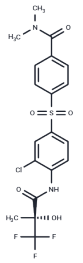
Data Sheet (Cat.No.T2447)

TargetMol

AZD7545

Chemical Properties



CAS No. : 252017-04-2

Formula: C19H18ClF3N2O5S

Molecular Weight: 478.87

Appearance: no data available

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

Biological Description

Description	AZD7545 is a potent PDHK inhibitor.
Targets(IC50)	Dehydrogenase
In vitro	In obese, insulin-resistant Zucker rats, AZD7545 eliminated postprandial hyperglycemia. AZD7545 increased the percentage of active PDH in the liver and skeletal muscle of Wistar rats.
In vivo	AZD7545 inhibits pyruvate dehydrogenase kinase (PDHK) activity by disrupting the interaction between the inner lipoic acid domain of PDHK2 and the dihydrolipoamide acetyltransferase component of the pyruvate dehydrogenase complex (PDC). It increases the activity of pyruvate dehydrogenase (PDH) in primary rat hepatocytes with an EC50 of 105 nM. In the presence of recombinant human PDHK2, AZD7545 also enhances PDH activity, achieving an EC50 of 5.2 nM.
Kinase Assay	Cellular Kinase Assays: NIH3T3 cells prepared by transfection of human KDR. The cells are cultured in a collagen type I coated 96-well plate in an amount of 1.5 × 104 per well. The medium is then replaced by a DMEM medium containing 0.1% FCS. Ki8751 diluted in DMSO is added to each well and cultured. rhVEGF is added to a final concentration of 100 ng/mL, and the stimulation of cells is carried out at 37 °C. The cells are washed with PBS (pH 7.4), 50 μL of a solubilization buffer (20 mM HEPES (pH 7.4), 150 mM NaCl, 0.2% Triton X-100, 10% glycerol, 5 mM Na3VO4, 5 mM disodium ethylenediamine tetraacetate, and 2 mM Na4P2O7) is then added and a cell extract is prepared. Separately, PBS (50 μL, pH 7.4) containing 5 μg/mL of antiphosphotyrosine antibody (PY20) is added to a microplate for ELISA. After washing of the plate, 300 μL of a blocking solution is added. The cell extract is transferred to the plate. An anti-VEGFR2 antibody and a peroxidase-labeled anti-rabbit Ig antibody are added. Next, a chromophoric substrate for peroxidase is added, and the absorbance at 450 nm is measured with microplate reader. The VEGFR2 phosphorylation activity for each well is determined by presuming the absorbance with the addition of VEGF and without the addition of the test sample to be 100% VEGFR2 phosphorylation activity and VEGF to be 0% VEGFR2 phosphorylation activity. The concentration of the inhibition (%) of VEGFR2 Phosphorylation is determined for each case, and IC50 value is calculated.

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 88 mg/mL (183.77 mM),Sonication is recommended. DMSO: 88 mg/mL (183.77 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0882 mL	10.4412 mL	20.8825 mL
5 mM	0.4176 mL	2.0882 mL	4.1765 mL
10 mM	0.2088 mL	1.0441 mL	2.0882 mL
50 mM	0.0418 mL	0.2088 mL	0.4176 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

Morrell JA, et al. Biochem Soc Trans. 2003, 31(Pt 6), 1168-1170.
Mayers RM, et al. Biochem Soc Trans. 2003, 31(Pt 6), 1165-1167.
Tuganova A, et al. Biochemistry. 2007, 46(29), 8592-8602.