YO-01027

Cat. No.: HY-13526
CAS No.: 209984-56-5
Molecular Formula: C_{26}H_{23}F_{2}N_{3}O_{3}
Molecular Weight: 463.48
Target: Notch; γ-secretase
Pathway: Neuronal Signaling; Stem Cell/Wnt
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 mg/mL (71.20 mM)
H_{2}O: < 0.1 mg/mL (insoluble)
* "≥" 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>1 mM</td>
<td></td>
<td>2.1576 mL</td>
<td>10.7880 mL</td>
<td>21.5759 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.4315 mL</td>
<td>2.1576 mL</td>
<td>4.3152 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.2158 mL</td>
<td>1.0788 mL</td>
<td>2.1576 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 (5.39 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.39 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
YO-01027 (Dibenzazepine;DBZ) is a potent γ-secretase inhibitor with IC_{50} values of 2.92 and 2.64 nM for Notch and APPL cleavage, respectively.

IC_{50} & Target
IC_{50}: 2.92±0.22 (Notch), 2.64±0.30 (APPL) nM[^1]
**In Vitro**

Increasing concentrations of DBZ administered to APPL- or Notch-expressing cells leads to the progressive accumulation of APPL CTF fragments and a decrease in NICD production in a strictly dose-dependent manner\[^{1}\]. The molecular targets of CE and DBZ are the N-terminal fragment of presenilin 1 within the γ-secretase complex\[^{2}\].

**In Vivo**

DBZ blocks activated Notch1 signaling in abdominal aortic aneurysm (AAA) tissue from both Ang II-infused Apo E\(^{-/-}\) mice and human undergoing AAA repair. DBZ markedly prevents Ang II-stimulated accumulation of macrophages and CD4+ T cells, and ERK-mediated angiogenesis, simultaneously reverses Th2 response, in vivo\[^{3}\]. Administration of DBZ markedly attenuates renal fibrosis and expression of fibrotic markers, including collagen 1α1/3α1, fibronectin, and α-smooth muscle actin. DBZ significantly inhibits ureteral obstruction-induced expression of transforming growth factor (TGF)-β, phosphorylated Smad 2, and Smad 3\[^{4}\].

---

**PROTOCOL**

**Cell Assay**\[^{1}\]

DBZ (0.1, 1, 2.5, 5, 7.5, 10, 25, 50, 100, 250 nM) are added to the S2 cell medium upon induction of Notch or APPL expression, 6 h before protein harvesting. For each sample, the same inhibitor is also included at the corresponding concentration in the lysis buffer for protein extraction and immunoblot analysis\[^{1}\].

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

**Animal Administration**\[^{3}\]

Mice: Male wild-type (WT) C57BL/6J and Apo E\(^{-/-}\) mice are used in the study. Ang II-treated mice are received an intraperitoneal injection of either saline vehicle or γ-secretase inhibitor, dibenzazepine (DBZ) (1 mg/kg/d, dissolved in saline) 1 day before mini-pump implantation, and the treatment continued daily for 4 weeks. The blood pressure is measured in conscious mice using a computerized tail-cuff system. All mice are anesthetized. The aortic tissues are removed and prepared for further histological and molecular analysis\[^{3}\].

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

---

**REFERENCES**


---

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

Tel: 609-228-6898       Fax: 609-228-5909       E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA