



上海源叶生物科技有限公司
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产品名称: **N-BENZYL-4-CHLORO-N-CYCLOHEXYLBENZAMIDE**
产品别名: **FPS-ZM1**

生物活性:				
Description	FPS-ZM1 is a high-affinity RAGE inhibitor with a K_i of 25 nM.			
IC ₅₀ & Target	K_i : 25 nM (RAGE)[1]			
In Vitro	FPS-ZM1 inhibits A β /RAGE binding in CHO cells with approximately 2-fold greater affinity than its parent molecule, FPS2. FPS-ZM1 inhibits binding of other known RAGE ligands to sRAGE, including S100 calcium-binding protein B and amphoterin. FPS-ZM1 is more effective than FPS2 in reducing A β 40-induced increases in BACE1 mRNA and protein levels and the generation of sAPP β , an APP cleavage product of BACE1 indicative of BACE1 activity[1].			
In Vivo	FPS-ZM1 is nontoxic to mice and readily crossed the blood-brain barrier. In aged APP ^{sw/0} mice overexpressing human A β -precursor protein, a transgenic mouse model of AD with established A β pathology, FPS-ZM1 inhibits RAGE-mediated influx of circulating A β 40 and A β 42 into the brain. In brain, FPS-ZM1 binds exclusively to RAGE, which inhibits β -secretase activity and A β production and suppresses microglia activation and the neuro-inflammatory response[1]. FPS-ZM1 treatment reduces the level of A β 1-40 and A β 1-42 in AGEs Rats. It inhibits AGEs-mediated increase of A β -metabolism-related proteins and downregulates AGEs-mediated increase of pro-inflammatory cytokines in the hippocampus. FPS-ZM1 up-regulates anti-oxidant defense system and attenuated AGEs induced memory impairment in AGEs rats[2].			
Solvent&Solubility	In Vitro: DMSO : \geq 100 mg/mL (305.02 mM) H₂O : < 0.1 mg/mL (insoluble) * " \geq " means soluble, but saturation unknown.			
		Solvent Mass Concentration	1 mg	5 mg
	Preparing	1 mM	3.0502 mL	15.2509 mL
	Stock Solutions	5 mM	0.6100 mL	3.0502 mL
		10 mM	0.3050 mL	1.5251 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 (7.63 mM); Suspended solution; Need ultrasonic				



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	<p>此方案可获得 2.5 mg/mL (7.63 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 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> <p>2.请依序添加每种溶剂: 10% DMSO\rightarrow 90% (20% SBE-β-CD in saline)</p> <p>Solubility: 2.5 mg/mL (7.63 mM); Suspended solution; Need ultrasonic</p> <p>此方案可获得 2.5 mg/mL (7.63 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 \rightarrow90% corn oil</p> <p>Solubility: \geq 2.5 mg/mL (7.63 mM); Clear solution</p> <p>此方案可获得 \geq 2.5 mg/mL (7.63 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]. Deane R, et al. A multimodal RAGE-specific inhibitor reduces amyloid β-mediated brain disorder in a mouse model of Alzheimer disease. J Clin Invest. 2012 Apr;122(4):1377-92.</p> <p>[2]. Hong Y, et al. Effects of RAGE-Specific Inhibitor FPS-ZM1 on Amyloid-β Metabolism and AGEs-Induced Inflammation and Oxidative Stress in Rat Hippocampus. Neurochem Res. 2016 May;41(5):1192-9.</p> <p>[3]. Lian YJ, et al. Ds-HMGB1 and fr-HMGB induce depressive behavior through neuroinflammation in contrast to nonoxid-HMGB1. Brain Behav Immun. 2017 Jan;59:322-332.</p>
实验参考:	
Cell Assay	<p>To determine whether FPS2 and FPS-ZM1 are toxic to CHO cells, the cells are treated for 72 hours with different concentrations of inhibitors ranging from 10 nM to 10 μM. The cellular toxicity is determined using the WST-8 Assay Kit[1].</p>
Animal Administration	<p>Rats: Starting from 1 week before intrahippocampal injection, FZM1 and AGEs+FZM1 rats are intraperitoneally injected with FPS-ZM1 (1 mg/kg/d at a volume of 2 mL) for 4 weeks; rats in the AGEs and the control groups are intraperitoneally injected with normal saline with the same volume for 4 weeks. Three weeks after AGEs intrahippocampal injection, the escape latency time of rats is assayed with Morris water maze test, and then all rats are sacrificed[2].</p> <p>Mice: FPS2 or FPS-ZM1 are administered i.v. (1 mg/kg) via the femoral vein and arterial blood samples (30 μL) collected at 1, 5, 10, 15, and 20 minutes via the cannulated femoral artery. Plasma is separated by centrifugation at 4°C and immediately stored at -80°C until analysis[1].</p>
Kinase Assay	<p>Human sRAGE is immobilized (10 μg/mL) overnight at 4°C in 96-well microtiter plates and blocked with 3% bovine serum albumin. ¹²⁵I-labeled Aβ40, HMGB1, or S100B at 5 nM in the absence and presence of various concentrations of FPS2 or FPS-ZM1 (10 to 1,000 nM) is added to the wells containing immobilized sRAGE and incubated for 1 hour at room temperature in PBS. Wells are washed with cold PBS to remove unbound radiolabeled ligands, and the radioactivity is analyzed[1].</p>



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