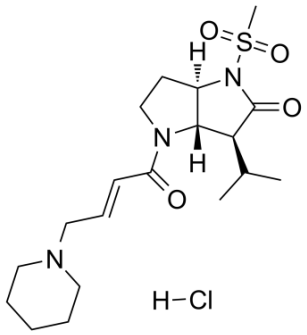
GW311616 hydrochloride

Cat. No.:	HY-15891A
CAS No.:	197890-44-1
Molecular Formula:	$C_{19}H_{32}ClN_3O_4S$
Molecular Weight:	433.99
Target:	Elastase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

H_2O : 100 mg/mL (230.42 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3042 mL	11.5210 mL	23.0420 mL
	5 mM	0.4608 mL	2.3042 mL	4.6084 mL
	10 mM	0.2304 mL	1.1521 mL	2.3042 mL

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

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].
GW311616A (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 is achieved 6 hours after dosing, with activity returning towards control values. Single oral dose of 2 mg/kg rapidly abolishes circulating enzyme activity, and greater than 90% inhibition is maintained for 4 days.

CUSTOMER VALIDATION

- J Invest Dermatol. 2020 Jul;140(7):1371-1378.e3.
- Cell Immunol. 2020 Jun;352:104101.
- Sci Rep. 2017 Nov 30;7(1):16628.
- Life Sci. 2020 Feb 1;242:117229.

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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