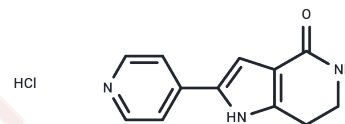


PHA-767491 hydrochloride

Chemical Properties

CAS No. : 942425-68-5
 Formula: C₁₂H₁₂ClN₃O
 Molecular Weight: 249.69
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
 Actual storage temperature shall be subject to the COA.



Biological Description

Description	PHA-767491 hydrochloride (CAY-10572 hydrochloride) is an effective ATP-competitive dual Cdc7/CDK9 inhibitor (IC ₅₀ : 10/34 nM). It has ~20-fold selectivity against GSK3-β and CDK1/2, 50-fold selectivity against CDK5 and MK2, 100-fold selectivity against CHK2 and PLK1.
Targets(IC ₅₀)	Apoptosis,CDK,GSK-3
In vitro	PHA-767491 inhibits proliferation of HCC1954 cells (IC ₅₀ : 0.64 μM) and Colo-205 cells (IC ₅₀ : 1.3 μM). PHA-767491 is effective DDK inhibitors in vitro (IC ₅₀ : 18.6 nM). PHA-767491 (2 μM) completely abolishes Mcm2 phosphorylation by 24 hours in HCC1954 cells [1]. PHA-767491 in combination with 5-FU exhibits much stronger cytotoxicity and induces significant apoptosis manifested by remarkably increased caspase 3 activation and poly(ADP-Ribose) polymerase fragmentation in HCC cells. PHA-767491 directly counteracts the 5-FU-induced phosphorylation of Chk1 and decreases the expression of the anti-apoptotic protein myeloid leukemia cell line [2]. PHA-767491 (0-10 μM) time- and dose-dependently decreases glioblastoma cell viability (IC ₅₀ : about 2.5 μM) for U87-MG and U251-MG cells.
In vivo	PHA-767491 decreases Chk1 phosphorylation and enhances apoptosis directly within sections of tumor tissues from HCC xenografts in nude mice.
Kinase Assay	20 ng of purified human DDK is pre-incubated with increasing concentrations of each DDK inhibitor for 5 min. Then 10 μCi (γ)- ³² P ATP and 1.5 μM cold ATP are added in a buffer containing 50 mM Tris-HCl (pH 7.5), 10 mM MgCl ₂ , and 1 mM DTT and incubated for 30 min at 30°C. The proteins are denatured in 1X Laemmli buffer at 100°C followed by SDS-PAGE and autoradiography on HyBlot CL film. Auto-phosphorylation of DDK is used as an indicator of its kinase activity. ³² P-labeled bands are quantified using ImageJ and the IC ₅₀ values are calculated using GraphPad.
Cell Research	For assays in 96 well plates 2500 cells are plated per well. After 24 hours, cells are treated with small molecule inhibitors and incubated for 72 hours at 37°C. Subsequently the cells are lysed and the ATP content is measured as an indicator of metabolically active cells using the CellTiter-Glo assay. IC ₅₀ values are calculated using the GraphPad software. For assays in six-well plates, 100,000 cells are plated per well. After 24 hours, cells are treated with small molecule inhibitors and incubated for varying time points. Cells are trypsinized and a suspension is made in 5 mL of phosphate buffered saline. 30 μL of this suspension is mixed with 30 μL of CellTiter-Glo reagent followed by a 10-

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Cell Research	minute incubation at room temperature. Luminescence is measured using EnVision 2104 Multilabel Reader and BioTek Synergy Neo Microplate Reader.
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Solubility Information

Solubility	H2O: 25 mg/mL (100.12 mM),Sonication is recommended. DMSO: 10.42 mg/mL (41.73 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (4 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	4.005 mL	20.0248 mL	40.0497 mL
5 mM	0.801 mL	4.005 mL	8.0099 mL
10 mM	0.4005 mL	2.0025 mL	4.005 mL
50 mM	0.0801 mL	0.4005 mL	0.801 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Montagnoli A, et al. Nat Chem Biol, 2008, 4(6), 357-365.

Yecies D, et al. Blood, 2010, 115(16), 3304-3313.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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