Palosuran hydrochloride

Cat. No.: HY-10655A

CAS No.: 2469274-58-4

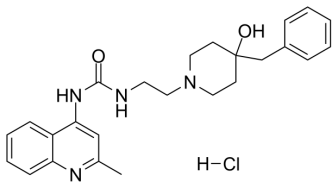
Molecular Formula: $C_{25}H_{31}ClN_4O_2$

Molecular Weight: 454.99

Target: Urotensin Receptor

Pathway: GPCR/G Protein

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (109.89 mM; Need ultrasonic)
H_2O : 7.14 mg/mL (15.69 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1979 mL	10.9893 mL	21.9785 mL
5 mM	0.4396 mL	2.1979 mL	4.3957 mL
10 mM	0.2198 mL	1.0989 mL	2.1979 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 (5.49 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.49 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.49 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Palosuran hydrochloride (ACT-058362 hydrochloride) is a potent, selective, and orally active antagonist of urotensin II receptor, with an IC_{50} of 3.6 nM for CHO cell membranes expressing human recombinant receptors. Palosuran hydrochloride can improves pancreatic and renal function in diabetic rats[1][2].

IC_{50} & Target

IC50: 3.6 nM (human urotensin II receptor)[1]

In Vitro

Palosuran (8 h) inhibits ^{125}I-U-II binding to human UT receptor, with IC_{50}s of 46.2 nM on TE 671 cells and 86 nM on recombinant CHO cells[1].

	Palosuran inhibits Ca^{2+} mobilization in response to human U-II in CHO cells expressing human and rat UT receptor with IC_{50}s of 17 and >10000 nM, respectively[1]. Palosuran (0.12-10000 nM; 20 min) inhibits human U-II induced MAPK phosphorylation in a dose-dependent manner in recombinant CHO cells, with an IC_{50} of 150 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ACT-058362 (10 mg/kg/h; i.v.) fully prevents the decrease in renal blood flow after ischemia in rats without decreasing blood pressure[1]. Palosuran (300 mg/kg/d; p.o. for 16 weeks) improves the survival, increases insulin, and slows the increase in glycemia, glycosylated hemoglobin, and serum lipids in streptozotocin-induced diabetic rats[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male Wistar rats with renal ischemia and reperfusion[1]
Dosage:	20 mg/kg/h for 135 min
Administration:	I.v. (continuous infusion) for 135 min
Result:	Restored renal blood flow to baseline values at 30 min after reperfusion and by 60 min increased renal blood flow by 12% above baseline values. Did not significantly alter mean arterial blood pressure (MAP) and heart rate (HR).

CUSTOMER VALIDATION

- Endocrinology. 2018 May 1;159(5):2253-2263.

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REFERENCES

[1]. Clozel M, et, al. Pharmacology of the urotensin-II receptor antagonist palosuran (ACT-058362; 1-[2-(4-benzyl-4-hydroxy-piperidin-1-yl)-ethyl]-3-(2-methyl-quinolin-4-yl)-urea sulfate salt): first demonstration of a pathophysiological role of the urotensin System. J Pharmacol Exp Ther. 2004 Oct;311(1):204-12.

[2]. Clozel M, et, al. The urotensin-II receptor antagonist palosuran improves pancreatic and renal function in diabetic rats. J Pharmacol Exp Ther. 2006 Mar;316(3):1115-21.

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