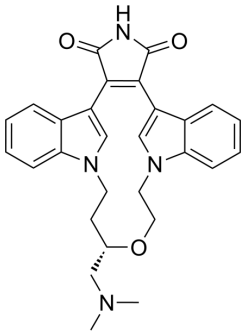
Ruboxistaurin



Cat. No.:	HY-10195
CAS No.:	169939-94-0
Molecular Formula:	$C_{28}H_{28}N_4O_3$
Molecular Weight:	468.55
Target:	PKC
Pathway:	Epigenetics; TGF-beta/Smad
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 : 25 mg/mL (53.36 mM; ultrasonic and warming and heat to 60°C)
THF : < 1 mg/mL (ultrasonic) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1342 mL	10.6712 mL	21.3424 mL
5 mM	0.4268 mL	2.1342 mL	4.2685 mL
10 mM	0.2134 mL	1.0671 mL	2.1342 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: ≥ 1.67 mg/mL (3.56 mM); Suspended solution

BIOLOGICAL ACTIVITY

Description

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

IC_{50} & Target

PKC-βI 4.7 nM (IC_{50})	PKC-βII 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 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.

Animal Model:	Rats[4]
Dosage:	0.1, 1.0, or 10.0 mg/kg
Administration:	P.o.
Result:	Dramatically reduced the number of leukocytes trapped in the retinal microcirculation of diabetic rats.

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 kinase C beta. J Med Chem. 1996;39(14):2664-2671.

[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.

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

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