

产品名称: **YO-01027**
 产品别名: 二苯并氮卓-**YO-01027**

生物活性:				
Description	YO-01027 (Dibenzazepine;DBZ) is a potent γ -secretase inhibitor with IC ₅₀ values of 2.92±0.22 and 2.64±0.30 nM for Notch and APPL cleavage, respectively.			
IC ₅₀ & Target	IC50: 2.92±0.22 (Notch), 2.64±0.30 (APPL) nM[1]			
In Vitro	Increasing concentrations of DBZ administered to APPL- or Notch-expressing cells leads to the progressive accumulation of APPL CTF fragments and a decrease in NICD production in a strictly dose-dependent manner[1]. The molecular targets of CE and DBZ are the N-terminal fragment of presenilin 1 within the γ -secretase complex[2].			
In Vivo	DBZ blocks activated Notch1 signaling in abdominal aortic aneurysm (AAA) tissue from both Ang II-infused Apo E ^{-/-} mice and human undergoing AAA repair. DBZ markedly prevents Ang II-stimulated accumulation of macrophages and CD4 ⁺ T cells, and ERK-mediated angiogenesis, simultaneously reverses Th2 response, in vivo[3]. Administration of DBZ markedly attenuates renal fibrosis and expression of fibrotic markers, including collagen 1 α 1/3 α 1, fibronectin, and α -smoothmuscle actin. DBZ significantly inhibits ureteral obstruction -induced expression of transforming growth factor (TGF)- β , phosphorylated Smad 2, and Smad 3[4].			
Solvent&Solubility	<i>In Vitro:</i> DMSO : ≥ 33 mg/mL (71.20 mM) H ₂ O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.			
	Preparing Stock Solutions	Solvent \ Mass Concentration	1 mg	5 mg
		1 mM	2.1576 mL	10.7880 mL
		5 mM	0.4315 mL	2.1576 mL
		10 mM	0.2158 mL	1.0788 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。 <i>In Vivo:</i> 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 (5.39 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.39 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μ L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μ L PEG300 中，混合均匀向上述体系中加入 50 μ L Tween-80，混合均匀；然后继续加入 450 μ L 生理盐水定容至 1 mL。			

	<p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (5.39 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.39 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 Solubility: ≥ 2.5 mg/mL (5.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.39 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]. Groth C, et al. Pharmacological analysis of <i>Drosophila melanogaster</i> gamma-secretase with respect to differential proteolysis of Notch and APP. <i>Mol Pharmacol</i>. 2010 Apr;77(4):567-74.</p> <p>[2]. Fuwa H, et al. Divergent synthesis of multifunctional molecular probes to elucidate the enzyme specificity of dipeptidic gamma-secretase inhibitors. <i>ACS Chem Biol</i>. 2007 Jun 15;2(6):408-18.</p> <p>[3]. Zheng YH, et al. Notch γ-secretase inhibitor dibenzazepine attenuates angiotensin II-induced abdominal aortic aneurysm in ApoE knockout mice by multiple mechanisms. <i>PLoS One</i>. 2013 Dec 16;8(12):e83310.</p> <p>[4]. Xiao Z, et al. The Notch γ-secretase inhibitor ameliorates kidney fibrosis via inhibition of TGF-β/Smad2/3 signaling pathway activation. <i>Int J Biochem Cell Biol</i>. 2014 Oct;55:65-71.</p>
实验参考：	
Cell Assay	<p>DBZ (0.1, 1, 2.5, 5, 7.5, 10, 25, 50, 100, 250 nM) are added to the S2 cell medium upon induction of Notch or APPL expression, 6 h before protein harvesting. For each sample, the same inhibitor is also included at the corresponding concentration in the lysis buffer for protein extraction and immunoblot analysis[1].</p>
Animal Administration	<p>Mice: Male wild-type (WT) C57BL/6J and Apo E^{-/-} mice are used in the study. Ang II-treated mice are received an intraperitoneal injection of either saline vehicle or γ-secretase inhibitor, dibenzazepine (DBZ) (1 mg/kg/d, dissolved in saline) 1 day before mini-pump implantation, and the treatment continued daily for 4 weeks. The blood pressure is measured in conscious mice using a computerized tail-cuff system. All mice are anesthetized. The aortic tissues are removed and prepared for further histological and molecular analysis[3].</p>
References	<p>[1]. Groth C, et al. Pharmacological analysis of <i>Drosophila melanogaster</i> gamma-secretase with respect to differential proteolysis of Notch and APP. <i>Mol Pharmacol</i>. 2010 Apr;77(4):567-74.</p> <p>[2]. Fuwa H, et al. Divergent synthesis of multifunctional molecular probes to elucidate the enzyme specificity of dipeptidic gamma-secretase inhibitors. <i>ACS Chem Biol</i>. 2007 Jun 15;2(6):408-18.</p> <p>[3]. Zheng YH, et al. Notch γ-secretase inhibitor dibenzazepine attenuates angiotensin II-induced abdominal aortic aneurysm in ApoE knockout mice by multiple mechanisms. <i>PLoS One</i>. 2013 Dec 16;8(12):e83310.</p> <p>[4]. Xiao Z, et al. The Notch γ-secretase inhibitor ameliorates kidney fibrosis via inhibition of TGF-β/Smad2/3 signaling pathway activation. <i>Int J Biochem Cell Biol</i>. 2014 Oct;55:65-71.</p>