Ramatroban

Cat. No.: HY-B0745

CAS No.: 116649-85-5

Molecular Formula: $C_{21}H_{21}FN_2O_4S$

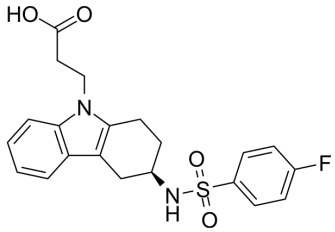
Molecular Weight: 416.47

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 : 125 mg/mL (300.14 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4011 mL	12.0057 mL	24.0113 mL
5 mM	0.4802 mL	2.4011 mL	4.8023 mL
10 mM	0.2401 mL	1.2006 mL	2.4011 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: ≥ 2.08 mg/mL (4.99 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.99 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.99 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Ramatroban is a selective thromboxane A_2 (TxA_2, IC_{50}=14 nM) antagonist, which also antagonizes CRTH2 (IC_{50}=113 nM) by inhibiting PGD_2 binding.

IC_{50} & Target

hTP	hDP2	hDP2
14 nM (IC_{50})	113 nM (IC_{50})	33.4 μM (IC_{50})

In Vitro

Ramatroban is a potent human thromboxane receptor (hTP) antagonist with an IC_{50} of 18 nM in a human TP binding assay.

	Ramatroban inhibits prostaglandin D_2 receptor DP2 (CRTH2) with an IC_{50} of 113 nM in a human DP2 binding assay. Ramatroban also inhibits human CYP isoform CYP2C9 with an IC_{50} of 15 μM[1]. Ramatroban is a selective thromboxane-type prostanoid (TP) receptor antagonist. PGD_2-stimulated human eosinophil migration is shown to be mediated exclusively through activation of CRTH2, and surprisingly, these effects are completely inhibited by Ramatroban. Ramatroban is an antagonist for CRTH2, and inhibits PGD_2-induced migration of eosinophils via CRTH2 blockade. ^3H-labeled PGD_2 binds to a single site on CRTH2 transfectants with high affinity (K_D=6.3 nM, B_{max}=450 pM). Nonlabeled PGD_2 inhibits the binding of ^3H-labeled PGD_2 to CRTH2 transfectants in a concentration-dependent manner with an EC_{50} value of 2.7 nM. Ramatroban shows significant inhibitory effects on the binding of ^3H-labeled PGD_2 to CRTH2, albeit with much lower potency (IC_{50}=100 nM). Ramatroban also inhibits PGD_2-induced Ca^{2+} mobilization in CRTH2 transfectants to almost the same extent with an IC_{50} value of 30 nM. Ramatroban completely inhibits the PGD_2-induced migration of eosinophils in a concentration-dependent manner with an IC_{50} value of 170 nM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Ramatroban is an orally bioavailable small molecule antagonist of CRTH2. Systemic administration of Ramatroban (30 mg/kg) in $CRTH2^{+/+}$ mice produces the same effects as seen in CRTH2 deficiency. Ramatroban completely blocks LPS-induced decreases in social and object exploratory behavior ($p<0.01$). In addition, tumor-impaired social interaction and object exploratory behavior in $CRTH2^{+/+}$ mice are completely reversed by a single injection of Ramatroban, even when the tumor is enlarged[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	CRTH2 transfectants are resuspended in binding buffer (50 mM Tris-HCl, pH 7.4, 40 mM $MgCl_2$, 0.1% BSA, 0.1% NaN_3). Cell suspension (2×10^5 cells), ^3H-labeled PGD_2, and various concentrations of Ramatroban (0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM and 10 μM) are then mixed in a 96-well U-bottomed polypropylene plate and incubated in a final volume of 100 μL for 60 min at room temperature. After incubation, the cell suspension is transferred to a filtration plate and washed three times with binding buffer. Scintillant is added to the filtration plate, and radioactivity remaining on the filter is measured by a scintillation counter. Nonspecific binding is determined by incubating the cell suspension and ^3H-labeled PGD_2 in the presence of 1 μM unlabeled PGD_2[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	Human eosinophils are purified and resuspended in migration buffer (20 mM HEPES, pH 7.6, 0.1% BSA, Hanks' solution) at a density of 6×10^6 cells/mL. Fifty microliters of the cell suspension (3×10^5 cells/well) is then dispensed into the upper chamber of a 96-well type chemotaxis chamber (pore diameter=5 μm), and 30 μL of ligand solution is added to the lower chamber. Cells are preincubated with various concentrations of Ramatroban (0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM and 10 μM) or BWA868C at 37°C for 10 min. The migration assays are performed in a humidified incubator at 37°C, 5% CO_2 for 2 h. The number of cells migrating into the lower chamber is counted[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Five micrograms of LPS (closed columns) or saline (open columns) are intraperitoneally injected into $CRTH2^{+/+}$ mice. $CRTH2^{+/+}$ mice are pretreated intraperitoneally for 1 h with 30 mg/kg Ramatroban. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Stearns BA, et al. Novel tricyclic antagonists of the prostaglandin D_2 receptor DP2 with efficacy in a murine modelof allergic rhinitis. Bioorg Med Chem Lett. 2009 Aug 15;19(16):4647-51.

[2]. Sugimoto H, et al. An orally bioavailable small molecule antagonist of CRTH2, ramatroban (BAY u3405), inhibits prostaglandin D_2-induced eosinophil migration in vitro. J Pharmacol Exp Ther. 2003 Apr;305(1):347-52.

[3]. Haba R, et al. Central CRTH2, a second prostaglandin D_2 receptor, mediates emotional impairment in the lipopolysaccharide and tumor-induced sickness behavior model. J Neurosci. 2014 Feb 12;34(7):2514-23.

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