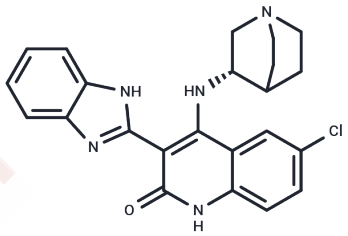
Data Sheet (Cat.No.T6350)

TargetMol

CHIR-124

Chemical Properties



CAS No. : 405168-58-3

Formula: C23H22ClN5O

Molecular Weight: 419.91

Storage: Store at low temperature,Keep away from direct sunlight
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	CHIR-124 is an effective Chk1 inhibitor (IC50: 0.3 nM). It has 2, 000-fold selectivity against Chk2, 500- to 5, 000-fold less activity against Cdc2 and CDK2/4.
Targets(IC50)	Apoptosis,FLT,Chk,GSK-3,PDGFR,Src
In vitro	CHIR-124 is a quinolone-based small molecule that is structurally unrelated to other known inhibitors of Chk1. CHIR-124 interacts synergistically with topoisomerase poisons (e.g., Camptothecin or SN-38) in causing growth inhibition in a variety of cancer cell lines, including breast carcinoma (MDA-MB-231 and MDA-MB-435) and colon carcinoma (SW-620 and Colo205), all of which contains the mutant p53 gene. CHIR-124 abrogates the SN-38-induced S and G2-M checkpoints and potentiates apoptosis in MDA-MD-435 breast cancer cells. The abrogation of the G2-Mcheckpoint and induction of apoptosis by CHIR-124 are enhanced by the loss of p53. [1] CHIR-124 also potently targets other kinases such as PDGFR and Flt3 with IC50 of 6.6 nM and 5.8 nM, respectively. [2]
In vivo	CHIR-124 potentiates the growth inhibitory effects of Irinotecan by abrogating the G2-M checkpoint and increasing tumor apoptosis in an orthotopic breast cancer xenograft model.
Kinase Assay	Chk1 Assay: For the Chk1 assay, the kinase domain is expressed in Sf9 insect cells, and a biotinylated cdc25c peptide containing the consensus Chk1/Chk2 phosphorylation site (*)(biotin-[AHX]SGSGS*GLYRSPSMP-ENLNRPR[CONH2]) is used as the substrate. A dilution series of CHIR-124 is mixed with a kinase reaction buffer containing a final concentration of 30 mM Tris-HCl (pH 7.5), 10 mM MgCl2, 2 mM DTT, 4 mM EDTA, 25 mMβ-glycerophosphate, 5 mM MnCl2, 0.01% bovine serum albumin, 1.35 nM CHK1 kinase domain, 0.5 μM peptide substrate, and 1 AM unlabeled ATP, plus 5 nM 33Pγ-labeled ATP (specific activity = 2,000 Ci/mmol). Reactions and detection of the phosphate transfer are carried out by a radioactive method. Reactions are incubated at room temperature for 1 to 4 hours and the phosphorylated peptide captured on streptavidin-coated microtiter plates containing stop reaction buffer (25 mM EDTA [ethylenediaminetetraacetic acid], 50 mMHEPES, pH 7.5). Phosphorylated peptide is measured with the DELFIA TRF system using a Europium-labeled anti-phosphotyrosine antibody PT66. The concentration of CHIR-124 for IC50 is calculated using nonlinear regression with XL-Fit data analysis software.

Cell Research	MDA-MB-231, MDA-MB-435, SW-620, and COLO 205 cells in log-phase are plated into 96-well microplates. CHIR-124 is serially diluted in the presence of six different concentrations of Camptothecin or 0 nM camptothecin. Camptothecin is also serially diluted in the absence of CHIR-124. CHIR-124 is added to cells in 96-well dishes and incubated at 37 °C for 48 hours. Each treatment condition is done in triplicate. Cell proliferation is monitored by the 3-(4,5-dimethylthiazol-2-yl)-5- (3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS), inner salt assay. MTS inner salt is added to the microplates, which are incubated for another 3 hours, and absorbance at 490 nm is read on a plate reader. The concentrations of each drug in the combinations required to produce 50% inhibition are plotted to generate the isoboles. Isobologram analysis of drug interaction is based the equation of Loewe additivity (1= D A /IC50, A + DB/IC50, B), where IC50, A and IC50, B are the concentrations of drugs to result in 50% inhibition for each drug alone, and DA and DB are concentrations of each drug in the combination that yield 50% overall inhibition. A diagonal line indicating Loewe additivity is included in each graph. Data points that fall below the line indicate synergy, whereas those that fall above the line will indicate antagonism(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 15 mg/mL (35.72 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Saline: < 1.5 mg/mL (3.57 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1.5 mg/mL (3.57 mM),Solution. 10% DMSO+40% PEG300+5% Tween-80+45% Saline: 0.5 mg/mL (1.19 mM),Sonication is recommended. *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.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3815 mL	11.9073 mL	23.8146 mL
5 mM	0.4763 mL	2.3815 mL	4.7629 mL
10 mM	0.2381 mL	1.1907 mL	2.3815 mL
50 mM	0.0476 mL	0.2381 mL	0.4763 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

Tse AN, et al, Clin Cancer Res, 2007, 13(2 Pt 1), 591-602.
Dai Y, et al, Clin Cancer Res, 2010, 16(2), 376-383

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Tel:781-999-4286 E_mail:info@targetmol.com Address:34 Washington Street,Wellesley Hills,MA 02481