Lomerizine dihydrochloride

Cat. No.: HY-B0768A

CAS No.: 101477-54-7

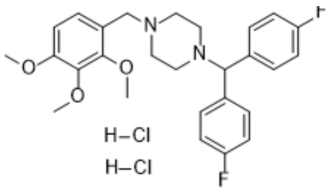
Molecular Formula: $C_{27}H_{32}Cl_2F_2N_2O_3$

Molecular Weight: 541.46

Target: Calcium Channel

Pathway: Membrane Transporter/Ion Channel; Neuronal Signaling

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (230.86 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8469 mL	9.2343 mL	18.4686 mL
	5 mM	0.3694 mL	1.8469 mL	3.6937 mL
	10 mM	0.1847 mL	0.9234 mL	1.8469 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 (3.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description Lomerizine dihydrochloride is an antagonist of L- and T-type voltagegated calcium channels.

IC_{50} & Target	T-type calcium channel	L-type calcium channel

In Vitro

Lomerizine is an antagonist of L- and T-type voltagegated calcium channels and transient receptor potential channel 5 transient receptor potential channels. Lomerizine is a dual L/T-type channel blocker used for prophylaxis of migraine. To demonstrate the effectiveness of Lomerizine in limiting intracellular [Ca^{2+}], its ability to inhibit glutamate-induced death of motor neurons and the associated rise in cytosolic [Ca^{2+}] is evaluated. Lomerizine inhibits the low- and high-voltage activated Ca^{2+} currents in dissociated rat brain neurons at a threshold concentration of 0.01 μM and IC_{50} of 1.9 μM and H_2O_2-

induced Ca^{2+} influx in hippocampal neurons is inhibited by 1 μM Lomerizine. Pre-treatment with 1 μM Lomerizine significantly reduces acute death of motor neurons in spinal cord-DRG cultures exposed to 50 μM glutamate, a concentration that kills approximately 40% of motor neurons in the culture by 6 h, and inhibits the rise in cytosolic [Ca^{2+}] that occurs with glutamate treatment. 0.5 μM Lomerizine is sufficient to significantly prevent the mitochondrial fragmentation of mitochondria induced by SOD1G93A[1]. Lomerizine increases the cytotoxicity of Adriamycin (ADM) and the apoptosis induced by ADM or Vincristine (VCR) in K562/ADM cells. At the concentration of 3, 10 and 30μM, Lomerizine reduces the IC_{50} value of ADM from 79.03 μM to 28.14, 8.16 and 3.16 μM, respectively. Lomerizine increases the intracellular accumulation of ADM and inhibits the efflux of Rh123 in K562/ ADM cells. No change in P-gp expression is observed after the treatment of Lomerizine for 72 h. Lomerizine has strong reversal effect on MDR in K562/ADM cells by inhibiting P-gp function [2].

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

In Vivo

To determine whether Ca^{2+} signaling molecules mediate NMDA-induced neurotoxicity in p50-deficient mice, the neuroprotective effects of chemical reagents are examined, which act on the Ca^{2+}-signaling pathway including CaN activation, on NMDA-induced RGC death. The p50-deficient mice at 2 months of age, showing normal RGC survival, undergo intraperitoneal pretreatments with a NMDA antagonist, MK801 or Memantine; calcium blocker, Lomerizine; and CaN inhibitor, Tacrolimus, daily for 1 week before the injection of 5 nM NMDA. The chronic administration of Lomerizine or Tacrolimus to KO mice for 6 months results in an increase in surviving RGC numbers ($p<0.0001$)[3]. Lomerizine (KB-2796; 0.3 and 1 mg/kg, i.v.) dose-dependently increases cerebral blood flow significantly at 30 min and 15 min, respectively, after its administration. Lomerizine (1 mg/kg, i.v.) significantly attenuates the expression of c-Fos-like immunoreactivity in the ipsilateral frontoparietal cortex[4].

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PROTOCOL

Cell Assay [2]

MTT assay is used to determine the influence of Lomerizine on the cytotoxicity of Adriamycin (ADM). The effect of Lomerizine (3, 10 and 30 μM) on the apoptosis induced by ADM and Vincristine (VCR) in K562/ADM cells is detected using flow cytometry. Intracellular accumulation of ADM is measured by fluorescence spectrophotometry. Flow cytometry is used to investigate the efflux of Rhodamine 123 (Rh123) and the expression of P-glycoprotein (P-gp) in K562/ADM cells[2].

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Animal Administration [3][4]

Mice[3]

The p50-deficient mice and wild-type mice aged 2 months are daily pre-treated intraperitoneally with Memantine (10 mg/kg), MK-801 (0.5 mg/kg), Lomerizine (1 mg/kg), or Tacrolimus (2, 0.5 and 0.2 mg/kg) for one week before the NMDA injection. These mice are given an intravitreous injection of 5 nM NMDA, which is a relatively low concentration for causing neurotoxicity[3].

Rats[4]

Male Wistar rats weighing 250 to 350 g are housed in an air-conditioned room at 25±0°C with 55±5% humidity and given food and water ad libitum. Lomerizine is injected i.v. in a volume of 1 mL/kg body weight. Effects of Lomerizine (0.3 mg/kg, i.v., or 1 mg/kg, i.v.) are measured on cerebral cortical blood flow measured by laser Doppler flowmetry (CBFLDF) in anaesthetized rats[4].

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

REFERENCES

[1]. Tran LT, et al. The voltage-gated calcium channel blocker Lomerizine is neuroprotective in motor neurons expressing mutant SOD1, but not TDP-43. J Neurochem. 2014 Aug;130(3):455-66.

[2]. Zhu HJ, et al. [Reversal of multidrug resistance by Lomerizine in K562/ADM cells]. Yao Xue Xue Bao. 2004 May;39(5):333-7.

[3]. Nakamura-Yanagidaira T, et al. Development of spontaneous neuropathy in NF-κBp50-deficient mice by calcineurin-signal involving impaired NF-κB activation. Mol Vis.

2011;17:2157-70.

[4]. Shimazawa M, et al. Effects of Ca2+ channel blockers on cortical hypoperfusion and expression of c-Fos-like immunoreactivity after cortical spreading depression in rats. Br J Pharmacol. 1995 Aug;115(8):1359-68.

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