N-Desmethylclozapine

Cat. No.: HY-G0021  
CAS No.: 6104-71-8  
Molecular Formula: C₁₇H₁₇ClN₄  
Molecular Weight: 312.8  
Target: mAChR; Opioid Receptor; Drug Metabolite; Virus Protease  
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 : ≥ 50 mg/mL (159.85 mM)  
* “≥” means soluble, but saturation unknown.  

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>1 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 mg</td>
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<tr>
<td></td>
<td></td>
<td>10 mg</td>
</tr>
<tr>
<td>1 mM</td>
<td>3.1969 mL</td>
<td>15.9847 mL</td>
</tr>
<tr>
<td></td>
<td>0.6394 mL</td>
<td>3.1969 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3197 mL</td>
<td>1.5985 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  >>  40% PEG300  >>  5% Tween-80  >>  45% saline  
   Solubility: ≥ 2.5 mg/mL (7.99 mM); Clear solution  
2. Add each solvent one by one:  
   10% DMSO  >>  90% (20% SBE-β-CD in saline)  
   Solubility: ≥ 2.5 mg/mL (7.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description  
N-Desmethylclozapine is a major active metabolite of the atypical antipsychotic drug Clozapine. N-Desmethylclozapine is a potent, allosteric and partial M1 receptors agonist (EC₅₀=115 nM) and is able to potentiate hippocampal N-methyl-d-aspartate (NMDA) receptor currents through M1 receptor activation. N-Desmethylclozapine is also a δ-opioid agonist[1][2].

IC₅₀ & Target  
EC50: 115 nM (M1 receptors)[1]  
δ-opioid[2]
### In Vitro

The brain penetrant metabolite N-desmethylclozapine preferentially bound to M1 muscarinic receptors with an IC\(_{50}\) of 55 nM and was a more potent partial agonist (EC\(_{50}\), 115 nM and 50% of acetylcholine response) at this receptor than clozapine\(^1\).

N-desmethylclozapine exhibits slight agonistic effects on the M1 mAChRs, and agonistic properties at the 5-HT1A receptor in the cerebral cortex and hippocampus. This compound also behaves as an agonist at the δ-opioid receptor in the cerebral cortex and striatum\(^2\).

N-desmethylclozapine (3 μM) greatly decreases the outward current in excitatory neurons, but not in inhibitory neurons. In excitatory neurons, N-desmethylclozapine alone is more effective than either clozapine alone or the combination of clozapine and N-desmethylclozapine. The effect of N-desmethylclozapine in excitatory neurons is significantly suppressed by 0.1 μM pirenzepine and 1 μM atropine. N-desmethylclozapine, but not clozapine, suppressed K\(^+\) channels via M1 receptors in excitatory cells\(^3\).

N-desmethylclozapine leads to a decrease in TxB2 levels under unstimulated conditions as well as under TSST-1 stimulation. Clozapine, N-desmethylclozapine and CPZ possibly act on neurotransmitter systems via modulation of TxA2 or TxB2 production\(^5\).

The IC\(_{50}\)s of N-desmethylclozapine, fluoxetine hydrochloride, and salmeterol xinafoate in Huh-7 cells infected with DENV-2 are 1 μM, 0.38 μM, and 0.67 μM, respectively. The levels of NS3 are reduced in cells treated with all three inhibitors compared to DMSO treatment, suggesting that the inhibitors act at a stage prior to viral protein translation. N-Desmethylclozapine-treated cells show a >75% reduction in negative-strand RNA levels\(^6\).

### In Vivo

N-desmethylclozapine in rat and human at M2 and M4 mAChRs underlying presynaptic modulation of GABA and glutamate release, respectively. In particular, N-desmethylclozapine maybe a M2 mAChR antagonist in the rat but has no activity at this receptor in human neocortex. However, N-desmethylclozapine has an agonistic effect at M4 mAChR in the human but no such effect in the rat neocortex\(^4\).

#### REFERENCES


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

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