NSC 663284

Cat. No.: HY-100034

CAS No.: 383907-43-5

Molecular Formula: $C_{15}H_{16}ClN_3O_3$

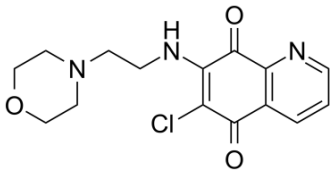
Molecular Weight: 321.76

Target: Phosphatase; Histone Methyltransferase

Pathway: Metabolic Enzyme/Protease; Epigenetics

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 150 mg/mL (466.19 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.1079 mL	15.5395 mL	31.0791 mL
5 mM	0.6216 mL	3.1079 mL	6.2158 mL
10 mM	0.3108 mL	1.5540 mL	3.1079 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: ≥ 2.5 mg/mL (7.77 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.77 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

NSC 663284 (DA-3003-1) is a potent, cell-permeable, and irreversible Cdc25 dual specificity phosphatase inhibitor, has an IC_{50} for Cdc25B2 of 0.21 μM. NSC 663284 exhibits mixed competitive kinetics against Cdc25A, Cdc25B(2), and Cdc25C with Ki values of 29, 95, and 89 nM, respectively[1]. NSC 663284 inhibits NSD2 (IC_{50} of 170 nM) through a direct interaction with the catalytic SET domain (K_d of 370 nM)[2].

IC_{50} & Target

IC50: 0.21 μM (Cdc25B2)[1]

In Vitro	NSC 663284 (3-100μM; 48 hours) has a mean IC_{50} value in the NCI 60 Cell human tumor panel of 1.5 ± 0.6 μM, has IC_{50} values of 0.2 μM in human breast cancer MDA-MB-435 and MDA-N cells, has an IC_{50} value of 1.7 μM in human breast MCF-7 cells in culture[1]. NSC 663284 has relative IC_{50} values for Cdc25B2 (IC_{50}=0.21 μM) are 20- and 450-fold lower than for VHR (IC_{50}=4.0 μM) or PTP1B (IC_{50}>4.0 μM), respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	NSC 663284 (intravenous injection; 2, 3, and 5mg/kg) inhibits the growth of subcutaneous human colon HT29 xenografts in SCID mice. After a single dose of 5 mg/kg, NSC 663284 is not detectable in plasma or tissues beyond 5 min. Following NSC 663284 treatment of tumor-bearing SCID mice, reduces glutathione concentrations in HT29 tumor are decreased to a greater extent and remained decreased for longer than the reduced glutathione concentrations in liver and kidneys[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice: C.B.-17 SCID mice bearing HT29 human colon carcinoma xenografts are stratified into the following groups of 9-10 animals: Control, vehicle control, positive control (gemcitabine, 50 mg/kg/dose i.v.), NSC 663284 at the following doses: 2, 3 or 5 mg/kg/dose i.v.. The mice are dosed every 4 days for 6 doses, and body weights and tumor volumes are recorded twice weekly. Tumors are measured with calipers, and tumor volumes are calculated. Mice are followed for 3 weeks following the completion of the dosing to monitor tumor regrowth. In a second study, C.B.-17 SCID mice bearing MDA-MB-435 human breast cancer xenografts are stratified to the same treatment groups, except that paclitaxel at 20 mg/kg i.v. every 7 days is used as the positive control[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Cancer Res. 2020 Jan;18(1):91-104.

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REFERENCES

[1]. Lazo JS, et al. Discovery and biological evaluation of a new family of potent inhibitors of the dual specificity protein phosphatase Cdc25. J Med Chem. 2001 Nov 22;44(24):4042-9.

[2]. Guo J, et al. Pharmacology and antitumor activity of a quinolinedione Cdc25 phosphatase inhibitor DA3003-1 (NSC 663284). Anticancer Res. 2007 Sep-Oct;27(5A):3067-73.

[3]. Coussens NP, et al. High-throughput screening with nucleosome substrate identifies small-molecule inhibitors of the human histone lysine methyltransferase NSD2. J Biol Chem. 2018 Aug 31;293(35):13750-13765.

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