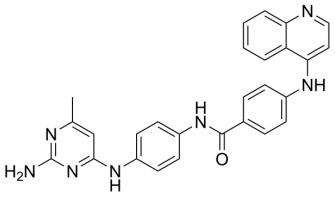
SGI-1027

Cat. No.:	HY-13962
CAS No.:	1020149-73-8
Molecular Formula:	$C_{27}H_{23}N_7O$
Molecular Weight:	462
Target:	DNA Methyltransferase; Apoptosis
Pathway:	Epigenetics; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 27 mg/mL (58.44 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1645 mL	10.8225 mL	21.6450 mL
	5 mM	0.4329 mL	2.1645 mL	4.3290 mL
	10 mM	0.2165 mL	1.0823 mL	2.1645 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 (5.41 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.41 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SGI-1027 is a DNA methyltransferase (DNMT) inhibitor, with IC_{50}s of 7.5 μM, 8 μM, and 12.5 μM for DNMT3B, DNMT3A, and DNMT1 with poly(dI-dC) as substrate.

IC_{50} & Target

DNMT3B	DNMT3A	DNMT1
7.5 μM (IC_{50})	8 μM (IC_{50})	12.5 μM (IC_{50})

In Vitro

SGI-1027 is a DNMT inhibitor, with IC_{50}s of 7.5 μM, 8 μM, and 12.5 μM for DNMT3B, DNMT3A, and DNMT1 with poly(dI-dC) as

substrate. SGI-1027 shows an IC_{50} of 6 μM for DNMT1 (hemimethylated DNA). SGI-1027 (1, 2.5, or 5 μM) causes selective degradation of DNMT1 in several human cancer cell lines, but shows little or no cytotoxic effect on rat hepatoma cells, and does not induce apoptosis in rat hepatoma cells[1]. SGI-1027 shows an EC_{50} of 0.9 μM for hDNMT3A, and causes cytotoxicity on KG-1 cells, with an EC_{50} of 4.4 μM[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

To determine the nature of inhibition of DNMTase activity by SGI-1027, DNMT1 enzyme activity is measured in presence of a fixed concentration of SGI-1027 (0, 2.5, 5, and 10 μM) while one of the two (Ado-Met or DNA) is varied in a particular reaction mixture. At a fixed concentration of DNA (500 ng) varying concentrations of Ado-Met used are from 25-500 nM, respectively. Similarly, final DNA concentrations are varied from (25-500 ng) at 75 nM Ado-Met[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

Rat hepatoma H4IIE cells are grown in DMEM supplemented with fetal bovine serum (10%) and calf serum (10%). Cells are seeded into 96-well plates and after 48 h exposed to SGI-1027 at concentrations ranging from 0 to 300 μM. The solubility is determined by Nephalometry techniques immediately after dosing and before harvesting the cells at 24 h. Following the exposure period, the cells or their supernatant (culture medium) are analyzed for changes in cell proliferation (propidium iodide), membrane leakage (α-GST), mitochondrial function [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide and cellular ATP], oxidative stress (intracellular GSH and 8-isoprostane), and apoptosis (caspase-3). The half-maximal toxic concentration (TC_{50}) is determined from the dose-response curves[1].

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CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- Pharmacol Res. 2022 Jun;180:106244.
- Aging Cell. 2021 Dec 7;e13526.
- Commun Biol. 2021 Mar 25;4(1):399.

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REFERENCES

[1]. Datta J, et al. A new class of quinoline-based DNA hypomethylating agents reactivates tumor suppressor genes by blocking DNA methyltransferase 1 activity and inducing its degradation. Cancer Res. 2009 May 15;69(10):4277-85.

[2]. Rilova E, et al. Design, synthesis and biological evaluation of 4-amino-N- (4-aminophenyl)benzamide analogues of quinoline-based SGI-1027 as inhibitors of DNA methylation. ChemMedChem. 2014 Mar;9(3):590-601.

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