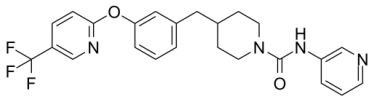
Data Sheet

Product Name:	PF-3845
Cat. No.:	CS-0419
CAS No.:	1196109-52-0
Molecular Formula:	C24H23F3N4O2
Molecular Weight:	456.46
Target:	Autophagy; FAAH
Pathway:	Autophagy; Metabolic Enzyme/Protease; Neuronal Signaling
Solubility:	DMSO : ≥ 100 mg/mL (219.08 mM)



BIOLOGICAL ACTIVITY:

PF-3845 is a selective fatty acid amide hydrolase (FAAH) inhibitor (Ki = 0.23 μM); showing negligible activity against FAAH2. IC50 value: 0.23 uM Target: FAAH PF-3845 selectively inhibits FAAH by carbamylating FAAH's serine nucleophile [1]. PF-3845 treated mice (10 mg/kg, i.p.) shows rapid and complete inactivation of FAAH in the brain, as judged by competitive activity-based protein profiling (ABPP) with the serine hydrolase-directed probe fluorophosphonate (FP)-rhodamine. PF-3845 shows a long duration of action up to 24 hour. PF-3845-treated mice also shows dramatic (>10-fold) elevation in brain levels of AEA and other NAEs (N-pamitoyl ethanolamine [PEA] and N-oleoyl ethanolamine [OEA]). FAAH is AEA-degrading enzyme fatty acid amide hydrolase. PF-3845 (1–30 mg/kg, oral administration [p.o.]) causes a dose dependent inhibition of mechanical allodynia with a minimum effective dose (MED) of 3 mg/kg (rats are analyzed at 4 hour post dosing with PF-3845). At higher doses (10 and 30 mg/kg), PF-3845 inhibits pain responses to an equivalent, if not greater, degree than the nonsteroidal anti-inflammatory drug naproxen (10mg/kg, p.o.) [1]. PF-3845 (10 mg/kg, i.p.) significantly reverses LPS-induced tactile allodynia, but doesn't modify paw withdrawal thresholds in the saline-injected paw [2].

PROTOCOL (Extracted from published papers and Only for reference)

Animal administration [1] For the inflammatory pain model, 0.15 ml of CFA (Sigma) was injected into the plantar surface of the left hind paw of the rat. The CFA injection immediately induces local inflammation, paw swelling, and pain that persist for at least two weeks post-injection. To assess mechanical allodynia, mechanical paw withdrawal thresholds (PWTs) were measured using a set of Von Frey Hairs on day 5 post injection as illustrated by the Dixon Up and Down Method (Dixon, 1980). Animals that exhibit the pain criteria of 9 g or less were then placed on study. Test compound was administered via either oral or intraperitoneal (i.p.) routes at the indicated concentrations (mg/kg) with the dosing vehicle 5% N,N-dimethylacetamide and 95% (40% 2-hydroxypropyl-β-cyclodextrin (Sigma) in water). PWTs were evaluated again at 4 hr post dosing. PWT measurements were averaged and statistical comparisons between groups were made using analysis of variance and unpaired T-tests.

References:

[1]. Ahn K, et al. Discovery and characterization of a highly selective FAAH inhibitor that reduces inflammatory pain. Chem Biol. 2009 Apr 24;16(4):411-20.

[2]. Booker L, et al. The fatty acid amide hydrolase (FAAH) inhibitor PF-3845 acts in the nervous system to reverse LPS-induced tactile allodynia in mice. Br J Pharmacol, 2012, 165(8), 2485-2496.

CAIndexNames:

1-Piperidinecarboxamide, N-3-pyridinyl-4-[[3-[[5-(trifluoromethyl)-2-pyridinyl]oxy]phenyl]methyl]-

SMILES:

O=C(N1CCC(CC2=CC=CC(OC3=NC=C(C=C3)C(F)(F)F)=C2)CC1)NC4=CN=CC=C4

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