



上海源叶生物科技有限公司
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产品名称: **LY 3000328**
产品别名: **LY 3000328**

生物活性:				
Description	LY 3000328 is a potent and selective Cathepsin S (Cat S) inhibitor with IC ₅₀ s of 7.7 and 1.67 nM for hCat S and mCat S, respectively.			
IC₅₀ & Target	IC ₅₀ : 7.7±5.85 nM (hCat S), 1.67±1.17 (mCat S) ^[1]			
In Vitro	LY3000328 maintains excellent in vitro potency and selectivity. LY3000328 shows low in vitro CYP450 inhibition (<15% at 10 µM for CYP3A4, CYP2D6, and CYP2C9); low in vitro metabolism in mouse, rat, dog, and human liver microsomes (<20% after 30 min incubation at 4 µM); and good permeability (MDCK A-B>4%). At a 100 µM concentration of LY3000328 there is only 6% displacement of [³ H]-astemizole in an assay with HEK293 membrane preparation, indicating low potential of hERG blockade ^[1] . LY3000328 is a potent and specific inhibitor of cathepsin S (CatS). Inhibition of CatS activity in plasma would be 50% of maximal when LY3000328 plasma concentration is approximately 60 ng/mL ^[2] .			
In Vivo	The efficacies of LY3000328 is studied in a mouse model of abdominal aortic aneurysm (AAA). In this model, inflammation is induced using CaCl ₂ applied to the abluminal surface. It is shown that features of the disease state in this model resemble those of human AAA. LY3000328 exhibits a dose-responsive aortic diameter reduction at 1, 3, 10, and 30 mg/kg. At the lowest dose of 1 mg/kg of LY3000328, the aortic diameter is reduced by 58%, then 83% at 3 mg/kg, and 87% at 10 mg/kg. The exposure (AUC) for both compounds increased in a dose-dependent manner, suggesting that the drug disposition properties of LY3000328 are favorable ^[1] .			
Solvent&Solubility	In Vitro: DMSO : ≥ 50 mg/mL (103.19 mM) * "≥" means soluble, but saturation unknown.			
		Solvent Mass Concentration	1 mg	5 mg
	Preparing	1 mM	2.0639 mL	10.3195 mL
	Stock Solutions	5 mM	0.4128 mL	2.0639 mL
		10 mM	0.2064 mL	1.0319 mL
*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。 In Vivo: 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: ——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 1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (5.16 mM); Clear solution				



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	此方案可获得 ≥ 2.5 mg/mL (5.16 mM, 饱和度未知) 的澄清溶液。 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。 2.请依序添加每种溶剂: 10% DMSO$\rightarrow$ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.16 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.16 mM, 饱和度未知) 的澄清溶液。 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 生理盐水水溶液中, 混合均匀。 3.请依序添加每种溶剂: 10% DMSO $\rightarrow$ 90% corn oil Solubility: ≥ 2.5 mg/mL (5.16 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.16 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。 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。
References	[1]. Jadhav PK, et al. Discovery of Cathepsin S Inhibitor LY3000328 for the Treatment of Abdominal Aortic Aneurysm. ACS Med Chem Lett. 2014 Aug 27;5(10):1138-42. [2]. Payne CD, et al. Pharmacokinetics and pharmacodynamics of the cathepsin S inhibitor, LY3000328, in healthy subjects. Br J Clin Pharmacol. 2014 Dec;78(6):1334-42.

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