A-740003

Cat. No.: HY-50697

CAS No.: 861393-28-4

Molecular Formula: $C_{26}H_{30}N_6O_3$

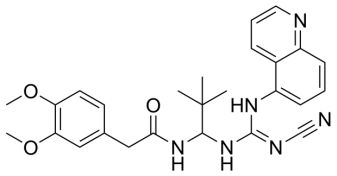
Molecular Weight: 474.55

Target: P2X Receptor

Pathway: Membrane Transporter/Ion Channel

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (105.36 mM; Need ultrasonic)

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

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 (5.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A-740003 is a potent, selective and competitive P2X7 receptor antagonist with IC_{50} values are 18 and 40 nM for rat and human P2X7 receptors, respectively.

IC_{50} & Target

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 (IC_{50}=156 nM) and pore formation (IC_{50}=92 nM) in differentiated human THP-1 cells[4].

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

In Vivo	Systemic administration of A-740003 produces dose-dependent antinociception in a spinal nerve ligation model (ED_{50}=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 (ED_{50}=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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [4]	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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Dis. 2019 Jan 8;10(1):20.
- Biochim Biophys Acta Mol Basis Dis. 2023 Sep 23;166895.
- Commun Biol. 2023 Jun 15;6(1):642.
- Prog Neuropsychopharmacol Biol Psychiatry. 2023 May 18;110796.
- Vet Res. 2022 Sep 5;53(1):69.

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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.

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

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