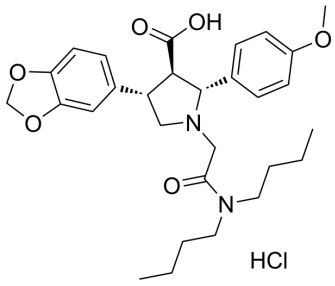
Atrasentan hydrochloride

Cat. No.:	HY-15403A
CAS No.:	195733-43-8
Molecular Formula:	$C_{29}H_{39}ClN_2O_6$
Molecular Weight:	547.08
Target:	Endothelin 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 : 28.57 mg/mL (52.22 mM; Need ultrasonic)

H_2O : 0.5 mg/mL (0.91 mM; ultrasonic and warming and adjust pH to 4 with HCl and heat to 60°C)

0.1 M HCL : < 1 mg/mL (ultrasonic;warming;adjust pH to 1 with HCl;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8279 mL	9.1394 mL	18.2789 mL
5 mM	0.3656 mL	1.8279 mL	3.6558 mL
10 mM	0.1828 mL	0.9139 mL	1.8279 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 (4.57 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.57 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.57 mM); Clear solution
4. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 0.75 mg/mL (1.37 mM); Clear solution; Need ultrasonic and warming

BIOLOGICAL ACTIVITY

Description

Atrasentan hydrochloride (ABT-627 hydrochloride) is a selective endothelin A receptor antagonist with an IC_{50} of 0.0551 nM for ET_A[1].

IC_{50} & Target

IC50: 0.055 nM (ET_A)

In Vitro	Atrasentan hydrochloride (ABT-627 hydrochloride) (0-50 μM) significantly inhibits LNCaP and C4-2b prostate cancer cell growth[2]. Atrasentan profoundly induces several CYPs and drug transporters (e.g. 12-fold induction of CYP3A4 at 50 μM). It is a moderate P-gp inhibitor (IC_{50} in P388/dx cells=15.1±1.6 μM) and a weak BCRP inhibitor (IC_{50} in MDCKII-BCRP cells=59.8±11 μM)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Atrasentan hydrochloride (ABT-627 hydrochloride) (3 mg/kg, p.o.) inhibits the pressor response induced by big endothelin-1 (1 nmol/kg) in pithed rats[1]. Aatrasentan (ABT-627, 10 mg/kg, i.p.) inhibits the C4-2b tumor growth within the bone environment to some extent in the SCID-hu model[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	All three prostate cancer cell lines (LNCaP, C4-2b, and PC-3 cells) are seeded at a density of 3×10^3 cells per well in 96-well microtiter culture plates. After overnight incubation, the medium is removed and replaced with a fresh medium containing different concentrations of ABT-627 (0-50 μM) diluted from a 10-mM stock. After 72 h of incubation with drug, 20 μL of MTT solution (5 mg/mL in PBS) are added to each well and incubated further for 2 h. Upon termination, the supernatant is aspirated and the MTT formazan formed by metabolically viable cells is dissolved in isopropanol (100 μL). The plates are mixed for 30 min on a gyratory shaker, and the absorbance is measured at 595 nm on a plate reader. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	YM598 (0.3, 1, and 3 mg/kg), atrasentan (0.3, 1, and 3 mg/kg), or 0.5% methyl cellulose as vehicle is orally administered to rats with a dosing cannula. Dosing volume of the test substances and vehicle is set at 5 mL/kg. Approximately 20 min after administration of compounds, the rats are anesthetized with NSC 10816, and then pithed and ventilated 30 min after dosing. Approximately 1 h after oral administration of compounds, big endothelin-1 (1 nmol/kg) is intravenously administered, and blood pressure is measured. In these two experiments, the dose of test compound that cause 50% inhibition (ID_{50}) of the big endothelin-1-induced increase in diastolic blood pressure is determined by linear regression analysis. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Commun Biol. 2022 Jul 28;5(1):750.
- Eur J Pharmacol. 2019 Mar 12;852:142-150.
- Mol Immunol. 2019 Oct;114:10-18.
- J Vet Intern Med. 2015 Nov;29(6):1584-94.
- Department Veterinary Clinical Medicine. University of Illinois. 2015.

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REFERENCES

[1]. Yuyama H, et al. Superiority of YM598 over atrasentan as a selective endothelin ETA receptor antagonist. Eur J Pharmacol. 2004 Sep 13;498(1-3):171-7.

[2]. Banerjee S, et al. In vitro and in vivo molecular evidence for better therapeutic efficacy of ABT-627 combination in prostate cancer. Cancer Res. 2007 Apr 15;67(8):3818-26.

[3]. Weiss J, et al. Interaction potential of the endothelin-A receptor antagonist atrasentan with drug transporters and drug-metabolising enzymes assessed in vitro. Cancer Chemother Pharmacol. 2011 Oct;68(4):1093-8.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA