

产品名称：SL-327

产品别名：SL327

生物活性:

Description	SL327 inhibits MEK1 and MEK2, with IC <sub>50</sub> values of 180 nM and 220 nM, respectively.				
IC <sub>50</sub> & Target	MEK1	MEK2			
	180 nM (IC <sub>50</sub> )	220 nM (IC <sub>50</sub> )			
In Vitro	The specificity of SL327 for MEK is investigated. Kinase activity is assessed by measuring the incorporation of [32P]phosphate during phosphorylation of substrate peptides specific for each kinase. Although SL327 inhibits MEK with an IC <sub>50</sub> of 0.27 μM, 10 μM SL327 has no significant effect on PKA, CaMKII, or PKC[2].				
In Vivo	SL327, which crosses the blood-brain barrier, is administered intraperitoneally at several concentrations to animals prior to cue and contextual fear conditioning. Administration of SL327 completely blocks contextual fear conditioning and significantly attenuates cue learning when measure 24 hr after training. Animals treated with SL327 exhibit significant attenuation of water maze learning; they take significantly longer to find a hidden platform compared with vehicle-treated controls and also fail to use a selective search strategy during subsequent probe trials in which the platform is removed. Mice are injected with various concentrations of SL327 (10, 30, 50 mg/kg i.p.), and 1 hr later their hippocampi are removed and assayed for activated MAPK. SL327 attenuates phosphorylated MAPK levels in a dose-dependent manner. Administration of 10, 30, or 50 mg/kg SL327 significantly attenuates p42 phospho-MAPK levels (F=20.90, P<0.0001; 10 mg/kg SL327 vs. vehicle, P<0.05, and 30 and 50 mg/kg SL327 vs. vehicle, P<0.001). Injection with 30 or 50 mg/kg SL327 also significantly reduces p44 phospho-MAPK levels (F=5.627, P<0.005; 30 mg/kg vs. vehicle, P<0.05, and 50 mg/kg SL327 vs. vehicle, P<0.01)[2].				
Solvent&Solubility	<b>In Vitro:</b> <b>DMSO : 68 mg/mL (202.77 mM; Need ultrasonic)</b> <b>Ethanol : 0.1 mg/mL (0.30 mM; Need ultrasonic and warming)</b>				
	Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg	10 mg
		1 mM	2.9820 mL	14.9098 mL	29.8196 mL
		5 mM	0.5964 mL	2.9820 mL	5.9639 mL
		10 mM	0.2982 mL	1.4910 mL	2.9820 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℃, 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。 <b>In Vivo:</b> 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 (7.45 mM); Clear solution				
	此方案可获得 ≥ 2.5 mg/mL (7.45 mM，饱和度未知) 的澄清溶液。				

	<p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中，混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80，混合均匀；然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-<math>\beta</math>-CD in saline) Solubility: <math>\geq</math> 2.5 mg/mL (7.45 mM); Clear solution 此方案可获得 <math>\geq</math> 2.5 mg/mL (7.45 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-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: <math>\geq</math> 2.5 mg/mL (7.45 mM); Clear solution 此方案可获得 <math>\geq</math> 2.5 mg/mL (7.45 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 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中，混合均匀。</p>
References	<p>[1]. Cheng Y, et al. Current Development Status of MEK Inhibitors. Molecules. 2017 Sep 26;22(10). pii: E1551.</p> <p>[2]. Selcher JC, et al. A necessity for MAP kinase activation in mammalian spatial learning. Learn Mem. 1999 Sep-Oct;6(5):478-90.</p>
实验参考：	
Animal Administration	<p>Mice[2] Adult male 129S3/SvImJ mice are used. In the 1<math>\times</math>-pairing paradigm of cue and contextual fear conditioning, animals are placed in the fear conditioning apparatus for 3 min, then a 30-sec acoustic conditioned stimulus (CS; white noise, 80 dB) is delivered. During the last second of the CS, a 1-sec shock unconditioned stimulus (US; 0.5 mA) is applied to the grid floor. To assess contextual learning, the animals are returned to the training context 24 hr post-training, and freezing behavior is scored for 5 min. To assess cue learning, the animals are placed in a different context (novel odor, lighting, cage floor, and visual cues) following contextual testing. Baseline behavior is measured for 3 min in the novel context (Pre-CS), then the tone is presented for 3 min. Freezing behavior is assessed with a time sampling procedure whereby the animal was observed for ~1 sec every 5 sec. The experimenter is blind to drug treatment. Animals are injected with either vehicle (2 mL/kg, 100% DMSO) or SL327 (10, 30, and 50 mg/kg; at 2 mL/kg, dissolved in 100% DMSO) intraperitoneally 1 hr before training[2].</p>
Kinase Assay	<p>Protein kinase assays are performed. All kinase assays are started by adding enzyme to a mixture that included [<math>\gamma</math>-<sup>32</sup>P]ATP and substrate. This mixture is then incubated at 30°C or 37°C for 10 min. The reaction is stopped by spotting aliquots of the reaction mixture onto Whatman P-81 phosphocellulose filter paper. The papers are then washed in 150 mM H<sub>3</sub>PO<sub>4</sub>, dried, and subjected to scintillation counting. The catalytic subunit of PKA is assayed by measuring [<sup>32</sup>P]phosphate incorporation into the substrate Kemptide (100 <math>\mu</math>M). The activity of CaMKII is determined by measuring phosphorylation of the synthetic peptide Autocamtide (100 <math>\mu</math>M) in the presence of 100 <math>\mu</math>M Calcium and 10 <math>\mu</math>g/mL Calmodulin. A synthetic peptide analog of a fragment of neurogranin, NG(28-43) (10 <math>\mu</math>M) is used as a specific substrate for the catalytic subunit of PKC. In all cases, substrate phosphorylation was linear with respect to time and enzyme concentration[2].</p>
	<p>[1]. Cheng Y, et al. Current Development Status of MEK Inhibitors. Molecules. 2017 Sep 26;22(10).</p>

<b>References</b>	<p><a href="#">pii: E1551.</a></p> <p>[2]. <a href="#">Selcher JC, et al. A necessity for MAP kinase activation in mammalian spatial learning. Learn Mem. 1999 Sep-Oct;6(5):478-90.</a></p>
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源叶生物