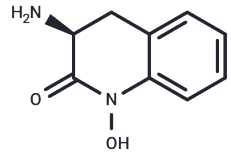
Data Sheet (Cat.No.T28368)

TargetMol

PF-04859989 HCl

Chemical Properties



CAS No. : 177943-33-8

Formula: C9H11ClN2O2

Molecular Weight: 214.65

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-04859989 HCl is a brain-penetrable and irreversible inhibitor of kynurenine amino transferase II (KAT II), which is the enzyme responsible for most of the brain synthesis of kynurenic acid.
Targets(IC50)	Others
In vitro	The IC50s values are 23 and 263 nM for hKAT II and rKAT II. PF-04859989 HCl is selective for KAT II over human KAT I, KAT III, and KAT IV (IC50s of 22, 11, and >50 μM, respectively) [3].
In vivo	Acute administration of the KAT II inhibitor PF-04859989 (5 or 10 mg/kg) was associated with a short-onset, time-dependent decrease in firing rate and burst activity of DA neurons, both parameters reaching a 50% reduction within 45 min. Furthermore, PF-04859989 reduced the number of spontaneously active DA cells as measured 4-6 after administration. Pretreatment with d-cycloserine (30 mg/kg) or CGP-52432 (10 mg/kg) prevented the inhibitory action of PF-04859989 (5 mg/kg) on firing rate and burst firing activity. In contrast, pretreatment with methyllycaconitine (MLA, 4 mg/kg) did not change the response, whereas picrotoxin (4.5 mg/kg) partially prevented the inhibitory effects of PF-04859989 (5 mg/kg, i.v.)[2].

Solubility Information

Solubility	DMSO: 120 mg/mL (559.05 mM),Sonication is recommended. H2O: 100 mg/mL (465.87 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: 4 mg/mL (18.63 mM),Sonication is recommended. 10% DMSO+90% Saline: 10 mg/mL (46.59 mM),Solution. *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	4.6587 mL	23.2937 mL	46.5875 mL
5 mM	0.9317 mL	4.6587 mL	9.3175 mL
10 mM	0.4659 mL	2.3294 mL	4.6587 mL
50 mM	0.0932 mL	0.4659 mL	0.9317 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

Nematollahi A, Sun G, Jayawickrama GS, Hanrahan JR, Church WB. Study of the Activity and Possible Mechanism of Action of a Reversible Inhibitor of Recombinant Human KAT-2: A Promising Lead in Neurodegenerative and Cognitive Disorders. Molecules. 2016 Jun 29;21(7). pii: E856. doi: 10.3390/molecules21070856. PubMed PMID: 27367665.

Liang X, Du W, Huang L, et al.Helicobacter pylori promotes gastric intestinal metaplasia through activation of IRF3-mediated kynurenine pathway.Cell Communication and Signaling.2023, 21(1): 1-14.

Linderholm KR, Alm MT, Larsson MK, Olsson SK, Goiny M, Hajos M, Erhardt S, Engberg G. Inhibition of kynurenine aminotransferase II reduces activity of midbrain dopamine neurons. Neuropharmacology. 2016 Mar;102:42-7. doi: 10.1016/j.neuropharm.2015.10.028. Epub 2015 Oct 24. PubMed PMID: 26514401.

Kozak R, Campbell BM, Strick CA, Horner W, Hoffmann WE, Kiss T, Chapin DS, McGinnis D, Abbott AL, Roberts BM, Fonseca K, Guanowsky V, Young DA, Seymour PA, Dounay A, Hajos M, Williams GV, Castner SA. Reduction of brain kynurenic acid improves cognitive function. J Neurosci. 2014 Aug 6;34(32):10592-602. doi: 10.1523/JNEUROSCI.1107-14.2014. PubMed PMID: 25100593.

Koshy Cherian A, Gritton H, Johnson DE, Young D, Kozak R, Sarter M. A systemically-available kynurenine aminotransferase II (KAT II) inhibitor restores nicotine-evoked glutamatergic activity in the cortex of rats. Neuropharmacology. 2014 Jul;82:41-8. doi: 10.1016/j.neuropharm.2014.03.004. Epub 2014 Mar 16. PubMed PMID: 24647121; PubMed Central PMCID: PMC4372264.