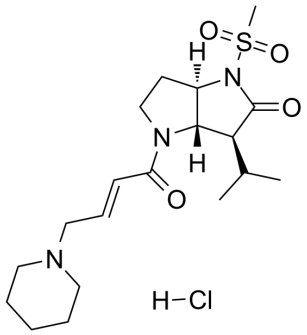
GW311616 hydrochloride

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:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.76 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.76 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.76 mM); Clear solution

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

- 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.

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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.

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