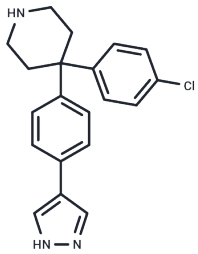
Data Sheet (Cat.No.T6304)

TargetMol

AT7867

Chemical Properties



CAS No. : 857531-00-1

Formula: C20H20ClN3

Molecular Weight: 337.85

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	AT7867 is a potent ATP-competitive inhibitor of Akt1/2/3 and p70S6K/PKA with IC50 values of 32 nM, 17 nM, 47 nM, 85 nM, and 20 nM, respectively, exhibiting little activity outside the AGC kinase family.
Targets(IC50)	Akt,PKA,S6 Kinase
In vitro	AT7867 also inhibits structurally related AGC kinases p70S6K and PKA with IC50 of 20 nM and 85 nM, respectively. AT7867 shows ATP-competitive activity to Akt2 with Ki of 18 nM. AT7867 exhibits antiproliferation in cell lines with PTEN or PIK3CA mutations and shows great potent to MES-SA, MDA-MB-468, MCF-7, HCT116 and HT29 with IC50 of 0.94 μM, 2.26 μM, 1.86 μM, 1.76 μM and 3.04 μM, respectively. AT7867 also suppresses the cell growth of U87 mg, PC-3 and DU145 cells with IC50 of 8.22 μM, 10.37 μM and 11.86 μM, respectively. AT7867 suppresses Akt activity by inhibiting phosphorylation of GSK-3β in human tumor cells with IC50 of 2-4 μM. AT7867 also induces the phosphorylation of the following Akt direct substrates including proapoptotic transcription factors FKHR (FoxO1a), FKHRL1 (FoxO3a) and the downstream target S6RP in U87 mg cells. [1]
In vivo	AT7867 shows bioavailability of 44% in mice by p.o. route. AT7867 could increase the cleaved PARP in MES-SA xenografts at 20 mg/kg i.p. or 90 mg/kg p.o. AT7867 significantly inhibits the tumor growth in MES-SA xenografts or U87 mg xenografts with T/C of 0.37 and 0.51, respectively. [1]
Kinase Assay	In vitro kinase assays : Kinase assays for Akt2, PKA, p70S6K, and CDK2/cyclin A are all carried out in a radiometric filter binding format. Assay reactions are set up in the presence of AT7867. For Akt2, the Akt2 enzyme and 25 μM Aktide-2T peptide (HARKRERTYSFGHHA) are incubated in 20 mM MOPS (pH 7.2), 25 mM β-glycerophosphate, 5 mM EDTA, 15 mM MgCl2, 1 mM sodium orthovanadate, 1 mM DTT, 10 μg/mL bovine serum albumin, and 30 μM ATP (1.16 Ci/mmol) for 4 hours. For PKA, the PKA enzyme and 50 μMpeptide (GRTGRRNSI) are incubated in 2 mM MOPS (pH 7.2), 25 mM β-glycerophosphate, 5 mM EDTA, 15 mM MgCl2, 1 mM orthovanadate, 1 mM DTT, and 40 μM ATP (0.88 Ci/mmol) for 20 minutes. For p70S6K, the p70S6K enzyme and 25 μMpeptide substrate (AKRRRLSSLRA) are incubated in 10 mM MOPS (pH 7), 0.2 mM EDTA, 1 mM MgCl2, 0.01% β-mercaptoethanol, 0.1 mg/mL bovine serum albumin, 0.001% Brij-35, 0.5% glycerol, and 15 μM ATP (2.3 Ci/mmol) for 60 min. For CDK2, the CDK2/cyclin A enzyme and 0.12 μg/mL histone H1 are incubated in 20 mM MOPS (pH 7.2), 25 mM β-glycerophosphate, 5 mM EDTA, 15 mM MgCl2, 1 mM sodium orthovanadate, 1 mM DTT, 0.1 mg/mL bovine serum albumin, and 45 μM ATP (0.78 Ci/mmol) for 4 hours. Assay

Kinase Assay	reactions are stopped by adding an excess of orthophosphoric acid, and the stopped reaction mixture is then transferred to Millipore MAPH filter plates and filtered. The plates are then washed, scintillant is added, and radioactivity is measured by scintillation counting on a Packard TopCount. IC50 values are calculated from replicate curves using GraphPad Prism software. Akt1 and Akt3 enzyme assays are carried out.
Cell Research	Cells are plated in 96-well microplates at 5 × 103 per well in medium supplemented with 10% fetal bovine serum and grown for 24 hours before treatment with AT7867. AT7867 or vehicle control is added to the cells for 72 hours. Following this, Alamar Blue solution is added. The IC50 value for AT7868 is calculated in GraphPad Prism using nonlinear regression analysis and a sigmoidal dose-response (variable slope) equation.(Only for Reference)

Solubility Information

Solubility	DMSO: 63 mg/mL (186.47 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 5 mg/mL (14.8 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 (2.96 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	2.9599 mL	14.7995 mL	29.5989 mL
5 mM	0.592 mL	2.9599 mL	5.9198 mL
10 mM	0.296 mL	1.4799 mL	2.9599 mL
50 mM	0.0592 mL	0.296 mL	0.592 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

Grimshaw KM, Mol Cancer Ther, 2010, 9(5), 1100-1110.