Reparixin

Cat. No.: HY-15251
CAS No.: 266359-83-5
Molecular Formula: C₁₄H₂₁NO₃S
Molecular Weight: 283.39
Target: CXCR
Pathway: GPCR/G Protein; Immunology/Inflammation
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 : ≥ 100 mg/mL (352.87 mM)
H₂O : < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.

Preparation of Stock Solutions

<table>
<thead>
<tr>
<th>Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>3.5287 mL</td>
<td>17.6435 mL</td>
<td>35.2871 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.7057 mL</td>
<td>3.5287 mL</td>
<td>7.0574 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3529 mL</td>
<td>1.7644 mL</td>
<td>3.5287 mL</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: ≥ 2.5 mg/mL (8.82 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.82 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.82 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Reparixin is a non-competitive allosteric inhibitor of the chemokine receptors CXCR1 and CXCR2 activation with IC₅₀ of 1 and 100 nM, respectively.

IC₅₀ & Target | CXCR1<sup>wt</sup> | CXCR1<sup>Ile43Val</sup> | CXCR1 | CXCR2
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<table>
<thead>
<tr>
<th>IC_{50} Values</th>
<th>In Vitro</th>
<th>In Vivo</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.6 nM (IC_{50} in L1.2 cells)</td>
<td>Reparixin is a potent functional inhibitor of CXCL8-induced biological activities on human PMNs with a marked selectivity (around 400-fold) for CXCR1, as shown in specific experiments on CXCR1/L1.2 and CXCR2/L1.2 transfected cells and on human PMNs. The efficacy of Reparixin is significantly lower in L1.2 cells expressing Ile43Val CXCR1 mutant (IC_{50} values of 5.6 nM and 80 nM for CXCR1 wt and CXCR1 Ile43Val, respectively)(^1). Reparixin is a non-competitive allosteric inhibitor of IL-8 receptors with a 400-fold higher efficacy in inhibiting CXCR1 activity than CXCR2(^2).</td>
<td>Reparixin is an inhibitor of CXCL8 receptor CXCR1 and CXCR2 activation, has been shown to attenuate inflammatory responses in various injury models. Spontaneously hypertensive rats (SHR) are administered a subcutaneous injection of Reparixin (5 mg/kg) daily for 3 weeks. Reparixin effectively decreases systolic blood pressure and increased the blood flow(^3). Reparixin reduces the levels of IL-1(\beta) in the brain after middle cerebral artery occlusion/reperfusion (MCAo) in mice. Bars represent levels of IL-1(\beta) (pg/100 mg) measured by ELISA in the brain tissues of mice subjected or not (SHAM) to MCAo and pretreated with vehicle or Reparixin (30 mg/kg, s.c.)(^4).</td>
</tr>
<tr>
<td>80 nM (IC_{50} in L1.2 cells)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 nM (IC_{50} in cells)</td>
<td></td>
<td></td>
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<tr>
<td>-100 nM (IC_{50} in cells)</td>
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</tr>
</tbody>
</table>

**PROTOCOL**

**Cell Assay**\(^1\)

L1.2 Cell suspension (1.5-3×10^6 cells/mL) is incubated at 37°C for 15 min in the presence of vehicle or of Reparixin (1 nM-1\(\mu\)M) and next seeded in triplicates in the upper compartment of the chemotactic chamber. Different agonists are seeded in the lower compartment of the chamber at the following concentrations: 1 nM CXCL8, 0.03 nM fMLP, 10 nM CXCL1, 2.5 nM CCL2, 30 nM C5a. The chemotactic chamber is incubated at 37°C in air with 5% CO\(_2\) for 45 min (human PMNs) or 2 h (monocytes). At the end of incubation, the filter is removed, fixed, and stained and five oil immersion fields at high magnification (100×) are counted for each migration well after sample coding. L1.2 migration is evaluated using 5 \(\mu\)m pore size Transwell filters\(^1\). MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Animal Administration**\(^3\)\(^4\)

**Rats**\(^3\)

The Reparixin-treated group contained 5 SHR (SHR-R), where equal numbers of normal saline-treated SHR (SHR-N) and WKY (WKY-N) served as controls. Eighteen-week-old SHR received a subcutaneous injection of Reparixin (5 mg/kg) once per day for 3 weeks. Reparixin effects on blood flow, blood pressure and body weight are measured before treatment and then weekly until 1 week after the final injection. The effect of Reparixin on the expression of hypertension-related mediators in thoracic aortas, as well as nitric oxide (NO) plasma levels, is examined 1 week after the final injection.

**Mice**\(^4\)

C57BL/6J mice (8-10 weeks old/20-25 g) are used. The subcutaneous administration of Reparixin (30 mg/kg) is performed 60 minutes before cerebral ischemia induction. The animals are divided into the following three experimental groups: Sham (i.e., the group in which the arteries are visualized, but there is no occlusion of the middle cerebral artery), Vehicle (i.e., the group pre-treated with the vehicle, phosphate buffer solution, 60 minutes before MCAo) and Reparixin (i.e., the group pre-treated with the drug 60 minutes before MCAo). To evaluate neurological signs secondary to MCAo, the animals are assessed with the SHIRPA battery 24 h after reperfusion. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**CUSTOMER VALIDATION**

REFERENCES


