Tipranavir

Cat. No.: HY-15148

CAS No.: 174484-41-4

Molecular Formula: $C_{31}H_{33}F_3N_2O_5S$

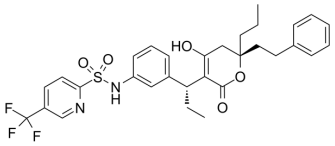
Molecular Weight: 602.66

Target: HIV Protease; HIV; SARS-CoV

Pathway: Anti-infection; Metabolic Enzyme/Protease

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 : 200 mg/mL (331.86 mM; Need ultrasonic)

Ethanol : ≥ 50 mg/mL (82.97 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6593 mL	8.2966 mL	16.5931 mL
5 mM	0.3319 mL	1.6593 mL	3.3186 mL
10 mM	0.1659 mL	0.8297 mL	1.6593 mL

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: 5 mg/mL (8.30 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (8.30 mM); Clear solution
3. 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
4. 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
5. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.15 mM); Clear solution
6. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.5 mg/mL (4.15 mM); Suspended solution; Need ultrasonic

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 IC_{50}s of 66-410 nM[1][2]. Tipranavir inhibits SARS-CoV-2 $3CL^{pro}$ activity[3].
IC_{50} & Target	IC50: 66-410 nM (HIV-1 isolates)[1]
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}^{P10}]) 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice[2] 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

- Signal Transduct Target Ther. 2021 May 29;6(1):212.
- Nat Commun. 2020 Sep 4;11(1):4417.
- Int J Antimicrob Agents. 2019 Dec;54(6):814-819.
- Talanta. 2018 May 1;181:182-189.
- Antimicrob Agents Chemother. 2020 Aug 20;64(9):e00872-20.

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REFERENCES

[1]. Aoki M, et al. Loss of the protease dimerization inhibition activity of tipranavir (TPV) and its association with the acquisition of resistance to TPV by HIV-1. J Virol. 2012 Dec;86(24):13384-96.

[2]. Li F, et al. Metabolism-mediated drug interactions associated with ritonavir-boosted tipranavir in mice. Drug Metab Dispos. 2010 May;38(5):871-8.

[3]. Qi Sun, et al. Bardoxolone and bardoxolone methyl, two Nrf2 activators in clinical trials, inhibit SARS-CoV-2 replication and its 3C-like protease. Signal Transduct Target Ther. 2021 May 29;6(1):212.

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