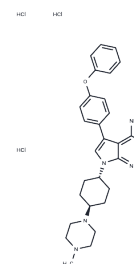


A 419259 trihydrochloride

Chemical Properties

CAS No. :	1435934-25-0
Formula:	C ₂₉ H ₃₇ Cl ₃ N ₆ O
Molecular Weight:	592
Storage:	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	A 419259 trihydrochloride (RK 20449 trihydrochloride) is an Src family kinases inhibitor (IC50s: 9 nM, 3 nM and 3 nM for Src, Lck and Lyn).
Targets(IC50)	Apoptosis,Src
In vitro	A-419259 inhibits K-562 cells (IC50: 0.1~0.3 μM), and Meg-01 proliferation (IC50: ~0.1 μM). A-419259 also potently induces apoptosis in K-562 cells beginning at 0.1 μM and increasing in a dose-dependent manner. PP2 inhibits Src kinase autophosphorylation in both Ph+ cell lines (K-562 and Meg-01) with an IC50 between 3 and 10 μM, while A-419259 blocks kinase activation between 0.1 and 0.3 μM. A-419259 strongly inhibits DAGM/Bcr-Abl cell proliferation in the absence of IL-3 (IC50: 0.1~0.3 μM) [1]. A-419259 inhibits overall SFK activity in K562 and other CML cell lines with an IC50 value of 0.1-0.3 μM [2].
Kinase Assay	In vitro kinase assays are performed on His(6)-tagged Lck (residues 62-509) and full-length c-Abl purified from Sf-9 cells, and commercial sources of Lyn, Src and PKC. Lck, Lyn, Src and Abl activities are measured with an ELISA-based assay. Flat bottom 96-well ELISA plates are incubated with a 200 μg/mL solution of Poly(Glu, Tyr) 4 : 1 substrate in phosphate-buffered saline (PBS) for 1 h at 37°C and then washed with PBS containing 0.1% Tween-20 (PBS-T). Inhibitor dilutions are added to the washed plates already containing the appropriate enzyme in kinase assay buffer (250 mM Mopso, pH 6.75, 10 mM MgCl ₂ , 2 mM MnCl ₂ , 2.5 mM DTT, 0.02% BSA, 2 mM Na ₃ VO ₄ , 5% DMSO, 5 μM ATP). After incubation at room temperature for 20 min, plates are washed three times with PBS-T and plate-bound phosphotyrosine is detected with an anti-phosphotyrosine-HRP antibody conjugate and subsequent color development with K-Blue reagents [1].
Cell Research	K-562 cells are grown in RPMI 1640 supplemented with 10% fetal calf serum (FCS), and 50 g/mL Gentamycin. Meg-01 cells are cultured in Vitacell modified RPMI 1640 (ATCC), supplemented with 10% FCS and 50 μg/mL Gentamycin. The human GM-CSF-dependent myeloid leukemia cell line TF-1 is grown in RPMI 1640 supplemented with 10% FCS, 50 μg/mL Gentamycin, and 1 ng/mL of recombinant human GM-CSF. DAGM murine myeloid leukemia cells are cultured in RPMI 1640 supplemented with 10% FCS, 50 μg/mL Gentamycin, and 0.5 ng/mL recombinant IL-3. Concentrated stock solutions of PP2 (5 mM) and A-419259 (2 mM) are prepared in DMSO and stored at -20°C. Cellular proliferation is measured using the Live/Dead growth assay. This assay employs calcein-AM, a fluorogenic esterase substrate that is taken up by viable cells and

Cell Research	hydrolyzed intracellularly, releasing a green fluorescent product. Briefly, 10 ⁴ cells are plated per well in 96-well plates for each day of a 4-day time course. Various concentrations of PP2, A-419259 or vehicle control are added to the wells (five wells per concentration per day) and the plates are incubated at 37°C. At each time point, one plate is centrifuged at 1500 g for 10 min to pellet the cells. Cells are washed with PBS, and calcein-AM is added to each well to a final concentration of 1 μM. Plates are incubated in the dark at room temperature for 1 h. The plates are then read at 485/530 nm (excitation/emission) using a fluorescent plate reader and data are analyzed with SoftMax Pro software [1].
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Solubility Information

Solubility	H2O: ≥53 mg/mL (89.53 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6892 mL	8.4459 mL	16.8919 mL
5 mM	0.3378 mL	1.6892 mL	3.3784 mL
10 mM	0.1689 mL	0.8446 mL	1.6892 mL
50 mM	0.0338 mL	0.1689 mL	0.3378 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

Wilson MB, et al. Selective pyrrolo-pyrimidine inhibitors reveal a necessary role for Src family kinases in Bcr-Abl signal transduction and oncogenesis. *Oncogene*. 2002 Nov 21;21(53):8075-88.

Pene-Dumitrescu T, et al. An inhibitor-resistant mutant of Hck protects CML cells against the antiproliferative and apoptotic effects of the broad-spectrum Src family kinase inhibitor A-419259. *Oncogene*. 2008 Nov 27;27(56):7055-69.

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