Atrasentan hydrochloride

Cat. No.: HY-15403A
CAS No.: 195733-43-8
Molecular Formula: C₂₉H₃₉ClN₂O₆
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 : ≥ 33.3 mg/mL (60.87 mM)
* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td></td>
<td>1.8279 mL</td>
<td>9.1394 mL</td>
<td>18.2789 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.3656 mL</td>
<td>1.8279 mL</td>
<td>3.6558 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.1828 mL</td>
<td>0.9139 mL</td>
<td>1.8279 mL</td>
</tr>
</tbody>
</table>

Preparing Stock Solutions

1. 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

**In Vivo**
1. 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 ETₐ[1].

**IC₅₀ & Target**
IC₅₀: 0.055 nM (ETₐ)

**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 (IC₅₀ in P388/dx cells=15.1±1.6 μM) and a weak BCRP inhibitor (IC₅₀ in MDCKII-BCRP cells=59.8±11 μM)[3].
**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\(^2\).

**PROTOCOL**

**Cell Assay**\(^2\)

All three prostate cancer cell lines (LNCaP, C4-2b, and PC-3 cells) are seeded at a density of \(3 \times 10^3\) 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 \(\mu\)M) diluted from a 10-mM stock. After 72 h of incubation with drug, 20 \(\mu\)L 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 \(\mu\)L). 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**

- **Department Veterinary Clinical Medicine**. University of Illinois. 2015.

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**REFERENCES**


