NSC 74859

Cat. No.: HY-15146

CAS No.: 501919-59-1

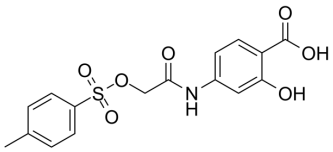
Molecular Formula: $C_{16}H_{15}NO_7S$

Molecular Weight: 365.36

Target: STAT

Pathway: JAK/STAT Signaling; Stem Cell/Wnt

Storage: Powder -20°C 3 years
4°C 2 years
* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (273.70 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7370 mL	13.6851 mL	27.3703 mL
	5 mM	0.5474 mL	2.7370 mL	5.4741 mL
	10 mM	0.2737 mL	1.3685 mL	2.7370 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: ≥ 7.5 mg/mL (20.53 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 7.5 mg/mL (20.53 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 7.5 mg/mL (20.53 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (6.84 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NSC 74859 (S3I-201) is a selective Stat3 inhibitor with an IC_{50} of 86 μM[1].

IC_{50} & Target

STAT3
86 μM (IC_{50})

In Vitro	NSC 74859 (S3I-201) preferentially inhibits Stat3 DNA-binding activity over that of Stat1 (IC_{50} values, Stat3•Stat3, 86±33 μM; Stat1•Stat3, 160±43 μM; and Stat1•Stat1, >300 μM) and inhibits that of Stat5 with IC_{50} of 166±17 μM). NSC 74859 significantly reduces viable cell numbers and inhibits growth of transformed mouse fibroblasts NIH 3T3/v-Src and breast carcinoma cell lines (MDA-MB-231, MDA-MB-435, and MDA-MB-468). At 30-100 μM, NSC 74859 induces significant apoptosis in the representative human breast carcinoma cell line MDA-MB-435 and NIH 3T3/v-Src, both of which harbor constitutively active Stat3. The breast carcinoma MDA-MB-435 cell line is more sensitive to 30 μM NSC 74859. By contrast, the human breast cancer MDA-MB-453 cells and the normal mouse fibroblasts (NIH 3T3), which do not contain abnormal Stat3 activity, are less sensitive to NSC 74859 at 100 μM or less. At 300 μM or higher, NSC 74859 induced general, nonspecific cytotoxicity independent of Stat3 activation status[1]. Huh-7 cells do not express β2SP or TBGFR2 and are sensitive to STAT3 inhibition, with an IC_{50} of 100 μM for NSC 74859, regardless of $CD133^+$ status. The IC_{50} of NSC 74859 is 150 μM for Huh-7 and SNU-398 cells, 15 μM for SNU-475 cells and 200 μM for SNU-182 cells. NSC 74859 inhibits breast carcinoma MDA-MB-435, MDA-MB-453 and MDA-MB-231 cell lines with an IC_{50} close to 100 μM[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Human breast (MDA-MB-231) tumor-bearing mice are given an i.v. injection of NSC 74859 (S3I-201) or vehicle every 2 or every 3 days for 2 weeks, and tumor measurements are taken every 2-3 days. Compared with control (vehicle-treated) tumors, which continued to grow, human breast tumors in mice that received S3I-201 display strong growth inhibition. Continued evaluation of treated mice on termination of treatment shows no resumption of tumor growth, suggesting potentially a long-lasting effect of S3I-201 on tumor growth[1]. Compared with vehicle-treated control tumors (n=15), which continued to grow, S3I-201 treatment of somatotroph tumor xenografts (n=15) significantly attenuated tumor growth for the duration of the experiment. Tumors derived from NSC 74859-treated rats are significantly smaller than those from the untreated group (220±16 mm^3 vs. 287±16 mm^3, P<0.01) as early as 5 days after NSC 74859 injection. Fifteen days after treatments, the average tumor volume of NSC 74859-treated rats is 64% of that of controls (449±40 mm^3 vs. 708±83 mm^3, P<0.01). Rats are sacrificed and tumors are harvested 15 days after treatment initiation. The average tumor weight of NSC 74859-treated rats is 78±8 mg, while tumors derived from control rats weighed 114±13 mg (32% reduction; P<0.05)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Proliferating cells are treated with or without NSC 74859 (30-100 μM) for up to 48 h. In some cases, cells are first transfected with Stat3C, ST3-NT, or ST3-SH2 domain or mock-transfected for 24 h before treatment with compound for an additional 24-48 h. Cells are then detached and analyzed by annexin V binding and flow cytometry to quantify the percent apoptosis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][3]	Mice[1] Six-week-old female athymic nude mice are used. Athymic nude mice are injected in the left flank area s.c. with $5×10^6$ human breast cancer MDA-MB-231 cells in 100 μL of PBS. After 5-10 days, tumors with a diameter of 3 mm are established. Animals are given NSC 74859 i.v. at 5 mg/kg every 2 or 3 days for 2 weeks and monitored every 2 or 3 days. Animals are stratified so that the mean tumor sizes in all treatment are nearly identical. Tumor volume is calculated according to the formula $V=0.52×a^2×b$, where a is the smallest superficial diameter and b is the largest superficial diameter. Rats[3] Four-week-old female Wistar Furth rats are used. GH3 cells ($5×10^5$ cells in 100 μL Matrigel) are subcutaneously injected into the left lumbar area. After 7 days, tumors with a volume of approximately 100 mm^3 are established. Rats are given NSC 74859 intravenously at 5 mg/kg every 2 or 3 days for 2 weeks. Tumor size is measured by caliper measurements twice a week, and volume is calculated as follows: $volume=(length×width^2)/2$. Three weeks after cell inoculations, animals are euthanized and excised tumors are weighed. Blood samples are collected 1 day before S3I-201 treatment and again on the day of euthanization. Serum GH and prolactin are assessed by RIA or ELISA, respectively. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2023 Apr 24;14(1):2342.
- Adv Sci (Weinh). 2020 Sep 24;7(21):2002518.
- Brain Behav Immun. 2018 Oct;73:504-519.
- Theranostics. 2022 Apr 4;12(7):3196-3216.
- J Exp Clin Cancer Res. 2023 Feb 27;42(1):51.

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REFERENCES

[1]. Siddiquee K, 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 May 1;104(18):7391-6.

[2]. Lin L, et al. The STAT3 inhibitor NSC 74859 is effective in hepatocellular cancers with disrupted TGF-β signaling. Oncogene. 2009 Feb 19;28(7):961-72.

[3]. Zhou C, et al. STAT3 upregulation in pituitary somatotroph adenomas induces hypersecretion. J Clin Invest. 2015 Apr;125(4):1692-702

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