

Product Data Sheet

Product Name: Clozapine

Cat. No.: GC17760

Chemical Properties

Cas. No. 5786-21-0

Chemical Name 3-chloro-6-(4-methylpiperazin-1-yl)-5H-benzo[b][1,4]benzodiazepine

SMILES CN1CCN(CC1)C2=C3C=CC=CC3=NC4=C(N2)C=C(C=C4)Cl

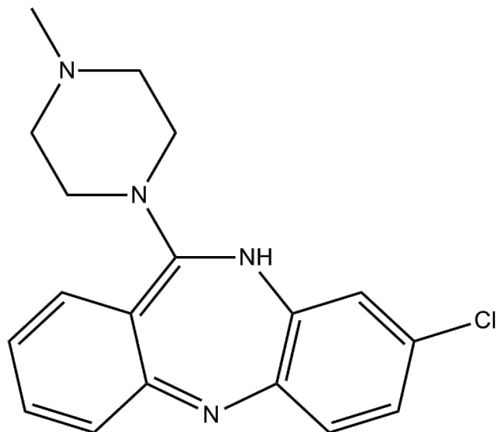
Formula $C_{18}H_{19}ClN_4$ M.Wt 326.82

Solubility 50mg/ml in DMSO Storage Store at RT

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines A549 cells

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

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Preparation Method	A549 cells were cultured in F12K medium supplemented with 10% fetal bovine serum, 100U/ml penicillin, and 100µg/ml streptomycin at 37°C with 5% CO ₂ and 95% saturated atmospheric humidity. Cells were seeded into 96-well microplates at a density of 5×10^3 cells/ml for 24h. Various concentrations of Clozapine (0, 5, 10, 15, 20, 25, and 50µM) were added to each well. At the end of the incubation period (72h at 37°C), cell viability was analyzed.
Reaction Conditions	0, 5, 10, 15, 20, 25, and 50µM; 72h
Applications	Clozapine treatment significantly induced cell death of A549 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	Male Balb/C mice
Preparation Method	Male Balb/C mice (6 weeks old) were maintained under a 12h light and 12h dark cycle at a temperature of 25°C and humidity of 50%±10%, free with water and diet. At around 11 a.m. every day, a 25mg/kg dose of Clozapine was injected intraperitoneally, and the administration was continued for 14 days. Then, the mouse heart tissues were collected for analysis.
Dosage form	25mg/kg/day for 14 days; i.p.
Applications	Clozapine treatment caused extensive inflammatory lesions within the myocardium in mice.

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References:

- [1] Yin Y C, Lin C C, Chen T T, et al. Clozapine induces autophagic cell death in non-small cell lung cancer cells[J]. Cellular Physiology and Biochemistry, 2015, 35(3): 945-956.
- [2] Wang J F, Min J Y, Hampton T G, et al. Clozapine-induced myocarditis: role of catecholamines in a murine model[J]. European journal of pharmacology, 2008, 592(1-3): 123-127.

Background

Clozapine is an antipsychotic agent that inhibits dopamine D2, muscarinic M1 receptor, and serotonin 5HT2A receptor with K_i values of 75nM, 9.5nM, and 4nM, respectively [1]. Clozapine is an agonist at the muscarinic M4 receptor (EC_{50} =11nM), producing inhibition of forskolin-stimulated cAMP accumulation [2]. Clozapine can stimulate autonomic nerve responses and activate muscarinic receptors in the salivary glands, resulting in excessive salivary secretion[3]. Clozapine has been widely used to down-regulate the 5-HT6 receptor in HeLa cells and up-regulate the 5-HT7 receptor[4].

In vitro, Clozapine treatment (50 μ M) for 24 hours induced an increase in mitochondrial volume and a decrease in mitochondrial membrane potential, as well as a reduction in ATP production in SKNSH cells[5]. Clozapine (1 μ M) pretreatment for 24 hours alleviated the production of superoxide and intracellular reactive oxygen species (ROS) in microglial cells after lipopolysaccharide (LPS) stimulation, as well as the generation of nitric oxide and TNF- α [6]. Treatment with 50 μ M Clozapine for 24 hours significantly inhibited the viability of A549 cells, induced cell cycle arrest, and upregulated the protein levels of p21 and p27[7].

In vivo, Clozapine treatment via intraperitoneal injection at a dose of 25mg/kg/day for 21 days significantly alleviated the head-twitch behavior induced by lysergic acid diethylamide (LSD) in mice, and decreased the level of 5-HT2A mRNA in the somatosensory cortex[8]. Daily intraperitoneal injection of a 25mg/kg dose of Clozapine for 14 days significantly induced myocardial inflammation in Balb/C mice and increased the level of TNF- α [9].

References:

- [1] Seeman P. Clozapine, a fast-off-D2 antipsychotic[J]. ACS chemical neuroscience, 2014, 5(1): 24-

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- [2] Zorn S H, Jones S B, Ward K M, et al. Clozapine is a potent and selective muscarinic M4 receptor agonist[J]. European Journal of Pharmacology: Molecular Pharmacology, 1994, 269(3): R1-R2.
- [3] Meltzer H Y. An overview of the mechanism of action of clozapine[J]. The journal of clinical psychiatry, 1994, 55: 47-52.
- [4] Zhukovskaya N L, Neumaier J F. Clozapine downregulates 5-hydroxytryptamine6 (5-HT6) and upregulates 5-HT7 receptors in HeLa cells[J]. Neuroscience letters, 2000, 288(3): 236-240.
- [5] Contreras-Shannon V, Heart D L, Paredes R M, et al. Clozapine-induced mitochondria alterations and inflammation in brain and insulin-responsive cells[J]. PloS one, 2013, 8(3): e59012.
- [6] Hu X, Zhou H, Zhang D, et al. Clozapine protects dopaminergic neurons from inflammation-induced damage by inhibiting microglial overactivation[J]. Journal of Neuroimmune Pharmacology, 2012, 7(1): 187-201.
- [7] Yin Y C, Lin C C, Chen T T, et al. Clozapine induces autophagic cell death in non-small cell lung cancer cells[J]. Cellular Physiology and Biochemistry, 2015, 35(3): 945-956.
- [8] Moreno J L, Holloway T, Umali A, et al. Persistent effects of chronic clozapine on the cellular and behavioral responses to LSD in mice[J]. Psychopharmacology, 2013, 225(1): 217-226.
- [9] Wang J F, Min J Y, Hampton T G, et al. Clozapine-induced myocarditis: role of catecholamines in a murine model[J]. European journal of pharmacology, 2008, 592(1-3): 123-127.

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