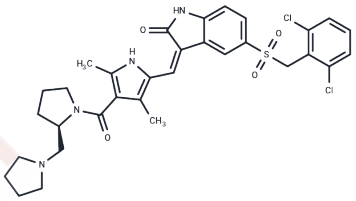
Data Sheet (Cat.No.T6128)

TargetMol

PHA-665752

Chemical Properties



CAS No. : 477575-56-7

Formula: C32H34Cl2N4O4S

Molecular Weight: 641.61

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-665752 is an effective, specific and ATP-competitive c-Met inhibitor (IC50: 9 nM), >50-fold selectivity for c-Met than STKs or RTKs.
Targets(IC50)	Apoptosis,FGFR,Bcr-Abl,Autophagy,c-Met/HGFR,VEGFR
In vitro	PHA-665752 significantly inhibits c-Met kinase activity with Ki of 4 nM, and exhibits >50-fold selectivity for c-Met compared with various tyrosine and serine-threonine kinases. PHA-665752 potently inhibits the HGF-stimulated c-Met autophosphorylation with IC50 of 25-50 nM. PHA-665752 also significantly blocks HGF- and c-Met-dependent functions such as cell motility and cell proliferation with IC50 of 40-50 nM and 18-42 nM, respectively. In addition, PHA-665752 potently inhibits HGF-stimulated or constitutive phosphorylation of mediators of downstream of c-Met such as Gab-1, ERK, Akt, STAT3, PLC-γ, and FAK in multiple tumor cell lines. [1] PHA-665752 inhibits cell growth in TPR-MET-transformed BaF3 cells with IC50 of <60 nM, and inhibits constitutive cell motility and migration by 92.5% at 0.2 μM. Inhibition of c-Met by PHA665752 (0.2 μM) also induces cell apoptosis of 33.1% and G1 cell cycle arrest with cells in G1 phase increasing from 42.4% to 77.0%. PHA665752 can cooperate with rapamycin to inhibit cell growth of TPR-MET-transformed BaF3 cells and non-small cell lung cancer H441 cells. [2]
In vivo	Administration of PHA-665752 induces a dose-dependent tumor growth inhibition of S114 xenografts by 20 %, 39% and 68%, at dose of 7.5, 15, and 30 mg/kg/day, respectively. [1] PHA665752 treatment significantly reduces the tumor growth of NCI-H69, NCI-H441 and A549 in mouse xenografts by 99%, 75%, and 59%, respectively. PHA665752 also significantly inhibits angiogenesis by >85%, due to decreasing the production of vascular endothelial growth factor and increasing the production of the angiogenesis inhibitor thrombospondin-1. [3]
Kinase Assay	In vitro enzyme assay: The c-Met kinase domain GST-fusion protein is used for the c-Met assay. The IC50 value of PHA-665752 for the inhibition of c-Met is based on phosphorylation of kinase peptide substrates or poly-glu-tyr in the presence of ATP and divalent cation (MgCl2 or MnCl2 10-20 mM). The linear range (i.e., the time period over which the rate remains equivalent to the initial rate) is determined for c-Met, and the kinetic measurement and IC50 determination are performed within this range.
Cell Research	For proliferation assays, cells are grown in medium with 0.1% FBS for 48 hours after which they are treated with various concentrations of PHA-665752 in HGF (50 ng/mL) in a medium containing 2% FBS. After 18 hours, cells are incubated with BrdUrd for 1 hour,

Cell Research	fixed, and stained with anti-BrdUrd peroxidase-conjugated antibody, and plates are read at 630 nm. For apoptosis assays, cells are grown in medium with 2% FBS in presence and absence of HGF (50 ng/mL) and various concentrations of PHA-665752 for 72 hours. After 72 hours, a mixture containing ethidium bromide and acridine orange is added, and apoptotic cells (bright orange cells or cell fragments) are counted by fluorescence microscopy.(Only for Reference)

Solubility Information

Solubility	DMSO: 50 mg/mL (77.93 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: 2 mg/mL (3.12 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	1.5586 mL	7.7929 mL	15.5858 mL
5 mM	0.3117 mL	1.5586 mL	3.1172 mL
10 mM	0.1559 mL	0.7793 mL	1.5586 mL
50 mM	0.0312 mL	0.1559 mL	0.3117 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

Christensen JG, et al. Cancer Res, 2003, 63(21), 7345-7355.
Yuan S, Gong Y, Chen R, et al. Chinese herbal formula QHF inhibits hepatocellular carcinoma metastasis via HGF/c-Met signaling pathway. Biomedicine & Pharmacotherapy. 2020, 132: 110867.
Ma PC, et al. Clin Cancer Res, 2005, 11(6), 2312-2319.
Puri N, et al. Cancer Res, 2007, 67(8), 3529-3534.