上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：
(3S,3AS,6AR)-3-ISOPROPYL-1-(METHANESULFONYL)-4-[4-(1-PIPERIDINYL)-2(E)-BUTENOYL]PERHYDROPYRROLO[3,2B]PYRROL-2(1H)-ONE HYDROCHLOR

产品别名：GW311616

生物活性：		
Description	GW-311616 is a potent, orally bioavailable, long duration and selective human neutrophil elastase (HNE) inhibitor with IC50 value of 22 nM and Ki 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].	
	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 (t1/2) of 1.1 hours and 1.5 hours for dog (2 mg/kg, oral), rat (2 mg/kg, oral), respectively[3].	
	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

<table>
<tr><td></td><td>Result:</td><td>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.</td></tr>
<tr><td>Solvent&Solubility</td><td colspan="2">In Vitro:
DMSO : ≥ 44 mg/mL (110.68 mM)
* "≥" means soluble, but saturation unknown.

<table>
<tr><td rowspan="4">Preparing Stock Solutions</td><td>Solvent / Mass / Concentration</td><td>1 mg</td><td>5 mg</td><td>10 mg</td></tr>
<tr><td>1 mM</td><td>2.5155 mL</td><td>12.5777 mL</td><td>25.1553 mL</td></tr>
<tr><td>5 mM</td><td>0.5031 mL</td><td>2.5155 mL</td><td>5.0311 mL</td></tr>
<tr><td>10 mM</td><td>0.2516 mL</td><td>1.2578 mL</td><td>2.5155 mL</td></tr>
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*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。
储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。</td></tr>
<tr><td>References</td><td colspan="2">[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.</td></tr>
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