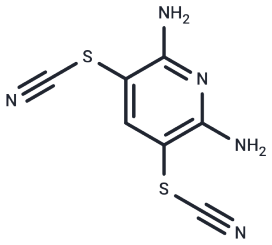
Data Sheet (Cat.No.T1862)

TargetMol

PR-619

Chemical Properties



CAS No. : 2645-32-1

Formula: C7H5N5S2

Molecular Weight: 223.28

Storage: Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PR-619 (2,6-Diamino-3,5-dithiocyanopyridine) is a DUB inhibitor that inhibits USP2/4/5/7/8 (EC50=7.2/3.93/8.61/6.86/4.9 μM). PR-619 induces endoplasmic reticulum stress and activates autophagy.
Targets(IC50)	Apoptosis,Autophagy,DUB
In vitro	**METHODS**: HEK293T cells were treated with PR-619 (5-50 μM) for 6 h. Target protein expression levels were measured by Western Blot. **RESULTS**: PR-619 interfered with probe labeling at concentrations of 5 μM and above. PR-619 inhibited probe labeling of USP7, but also targeted many other DUBs in the same concentration range, consistent with its broader inhibitory profile. [1] **METHODS**: The leukemia cell line K562 was treated with PR-619 (40 μM) for 2 h. Targeting was detected by Immunofluorescence. **RESULTS**: PR-619 induced a different distribution of TOP2A and TOP2B fluorescence signals, consisting of large signal foci. FK2 ubiquitin fluorescence signals partially overlapped with those of TOP2A and TOP2B, as well as SUMO2/3. [2]
In vivo	**METHODS**: To detect anti-tumor activity in vivo, PR-619 (10 mg/kg once daily) and cisplatin (10 mg/kg three times weekly) were intraperitoneally injected into Nude mice bearing T24 or BFTC-905 xenografts for three weeks. **RESULTS**: The combination of cisplatin and PR-619 showed the most significant antitumor effects on T24 and BFTC-905 xenograft tumors compared to monotherapy. [3]
Kinase Assay	Ub-PLA2 assay: Recombinant enzymes in 20 mM Tris-HCl, pH 8.0, 2 mM CaCl2 and 2 mM β-mercaptoethanol (DUB assay buffer) are preincubated with single doses or dose ranges of PR-619 or P22077 for 30 minutes in a 96 well plate before the addition of Ub-PLA2 and NBD C6-HPC. The liberation of a fluorescent product within the linear range of the assay is monitored at room temperature using a fluorescence plate reader. Vehicle (2%(v/v) DMSO) and 10 mM N-ethylmaleimide are included as controls. Where ≥60% inhibition is observed, EC50 values are determined using a sigmoidal dose response equation.
Cell Research	72 h hours later, 0.2 mg/mL resazurin prepared in phosphate-buffered saline is added to each well and the cells are incubated for an additional 3-6 h. The fluorescence of the resazurin reduction product is measured using Ex=535 nm and Em=590 nm filters on a fluorimeter. The EC50 values are calculated in Prism.(Only for Reference)

Solubility Information

Solubility	DMSO: 55 mg/mL (246.33 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	4.4787 mL	22.3934 mL	44.7868 mL
5 mM	0.8957 mL	4.4787 mL	8.9574 mL
10 mM	0.4479 mL	2.2393 mL	4.4787 mL
50 mM	0.0896 mL	0.4479 mL	0.8957 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Altun M, et al. Activity-based chemical proteomics accelerates inhibitor development for deubiquitylating enzymes. Chem Biol. 2011 Nov 23;18(11):1401-12.
Song P, Yang S, Hua H, et al. The regulatory protein GADD34 inhibits TRAIL-induced apoptosis via TRAF6/ERK-dependent stabilization of myeloid cell leukemia 1 in liver cancer cells. Journal of Biological Chemistry. 2019: jbc. RA118. 006029
Cowell IG, et al. The Deubiquitinating Enzyme Inhibitor PR-619 is a Potent DNA Topoisomerase II Poison. Mol Pharmacol. 2019 Nov;96(5):562-572.
Kuo KL, et al. The Deubiquitinating Enzyme Inhibitor PR-619 Enhances the Cytotoxicity of Cisplatin via the Suppression of Anti-Apoptotic Bcl-2 Protein: In Vitro and In Vivo Study. Cells. 2019 Oct 17;8(10):1268.