

Product Data Sheet

Product Name: NSC 74859

Cat. No.: GC14653

Chemical Properties

Cas. No. 501919-59-1

Chemical Name 2-hydroxy-4-[[2-(4-methylphenyl)sulfonyloxyacetyl]amino]benzoic acid

SMILES CC1=CC=C(C=C1)S(=O)(=O)OCC(=O)NC2=CC(=C(C=C2)C(=O)O)O

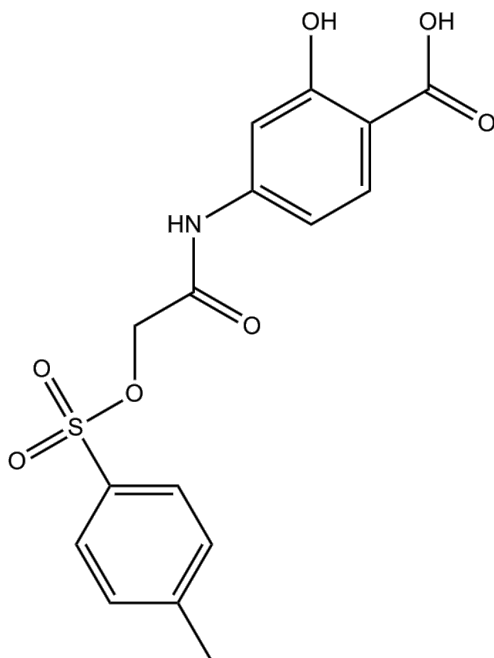
Formula $C_{16}H_{15}NO_7S$ M.Wt 365.36

Solubility $\geq 18.25\text{mg/mL}$ in DMSO Storage Store at -20°C , unstable in solution, ready to use.

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

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

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Cell experiment [1]:

Cell lines HepG2, Huh-7 and SK-HEP1 cells

Human hepatoma cell lines (HepG2, SK-Hep1 and Huh-7) were propagated in RPMI-1640 medium, supplemented with 10% fetal bovine serum, 100 units/ml penicillin and 100mg/ml streptomycin. Cells were plated in six-well plates (2×10^5 cells/well) and treated with 100μM NSC 74859 for 48h. The cells were washed with ice-cold PBS and harvested in 100μl of cell lysis buffer containing protease inhibitors. Protein concentration of lysates was determined using the bicinchoninic acid (BCA) method. Cell lysates (40μg/lane) were separated using 10% SDS-PAGE, and transferred electrophoretically onto a polyvinylidene

Preparation Method difluoride membrane. Membranes were blocked with tris-buffered saline TBS/0.1% Tween 20 (TBS/T) containing 5% bovine serum albumin and then incubated overnight at 4°C with anti-EGFR, phospho-STAT3 (Tyr705) or anti-STAT3 antibodies (1:1000). The membranes were washed thrice with TBS/T and incubated for 1h at room temperature with the appropriate secondary antibodies conjugated to goat anti-mouse horseradish peroxidase (1:2000). The membranes were washed and immunoreactive bands were developed using ECL and visualized using autoradiography on X-ray film. Protein loading was normalized by immunoblotting with a GAPDH antibody (1:5000).

Reaction
Conditions 100μM; 48h

Applications NSC 74859 significantly inhibited STAT3 Tyr705 phosphorylation in HepG2, SK-HEP1 and Huh-7 human hepatoma cells.

Animal experiment [2]:

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Animal models C57BL/6NHsd male and female mice

Six-week-old C57BL/6NHsd male and female mice, weighing 18–22 grams, housed and bred under Specific Pathogen Free (SPF) conditions. Homotopic heart transplantation was performed using microsurgery. Cold ischemia times were controlled to be less than 25min. Graft survival time was defined as the last day of transabdominally palpable cardiac contractions. Recipients remained

Preparation Method untreated or were treated by oral gavage every other day for 14 days (6 treatments) with 10mg/kg NSC 74859. Control group mice were subjected to heart transplantation and treated with DMSO alone. The results, expressed as mean survival time $\pm$ standard deviation, were assessed for statistical significance by the Gehan survival test. myocardium samples were collected for real-time qPCR and Immunohistochemistry analyses.

