁₈H₁₉ClN₄O
Molecular Weight: 342.82
Target: Dopamine Receptor; mAChR; Drug Metabolite
Pathway: GPCR/G Protein; Neuronal Signaling; Metabolic Enzyme/Protease
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 : ≥ 100 mg/mL (291.70 mM)
Methanol : ≥ 28.6 mg/mL (83.43 mM)
H₂O : 1 mg/mL (2.92 mM; Need ultrasonic)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Concentration</th>
<th>Mass (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>2.9170</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>14.5849</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>29.1798</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 >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (7.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Clozapine (N-oxide) is a pharmacologically inert metabolite of Clozapine, an antipsychotic drug. Clozapine (N-oxide) is an agonist for the DREADD (Designer Receptors Exclusively Activated by Designer Drug) system[1][2]. Clozapine is a potent antagonist of dopamine. Clozapine is also a potent and selective agonist at the muscarinic M4 receptor (EC₅₀ =11 nM)[3][4].

In Vivo
After a single intraperitoneal (i.p.) injection of Clozapine N-oxide (1 mg/kg) into mice, Clozapine N-oxide (CNO)
plasma levels peak at 15 min and are very low after 2 h. Acutely administered CNO can be metabolically converted to Clozapine in other species such as human and guinea-pig. The metabolites that may form after chronic administration of CNO to DREADD-expressing mice (or other species) have not been studied systematically. However, even if back-transformation to Clozapine occurs after chronic CNO administration, it should be noted that Clozapine is a more potent (by ~10-fold) DREADD agonist than CNO itself. Moreover, confounding biological effects of potential CNO metabolites can be easily identified by including both saline- and CNO-treated WT animals in a particular DREADD study. Despite the short plasma half-life of CNO in mice, the biological effects that have been described after acute treatment of DREADD-expressing experimental animals are usually much longer (6-10 h). One possibility is that CNO tends to accumulate in tissues, although other scenarios are also feasible[1]. Using a general pharmacokinetic model for the interconversion process, the mean total clearances of Clozapine and Clozapine N-oxide (CNO) are 28.45 L/hr and 45.30 L/hr, respectively[2].

REFERENCES


