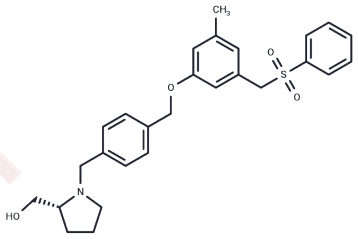
Data Sheet (Cat.No.T6085)

TargetMol

PF-543

Chemical Properties



CAS No. : 1415562-82-1

Formula: C27H31NO4S

Molecular Weight: 465.6

Appearance: no data available

Storage: store at low temperature
Pure form: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	PF-543 (Sphingosine Kinase 1 Inhibitor II), a novel sphingosine-competitive inhibitor of SphK1, inhibits SphK1 with IC50 of 2.0 nM and Ki of 3.6 nM.
Targets(IC50)	Apoptosis,Autophagy,LPL Receptor,S1P Receptor
In vitro	PF543 is a cell-permeable hydroxyl methylpyrrolidine compound that inhibits SphK-1/SphK1-catalyzed sphingosine phosphorylation in a reversible and sphingosine-competitive manner, exhibiting no affinity toward S1P receptors and much reduced inhibitory activity against Sphk2 (6.8% inhibition at 10 μM) or 46 other lipid and portein kinases (IC50 >10 μM). In the SphK1-overexpression 1483 head and neck carcinoma cells, PF-543 decreases the level of endogenous S1P 10-fold with a proportional increase in the level of sphingosine. PF-543 binds SphK1 reversibly (k off t1/2=8.5 min) and with high affinity and the binding constant (Kd) is 5 nM. PF543 had no effect on the proliferation and survival of 1483, A549, LN229, Jurkat, U937 and MCF-7 cells, despite a dramatic change in the cellular S1P/sphingosine ratio. PF-543 is effective as a potent inhibitor of S1P formation in whole blood, indicating that the SphK1 isoform of sphingosine kinase is the major source of S1P in human blood. [1]
In vivo	Administration of the potent sphingosine kinase 1 inhibitor, PF-543 in a mouse hypoxic model of pulmonary hypertension has no effect on vascular remodelling but reduces right ventricular hypertrophy. Administration of 10 mg/kg PF-543 for 24 h to mice induces a decrease in SK1 expression in pulmonary vessels[2].
Kinase Assay	FITC-S1P quantification/Caliper assay: A 384-well format of the SphK enzyme assay based on separation of FITC-S1P from unreacted FITC-sphingosine substrate using a microfluidic capillary electrophoresis mobility-shift system is developed. Briefly, 3 nM SphK1-His6 is incubated with 1 μM FITC-sphingosine, 20 μM ATP and 10 μM compound (a final concentration of DMSO of 2 %) in a buffer containing 100 mM Hepes (pH 7.4), 1 mM MgCl2,0.01% Triton X-100, 10% glycerol, 100 μM sodium orthovanadate and 1 mM DTT for 1 h in a 384-well Matrical MP-101-1-PP plate. Reaction mixtures (10 μL) are quenched by the addition of 20 μL of 30 mM EDTA and 0.15% Coating Reagent-3 in 100 mM Hepes, and a small aliquot of each reaction (a few nanolitres) is analysed in the Caliper LabChip 3000 instrument under -1.5 psi (psi=6.9 kPa) pressure, a downstream voltage of -1900 V and a sip time of 0.2 s. Phosphorylated fluorescent product and unphosphorylated fluorescent substrate appeared as distinctive peaks and are

	quantified using the Caliper data.
Cell Research	CellTiter-Glo Assay (Only for Reference)

Solubility Information

Solubility	H2O: <1 mg/mL, DMSO: 93 mg/mL (199.74 mM),Sonication is recommended. Ethanol: 93 mg/mL (199.74 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1478 mL	10.7388 mL	21.4777 mL
5 mM	0.4296 mL	2.1478 mL	4.2955 mL
10 mM	0.2148 mL	1.0739 mL	2.1478 mL
50 mM	0.043 mL	0.2148 mL	0.4296 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.

Reference

Schnute ME, et al. Biochem J, 2012, 444(1), 79-88.
Wen M, Sun X, Pan L, et al.Dihydromyricetin ameliorates diabetic renal fibrosis via regulating SphK1 to suppress the activation of NF-κB pathway.European Journal of Pharmacology.2024: 176799.
MacRitchie N, et al. Effect of the sphingosine kinase 1 selective inhibitor, PF-543 on arterial and cardiac remodelling in a hypoxic model of pulmonary arterial hypertension. Cell Signal. 2016 Aug;28(8):946-55.