Reparixin

Cat. No.: HY-15251

CAS No.: 266359-83-5

Molecular Formula: $C_{14}H_{21}NO_3S$

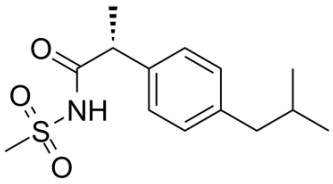
Molecular Weight: 283.39

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 : ≥ 100 mg/mL (352.87 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	3.5287 mL	17.6435 mL	35.2871 mL
5 mM	0.7057 mL	3.5287 mL	7.0574 mL
10 mM	0.3529 mL	1.7644 mL	3.5287 mL

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 (8.82 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.82 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.82 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

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.

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

PROTOCOL

Cell Assay [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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Ann Rheum Dis. 2016 Apr;75(4):721-9.
- Ann Rheum Dis. 2016 Apr;75(4):730-8.
- Sci Adv. 2019 May 8;5(5):eaav7384.
- Nat Commun. 2017 May 26;8:15584.
- J Allergy Clin Immunol. 2018 Jun;141(6):2286-2289.e5.

See more customer validations on www.MedChemExpress.com

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.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA