

## Clozapine N-Oxide

## Chemical Properties

CAS No. : 34233-69-7

Formula: C<sub>18</sub>H<sub>19</sub>ClN<sub>4</sub>O

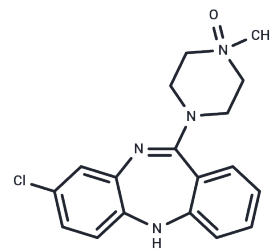
Molecular Weight: 342.82

The compound is unstable in solution. Please use soon

Storage:

Powder: -20°C for 3 years

Actual storage temperature shall be subject to the COA.



## Biological Description

Description	Clozapine N-oxide is the major metabolite of Clozapine and is blood-brain barrier permeable. Clozapine N-oxide is an agonist of DREADDs and activates the DREADD receptors hM3Dq and hM4Di. Clozapine N-oxide is also a dopamine antagonist and selective muscarinic M4 receptor agonist.
Targets(IC50)	5-HT Receptor, AChR, Dopamine Receptor, Drug Metabolite
In vitro	<p><b>METHODS:</b> hM4Di-transduced primary embryonic rat neuronal cultures were treated with Clozapine N-oxide (0.01-1000 nM), and activity on hM4Di receptors was detected by FLIPR assay.</p> <p><b>RESULTS:</b> The EC<sub>50</sub> value for Clozapine N-oxide was 8.1 nM. [1]</p> <p><b>METHODS:</b> WT and hM3Dq-transfected mouse embryoma cells ATDC5 were treated with Clozapine N-oxide (750 nM) to detect intracellular calcium signaling.</p> <p><b>RESULTS:</b> Administration of Clozapine N-oxide resulted in immediate coordinated induction of single [Ca<sup>2+</sup>]<sub>i</sub> spines in hM3Dq-ATDC5 cells, and only spontaneous [Ca<sup>2+</sup>]<sub>i</sub> signaling was observed in Clozapine N-oxide-treated WT controls. [2]</p>
In vivo	<p><b>METHODS:</b> To investigate potential effects on sleep, Clozapine N-oxide (1-10 mg/kg) was injected intraperitoneally into C57BL/6J mice.</p> <p><b>RESULTS:</b> Clozapine N-oxide altered sleep in mice. Sleep was analyzed using electroencephalography (EEG) and electromyography (EMG), revealing dose-dependent suppression of rapid eye movement (REM) sleep, changes in EEG spectral power during non-rapid eye movement (NREM) sleep, and alterations in sleep structure. [3]</p> <p><b>METHODS:</b> To investigate the effects on reward-seeking behavior, Clozapine N-oxide (0.1-10 mg/kg) was administered intraperitoneally to C57BL6/JJcl mice.</p> <p><b>RESULTS:</b> The off-target effects of commonly used doses of Clozapine N-oxide on motivated reward seeking were negligible. [4]</p>

## Solubility Information

Solubility	<p>H<sub>2</sub>O: 1 mg/mL (2.92 mM), Sonication is recommended. The compound is unstable in solution, please use soon.</p> <p>Ethanol: 10 mg/mL (29.17 mM), Sonication is recommended. The compound is unstable in solution, please use soon.</p>
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## A DRUG SCREENING EXPERT

Solubility	DMSO: 252.5 mg/mL (736.54 mM), Sonication is recommended. The compound is unstable in solution, please use soon. ( $< 1$ mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 3.3 mg/mL (9.63 mM), Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

### Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.917 mL	14.5849 mL	29.1698 mL
5 mM	0.5834 mL	2.917 mL	5.834 mL
10 mM	0.2917 mL	1.4585 mL	2.917 mL
50 mM	0.0583 mL	0.2917 mL	0.5834 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

### Reference

- Jendryka M, et al. Pharmacokinetic and pharmacodynamic actions of clozapine-N-oxide, clozapine, and compound 21 in DREADD-based chemogenetics in mice. *Sci Rep.* 2019 Mar 14;9(1):4522.
- Ma X, Li L, Li Z, et al. eEF2 in the prefrontal cortex promotes excitatory synaptic transmission and social novelty behavior. *EMBO reports.* 2022: e54543.
- Wang Y, Liu N, Ma L, et al. Ventral Hippocampal CA1 Pyramidal Neurons Encode Nociceptive Information. *Neuroscience Bulletin.* 2023: 1-17.
- McDonough RC, et al. DREADD-based synthetic control of chondrocyte calcium signaling in vitro. *J Orthop Res.* 2019 Jul;37(7):1518-1529.
- Traut J, et al. Effects of clozapine-N-oxide and compound 21 on sleep in laboratory mice. *Elife.* 2023 Mar 9;12:e84740.
- Aomine Y, et al. Clozapine N-oxide, compound 21, and JHU37160 do not influence effortful reward-seeking behavior in mice. *Psychopharmacology (Berl).* 2024 Jan;241(1):89-96.

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