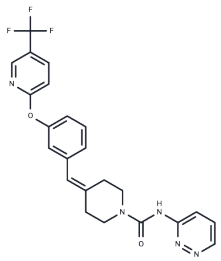
Data Sheet (Cat.No.T4323)

TargetMol

PF-04457845

Chemical Properties



CAS No. : 1020315-31-4

Formula: C23H20F3N5O2

Molecular Weight: 455.43

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	PF-04457845 is a greatly and effctive FAAH inhibitor, and for hFAAH(IC50=7.2±0.63 nM) and rFAAH(IC50=7.4±0.62 nM).
Targets(IC50)	FAAH,Autophagy
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 (kinact/Ki and IC50 values of 40300 M-1s-1 and 7.2 nM, respectively, for human FAAH).
In vivo	In a rat model, 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. FAAH is confirmed to be completely inhibited in mice treated with PF-04457845 (1 and 10 mg/kg p.o.).
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 the substrate oleamide. Mouse and human tissues are prepared and inhibitor selectivity is assessed by competitive activity-based protein profiling.
Cell Research	PF-04457845 is formulated as a nanocrystalline suspension in 2% polyvinylpyrrolidone and 0.15% sodium dodecyl sulfate in H2O (Rats). PF-04457845 is prepared in polyethyleneglycol 300 (Mice).RatsPF-04457845 is administered orally to male Sprague-Dawley rats (200 g-250 g) at the indicated dose (mg/kg) as a nanocrystalline suspension in 2% polyvinylpyrrolidone and 0.15% sodium dodecyl sulfate in H2O. 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.Mice 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.

Animal Research	Male C57BL6/J mice (7 weeks old) are treated with PF-04457845 (1 or 10 mg/kg in polyethyleneglycol 300 vehicle by oral administration in a volume of 4 mL/kg).

Solubility Information

Solubility	DMSO: 50 mg/mL (109.79 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween-80+45% Saline: 2.5 mg/mL (5.49 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0439 mL	0.2196 mL	0.4391 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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.

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.

Buntyn RW, et al. Inhibition of Endocannabinoid-Metabolizing Enzymes in Peripheral Tissues Following Developmental Chlorpyrifos Exposure in Rats. Int J Toxicol. 2017 Sep/Oct;36(5):395-402.

Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481