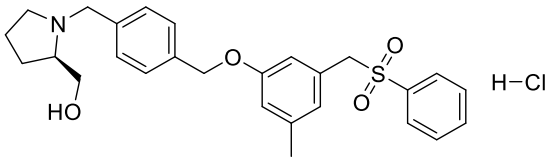
Product data sheet

MedKoo Cat#: 406142 Name: PF-543 HCl CAS#: 1706522-79-3 (HCl) Chemical Formula: $C_{27}H_{32}ClNO_4S$ Molecular Weight: 502.07	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

PF-543 is a novel selective SK-1 inhibitor which inhibited SK-1 activity in a competitive manner with sphingosine. PF-543 inhibits SphK1 with a K(i) of 3.6 nM, is sphingosine-competitive and is more than 100-fold selective for SphK1 over the SphK2 isoform. PF-543 was 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. PF-543 is the most potent inhibitor of SphK1 described to date and it will be useful for dissecting specific roles of SphK1-driven S1P signalling.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	50.21	100
Water	5.02	10

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.99 mL	9.96 mL	19.92 mL
5 mM	0.4 mL	1.99 mL	3.98 mL
10 mM	0.20 mL	1.00 mL	1.99 mL
50 mM	0.04 mL	0.20 mL	0.40 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Kim SB, Limbu KR, Oh YS, Kim SL, Park SK, Baek DJ, Park EY. Novel Dimer Derivatives of PF-543 as Potential Antitumor Agents for the Treatment of Non-Small Cell Lung Cancer. Pharmaceutics. 2022 Sep 24;14(10):2035. doi: 10.3390/pharmaceutics14102035. PMID: 36297469; PMCID: PMC9611471.
2. Hamada M, Kameyama H, Iwai S, Yura Y. 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. doi: 10.1038/cddiscovery.2017.47. PMID: 29109864; PMCID: PMC5554793.

In vivo study

1. MacRitchie N, Volpert G, Al Washih M, Watson DG, Futerman AH, Kennedy S, Pyne S, Pyne NJ. 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. doi: 10.1016/j.cellsig.2016.03.014. Epub 2016 Apr 6. PMID: 27063355; PMCID: PMC4913619.
2. Ju T, Gao D, Fang ZY. Targeting colorectal cancer cells by a novel sphingosine kinase 1 inhibitor PF-543. Biochem Biophys Res Commun. 2016 Feb 12;470(3):728-734. doi: 10.1016/j.bbrc.2016.01.053. Epub 2016 Jan 15. PMID: 26775841.

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7. Bioactivity

Biological target:

PF-543 HCl is a potent and selective SphK1 inhibitor (IC50 = 2 nM; Ki = 3.6 nM). PF-543 HCl exhibits >100-fold selectivity for Sphk1 over Sphk2. It exhibits >5,000 fold selectivity over S1P1-5 receptors and 48 protein and lipid kinases. PF-543 HCl attenuates proliferation and induces necrosis in human colorectal cancer cells in vitro. PF-543 HCl suppresses HCT-116 tumor xenograft growth in mice. It also reduces sickling, hemolysis and inflammation in a transgenic mouse model of sickle cell disease.

In vitro activity

Treatment of head and neck squamous cell carcinoma cells with autophagy inhibitors and PF-543 increased the proportion of cells with necrosis and apoptosis, indicating that autophagy acts to promote cell survival. These results demonstrate that PF-543 induces apoptosis, necrosis, and autophagy in human head and neck squamous cell carcinoma cells, and that autophagy antagonizes either necrosis or apoptosis.

Reference: Cell Death Discov. 2017 Aug 14;3:17047. https://pubmed.ncbi.nlm.nih.gov/29109864/

In vivo activity

Administration of PF-543 in a mouse hypoxic model of pulmonary hypertension reduced right ventricular hypertrophy. The findings of this study with PF-543 suggest an important role for sphingosine kinase 1 in the development of hypertrophy in pulmonary arterial hypertension.

Reference: Cell Signal. 2016 Aug;28(8):946-55. https://pubmed.ncbi.nlm.nih.gov/27063355/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.