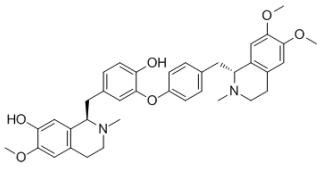
Daurisoline

Cat. No.:	HY-N0221
CAS No.:	70553-76-3
Molecular Formula:	$C_{37}H_{42}N_2O_6$
Molecular Weight:	610.74
Target:	Autophagy; Potassium Channel
Pathway:	Autophagy; Membrane Transporter/Ion Channel
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (81.87 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6374 mL	8.1868 mL	16.3736 mL
	5 mM	0.3275 mL	1.6374 mL	3.2747 mL
	10 mM	0.1637 mL	0.8187 mL	1.6374 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: ≥ 3 mg/mL (4.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Daurisoline is a hERG inhibitor and also an autophagy blocker.

IC_{50} & Target

hERG[1], autophagy[2]

In Vitro

Daurisoline (compound 1) shows a maximal inhibitory effect on the end of depolarization ($I_{hERG\text{-}step}$) at +20 mV and on the peak tail current ($I_{hERG\text{-}tail}$) at +60 mV. At concentrations of 1, 3, 10, and 30 μM, the inhibition ratios for current amplitude at the end of depolarization ($I_{hERG\text{-}step}$) are 32.2±4.2%, 41.6±2.6%, 62.1±5.9%, and 74.8±6.8%, respectively; the IC_{50} is 9.1 μM. In turn, the inhibition ratios for $I_{hERG\text{-}tail}$ are 16.7±5.8%, 31.1±4.5%, 55.1±7.2%, and 81.2±7.0%, respectively; the IC_{50} is 9.6 μM[1]. Daurisoline (DAS) inhibits the CPT-induced autophagy in different cancer cell lines, with IC_{50}s of 74.75±1.03, 50.54±1.02 and 80.81±1.10 μM in HeLa, A549 and HCT-116 cells, respectively. DAC and Daurisoline also impair lysosomal function and lysosomal acidification, via inhibiting the lysosome V-type ATPase acitivity in DAC and Daurisoline treated cells[2].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The results show that plasma concentration exists a biexponential decline following iv administration of Daurisoline (DS) or dauricine (Dau) 6 mg/kg. After iv Daurisoline and Dau 6 mg/kg in beagle dogs, HR, LVSP, dp/dtmax, and SBP are decreased. But the maximum pharmacological effects of both drugs peak at 10 to15 min later than the maximum plasma concentration is observed[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	HEK293 cells are incubated overnight with 35 μg/mL Dx-OG514. Cells are washed and incubated with serum-free Dulbecco's modified Eagle's medium (DMEM) for 2 h. 15 minutes prior to lysis, FCCP is added into the medium to a final concentration of 1 μM. Cells are scraped in fraction buffer (50 mM KCl, 90 mM K-Gluconate, 1 mM EGTA, 50 mM Glucose, 20 mM HEPES, protease inhibitor cocktail, pH=7.4) supplemented with 1 μM FCCP. After spraying with needle, cells are spun down at 10,000 rpm for 15 sec. at 4°C. Then, re-centrifuge the supernatant at max speed for another 20 minutes. The pellet is resuspended in pre-warmed fractionation buffer supplemented with 1% BSA, and split into several aliquots with DAC, Daurisoline (DAS) or BAF treatment for 30 min. Baseline fluorescence is measured at 530 nm upon 511 nm excitation in 96-well plate at 30 s intervals for 5 min[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Cell proliferation is determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. HeLa cells are seeded at 7000 cells per well in 96-well plates in DMEM (1% serum). After cells are treated with different compounds (including Daurisoline) for indicated times, 20 μL of MTT (2.5 mg/mL in PBS) is added to each well. The plates are incubated for an additional 4 h at 37°C. Then the purple-blue MTT formazan precipitate is dissolved in 100 μL DMSO. The cell viability of HeLa cell is evaluated by measuring optical density at 572 nm with a microplate reader[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	After the beagle dogs are anesthetized with sodium pentobarbital (30 mg/kg, iv) a canula is advanced into the left ventricle through the right common carotid artery. And the canula is connected to a pressure transducer which is connected to an amplifier and polygraph. The right femoral artery is canulated to measure the blood pressure wave. ECG (lead II) is observed simultaneously. After iv injection of Daurisoline (DS) (n=4) or Dau (n=4) to beagle dogs, the ECG, BP, and LVP signals are recorded. Blood samples are taken before dosing and at 2, 5, 10, 15, 20, 30, 45 min, and 1, 1.5, 2, 3, 4, 6, 8 h after dosing[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biochem Biophys Res Commun. 2020 Nov 16;S0006-291X(20)31815-5.

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REFERENCES

[1]. Liu Q, et al. Effect of daurisoline on HERG channel electrophysiological function and protein expression. J Nat Prod. 2012 Sep 28;75(9):1539-45.

[2]. Wu MY, et al. Natural autophagy blockers, dauricine (DAC) and daurisoline (DAS), sensitize cancer cells tocamptothecin-induced toxicity. Oncotarget. 2017 Sep 8;8(44):77673-77684.

[3]. Shi SJ, et al. Pharmacokinetic-pharmacodynamic modeling of daurisoline and dauricine in beagle dogs. Acta Pharmacol Sin. 2003 Oct;24(10):1011-5.

Caution: Product has not been fully validated for medical applications. For research use only.

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