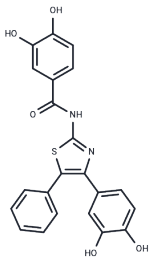
Data Sheet (Cat.No.T3157)

TargetMol

COH29

Chemical Properties



CAS No. : 1190932-38-7

Formula: C22H16N2O5S

Molecular Weight: 420.44

Appearance: no data available

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

Biological Description

Description	COH29 (RNR Inhibitor COH29) is an orally available, aromatically substituted thiazole and human ribonucleotide reductase (RNR) inhibitor with potential antineoplastic activity. COH29 binds to the ligand-binding pocket of the RNR M2 subunit (hRRM2) near the C-terminal tail, decreasing the pool of deoxyribonucleotide triphosphates needed for DNA synthesis, leading to cell cycle arrest and growth inhibition. It may also inhibit the nuclear enzyme poly (ADP-ribose) polymerase (PARP) 1, preventing DNA repair, causing accumulation of DNA breaks, and inducing apoptosis.
Targets(IC50)	DNA/RNA Synthesis
In vitro	COH29 overcome gemcitabine and hydroxyurea resistance in Y cells. It potently inhibits proliferation of most cell lines in the NCI 60 human Y panel, most especially leukemia and ovarian Y, but exerts little effect on normal fibroblasts or endothelial cells. NMR, site-directed mutagenesis, and surface plasmon resonance biosensor studies confirm COH29 binding to the proposed ligand-binding pocket and offer evidence for assembly blockade of the RRM1-RRM2 quaternary structure[1].
In vivo	COH29 (50/100 mg/kg, b.i.d., p.o.)results in a dose-dependent inhibition of MOLT-4 tumor xenograft growth, which is pronounced by Day 12 of treatment. In mice bearing TOV11D xenografts, 7 days of treatment with COH29 (200/300/400 mg/kg/day) results in a dose-dependent inhibition of tumor xenograft growth. Compared with the control group, tumor growth is significantly inhibited [1].
Kinase Assay	For kinase assays following immunoprecipitation of FLAG-CDK7 protein from HCT116 or FLAG-CDK12 from 293A cellular lysates, cells are first treated with THZ1, THZ1-R, or DMSO for 4 hrs at 37°C. Cells are then harvested by lysis in 50 mM Tris HCl pH 8.0, 150 mM NaCl, 1% NP-40, 5 mM EDTA, and protease/phosphatase cocktails. Exogenous CDK7 or CDK12 proteins are immunoprecipitated from cellular lysates using FLAG antibody-conjugated agarose beads. Precipitated proteins are washed with lysis buffer 6 times, followed by 2 washes with kinase buffer (40 mM Hepes pH 7.5, 150 mM NaCl, 10 mM MgCl2, 5% glycerol) and subjected to in vitro kinase assays at 30°C for 45 minutes using 1 μg of the large subunit of RNAPII (RPB1) as substrate and 25 μM ATP and 10 μCi of 32P ATP. Kinase assays using recombinant CDK7/TFIIH/MAT1 are conducted in the manner as described above using 25 ng of CAK complex per reaction. For kinase assays designed to test time-dependent inactivation of CDK7 kinase activity, CAK complex is pre-incubated with indicated concentrations of THZ1, THZ1-R, or DMSO in kinase buffer without ATP for 4 hrs at 30°C prior to being subjected to kinase assay conditions[1].

Cell Research	Cells is seeded into 96-well plates in 100 μL of complete medium at 2000 to 5000 cells per well, depending on the cell line's growth rate. After overnight incubation, test compound is added to each well at various concentrations in 50 μL of culture medium. After a further incubation for 96 hours at 37°C, fluorescein diacetate (final concentration: 10 mg/mL) and eosin Y [final concentration: 0.1% (w/v)] is added to each well, and the cells is incubated for an additional 20 minutes at 37°C. Cytotoxicity is assessed by Digital Imaging Microscopy System detection Viability is assessed using MTS [(3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium)] as previously described[1].

Solubility Information

Solubility	DMSO: 50 mg/mL (118.92 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.3785 mL	11.8923 mL	23.7846 mL
5 mM	0.4757 mL	2.3785 mL	4.7569 mL
10 mM	0.2378 mL	1.1892 mL	2.3785 mL
50 mM	0.0476 mL	0.2378 mL	0.4757 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

Zhou B, et al. A small-molecule blocking ribonucleotide reductase holoenzyme formation inhibits cancer cell growth and overcomes drug resistance.Cancer Res. 2013 Nov 1;73(21):6484-93.
Wang R, Xu Z, Tian J, et al. Pterostilbene inhibits hepatocellular carcinoma proliferation and HBV replication by targeting ribonucleotide reductase M2 protein. American Journal of Cancer Research. 2021, 11(6): 2975.
Chen MC, et al. The Novel Ribonucleotide Reductase Inhibitor COH29 Inhibits DNA Repair In Vitro. Mol Pharmacol. 2015 Jun;87(6):996-1005.

Tel:781-999-4286 E_mail:info@targetmol.com Address:36 Washington Street,Wellesley Hills,MA 02481