Dosage form 10mg/kg; p.o.; every other day for 14 days

Applications NSC 74859 attenuated cardiac allograft rejection and prolonged survival in mice.

References:

- [1] Chen W, Shen X, Xia X, et al. NSC 74859-mediated inhibition of STAT3 enhances the anti-proliferative activity of cetuximab in hepatocellular carcinoma. Liver Int. 2012;32(1):70-77.
- [2] Lai Y, Kuang F, Shan Z, Liu H. A New Concept of the Old Inhibitor NSC 74859 in Alleviating Cardiac Allograft Rejection and Extending Allograft Survival in Mice. Ann Transplant. 2017;22:656-662.

Background

NSC 74859 is a selective STAT3 inhibitor with an IC_{50} of $86\mu M$ ^[1]. STAT3(Signal Transducer and

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activator of Transcription 3), a pivotal transcription factor governing cell proliferation, survival and immune responses, is aberrantly activated in numerous cancers and inflammatory diseases^[2]. NSC 74859 is mainly applied in tumor-targeted therapy, tumor immunology research^{[3][4]}.

In vitro, NSC 74859 (100μM; 48h) significantly inhibited STAT3 Tyr705 phosphorylation in HepG2, SK-HEP1 and Huh-7 human hepatoma cells, and synergically enhanced the antiproliferative activity of cetuximab^[5].

In vivo, NSC 74859 (10mg/kg; p.o.; every other day for 14 days) attenuated cardiac allograft rejection and prolonged survival in mice by reducing infiltration of CD4⁺, CD8⁺ T cells and CD14⁺ monocytes/macrophages and by down-regulating IL-2, IL-15 and IL-6 expression within the graft^[6]. NSC 74859(2.5mg/kg; i.p.; 16 weeks) significantly reduced renal collagen deposition, down-regulated fibrotic molecules (TGF-β1, ACE, AT1, VEGF), attenuated albuminuria, and reversed tubulointerstitial fibrosis and functional impairment in streptozocin-induced diabetic mice^[7].

References:

- [1] Siddiquee K, Zhang S, Guida WC, et al. Selective chemical probe inhibitor of Stat3, identified through structure-based virtual screening, induces antitumor activity. Proc Natl Acad Sci U S A. 2007;104(18):7391-7396.
- [2] Zou S, Tong Q, Liu B, Huang W, Tian Y, Fu X. Targeting STAT3 in Cancer Immunotherapy. Mol Cancer. 2020;19(1):145.
- [3] Lin L, Amin R, Gallicano GI, et al. The STAT3 inhibitor NSC 74859 is effective in hepatocellular cancers with disrupted TGF-beta signaling. Oncogene. 2009;28(7):961-972.
- [4] Brady MT, Miller A, Sait SN, et al. Down-regulation of signal transducer and activator of transcription 3 improves human acute myeloid leukemia-derived dendritic cell function. Leuk Res. 2013;37(7):822-828.
- [5] Chen W, Shen X, Xia X, et al. NSC 74859-mediated inhibition of STAT3 enhances the anti-proliferative activity of cetuximab in hepatocellular carcinoma. Liver Int. 2012;32(1):70-77.
- [6] Lai Y, Kuang F, Shan Z, Liu H. A New Concept of the Old Inhibitor NSC 74859 in Alleviating Cardiac Allograft Rejection and Extending Allograft Survival in Mice. Ann Transplant. 2017;22:656-662.
- [7] Zheng C, Huang L, Luo W, et al. Inhibition of STAT3 in tubular epithelial cells prevents kidney fibrosis and nephropathy in STZ-induced diabetic mice. Cell Death Dis. 2019;10(11):848.

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