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产品名称：ZL006
产品别名：ZL006

生物活性：

Description	ZL006 is a potent inhibitor of nNOS/PSD-95 interaction, and inhibits NMDA receptor-mediated NO synthesis.
In Vitro	ZL006 presents little cytotoxicity, and a growth inhibition of BCECs is not found at low concentration of 0.001, 0.01, 0.1, 1 and 10 μg/mL. The cytotoxicity of T7-P-LPs/ZL006 is significantly enhanced at the concentration of 10 μg/mL. Cellular uptake of ZL006 loads P-LPs and T7-P-LPs after incubation for 0.5 h at the concentrations range from 100 μg/mL to 600 μg/mL in BCECs[1]. ZL006 does not inhibit the nNOS-PDZ/PSD-95-PDZ interaction, or perturb the nNOS β-finger[2].
In Vivo	Compared with P-LPs/ZL006 and free ZL006, T7-P-LPs/ZL006 exhibits a significant increase of drug accumulation in the brain tissue due to its better brain targeting delivery. Compared with free ZL006, P-LPs/ZL006 and T7-P-LPs/ZL006 exhibit a significant decrease of drug accumulation in the liver and kidney[1].
Solvent&Solubility	***In Vitro:*** **DMSO： ≥ 29 mg/mL (88.37 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0474 mL	15.2369 mL	30.4739 mL
5 mM	0.6095 mL	3.0474 mL	6.0948 mL
10 mM	0.3047 mL	1.5237 mL	3.0474 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 (7.62 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (7.62 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→ 90% (20% SBE-β-CD in saline)

Solubility: ≥ 2.5 mg/mL (7.62 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (7.62 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 →90% corn oil Solubility: ≥ 2.5 mg/mL (7.62 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.62 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]. Wang Z, et al. Enhanced anti-ischemic stroke of ZL006 by T7-conjugated PEGylated liposomes drug delivery system. Sci Rep. 2015 Jul 29;5:12651. [2]. Bach A, et al. Biochemical investigations of the mechanism of action of small molecules ZL006 and IC87201 as potential inhibitors of the nNOS-PDZ/PSD-95-PDZ interactions. Sci Rep. 2015 Jul 16;5:12157.

实验参考：

Cell Assay	BCECs are seeded in 96-well plates in 200 μL of DMEM medium to obtain a concentration of 2000 cells per well, and incubated for 24 h. The medium in each well is then incubated for 72 h with 200 μL medium containing blank vehicle, P-LPs/ZL006, T7-P-LPs/ZL006 and ZL006 (free drug dissolved in DMSO) with a series of concentrations ranging from 0.001 to 100 μg/mL. The MTT absorbance at 570 nm of each well is measured by a microplate reader.
Animal Administration	ICR mice weighting 20 ± 2 g are divided into three groups at random (n=12). Free ZL006, P-LPs/ZL006 and T7-P-LPs/ZL006 (all containing ZL006 4 mg/kg) are administered to each group through intravenous route, respectively. At designated time intervals (0.5, 1 and 2 h), the mice are executed and the major organs samples including brain, heart, liver, spleen, lung and kidney are collected. Before pretreatment, these tissues are rinsed with cold saline solution to remove the blood and then blotted with paper towel. Protein precipitation of the samples is performed before analysis. Then the samples are injected into the LC-MS/MS systems for analysis. The LC-MS/MS system consists of an Agilent Series 1200 HPLC system and a 6410 Triple Quad LC/MS mass spectrometer. The data is collected and processed using the Agilent MassHunter Workstation Software.
References	[1]. Wang Z, et al. Enhanced anti-ischemic stroke of ZL006 by T7-conjugated PEGylated liposomes drug delivery system. Sci Rep. 2015 Jul 29;5:12651. [2]. Bach A, et al. Biochemical investigations of the mechanism of action of small molecules ZL006 and IC87201 as potential inhibitors of the nNOS-PDZ/PSD-95-PDZ interactions. Sci Rep. 2015 Jul 16;5:12157.