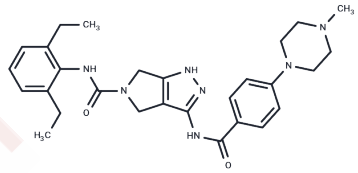
Data Sheet (Cat.No.T6338)

TargetMol

PHA-680632

Chemical Properties



CAS No. : 398493-79-3

Formula: C28H35N7O2

Molecular Weight: 501.62

Appearance: no data available

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

Biological Description

Description	PHA-680632 is potent inhibitor of Aurora A, Aurora B and Aurora C with IC50 of 27 nM, 135 nM and 120 nM, respectively. It has 10- to 200-fold higher IC50 for FGFR1, FLT3, LCK, PLK1, STLK2, and VEGFR2/3.
Targets(IC50)	FGFR,Aurora Kinase,PLK
In vitro	PHA-680632 potently inhibits all three Aurora kinases (A, B, and C) with IC50 values of 27, 135, and 120 nM, respectively. PHA-680632 is selective for Aurora kinases, with 10- to 200-fold higher IC50 for FGFR1, FLT3, LCK, PLK1, STLK2, VEGFR2, and VEGFR3, and with IC50 higher than 10 μM for another 22 kinases. PHA-680632 shows potent anti-proliferative effects in a wide range of cell types with IC50 values of 0.06–7.15 μM, including HeLa, HCT116, HT29, LOVO, DU145, and NHDF cells. PHA-680632 (0.5 μM) causes polyploidy in tumor cells. The mechanism of action of PHA-680632 is in agreement with inhibition of Aurora kinases. [1] PHA680632 in association with radiation leads to additive effects in cancer cells, especially in the p53-deficient cells. Combined ionising radiation (IR) and treatment of PHA680632 (100–400 nM) prior to IR leads to an enhancement of radiation-induced Annexin V positive cells, micronuclei formation, and Brca1 foci formation only in HCT116 cells with deficient p53, other than the p53 wild-type counterparts. [2]
In vivo	HA-680632 (15-60 mg/kg) inhibits tumor growth in mice xenografts models of HL60, A2780, and HCT116 cells, by reducing tumor cell proliferation and increasing apoptosis. PHA-680632 (45 mg/kg) suppresses growth of activated ras-driven mammary tumors in mouse mammary tumor virus v-Ha-ras transgenic mice and results in complete tumor stabilization and partial regression. [1]
Kinase Assay	Aurora Kinase Inhibition Assay: Inhibition of kinase activity by PHA-680632 is assessed using a scintillation proximity assay format. The biotinylated substrate is transphosphorylated by the kinase in presence of ATP traced with γ33-ATP. The phosphorylated substrate is then captured using streptavidin-coated scintillation proximity assay beads and the extent of phosphorylation is evaluated by β-counter after a 4-hour rest for the floatation of the beads on a dense 5 M CsCl solution. In particular, a peptide derived from the Chocktide sequence (LRRWSLGL) is used as substrate for Aurora A, whereas the optimized peptide Auroratide is employed for Aurora B and C. The assay is run in a robotized format on 96-well plates. The potency of the compound toward Aurora kinases is evaluated and IC50 values are determined.

Cell Research	Cells (5 × 103 to 1.5 × 104 per cm2) are seeded in 24-well plate. After 24 hours, plates are treated with PHA-680632 and incubated for 72 hours. At the end of incubation time, cells are detached from each plate and counted using a cell counter. IC50s are calculated using percentage of growth versus untreated cont(Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 93 mg/mL (185.4 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.9935 mL	9.9677 mL	19.9354 mL
5 mM	0.3987 mL	1.9935 mL	3.9871 mL
10 mM	0.1994 mL	0.9968 mL	1.9935 mL
50 mM	0.0399 mL	0.1994 mL	0.3987 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

Soncini C, et al. Clin Cancer Res, 2006, 12(13), 4080-4089.
Tao Y, et al. Br J Cancer, 2007, 97(12), 1664-1672.

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