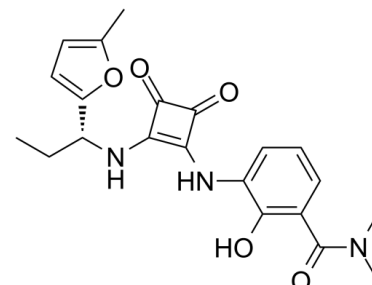


Data Sheet

Product Name:	Navarixin
Cat. No.:	CS-0609
CAS No.:	473727-83-2
Molecular Formula:	C ₂₁ H ₂₃ N ₃ O ₅
Molecular Weight:	397.42
Target:	CXCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
Solubility:	H ₂ O : < 0.1 mg/mL (insoluble); DMSO : ≥ 50 mg/mL (125.81 mM)



BIOLOGICAL ACTIVITY:

Navarixin is a potent, allosteric antagonist of both **CXCR1** and **CXCR2**, with K_d 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. IC₅₀ & Target: K_d: 41 nM (cynomolgus CXCR1), 0.20 nM (mouse CXCR2), 0.20 nM (rat CXCR2), 0.08 nM (cynomolgus monkey CXCR2)^[1] **In Vitro**: Navarixin is a potent, allosteric antagonist of both CXCR1 and CXCR2, with K_d 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 (Extracted from published papers and Only for reference)

Cell Assay: ^[2] **Recombinant cells** are resuspended at 1×10^6 /mL in assay buffer (phenol red free-RPMI 1640 supplemented with 2% FBS). Human neutrophils are resuspended at 2×10^6 /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].

Animal Administration: Navarixin is suspended in 0.4% methylcellulose vehicle for both mice and rat assay^[1].^[1] Mice^[1]

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^[1]

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].

References:

- [1]. Gonsiorek W, et al. Pharmacological characterization of Sch527123, a potent allosteric CXCR1/CXCR2 antagonist. J Pharmacol Exp Ther. 2007 Aug;322(2):477-85.
- [2]. Chapman RW, et al. A novel, orally active CXCR1/2 receptor antagonist, Sch527123, inhibits neutrophil recruitment, mucus production, and goblet cell hyperplasia in animal models of pulmonary inflammation. J Pharmacol Exp Ther. 2007 Aug;322(2):486-93.
- [3]. Ning Y, et al. The CXCR2 antagonist, SCH-527123, shows antitumor activity and sensitizes cells to NSC 266046 in preclinical colon cancer models. Mol Cancer Ther. 2012 Jun;11(6):1353-64.

CAIndexNames:

Benzamide, 2-hydroxy-N,N-dimethyl-3-[[2-[[[(1R)-1-(5-methyl-2-furanyl)propyl]amino]-3,4-dioxo-1-cyclobuten-1-yl]amino]-

SMILES:

O=C1C(C(NC2=CC=CC(C(N(C)C)=O)=C2O)=C1N[C@H](CC)C3=CC=C(O3)C)=O

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

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