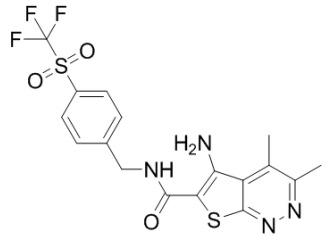
VU0467154

Cat. No.:	HY-112209
CAS No.:	1451993-15-9
Molecular Formula:	$C_{17}H_{15}F_3N_4O_3S_2$
Molecular Weight:	444.45
Target:	mAChR
Pathway:	GPCR/G Protein; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 13.89 mg/mL (**31.25 mM;** Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2500 mL	11.2499 mL	22.4997 mL
5 mM	0.4500 mL	2.2500 mL	4.4999 mL
10 mM	0.2250 mL	1.1250 mL	2.2500 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: **10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline**
   Solubility: 1.39 mg/mL (3.13 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

VU0467154 is a positive allosteric modulator of the **M4 muscarinic acetylcholine receptor (mAChR)**, potentiating the response to ACh with **pEC$_{50}$**s of 7.75, 6.2 and 6 for rat, human and cynomolgus monkey M4 receptor, respectively.

IC$_{50}$ & Target

pEC50: of 7.75 (Rat M4 receptor), 6.2 (Human M4 receptor), 6 (Cynomolgus monkey M4 receptor)[1]

In Vitro

VU0467154 is a positive allosteric modulators of the M4 muscarinic acetylcholine receptor (mAChR), robustly potentiates the response to ACh with pEC$_{50}$s of 7.75, 6.2 and 6 for rat, human and cynomolgus monkey (cyno) M4 receptor, respectively. VU0467154 does not potentiate the ACh response at rat and human M1, M2, M3, or M5[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

VU0467154 (1-56.6 mg/kg, p.o. or i.p.) reverses amphetamine-induced hyperlocomotion in rats. VU0467154 (0.3-30

mg/kg, i.p.) reverses amphetamine- and MK-801-induced hyperlocomotion in wild-type but not M4 KO mice. VU0467154 alone also enhances the acquisition of both contextual and cue-mediated fear conditioning in wild-type mice[1].

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PROTOCOL

Animal Administration [1]

Rats[1]

To determine the relationship between in vivo efficacy of VU0467154 and brain concentrations in **rats**, the efficacy of **VU0467154 (1, 3, 10, 30, and 56.6 mg/kg, PO; n ≥ 8 per dose level)** in reversing amphetamine-induced hyperlocomotion is correlated to the brain concentrations of VU0467154 in the same animals upon study completion (1.5 h postadministration). In mice, the in vivo concentration-effect relationship for VU0467154 is determined by correlating the efficacy of **VU0467154** in reversing amphetamine-induced hyperlocomotion (**0.3, 1, 3, 10, and 30 mg/kg, IP**) to the brain concentrations of VU0467154 in the same animals upon study completion (2.5 h postadministration). Terminal unbound brain concentrations for all treatment groups are plotted versus each animal's efficacy in reversing amphetamine-induced hyperlocomotion. Nonlinear regression analysis of the plotted data are calculated to determine the in vivo EC_{50} value (nM) for VU0467154 in reversing amphetamine-induced hyperlocomotion in rats using GraphPad Prism 5.0[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bubser M, et al. Selective activation of M4 muscarinic acetylcholine receptors reverses MK-801-induced behavioral impairments and enhances associative learning in rodents. ACS Chem Neurosci. 2014 Oct 15;5(10):920-42.

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