

Product Data Sheet

Product Name: NSC 87877

Cat. No.: GC10169

Chemical Properties

Cas. No. 56990-57-9

Chemical Name (7E)-8-oxo-7-[(6-sulfonaphthalen-2-yl)hydrazinylidene]quinoline-5-sulfonic acid

SMILES C1=CC2=C(C(=O)C(=NNC3=CC4=C(C=C3)C=C(C=C4)S(=O)(=O)O)C=C2S(=O)(=O)O)N=C1

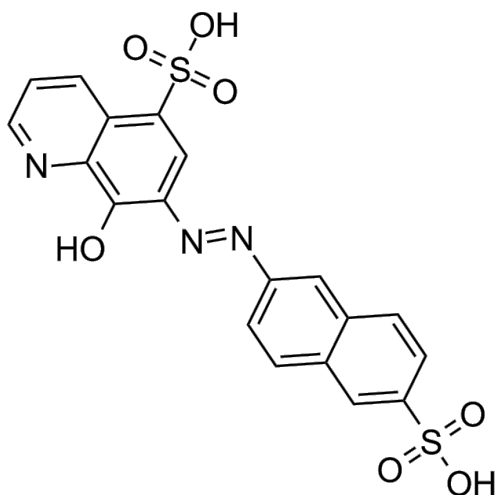
Formula $C_{19}H_{13}N_3O_7S_2$ M.Wt 459.45

Solubility $\geq 45.9\text{mg/mL}$ in DMSO, $\geq 16.6\text{mg/mL}$ in Water with ultrasonic 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



Background

IC₅₀: NSC-87877 potently inhibited Shp2 with an IC₅₀ of $0.318 \pm 0.049\ \mu\text{M}$. NSC-87877 seemed to have no selectivity between human Shp2 and Shp1 (IC₅₀ $0.355 \pm 0.073\ \mu\text{M}$). In addition, NSC-87877

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

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showed approximately 5-, 24-, 206-, 266-, and 475-fold selectivity for Shp2 over PTP1B (IC₅₀ 1.691 ± 0.407 μM), HePTP (IC₅₀ 7.745 ± 1.561 μM), DEP1 (IC₅₀ 65.617 ± 4.120 μM), CD45 (IC₅₀ 84.473 ± 16.185 μM), and LAR (IC₅₀ 150.930 ± 9.077 μM), respectively [1].

Shp2, a nonreceptor protein tyrosine phosphatase (PTP) encoded by the PTPN11 gene, is involved in the growth factor-induced activation of mitogen-activated protein kinases Erk1 and Erk2. Moreover, gain-of-function Shp2 mutations have been found in Noonan syndrome and childhood leukemias.

Therefore, Shp2 PTP inhibitors are required for the evaluation of Shp2 as a therapeutic target.

NSC87877, a novel SHP-2 inhibitor, has been observed dose-dependent cytotoxicity in leukemic cell lines.

In vitro: Molecular modeling and site-directed mutagenesis studies suggested that NSC-87877 binds to the catalytic cleft of Shp2 PTP. It is noteworthy that NSC-87877 inhibited epidermal growth factor (EGF)-induced activation of Shp2 PTP, Ras, and Erk1/2 in cell cultures but did not block EGF-induced Gab1 tyrosine phosphorylation or Gab1-Shp2 association. Furthermore, NSC-87877 inhibited Erk1/2 activation by a Gab1-Shp2 chimera but did not affect the Shp2-independent Erk1/2 activation by phorbol 12-myristate 13-acetate. These results identified NSC-87877 as the first PTP inhibitor capable of inhibiting Shp2 PTP in cell cultures without a detectable off-target effect [1].

In vivo: An mice in-vivo study aimed to investigate the effects of S NSC-87877 on inflammatory pain and its underlying mechanisms. In this study, immediately after behavioral tests, sinistral spinal dorsal horn was collected for immunoblotting analysis of the expression of NMDA receptors. Results showed that NSC-87877 alleviated CFA-induced mechanical allodynia, which had no effects on the nociceptive responses in naive mice. Moreover, NSC-87877 specifically abolished the increase in the synaptic expression of NMDA receptor NR2B subunits in inflamed mice. These findings indicated that NSC-87877 could ameliorate inflammatory pain by inhibiting the synaptic accumulation of NR2B in spinal dorsal horn [2].

Clinical trial: NSC-87877 is currently in the preclinical development and no clinical trial is ongoing.

Reference:

[1] Liwei Chen, Shen-Shu Sung, M. L. Richard Yip, Harshani R. Lawrence, Yuan Ren, Wayne C. Guida, Said M. Sebti, Nicholas J. Lawrence, and Jie Wu. *Discovery of a Novel Shp2 Protein Tyrosine Phosphatase Inhibitor. Mol Pharmacol* 2006,70:562–570

[2] YANG Hong-bin, YANG Xian, CAO Jing, LI Shuai, LIU Yan-ni, SUO Zhan-wei, ZHENG Cheng-rong, CUI Hong-bin, GUO Zhong, HU Xiao-dong. *Inhibitory effects of SHP2 blocker NSC-87877 on inflammatory pain and its underlying mechanisms. Chinese Pharmacological Bulletin* 2010-09

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