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产品名称: 3-[[5-(2,3-二氯苯基)-1H-四唑-1-基]甲基]吡啶  
产品别名: A 438079

生物活性:	
Description	A 438079 is a potent, and selective P2X <sub>7</sub> receptor antagonist with pIC <sub>50</sub> of 6.9.
IC <sub>50</sub> & Target	pIC <sub>50</sub> : 6.9 (P2X <sub>7</sub> receptor)
In Vitro	In 1321N1 cells stably expressing rat P2X <sub>7</sub> receptors, A 438079 blocks BzATP-(10 μM) evoked changes in intracellular calcium concentrations with an IC <sub>50</sub> of 321 nM. A 438079 is also selective for the P2X <sub>7</sub> receptor, at concentrations up to 100 μM[1].
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.) significantly 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 significantly prevents the 6-OHDA-induced depletion of striatal DA stores[3]. Pretreatment with A 438079 reduces nociceptive behaviour scores in the HC model[4].
Solvent&Solubility	<b>In Vitro:</b> H <sub>2</sub> O : 0.2 mg/mL (0.65 mM; Need ultrasonic)
References	[1]. McGaraughty S, et al. P2X <sub>7</sub> -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 P2X <sub>7</sub> purinergic receptors in inflammatory and nociceptive changes accompanying cyclophosphamide-induced haemorrhagic cystitis in mice. Br J Pharmacol. 2012 Jan;165(1):183-96.
实验参考:	
Animal Administration	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. [2]
	Human astrocytoma cells, 1321N1, are grown to stably express rat P2X <sub>7</sub> , human P2X <sub>4</sub> , P2X <sub>2a</sub> , P2X <sub>2/3</sub> , P2X <sub>1</sub> , P2Y <sub>1</sub> and P2Y <sub>2</sub> recombinant receptors. Agonist, BzATP, 2,3-O-(4-ben-zoylbenzoyl)-ATP or ATP-induced changes in intracellular Ca <sup>2+</sup> concentrations are assessed in all of the cell lines using the Ca <sup>2+</sup> 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



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<b>Kinase Assay</b>	Ca <sup>2+</sup> concentrations are recorded, per second, for 3 min. Ligands are tested at 11 half-log concentrations from 10 <sup>-10</sup> to 10 <sup>-4</sup> M. BzATP or ATP concentrations corresponds to the EC <sub>70</sub> 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 <sub>50</sub> or pIC <sub>50</sub> values are derived from a single curve fit. [1]
<b>References</b>	<p>[1]. McGaraughty S, et al. P2X7-related modulation of pathological nociception in rats. Neuroscience. 2007 Jun 8;146(4):1817-28.</p> <p>[2]. Mesuret G, et al. CNS Neurosci Ther. 2014 Jun;20(6):556-64.</p> <p>[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.</p> <p>[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.</p>

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