产品名称：**SGI-1027**
产品别名：**SGI-1027**

生物活性：

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 IC50s 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 IC50 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 EC50 of 0.9 μM for hDNMT3A, and causes cytotoxicity on KG-1 cells, with an EC50 of 4.4 μM[2].

Solvent&Solubility

In Vitro:

DMSO : 27 mg/mL (**58.50 mM;** Need ultrasonic and warming)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1668 mL	10.8338 mL	21.6675 mL
	5 mM	0.4334 mL	2.1668 mL	4.3335 mL
	10 mM	0.2167 mL	1.0834 mL	2.1668 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: 2.5 mg/mL (5.42 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.42 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)

Solubility: 2.5 mg/mL (5.42 mM); Suspended solution; Need ultrasonic

此方案可获得 2.5 mg/mL (5.42 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

	3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.42 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.42 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	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 (TC50) is determined from the dose-response curves[1].
Kinase Assay	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].
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.