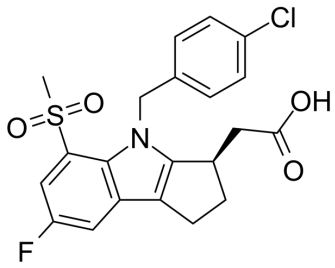
Laropiprant

Cat. No.:	HY-50175
CAS No.:	571170-77-9
Molecular Formula:	$C_{21}H_{19}ClFNO_4S$
Molecular Weight:	435.9
Target:	Prostaglandin Receptor
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (229.41 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2941 mL	11.4705 mL	22.9410 mL
5 mM	0.4588 mL	2.2941 mL	4.5882 mL
10 mM	0.2294 mL	1.1471 mL	2.2941 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 (5.74 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Laropiprant is a potent and selective DP receptor antagonist with K_i values of 0.57 nM and 2.95 nM for DP receptor and TP Receptor, respectively[1][2][3].

IC_{50} & Target

DP	TP Receptor
0.57 nM (Ki)	2.95 nM (Ki)

In Vitro

Laropiprant (0.01-1000 μM; 10 mins; HEK293 cells) is an inverse agonist of DP1 cAMP signaling and reduces DP1 cAMP signaling below basal levels[1].

Laropiprant (1 μM; 0-24 h; HEK293 cells) is a pharmacochaperone in promoting DP1 cell surface expression[1].

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

In Vivo

Laropiprant (0-100 mg/kg; p.o. and i.v.; male Sprague-Dawley rats) exhibits good pharmacokinetic profiles[3].

Pharmacokinetic Analysis in Male Sprague-Dawley rats[3]

Route	Dose (mg/kg)	$AUC_{0-\infty}$ (μM·hr)	Cl_p (mL/min/kg)	V_{dss} (L/kg)	$T_{1/2}$ (hr)
PO	1	22.7	1.9	0.7	7.4
PO	5	96.0	2.1	0.9	7.6
Route	Dose (mg/kg)	$AUC_{0-\infty}$ (μM·hr)	C_{max} (μM)	T_{max} (hr)	F(%)
IV	5	52.6	15.6	1.2	/

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PROTOCOL

Cell Assay [2]

Vena8Fluoro+ Biochips are coated with collagen (200 μg/mL) at 4°C overnight and thereafter blocked with bovine serum albumin (10 μg/mL) for 30 minutes at room temperature followed by washing steps. Whole blood collected in sodium citrate is incubated with 3, 3-dihexyloxacarbocyanine iodide (1 μM) in the dark for 10 minutes. PGD2 (30 nM), BW245c (3 nM) are added 10 min before the start of perfusion, and the DP antagonist BWA868c or Laropiprant (1 μM) are added 10 min before the agonists. In another set of experiments whole blood is treated with niacin (3 mM), acetylsalicylic acid (1 mM) or Laropiprant (1 μM and 10 μM) for 30 min. $CaCl_2$ at a final concentration of 1 mM is added 2 minutes before the perfusion over the collagen-coated chip. Perfusion is carried out at a shear rate of 30 dynes cm^2. Thrombus formation is recorded. Computerized image analysis is performed by DucoCell analysis software, where the area covered by the thrombus is calculated. Data are expressed as percent of area covered in a control sample[2].

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REFERENCES

[1]. Labrecque P, et, al. Inverse agonist and pharmacochaperone properties of MK-0524 on the prostanoid DP1 receptor. PLoS One. 2013 Jun 10;8(6):e65767.

[2]. Sturino CF, et, al. Discovery of a potent and selective prostaglandin D2 receptor antagonist, [(3R)-4-(4-chloro-benzyl)-7-fluoro-5-(methylsulfonyl)-1,2,3,4-tetrahydrocyclopenta[b]indol-3-yl]-acetic acid (MK-0524). J Med Chem. 2007 Feb 22;50(4):794-806.

[3]. Chang SW, et, al. The pharmacokinetics and disposition of MK-0524, a Prosglandin D2 Receptor 1 antagonist, in rats, dogs and monkeys. Xenobiotica. 2007 May;37(5):514-33.

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