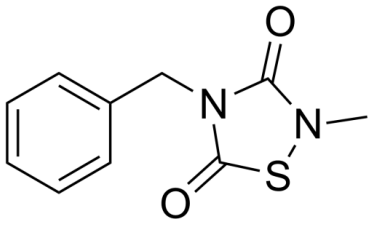
Data Sheet

Product Name:	TDZD-8
Cat. No.:	CS-1671
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
Solubility:	DMSO : ≥ 100 mg/mL



BIOLOGICAL ACTIVITY:

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. IC50 & Target: IC50: 2 μM (GSK-3β)[1] ***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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **Animal Administration:** TDZD-8 is dissolved in DMSO.[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].

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.

CAIndexNames:

1,2,4-Thiadiazolidine-3,5-dione, 2-methyl-4-(phenylmethyl)-

SMILES:

O=C(N1CC2=CC=CC=C2)N(C)SC1=O

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