Bosentan

Cat. No.: HY-A0013
CAS No.: 147536-97-8
Molecular Formula: C_{27}H_{29}N_{5}O_{6}S
Molecular Weight: 551.61
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: ≥ 275 mg/mL (498.54 mM)
* "≥" means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>1.8129 mL</td>
<td>9.0644 mL</td>
<td>18.1287 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.3626 mL</td>
<td>1.8129 mL</td>
<td>3.6258 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.1813 mL</td>
<td>0.9064 mL</td>
<td>1.8129 mL</td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Bosentan is prepared fresh every day as a suspension in 5% gum arabic[^4].

BIOLOGICAL ACTIVITY

Description
Bosentan is a competitive and dual antagonist of endothelin-1 (ET) for the ET\textsubscript{A} and ET\textsubscript{B} receptors with \(K_i\) of 4.7 nM and 95 nM in human SMC, respectively.

IC\textsubscript{50} & Target

\(K_i\): 4.7 nM (ET\textsubscript{A} receptor, in human SMC), 95 nM (ET\textsubscript{A} receptor, in human SMC)[\(^{[1]}\)]

In Vitro

Bosentan (BOS) competitively and specifically antagonizes binding of \(^{125}\)I-labelled ET-1 to ET\textsubscript{A} receptors on human smooth muscle cells (SMC) and ET\textsubscript{B} receptors on human placenta cells. The in vitro binding affinity of Bosentan to ET\textsubscript{A} receptors on human SMC is 4.7 nM and to ET\textsubscript{B} receptors on human SMC or placenta cells is 41 or 95 nM. Bosentan has 67-fold greater selectivity for ET\textsubscript{A} than ET\textsubscript{B} receptors (mean IC\textsubscript{50}=7.1 vs 474.8 nM) in an in vitro \(^{125}\)I-labeling assay[^1].

[^1]: www.MedChemExpress.com
In Vivo

Single-dose Bosentan 62.5 mg significantly (p<0.01 vs baseline) plasma ET-1 levels by 2-fold in 7 pts with WHO class II or III idiopathic or CTD-associated PAH, with peak levels achieved at 8 h[1]. In hypertensive rats, Macitentan 30 mg/kg further decreases mean arterial blood pressure (MAP) by 19 mm Hg when given on top of Bosentan 100 mg/kg. Conversely, Bosentan given on top of Macitentan fails to induce an additional MAP decrease. In pulmonary hypertensive rats, Macitentan 30 mg/kg further decreases mean pulmonary artery pressure (MPAP) by 4 mm Hg on top of Bosentan, whereas a maximal effective dose of Bosentan given on top of Macitentan does not cause any additional MPAP decrease[3].

PROTOCOL

Cell Assay[2]

Cell viability is evaluated by the trypan blue exclusion test. Human dermal fibroblasts are treated with the indicated concentration of Bosentan (10, 20 and 40 μM). Cell viability is examined at 24 and 48 hours. Stained (dead) and unstained (viable) cells are counted with a hematocytometer[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration[3]

Rats[3]

Two-month-old DSS rats and two-month-old Wistar rats are used. Pharmacological effects on mean arterial pressure (MAP) or mean pulmonary arterial pressure (MPAP) and heart rate (HR) are measured up to 120 h after a single gavage at doses ranging from 0.1 to 100 mg/kg (Macitentan) or 3 to 600 mg/kg (Bosentan). To determine whether Macitentan can provide superior pharmacological activity vs. Bosentan, a study is designed in which: 1) Macitentan is administered on top of the maximal effective dose of Bosentan established by the dose-response curve. 2) the same dose of Bosentan is administered on top of the maximal effective dose of Macitentan. The maximal effective dose of the second compound is administered at T_{max} of the first tested compound.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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REFERENCES


