上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：SR-3306
产品别名：SR-3306

生物活性：

Description	SR-3306 is a selective, potent, highly brain penetrant JNK inhibitor.
IC_{50} & Target	JNK
In Vitro	The effect of SR-3306 or Tat-Sab on cell viability in response to oxidative stress is measured by an MTT assay. H9c2 cells treated with 100 μM H_2O_2/$FeSO_4$ are ~40% viable, whereas the addition of 500 nM SR-3306 or 500 nM SR3562 to cells treated with 100 μM H_2O_2/$FeSO_4$ increases viability to ~90%, and the addition of 10 μM Tat-Sab peptide to cells treated with 100 μM H_2O_2/$FeSO_4$ increases viability to ~70% compared with 98% viability in untreated cells. Similar results are found for primary human cardiomyocytes [2].
In Vivo	Administration of SR-3306 [10 mg/kg/day (s.c.) for 14 days] increases the number of tyrosine hydroxylase immunoreactive (TH^+) neurons in the SNpc by 6-fold and reduces the loss of the TH^+ terminals in the striatum relative to the corresponding side of 6-OHDA-lesioned rats that receive only vehicle ($p<0.05$). In addition, SR-3306 [10 mg/kg/day (s.c.) for 14 days] decreases d-amphetamine-induced circling by 87% compared to 6-hydroxydopamine (6-OHDA)-lesioned animals given vehicle. Steady-state brain levels of SR-3306 at day 14 are 347 nM, which is approximately 2-fold higher than the cell-based IC50 for this compound. Finally, immunohistochemical staining for phospho-c-jun (p-c-jun) reveals that SR-3306 [10 mg/kg/day (s.c.) for 14 days] produces a 2.3-fold reduction of the number of immunoreactive neurons in the substantia nigra pars compacta (SNpc) relative to vehicle treated rats[1]. In lean mice, intraperitoneal (i.p.) or intracerebroventricular (i.c.v.) administration of SR-3306 reduces food intake and body weight. Moreover, i.p. and i.c.v. administrations of SR11935 exert similar anorectic effects as SR3306, which suggests JNK2 or JNK3 mediates aspect of the anorectic effect by pan-JNK inhibition. Furthermore, daily i.p. injection of SR-3306 (7 days) prevents the increases in food intake and weight gain in lean mice upon high-fat diet feeding, and this injection paradigm reduced high-fat intake and obesity in diet-induced obese (DIO) mice[3].

In Vitro:

DMSO : 125 mg/mL (**254.81 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.0385 mL	10.1924 mL	20.3849 mL
	5 mM	0.4077 mL	2.0385 mL	4.0770 mL
	10 mM	0.2038 mL	1.0192 mL	2.0385 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

Solvent&Solubility	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: ≥ 2.08 mg/mL (4.24 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.24 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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。
References	[1]. Crocker CE, et al. JNK Inhibition Protects Dopamine Neurons and Provides Behavioral Improvement in a Rat 6-hydroxydopamine Model of Parkinson's Disease. ACS Chem Neurosci. 2011 Apr 20;2(4):207-212. [2]. Gao S, et al. Pharmacological Inhibition of c-Jun N-terminal Kinase Reduces Food Intake and Sensitizes Leptin's Anorectic Signaling Actions. Sci Rep. 2017 Feb 6;7:41795. [3]. Chambers JW, et al. Inhibition of JNK mitochondrial localization and signaling is protective against ischemia/reperfusion injury in rats. J Biol Chem. 2013 Feb 8;288(6):4000-11.

实验参考：

Cell Assay	H9c2 cells and primary human cardiomyocytes are grown under normal cell culture conditions (37 °C and 5% CO_2) in DMEM supplemented with 10% fetal bovine serum and penicillin/streptomycin. To assure that the cells are actively growing, only cells at ~80% confluency and between passages 5 and 15 are used in our experiments. H9c2 cells and primary human cardiomyocytes are exposed to 500 nM SR-3306, 500 nM SR-3562, 0.01% DMSO vehicle control, 10 μM Tat-Sab_{KIM1}, and 10 μM Tat-scramble for 30 min prior to the addition of stress. To induce oxidative stress and mitochondrial dysfunction in H9c2 cells and primary human cardiomyocytes, 100 μM hydrogen peroxide (H_2O_2)/$FeSO_4$ or 100 μM hydrogen peroxide (H_2O_2)/$FeSO_4$ is added directly to the media of the cells. The cells are exposed to H_2O_2/$FeSO_4$ for the times indicated in the experiments[2].
Animal Administration	Rats[1] Four Sprague-Dawley rats are used. SR-3306 is dosed at 2.5 or 10 mg/kg in subcutaneous minipumps at a rate of 5 μL/h, and after 24 h on days 1, 2, 3, 4, 6, 7, 8, 9, 10, 13, and 14 blood, and day 14 brain are collected. Plasma is generated, and the samples are frozen at -80 °C. The plasma and brain are mixed with Acetonitrile (1:5 v/v or 1:5 w/v, respectively). The brain sample is sonicated with a probe tip sonicator to break up the tissue, and samples are analyzed for compound levels by LC-MS/MS. Plasma compound levels are determined against standards made in plasma and brain levels against standards made in blank brain matrix[1]. Mice[3] Male, lean or DIO C57BL/6 mice are used. The mice are trained to scheduled, daily, 2-hour water access during the light for 2 weeks. On the first day of the conditioned taste aversion (CTA) test, the trained mice are given a novel 0.15% saccharin solution to drink for the first 50 minutes, and are then given an i.p. injection of SR-3306 (30 mg/kg or 60 mg/kg) or the vehicle. The injected mice are then provided water for the remaining 70 min. The next day, the mice are allowed to choose

	between water and 0.15% saccharin for 50 min. Fluid consumption is calculated[3].
References	[1]. Crocker CE, et al. JNK Inhibition Protects Dopamine Neurons and Provides Behavioral Improvement in a Rat 6-hydroxydopamine Model of Parkinson's Disease. ACS Chem Neurosci. 2011 Apr 20;2(4):207-212. [2]. Gao S, et al. Pharmacological Inhibition of c-Jun N-terminal Kinase Reduces Food Intake and Sensitizes Leptin's Anorectic Signaling Actions. Sci Rep. 2017 Feb 6;7:41795. [3]. Chambers JW, et al. Inhibition of JNK mitochondrial localization and signaling is protective against ischemia/reperfusion injury in rats. J Biol Chem. 2013 Feb 8;288(6):4000-11.

源叶生物