A 438079 hydrochloride

Cat. No.: HY-15488A

CAS No.: 899431-18-6

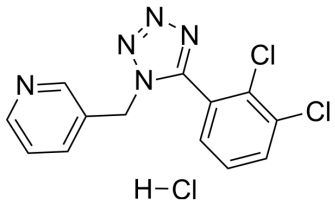
Molecular Formula: $C_{13}H_{10}Cl_3N_5$

Molecular Weight: 342.61

Target: P2X Receptor

Pathway: Membrane Transporter/Ion Channel

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (291.88 mM)

H_2O : 1 mg/mL (2.92 mM; ultrasonic and warming and heat to 80°C)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.9188 mL	14.5939 mL	29.1877 mL
5 mM	0.5838 mL	2.9188 mL	5.8375 mL
10 mM	0.2919 mL	1.4594 mL	2.9188 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 (7.30 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.30 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A 438079 (hydrochloride) is a potent, and selective $P2X_7$ receptor antagonist with pIC_{50} of 6.9.

IC_{50} & Target

P2X7 Receptor

In Vitro

In 1321N1 cells stably expressing rat $P2X_7$?receptors, A 438079 blocks BzATP-(10 μM) evoked changes in intracellular calcium concentrations with an IC_{50} of 321 nM. A 438079 is also selective for the $P2X_7$ receptor, at concentrations up to 100 μM[1].

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

In Vivo	A 438079 (80 μmol/kg, i.v.) reduces noxious and innocuous evoked activity of different classes of spinal neurons in neuropathic rats. A 438079 (100 and 300 μmol/kg, i.p.) signi?cantly raises withdrawal thresh-olds in both the SNL and CCI models[1]. Intraperitoneal injection of A 438079 (5 and 15 mg/kg) 60 min after triggering seizures reduces seizure severity and neuronal death within the hippocampus. A 438079 has superior neuroprotective effects compared with an equally dose of phenobarbital (25 mg/kg)[2]. ?A 438079 partially but signi?cantly prevents the 6-OHDA-induced depletion of striatal DA stores[3]. Pretreatment with A 438079 reduces nociceptive behaviour scores in the HC model[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Human astrocytoma cells, 1321N1, are grown to stably express rat $P2X_7$, human P2X4, P2X2a, P2X2/3, P2X1, P2Y1 and P2Y2 recombinant receptors. Agonist, BzATP, 2,3-O-(4-ben-zoylbenzoyl)-ATP or ATP-induced changes in intracellular Ca^{2+} concentrations are assessed in all of the cell lines using the Ca^{2+} chelating dye, Fluo-4, in conjunction with a Fluorometric Imaging Plate Reader. The cells are plated out the day before the experiment onto poly-D-lysine-coated black 96 well plates. After the agonist addition, changes in intracellular Ca^{2+} concentrations are recorded, per second, for 3 min. Ligands are tested at 11 half-log concentrations from 10^{-10} to 10^{-4} M. BzATP or ATP concentrations corresponds to the EC_{70} values for each receptor to enable comparison of antagonist potencies across the multiple P2 receptor subtypes. A 438079 is added to the cell plate and fluorescence data are collected for 3 min before the addition of agonist, subsequently, data are then collected for another 2 min. The pEC_{50} or pIC_{50} values are derived from a single curve fit. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	To confirm A 438079 reach the brain after systemic administration, P10 rat pups are injected with 5 mg/kg A 438079 and killed either 10 min, 30 min, or 2 h later (n=4 per group). Blood samples are centrifuged at 1000×g for 10 min to isolate the plasma. Samples are analyzed using liquid chromatography-mass spectrometry (LC-MS/MS) by a service provider. Briefly, protein is precipitated from 50 μL aliquots of the individual plasma or brain tissue homogenate, and A 438079 is quantified by LC-MS/MS from a five-point standard curve. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Brain, Behavior, and Immunity. 2020 Aug;88:507-514.
- Cancer Immunol Res. 2020 Nov;8(11):1426-1439.
- Neural Regen Res. 2021 Aug;16(8):1582-1591.
- Int J Mol Sci. 2022 May 17;23(10):5586.
- Front Mol Neurosci. 2018 Nov 6;11:401.

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REFERENCES

[1]. McGaraughty S, et al. P2X7-related modulation of pathological nociception in rats. Neuroscience. 2007 Jun 8;146(4):1817-28.

[2]. Mesuret G, et al. CNS Neurosci Ther. 2014 Jun;20(6):556-64.

[3]. Marcellino D, et al. On the role of P2X(7) receptors in dopamine nerve cell degeneration in a rat model of Parkinson's disease: studies with the P2X(7) receptor antagonist A-438079. J Neural Transm (Vienna). 2010 Jun;117(6):681-7.

[4]. Martins JP, et al. The role of P2X7 purinergic receptors in inflammatory and nociceptive changes accompanying cyclophosphamide-induced haemorrhagic cystitis in mice. Br J Pharmacol. 2012 Jan;165(1):183-96.

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