Product Data Sheet

Product Name: ABT 702 dihydrochloride
Cat. No.: GC13416

Chemical Properties

Cas. No.	1188890-28-9		
Chemical Name	5-(3-bromophenyl)-7-(6-morpholinopyridin-3-yl)pyrido[2,3-d]pyrimidin-4-amine dihydrochloride		
SMILES	BrC1=CC=CC(C2=CC(C3=CN=C(N4CCOCC4)C=C3)=NC5=NC=NC(N)=C25)=C1.Cl.Cl		
Formula	$C_{22}H_{19}N_6OBr.2HCl$	M.Wt	536.26
Solubility	≥ 107.2 mg/mL in DMSO, ≥ 9.84 mg/mL in EtOH with ultrasonic and warming	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	ABT 702 dihydrochloride		

Protocol

Cell experiment [1]:

Cell lines	The mouse micrgolial cell line EOC-20
Preparation Method	Cells were pretreated with ABT 702 (20μM) for 30min at 37°C before LPS (50ng/ml for 24h) treatment. Subsequently, Western blotting and immunofluorescence detection were performed.
Reaction Conditions	20μM; 30min
Applications	The treatment of retinal microglia cells with LPS triggered a prominent increase in TNF-α release and activated MAP Kinase signaling. ABT 702 treatment significantly attenuated p-ERK1/2 and p-P38 activation in LPS induced activated mouse microglia.

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Animal experiment [2]:

Animal models	Rats
Preparation Method	All rats were fasted for 16 hours prior to use. Anesthetized using 5% isoflurane for induction and 2.5% for maintenance. Rats were then given an intraperitoneal (i.p.) injection of the adenosine A1 receptor antagonist DPCPX (3mg/kg), the adenosine kinase inhibitor ABT 702 (3mg/kg), or an equivalent volume of vehicle to manipulate the effect of endogenous adenosine on neuronal activities. Ten minutes after i.p. injection, rats were administered FDG (15.4±0.7MBq) in 0.3-0.5ml saline by intravenous (i.v.) tail vein injection. Rats were allowed to recover from anesthesia and reanesthetized for 15-minute-static PET scan. Reconstructed PET images were spatially normalized to FDG PET template for rats and standard uptake values (SUVs) were calculated.
Dosage form	3mg/kg; 10min; i.p.
Applications	ABT 702 inhibit FDG accumulation in rat cerebellum, pons, mesencephalic region and medulla compared to the vehicle-treated rats, this revealed significant regional hypometabolism.

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References:
[1]. Ahmad S, Elsherbiny NM, Bhatia K, Elsherbini AM, Fulzele S, Liou GI. Inhibition of adenosine kinase attenuates inflammation and neurotoxicity in traumatic optic neuropathy. *J Neuroimmunol*. 2014;277(1-2):96-104.
[2]. Parkinson FE, Paul S, Zhang D, Mzengeza S, Ko JH. The Effect of Endogenous Adenosine on Neuronal Activity in Rats: An FDG PET Study. *J Neuroimaging*. 2016;26(4):403-405.

Background

ABT 702 dihydrochloride is a novel, potent non-nucleoside adenosine kinase (AK) inhibitor with an IC_{50} values of 1.7nM [1]. ABT 702 increases extracellular adenosine concentrations at sites of tissue trauma thereby attenuates neuronal response [1]. ABT 702 has therapeutic potential as analgesic and anti-inflammatory agents [1].

In vitro, treatment of ABT 702 (3μM) to the isolated neonatal rat spinal cord for 20 minutes, gradually decreased slow ventral root potentials (VRP) with a slight decline in monosynaptic

reflex potentials (MSR), leading to the inhibition of spinal nociceptive transmission [2]. ABT 702 highly inhibited AK activity in IMR-32 cells with an IC_{50} value of 1.7nM [1]. ABT 702 (20μM) attenuated p-ERK1/2 and p-P38 activation in LPS induced activated mouse microglia cells (EOC-20) [3].

In vivo, ABT 702 reduced acute somatic nociception in the mouse hot-plate assay following oral administration of 65μmol/kg or intraperitoneal injection of 8μmol/kg [1]. ABT 702 decreased regional FDG levels in the rat cerebellum, pons, mesencephalic region and medulla, via intraperitoneal (i.p.) injection of 3mg/kg [4]. Subcutaneous injection of ABT 702 (10mg/kg) for 1 hour significantly reduced the electrical evoked responses of spinal neurons in spiral never ligation (SNL) rats, thus demonstrating effective analgesia [5].

References:
[1] Jarvis MF, Yu H, Kohlhaas K, 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;295(3):1156-1164.
[2] Otsuguro K, Tomonari Y, Otsuka S, Yamaguchi S, Kon Y, Ito S. An adenosine kinase inhibitor, ABT-702, inhibits spinal nociceptive transmission by adenosine release via equilibrative nucleoside transporters in rat. *Neuropharmacology*.2015;97:160-170.
[3] Ahmad S, Elsherbiny NM, Bhatia K, Elsherbini AM, Fulzele S, Liou GI. Inhibition of adenosine kinase attenuates inflammation and neurotoxicity in traumatic optic neuropathy. J Neuroimmunol. 2014;277(1-2):96-104.
[4] Parkinson FE, Paul S, Zhang D, Mzengeza S, Ko JH. The Effect of Endogenous Adenosine on Neuronal Activity in Rats: An FDG PET Study. *J Neuroimaging*. 2016;26(4):403-405.
[5] Suzuki R, Stanfa LC, Kowaluk EA, Williams M, Jarvis MF, Dickenson AH. The effect of ABT-702, a novel adenosine kinase inhibitor, on the responses of spinal neurones following carrageenan inflammation and peripheral nerve injury. *Br J Pharmacol*. 2001;132(7):1615-1623.

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