Ruboxistaurin hydrochloride

Cat. No.: HY-10195B

CAS No.: 169939-93-9

Molecular Formula: $C_{28}H_{29}ClN_4O_3$

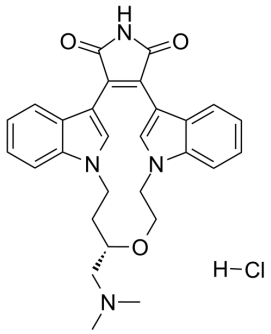
Molecular Weight: 505.01

Target: PKC

Pathway: Epigenetics; TGF-beta/Smad

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 : 6.67 mg/mL (13.21 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.9802 mL	9.9008 mL	19.8016 mL
	5 mM	0.3960 mL	1.9802 mL	3.9603 mL
	10 mM	0.1980 mL	0.9901 mL	1.9802 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: ≥ 0.67 mg/mL (1.33 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.67 mg/mL (1.33 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ruboxistaurin (LY333531) hydrochloride is an orally active, selective PKC beta inhibitor (K_i=2 nM). Ruboxistaurin hydrochloride exhibits ATP dependent competitive inhibition of PKC beta I with an IC_{50} of 4.7 nM. Ruboxistaurin hydrochloride inhibits PKC beta II with an IC_{50} of 5.9 nM[1][2].

IC_{50} & Target

PKCβI 4.7 nM (IC_{50})	PKCβII 5.9 nM (IC_{50})	PKCη 52 nM (IC_{50})	PKCδ 250 nM (IC_{50})
PKCγ 300 nM (IC_{50})	PKCα 360 nM (IC_{50})	PKCε 600 nM (IC_{50})	

In Vitro

Ruboxistaurin hydrochloride is a selective and ATP-competitive PKCβ inhibitor, with IC_{50}s of 4.7 and 5.9 nM for PKCβI and

	PKCβII, shows less potent inhibition on PKCη (IC_{50}, 52 nM), PKCα (IC_{50}, 360 nM), PKCγ (IC_{50}, 300 nM), PKCδ (IC_{50}, 250 nM), and has no effect on PKCζ (IC_{50}, >100 μM)[1]. Ruboxistaurin (10 and 400 nM) dramatically inhibits glucose-induced monocyte adherence to levels that are not different from baseline adherence of monocytes to endothelial cells under NG conditions. Ruboxistaurin (10 and 400 nM) dose not alter the endothelial expression of adhesion molecules or modify endothelial cell growth[2]. Ruboxistaurin (LY333531; 10 nM) reduces high-glucose (HG)-induced human renal glomerular endothelial cells (HRGECs) viability, and inhibits the increases in swiprosin-1 in HRGECs incubated with HG[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ruboxistaurin (1 mg/kg; 8 weeks) markedly reduces GEC apoptosis as well as swiprosin-1 upregulation, and ameliorates renal glomerular injury in the diabetic mice. Ruboxistaurin also potently attenuates the expression of PARP, cleaved-caspase9, cleaved-caspase3, and the Bax/Bcl-2 ratio, in diabetic mice[3]. Ruboxistaurin (0.1, 1.0, or 10.0 mg/kg; p.o.) dramatically reduces the number of leukocytes trapped in the retinal microcirculation of diabetic rats[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The second passages of human umbilical vein endothelial cells (HUVEC) are grown to confluence in microtiter plates coated with gelatin. The medium contains 5.5 mM glucose. If endothelial cells are stimulated with 27.7 mM glucose for 4 days, they are seeded in the well at a calibrated higher cell concentration in order to achieve comparable cell density at the day adhesion assays are performed. Therefore, cell density in the wells is tested thoroughly in control wells of each glucose concentration prior to monocyte adhesion assays. If Ruboxistaurin is used in this assay, it is added to the cultures for the whole period[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Rats[4] Leukocyte entrapment is evaluated only once after a 4-week diabetic period in both groups of rats with and without Ruboxistaurin treatment, using one eye (right eye) of each rat. Ruboxistaurin is administered orally at dosages of 0.1 (n = 8), 1.0 (n = 16), and 10.0 mg/kg/d (n = 8) for 4 weeks, from the time streptozotocin is injected in the rats[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Acta Pharm Sin B. 2022.
- Cell Biosci. 2021 Feb 8;11(1):32.
- Endocrinology. 2018 May 1;159(5):2253-2263.
- ACS Omega. 2020 Oct 12;5(41):26551-26561.

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REFERENCES

[1]. Jirousek MR, et al. (S)-13-[(dimethylamino)methyl]-10,11,14,15-tetrahydro-4,9:16, 21-dimetheno-1H, 13H-dibenzo[e,k]pyrrolo[3,4-h][1,4,13]oxadiazacyclohexadecene-1,3(2H)-d ione (LY333531) and related analogues: isozyme selective inhibitors of protein kinas

[2]. Ruboxistaurin: LY 333531. Drugs R D. 2007;8(3):193-199.

[3]. Kunt T, et al. The beta-specific protein kinase C inhibitor ruboxistaurin (LY333531) suppresses glucose-induced adhesion of human monocytes to endothelial cells in

vitro. J Diabetes Sci Technol. 2007 Nov;1(6):929-35.

[4]. Nonaka A, et al. PKC-beta inhibitor (LY333531) attenuates leukocyte entrapment in retinal microcirculation of diabetic rats. Invest Ophthalmol Vis Sci. 2000 Aug;41(9):2702-6.

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