Zamicastat

Cat. No.: HY-106004
CAS No.: 1080028-80-3
Molecular Formula: C₂₁H₂₁F₂N₃OS
Molecular Weight: 401.47
Target: Dopamine β-hydroxylase; P-glycoprotein; BCRP
Pathway: Metabolic Enzyme/Protease; Membrane Transporter/Ion Channel
Storage:
- Powder: -20°C 3 years
- Powder: 4°C 2 years
- In solvent: -80°C 6 months
- In solvent: -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro
DMSO: 150 mg/mL (373.63 mM; need ultrasonic)
H₂O: < 0.1 mg/mL (insoluble)

<table>
<thead>
<tr>
<th>Solvent &amp; Mass Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.4908 mL</td>
<td>12.4542 mL</td>
<td>24.9085 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4982 mL</td>
<td>2.4908 mL</td>
<td>4.9817 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2491 mL</td>
<td>1.2454 mL</td>
<td>2.4908 mL</td>
</tr>
</tbody>
</table>

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 (6.23 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.23 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.23 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Zamicastat (BIA 5-1058) is a dopamine β-hydroxylase (DBH) inhibitor and can cross the blood-brain barrier (BBB) to cause central as well as peripheral effects. Zamicastat is also a concentration-dependent dual P-gp and BCRP inhibitor with IC₅₀ values of 73.8 μM and 17.0 μM, respectively[1]. Zamicastat reduces high blood pressure[2].

IC₅₀ & Target
Dopamine β-hydroxylase (DBH)[1]
**IC50:** 73.8 μM (P-gp), 17.0 μM (BCRP)[1]

### In Vitro

Following 4 hours of incubation (5, 10, 20, 50, 80, 100 μM), a significant loss of cell viability is verified with 100 μM Zamicastat (p=0.010) in MDCK-BCRP cells. No significant losses of cell viability are observed after 4 h of incubation for other concentrations in all cell lines. By decreasing the incubation period to 30 min, there is no significant loss of cell viability (p>0.05) at 100 μM in all cell lines[1].

**Cell Viability Assay[1]**

<table>
<thead>
<tr>
<th>Cell Line:</th>
<th>MDCK II, MDCK-MDR1 and MDCK-BCRP cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration:</td>
<td>5, 10, 20, 50, 80, 100 μM</td>
</tr>
<tr>
<td>Incubation Time:</td>
<td>4 hours (5, 10, 20, 50, 80, 100 μM) or 30 min (only 100 μM)</td>
</tr>
<tr>
<td>Result:</td>
<td>A significant loss of cell viability was verified with 100 μM in MDCK-BCRP cells.</td>
</tr>
</tbody>
</table>

### In Vivo

Zamicastat (10, 30 and 100 mg/kg/day; oral bolus, 7 days) is tested acutely against salt-induced hypertension in the Dahl SS rat. Zamicastat produces a dose-dependent decrease in blood pressure. 24 h after Zamicastat administration mean systolic blood pressure (SBP) decrease is -12.6±4.1 mm Hg (P=0.0284), -15.2±2.7 mm Hg (P=0.0026) and -19.0±3.7 mm Hg (P=0.0036) for the 10, 30, and 100 mg/kg body weight dose, respectively. Zamicastat administration also produces a significant 24-h average decrease in diastolic blood pressure (DBP) of -14.6±3.4 mm Hg (P=0.0073) with 10 mg/kg body weight dose, -13.0±4.5 mm Hg (P=0.0347) with 30 mg/kg body weight dose and -15.0±3.1 mm Hg (P=0.0046) with 100 mg/kg body weight dose. Zamicastat administration leads to a decrease in the 24h post-dose mean arterial pressure (MAP) of -13.4±3.8 mm Hg (P=0.0162), -14.0±3.5 mm Hg (P=0.0101) and -20.6±3.7 mm Hg (P=0.0026) for the 10, 30, and 100 mg/kg body weight dose, respectively. There is a small, but significant, effect of Zamicastat on the 24-h mean heart rate (HR) post-dose for all tested doses (10 mg/kg: -19.1±3.2 beats/min, P=0.0019; 30 mg/kg: -13.0±4.5 beats/min, P=0.0347; 100 mg/kg: -21.6±6.6 beats/min, P=0.0235)[2].

**Animal Model:** Six-week-old male inbred male Dahl SS rats[2]

**Dosage:** 10, 30, or 100 mg/kg; 4 mL/kg

**Administration:** Oral bolus, daily, seven days

**Result:** Treatment produced a dose-dependent decrease in blood pressure. Twenty four hours after administration mean SBP decrease was -12.6±4.1 mm Hg (P=0.0284), -15.2±2.7 mm Hg (P=0.0026) and -19.0±3.7 mm Hg (P=0.0036) for the 10, 30, and 100 mg/kg body weight dose, respectively.

**Animal Model:** Ten-week-old male Wistar Han rats[2]

**Dosage:** 30 mg/kg/day

**Administration:** in animal feedings (mixed in meal rodent food) everyday

**Result:** lead to a significant 51% decrease in noradrenaline levels excreted in urine

### REFERENCES


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

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