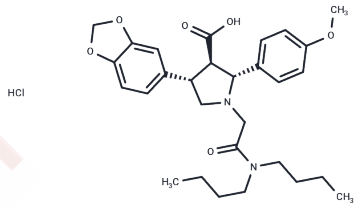
Data Sheet (Cat.No.TQ0270)

TargetMol

Atrasentan hydrochloride

Chemical Properties



CAS No. : 195733-43-8

Formula: C29H39ClN2O6

Molecular Weight: 547.08

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Atrasentan hydrochloride (ABT-627 hydrochloride) is an endothelin receptor antagonist with an IC50 of 55.1 μM for ETA.
Targets(IC50)	Endothelin Receptor
In vitro	Atrasentan (0-50 μM) significantly inhibits LNCaP and C4-2b prostate cancer cell growth. ABT-627 in combination with Taxotere elicits a significantly greater loss of viable prostate cancer cells relative to either agent alone and shows a greater degree of down-regulation of the NF-κB DNA binding activity [2]. Atrasentan profoundly induces several CYPs and drug transporters. It is a moderate P-gp inhibitor (IC50: 15.1 μM in P388/dx cells) and a weak BCRP inhibitor (IC50: 59.8 μM in MDCKII-BCRP cells) [3].
In vivo	Atrasentan (3 mg/kg, p.o.) inhibits the pressor response induced by big endothelin-1 (1 nmol/kg) in pithed rats [1]. Aatrasentan (10 mg/kg, i.p.) inhibited the C4-2b tumor growth within the bone environment to some extent in the SCID-hu model [2].
Kinase Assay	Cells are incubated and treated with Atrasentan. They are then washed twice with PBS and lysed in ice-cold lysis buffer [20 mM Tris (pH 7.4), 150 mM NaCl, 1% Triton X-100, 1 mM EDTA, 1 mM EGTA, 2.5 mM sodium PPi, 1 mM β-glycerophosphate, 1 mM sodium orthovanadate, 1 μg/mL leupeptin, and 1 mM PMSF]. The extracts are centrifuged to remove cellular debris, and the protein content of the supernatants is determined using the bicinchoninic acid (BCA) protein assay reagent. Proteins (150 μg) are incubated with gentle rocking at 4°C overnight with immobilized Akt antibody cross-linked to agarose hydrazide beads. After the Akt is selectively immunoprecipitated from the cell lysates, the immunoprecipitated products are washed twice with lysis buffer and twice with kinase assay buffer [25 mM Tris (pH 7.5), 10 mM MgCl2, 5 mM β-glycerol phosphate, 0.1 mM sodium orthovanadate, 2 mM DTT] and then resuspended in 40 μL of kinase assay buffer containing 200 μM ATP and 1 μg GSK-3α/β fusion protein. The kinase assay reaction is allowed to proceed at 30°C for 30 min and stopped by the addition of Lamelli SDS sample buffer. Reaction products are resolved by 10% SDS-PAGE, followed by Western blotting with antiphosphorylated GSK-3α/β antibody. For analysis of the total amount of Akt, 40 μg of protein from the lysate samples are resolved by 10% SDS-PAGE, followed by Western blotting with anti-Akt antibody [2].
Cell Research	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

Cell Research	concentrations of ABT-627 (0-50 μM) diluted from a 10-mM stock. After 72 h of incubation with the drug, 20 μL of MTT solution (5 mg/mL in PBS) is 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 [2].
Animal Research	YM598 (0.3, 1, and 3 mg/kg), atrasentan (0.3, 1, and 3 mg/kg), or 0.5% methylcellulose as vehicle is orally administered to rats with a dosing cannula. The 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 sodium pentobarbital, 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 causes 50% inhibition (ID50) of the big endothelin-1-induced increase in diastolic blood pressure is determined by linear regression analysis [1].

Solubility Information

Solubility	H2O: 0.4 mg/mL (0.73 mM),when pH is adjusted to 4 with HCl. Sonication and heating to 60℃ are recommended. DMSO: 30 mg/mL (54.84 mM),Sonication is recommended. 0.1 M HCl: < 1 mg/mL (insoluble) (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.66 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0366 mL	0.1828 mL	0.3656 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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

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