上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：N-[1-[[(氰基氨基)(5-喹啉亚氨基)甲基]氨基]-2,2-二甲基丙基]-3,4-二甲氧基苯乙酰胺
产品别名：A-740003

生物活性：

Description	A-740003 is a potent, selective and competitive P2X7 receptor antagonist with IC50 values are 18 and 40 nM for rat and human P2X7 receptors, respectively.
IC_{50} & Target	IC50: 18 nM (rat P2X7 receptor), 40 nM (human P2X7 receptor)
In Vitro	A 438079 or A 740003 (10 μM) significantly blocks the sustained phase of the BzATP-induced response[1]. A-740003 infusion reduces SE-induced TNF-α expression in dentate granule cells. A-740003 infusions increases SE-induced neuronal death[2]. A-740003 and A-438079 show significantly greater potency in blocking P2X7 receptor activation across all species compared with other antagonists. A-740003 and A-438079 show greater activity at rat and human, as compared with mouse P2X7 receptors[3]. A-740003 potently blocks agonist-evoked IL-1β release with (IC50=156 nM) and pore formation (IC50=92 nM) in differentiated human THP-1 cells[4].
In Vivo	Systemic administration of A-740003 produces dose-dependent antinociception in a spinal nerve ligation model (ED50=19 mg/kg i.p.) in the rat. A-740003 also attenuates tactile allodynia in two other models of neuropathic pain, chronic constriction injury of the sciatic nerve and vincristine-induced neuropathy. In addition, A-740003 effectively reduces thermal hyperalgesia observed following intraplantar administration of carrageenan or complete Freund's adjuvant (ED50=38-54 mg/kg i.p.). A-740003 is ineffective in attenuating acute thermal nociception in normal rats and does not alter motor performance at analgesic doses[4].
Solvent&Solubility	***In Vitro:*** **DMSO : 50 mg/mL** (**105.36 mM;** Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1073 mL	10.5363 mL	21.0726 mL
5 mM	0.4215 mL	2.1073 mL	4.2145 mL
10 mM	0.2107 mL	1.0536 mL	2.1073 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 (5.27 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.27 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。
References	[1]. Grol MW, et al. P2X?-mediated calcium influx triggers a sustained, PI3K-dependent increase in metabolic acid production by osteoblast-like cells. Am J Physiol Endocrinol Metab. 2012 Mar 1;302(5):E561-75. [2]. Kim JE, et al. P2X7 receptor activation ameliorates CA3 neuronal damage via a tumor necrosis factor-α-mediated pathway in the rat hippocampus following status epilepticus. J Neuroinflammation. 2011 Jun 2;8:62. [3]. Donnelly-Roberts DL, et al. Mammalian P2X7 receptor pharmacology: comparison of recombinant mouse, rat and human P2X7 receptors.Br J Pharmacol. 2009 Aug;157(7):1203-14. Epub 2009 Jun 22. [4]. Honore P, et al. A-740003 [N-(1-{[(cyanoimino)(5-quinolinylamino) methyl]amino}-2,2-dimethylpropyl)-2-(3,4-dimethoxyphenyl)acetamide], a novel and selective P2X7 receptor antagonist, dose-dependently reduces neuropathic pain in the rat. J Pharmacol Exp Ther. 2006 Dec;319(3):1376-85. Epub 2006 Sep 18. [5]. Y. H. Gao, et al. Effect of electroacupuncture on the cervicospinal P2X7 receptor/fractalkine/CX3CR1 signaling pathway in a rat neck-incision pain model. Purinergic Signal. 2017 Jun;13(2):215-225.

实验参考：

Animal Administration	The response to acute thermal stimulation is determined using a commercially available paw thermal stimulator. Rats are placed individually in Plexiglas cubicles mounted on a glass surface maintained at 30°C and allowed a 30-min habituation period. A thermal stimulus, in the form of radiant heat emitted from a focused projection bulb, is then applied to the plantar surface of each hind paw. In each test session, each rat is tested in three sequential trials at approximately 5-min intervals. Paw-withdrawal latencies (PWLs) are calculated as the median of the two shortest latencies. An assay cut off is set at 20.5 s. A-740003 is injected i.p. 30 min before testing for acute thermal pain. [4]
References	[1]. Grol MW, et al. P2X?-mediated calcium influx triggers a sustained, PI3K-dependent increase in metabolic acid production by osteoblast-like cells. Am J Physiol Endocrinol Metab. 2012 Mar 1;302(5):E561-75. [2]. Kim JE, et al. P2X7 receptor activation ameliorates CA3 neuronal damage via a tumor necrosis factor-α-mediated pathway in the rat hippocampus following status epilepticus. J Neuroinflammation. 2011 Jun 2;8:62. [3]. Donnelly-Roberts DL, et al. Mammalian P2X7 receptor pharmacology: comparison of recombinant mouse, rat and human P2X7 receptors.Br J Pharmacol. 2009 Aug;157(7):1203-14. Epub 2009 Jun 22. [4]. Honore P, et al. A-740003 [N-(1-{[(cyanoimino)(5-quinolinylamino) methyl]amino}-2,2-dimethylpropyl)-2-(3,4-dimethoxyphenyl)acetamide], a novel and selective P2X7 receptor antagonist, dose-dependently reduces neuropathic pain in the rat. J Pharmacol Exp Ther.

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