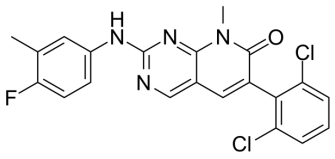
PD180970

Cat. No.:	HY-103274
CAS No.:	287204-45-9
Molecular Formula:	$C_{21}H_{15}Cl_2FN_4O$
Molecular Weight:	429.27
Target:	Bcr-Abl; Src; c-Kit; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (232.95 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3295 mL	11.6477 mL	23.2954 mL
	5 mM	0.4659 mL	2.3295 mL	4.6591 mL
	10 mM	0.2330 mL	1.1648 mL	2.3295 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PD180970 is a highly potent and ATP-competitive $p210^{Bcr\text{-}Abl}$ kinase inhibitor, with an IC_{50} of 5 nM for inhibiting the autophosphorylation of $p210^{Bcr\text{-}Abl}$. PD180970 also inhibits Src and KIT kinase with IC_{50}s of 0.8 nM and 50 nM, respectively. PD180970 indcues apoptosis of K562 leukemic cells, and can be used for chronic myelogenous leukemia research[1][2][3].

IC_{50} & Target

Bcr-Abl	Src	KIT
5 nM (IC_{50}, $p210^{Bcr\text{-}Abl}$ kinase)	0.8 nM (IC_{50})	50 nM (IC_{50})

In Vitro

PD180970 (0.5 μM; 24-96 hours) treatment causes cell death K562 cells[1].
PD180970 (0.5 μM; 24-48 hours) treatment induces apoptosis of K562 cells. The result shows increase in annexin V-PI double-positive cells[1].
PD180970 inhibits tyrosine phosphorylation of p210Bcr-Abl, Gab2, and CrkL in K562 cells with IC50 values of 170 nM, 80 nM,

and 80 nM, respectively. In vitro, PD180970 potently inhibits autophosphorylation of $p210^{Bcr\text{-}Abl}$ (IC_{50} of 5 nM) and the kinase activity of purified recombinant Abl tyrosine kinase (IC_{50} of 2.2 nM)[1].
The blocking Bcr-Abl kinase activity using PD180970 in the human K562 CML cell line resulted in inhibition of Stat5 DNA-binding activity with an IC_{50} of 5 nM[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	K562 cells
Concentration:	0.5 μM
Incubation Time:	24 hours, 48 hours, 72 hours, 96 hours
Result:	Resulted in cell death.

Apoptosis Analysis[1]

Cell Line:	K562 cells
Concentration:	0.5 μM
Incubation Time:	24 hours, 48 hours
Result:	Increased annexin V-positive/PI-negative cells.

In Vivo

PD180970 (5 mg/kg; intraperitonial injection; daily; for 7 days) mitigates MPTP-induced neuronal loss in mice. PD180970 has the neuroprotective ability in a preclinical mouse model of Parkinson's disease (PD)[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL/6J mice (3-4 months old) injected with MPTP[4]
Dosage:	5 mg/kg
Administration:	Intraperitonial injection; daily; for 7 days
Result:	Decreased number of activated microglia on activation by MPTP in mice brains. And showed significant reduction in intensity of Iba1 expression in activated microglia.

REFERENCES

[1]. J F Dorsey, et al. The pyrido[2,3-d]pyrimidine derivative PD180970 inhibits p210Bcr-Abl tyrosine kinase and induces apoptosis of K562 leukemic cells. Cancer Res. 2000 Jun 15;60(12):3127-31.

[2]. Mei Huang, et al. Inhibition of Bcr-Abl kinase activity by PD180970 blocks constitutive activation of Stat5 and growth of CML cells. Oncogene. 2002 Dec 12;21(57):8804-16.

[3]. Amie S Corbin, et al. Sensitivity of oncogenic KIT mutants to the kinase inhibitors MLN518 and PD180970. Blood. 2004 Dec 1;104(12):3754-7.

[4]. Suresh Sn, et al. Small molecule modulator of aggrephagy regulates neuroinflammation to curb pathogenesis of neurodegeneration. EBioMedicine. 2019 Dec;50:260-273.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA