Ledipasvir

Cat. No.: HY-15602
CAS No.: 1256388-51-8
Molecular Formula: C₄₉H₅₄F₂N₈O₆
Molecular Weight: 889
Target: HCV; SARS-CoV
Pathway: Anti-infection
Storage: Powder -20°C 3 years
        4°C 2 years
        In solvent -80°C 2 years
        -20°C 1 year

SOLVENT & SOLUBILITY

In Vitro
DMSO: 50 mg/mL (56.24 mM; Need ultrasonic)

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>Mass</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td></td>
<td>1.1249 mL</td>
<td>5.6243 mL</td>
<td>11.2486 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.2250 mL</td>
<td>1.1249 mL</td>
<td>2.2497 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.1125 mL</td>
<td>0.5624 mL</td>
<td>1.1249 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 (2.81 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.81 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Ledipasvir (GS-5885) is an inhibitor of the hepatitis C virus NS5A, with EC₅₀ values of 34 pM and 4 pM against genotype 1a and 1b replicon, respectively. Ledipasvir is also a SARS-CoV 3CLpro inhibitor with an IC₅₀ of 1.62 μM[3].

IC₅₀ & Target
EC₅₀: 34 pM (GT1a), 4 pM (GT1b)[1]

In Vitro
Ledipasvir has GT1a and 1b EC₅₀ values of 31 and 4 pM, respectively, and protein-adjusted EC₅₀ values of 210 pM (GT1a) and 27 pM (GT1b) and the intrinsic EC₅₀ of 39 is 310 fM for GT1a and 40 fM for GT1b. Ledipasvir is highly protein-bound both in human serum and in the cell-culture medium (containing 10% BSA) of the replicon assay[1]. Ledipasvir exhibits an EC₅₀ value of 141 nM against the JFH/3a-NS5A replicon[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Ledipasvir is remarkable not only on the basis of its high replicon potency but also on the basis of its low clearance, good bioavailability, and long half-lives in rat, dog, and monkey and low predicted clearance in human. The pharmacokinetics of Ledipasvir is measured in rats and dogs. Ledipasvir shows good half-lives (rat $1.83 \pm 0.22$ hr, dog $2.63 \pm 0.18$ hr) in plasma, low systemic clearance (CL), and moderate volumes of distribution (Vss) that are greater than total body water volume $^{[1]}$. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration $^{[1]}$

Pharmacokinetic studies are performed in male naïve Sprague-Dawley(SD) rats, non-naive beagle dogs, and cynomolgus monkeys (three animals per dosing route). Intravenous (IV) administration is dosed via infusion over 30 min in a vehicle containing 5% ethanol, 20% PEG400, and 75% water (pH adjusted to 3.0 with HCl). Oral dosing is administered by gavage in a vehicle containing 5% ethanol, 45% PEG 400, and 50% of 50 mM citrate buffer, pH 3. Blood samples are collected over a 24 h period postdose into Vacutainer tubes containing EDTA-K2. Plasma was isolated, and the concentration of the test compound in plasma was determined with LC/MS/MS after protein precipitation with acetonitrile.

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

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2021 May 29;6(1):212.

See more customer validations on www.MedChemExpress.com

REFERENCES

