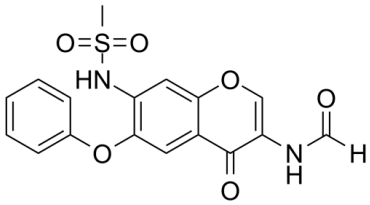
Data Sheet

Product Name:	Iguratimod
Cat. No.:	CS-0617
CAS No.:	123663-49-0
Molecular Formula:	C17H14N2O6S
Molecular Weight:	374.37
Target:	COX
Pathway:	Immunology/Inflammation
Solubility:	DMSO : 33.33 mg/mL (89.03 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

Iguratimod is an antirheumatic agent, acts as an inhibitor of **COX-2**, with an **IC_{50}** of 20 μM (7.7 μg/mL), but shows no effect on COX-1. Iguratimod also inhibits macrophage migration inhibitory factor (**MIF**) with an **IC_{50}** of 6.81 μM. IC50 & Target: IC50: 20 μM (COX-2)[1], 6.81 μM (MIF)[3] **In Vitro:** Iguratimod (T-614) is an antirheumatic agent, acts as an inhibitor of COX-2, with an IC_{50} 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 IC_{50} 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 IC_{50} 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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [3]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: [3]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.

CAIndexNames:

Methanesulfonamide, N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]-

SMILES:

O=C1C2=CC(OC3=CC=CC=C3)=C(C=C2OC=C1NC([H])=O)NS(=O)(C)=O

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