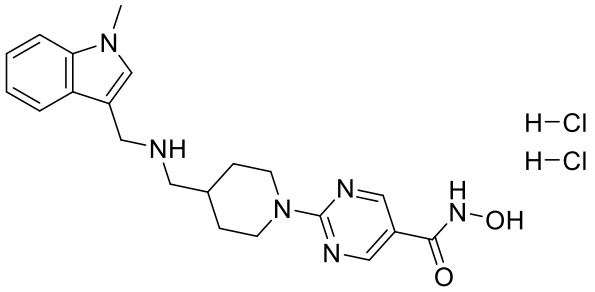
Product data sheet

MedKoo Cat#: 201612 Name: Quisinostat HCl CAS#: 875320-31-3 (2HCl) Chemical Formula: $C_{21}H_{28}Cl_2N_6O_2$ Exact Mass: 394.21172 Molecular Weight: 467.4	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Quisinostat, also known as JNJ-26481585, is an orally bioavailable, second-generation, hydroxamic acid-based inhibitor of histone deacetylase (HDAC) with potential antineoplastic activity. HDAC inhibitor JNJ-26481585 inhibits HDAC leading to an accumulation of highly acetylated histones, which may result in an induction of chromatin remodeling; inhibition of the transcription of tumor suppressor genes; inhibition of tumor cell division; and the induction of tumor cell apoptosis. HDAC, an enzyme upregulated in many tumor types, deacetylates chromatin histone proteins. Compared to some first generation HDAC inhibitors, JNJ-26481585 may induce superior HSP70 upregulation and bcl-2 downregulation.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	46.7	99.9

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.14 mL	10.70 mL	21.39 mL
5 mM	0.43 mL	2.14 mL	4.28 mL
10 mM	0.21 mL	1.07 mL	2.14 mL
50 mM	0.04 mL	0.21 mL	0.43 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Arts J, King P, Mariën A, Floren W, Beliën A, Janssen L, Pilatte I, Roux B, Decrane L, Gilissen R, Hickson I, Vreys V, Cox E, Bol K, Talloen W, Goris I, Andries L, Du Jardin M, Janicot M, Page M, van Emelen K, Angibaud P. 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. doi: 10.1158/1078-0432.CCR-09-0547. Epub 2009 Oct 27. PMID: 19861438.
2. He B, Dai L, Zhang X, Chen D, Wu J, Feng X, Zhang Y, Xie H, Zhou L, Wu J, Zheng S. The HDAC Inhibitor Quisinostat (JNJ-26481585) Supresses Hepatocellular Carcinoma alone and Synergistically in Combination with Sorafenib by G0/G1 phase arrest and Apoptosis induction. Int J Biol Sci. 2018 Oct 20;14(13):1845-1858. doi: 10.7150/ijbs.27661. PMID: 30443188; PMCID: PMC6231215.

In vivo study

1. Capasso KE, Manners MT, Quershi RA, Tian Y, Gao R, Hu H, Barrett JE, Sacan A, Ajit SK. Effect of histone deacetylase inhibitor JNJ-26481585 in pain. J Mol Neurosci. 2015 Mar;55(3):570-8. doi: 10.1007/s12031-014-0391-7. Epub 2014 Aug 2. PMID: 25085711.

2. Arts J, King P, Mariën A, Floren W, Beliën A, Janssen L, Pilatte I, Roux B, Decrane L, Gilissen R, Hickson I, Vreys V, Cox E, Bol K, Talloen W, Goris I, Andries L, Du Jardin M, Janicot M, Page M, van Emelen K, Angibaud P. 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. doi: 10.1158/1078-0432.CCR-09-0547. Epub 2009 Oct 27. PMID: 19861438.

7. Bioactivity

Biological target:

Quisinostat dihydrochloride (JNJ-26481585 dihydrochloride) is a potent pan-HDAC inhibitor with IC_{50}s of 0.11 nM, 0.33 nM, 0.64 nM, 0.46 nM, and 0.37 nM for HDAC1, HDAC2, HDAC4, HDAC10 and HDAC11, respectively.

In vitro activity

Flow cytometry analysis was performed to explore mechanism of cell cycle arrest induced by quisinostat. As shown in Figure 3A-B, in contrast to DMSO group, it was observed that quisinostat substantially induced G0/G1 phase arrest both in HCCLM3 and SMMC-7721 cells. Moreover, in order to verify the influence of quisinostat on cell cycle arrest, expressions of p21, cdk2, cdk4, cdk6, cyclinD1, cyclinE1 and cyclinA2 were detected by Western blotting (Fig.3C-D). Consequently the results supported that quisinostat did play a role in G0/G1 cell cycle arrest by upregulating expression of p21 as well as downregulating levels of cdk2/cdk4/cdk6/ cyclinD1/cyclinE1/cyclinA2 proteins. Accordingly apoptosis assay demonstrated that quisinostat could facilitate apoptosis in HCC cells more effectively when compared with DMSO group (Fig.4A-B). In agreement with the data of apoptosis assay, quisinostat enhanced expression levels of proapoptosis proteins, cleaved-Caspase-3, cleaved-Caspase-9, cleaved-PARP and Bax and decreased levels of antiapoptosis proteins, Bcl-xl, Bcl2 and survivin in HCC cells in contrast to DMSO group (Fig.4C). The findings suggested that quisinostat induced apoptotic events both in HCCLM3 and SMMC-7721 cells. Our study indicated that quisinostat, as a novel chemotherapy for HCC, exhibited excellent antitumor activity in vitro.

Int J Biol Sci. 2018; 14(13): 1845–1858. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6231215/

In vivo activity

JNJ-26481585 administered continuously for 14 days (once daily, 10 mg/kg i.p.) in male nude mice strongly inhibited the growth of large pre-established HCT116 colon xenografts (320 ± 10 mm3 at start of treatment). At the end of the study, JNJ-26481585 inhibited tumor volume by 76% (treated versus control = 24), which is superior to the activity of the clinical standard of care agent 5-FU (41% inhibition). In agreement with its low antitumor potency, vorinostat only slightly increased H3 acetylation levels at 4 hours postdose (0.03 ± 0.02 ng/μg protein), whereas JNJ-26481585 showed a more potent effect (0.22 ± 0.07 ng/μg protein; data not shown). A subsequent dose-response study to further explore the potency of JNJ-26481585 showed similar tumor growth inhibition at 5 mg/kg compared with 20 mg/kg (87% and 93% inhibition, respectively, Fig. 6B), whereas half-maximal inhibition was obtained at the low dose of 2.5 mg/kg in the pre-established setting (69% inhibition). JNJ-26481585 was also tested in a C170HM2 colorectal liver metastasis model. As shown in Fig. 6D, there was a significant 87% reduction in mean liver tumor burden in the JNJ-26481585–treated group (0.380 g reduced to 0.050 g; P = 0.016).

Clin Cancer Res. 2009 Nov 15;15(22):6841-51. https://clincancerres.aacrjournals.org/content/15/22/6841.long

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.