产品名称：Quisinostat(JNJ-26481585)
产品别名：Quisinostat

生物活性：

Description

Quisinostat (JNJ-26481585) is an orally available, potent HDAC inhibitor with an IC_{50} of 0.11 nM for HDAC1.

IC_{50} & Target

HDAC1	HDAC2	HDAC11	HDAC10	HDAC5	HDAC8
0.11 nM (IC_{50})	0.33 nM (IC_{50})	0.37 nM (IC_{50})	0.46 nM (IC_{50})	3.69 nM (IC_{50})	4.26 nM (IC_{50})
HDAC3	HDAC9	HDAC6	HDAC7		
4.86 nM (IC_{50})	32.1 nM (IC_{50})	76.8 nM (IC_{50})	119 nM (IC_{50})		

In Vitro

Quisinostat exerts broad-spectrum antiproliferative activity against a wide panel of cancer cell lines including lung, colon, breast, prostate, and ovarian cell lines at nanomolar concentrations. JNJ-26481585 shows activity toward all HDAC enzymes tested with highest potency in vitro observed toward recombinant HDAC1 (IC_{50}, 0.11±0.03 nM), which is comparable with the potency observed toward HDAC1-immunoprecipitated complexes from tumor cells (IC_{50}, 0.16±0.02 nM). Lowest in vitro potency is observed toward HDAC6, 7 and 9 (IC_{50}, 32.1-119 nM) [1].

In Vivo

JNJ-26481585 induces continuous H3 acetylation in tumor tissue in vivo. JNJ-26481585, a "second-generation" HDAC inhibitor with prolonged pharmacodynamic response in vivo. In agreement with the hypothesis, JNJ-26481585 showed superior efficacy compared with both standard of care agents and first-generation HDAC inhibitors in preclinical tumor models. These studies suggest that an HDAC inhibitor with continuous pharmacodynamic activity may show activity in solid tumor malignancies[1].

Solvent&Solubility

In Vitro:

DMSO : 50 mg/mL (126.75 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5350 mL	12.6752 mL	25.3505 mL
	5 mM	0.5070 mL	2.5350 mL	5.0701 mL
	10 mM	0.2535 mL	1.2675 mL	2.5350 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 (6.34 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.34 mM，饱和度未知) 的澄清溶液。

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 (6.34 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.34 mM，饱和度未知) 的澄清溶液。 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 (6.34 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.34 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]. Arts J, et al. JNJ-26481585, a novel "second-generation" oral histone deacetylase inhibitor, shows broad-spectrum preclinical antitumoral activity. Clin Cancer Res. 2009 Nov 15;15(22):6841-51.

实验参考：

Animal Administration	JNJ-26481585 is dissolved in DMSO as 5mM stock solution and diluted with appropriate medium. Human A2780 ovarian tumor cells (107 cells/mouse) are injected s.c. into the inguinal region of male athymic nu/nu CD-1 mice. When palpable tumors are obtained, mice are treated once daily with vehicle (10% hydroxypropyl-β-cyclodextrin) or JNJ-26481585 at 10 mg/kg i.p., and tumor and plasma is harvested at day 1 and at day 7 at the indicated time points (5 mice/point). Levels of AcH3 are determined using a quantitative ELISA (300 ng tumor protein/well) and described on the basis of an indirect response pharmacodynamic model[1]
References	[1]. Arts J, et al. JNJ-26481585, a novel "second-generation" oral histone deacetylase inhibitor, shows broad-spectrum preclinical antitumoral activity. Clin Cancer Res. 2009 Nov 15;15(22):6841-51.

源叶生物