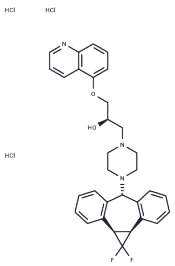
Data Sheet (Cat.No.T6018)

TargetMol
YOUR TARGET MOLECULES

Zosuquidar trihydrochloride

Chemical Properties



CAS No. : 167465-36-3

Formula: C32H31F2N3O2·3HCl

Molecular Weight: 636.99

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Zosuquidar trihydrochloride (LY-335979 trihydrochloride) is a potent modulator of P-glycoprotein-mediated multi-drug resistance with Ki of 60 nM. Phase 3.
Targets(IC50)	P-gp
In vitro	LY335979 competitively inhibits equilibrium binding of [3H]vinblastine to Pgp by blocking [3H]azidopine photoaffinity labeling of the Pgp in CEM/VLB100 plasma membranes. [1] LY335979 alone shows the cytotoxicity to drug-sensitive and MDR cell lines with IC50 ranging from 6 μM-16 μM and produces its ability to completely reverse the resistance of the oncolytics (vinblastine, doxorubicin, or etoposide) to the MDR cell lines P388/ADR, MCF7/ADR, 2780AD, or UCLA-P3.003VLB at concentration of 0.1 and 0.5 μM. [1] LY335979 significantly restores drug sensitivity in P-gp-expressing leukemia cell lines including K562/HHT40, K562/HHT90, K562/DOX and HL60/DNR, and enhances the cytotoxicity of anthracyclines (daunorubicin, idarubicin, mitoxantrone) and gemtuzumab ozogamicin (Mylotarg) in primary AML blasts with active P-gp. [2] A latest paper indicates that LY335979 completely inhibits apically directed transport of (Z)-endoxifen in the ABCB1-transduced cells. [3]
In vivo	Zosuquidar trihydrochloride is only moderately active as an inhibitor of P-gp at the blood-brain. Zosuquidar trihydrochloride at an oral dose of 25 mg/kg increases the brain concentrations by about 2.5-fold at 1 h and 5-fold at 24 h after paclitaxel administrationbarrier[4]. Zosuquidar enhances the brain uptake of nelfinavir in a dose-dependent manner. Brain tissue/plasma nelfinavir concentration ratios increase from 0.06±0.03 in the absence of zosuquidar administration and 0.09±0.02 between 2 and 6 h after a 2 mg/kg intravenous dose of zosuquidar to 0.85±0.19 after 6h and 1.58±0.67 after 20 mg/kg zosuquidar[5].
Kinase Assay	ATPase Assay : P-Glycoprotein ATPase activity is measured by the liberation of inorganic phosphate from ATP. The assay is measured in a 96-well plate for 90 min at 37 °C. Membranes (8 μg-10 μg protein) are incubated in a total volume of 100 μL of buffer A containing 5 mM sodium azide, 1 mM ouabain, 1 mM EGTA, 3 mM ATP, an ATP regenerating system composed of 5 mM phosphoenolpyruvate, and 3.6 units/mL pyruvate kinase in the presence and absence of 1 mM sodium vanadate. Pgp-ATPase activity is defined as the vanadate-sensitive portion of the total ATPase activity. Plates are read 3 minutes after the addition of the detection solution. The absorbance is measured at 690 nm by a microtiter dish reader. A phosphate standard curve is used to calculate the μMol of phosphate formed. Samples are measured in triplicate.

Cell Research	Cell viability is determined using a modified 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide dye reduction method. Cells are harvested during logarithmic growth phase, and seeded in 96-well plates. The cells are then cultured for 72 hours in the presence of oncolytics with or without modulators. MCF-7 and MCF-7/ADR cells are incubated 24 hours before the addition of the drug with and without the LY335979. LY335979 is prepared as 2 mM DMSO stocks and added to wells to give final concentrations ranging from 0.05 to 5 μM. After 72 hours, 20 μL of freshly prepared 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (5 mg/mL in Dulbecco's PBS) is added to each well and incubated for 4 hours in a 37 °C incubator containing 5% CO2. Cells are pelleted in a Sorvall RT6000B centrifuge, 70 μL of medium is carefully removed from each well, and 100 μL of 2-propanol/0.04 N HC1 is added. Cells are resuspended 5-10 times with a Multipipettor or until no particulate matter is visible. Plates are immediately read on a Titertek Multiskan MCC/340 microplate reader Flow Laboratories with a test wavelength of 570 nm and a reference wavelength of 630 nm. Controls are measured in quadruplicate and modulators are measured in duplicate. Cytotoxicity analyses are also performed using the CeliTiter 96 AQueous assay kit.(Only for Reference)

Solubility Information

Solubility	DMSO: 31.9 mg/mL (50 mM), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.5699 mL	7.8494 mL	15.6988 mL
5 mM	0.314 mL	1.5699 mL	3.1398 mL
10 mM	0.157 mL	0.7849 mL	1.5699 mL
50 mM	0.0314 mL	0.157 mL	0.314 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.

Reference

Dantzig AH, et al. Cancer Res. 1996, 56(18), 4171-4179.
Tang R, et al. BMC Cancer. 2008, 8,51.