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产品名称：SCH 527123
产品别名：Navarixin；MK-7123

生物活性：

Description

Navarixin is a potent, allosteric antagonist of both CXCR1 and CXCR2, with Kd values of 41 nM for cynomolgus CXCR1 and 0.20 nM, 0.20 nM, 0.08 nM for mouse, rat and cynomolgus monkey CXCR2, respectivelly.

IC_{50} & Target

Cynomolgus CXCR2	Mouse CXCR2	Rat CXCR2	Cynomolgus CXCR1
0.08 nM (Kd)	0.2 nM (Kd)	0.2 nM (Kd)	41 nM (Kd)

In Vitro

Navarixin is a potent, allosteric antagonist of both CXCR1 and CXCR2, with Kd values of 41 nM for cynomolgus CXCR1 and 0.20 nM, 0.20 nM, 0.08 nM for mouse, rat and cynomolgus monkey CXCR2, respectivelly[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].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (125.81 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5162 mL	12.5811 mL	25.1623 mL
5 mM	0.5032 mL	2.5162 mL	5.0325 mL
10 mM	0.2516 mL	1.2581 mL	2.5162 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

	Solubility: ≥ 2.5 mg/mL (6.29 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.29 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (6.29 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.29 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.29 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.29 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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 CO_2 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 CO_2 incubator), the filters are removed[2].
Animal Administration	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.