AZD9056 hydrochloride

Cat. No.: HY-19427A

CAS No.: 345303-91-5

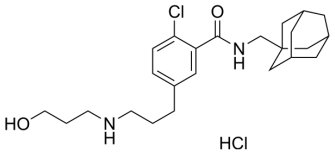
Molecular Formula: $C_{24}H_{36}Cl_2N_2O_2$

Molecular Weight: 455.46

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 : 50 mg/mL (109.78 mM; Need ultrasonic)
H_2O : 1.67 mg/mL (3.67 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Mass / Solvent / Concentration	1 mg	5 mg	10 mg
1 mM	2.1956 mL	10.9779 mL	21.9558 mL
5 mM	0.4391 mL	2.1956 mL	4.3912 mL
10 mM	0.2196 mL	1.0978 mL	2.1956 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 (5.49 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.49 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.49 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AZD9056 hydrochloride is a selective orally active inhibitor of P2X7 which plays a significant role in inflammation and pain-causing diseases.

IC_{50} & Target

P2X7 Receptor

In Vitro

The antagonist AZD9056 blocks P2X7 receptors with an IC_{50} of 11.2 nM in HEK-hP2X7 cell line, indicating a high selectivity of the antagonist for the P2X7 receptor. The P2X7-receptor antagonist AZD9056 has a clear inhibitory effect (IC_{50}=1-3 μM) in mouse microglia BV2 cells[1]. AZD9056 is an inhibitor of BCRP and weakly inhibits BCRP-mediated transport of methotrexate

	(IC_{50}=92 μM)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Treatment with AZD9056 exerts pain-relieving and anti-inflammatory effects. The upregulated expression of interleukin (IL)-1β, IL-6, tumor necrosis factor-α (TNF-α), matrix metalloproteinase-13 (MMP-13), substance P (SP) and prostaglandin E2 (PGE2) which is induced by MIA in cartilage tissues is reversed by AZD9056[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	AZD9056 is used as a stock solution in DMSO. Final DMSO concentrations in experiments does not exceed 1.0% (v/v). The effect of agonists on cell viability is assessed in parental HEK293 cells and HEK–hP2X7 cells using the CellTiter-Blue assay. For inhibition experiments, AZD9056 is added to the cells at concentrations up to 10 μmol/L 5 min prior to the addition of ATP (2.5 mM) or BzATP (0.25 mM). After incubation for 30 min at 37°C, an aliquot (20 μL) of the prewarmed CellTiter-Blue reagent is added. Samples are incubated for 1 h at 37°C. Fluorescence signals are measured[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Rats: To reveal the molecular mechanisms of action of P2X7R in articular cartilage in OA-induced pain and inflammation, the antagonist of P2X7R AZD9056 is used. Wistar rats are administered (by intra-articular injection) monosodium iodoacetate (MIA), and the rats with OA are then treated with the P2X7R antagonist, AZD9056[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Front Immunol. 2021 Jan 8;11:602016.

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REFERENCES

[1]. Seeland S, et al. ATP-induced cellular stress and mitochondrial toxicity in cells expressing purinergic P2X7 receptor. Pharmacol Res Perspect. 2015 Mar;3(2):e00123.

[2]. Elsby R, et al. In vitro risk assessment of AZD9056 perpetrating a transporter-mediated drug-drug interaction with methotrexate. Eur J Pharm Sci. 2011 May 18;43(1-2):41-9.

[3]. Hu H, et al. Blocking of the P2X7 receptor inhibits the activation of the MMP-13 and NF-κB pathways in the cartilage tissue of rats with osteoarthritis. Int J Mol Med. 2016 Dec;38(6):1922-1932.

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