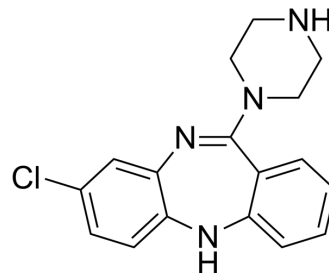


N-Desmethylclozapine

Cat. No.:	HY-G0021		
CAS No.:	6104-71-8		
Molecular Formula:	C ₁₇ H ₁₇ ClN ₄		
Molecular Weight:	312.8		
Target:	mAChR; Opioid Receptor; Drug Metabolite; Virus Protease		
Pathway:	GPCR/G Protein; Neuronal Signaling; Metabolic Enzyme/Protease; Anti-infection		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (159.85 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent		Mass		
	Concentration		1 mg	5 mg	10 mg
	1 mM		3.1969 mL	15.9847 mL	31.9693 mL
	5 mM		0.6394 mL	3.1969 mL	6.3939 mL
	10 mM		0.3197 mL	1.5985 mL	3.1969 mL

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

In Vivo

- 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
- 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 agent 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

mAChR1

δ Opioid Receptor/DOR

In Vitro

The brain penetrant metabolite N-desmethylclozapine preferentially bound to M1 muscarinic receptors with an IC₅₀ of 55 nM and was a more potent partial agonist (EC₅₀, 115 nM and 50% of acetylcholine response) at this receptor than clozapine [1].

N-desmethylclozapine exhibits slight agonistic effects on the M1 mAChR, 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 μ M) 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 μ M pirenzepine and 1 μ M 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 IC₅₀s of N-desmethylclozapine, fluoxetine hydrochloride, and salmeterol xinafoate in Huh-7 cells infected with DENV-2 are 1 μ M, 0.38 μ M, and 0.67 μ M, 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

- [1]. Li Z, et al. N-desmethylclozapine, a major metabolite of clozapine, increases cortical acetylcholine and dopamine release in vivo via stimulation of M1 muscarinic receptors. *Neuropsychopharmacology*. 2005 Nov;30(11):1986-95.
- [2]. Odagaki Y, et al. Comparative analysis of pharmacological properties of xanomeline and N-desmethylclozapine in rat brain membranes. *J Psychopharmacol*. 2016 Sep;30(9):896-912
- [3]. Sugawara Y, et al. Electrophysiological evidence showing muscarinic agonist-antagonist activities of N-desmethylclozapine using hippocampal excitatory and inhibitory neurons. *Brain Res*. 2016 Jul 1;1642:255-62
- [4]. Gigout S, et al. Different pharmacology of N-desmethylclozapine at human and rat M2 and M4 mAChRs in neocortex. *Naunyn Schmiedebergs Arch Pharmacol*. 2015 May;388(5):487-96
- [5]. Himmerich H, et al. Impact of clozapine, N-desmethylclozapine and chlorpromazine on thromboxane production in vitro. *Med Chem*. 2012 Nov;8(6):1032-8.
- [6]. Medigeshi GR, et al. N-Desmethylclozapine, Fluoxetine and Salmeterol inhibit post-entry stages of dengue virus life-cycle. *Antimicrob Agents Chemother*. 2016 Aug 29.

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