Navarixin

Cat. No.: HY-10198
CAS No.: 473727-83-2
Molecular Formula: C₂₁H₂₃N₃O₅
Molecular Weight: 397.42
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 : ≥ 50 mg/mL (125.81 mM)
H₂O : < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.

<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>2.5162 mL</td>
<td>12.5811 mL</td>
<td>25.1623 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.5032 mL</td>
<td>2.5162 mL</td>
<td>5.0325 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2516 mL</td>
<td>1.2581 mL</td>
<td>2.5162 mL</td>
</tr>
</tbody>
</table>

Preparing Stock Solutions

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 (6.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.29 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.29 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Navarixin (SCH 527123) is a potent, allosteric and orally active antagonist of both CXCR1 and CXCR2, with Kᵦ values of 41 nM for cynomolgus CXCR1 and 0.20 nM, 0.20 nM, 0.08 nM for mouse, rat and cynomolgus monkey CXCR2, respectively[1][2].
<table>
<thead>
<tr>
<th>IC₅₀ &amp; Target</th>
<th>125I-CXCL8-CXCR2</th>
<th>Cynomolgus CXCR2</th>
<th>Mouse CXCR2</th>
<th>Rat CXCR2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.97 nM (IC₅₀)</td>
<td>0.08 nM (Kd)</td>
<td>0.2 nM (Kd)</td>
<td>0.2 nM (Kd)</td>
<td></td>
</tr>
<tr>
<td>43 nM (IC₅₀)</td>
<td>Cynomolgus CXCR1</td>
<td>41 nM (Kd)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**In Vitro**

Navarixin is a potent, allosteric antagonist of both CXCR1 and CXCR2, with Kₜ values of 41 nM for cynomolgus CXCR1 and 0.20 nM, 0.20 nM, 0.08 nM for mouse, rat and cynomolgus monkey CXCR2, respectively\[^1\]. Navarixin (1 nM) reduces CXCL8 potency in stimulating Ba/F3-hCXCR2 chemotaxis. Navarixin (3 nM) significantly inhibits the potency and efficacy of CXCL1-induced neutrophils (PMN) chemotaxis. Navarixin (300 nM) significantly decreases chemokine potency and slightly decreases maximal cell movement for Ba/F3-CXCR1 cells\[^2\]. Navarixin (25 μM) is sufficient to block IL-8-mediated CXCR2 activation in HCT116, E2, Caco2, and IIIe cells, in which phosphorylation of downstream kinases of CXCR2 is reduced in a concentration-dependent manner\[^3\].

**In Vivo**

Navarixin (0.1–10 mg/kg, p.o.) blocks pulmonary neutrophilia (ED₅₀=1.2 mg/kg) and goblet cell hyperplasia (32–38% inhibition at 1–3 mg/kg) in mice following the intranasal lipopolysaccharide (LPS) administration. In rats, Navarixin (0.1–3 mg/kg p.o.) suppresses the pulmonary neutrophilia (ED=1.8 mg/kg) and increase in bronchoalveolar lavage (BAL) mucin content (ED₅₀=0.1 mg/kg) induced by intratracheal (i.t.) LPS\[^1\].

**PROTOCOL**

**Cell Assay**\[^2\]

Recombinant cells are resuspended at 1×10⁶/mL in assay buffer (phenol red free-RPMI 1640 supplemented with 2% FBS). Human neutrophils are resuspended at 2 × 10⁶/mL in the same assay buffer containing 5% FBS. CXCL1 binds only CXCR2 with high affinity, whereas CXCL8 binds both CXCR1 and CXCR2 with high affinity. Chemoattractants (30 μL) diluted in assay buffer are dispensed into the bottom wells of disposable microchemotaxis plates, which are then covered with filter. Cells are preincubated with Navarixin (1-300 nM) in a CO₂ incubator for 90 min. Cell aliquots (25 μL) are applied to each spot on the filter. After incubation (90 min for BaF/3 cells and 30 min for PMN in a CO₂ incubator), the filters are removed\[^2\].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Animal Administration**\[^1\]

**Mice**

Male BALB/c mice weighing between 20 and 25 g are used. Control mice receive intranasal injection of 50 μL of isotonic (0.9%) saline. Navarixin (0.1–10 mg/kg, p.o.) is suspended in 0.4% methylcellulose and given orally by gavage 2 h before and 4 h after each intranasal administration of LPS. Control animals receive 0.4% methylcellulose (10 mL/kg). In total, four doses of Navarixin or vehicle are given\[^1\].

**Rats**

Male Sprague-Dawley rats (200 g) are used. Control animals receive 100 μL of isotonic saline. Navarixin (0.1–3 mg/kg, p.o.) is suspended in 0.4% methylcellulose vehicle and given orally 2 h before the LPS challenge. Control rats receive oral methylcellulose (10 mL/kg). Only one dose of Navarixin or vehicle is given in these experiments\[^1\].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**CUSTOMER VALIDATION**

- [Nat Microbiol.](https://www.nature.com/articles/s41564-017-0037-x) 2017 May 15;2:17072.
REFERENCES


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