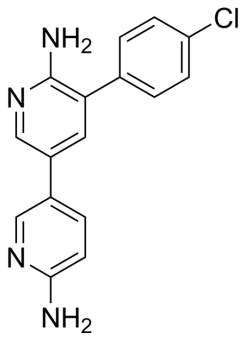
PF-06260933

Cat. No.:	HY-19562
CAS No.:	1811510-56-1
Molecular Formula:	$C_{16}H_{13}ClN_4$
Molecular Weight:	296.75
Target:	MAP4K
Pathway:	MAPK/ERK Pathway
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 30 mg/mL (101.10 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.3698 mL	16.8492 mL	33.6984 mL
	5 mM	0.6740 mL	3.3698 mL	6.7397 mL
	10 mM	0.3370 mL	1.6849 mL	3.3698 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: ≥ 2.5 mg/mL (8.42 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-06260933 is an orally active and highly selective inhibitor of MAP4K4 with IC_{50}s of 3.7 and 160 nM for kinase and cell, respectively.

IC_{50} & Target

MAP4K4
3.7 nM (IC_{50})

In Vitro

PF-06260933 treatment of human aortic endothelial cell (EC) robustly prevents TNF-α-mediated endothelial permeability in vitro, similar to MAP4K4 knockdown[2].

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

In Vivo	In the mice model, PF-06260933 treatment does not alter plasma lipid content, although reductions in glucose levels are observed, which is consistent with whole-body-inducible Map4k4 knockout animals. PF-06260933 administration ameliorates further plaque development and/or promotes plaque regression in this animal model (46.0% versus 25.5%), and a reduction in plasma glucose as well as lipid content is also observed[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	HUVECs are maintained in EGM2 media at 37°C and 5% CO_2. HUVECs or peritoneal macrophages are treated with vehicle or PF-06260933 in vitro to determine whether pharmacological inhibition of MAP4K4 alteres MAPK signalling in response to TNF-α[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Compound PF-06260933 (10 mg/kg, dissolved in dH_2O) is orally administered to 8 to 10-week-old male Apoe$^{-/-}$ mice twice daily for 6 weeks. Ldlr$^{-/-}$ male mice are placed on high-fat diet (HFD) for 10 weeks before drug administration. Compound PF-06260933 is administered to male 8 to 10-week-old Ldlr$^{-/-}$ mice as above for 10 weeks. Oral administration of water is used as vehicle control in all studies. Mice are euthanized by CO_2 inhalation followed by bilateral pneumothorax[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Life Sci Alliance. 2023 Jun 27;6(9):e202302196.

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REFERENCES

[1]. Ammirati M, et al. Discovery of an in Vivo Tool to Establish Proof-of-Concept for MAP4K4-Based Antidiabetic Treatment. ACS Med Chem Lett. 2015 Oct 6;6(11):1128-33.

[2]. Roth Flach RJ, et al. Endothelial protein kinase MAP4K4 promotes vascular inflammation and atherosclerosis. Nat Commun. 2015 Dec 21;6:8995.

Caution: Product has not been fully validated for medical applications. For research use only.

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