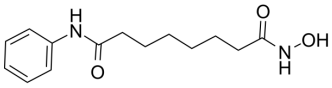
Vorinostat

Cat. No.: HY-10221

CAS No.: 149647-78-9

Molecular Formula: $C_{14}H_{20}N_2O_3$

Molecular Weight: 264.32



Target: HDAC; Autophagy; Mitophagy; Filovirus; Apoptosis; HPV

Pathway: Cell Cycle/DNA Damage; Epigenetics; Autophagy; Anti-infection; Apoptosis

Storage:

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

SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (378.33 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.7833 mL	18.9165 mL	37.8329 mL
	5 mM	0.7567 mL	3.7833 mL	7.5666 mL
	10 mM	0.3783 mL	1.8916 mL	3.7833 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 20% HP-β-CD in saline
   Solubility: 3.33 mg/mL (12.60 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (9.46 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (9.46 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (7.87 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (7.87 mM); Clear solution
6. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.87 mM); Clear solution
7. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.87 mM); Clear solution
8. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.87 mM); Clear solution

	9. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.08 mg/mL (7.87 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Vorinostat (SAHA) is a potent and orally active pan-inhibitor of HDAC1, HDAC2 and HDAC3 (Class I), HDAC6 and HDAC7 (Class II) and HDAC11 (Class IV), with ID_{50} values of 10 nM and 20 nM for HDAC1 and HDAC3, respectively. Vorinostat induces cell apoptosis[1][4]. Vorinostat is also an effective inhibitor of human papillomaviruse (HPV)-18 DNA amplification[7].

IC_{50} & Target				
	HDAC1 10 nM (ID50)	HDAC3 20 nM (ID50)	HDAC2	HDAC7
	HDAC11	Autophagy	Mitophagy	

In Vitro	Vorinostat efficiently suppresses MES-SA cell growth at a low dosage (3 μM) already after 24 hours treatment. HDACs class I (HDAC2 and 3) as well as class II (HDAC7) are preferentially affected by this treatment. Vorinostat significantly increases $p21^{WAF1}$ expression and apoptosis in MES-SA cells[1]. Vorinostat inhibits SK-N-SH and SK-N-Be(2)C with the IC_{25} values of 1 μM and 0.5 μM, respectively[2]. Vorinostat is an effective inhibitor of HPV-18 DNA amplification, reduces oncoproteins E6 and E7 activities and triggers apoptosis in HPV-infected, differentiated cells[7]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Vorinostat (50 mg/kg/day) reduces tumor growth by more than 50% in nude mice injected with $5×10^6$ MES-SA cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cell lysates are prepared by using RIPA buffer (25 mM Tris-HCl pH 7.6, 150 mM NaCl, 1% NP-40, 1% sodium deoxycholate, 0.1% SDS), and the protein concentration is determined by Bio-Rad DC Protein Assay. Protein lysates are separated by SDS-PAGE and transferred to nitrocellulose membrane. Following antibodies and dilutions are used: rabbit anti HDAC1 (1 μg/mL); rabbit anti HDAC2 (1 μg/mL); rabbit anti HDAC3 (9 μg/mL); rabbit anti HDAC7 (3 μg/mL); mouse anti p21WAF1 (0.5 μg/mL). As secondary antibodies, the rabbit anti-mouse and swine anti-rabbit HRP-coupled antibodies at a final concentration of 1 μg/mL. An overnight incubation at 4°C is used for all primary antibodies, followed by washing and 2-hours incubation at RT with secondary antibodies. Specific protein bands are visualized by enhanced chemiluminescence assay. To demonstrate equal loading of protein samples all western blots are probed for β-tubulin. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Twelve weeks old male mice (n=14) are anesthetized with Isofluran and $5×10^6$ MES-SA cells are injected subcutaneously into the right flank of the animal. Mice from a control group receives placebo containing 300 μL of empty HOP-β-CD (2-hydroxypropyl-β-cyclodextrin) vesicles. Another group of mice receives vorinostat dissolved in HOP-β-CD at a concentration of 50 mg/kg/day. Both, empty vesicles and vorinostat are administered intraperitoneally, starting on the day 4 after the injection of MES-SA tumor cells. Mice body weight and tumor size ($w^2 × l × 0.52$; measured by caliper) are estimated twice a week. All mice are treated for 21 days and afterwards sacrificed by cervical dislocation. Each tumor is isolated as a whole and different tumor parameters are determined. Finally, tumor slices are cryo preserved and formalin fixed (4%) for further analyses. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Protein Cell. 2023 Nov 27:pwad056.
- Mil Med Res. 2022 Sep 27;9(1):54.
- Nat Commun. 2020 Apr 14;11(1):1792.
- Nat Commun. 2021 Mar 3;12(1):1407.
- Nat Commun. 2017 Dec 20;8(1):2207.

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[1]. Hrzenjak A et al. Histone deacetylase inhibitor vorinostat suppresses the growth of uterine sarcomas in vitro and in vivo. Mol Cancer. 2010 Mar 4;9:49.

[2]. Lautz TB, et al. The effect of vorinostat on the development of resistance to NSC 123127 in neuroblastoma.PLoS One. 2012;7(7):e40816.

[3]. Richon VM, et al. A class of hybrid polar inducers of transformed cell differentiation inhibits histone deacetylases. Proc Natl Acad Sci U S A. 1998 Mar 17;95(6):3003-7.

[4]. Xu WS, et al. Histone deacetylase inhibitors: molecular mechanisms of action. Oncogene. 2007 Aug 13;26(37):5541-52.

[5]. Pérez-Cañamás A, et al. Sphingomyelin-induced inhibition of the plasma membrane calcium ATPase causes neurodegeneration in type A Niemann-Pick disease. Mol Psychiatry. 2017 May;22(5):711-723.

[6]. Wang J, et al. Snail determines the therapeutic response to mTOR kinase inhibitors by transcriptional repression of 4E-BP1. Nat Commun. 2017 Dec 20;8(1):2207.

[7]. Banerjee NS, et al. Vorinostat, a pan-HDAC inhibitor, abrogates productive HPV-18 DNA amplification. Proc Natl Acad Sci U S A. 2018 Nov 20;115(47):E11138-E11147.

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