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产品名称：Iguratimod
产品别名：艾拉莫德；T614

生物活性：

Description	Iguratimod is an antirheumatic agent, acts as an inhibitor of COX-2, with an IC50 of 20 μM (7.7 μg/mL), but shows no effect on COX-1. Iguratimod also inhibits macrophage migration inhibitory factor (MIF) with an IC50 of 6.81 μM.	
IC_{50} & Target	COX-2	MIF
	20 μM (IC_{50})	6.81 μM (IC_{50})
In Vitro	Iguratimod (T-614) is an antirheumatic agent, acts as an inhibitor of COX-2, with an IC50 of 20 μM (7.7 μg/mL), but shows no effect on COX-1. Iguratimod (0.1, 1, 10 μg/mL) inhibits bradykinin-stimulated PGE2 release from fibroblasts. Iguratimod suppresses the COX activity from bradykinin stimulated fibroblasts in a concentration-dependent manner, with an IC50 of 48 μg/mL. Iguratimod (10 and 30 μg/mL) also dose-dependently inhibits COX-2 mRNA levels[1]. In addition, Iguratimod potently inhibits macrophage migration inhibitory factor (MIF) with an IC50 of 6.81 μM. Iguratimod is synergetic with glucocorticoids in vitro[3].	
In Vivo	Iguratimod (5 or 20 mg/kg) shows analgesic effect, significantly improves the pain withdrawal threshold of the left hind paw in dose-dependent manner in rats. Iguratimod (5 or 20 mg/kg) reduces the elevation of pERK1/2 and c-Fos in the spinal cord induced by cancer cell inoculation. Iguratimod also dose-dependently decreases the IL-6 levels in rats. In Iguratimod-treated rats, the activity of osteoclasts is weaker than the control group[2]. Iguratimod (20 mg/kg i.p.) shows significantly increased survival in BALB/c mice that are vulnerable to endotoxemia, and attenuates TNFα release measured in serum isolated 90 min post-LPS administration in wild-type C57BL/6 mice[3].	

Solvent&Solubility

In Vitro:

DMSO : 33.33 mg/mL (**89.03 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6712 mL	13.3558 mL	26.7115 mL
5 mM	0.5342 mL	2.6712 mL	5.3423 mL
10 mM	0.2671 mL	1.3356 mL	2.6712 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→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (6.68 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.68 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。
References	[1]. Tanaka K, et al. T-614, a novel antirheumatic drug, inhibits both the activity and induction of cyclooxygenase-2 (COX-2) in cultured fibroblasts. Jpn J Pharmacol. 1995 Apr;67(4):305-14. [2]. Sun Y, et al. Anti-rheumatic drug iguratimod protects against cancer-induced bone pain and bone destruction in a rat model. Oncol Lett. 2017 Jun;13(6):4849-4856. [3]. Iguratimod, et al. Identification of Iguratimod as an Inhibitor of Macrophage Migration Inhibitory Factor (MIF) with Steroid-sparing Potential. J Biol Chem. 2016 Dec 16;291(51):26502-26514.

实验参考：

Cell Assay	Briefly, human Raji B cells are plated at a density of 0.5 × 10^4 cells/well in a 96-well plate and synchronized by incubation for 24 h in RPMI 1640 medium supplemented with 0.1-0.5% FBS. Synchronized cells are pretreated with Iguratimod or vehicle for 30 min prior to stimulation with macrophage migration inhibitory factor (MIF) for 24 h. At 20 h BrdU is added to cells and quantified using a BrdU Cell proliferation assay kit[3].
Animal Administration	Mice[3] Endotoxemia is induced by intraperitoneal injection of LPS from E. coli O111:B4. In BALB/c animals, 5 mg/kg LPS is used as a lethal dose for survival experiments; animals are treated with Iguratimod (20 mg/kg i.p.) 0.5 h prior to LPS, 6 h after LPS, and then once daily for 3 days and monitored for survival over 2 weeks. In C57BL/6 animals, 20 mg/kg LPS is used as non-lethal dose for plasma cytokine experiments; animals are pretreated with Iguratimod (20 mg/kg i.p.) twice, one dose each at 2 and 0.5 h prior to LPS administration, and euthanized at 90 min post-LPS by CO_2 asphyxiation with cervical dislocation. Blood is collected by cardiac puncture and allowed to clot 20 min at room temperature and 20 min at 4°C; sera are isolated by centrifugation at 300 × g for 10 min and stored at −20°C for further analysis by TNFα ELISA (1:3 dilution)[3].
References	[1]. Tanaka K, et al. T-614, a novel antirheumatic drug, inhibits both the activity and induction of cyclooxygenase-2 (COX-2) in cultured fibroblasts. Jpn J Pharmacol. 1995 Apr;67(4):305-14. [2]. Sun Y, et al. Anti-rheumatic drug iguratimod protects against cancer-induced bone pain and bone destruction in a rat model. Oncol Lett. 2017 Jun;13(6):4849-4856. [3]. Iguratimod, et al. Identification of Iguratimod as an Inhibitor of Macrophage Migration Inhibitory Factor (MIF) with Steroid-sparing Potential. J Biol Chem. 2016 Dec 16;291(51):26502-26514.