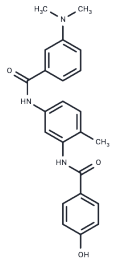
Data Sheet (Cat.No.T1851)

TargetMol

ZM 336372

Chemical Properties



CAS No. : 208260-29-1

Formula: C23H23N3O3

Molecular Weight: 389.45

Appearance: no data available

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

Biological Description

Description	ZM 336372 is a potent and selective c-Raf inhibitor.
Targets(IC50)	Apoptosis,Raf
In vivo	1 μM ZM 336372 abrogated the up-regulation of eNOS after hydrogen peroxide treatment.ZM 336372 induced inhibition of proliferation, inhibition of hormone secretion and up-regulation of cell cycle inhibitors in a dose-dependent manner in HepG2.ZM 336372 acted selectively on C-Raf 10-fold compared to B-Raf.ZM 336372 inhibited proliferation and suppressed NE vasoactive peptide in pheochromocytoma cells.ZM 336372 inhibited proliferation of pheochromocytoma cells. ZM 336372 weakly inhibited SAPK2a/p38α and SAPK2b/p38β with an IC50 of 2 μM, and was more selective for C-Raf than for 17 other protein kinases, including PKA, PKC, AMPK, p42 MAPK, MKK1, SAPK1/JNK, and CDK1, at a concentration of up to 50 μM. ZM 336372 does not prevent growth factor or fobol ester-induced activation of MKKl or p42 MAPK/ERK2. By inhibiting the MAPK cascade, protein kinase C or phosphatidylinositol 3-kinase did not prevent ZM 336372-induced activation of c-Raf. ZM 336372 treatment induced the activation of c-Raf and B-Raf isoforms > 100, but it did not trigger any activation of MKKI or p42 MAPK/ERKP or induce any increase in GTP loading of Ras. , suggesting that the feedback control loop Raf isoform inhibits its own activation, and thus the inhibition is always counteracted by reactivation.ZM 336372 also induces apoptosis in pancreatic cancer cell lines by inhibiting glycogen synthase kinase-3β via phosphorylation of GSK-3β on Ser 9.
Kinase Assay	In vitro kinase assay: c-Raf kinase activity is assayed directly in Sl9 cell lysates. Human c-Raf is activated in Sf9 cells by cotransfection from baculovirus vectors containing DNA encoding v-Ras and Lck in the absence of ZM 336372. The cell lysates are then assayed for c-Raf activity in the presence of increasing concentrations of ZM 336372.
Cell Research	Cells are exposed to various concentrations of ZM 336372 for 48 and 72 hours. After incubation, the medium is removed and cells are trypsinized. Cells are incubated on ice, and 2.5 μg/mL propidium iodide is added 5 minutes before flow cytometry. Data is acquired using a FACSCalibur benchtop flow cytometer using CellQuest acquisition and analysis software. Cytotoxicity is done using Cell Titer Glo Assay. Cell proliferation is measured using MTT assay.(Only for Reference)

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 2 mg/mL (5.14 mM),Sonication is recommended. DMSO: 72 mg/mL (184.88 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5677 mL	12.8386 mL	25.6772 mL
5 mM	0.5135 mL	2.5677 mL	5.1354 mL
10 mM	0.2568 mL	1.2839 mL	2.5677 mL
50 mM	0.0514 mL	0.2568 mL	0.5135 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

Hall-Jackson CA, et al. Chem Biol, 1999, 6(8), 559-568.
Wartenberg M, et al. Int J Cancer, 2003, 104(3), 274-282.
Van Gompel JJ, et al. Mol Cancer Ther, 2005, 4(6), 910-917.
Kappes A, et al. J Surg Res, 2006, 133(1), 42-55.
Deming D, et al. J Gastrointest Surg, 2008, 12(5), 852-857.