LY 3000328

Cat. No.: HY-15533
CAS No.: 1373215-15-6
Molecular Formula: C₂₅H₂₉FN₄O₅
Molecular Weight: 484.52
Target: Cathepsin
Pathway: Metabolic Enzyme/Protease
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 : ≥ 50 mg/mL (103.19 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>2.0639 mL</td>
<td>10.3195 mL</td>
<td>20.6390 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.4128 mL</td>
<td>2.0639 mL</td>
<td>4.1278 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.2064 mL</td>
<td>1.0319 mL</td>
<td>2.0639 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 (5.16 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.16 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.16 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
LY 300328 is a potent and selective Cathepsin (Cat S) inhibitor with IC₅₀s of 7.7 and 1.67 nM for hCat S and mCat S, respectively.

IC₅₀ & Target
IC₅₀: 7.7±5.85 nM (hCat S), 1.67±1.17 (mCat S)[¹]
**In Vitro**

LY3000328 maintains excellent in vitro potency and selectivity. LY3000328 shows low in vitro CYP450 inhibition (<15% at 10 μM for CYP3A4, CYP2D6, and CYP2C9); low in vitro metabolism in mouse, rat, dog, and human liver microsomes (<20% after 30 min incubation at 4 μM); and good permeability (MDCK A-B>4%). At a 100 μM concentration of LY3000328 there is only 6% displacement of [3H]-astemizole in an assay with HEK293 membrane preparation, indicating low potential of hERG blockade[1]. LY3000328 is a potent and specific inhibitor of cathepsin S (CatS). Inhibition of CatS activity in plasma would be 50% of maximal when LY3000328 plasma concentration is approximately 60 ng/ml[2].

**In Vivo**

The efficacies of LY3000328 is studied in a mouse model of abdominal aortic aneurysm (AAA). In this model, inflammation is induced using CaCl₂ applied to the ablumenal surface. It is shown that features of the disease state in this model resemble those of human AAA. LY3000328 exhibits a dose-responsive aortic diameter reduction at 1, 3, 10, and 30 mg/kg. At the lowest dose of 1 mg/kg of LY3000328, the aortic diameter is reduced by 58%, then 83% at 3 mg/kg, and 87% at 10 mg/kg. The exposure (AUC) for both compounds increased in a dose-dependent manner, suggesting that the drug disposition properties of LY3000328 are favorable[1].

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**REFERENCES**


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

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