5-Iodotubercidin

Cat. No.: HY-15424

CAS No.: 24386-93-4

Molecular Formula: $C_{11}H_{13}IN_4O_4$

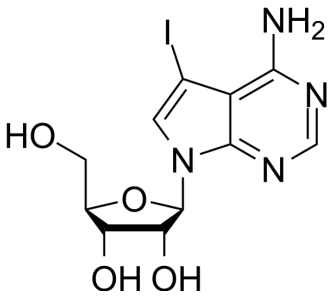
Molecular Weight: 392

Target: Adenosine Kinase

Pathway: Metabolic Enzyme/Protease; Neuronal Signaling

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (63.78 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5510 mL	12.7551 mL	25.5102 mL
	5 mM	0.5102 mL	2.5510 mL	5.1020 mL
	10 mM	0.2551 mL	1.2755 mL	2.5510 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 (6.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.38 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (6.38 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.38 mM); Clear solution
6. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: ≥ 0.5 mg/mL (1.28 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

5-Iodotubercidin (NSC 113939), an ATP mimetic, is a potent adenosine kinase inhibitor with an IC_{50} of 26 nM. 5-

	Iodotubercidin (NSC 113939) initiates glycogen synthesis in isolated hepatocytes by causing inactivation of phosphorylase and activation of glycogen synthase. 5-Iodotubercidin (NSC 113939) also inhibits CK1, insulin receptor tyrosine kinase, phosphorylase kinase, PKA, CK2, PKC and Haspin[1][2][3].
IC_{50} & Target	IC50: 26 nM (adenosine kinase)
In Vitro	5-Iodotubercidin (NSC 113939) inhibits CK1, insulin receptor tyrosine kinase, phosphorylase kinase, PKA, CK2 and PKC, and the IC_{50} values are 0.4, 3.5, 5-10, 5-10, 10.9 and 27.7 μM respectively[1]. 5-Iodotubercidin (20 μM) causes an important decrease in ATP concentration, and a concomitant smaller increase in AMP concentration. 5-Iodotubercidin decreases the activity of ACC and the rates of synthesis of fatty acids and cholesterol. In line with the iodotubercidin-mediated inhibition of ACC, 5-iodotubercidin induces a marked decrease in the intracellular concentration of malonyl-CoA[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	5-Iodotubercidin (1 mL/kg, i.p.) is in agreement with activity observed against bicuculline-induced seizures following local administration of the AKI into the prepiriform cortex[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	AK activity is measured in a radiochemical assay. The final reaction volume is 100 μL and contained 70 mM Tris-maleate (pH 7.0), 0.1% (w/v) bovine serum albumin, 1.0 mM $MgCl_2$, 1.0 mM ATP, 1.0 μM [U-^{14}C]adenosine (400-600 mCi/mmol) and various inhibitor concentrations. Inhibitors are prepared as 10 mM stock solutions in DMSO. The final DMSO concentration in the assay is 5% (v/v). Eleven different concentration of the test solutions ranging from 0.001 to 10.0 μM are utilized to determine a dose response curve of the inhibition of the enzyme. Reactions are started by adding the appropriate amount of purified human recombinant AK and incubated for 20 min at 37°C. The reactions are terminated by addition of the potent AKI GP3269. A 30-μL aliquot of each reaction is spotted on DEAE cellulose filter paper (cut in squares of appr 1×1 cm) and air-dried for 30 min. The dry filters are then washed for 3 min in deionized water to remove residual [U-^{14}C]adenosine, rinsed with ethanol and dried at 90°C for 20 min. The filter papers are counted in 5.5 mL of Ready Safe liquid scintillation cocktail using a Beckman LS3801 scintillation counter. Control AK activity is determined from the amount of [^{14}C]AMP formed in the presence of 5% DMSO. The concentration of inhibitor required to inhibit 50% of the AK activity (IC_{50}) is determined graphically from plots of inhibitor concentration versus percent (%) control enzyme activity. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [4]	HeLa cells are grown in DME supplemented with 10% fetal bovine serum (FBS) and 2 mM l-glutamine. Nocodazole is used at a concentration of 3.3 μM unless differently specified. Thymidine (2.5 mM) is used in the asssay. For transfection, FuGENE 6 Transfection Agent is used at a 3:1 ratio with plasmid DNA. Cells are analyzed 24-48 h after transfection. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Male SA rats (100-150 g) are maintained on a 12:12 light:dark cycle in temperaturecontrolled facilities with free access to food and water. One hour prior to seizure testing, the animals are injected intraperitoneally (1 mL/kg) with DMSO vehicle or with test compound dissolved in DMSO. At the time of the test, an electrolyte solution (2% lidocaine in 0.9% sodium chloride) is applied to the eyes. Maximal electroshock seizures are induced by administering a 60-Hz current of 150 mA for 0.2 s via corneal electrodes, using a Wahlquist Model H stimulator. The endpoint measured is suppression of hindlimb tonic extension (HTE) and expressed as percentage of animals in which the response is inhibited. At this supramaximal stimulation level, virtually 100% of control (vehicle-treated) animals show HTE. ED_{50} values are calculated from a dose-response curve using probit analysis. The N for the screening doses is 6-8; doseresponse determinations are conducted with at least 5 animals/dose. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Stem Cell. 2023 Apr 6;30(4):450-459.e9.
- Sci Transl Med. 2020 May 6;12(542):eaba0769.
- Cell Rep. 2023 May 23;42(6):112547.
- Front Mol Neurosci. 2016 Jun 3;9:42.
- Sci Rep. 2017 Feb 21;7:42885.

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REFERENCES

[1]. Massillon D, et al. Identification of the glycogenic compound 5-iodotubercidin as a general protein kinase inhibitor. Biochem J. 1994 Apr 1;299 (Pt 1):123-8.

[2]. Ugarkar BG, et al. Adenosine kinase inhibitors. 1. Synthesis, enzyme inhibition, and antiseizure activity of 5-iodotubercidin analogues. J Med Chem. 2000 Jul 27;43(15):2883-93.

[3]. García-Villafranca J, et al. Effects of 5-iodotubercidin on hepatic fatty acid metabolism mediated by the inhibition of acetyl-CoA carboxylase. Biochem Pharmacol. 2002 Jun 1;63(11):1997-2000.

[4]. De Antoni A, et al. A small-molecule inhibitor of Haspin alters the kinetochore functions of Aurora B. J Cell Biol. 2012 Oct 15;199(2):269-84.

[5]. Acharya MM, et al. Adenosine Kinase Inhibition Protects against Cranial Radiation-Induced Cognitive Dysfunction. Front Mol Neurosci. 2016 Jun 3;9:42.

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