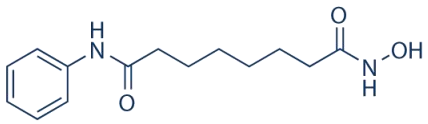
Product Introduction

Vorinostat (SAHA)

Vorinostat (suberoylanilide hydroxamic acid, SAHA) is an HDAC inhibitor with IC50 of ~10 nM.

Technical Data:

Molecular Weight (MW):	264.3
Formula:	C14H20N2O3
Solubility:	DMSO 53mg/mL Water <1mg/mL Ethanol 3mg/mL
Purity:	>98%
Storage:	2 years -20℃ Powder 6 months-80℃ in DMSO
CAS No.:	149647-78-9
Synonym:	Zolinza, MK-0683



Biological Activity

Vorinostat inhibits the activities of HDAC1 and HDAC3 with IC50 of 10 nM and 20 nM, respectively. Vorinostat also results in a marked hyperacetylation of histone H4. [1] Vorinostat inhibits the growth of three prostate cancer cell lines LNCaP, PC-3 and TSU-Pr1 at micromolar concentrations (2.5-7.5 μM), and induces dose-dependent cell death in LNCaP cells. [2] Vorinostat treatment in MCF-7 cells inhibits cell proliferation at an IC50 of 0.75 μM resulting in the accumulation of cells in the G1 and G2-M phase of the cell cycle. Vorinostat also induces differentiation in the estrogen receptor-negative cell line SKBr-3 and the retinoblastoma-negative cell line MDA-468. [3] Vorinostat treatment at 1 μM for 8 hours or more is sufficient to irreversibly induce apoptosis of human multiple myeloma (MM) cells. The gene expression profiles of Vorinostat treated MM cells are not hallmarked by global transcriptional activation, but by coordinated transcriptional changes of specific functional groups of genes such as cytokine-induced

proliferative/survival signaling cascades, oncogenes-tumor suppressor genes, regulators of apoptosis, DNA synthesis-repair and cell cycle, and proteasome-ubiquitin function. [4]

Administration of Vorinostat (~100 mg/kg/day) significantly inhibits the growth of CWR22 human prostate xenografts in nude mice with tumor reductions of 78%, 97% and 97%, at doses of 25 mg/kg/day, 50 mg/kg/day and 100 mg/kg/day, respectively, compared with control. Vorinostat induces the accumulation of acetylated core histones and prostate-specific antigen mRNA expression in CWR22 cells, resulting in higher levels of serum prostate-specific antigen than predicted from tumor volume alone. [2] Oral administration of Vorinostat (0.67g/L) crosses the blood-brain barrier, increases histone acetylation in the brain, and dramatically improves the motor impairment in the R6/2 mice model of Huntington's disease. [5]

References

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[3] Munster PN, et al. Cancer Res, 2001, 61(23), 8492-8497.

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[6] Pei XY, et al. Clin Cancer Res, 2004, 10(11), 3839-3852.

[7] Zhang G, et al. Clin Cancer Res, 2008, 14(17), 5385-5399.

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