Product Data Sheet

Product Name: PF-2545920
Cat. No.: GC15194

Chemical Properties

Cas. No.	1292799-56-4		
Chemical Name	2-[[4-(1-methyl-4-pyridin-4-ylpyrazol-3-yl)phenoxy]methyl]quinoline		
SMILES	CN1C=C(C(=N1)C2=CC=C(C=C2)OCC3=NC4=CC=CC=C4C=C3)C5=CC=NC=C5		
Formula	$C_{25}H_{20}N_4O$	M.Wt	392.45
Solubility	≥ 19.35 mg/mL in DMSO, ≥ 99.8 mg/mL in EtOH	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	PF-2545920		

Protocol

Cell experiment [1]:

Cell lines	Rat striatal cells
Preparation method	The solubility of this compound in DMSO is >19.35 mg/ml. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting condition	1 μM for 30 min at 30°C

Caution: Product has not been fully validated for medical applications. For research use only.
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Applications	Biochemical characterization of PF-2545920 showed that it could modulate both the dopamine D1-direct and D2-indirect striatal pathways and regulate the phosphorylation status of a panel of glutamate receptor subunits in the striatum. It was striking that PDE10A inhibition increased the phosphorylation of the (+/-)-alpha-amino-3-hydroxy-5-methylisoxazole-4-proprionic acid receptor GluR1 subunit at residue serine 845 at the cell surface.

Animal experiment [1]:

Animal models	Male CF-1 mice or Sprague-Dawley rats
Dosage form	1-30 mg/kg, i.p.
Application	PF-2545920 was active in a range of antipsychotic models, antagonizing apomorphine-induced climbing in mice, inhibiting conditioned avoidance responding in both rats and mice, and blocking N-methyl-D-aspartate antagonist-induced deficits in prepulse inhibition of acoustic startle response in rats, while improving baseline sensory gating in mice, all of which strengthen previously reported observations.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1] Grauer SM, et al. Phosphodiesterase 10A inhibitor activity in preclinical models of the positive, cognitive, and negative symptoms of schizophrenia. J Pharmacol Exp Ther, 2009, 331(2), 574-590.

Background

PF-2545920 is an inhibitor of phosphodiesterase 10A (PDE10A) with IC50 value of 0.37nM [1].

PDE10A is highly expressed in the medium spiny neurons of the striatum and regulates both cGMP and cAMP. The PDE10A inhibitors are believed to regulate cyclic nucleotide signaling in the cortices-triatothalamic circuit. Previous inhibitors of PDE have potential therapeutic utility but also have potential safety risks due to off-target PDE inhibition. Thereby PF-2545920 is developed as a more selective inhibitor. PF-2545920 is shown to be efficacious both in vitro and in vivo with improved penetration in CNS. It has excellent in vivo efficacy in neurochemical elevation of cyclic nucleotides and in models predictive of antipsychotic activity. Administration of PF-2545920 to mice can cause increase in striatal cGMP with the minimal effective dose at about 1mg/kg [1].

References:
[1] Verhoest PR, Chapin DS, Corman M, Fonseca K, Harms JF, Hou X, Marr ES, Menniti FS, Nelson F, O'Connor R, Pandit J, Proulx-Lafrance C, Schmidt AW, Schmidt CJ, Suiciak JA, Liras S. Discovery of a novel class of phosphodiesterase 10A inhibitors and identification of clinical candidate 2-[4-(1-methyl-4-pyridin-4-yl-1H-pyrazol-3-yl)-phenoxymethyl]-quinoline (PF-2545920) for the treatment of schizophrenia. J Med Chem. 2009 Aug 27;52(16):5188-96.

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