产品名称：**TDZD-8**
产品别名：**TDZD-8**

生物活性：

Description	TDZD-8 is an inhibitor of GSK-3β, with an IC_{50} of 2 μM; TDZD-8 shows less potent activities against Cdk-1/cyclin B, CK-II, PKA, and PKC, with all IC_{50}s of >100 μM.
IC_{50} & Target	GSK-3β [1]
	2 μM (IC_{50})
In Vitro	TDZD8 results in a significant decline of cellular ATP levels in PC-3 cells. TDZD8 (10 μM) treatment also triggers a drastic autophagy response and AMPK activation in PC-3 cells. Furthermore, TDZD8 (10 μM) reduces mTOR phosphorylation levels at the S2448 site. In addition, TDZD8 (10 μM) induces LKB1 nuclear-cytoplasm translocation[3].
In Vivo	TDZD-8 (TDZD8, 1 or 2 mg/kg, i.p.) both reduces the induction of p-DARPP32 following chronic L-dopa treatment in parkinsonian animals. TDZD8 treatment of 21 days induces a significant reduction in PKA expression in rats with established dyskinesia. Moreover, TDZD8 reduces FosB mRNA level in the striatum and lowers the expression of PPEB mRNA to similar levels as in 6-OHDA-lesioned rats without treated with L-dopa. The decrease in dyskinesia induced by TDZD8 is overcome by dopamine rceptor-1 agonist[2].

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (449.92 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.4992 mL	22.4962 mL	44.9924 mL
	5 mM	0.8998 mL	4.4992 mL	8.9985 mL
	10 mM	0.4499 mL	2.2496 mL	4.4992 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 (11.25 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (11.25 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 (11.25 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (11.25 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 (11.25 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (11.25 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]. Martinez A, et al. First non-ATP competitive glycogen synthase kinase 3 beta (GSK-3beta) inhibitors: thiadiazolidinones (TDZD) as potential drugs for the treatment of Alzheimer's disease. J Med Chem. 2002 Mar 14;45(6):1292-9. [2]. Xie CL, et al. Inhibition of Glycogen Synthase Kinase-3β (GSK-3β) as potent therapeutic strategy to ameliorates L-dopa-induced dyskinesia in 6-OHDA parkinsonian rats. Sci Rep. 2016 Mar 21;6:23527. [3]. Sun A, et al. GSK-3β controls autophagy by modulating LKB1-AMPK pathway in prostate cancer cells. Prostate. 2016 Feb;76(2):172-83.

实验参考：

Animal Administration	Apomorphine hydrochloride is administered (0.5 mg/kg). L-dopa (25 mg/kg) plus benserazide-HCl (6.25 mg/kg) are given once-daily. TDZD8, a non-ATP competitive inhibitor of GSK-3β, is dissolved in 10% DMSO and is administered i.p. (TDZD8-L group, 1 mg/kg; TDZD8-H group, 2 mg/kg, respectively) 30 min prior to L-dopa intake for 3 weeks. (±)-1-Phenyl-2,3,4,5-tetrahydro-(1H)-3-benzazepine-7,8-diol hydrochloride (SKF38393), a D1 Dopamine receptor agonist, is dissolved in saline and is administered i.p. (SKF38393-L group, 5 mg/kg; SKF38393-H group, 10 mg/kg, respectively) 30 min prior to L-dopa intake for 3 weeks[2].
Kinase Assay	GSK-3 activity is assayed in 50 mM Tris-HCl, pH 7.5, 10 mM $MgCl_2$, 1 mM EGTA, and 1 mM EDTA buffer, at 37°C, in the presence of 15 μM GS-1 (substrate), 15 μM [γ-^{32}P]ATP in a final volume of 12 μL. After 20 min incubation at 37°C, 4 μL aliquots of the supernatant are spotted onto 2×2 cm pieces of Whatman P81 phosphocellulose paper, and 20 s later, the filters are washed four times (for at least 10 min each time) in 1% phosphoric acid. The dried filters are transferred into scintillation vials, and the radioactivity is measured in a liquid scintillation counter. Blank values are subtracted, and the GSK-3β activity is expressed in picomoles of phosphate incorporated in GS-1 per 20 min or in percentage of maximal activity[1].
References	[1]. Martinez A, et al. First non-ATP competitive glycogen synthase kinase 3 beta (GSK-3beta) inhibitors: thiadiazolidinones (TDZD) as potential drugs for the treatment of Alzheimer's disease. J Med Chem. 2002 Mar 14;45(6):1292-9. [2]. Xie CL, et al. Inhibition of Glycogen Synthase Kinase-3β (GSK-3β) as potent therapeutic strategy to ameliorates L-dopa-induced dyskinesia in 6-OHDA parkinsonian rats. Sci Rep. 2016 Mar 21;6:23527. [3]. Sun A, et al. GSK-3β controls autophagy by modulating LKB1-AMPK pathway in prostate cancer cells. Prostate. 2016 Feb;76(2):172-83.