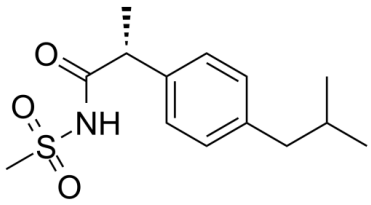
Data Sheet

Product Name:	Reparixin
Cat. No.:	CS-1379
CAS No.:	266359-83-5
Molecular Formula:	C14H21NO3S
Molecular Weight:	283.39
Target:	CXCR
Pathway:	GPCR/G Protein; Immunology/Inflammation
Solubility:	H2O : < 0.1 mg/mL (insoluble); DMSO : ≥ 100 mg/mL (352.87 mM)



BIOLOGICAL ACTIVITY:

Reparixin is a non-competitive allosteric inhibitor of the chemokine receptors **CXCR1** and **CXCR2** activation with **IC_{50}**s of 1 and 100 nM, respectively. IC50 & Target: IC50: 5.6/80 nM ($CXCR1^{wt}$/$CXCR1^{Ile43Val}$, in L1.2 cell)[1] **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 (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]. **In Vivo:** 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-1β in the brain after middle cerebral artery occlusion/reperfusion (MCAo) in mice. Bars represent levels of IL-1β (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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Reparixin is dissolved in saline at the appropriate dilution[1].[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-1μM) 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:** Reparixin is dissolved in saline and administered subcutaneously (Mice and Rats).[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.

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]. Kim HY, et al. Reparixin, an inhibitor of CXCR1 and CXCR2 receptor activation, attenuates blood pressure and hypertension-related mediators expression in spontaneously hypertensive rats. Biol Pharm Bull. 2011;34(1):120-7.

[4]. Sousa LF, et al. Blockade of CXCR1/2 chemokine receptors protects against brain damage in ischemic stroke in mice. Clinics (Sao Paulo). 2013;68(3):391-4.

[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.

[6]. Krishnamurthy A, et al. Identification of a novel chemokine-dependent molecular mechanism underlying rheumatoid arthritis-associated autoantibody-mediated bone loss. Ann Rheum Dis. 2016 Apr;75(4):721-9.

[7]. Crespo J, et al. Human Naive T Cells Express Functional CXCL8 and Promote Tumorigenesis. J Immunol. 2018 Jul 15;201(2):814-820.

CAIndexNames:

Benzeneacetamide, α-methyl-4-(2-methylpropyl)-N-(methylsulfonyl)-, (αR)-

SMILES:

CS(=O)(NC([C@@H](C1=CC=C(CC(C)C)C=C1)C)=O)=O

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