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产品名称：Reparixin (L-lysine salt)
产品别名：瑞帕利辛 L-赖氨酸盐；Repertaxin L-lysine salt

生物活性：

Description	Reparixin L-lysine salt is an allosteric inhibitor of chemokine receptor 1/2 (CXCR1/2) activation.			
IC_{50} & Target	$CXCR1^{wt}$	$CXCR1^{Ile43Val}$	CXCR1	CXCR2
	5.6 nM (IC_{50}, in L1.2 cells)	80 nM (IC_{50}, in L1.2 cells)	1 nM (IC_{50}, in cells)	~100 nM (IC_{50}, in cells)
In Vitro	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 (IC50 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].			
In Vivo	The pharmacokinetics and metabolism of Reparixin are investigated in rats and dogs after intravenous administration of [^{14}C]-Reparixin L-lysine salt. Plasma protein binding of Reparixin is >99% in the laboratory animals and humans up to 50 μg/mL, but lower at higher concentrations. Although radioactivity is rapidly distributed into rat tissues, V_{ss} is low (about 0.15 L/kg) in both rat and dog. Nevertheless, Reparixin is more rapidly eliminated in rats ($t_{1/2}$~0.5 h) than in dogs ($t_{1/2}$~10 h)[3].			
Solvent&Solubility	***In Vitro:*** **H_2O : ≥ 200 mg/mL (465.58 mM)** * "≥" means soluble, but saturation unknown.			

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3279 mL	11.6395 mL	23.2791 mL
	5 mM	0.4656 mL	2.3279 mL	4.6558 mL
	10 mM	0.2328 mL	1.1640 mL	2.3279 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:

1.Reparixin L-lysine salt is prepared in saline[4].

References

[1]. Moriconi A, et al. Design of noncompetitive interleukin-8 inhibitors acting on CXCR1 and CXCR2. J Med Chem. 2007 Aug 23;50(17):3984-4002.

[2]. Bertini R, et al. Receptor binding mode and pharmacological characterization of a potent and selective dual CXCR1/CXCR2non-competitive allosteric inhibitor. Br J Pharmacol. 2012 Jan;165(2):436-54.

[3]. Midgley I, et al. Species differences in the pharmacokinetics and metabolism of reparixin in rat and dog. Xenobiotica. 2006 May;36(5):419-40

[4]. Catrina, Anca, et al. METHODS AND COMPOUNDS FOR THE TREATMENT OF BONE LOSS AND/OR PAIN. US 20170105971 A1.

	[5]. Bertini R, et al. Noncompetitive allosteric inhibitors of the inflammatory chemokine receptors CXCR1 and CXCR2: prevention of reperfusion injury. Proc Natl Acad Sci U S A. 2004 Aug 10;101(32):11791-6.

实验参考：

Cell Assay	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 μM) 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 μm pore size Transwell filters[1].
Animal Administration	Rats and Dogs[3] Male and female Sprague-Dawley CD (albino) rats and male Lister Hooded (partially pigmented) rats are used. Male and female beagle Dogs (age about 15 months, bodyweight range 8.3-9.4 kg at the time of dosing) are used. Rats and Dogs are dosed i.v. with repurified [^{14}C]-Reparixin free acid and an equivalent quantity of L-lysine suitably radiodiluted with Reparixin L-lysine salt in a solution of sterile isotonic (0.9%, w/v) saline. Rats are dosed with a solution of total drug concentration 9 mg/mL at a dose volume of 5 mL/kg (30 mg free Reparixin /kg) by bolus injection into a caudal vein. Dogs are dosed with a solution of total drug concentration 100 mg/mL at a dose volume of 0.5 mL/kg (33 mg free Reparixin/kg) by bolus injection into a superficial forelimb vein.
References	[1]. Moriconi A, et al. Design of noncompetitive interleukin-8 inhibitors acting on CXCR1 and CXCR2. J Med Chem. 2007 Aug 23;50(17):3984-4002. [2]. Bertini R, et al. Receptor binding mode and pharmacological characterization of a potent and selective dual CXCR1/CXCR2non-competitive allosteric inhibitor. Br J Pharmacol. 2012 Jan;165(2):436-54. [3]. Midgley I, et al. Species differences in the pharmacokinetics and metabolism of reparixin in rat and dog. Xenobiotica. 2006 May;36(5):419-40 [4]. Catrina, Anca, et al. METHODS AND COMPOUNDS FOR THE TREATMENT OF BONE LOSS AND/OR PAIN. US 20170105971 A1. [5]. Bertini R, et al. Noncompetitive allosteric inhibitors of the inflammatory chemokine receptors CXCR1 and CXCR2: prevention of reperfusion injury. Proc Natl Acad Sci U S A. 2004 Aug 10;101(32):11791-6.