



上海源叶生物科技有限公司
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产品名称:

(S)-N-((R)-1-(Benzo[d][1,3]dioxol-5-yl)butyl)-3,3-diethyl-2-(4-(4methyl-piperazine-1-carbonyl)phenoxy)-4-oxoazetidine-1-carboxam

产品别名: **DMP 777; L-694458**

生物活性:

Description	DMP 777 is a potent, selective, and orally active human leukocyte elastase (HLE) inhibitor.				
IC ₅₀ & Target	Human leukocyte elastase (HLE) ^[2]				
In Vivo	DMP-777-treated rats show a marked decrease in H/K-ATPase staining parietal cells. DMP-777-induced loss of parietal cells is significantly ameliorated with coadministration of omeprazole. DMP-777-treated animals demonstrates marked foveolar hyperplasia in the fundus with prominent expansion of diastase-resistant, PAS-positive surface mucous cells. When DMP-777 is coadministered with omprazole there is a significant decrease in BrdUpositive S-phase cells compared with rats thatreceive DMP-777 alone[1]. After oral dosing of monkeys at 40 mg/kg with DMP-777 the only stereoisomer detected in the post-dose plasma samples is the starting material DMP-777, and no inversion of the configuration at positions 'a' and 'b' of DMP-777 has occurred in vivo[2]. Mist1-/- mice treated with DMP-777 show fewer chief cell to SPEM transitions. Mist1-/- mice treated with L635 demonstrates significantly fewer proliferative SPEM cells compared to control mice[3].				
Solvent&Solubility	In Vitro: DMSO : 38.33 mg/mL (67.88 mM; Need ultrasonic) H ₂ O : < 0.1 mg/mL (insoluble)				
	Preparing Stock Solutions	<div>SolventMassConcentration</div>	1 mg	5 mg	10 mg
		1 mM	1.7709 mL	8.8547 mL	17.7095 mL
		5 mM	0.3542 mL	1.7709 mL	3.5419 mL
		10 mM	0.1771 mL	0.8855 mL	1.7709 mL
	<p>*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。</p> <p>储备液的保存方式和期限 -80℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 储存时，请在 1 个月内使用。</p> <p>In Vivo:</p> <p>请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：</p> <p>——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶</p> <p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (4.43 mM，饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。</p>				



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	<p>2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: 2.5 mg/mL (4.43 mM); Suspended solution; Need ultrasonic</p> <p>此方案可获得 2.5 mg/mL (4.43 mM)的均匀悬浊液, 悬浊液可用于口服和腹腔注射。</p> <p>以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水溶液中, 混合均匀。</p> <p>3.请依序添加每种溶剂: 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (4.43 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (4.43 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。</p>
References	<p>[1]. Ogawa M, et al. Omeprazole treatment ameliorates oxyntic atrophy induced by DMP-777. Dig Dis Sci. 2006 Mar;51(3):431-9.</p> <p>[2]. Zagrobelny J, et al. Separation of the four stereoisomers of a potent inhibitor (L-694,458) of human leukocyte elastase and its determination in human plasma using achiral/chiral chromatography with column switching. J Pharm Biomed Anal. 1998 Sep 1;17(6-7</p> <p>[3]. Weis VG, et al. Maturity and age influence chief cell ability to transdifferentiate into metaplasia. Am J Physiol Gastrointest Liver Physiol. 2016 Nov 23;ajpgi.00326.2016</p>
实验参考:	
Animal Administration	<p>Groups 1A and 1B receive control vehicle instead of omeprazole and DMP-777. Group 2A and 2B are dosed with DMP-777 once daily on Study Day 3 or Days 3 and 4, respectively, and receive control vehicle instead of omeprazole. Groups 3A and 3B are treated with omeprazole twice daily on Study Days 1 to 3 or Days 1 to 4, respectively, and receive control vehicle instead of DMP-777. Groups 4A and 4B are dosed with both omeprazole and DMP-777. On Study Days 1 and 2, animals are pretreated with omeprazole twice daily, the dosing intervals separated by approximately 6 hr. On Study Day 3 (Group 4A) or Days 3 and 4 (Group 4B), omeprazole is coadministered with DMP-777. The first dose of omeprazole is administered approximately 1 hr prior to the dose of DMP-777. The second dose is approximately 6 hr after the last dose of DMP-777. Groups 1A, 2A, 3A, and 4A are sacrificed on Day 4. Groups 1B, 2B, 3B, and 4B are sacrificed on Day 5. Bromodeoxyuridine (BrdU) is administered by intraperitoneal injection to all the rats, 2 hr prior to necropsy. [1]</p>
References	<p>[1]. Ogawa M, et al. Omeprazole treatment ameliorates oxyntic atrophy induced by DMP-777. Dig Dis Sci. 2006 Mar;51(3):431-9.</p> <p>[2]. Zagrobelny J, et al. Separation of the four stereoisomers of a potent inhibitor (L-694,458) of human leukocyte elastase and its determination in human plasma using achiral/chiral chromatography with column switching. J Pharm Biomed Anal. 1998 Sep 1;17(6-7</p> <p>[3]. Weis VG, et al. Maturity and age influence chief cell ability to transdifferentiate into metaplasia. Am J Physiol Gastrointest Liver Physiol. 2016 Nov 23;ajpgi.00326.2016</p>