Abexinostat

Cat. No.: HY-10990

CAS No.: 783355-60-2

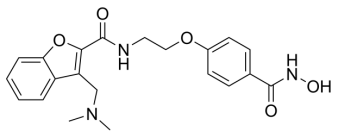
Molecular Formula: $C_{21}H_{23}N_3O_5$

Molecular Weight: 397.42

Target: HDAC

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage: Powder -20°C 3 years
4°C 2 years
* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 3.33 mg/mL (8.38 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5162 mL	12.5811 mL	25.1623 mL
	5 mM	0.5032 mL	2.5162 mL	5.0325 mL
	10 mM	---	---	---

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: 6 mg/mL (15.10 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Abexinostat (CRA 024781) is a novel pan-HDAC inhibitor mostly targeting HDAC1 with K_i of 7 nM. Abexinostat also inhibits metallo-β-lactamase domain-containing protein 2 (MBLAC2) hydrolase activity with an EC_{50} below 10 nM[1][4].

IC_{50} & Target

HDAC1 7 nM (Ki)	HDAC3/SMRT 8.2 nM (Ki)	HDAC6 17 nM (Ki)	HDAC2 19 nM (Ki)
HDAC10 24 nM (Ki)	HDAC8 280 nM (Ki)	MBLAC2 <10 nM (EC50)	

In Vitro

Abexinostat (CRA 024781) exhibits potent antitumor activity against a variety of tumor cell lines with $GI_{50\%}$ ranging from 0.15 μM to 3.09 μM. Abexinostat (CRA 024781) also has an antiproliferative effect on HUVEC endothelial cells with $GI_{50\%}$ of 0.43 μM. Abexinostat (CRA 024781) treatment causes dose-dependent accumulation of both acetylated histones and acetylated tubulin in HCT116 or DLD-1 cells, induces expression of p21, and leads to PARP cleavage and accumulation of the γH2AX[1].

	Inhibition of HDAC enzymes by Abexinostat (CRA 024781) leads to a significant reduction in the transcription of genes specifically associated with HR, including RAD51. Consistent with inhibition of HR, Abexinostat (CRA 024781) treatment results in a decreased ability to perform homology directed repair of I-SceI-induced chromosome breaks in transfected CHO cells[2]. Abexinostat (CRA 024781) induces S phase depletion, G2 cell cycle arrest, and apoptosis in soft tissue sarcoma (STS) cells. Abexinostat (CRA 024781) induces Rad51 transcriptional repression in STS cells potentially mediated via enhanced E2F1 binding to the Rad51 proximal promoter[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Abexinostat (CRA 024781) parenterally administered to mice harboring HCT116 or DLD-1 colon tumor xenografts results in a statistically significant reduction in tumor growth. Inhibition of tumor growth is accompanied by an increase in the acetylation of α-tubulin in peripheral blood mononuclear cells, and an alteration in the expression of many genes in the tumors, including several involved in apoptosis and cell growth[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Ten tumor cell lines and HUVEC are cultured for at least two doubling times, and growth is monitored at the end of compound exposure using an Alamar blue fluorometric cell proliferation assay. The compound is assayed in triplicate wells in 96-well plates at nine concentrations using half-log intervals ranging from 0.0015 to 10 μmol/L. The final DMSO concentration in each well is 0.15%. The concentration required to inhibit cell growth by 50% and 95% confidence intervals are estimated from nonlinear regression using a four-parameter logistic equation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	HCT116 and DLD-1 tumor cells are implanted s.c. in female BALB/c nu/nu mice at 3×10^6 per mouse. Treatment with Abexinostat (CRA 024781) started when the average tumor volume is -100 mm[1]. Mice bearing human colon tumor xenografts are dosed i.v. with Abexinostat (CRA 024781) using various dosages and schedules to assess the antitumor activity of Abexinostat (CRA 024781) [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- Viruses. 2020 Jun 3;12(6):609.
- Research Square Print. 2023 Mar 9.
- bioRxiv. 2021 Jan 5.
- Methods Mol Biol. 2018;1711:351-398.

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REFERENCES

[1]. Lechner S, et al. Target deconvolution of HDAC pharmacopoeia reveals MBLAC2 as common off-target. Nat Chem Biol. 2022 Aug;18(8):812-820.

[2]. Buggy JJ, et al. CRA-024781: a novel synthetic inhibitor of histone deacetylase enzymes with antitumor activity in vitro and in vivo. Mol Cancer Ther, 2006, 5(5), 1309-1317.

[3]. Adimoolam S, et al. HDAC inhibitor PCI-24781 decreases RAD51 expression and inhibits homologous recombination. Proc Natl Acad Sci U S A, 2007, 104(49), 19482-19487.

[4]. Lopez G, et al. Combining PCI-24781, a novel histone deacetylase inhibitor, with chemotherapy for the treatment of soft tissue sarcoma. Clin Cancer Res, 2009, 15(10), 3472-3483.

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