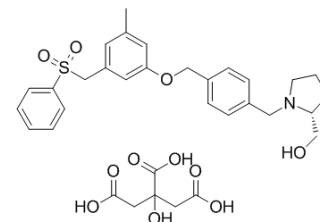


## PF-543 Citrate

<b>Cat. No.:</b>	HY-15425A		
<b>CAS No.:</b>	1415562-83-2		
<b>Molecular Formula:</b>	C <sub>33</sub> H <sub>39</sub> NO <sub>11</sub> S		
<b>Molecular Weight:</b>	657.73		
<b>Target:</b>	SPHK; LPL Receptor; Apoptosis; Autophagy		
<b>Pathway:</b>	Immunology/Inflammation; GPCR/G Protein; Apoptosis; Autophagy		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 100 mg/mL (152.04 mM)  
 H<sub>2</sub>O : 50 mg/mL (76.02 mM; Need ultrasonic)  
 \* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	1.5204 mL	7.6019 mL	15.2038 mL
	5 mM	0.3041 mL	1.5204 mL	3.0408 mL
	10 mM	0.1520 mL	0.7602 mL	1.5204 mL

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

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: ≥ 2.5 mg/mL (3.80 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (3.80 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
Solubility: ≥ 2.5 mg/mL (3.80 mM); Clear solution
- Add each solvent one by one: PBS  
Solubility: 100 mg/mL (152.04 mM); Clear solution; Need ultrasonic

### BIOLOGICAL ACTIVITY

#### Description

PF-543 Citrate (Sphingosine Kinase 1 Inhibitor II Citrate) is a potent, selective, reversible and sphingosine-competitive SPHK1 inhibitor with an IC<sub>50</sub> of 2 nM and a K<sub>i</sub> of 3.6 nM. PF-543 Citrate is >100-fold selectivity for SPHK1 over SPHK2. PF-543 Citrate is an effective potent inhibitor of sphingosine 1-phosphate (S1P) formation in whole blood with an IC<sub>50</sub> of 26.7 nM.

	PF-543 Citrate induces apoptosis, necrosis, and autophagy <sup>[1][2][3]</sup> .																
<b>IC<sub>50</sub> &amp; Target</b>	IC <sub>50</sub> : 2 nM (SPHK1); 26.7 nM (Sphingosine 1-phosphate (S1P)) <sup>[1]</sup> Ki: 3.6 nM (SPHK1) <sup>[1]</sup>																
<b>In Vitro</b>	<p>PF-543 (10-1000 nM; 24 hours; PASM cells) treatment abolishes SK1 expression at nM concentrations<sup>[2]</sup>.</p> <p>PF-543 (0.1-10 μM; 24 hours; PASM cells) treatment induces caspase-3/7 activity<sup>[2]</sup>.</p> <p>PF-543 inhibits C<sub>17</sub>-S1P formation in 1483 cells with an IC<sub>50</sub> of 1.0 nM<sup>[1]</sup>.</p> <p>SphK1 inhibition by PF-543 causes a dose-dependent depletion of the intracellular level of S1P with EC<sub>50</sub> 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<sup>[1]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <p>Western Blot Analysis<sup>[2]</sup></p> <table border="1"> <tr> <td>Cell Line:</td> <td>Human pulmonary arterial smooth muscle (PASM) cells</td> </tr> <tr> <td>Concentration:</td> <td>10 nM, 100 nM, 1000 nM</td> </tr> <tr> <td>Incubation Time:</td> <td>24 hours</td> </tr> <tr> <td>Result:</td> <td>Abolished SK1 expression at nM concentrations.</td> </tr> </table> <p>Apoptosis Analysis<sup>[2]</sup></p> <table border="1"> <tr> <td>Cell Line:</td> <td>Human pulmonary arterial smooth muscle (PASM) cells</td> </tr> <tr> <td>Concentration:</td> <td>0.1 μM, 1 μM, 10 μM</td> </tr> <tr> <td>Incubation Time:</td> <td>24 hours</td> </tr> <tr> <td>Result:</td> <td>Induced caspase-3/7 activity in cultured human pulmonary smooth muscle cells.</td> </tr> </table>	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.	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.
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<b>In Vivo</b>	<p>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<sup>[2]</sup>.</p> <p>Mice are initially dosed (ip) with 10 mg/kg or 30 mg/kg of PF-543 for 24 h and the T<sub>1/2</sub> is 1.2 h in blood samples.</p> <p>Administration of 10 mg/kg PF-543 for 24 h to mice induces a decrease in SK1 expression in pulmonary vessels<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tr> <td>Animal Model:</td> <td>Female C57BL/6 J mice (7-12 week-old) with hypoxic-induced pulmonary arterial hypertension<sup>[2]</sup></td> </tr> <tr> <td>Dosage:</td> <td>1 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>Intraperitoneal injection; every second day; for 21 days</td> </tr> <tr> <td>Result:</td> <td>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.</td> </tr> </table>	Animal Model:	Female C57BL/6 J mice (7-12 week-old) with hypoxic-induced pulmonary arterial hypertension <sup>[2]</sup>	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.								
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- Hum Cell. 2020 Jan;33(1):57-66.

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

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