Zardaverine

Cat. No.: HY-15485

CAS No.: 101975-10-4

Molecular Formula: $C_{12}H_{10}F_2N_2O_3$

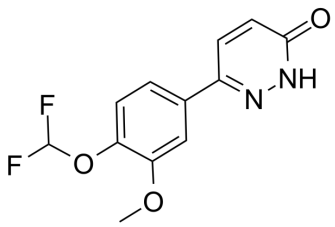
Molecular Weight: 268.22

Target: Phosphodiesterase (PDE); Apoptosis

Pathway: Metabolic Enzyme/Protease; Apoptosis

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (93.21 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.7283 mL	18.6414 mL	37.2828 mL
	5 mM	0.7457 mL	3.7283 mL	7.4566 mL
	10 mM	0.3728 mL	1.8641 mL	3.7283 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: ≥ 2.08 mg/mL (7.75 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zardaverine is an orally active and selective PDE3/4 inhibitor (IC_{50})=0.58 uM/0.17 uM) with potent bronchodilator activity. Zardaverine also selectively inhibits the proliferation of HCC cells and induces apoptosis and cycle arrest (G0/G1 phase). Zardaverine has good antitumor potential and is effective in both bronchial relaxation and reduction of inflammation in asthma[1][2][3].

IC_{50} & Target		
	PDE3	PDE4

In Vitro

Zardaverine (0-30 μM; 72 h) selectively inhibits the growth of human HCC cells in vitro[1].
Zardaverine shows selective antitumor activity that closely related to the regulation of cell cycle-associated proteins, but is independent of PDE3/4 inhibition[1].

Zardaverine (0.1 μM; 24 h) selectively causes G0/G1-phase arrest and dysregulates cell cycle-associated proteins in HCC cells [1].

Zardaverine (0.01, 0.03, 0.1, 0.3 1 μM/48h; 0.3 1 μM/24, 36, 48, 60, 72 h) induces apoptosis in a time- and concentration-dependent manner, in Bel-7402 and SMMC-7721 cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	Bel-7402, Bel-7404, QGY-7701 and SMMC-7721
Concentration:	0-30 μM
Incubation Time:	72 h
Result:	Selectively inhibited SMMC-7721, QGY-7701, Bel-7402 and Bel-7404 growth with IC_{50}s of 36.6, 51.0, 137.7 and 288.0, respectively.

Cell Cycle Analysis[1]

Cell Line:	Bel-7402, Bel-7404, QGY-7701 and SMMC-7721
Concentration:	0.1 μM
Incubation Time:	24 h
Result:	Induced accumulation of Bel-7402, Bel-7404, QGY-7701 and SMMC-7721 cells in the G0/G1 phase.

Western Blot Analysis[1]

Cell Line:	Bel-7402, SMMC-7721
Concentration:	0.01, 0.03, 0.1, 0.3 1 μM; 0.3 1 μM
Incubation Time:	48 h; 24, 36, 48, 60, 72 h
Result:	Induced a concentration- and time- dependent increase in the cleavage of PARP and caspase-3, -8 and -9, which are apoptosis markers.

In Vivo

Zardaverine (60, 200 mg/kg; p.o.; single daily for 14 days) inhibits the growth of human Bel-7402 xenografts in mice[1].

Zardaverine (8046.6 μg/kg; i.p.; single) blocks the LPS induced increase in responsiveness completely in airway inflammation and hyperresponsiveness rat model[2].

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

Animal Model:	Female Balb/cA-nude mice (5 to 6-week-old; human Bel-7402 xenografts model)[1].
Dosage:	60, 200 mg/kg
Administration:	Oral administration; single daily for 14 days
Result:	Inhibited the growth of Bel-7402 xenografts at the dose of 60 mg/kg for 14 consecutive days and caused the tumor regression at the dose of 200 mg/kg.

Animal Model:	Inbred male Fisher 344 (F344) rats (250-350 g; 3 to 4-month-old; airway inflammation and hyperresponsiveness model)[2].
Dosage:	8046.6 μg/kg (30 μmol/Kg)

Administration:	Intraperitoneal injection; single
Result:	Completely blocked LPS-induced hyperresponsiveness and airway inflammation.

REFERENCES

[1]. Sun L, et al. Phosphodiesterase 3/4 inhibitor zardaverine exhibits potent and selective antitumor activity against hepatocellular carcinoma both in vitro and in vivo independently of phosphodiesterase inhibition. PLoS One. 2014 Mar 5;9(3):e90627.

[2]. Kips JC, et al. The effect of zardaverine, an inhibitor of phosphodiesterase isoenzymes III and IV, on endotoxin-induced airway changes in rats. Clin Exp Allergy. 1993 Jun;23(6):518-23.

[3]. Schudt C, et al. Zardaverine: a cyclic AMP specific PDE III/IV inhibitor. Agents Actions Suppl. 1991;34:379-402.

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