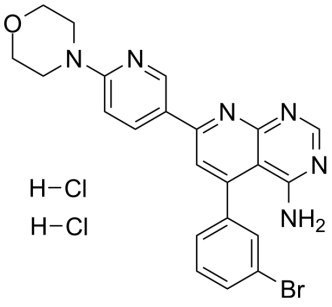
ABT-702 dihydrochloride

Cat. No.:	HY-103161
CAS No.:	1188890-28-9
Molecular Formula:	$C_{22}H_{21}BrCl_2N_6O$
Molecular Weight:	536
Target:	Adenosine Kinase
Pathway:	Metabolic Enzyme/Protease; Neuronal Signaling
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 33.33 mg/mL (62.18 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.8657 mL	9.3284 mL	18.6567 mL
5 mM	0.3731 mL	1.8657 mL	3.7313 mL
10 mM	0.1866 mL	0.9328 mL	1.8657 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 (4.66 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.66 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ABT-702 dihydrochloride is a potent adenosine kinase (AK) inhibitor (IC_{50}=1.7 nM).

IC_{50} & Target

IC50: 1.7 nM (Adenosine kinase, AK)[1]

In Vitro

ABT-702 is an orally effective adenosine kinase inhibitor that has several orders of magnitude selectivity over other sites of adenosine (ADO) interaction (A_1, A_{2A}, A_3 receptors, ADO transporter, and ADO deaminase). ABT-702 is equipotent (IC_{50} =1.5±0.3 nM) in inhibiting native human AK (placenta), two human recombinant isoforms (AK_{long} and AK_{short}), and AK from monkey, dog, rat, and mouse brain. ABT-702 potently inhibits the activity of rat brain cytosolic AK in a concentration-

dependent manner with an IC_{50} value of 1.7 nM. ABT-702 also potently inhibits AK activity in intact cultured IMR-32 human neuroblastoma cells (IC_{50}=51 nM), indicating that ABT-702 can penetrate the cell membrane and potently inhibit AK at its intracellular site[1].

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

In Vivo

ABT-702 significantly reduces acute thermal nociception in a dose-dependent manner after both intraperitoneal (ED_{50}=8 μmol/kg i.p.) and oral (ED_{50}=65 μmol/kg p.o.) administration in the mouse hot-plate test. Consistent with its antinociceptive effects in the hot-plate assay, ABT-702 also produces dose-dependent antinociceptive effects (ED_{50}=2 μmol/kg i.p.) in the abdominal constriction assay. ABT-702 exhibits full efficacy in this model of persistent chemical pain[1]. Rats are given an intraperitoneal injection of the adenosine A_1 receptor antagonist DPCPX (3 mg/kg), ABT-702 (3 mg/kg), or vehicle 10 minutes prior to an intravenous injection of 2-^{18}F-fluorodeoxy-D-glucose (FDG) (FDG, 15.4±0.7 MBq per rat). Rats are then subjected to a 15 minute static positron emission tomography (PET) scan. Reconstructed images are normalized to FDG PET template for rats and standard uptake values (SUVs) are calculated. To examine the regional effect of active treatment compared to vehicle, statistical parametric mapping analysis is performed. Whole-brain FDG uptake is not affected by drug treatment. Significant regional hypometabolism is detected, particularly in cerebellum, of DPCPX and ABT-702 treated rats, relative to vehicle-treated rats. Thus, endogenous adenosine can affect FDG accumulation although this effect is modest in quiescent rats. Body weight (316.8±28.4 g; mean±SD) and blood glucose (5.5±1.7 mM) are not significantly different among three groups. Whole-brain PET SUV values are 1.6±0.4, 1.6±0.6, and 1.8±0.6 for vehicle, ABT-702, and DPCPX-treated rats, respectively ($F(2,9)=0.298$, $P=0.75$). statistical parametric mapping (SPM) analysis reveals significant regional hypometabolism in the cerebellum, mesencephalic region, and medulla in the ABT-702-treated rats compared to the vehicle-treated rats[2].

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

PROTOCOL

Animal Administration [2]

Rats[2]

Rats are fasted for 16 hours prior to use. At the beginning of the experiment, each rat is weighed, and then anesthetized using 5% isoflurane for induction and 2.5% for maintenance. A blood sample from tail vein is collected for a fasting blood glucose determination using a standard glucometer. Rats are then given an intraperitoneal (i.p.) injection of DPCPX (3 mg/kg, n=4), ABT-702 (3 mg/kg, n=4), or an equivalent volume of vehicle (15% dimethyl sulfoxide, 15% cremophor EL, 70% saline, n=4) to manipulate the effect of endogenous adenosine on neuronal activities. Ten minutes after i.p. injection, rats are administered FDG (15.4±0.7 MBq) in 0.3-0.5 mL saline by intravenous (i.v.) tail vein injection. Rats are allowed to recover from anesthesia after the FDG injection but are reanesthetized for 15-minute-static PET scan with the head in the center of the field of view. All images are reconstructed[2].

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

REFERENCES

[1]. Jarvis MF, et al. ABT-702 (4-amino-5-(3-bromophenyl)-7-(6-morpholinopyridin-3-yl)pyrido[2, 3-d]pyrimidine), a novel orally effective adenosine kinase inhibitor with analgesic and anti-inflammatory properties: I. In vitro characterization and acute antinociceptive effects in the mouse. J Pharmacol Exp Ther. 2000 Dec;295(3):1156-64.

[2]. Parkinson FE, et al. The Effect of Endogenous Adenosine on Neuronal Activity in Rats: An FDG PET Study. J Neuroimaging. 2016 Jul;26(4):403-5.

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