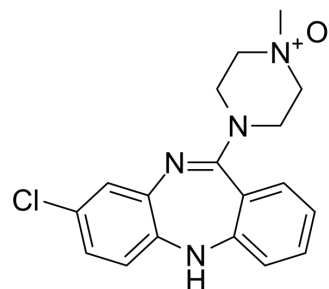


## Clozapine N-oxide

<b>Cat. No.:</b>	HY-17366		
<b>CAS No.:</b>	34233-69-7		
<b>Molecular Formula:</b>	C <sub>18</sub> H <sub>19</sub> ClN <sub>4</sub> O		
<b>Molecular Weight:</b>	342.82		
<b>Target:</b>	mAChR; Drug Metabolite; Dopamine Receptor		
<b>Pathway:</b>	GPCR/G Protein; Neuronal Signaling; Metabolic Enzyme/Protease		
<b>Storage:</b>	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)  
 H<sub>2</sub>O : 1 mg/mL (2.92 mM; Need ultrasonic)  
 \* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.9170 mL	14.5849 mL	29.1698 mL
	5 mM	0.5834 mL	2.9170 mL	5.8340 mL
	10 mM	0.2917 mL	1.4585 mL	2.9170 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 (7.29 mM); Clear solution
- 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
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (7.29 mM); Clear solution
- Add each solvent one by one: PBS  
Solubility: 2.44 mg/mL (7.12 mM); Clear solution; Need ultrasonic and warming and heat to 60°C
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline  
Solubility: ≥ 0.5 mg/mL (1.46 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)  
Solubility: ≥ 0.5 mg/mL (1.46 mM); Clear solution

### BIOLOGICAL ACTIVITY

<b>Description</b>	Clozapine N-oxide is a major metabolite of Clozapine and a human muscarinic designer receptors (DREADDs) agonist. Clozapine N-oxide activates the DREADD receptor hm3Dq and hm4Di. Clozapine N-oxide can cross the blood-brain barrier <sup>[1]</sup> [2][3][4]. Clozapine is a potent dopamine antagonist and also a potent and selective muscarinic M4 receptor (EC <sub>50</sub> =11 nM) agonist <sup>[5][6]</sup> .
<b>IC<sub>50</sub> &amp; Target</b>	Human muscarinic designer receptors (DREADDs) <sup>[1]</sup>
<b>In Vitro</b>	Clozapine N-oxide (CNO) can bind to non-DREADD receptors at concentrations required for DREADD activation, and undergoes reverse-metabolism to its parent compound clozapine, an atypical antipsychotic that acts at a variety of pharmacological targets and produces numerous physiological and behavioral effects <sup>[2]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
<b>In Vivo</b>	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. 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) <sup>[1]</sup> . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Cell Metab. 2022 Feb 1;34(2):285-298.e7.
- Nat Commun. 2022 Apr 25;13(1):2233.
- Nat Commun. 2020 Nov 27;11(1):6045.
- Nat Commun. 2020 Jun 5;11(1):2847.
- Biol Psychiatry. 2017 May 1;81(9):737-747.

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## REFERENCES

- [1]. Wess J, et al. Novel designer receptors to probe GPCR signaling and physiology. Trends Pharmacol Sci. 2013 Jul;34(7):385-92.
- [2]. Silva RR, et al. Evaluation of Functional Selectivity of NSC 170973, Clozapine, and LASSBio-579, an Experimental Compound With Antipsychotic-Like Actions in Rodents, at G Protein and Arrestin Signaling Downstream of the Dopamine D2 Receptor. Front Pharmac
- [3]. Zorn SH, et al. Clozapine is a potent and selective muscarinic M4 receptor agonist. Eur J Pharmacol. 1994 Nov 15;269(3):R1-2.
- [4]. Manvich DF, et al. The DREADD agonist clozapine N-oxide (CNO) is reverse-metabolized to clozapine and produces clozapine-like interoceptive stimulus effects in rats and mice. Sci Rep. 2018 Mar 1;8(1):3840.
- [5]. van der Peet PL, et al. Gram scale preparation of clozapine N-oxide (CNO), a synthetic small molecule actuator for muscarinic acetylcholine DREADDs. MethodsX. 2018 Mar 23;5:257-267.
- [6]. Joseph Cichon, et al. Branch-specific dendritic Ca(2+) spikes cause persistent synaptic plasticity. Nature. 2015 Apr 9;520(7546):180-5.

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

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