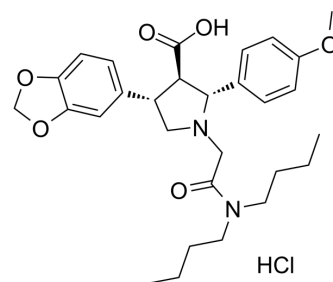


Atrasentan hydrochloride

Cat. No.:	HY-15403A		
CAS No.:	195733-43-8		
Molecular Formula:	C ₂₉ H ₃₉ ClN ₂ O ₆		
Molecular Weight:	547.08		
Target:	Endothelin Receptor		
Pathway:	GPCR/G Protein		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (182.79 mM)
 H₂O : 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)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

- 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
- 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
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (4.57 mM); Clear solution
- 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 IC₅₀ of 0.0551 nM for ET_A^[1].

IC₅₀ & Target	IC ₅₀ : 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] . Atrasentan (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 (ID₅₀) 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

- Mol Immunol. 2019 Oct;114:10-18.
- Eur J Pharmacol. 2019 Mar 12;852:142-150.
- 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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