Tipranavir

Cat. No.: HY-15148
CAS No.: 174484-41-4
Molecular Formula: C₃₁H₃₃F₃N₂O₅S
Molecular Weight: 602.66
Target: HIV Protease; HIV
Pathway: Anti-infection; 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
Ethanol: ≥ 50 mg/mL (82.97 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>1 mM</td>
<td></td>
<td>1.6593 mL</td>
<td>8.2966 mL</td>
<td>16.5931 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.3319 mL</td>
<td>1.6593 mL</td>
<td>3.3186 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.1659 mL</td>
<td>0.8297 mL</td>
<td>1.6593 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% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (4.15 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.15 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Tipranavir (PNU-140690) inhibits the enzymatic activity and dimerization of HIV-1 protease, exerts potent activity against multi-protease inhibitor (PI)-resistant HIV-1 isolates with IC₅₀ values of 66-410 nM.

IC₅₀ & Target
IC₅₀: 66-410 nM (HIV-1 isolates)
In Vitro
Tipranavir (PNU-140690) inhibits the enzymatic activity of HIV-1 protease, blocks the dimerization of protease subunits, and exerts potent activity against a wide spectrum of wild-type and multi-PI-resistant HIV-1 variants. When a mixture of 11 multi-PI-resistant (but TPV-sensitive) clinical isolates (HIV_{11MIX}), which include HIV$_B$ and HIV$_C$, is selected against Tipranavir, HIV$_{11MIX}$ rapidly (by 10 passages [HIV$_{11MIX}^{P_{10}}$]) acquires high-level Tipranavir (PNU-140690) resistance and replicates at high concentrations of Tipranavir (PNU-140690). cHIV$_B^{I54V}$ and cHIV$_B^{I54V/V82T}$ are significantly resistant to Tipranavir (PNU-140690), with IC$_{50}$s of 2.9 and 3.2 μM, respectively, which are 11- and 12-fold increases in comparison to the IC$_{50}$ against cHIV$_B$, respectively.$^1$

In Vivo
Tipranavir (PNU-140690) is administered orally twice daily and must be given in combination with low-dose ritonavir (RTV) to boost Tipranavir bioavailability. In Tipranavir/r-cotreated mice, the Tipranavir (PNU-140690) abundance in the liver, spleen, and eyes is significantly higher than that in mice treated with Tipranavir alone. Tipranavir (PNU-140690) metabolites accounts for 31 and 38% in the serum and liver in the Tipranavir-alone group. In Tipranavir (PNU-140690) and Tipranavir (TPV/r)-cotreated mice, only 1 and 2% of metabolites are detected in the serum and liver. Sprague-Dawley rats are administered a single dose of [$^{14}$C]Tipranavir (PNU-140690) with coadministration of RTV. The most abundant metabolite in feces is an oxidation metabolite. In urine, no single metabolite is found to be significantly present.$^2$

PROTOCOL

Animal Administration $^2$

Mice

All mice (2-4 months old) are maintained under a standard 12-h dark and 12-h light cycle with water and chow provided ad libitum. For metabolomic analysis, Tipranavir (PNU-140690) (40 mg/kg) is administered via ball-tipped gavage needles, and the mice are housed in separate metabolic cages for 18 h. Urine and feces samples are collected and stored at −20°C for further analysis. For tissue distribution and inhibition studies, three groups of mice are used and are orally treated with Tipranavir (100 mg/kg), RTV (40 mg/kg), and Tipranavir (PNU-140690) (100 mg/kg Tipranavir and 40 mg/kg RTV), respectively. Tissues including the liver, brain, lung, kidney, spleen, and eyes are collected 30 min after treatment and stored at −20°C for further analysis.

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

CUSTOMER VALIDATION


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REFERENCES


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

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