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# 产品名称：PF-04457845
# 产品别名：PF-04457845

## 生物活性：

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| **Description** | PF-04457845 is a highly efficacious and selective FAAH inhibitor with IC50 values is 7.2±0.63 nM and 7.4±0.62 nM for hFAAH and rFAAH, respectively. |
| **$IC_{50}$ & Target** | IC50: 7.2±0.63 nM (hFAAH), 7.4±0.62 nM (rFAAH)[1] |
| **In Vitro** | PF-04457845 inhibits FAAH by a covalent, irreversible mechanism involving carbamylation of the active-site serine nucleophile of FAAH with high in vitro potency ($k_{inact}/K_i$ and $IC_{50}$ values of 40300 $M^{-1}s^{-1}$ and 7.2 nM, respectively, for human FAAH). PF-04457845 has exquisite selectivity for FAAH relative to other members of the serine hydrolase superfamily as demonstrated by competitive activity-based protein profiling. PF-04457845 completely inhibits FAAH in human and mouse membrane proteomes at both 10 and 100 μM with no off targets[1]. PF-04457845 is completely selective for FAAH, and none of the other FP-reactive serine hydrolases in the tested tissues are inhibited by PF-04457845 even at 100 μM[2]. |
| **In Vivo** | Oral administration of PF-04457845 at 0.1 mg/kg results in efficacy comparable to that of naproxen at 10 mg/kg in a rat model of inflammatory pain. Oral administration of PF-04457845 causes a significant inhibition of mechanical allodynia measured after 4 h with a minimum effective dose (MED) of 0.1 mg/kg. Furthermore, at 0.1 mg/kg (p.o.), PF-04457845 inhibits the pain response to a comparable degree as the nonsteroidal anti-inflammatory drug naproxen at 10 mg/kg[1]. FAAH is confirmed to be completely inhibited in mice treated with PF-04457845 at 1 and 10 mg/kg p.o. by competitive activity-based protein profiling (ABPP) study[2]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO : ≥ 100 mg/mL (219.57 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 | 2.1957 mL | 10.9786 mL | 21.9573 mL |
| | 5 mM | 0.4391 mL | 2.1957 mL | 4.3915 mL |
| | 10 mM | 0.2196 mL | 1.0979 mL | 2.1957 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

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.75 mg/mL (6.04 mM); Clear solution

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| | 此方案可获得 ≥ 2.75 mg/mL (6.04 mM，饱和度未知) 的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 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: ≥ 2.75 mg/mL (6.04 mM); Clear solution<br>此方案可获得 ≥ 2.75 mg/mL (6.04 mM，饱和度未知) 的澄清溶液。<br>以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 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: ≥ 2.75 mg/mL (6.04 mM); Clear solution<br>此方案可获得 ≥ 2.75 mg/mL (6.04 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 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **References** | [1]. Johnson DS, et al. Discovery of PF-04457845: A Highly Potent, Orally Bioavailable, and Selective Urea FAAH Inhibitor. ACS Med Chem Lett. 2011 Feb 10;2(2):91-96.<br>[2]. Ahn K, et al. Mechanistic and pharmacological characterization of PF-04457845: a highly potent and selective fatty acid amide hydrolase inhibitor that reduces inflammatory and noninflammatory pain. J Pharmacol Exp Ther. 2011 Jul;338(1):114-24.<br>[3]. Buntyn RW, et al. Inhibition of Endocannabinoid-Metabolizing Enzymes in Peripheral Tissues Following Developmental Chlorpyrifos Exposure in Rats. Int J Toxicol. 2017 Jan 1:1091581817725272. |

**实验参考：**

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| **Animal Administration** | Rats[1]<br>PF-04457845 is administered orally to male Sprague-Dawley rats (200g-250g) at the indicated dose (mg/kg) as a nanocrystalline suspension in 2% polyvinylpyrrolidone and 0.15% sodium dodecyl sulfate in $H_2O$. The dose volume is 10 mL/kg. The Paw Withdrawal Threshold (PWT) is evaluated at 4 h post dose. PWT measurements are averaged and statistical comparisons between groups are made using analysis of variance and unpaired T-tests.<br>Mice[2]<br>Male C57BL6/J mice (7 weeks old; n=8) are treated with PF-04457845 (1 or 10 mg/kg in polyethyleneglycol 300 vehicle by oral administration in a volume of 4 mL/kg), the synthetic cannabinoid agonist WIN 55,212-2 (1 or 10 mg/kg in 18:1:1 saline/Emulphor/ethanol vehicle by intraperitoneal administration in a volume of 10 mL/kg), or the corresponding vehicle. Mice are evaluated for hypomotility, hypothermia, antinociceptive, and cataleptic effects at 4 h or 30 min after PF-04457845 or WIN 55,212-2 administration, respectively, using the tetrad tests except that catalepsy is assessed for 60 s instead of 10 s. Statistical analysis is performed using the Student's t test comparing each treatment group with vehicle. |
| **Kinase Assay** | The IC50 values for the inhibition of hFAAH and rFAAH by PF-04457845 is determined. PF-04457845 is preincubated with FAAH for 60 min before initiating the reaction by the addition of |

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| | the substrate oleamide. Mouse and human tissues are prepared and inhibitor selectivity is assessed by competitive activity-based protein profiling[1]. |
| **References** | [1]. Johnson DS, et al. Discovery of PF-04457845: A Highly Potent, Orally Bioavailable, and Selective Urea FAAH Inhibitor. ACS Med Chem Lett. 2011 Feb 10;2(2):91-96.<br>[2]. Ahn K, et al. Mechanistic and pharmacological characterization of PF-04457845: a highly potent and selective fatty acid amide hydrolase inhibitor that reduces inflammatory and noninflammatory pain. J Pharmacol Exp Ther. 2011 Jul;338(1):114-24.<br>[3]. Buntyn RW, et al. Inhibition of Endocannabinoid-Metabolizing Enzymes in Peripheral Tissues Following Developmental Chlorpyrifos Exposure in Rats. Int J Toxicol. 2017 Jan 1:1091581817725272. |