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# 产品名称：Tipranavir
# 产品别名：替拉那韦；PNU-140690

## 生物活性：

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| **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. |
| **$IC_{50}$ & 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]. |
| **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]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**Ethanol : ≥ 50 mg/mL (82.97 mM)**<br>* "≥" means soluble, but saturation unknown. |

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
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| 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 |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

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| | 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline<br>Solubility: 2.5 mg/mL (4.15 mM); Suspended solution; Need ultrasonic<br>此方案可获得 2.5 mg/mL (4.15 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。<br><br>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)<br>Solubility: 2.5 mg/mL (4.15 mM); Suspended solution; Need ultrasonic<br>此方案可获得 2.5 mg/mL (4.15 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。<br><br>3.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 2.5 mg/mL (4.15 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (4.15 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 EtOH 储备液加到 900 μL 玉米油中，混合均匀。 |
| **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.<br>[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. |

**实验参考：**

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| **Animal Administration** | Mice[2]<br>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. |
| **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.<br>[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. |