产品名称：**Ruboxistaurin Hydrochloride**
产品别名：鲁伯斯塔盐酸盐；**LY 333531 hydrochloride**

生物活性：

Description

Ruboxistaurin hydrochloride is a selective and ATP-competitive PKCβ inhibitor, with IC50s of 4.7 and 5.9 nM for PKCβI and PKCβII, shows less potent inhibition on PKCη (IC50, 52 nM), PKCα (IC50, 360 nM), PKCγ (IC50, 300 nM), PKCδ (IC50, 250 nM), and has no effect on PKCζ (IC50, >100 μM).

IC_{50} & Target

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

In Vitro

Ruboxistaurin hydrochloride is a selective and ATP-competitive PKCβ inhibitor, with IC50s of 4.7 and 5.9 nM for PKCβI and PKCβII, shows less potent inhibition on PKCη (IC50, 52 nM), PKCα (IC50, 360 nM), PKCγ (IC50, 300 nM), PKCδ (IC50, 250 nM), and has no effect on PKCζ (IC50, >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].

In Vivo

Ruboxistaurin (LY333531; 1 mg/kg/d for 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 (LY333531; 0.1, 1.0, or 10.0 mg/kg/d, po.o.) dramatically reduces the number of leukocytes trapped in the retinal microcirculation of diabetic rats[4].

Solvent&Solubility

In Vitro:

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

Preparing Stock Solutions	Solvent / Mass / Concentration	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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 0.67 mg/mL (1.33 mM); Clear solution

	此方案可获得 ≥ 0.67 mg/mL (1.33 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 6.7000003 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 0.67 mg/mL (1.33 mM); Clear solution 此方案可获得 ≥ 0.67 mg/mL (1.33 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 6.7000003 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 0.67 mg/mL (1.33 mM); Precipitated solution 此方案可获得 ≥ 0.67 mg/mL (1.33 mM，饱和度未知) 以 1 mL 工作液为例，取 100 μL 6.7000003 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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 Jul 5;39(14):2664-71. [2]. 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. [3]. Wang ZB, et al. LY333531, a PKCβ inhibitor, attenuates glomerular endothelial cell apoptosis in the early stage of mouse diabetic nephropathy via down-regulating swiprosin-1. Acta Pharmacol Sin. 2017 Jul;38(7):1009-1023. [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.

实验参考：

Cell Assay	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].
Animal Administration	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].
	[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

References	Chem. 1996 Jul 5;39(14):2664-71. [2]. 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. [3]. Wang ZB, et al. LY333531, a PKCβ inhibitor, attenuates glomerular endothelial cell apoptosis in the early stage of mouse diabetic nephropathy via down-regulating swiprosin-1. Acta Pharmacol Sin. 2017 Jul;38(7):1009-1023. [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.