

Product Data Sheet

Product Name: Ruboxistaurin

Cat. No.: GC63177

Chemical Properties

Cas. No. 169939-94-0

Formula $C_{28}H_{28}N_4O_3$

M.Wt 468.55

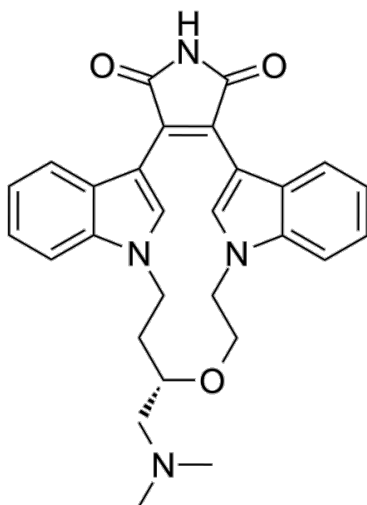
Solubility DMSO : 50 mg/mL (106.71 mM;
ultrasonic and warming and heat to
60°C)

Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Human umbilical vein endothelial cells (HUVECs)

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

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Preparation Method HUVECs were seeded into 96-well plates at a density of 2000 cells per well at 37°C for 12h, and preincubated in HuMedia-EB2 containing 2% fetal bovine serum (FBS) at 37°C for 6h. The HUVECs were incubated for 48h in fresh medium containing VEGF (10ng/ml), with various concentrations of Ruboxistaurin (0, 0.1, 0.5, 1.0μM), and then incubated for a further 48h in the fresh medium. After incubation, the viable cell numbers were measured.

Reaction Conditions 0, 0.1, 0.5, 1.0μM; 48h

Applications Ruboxistaurin treatment significantly reduced cell proliferation of HUVECs induced by VEGF in a dose-dependent manner.

Animal experiment [2]:

Animal models Male farm pigs

Preparation Method Male farm pigs (8-10kg) were anesthetized with intramuscular ketamine-HCl (20mg/kg) and xylazine-HCl (2mg/kg). Pupillary dilation was achieved using 1% tropicamide and 2.5% phenylephrine-HCl. Baseline fundus photographs were obtained, including stereo photography of the optic disc, using a fundus camera. After intravenous injection of rose bengal dye (10mg/kg), selected branch retinal veins were treated with an argon laser with green light using a slit-lamp delivery system and a corneal-contact lens. At least 50% of the total venous area of the retina was occluded by treating the large superior branch vein at the first branch point and one of the inferior vessels at the first branch point. Five pigs were given Ruboxistaurin orally with the standard chow at a dose of 0.5mg/kg twice daily for 12 weeks. Intraocular neovascularization in pigs was determined.

Dosage form 0.5mg/kg; twice a day for 12 weeks; p.o.

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Applications Ruboxistaurin treatment inhibited pre-retinal and optic nerve head neovascularization in the pig model of branch retinal vein occlusion.

References:

- [1] Nakamura S, Chikaraishi Y, Tsuruma K, et al. Ruboxistaurin, a PKC β inhibitor, inhibits retinal neovascularization via suppression of phosphorylation of ERK1/2 and Akt[J]. Experimental eye research, 2010, 90(1): 137-145.
- [2] Danis R P, Bingaman D P, Jirousek M, et al. Inhibition of intraocular neovascularization caused by retinal ischemia in pigs by PKC β inhibition with LY333531[J]. Investigative ophthalmology & visual science, 1998, 39(1): 171-179.

Background

Ruboxistaurin is an orally available inhibitor of protein kinase C (PKC), with IC₅₀ values of 0.36 μ M, 0.0047 μ M, and 0.0059 μ M for PKC α , β I, and β II, respectively^[1]. Ruboxistaurin can reduce the adhesion of macrophages to endothelial cells by lowering the expression of inflammatory cytokines and enhancing the antioxidant stress capacity of cells^[2]. Ruboxistaurin has been widely used to reduce the degree of glomerular sclerosis and tubulointerstitial fibrosis in mice with kidney removal, and to improve renal function^[3].

In vitro, Ruboxistaurin treatment for 24 hours significantly induced cell death in MOLM13 cells and MV4-11 cells, with IC₅₀ values of 0.7 μ M and 1.5 μ M, respectively^[4]. Treatment with 1 μ M Ruboxistaurin for 48 hours significantly inhibited VEGF-induced proliferation of human umbilical vein endothelial cells (HUVECs) and phosphorylation of ERK1/2 and Akt^[5]. Treatment with 1 μ M Ruboxistaurin for 6 days inhibited the overall size of the podosome actin belts in mouse bone marrow-derived macrophages (BMMs) induced by RANKL, resulting in a significant reduction in osteoclast formation^[2].

In vivo, Ruboxistaurin treatment via oral administration at a dose of 10mg/kg/day for 6 weeks significantly reduced the mRNA expressions of TGF- β 1, Smad2, and Smad3 in the kidneys of diabetic rats, and alleviated diabetic nephropathy^[6]. Oral administration of Ruboxistaurin (0.5mg/kg) twice daily for 12 weeks effectively inhibited pre-retinal and optic nerve head neovascularization in

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the pig model of branch retinal vein occlusion^[7].

References:

- [1] Jirousek M R, Gillig J R, Gonzalez C M, et al. (S)-13-[(Dimethylamino) methyl]-10, 11, 14, 15-tetrahydro-4, 9: 16, 21-dimetheno-1 H, 13 H-dibenzo [e, k] pyrrolo [3, 4-h][1, 4, 13] oxadiazacyclohexadecene-1, 3 (2 H)-dione (LY333531) and related analogues: isozyme selective inhibitors of protein kinase C β [J]. Journal of medicinal chemistry, 1996, 39(14): 2664-2671.
- [2] Pang C, Wen L, Lu X, et al. Ruboxistaurin maintains the bone mass of subchondral bone for blunting osteoarthritis progression by inhibition of osteoclastogenesis and bone resorption activity[J]. Biomedicine & Pharmacotherapy, 2020, 131: 110650.
- [3] Kelly D J, Edgley A J, Zhang Y, et al. Protein kinase C- β inhibition attenuates the progression of nephropathy in non-diabetic kidney disease[J]. Nephrology Dialysis Transplantation, 2009, 24(6): 1782-1790.
- [4] Fedorov O, Marsden B, Pogacic V, et al. A systematic interaction map of validated kinase inhibitors with Ser/Thr kinases[J]. Proceedings of the National Academy of Sciences, 2007, 104(51): 20523-20528.
- [5] Nakamura S, Chikaraishi Y, Tsuruma K, et al. Ruboxistaurin, a PKC β inhibitor, inhibits retinal neovascularization via suppression of phosphorylation of ERK1/2 and Akt[J]. Experimental eye research, 2010, 90(1): 137-145.
- [6] Al-Onazi A S, Al-Rasheed N M, Attia H A, et al. Ruboxistaurin attenuates diabetic nephropathy via modulation of TGF- β 1/Smad and GRAP pathways[J]. Journal of Pharmacy and Pharmacology, 2016, 68(2): 219-232.
- [7] Danis R P, Bingaman D P, Jirousek M, et al. Inhibition of intraocular neovascularization caused by retinal ischemia in pigs by PKC β inhibition with LY333531[J]. Investigative ophthalmology & visual science, 1998, 39(1): 171-179.

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