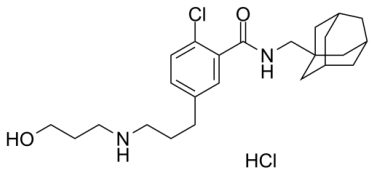
Data Sheet

Product Name:	AZD9056 (hydrochloride)
Cat. No.:	CS-6172
CAS No.:	345303-91-5
Molecular Formula:	C24H36Cl2N2O2
Molecular Weight:	455.46
Target:	P2X Receptor
Pathway:	Membrane Transporter/Ion Channel
Solubility:	DMSO : ≥ 34 mg/mL (74.65 mM)



BIOLOGICAL ACTIVITY:

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

PROTOCOL (Extracted from published papers and Only for reference)

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]. **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].

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.

CAIndexNames:

Benzamide, 2-chloro-5-[3-[(3-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.13,7]dec-1-ylmethyl)-, hydrochloride (1:1)

SMILES:

O=C(C1=CC(CCCNCCCO)=CC=C1Cl)NCC2(C[C@H](C3)C4)C[C@H]4C[C@H]3C2.Cl

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

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