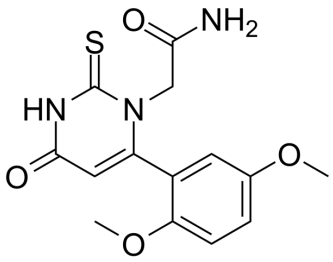
PF-1355

Cat. No.:	HY-100873
CAS No.:	1435467-38-1
Molecular Formula:	$C_{14}H_{15}N_3O_4S$
Molecular Weight:	321.35
Target:	Glutathione Peroxidase
Pathway:	Metabolic Enzyme/Protease
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 : 50 mg/mL (155.59 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.1119 mL	15.5594 mL	31.1187 mL
	5 mM	0.6224 mL	3.1119 mL	6.2237 mL
	10 mM	0.3112 mL	1.5559 mL	3.1119 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: ≥ 2.08 mg/mL (6.47 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.47 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PF-1355 is a selective 2-thiouracil mechanism-based MPO inhibitor, used for treatment of vasculitic diseases.

In Vitro

In a dose-responsive fashion, PF-1355 inhibits MPO activity in phorbol ester-stimulated human neutrophils as measured by taurine chlorination (EC_{50}=1.47 μM) as well as lipopolysaccharide-treated human blood measuring residual MPO activity (EC_{50}=2.03 μM)[1].

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

In Vivo	Oral administration of PF-1355 reduces plasma MPO activity, vascular edema, neutrophil recruitment, and elevates circulating cytokines. In a model of anti-glomerular basement membrane disease, formerly known as Goodpasture disease, albuminuria and chronic renal dysfunction are completely suppressed by PF-1355 treatment[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Plates are coated with the MPO capture antibody (1:200) overnight at 4°C, washed with PBS, and then nonspecific binding blocked with PBS/1% BSA. Plasma or peritoneal exudate samples are diluted 1:4 in PBS and 50 µL is added to triplicate wells for 1 hour at room temperature. Plates are washed three times with PBS containing 0.05% Tween, followed by PBS ishes. Assay buffer (50 µL containing 50 nM phosphate buffer, pH 7.4, containing 140 mM NaCl, 10 mM Na_2NO_2, 40 µM Amplex Red, and 10 µM H_2O_2) is added with kinetic reads and an excitation/emission wavelength of 530/580 nm on a fluorescence plate reader. Assay linearity is typically maintained for >300 seconds (R2 > 0.99) and Vmax represented by the change in relative fluorescence units divided by time to yield MPO activity. Active MPO is back-calculated using purified human MPO standard. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Animals receive an intraperitoneal injection of 4% thioglycollate broth in phosphate-buffered saline (PBS) for neutrophil recruitmen. Twenty hours later, PF-1355 or vehicle (1% hydroxypropyl methylcellulose, 0.5% 2-amino-2-hydroxymethyl-propane-1,3-diol, 0.5% hypromellose acetate succinate, pH 9.5) is administered p.o., followed by intraperitoneal administration of opsonized zymosan or saline. After 3 hours, the mice are euthanized and receive intraperitoneal injection of 2 mL cold PBS. Blood is collected and animals are shaken vigorously before the collection of peritoneal lavage. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- EBioMedicine. 2023 Mar 2;90:104499.

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REFERENCES

[1]. Zheng W, et al. PF-1355, a mechanism-based myeloperoxidase inhibitor, prevents immune complex vasculitis and anti-glomerular basement membrane glomerulonephritis. J Pharmacol Exp Ther. 2015 May;353(2):288-98

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