Zosuquidar trihydrochloride

Cat. No.: HY-50671

CAS No.: 167465-36-3

Molecular Formula: $C_{32}H_{34}Cl_3F_2N_3O_2$

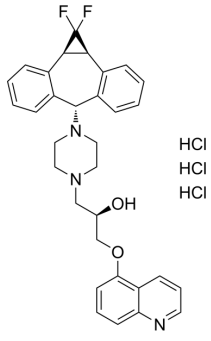
Molecular Weight: 636.99

Target: P-glycoprotein

Pathway: Membrane Transporter/Ion Channel

Storage: 4°C, sealed storage, away from moisture

* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

H_2O : 5 mg/mL (7.85 mM; Need ultrasonic)

DMSO : 1 mg/mL (1.57 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5699 mL	7.8494 mL	15.6988 mL
5 mM	0.3140 mL	1.5699 mL	3.1398 mL
10 mM	---	---	---

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Zosuquidar is dissolved in 20% ethanol-saline[5].

BIOLOGICAL ACTIVITY

Description

Zosuquidar (LY335979) trihydrochloride is a P-glycoprotein (P-gp) inhibitor (K_i=59 nM). Zosuquidar trihydrochloride shows anti-tumor activities, and can be used in acute myelogenous leukemia (AML) research[1][2][3].

IC_{50} & Target

Ki: 59nM (P-glycoprotein)[1].

In Vitro

Zosuquidar (0.3 μM; 48 h) enhances the cytotoxicity of DNR (substrates for P-glycoproteins) in P-glycoproteins active cell lines[2].

?Zosuquidar (5-16 μM; 72 h) treatment alone shows high cytotoxic concentration to drug-sensitive and MDR cell lines[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Cytotoxicity Assay[2]

Cell Line:	K562 and HL60 cells

Concentration:	0.3 μM
Incubation Time:	48 hours
Result:	Enhanced the cytotoxicity of DNR (substrates for P-glycoproteins) in K562/DOX cells more than 45.5-fold.

Cell Cytotoxicity Assay[1]

Cell Line:	CCRF-CEM, CEM/VLB100, P388, P388/ADR, MCF7, MCF7/ADR, 2780, 2780AD, UCLA-P3, UCLA-P3.003VLB cells
Concentration:	5-16 μM
Incubation Time:	72 hours
Result:	Showed IC_{50}s of 6, 7, 15, 8, 7, 15, 11, 16, >5, >5 μM for CCRF-CEM, CEM/VLB100, P388, P388/ADR, MCF7, MCF7/ADR, 2780, 2780AD, UCLA-P3, UCLA-P3.003VLB cells, respectively.

In Vivo

Zosuquidar (intraperitoneal injection; 30, 10, 3, or 1 mg/kg; once daily; 5 d) treatment shows a significant increase in life span[1].

?Zosuquidar (intraperitoneal injection; 30 mg/kg; once daily; 5 d) treatment shows the potentiation with a combined of Doxorubicin[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mice implanted with P388/ADR tumors[1]
Dosage:	30, 10, 3, or 1 mg/kg
Administration:	Intraperitoneal injection; 30, 10, 3, or 1 mg/kg; once daily; 5 days
Result:	Exihibited a significantly increased survival compared to the group treated with Doxorubicin alone (P<0.001).

Animal Model:	Mice implanted with P388 or P388/ADR murine leukemia cells[1]
Dosage:	30 mg/kg
Administration:	Intraperitoneal injection; 30 mg/kg; once daily; 5 days
Result:	Observed significant antitumor activity against the MDR P388/ADR cell lines when mice were treated with a combined dose of 30 mg/kg LY335979 and 1 mg/kg Doxorubicin (P=0.1).

CUSTOMER VALIDATION

- Cancer Cell. 2017 Apr 10;31(4):501-515.e8.
- Antiviral Res. 2021 Jun 28;105124.
- Blood Adv. 2020 Oct 27;4(20):5062-5077.
- Biomed Pharmacother. 2020 Sep;129:110506.
- Pharmaceutics. 2021, 13(4), 559.

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REFERENCES

[1]. A H Dantzig, et al. Reversal of P-glycoprotein-mediated multidrug resistance by a potent cyclopropyldibenzosuberane modulator, LY335979. Cancer Res. 1996 Sep 15;56(18):4171-9.

[2]. Ruoping Tang, et al. Zosuquidar restores drug sensitivity in P-glycoprotein expressing acute myeloid leukemia (AML). BMC Cancer. 2008 Feb 13;8:51.

[3]. Larry D Cripe, et al. Zosuquidar, a novel modulator of P-glycoprotein, does not improve the outcome of older patients with newly diagnosed acute myeloid leukemia: a randomized, placebo-controlled trial of the Eastern Cooperative Oncology Group 3999. Blood. 2010 Nov 18;116(20):4077-85.

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