Clozapine

Cat. No.: HY-14539

CAS No.: 5786-21-0

Molecular Formula: $C_{18}H_{19}ClN_4$

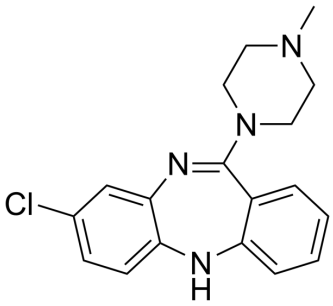
Molecular Weight: 326.82

Target: Dopamine Receptor; mAChR; Adrenergic Receptor; 5-HT Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (152.99 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.0598 mL	15.2989 mL	30.5979 mL
	5 mM	0.6120 mL	3.0598 mL	6.1196 mL
	10 mM	0.3060 mL	1.5299 mL	3.0598 mL

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 (7.65 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.65 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.65 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Clozapine (HF 1854) is an antipsychotic used for the research of schizophrenia. Clozapine has high affinity for a number of neuroreceptors. Clozapine is a potent antagonist of dopamine D2 with a K_i of 75 nM. Clozapine inhibits the muscarinic M1 receptor and serotonin 5HT2A receptor with K_is of 9.5 nM and 4 nM, respectively[1][2][3]. Clozapine is also a potent and selective agonist at the muscarinic M4 receptor (EC_{50}=11 nM)[4].

IC_{50} & Target				
	5-HT_{2A} Receptor 4 nM (Ki, Inhibitor)	5-HT_6 Receptor (Inhibitor)	5-HT_7 Receptor (Activator)	mAChR1 9.5 nM (Ki, Antagonist)

	mAChR4 11 nM (EC50, Agonist)	α2-adrenergic receptor 51 nM (Ki, Inhibitor)	D_2 Receptor 75 nM (Ki, Antagonist)

In Vitro

Clozapine (HF 1854) is a D2 receptor antagonist with a K_i of 75 nM, blocks the serotonin 5HT2A receptor with a K_i of 4 nM, inhibits the muscarinic M1 receptor with a K_i of 9.5 nM, blocks α2-adrenoceptor with a K_i value of 51 nM[1].
?Clozapine (0-1 μM; 24 h) downregulates 5-HT_6 and upregulates 5-HT_7 receptors in HeLa cells[2].
?Clozapine is a full agonist at the muscarinic M4 receptor (EC_{50}=11 nM) expressed in CHO cells[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Clozapine (HF 1854) (25 mg/kg/day; i.p.; 21 days) shows antipsychotic effects in lysergic acid diethylamide-induced psychosis mouse model[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male 129 S6/Sv mice, lysergic acid diethylamide (LSD)-induced psychosis model[3]
Dosage:	25 mg/kg/day
Administration:	Intraperitoneal injection, 21 days
Result:	Decreased head-twitch response, reduced 5-HT_{2A} mRNA, rescued induction of c-fos, but not egr-1 and egr-2.

CUSTOMER VALIDATION

- Mol Psychiatry. 2021 Jun;26(6):2514-2532.
- Eur J Pharm Sci. 2023 May 22;106475.
- Eur J Pharm Sci. 2021, 105889.

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REFERENCES

[1]. Seeman P, et al. Clozapine, a fast-off-D2 antipsychotic. ACS Chem Neurosci. 2014 Jan 15;5(1):24-9.

[2]. Zhukovskaya NL, et al. Clozapine downregulates 5-hydroxytryptamine6 (5-HT6) and upregulates 5-HT7 receptors in HeLa cells. Neurosci Lett. 2000 Jul 21;288(3):236-40.

[3]. Moreno JL, et al. Persistent effects of chronic clozapine on the cellular and behavioral responses to LSD in mice. Psychopharmacology (Berl). 2013 Jan;225(1):217-26.

[4]. Zorn SH, et al. Clozapine is a potent and selective muscarinic M4 receptor agonist. Eur J Pharmacol. 1994 Nov 15;269(3):R1-2.

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