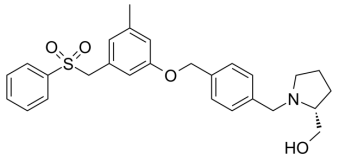
PF-543

Cat. No.:	HY-15425
CAS No.:	1415562-82-1
Molecular Formula:	$C_{27}H_{31}NO_4S$
Molecular Weight:	465.6
Target:	SphK; Apoptosis; Autophagy; LPL Receptor
Pathway:	Immunology/Inflammation; Apoptosis; Autophagy; GPCR/G Protein
Storage:	-20°C, protect from light, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (214.78 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 5 mg/mL (10.74 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (10.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-543 (Sphingosine Kinase 1 Inhibitor II) is a potent, selective, reversible and sphingosine-competitive SPHK1 inhibitor with an IC_{50} of 2 nM and a K_i of 3.6 nM. PF-543 is >100-fold selectivity for SPHK1 over SPHK2. PF-543 is an effective potent inhibitor of sphingosine 1-phosphate (S1P) formation in whole blood with an IC_{50} of 26.7 nM. PF-543 induces apoptosis, necrosis, and autophagy[1][2][3].

IC_{50} & Target

IC50: 2 nM (SPHK1); 26.7 nM (Sphingosine 1-phosphate (S1P))[1]
Ki: 3.6 nM (SPHK1)[1]

In Vitro

PF-543 (10-1000 nM; 24 hours; PASM cells) treatment abolishes SK1 expression at nM concentrations[2].
PF-543 (0.1-10 μM; 24 hours; PASM cells) treatment induces caspase-3/7 activity[2].
PF-543 inhibits C_{17}-S1P formation in 1483 cells with an IC_{50} of 1.0 nM[1].

SphK1 inhibition by PF-543 causes a dose-dependent depletion of the intracellular level of S1P with EC_{50} concentration of 8.4 nM and a concomitant elevation of the intracellular level of sphingosine in 1483 cells. The level of endogenous S1P in 1483 cells after a 1 h treatment with 200 nM PF-543 is decreased 10-fold, producing a proportional increase in the level of sphingosine[1].

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

Western Blot Analysis[2]

Cell Line:	Human pulmonary arterial smooth muscle (PASM) cells
Concentration:	10 nM, 100 nM, 1000 nM
Incubation Time:	24 hours
Result:	Abolished SK1 expression at nM concentrations.

Apoptosis Analysis[2]

Cell Line:	Human pulmonary arterial smooth muscle (PASM) cells
Concentration:	0.1 μM, 1 μM, 10 μM
Incubation Time:	24 hours
Result:	Induced caspase-3/7 activity in cultured human pulmonary smooth muscle cells.

In Vivo

PF-543 (1 mg/kg; intraperitoneal injection; every second day; for 21 days; female C57BL/6 J mice) treatment has no effect on vascular remodelling but reduces right ventricular hypertrophy. The protection involves a reduction in the expression of p53 and an increase in the expression of anti-oxidant nuclear factor Nrf-2[2].

Mice are initially dosed (ip) with 10 mg/kg or 30 mg/kg of PF-543 for 24 h and the $T_{1/2}$ is 1.2 h in blood samples. Administration of 10 mg/kg PF-543 for 24 h to mice induces a decrease in SK1 expression in pulmonary vessels[2].

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

Animal Model:	Female C57BL/6 J mice (7-12 week-old) with hypoxic-induced pulmonary arterial hypertension[2]
Dosage:	1 mg/kg
Administration:	Intraperitoneal injection; every second day; for 21 days
Result:	Reduced right ventricular hypertrophy. The protection involves a reduction in the expression of p53 (that promotes cardiomyocyte death) and an increase in the expression of anti-oxidant nuclear factor Nrf-2.

CUSTOMER VALIDATION

- Mol Cell. 2020 Mar 19;77(6):1294-1306.e5.
- Sci China Life Sci. 2021 May 27;1-21.
- Cancer Sci. 2020 Jul;111(7):2259-2274.
- Inflammation. 2021 Dec;44(6):2170-2179.
- FASEB J. 2024 Jan 31;38(2):e23417.

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REFERENCES

[1]. Schnute ME, et al. Modulation of cellular S1P levels with a novel, potent and specific inhibitor of sphingosine kinase-1. Biochem J. 2012 May 15;444(1):79-88.

[2]. 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.

[3]. Hamada M, et al. Induction of autophagy by sphingosine kinase 1 inhibitor PF-543 in head and neck squamous cell carcinoma cells. Cell Death Discov. 2017 Aug 14;3:17047.

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