

Product Data Sheet

Product Name: ST 045849

Cat. No.: GC50570

Chemical Properties

Cas. No. 442665-87-4

SMILES OC(C1CC(N(/C(S1)=N/C2=CC=C(C=C2)Cl)CCC34CC5CC(C4)CC(C3)C5)=O)=O

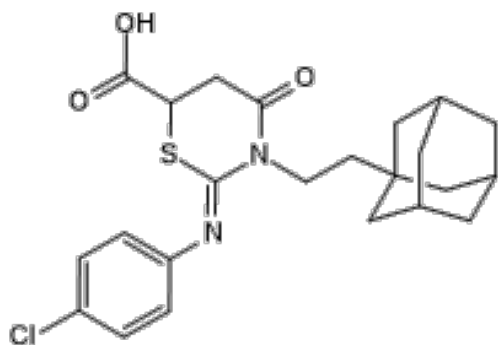
Formula C₂₃H₂₇ClN₂O₃S M.Wt 446.99

Solubility 44.7mg/mL in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines ATDC5 cells

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

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The chondrocytes (ATDC5 cells) were cultured in Dulbecco's modified Eagle's medium (DMEM) containing 10% foetal bovine serum (FBS) and 1% P/S. ATDC5 cells were maintained at 37°C under humidified air with 5% CO₂. In order to set up the osteoarthritis cell model, ATDC5 cells were stimulated with 10µg/mL lipopolysaccharide (LPS) for 12h. Meanwhile, ST 045849 was incubated with the cells at a concentration of 10µM for 24 hours. Cell viability of the indicated ATDC5 cells was assessed with the CCK-8 kit. In brief, cells were seeded into 96-well plates at a density of 5000 cells/well and incubated for 48h. After that, each well was added with 10µL CCK-8 cocktail and subjected to further incubation at 37°C for 2h. A microplate reader was used to measure the absorbance value at a wavelength of 450nm.

Reaction Conditions 10µM; 24h

Applications ST 045849 significantly restored the decreased cell viability of ATDC5 cells induced by LPS.

Animal experiment [2]:

Animal models C57BL/6J female mice

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Preparation Method	Ten-week-old female C57BL/6J mice were injected with streptozotocin in 0.1mM citrate buffer at 65mg/kg body weight intravenously. Blood glucose level was measured by tail clipping using Blood Glucose Monitoring System. The value $\geq 250\text{mg/dl}$ or 14mM indicated diabetes Mellitus (DM). The normal glucose level ($\sim 150\text{mg/dl}$ or $\sim 8\text{mM}$) was restored by subcutaneous implantation of insulin pellets. A group of sham-operated mice was used as non-diabetic (ND) controls. Female mice were mated with normal male mice in the afternoon. The presence of vaginal plug on the following morning was denoted as embryonic (E) day 0.5. Insulin pellets were removed at E5.5 to make the female animals of the DM group hyperglycemic again before the beginning of neurulation at E8.5. Diabetic pregnant mice were given gavage feeding with an OGT inhibitor ST 045849 (20mg/kg/day), suspended in water (vehicle), at E6.5 for 4 days. At E10.5 (late neurulation), mice were sacrificed and the embryos were collected for examination.
Dosage form	20mg/kg/day for 4 days; p.o.
Applications	ST 045849 treatment significantly reduced the incidence of neural tube defects in the embryos of diabetic pregnant mice.

References:

- [1] He C, Wu Q, Zeng Z, et al. OGT-induced O-GlcNAcylation of NEK7 protein aggravates osteoarthritis progression by enhancing NEK7/NLRP3 axis[J]. Autoimmunity, 2024, 57(1): 2319202.
 [2] Kim G, Cao L, Reece E A, et al. Impact of protein O-GlcNAcylation on neural tube malformation in diabetic embryopathy[J]. Scientific Reports, 2017, 7(1): 11107.

Background

ST 045849 is an inhibitor of O-GlcNAc transferase (OGT), with an IC_{50} value of $53\mu\text{M}$ ^[1]. ST 045849 is currently widely used in the research for screening low toxicity OGT inhibitors^[2].

In vitro, ST 045849 treatment significantly inhibited the growth of HKCI-2 cells after 72 hours, with an IC_{50} value of 50.44nM ^[3]. Mouse embryonic stem cells were treated with ST 045849 (0.2nM) for

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30min exhibited the reduced O-GlcNAcylated Notch1 and Notch1 protein expression in the plasma membrane, accompanied by a reduction in glucose production^[4]. ST 045849 treatment (15 μ M; 6h) can significantly reduce the reactive oxygen species (ROS) levels in NE-4C cells cultured under high glucose concentration (500mg/dl)^[5]. ST 045849 treatment (0.4mM) for 2h can significantly inhibit the overall O-GlcNAc glycosylation in adipocytes, and induce an increase in the number of small lipid droplets and the appearance of a small number of extremely large lipid droplets in oleic acid-treated adipocytes^[6].

In vivo, ST 045849 treatment (20mg/kg/day) via gavage for 4 days in mouse model of diabetic pregnancy significantly reduced the incidence of neural tube defects in the embryos^[5].

References:

- [1] Wu X, Wang M, Cao Y, et al. Discovery of a novel OGT inhibitor through high-throughput screening based on homogeneous time-resolved fluorescence (HTRF)[J]. Bioorganic Chemistry, 2023, 139: 106726.
- [2] Liu Y, Ren Y, Cao Y, et al. Discovery of a low toxicity O-GlcNAc transferase (OGT) inhibitor by structure-based virtual screening of natural products[J]. Scientific reports, 2017, 7(1): 12334.
- [3] Xu W, Zhang X, Wu J, et al. O-GlcNAc transferase promotes fatty liver-associated liver cancer through inducing palmitic acid and activating endoplasmic reticulum stress[J]. Journal of hepatology, 2017, 67(2): 310-320.
- [4] Jeon J H, Suh H N, Kim M O, et al. Glucosamine-induced OGT activation mediates glucose production through cleaved Notch1 and FoxO1, which coordinately contributed to the regulation of maintenance of self-renewal in mouse embryonic stem cells[J]. Stem cells and development, 2014, 23(17): 2067-2079.
- [5] Kim G, Cao L, Reece E A, et al. Impact of protein O-GlcNAcylation on neural tube malformation in diabetic embryopathy[J]. Scientific Reports, 2017, 7(1): 11107.
- [6] Yang Y, Fu M, Li M D, et al. O-GlcNAc transferase inhibits visceral fat lipolysis and promotes diet-induced obesity[J]. Nature communications, 2020, 11(1): 181.

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