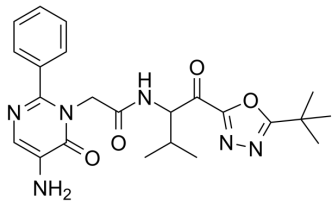
Freselestat

Cat. No.:	HY-15652
CAS No.:	208848-19-5
Molecular Formula:	$C_{23}H_{28}N_6O_4$
Molecular Weight:	452.51
Target:	Elastase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (220.99 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2099 mL	11.0495 mL	22.0990 mL
	5 mM	0.4420 mL	2.2099 mL	4.4198 mL
	10 mM	0.2210 mL	1.1049 mL	2.2099 mL

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

BIOLOGICAL ACTIVITY

Description

Freselestat (ONO-6818) is a potent and orally active neutrophil elastase inhibitor with a K_i of 12.2 nM. Freselestat is >100-fold less-active against other proteases such as trypsin, protein-ase 3, pancreatic elastase, plasmin, thrombin, collagenase, cathepsin G, and murine macrophage elastase. Freselestat has a potent anti-inflammatory activity[1][2][3][4].

IC_{50} & Target

Ki: 12.2 nM (Neutrophil elastase)[3]

In Vitro

Simulated extracorporeal circulation is established by recirculating fresh heparinized (3.75 U/mL) human blood for 120 minutes in a membrane oxygenator and a roller pump with and without 1.0 μM of Freselestat (ONO-6818). Neutrophil elastase levels are significantly lower in the Freselestat group. Freselestat significantly reduces interleukin 8 and C5b-9 production. Freselestat does not modulate changes of CD11b and L-selectin during recirculation[3].

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

In Vivo

Freselestat (ONO-6818; 10-100 mg/kg; oral administration; daily; for 8 weeks) treatment attenuates dose-dependently HNE-induced increases in lung myeloperoxidase activity, hemoglobin, and neutrophil count in bronchoalveolar lavage fluid. ONO-6818 inhibits acute lung injury induced by HNE by minimizing lung hemorrhage and accumulation of neutrophils in the lung[1].

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

Animal Model:	Male Wistar rats (228 g) induced by human neutrophil elastase (HNE)[1]
Dosage:	10 mg/kg, 100 mg/kg
Administration:	Oral administration; daily; for 8 weeks
Result:	Attenuated dose-dependently HNE-induced increases in lung myeloperoxidase activity, hemoglobin, and neutrophil count in bronchoalveolar lavage fluid.

REFERENCES

[1]. Am J Respir Crit Care Med. 2002 Aug 15;166(4):496-500.

[2]. K Ohmoto, et al. Design and synthesis of new orally active inhibitors of human neutrophil elastase. Bioorg Med Chem. 2001 May;9(5):1307-23.

[3]. Yasushi Hirota, et al. Effects of the neutrophil elastase inhibitor (ONO-6818) on acetic acid induced colitis in Syrian hamsters. J Vet Med Sci. 2004 Oct;66(10):1223-8.

[4]. Yukihiro Yoshimura, et al. ONO-6818, a novel, potent neutrophil elastase inhibitor, reduces inflammatory mediators during simulated extracorporeal circulation. Ann Thorac Surg. 2003 Oct;76(4):1234-9.

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