TDZD-8

Cat. No.: HY-11012

CAS No.: 327036-89-5

Molecular Formula: $C_{10}H_{10}N_2O_2S$

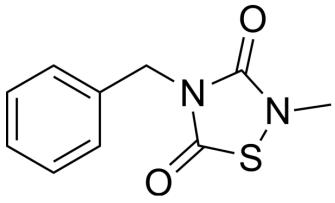
Molecular Weight: 222.26

Target: GSK-3

Pathway: PI3K/Akt/mTOR; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (11.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (11.25 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (11.25 mM); Clear solution

BIOLOGICAL ACTIVITY

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

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Death Differ. 2021 Jan;28(1):337-348.
- J Neuroinflammation. 2023 Feb 24;20(1):49.
- Oncogene. 2023 Jun 22.
- Eur J Med Chem. 2017 Apr 19;135:370-381.
- Acta Biochim Biophys Sin (Shanghai). 2020 Apr 20;52(4):363-370.

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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.

Caution: Product has not been fully validated for medical applications. For research use only.

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