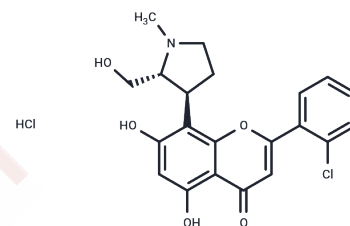


Rivaciclib hydrochloride

Chemical Properties

CAS No. :	920113-03-7
Formula:	C ₂₁ H ₂₀ ClNO ₅ ·HCl
Molecular Weight:	438.3
Appearance:	no data available
Storage:	Powder: -20°C for 3 years In solvent: -80°C for 1 year



Biological Description

Description	Rivaciclib hydrochloride (P276-00) is a novel inhibitor of CDK1, CDK4, and CDK9, with IC ₅₀ values of 79 nM, 63 nM, and 20 nM, respectively, currently in Phase 2/3.
Targets(IC ₅₀)	Apoptosis,CDK
In vitro	Rivaciclib shows 40-fold selectivity toward Cdk4-D1, compared with Cdk2-E[1]. It shows potent antiproliferative effects against various human cancer cell lines, including HCT-116, U2OS, H-460, HL-60, HT-29, SiHa, MCF-7, Colo-205, SW-480, PC-3, Caco2, T-24 with an IC ₅₀ ranging from 300 to 800 nmol/L, and is found to be highly selective for cancer cells as compared with normal fibroblast cells[1]. Rivaciclib can down-regulate cyclin D1 and Cdk4 in an ATP- competitive manner and decrease Cdk4-specific pRb Ser780 phosphorylation. Rivaciclib also induces apoptosis by activating cellular caspase-3 activity and DNA ladder formation[1].
In vivo	Rivaciclib, administered i.p. at 50 mg/kg daily for 20 treatments can significantly induce growth inhibition of murine colon cancer (CA-51). However, in murine lung carcinoma model (Lewis lung), an increased dose of 60 mg/kg (30 mg/kg twice daily) administered every alternate day i.p. for 7 treatments shows significant inhibition in the growth[2]. And it also inhibit the growth of human colon carcinoma HCT-116 xenograft and human non-small cell lung carcinoma H-460 xenograft[2]. Efficacy Studies show its maximum tolerated dose is 78 mg/kg/d[2].
Kinase Assay	Cdk4-D1/Cdk2-E enzyme assay: The Cdk4-D1/Cdk2-E enzyme assay is run in 96-well format using Millipore Multiscreen filtration plates. All assay steps are done in a single filter plate. The filtration wells are prewetted with 100 µL of kinase buffer [50 mmol/L HEPES (pH, 7.5), 10 mmol/L MgCl ₂ , 1 mmol/L EGTA], and then the solution is removed by vacuum. With filter plate on vacuum manifold, 50 µL GST-Rb bound to GSH-Sepharose beads in kinase buffer (0.5 µg GST-Rb/50 µL) is added to each well, and vacuum is applied to the filter plate. About 25 µL of a reaction mix containing ATP (cold + hot) and 4x phosphatase inhibitor mix (40 µMol/L unlabeled ATP, 10 µCi/mL γ ³² P-ATP, 40 mmol/L h-glycerophosphate, 4 mmol/L DTT, 0.4 mmol/L NaF, 0.4 mmol/L sodium orthovanadate) diluted in kinase buffer is added to each well. The test compound (4x final concentration in kinase buffer) or kinase buffer alone (control) is then added in an additional 25 µL volume. To each well, 50 µL (100 ng) of human Cdk4-D1/Cdk2-E enzyme in kinase buffer is added to initiate the reaction, which is allowed to continue for 30 min at 30°C. When the reaction is completed, vacuum is applied again, and the plate is washed with the TNEN buffer [20 mmol/L Tris (pH, 8.0), 100 mmol/L NaCl, 1

mmol/L EDTA, 0.5% nonidet-P40] thrice; the filter plate is air-dried and is placed in a Multiscreen adapter plate. Packard Microscint-O cocktail (30 µL) is added, and the plate is covered with a Top-Seal A film. Quantitation of ³²P-GST-Rb in 96-well filter plates is carried out by Top Count scintillation counter. All compounds are tested initially at 1 µMol/L concentration. Compounds showing more than or equal to 50% inhibition are further profiled for IC₅₀ determination.

Cell Research

The cells are seeded at a density of 3,000-5,000 cells per well, depending on cell type in 180 µL of culture medium in 96-well plate and incubated overnight to allow the cells to adhere. Varying concentrations of compounds are added to the wells and incubated for 48 h at 37°C. 3H-thymidine (0.25 µCi) is added to each well, and incorporation of the radiolabel is allowed to proceed for 5 to 7 h. Following this incubation, cells are harvested onto GF/B unfilter plates using a Packard Filtermate Universal harvester, and the plates are counted in a Packard Top Count 96-well liquid scintillation counter. (Only for Reference)

Solubility Information

Solubility

Ethanol: 7 mg/mL (15.97 mM), Sonication is recommended.
DMSO: 82 mg/mL (187.09 mM), Sonication is recommended.
H₂O: 81 mg/mL (184.8 mM), Sonication is recommended.
(< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2815 mL	11.4077 mL	22.8154 mL
5 mM	0.4563 mL	2.2815 mL	4.5631 mL
10 mM	0.2282 mL	1.1408 mL	2.2815 mL
50 mM	0.0456 mL	0.2282 mL	0.4563 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

- Joshi KS, et al. Mol Cancer Ther, 2007, 6(3), 918-925.
Joshi KS, et al. Mol Cancer Ther, 2007, 6(3), 926-934.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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