Chemical Properties

Product Name: LY-411575
Cas No.: 209984-57-6
M.Wt: 479.48
Formula: C26H23F2N3O4
Synonyms: N/A
Chemical Name: (2S)-2-[(2S)-2-(3,5-difluorophenyl)-2-hydroxyacetyl]amino]-N-[(7S)-5-methyl-6-oxo-7H-benzo[d][1]benzazepin-7-yl]propanamide
Canonical SMILES: CC(C(=O)NC1C2=CC=CC=C2C3=CC=CC=C3N(C1=O)C)NC(=O)C(C4=CC(=CC(=C4)F)F)O
Solubility: ≥23.85mg/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: Proteases
Pathways: Gamma Secretase
Description:
LY-411575 is a potent inhibitor of γ-secretase with IC50 value of 0.078 nM in membrane assay.[1]
γ-Secretase is one of intramembrane-cleaving aspartyl protease which cleaves many type-I membrane proteins and many of them have important biological functions. γ-Secretase is a multi-subunit protease and it contains presenilin, nicastrin, APH-1(Anterior Pharynx- defective 1)
and PEN-2. Presenilin contains Asp258 and Asp385 embedded in the sixth and seventh transmembrane domain and forms the active site. The feature of being a membrane integrated protease complex makes it difficult to be purified as well as studying its mechanism. γ-secretase is responsible for the generation Aβ from the amyloid precursor protein. γ-Secertase has been considered as an important drug target for Alzheimer’s disease. γ-Secertase also is responsible for Notch processing which is related to cancer such as leukemia.[2]

LY-411,575 significantly inhibits they-secretase activity in vitro. LY-411,575 inhibits the production of Aβ production with IC50 value of 0.078 nM in membrane-assay and 0.082 nM in cell-based-secretase assays, respectively. LY-411,575 also affects the Notch pathway by inhibiting Notch S3 cleavage with IC50 value of 0.39 nM.[1] LY-411,575 treatment also significantly inhibited the Notch pathway by inhibiting the γ-secretase activity luciferase activity in primary KS cells. LY-411,575 also induced the apoptosis though Notch pathway inhibition in primary and immortalized Kaposi’s sarcoma (KS) tumor cells.[2]

LY-411,575 decreases the levels of brain and plasma Aβ40 and -42 at 10 mg/kg oral doses.[1] LY-411,575 also decreases cortical Aβ40 levels in transgenic CRND8 mice with ED50 ≈ 0.6 mg/kg. LY-411,575 also induced significantly intestinal goblet cell hyperplasia and thymus atrophy by inhibiting Notch signaling pathway at higher doses in vivo.[3]

**Reference:**

**Protocol**

**Cell experiment:**

**Cell lines**  
HEK293 cells expressing human APP carrying both the Swedish and London mutations or N E.

**Preparation method**  
Soluble in DMSO > 10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.

**Reacting conditions**  
4 h.

**Applications**  
In HEK293 cells expressing human APP or N E, LY-411,575 inhibits
Aβ40 and NICD production with IC50 values of 0.082 and 0.39 nM, respectively.

**Animal experiment [3]:**

<table>
<thead>
<tr>
<th>Animal models</th>
<th>Six-week-old female TgCRND8 or male C57BL/6 mice.</th>
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</thead>
<tbody>
<tr>
<td>Dosage form</td>
<td>1-10 mg/kg; dosed orally once/day for 5 or 15 days.</td>
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<tr>
<td>Applications</td>
<td>In TgCRND8 mice, LY-411,575 decreases brain and plasma Aβ40 and Aβ42. LY-411,575 (10 mg/kg) reduces weight of mice by 2 g. LY-411,575 induces a marked atrophy of the cortical zone of the thymus and reduces the amount of thymocyte cells.</td>
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<tr>
<td>Preparation method</td>
<td>Formulated as 10 mg/ml solutions in 50% polyethylene glycol, 30% propylene glycol, 10% ethanol and diluted in 0.4% methylcellulose for dosing.</td>
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<tr>
<td>Other notes</td>
<td>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.</td>
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</tbody>
</table>

**Reference:**


**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. Shortterm 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.
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