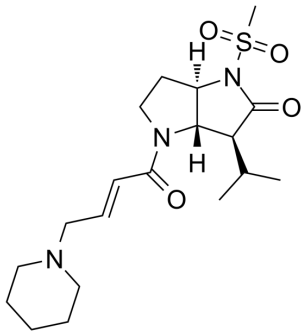
GW311616

Cat. No.:	HY-15891
CAS No.:	198062-54-3
Molecular Formula:	$C_{19}H_{31}N_3O_4S$
Molecular Weight:	397.53
Target:	Elastase
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 : 66.67 mg/mL (167.71 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5155 mL	12.5777 mL	25.1553 mL
5 mM	0.5031 mL	2.5155 mL	5.0311 mL
10 mM	0.2516 mL	1.2578 mL	2.5155 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: 2.5 mg/mL (6.29 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.29 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

GW-311616 is a potent, orally bioavailable, long duration and selective human neutrophil elastase (HNE) inhibitor with IC_{50} value of 22 nM and K_i value of 0.31 nM[1].

IC_{50} & Target

IC50: 22 nM (HNE)[1] Ki: 0.31 nM (HNE)[1]

In Vitro

GW-311616 (150 μM; 48 hours) markedly suppresses NE activity in U937 and K562 cells lines[2].
GW-311616 (20-320 μM; 48 hours; U937 cells) treatment inhibits proliferation and induces apoptosis in leukemia cells[2].
GW-311616 (150 μM; U937 cells) treatment can increase the protein expression levels of Bax and decrease the expression of Bcl-2[2].

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

Cell Viability Assay[2]

Cell Line:	U937 and K562 cells
Concentration:	150 μM
Incubation Time:	48 hours
Result:	Markedly suppressed NE activity.

Apoptosis Analysis[2]

Cell Line:	U937 cells
Concentration:	20 μM, 40 μM, 80 μM, 160 μM, 320 μM
Incubation Time:	48 hours
Result:	The rate of apoptosis was enhanced.

Western Blot Analysis[2]

Cell Line:	U937 cells
Concentration:	150 μM
Incubation Time:	48 hours
Result:	Increased the protein expression levels of Bax and decreased the expression of Bcl-2.

In Vivo

GW-311616 (2 mg/kg; oral administration) rapidly abolishes the circulation of neutrophil elastase (NE) in dogs, while >90% inhibition is maintained for 4 days. This prolonged effect is independent to be due to penetration of neutrophils in bone marrow by orally administrated GW-311616. GW-311616 has moderate terminal elimination half-life ($t_{1/2}$) of 1.1 hours and 1.5 hours for dog (2 mg/kg, oral), rat (2 mg/kg, oral), respectively[3].

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

Animal Model:	Dogs (9-month-old)[3]
Dosage:	0.22 mg/kg, 0.66 mg/kg and 2 mg/kg (Pharmacokinetic study)
Administration:	Oral administration
Result:	At 0.22 mg/kg, greater than 50% inhibition of elastase was achieved 6 hours after dosing, with activity returning towards control values. Single oral dose of 2 mg/kg rapidly abolished circulating enzyme activity, and greater than 90% inhibition was maintained for 4 days.

CUSTOMER VALIDATION

- Adv Sci (Weinh). 2023 Jun 22;e2302613.
- EMBO Rep. 2023 Aug 31;e57032.
- J Invest Dermatol. 2020 Jul;140(7):1371-1378.e3.
- Life Sci. 2020 Feb 1;242:117229.

- Int Immunopharmacol. 2022 Dec 7;114:109537.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Ohbayashi H,et al. Neutrophil elastase inhibitors as treatment for COPD. Expert Opin Investig Drugs. 2002 Jul;11(7):965-80.

[2]. Jiang KL, et al. Neutrophil elastase and its therapeutic effect on leukemia cells. Mol Med Rep. 2015 Sep;12(3):4165-4172.

[3]. Macdonald SJ, et al. The discovery of a potent, intracellular, orally bioavailable, long duration inhibitor of human neutrophil elastase--GW311616A a development candidate. Bioorg Med Chem Lett. 2001 Apr 9;11(7):895-8.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA