Ruboxistaurin hydrochloride

Cat. No.: HY-10195B
CAS No.: 169939-93-9
Molecular Formula: C₂₈H₂₉ClN₄O₃
Molecular Weight: 505.01
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: 6.67 mg/mL (13.21 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>1.9802 mL</td>
<td>9.9008 mL</td>
<td>19.8016 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.3960 mL</td>
<td>1.9802 mL</td>
<td>3.9603 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.1980 mL</td>
<td>0.9901 mL</td>
<td>1.9802 mL</td>
<td></td>
</tr>
</tbody>
</table>

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 hydrochloride (LY 333531 hydrochloride) is a selective and ATP-competitive PKCβ inhibitor with IC₅₀s of 4.7 nM and 5.9 nM for PKCβI and PKCβII, respectively. Ruboxistaurin hydrochloride 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].

**IC₅₀ & Target**

<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>PKCβI 4.7 nM (IC₅₀)</th>
<th>PKCβII 5.9 nM (IC₅₀)</th>
<th>PKCη 52 nM (IC₅₀)</th>
<th>PKCδ 250 nM (IC₅₀)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PKCγ</td>
<td></td>
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<tr>
<td>PKCα</td>
<td></td>
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</tr>
<tr>
<td>PKCε</td>
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</tbody>
</table>
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 PKCζ (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 adhesion to levels that are not different from baseline adhesion 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].

### 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

- Biosci Rep. 2018 Sep 7;38(5).
- Diabetes Metab Syndr Obes. 2019 Nov 4:2289-2302.

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### REFERENCES

