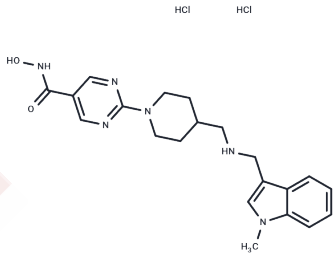
Data Sheet (Cat.No.T6865)

TargetMol

Quisinostat dihydrochloride

Chemical Properties



CAS No. : 875320-31-3

Formula: C21H28Cl2N6O2

Molecular Weight: 467.39

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Quisinostat dihydrochloride (JNJ26854165(Quisinostat) 2HCl) is a novel second-generation HDAC inhibitor with highest potency for HDAC1 with IC50 of 0.11 nM in a cell-free assay, modest potent to HDACs 2, 4, 10, and 11; greater than 30-fold selectivity against HDACs 3, 5, 8, and 9 and lowest potency to HDACs 6 and 7. Phase 2.
Targets(IC50)	Apoptosis,HDAC,Autophagy
In vitro	Quisinostat exhibits broad spectrum antiproliferative activity in solid and hematologic cancer cell lines, such as all lung, breast, colon, prostate, brain, and ovarian tumor cell lines, with IC50 ranging from 3.1-246 nM, which is more potent than vorinostat, R306465, panobinostat, CRA-24781, or mocetinostat in various human cancer cell lines tested. [1] A recent study shows that Quisinostat promotes myeloma cell death at low nanomolar concentrations by resulting in Mcl-1 depletion and Hsp72 induction. [2]
In vivo	In an HDAC1-responsive A2780 ovarian tumor screening model, Quisinostat dosing at its maximal tolerated dose (10 mg/kg i.p. and 40 mg/kg p.o.) for 3 days leads to an HDAC1-regulated fluorescence , which predicts tumor growth inhibition. Furthermore, Quisinostat also shows more potent inhibitory effects on the growth of C170HM2 colorectal liver metastases than 5-fluorouracil/Leucovorin. [1]
Kinase Assay	HDAC activity assays : In all cases, full-length HDAC proteins are expressed using baculovirus-infected Sf9 cells. In addition, HDAC3 is coexpressed as a complex with human NCOR2. For assessing activity of HDAC1-containing cellular complexes, immunoprecipitated HDAC1 complexes are incubated with an [3H]acetyl- labeled fragment of histone H4 peptide [biotin-(6-aminohexanoic)Gly-Ala-(acetyl[3H])Lys-Arg-His-Arg-Lys-Val-NH2] in a total volume of 50µL enzyme assay buffer (25 mM HEPES (pH 7.4), 1 M sucrose, 0.1 mg/mL BSA and 0.01% (v/v) Triton X-100). Incubation is performed for 45 minutes at 37 °C (immunoprecipitates) or 30 min at room temperature. Before addition of substrate, HDAC inhibitors are added at increasing concentrations and preincubated for 10 minutes at room temperature. After incubation, the reaction is quenched with 35µL stop buffer (1 M HCl and 0.4 M acetic acid). Released [3H]acetic acid is extracted with 800µL ethyl acetate and quantified by scintillation counting. Equal amounts of HDAC1 are immunoprecipitated as indicated by Western blot analysis. HDAC1 activity results are presented as mean ± SD of three independent experiments on a single lysate.
Cell Research	All cell lines are obtained from American Type Culture Collection and cultured according to instructions. The effect of HDAC inhibitors on cell proliferation is measured using an

MTT. Proliferation of non-small cell lung carcinoma (NSCLC) cell lines is assessed using an Alamar Blue-based assay. For proliferation of hematologic cell lines, cells are incubated for 72 hours and the cytotoxic activity is evaluated by MTS assay. Data are presented as mean IC50 or IC40 ± SD of at least three independent experiments.(Only for Reference)

Solubility Information

Solubility	DMSO: 73 mg/mL (156.19 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1395 mL	10.6977 mL	21.3954 mL
5 mM	0.4279 mL	2.1395 mL	4.2791 mL
10 mM	0.214 mL	1.0698 mL	2.1395 mL
50 mM	0.0428 mL	0.214 mL	0.4279 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Arts J, et al. Clin Cancer Res, 2009, 15(22), 6841-6851.
Stühmer T, et al. Br J Haematol 2010, 149(4), 529-536