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产品名称：3-[[5-(2,3-Dichlorophenyl)-1H-tetrazol-1-yl]methyl]pyridine Hydrochloride
产品别名：A 438079 hydrochloride

生物活性：

Description	A 438079 (hydrochloride) is a potent, and selective P2X7 receptor antagonist with pIC50 of 6.9.
IC_{50} & Target	pIC50: 6.9
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

In Vitro:

H_2O : ≥ 350 mg/mL (1021.57 mM)

DMSO : ≥ 100 mg/mL (291.88 mM)

* "≥" 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (7.30 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.30 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (7.30 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (7.30 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (7.30 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.30 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

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

References	[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.