MK-571

Cat. No.: HY-19989

CAS No.: 115104-28-4

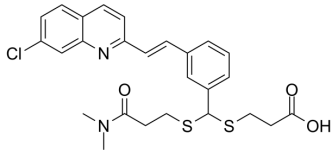
Molecular Formula: $C_{26}H_{27}ClN_2O_3S_2$

Molecular Weight: 515.09

Target: Leukotriene Receptor; LPL Receptor

Pathway: GPCR/G Protein

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

MK-571 (L-660711) is an orally active, potent and selective competitive leukotriene D_4 (LTD_4) receptor antagonist, with K_i values of 0.22 and 2.1 nM in guinea pig and human lung membranes, respectively. MK-571 is also a MRP4 and ABCC1 (MRP1) inhibitor. MK-571 inhibits constitutive and antigen-stimulated S1P (sphingosine-1-phosphate) release[1][2][3].

IC_{50} & Target

LTD_4	LTD_4	LTD_4	LTE_4
0.22 nM (Ki, In guinea pig lung)	2.1 nM (Ki, In human lung)	10.5 (pA2, on guinea pig ileum)	10.4 (pA2, on guinea pig ileum)

In Vitro

MK571 (15 μM, 1 h) markedly suppresses constitutive and Ag-stimulated S1P secretion from RBL-2H3 cells and mast cells, and inhibits Fluo-3 efflux[3].

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

Cell Viability Assay[3]

Cell Line:	RBL-2H3 cells, human LAD2 mast cells
Concentration:	15 μM
Incubation Time:	1 h
Result:	Inhibited S1P secretion by vector and SphK1 transfected RBL-2H3 cells, whereas it did not affect uptake and intracellular conversion of [3H]Sph to S1P. Inhibited Fluo-3 efflux, inhibited S1P export by LAD2 cells, and blocked Ag-stimulated release of S1P.

In Vivo

MK-571 (0-0.5 mg/kg, orally, once) produces dose-dependent inhibition of the duration of antigen-induced dyspnea in conscious sensitized rats treated with methysergide (3 μg/kg)[1].

MK-571 (0-1 mg/kg, orally, once) blocks LTD_4- and Ascaris-induced bronchoconstriction in conscious squirrel monkeys[1].

MK-571 (0-25 mg/kg, orally, daily, for 2 more weeks) shows reversal of hypoxic pulmonary hypertension (PH), and protects mice from hypoxic PH[2].

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

Animal Model:	Hyperreactive rats (male and female, 200-400 g, pretreated intravenously with 3μg/kg methysergide, 5 min before antigen chdlenge)[1]

Dosage:	0.5, 0.15, and 0.05 mg/kg
Administration:	Orally, once, 1 or 4 h before challenge
Result:	Produced dose-dependent inhibition of the duration of antigen-induced dyspnea, with ED_{50} values of 0.13 (95% confidence interval (CI), 0.03-0.62) and 0.11 (95% CI, 0.009-1.47) mg/kg, respectively. MK-571 was even more active when administered orally as a suspension in 1% Methocel (4 h pretreatment), with an ED_{50} of 0.068 (95% CI, 0.83-0.14) mg/kg.

Animal Model:	Csnscisus squirrel msnkeys[1]
Dosage:	0.1, 0.5, and 1 mg/kg
Administration:	Orally, once, 2 h prior to challenge with Ascaris antigen
Result:	Produced significant inhibition of the bronchoconstriction at 0.5 mg/kg, produced significant inhibition of the increases in R_L and decreases in C_{dyn} at 1 mg/kg.

Animal Model:	FVB (Friend virus B-type) mice ($Mrp4^{-/-}$ and WT, 6 weeks old, exposed to chronic hypoxia (10% O_2) in a ventilated chamber for 28 days)[2]
Dosage:	0, 5, and 25 mg/kg
Administration:	Orally, daily, for 2 more weeks, maintain in hypoxic conditions
Result:	Showed reversal of hypoxic pulmonary hypertension (PH), and mice were protected from hypoxic PH. MK-571-treated mice displayed lower RVSP and Fulton index and a decrease in the medial thickening of small pulmonary arteries and arterioles.

CUSTOMER VALIDATION

- Nat Commun. 2023 Sep 19;14(1):5709.
- Int J Nanomedicine. 2019 Nov 27;14:9217-9234.
- Biomed Pharmacother. 2020 Sep;129:110506.
- Biomed Pharmacother. 2018 Oct;106:1563-1569.
- Arch Toxicol. 2020 Nov;94(11):3799-3817.

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REFERENCES

[1]. Mitra P, et al. Role of ABCC1 in export of sphingosine-1-phosphate from mast cells. Proc Natl Acad Sci U S A. 2006 Oct 31;103(44):16394-9.

[2]. Jones TR, et al. Pharmacology of L-660,711 (MK-571): a novel potent and selective leukotriene D_4 receptor antagonist. Can J Physiol Pharmacol. 1989 Jan;67(1):17-28.

[3]. Hara Y, et al. Inhibition of MRP4 prevents and reverses pulmonary hypertension in mice. J Clin Invest. 2011 Jul;121(7):2888-97.

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

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