Product Data Sheet

Chemical Properties

Product Name: MK-0752
Cas No.: 471905-41-6
M.Wt: 442.9
Formula: C21H21ClF2O4S
Synonyms: MK 0752, MK0752
Chemical Name: 3-[4-(4-chlorophenyl)sulfonyl-4-(2,5-difluorophenyl)cyclohexyl]propanoic acid
Canonical SMILES: C1CC(CCC1CCC(=O)O)(C2=C(C=CC(=C2)F)F)S(=O)(=O)C3=CC=C(C=C3)Cl
Solubility: >22.2mg/mL in DMSO
Storage: Store at -20°C
General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Gamma Secretase
Pathways: Proteases >> Gamma Secretase
Description:
MK-0752 is a potent gamma secretase inhibitor in clinical development (IC50 ~50 nM). Gamma secretase is an important component in the NOTCH cleavage machinery that catalyzes the cleavage of receptor protein substrates within their transmembrane domain. Inhibition of Notch inhibits BC cell proliferation in vitro. Notch signaling requires gamma secretase, which cleaves Notch, releasing the Notch intracellular domain (NICD) to activate transcription of target genes.
NOTCH signaling plays an important role in normal tissue development, cell fate determination, proliferation, and survival. NOTCH signaling is activated following the binding of cognate ligands that include Delta1, Delta2, and Delta3 and Jagged1 and Jagged2.

**Reference:**

### Protocol

**Cell experiment:**

<table>
<thead>
<tr>
<th>Cell lines</th>
<th>SH-SY5Y cells</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preparation method</strong></td>
<td>The solubility of this compound in DMSO is &gt;10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.</td>
</tr>
<tr>
<td><strong>Reacting conditions</strong></td>
<td>IC50: 5 nM.</td>
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<tr>
<td><strong>Applications</strong></td>
<td>As a moderately potent γ-secretase inhibitor, MK-0752 inhibited the production of Aβ40 in a dose-dependent manner with an IC50 of 5 nM in human SH-SY5Y cells.</td>
</tr>
</tbody>
</table>

**Animal experiment [3]:**

<table>
<thead>
<tr>
<th>Animal models</th>
<th>Male CMP rhesus monkeys</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosage form</strong></td>
<td>Oral administration, 60 mg/kg and 240mg/kg</td>
</tr>
<tr>
<td><strong>Applications</strong></td>
<td>Oral administration of MK-0752 demonstrated a dose-related reduction of Aβ levels. After 48 h, the Aβ levels with 240mg/kg treatment only recovered to 50% of baseline, while the 60mg/kg treatment group reached baseline at 30 h without overshoot. Plasma Aβ levels rebounded above baseline after MK-0752 inhibition (60 mg/kg, h 33–48).</td>
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</tbody>
</table>
Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Product Validation

Plasma levels of Aβ during and after γ-secretase inhibition indicate peripheral Aβ rebound in rhesus monkeys treated with a CNS-penetrant GSI. A, Concentration of GSI in rhesus monkey plasma after dosing with GSI. B, Aβ levels in rhesus monkeys (n=6), measured by ELISA are shown normalized to baseline. A dose-response effect on Aβ levels was observed with 60 mg/kg and 240 mg/kg. Plasma Aβ levels in the 60 mg/kg dose group recovered to baseline after 24 h, and then increased above baseline. Means between vehicle and 60 mg/kg from hours 33-48 are significantly different (paired t test, ***p<0.0001). C, D, In an extended study (n = 6.3/group), animals were treated with either vehicle or 240 mg/kg GSI. C, Concentration of GSI in rhesus monkey plasma after dosing with 240 mg/kg GSI. D, Plasma Aβ levels overshoot baseline after 48 h in 240 mg/kg GSI-treated animals (unpaired t test, ***p<0.0001, h48-240). (vehicle, black circle; 60 mg/kg, blue square; 240 mg/kg, red triangle). Error bars indicate SEM.

Aβ during and after γ-secretase inhibition
No evidence of central Aβ rebound in rhesus monkeys treated with a CNS-penetrant GSI. A, Concentration of GSI in rhesus monkey CSF after dosing. B, C, Aβ levels in rhesus monkeys (n=6), measured by ELISA, were normalized to baseline. A dose-response effect on Aβ levels was observed with GSI treatment. A rebound effect was not observed in levels of CSF Aβ40 (B) or Aβ42 (C). After 48 h, the Aβ levels with 240 mg/kg treatment...
only recovered to 50% of baseline, while the 60 mg/kg treatment group reached baseline at 30 h without overshoot. D-F, In an extended study (n = 6,3/group) Aβ levels returned to baseline within 72 h of treatment (240 mg/kg), without rebound. (vehicle, black circle; 60 mg/kg, blue square; 240 mg/kg, red triangle). Error bars indicate SEM.

**Caution**

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

ApexBio Technology

[www.apexbt.com](http://www.apexbt.com)

7505 Fannin street, Suite 410, Houston, TX 77054.

Tel: +1-832-696-8203 | Fax: +1-832-641-3177 | Email: info@apexbt.com