ETP-45658

Cat. No.: HY-110109

CAS No.: 1198357-79-7

Molecular Formula: $C_{16}H_{17}N_5O_2$

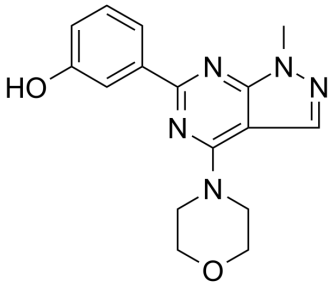
Molecular Weight: 311.34

Target: PI3K; DNA-PK; mTOR

Pathway: PI3K/Akt/mTOR; Cell Cycle/DNA Damage

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 : 250 mg/mL (802.98 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	3.2119 mL	16.0596 mL	32.1192 mL
	5 mM	0.6424 mL	3.2119 mL	6.4238 mL
	10 mM	0.3212 mL	1.6060 mL	3.2119 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (6.68 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.68 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.68 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ETP-45658 is a potent PI3K inhibitor, with IC_{50}s of 22.0 nM, 39.8 nM, 129.0 nM and 717.3 nM for PI3Kα, PI3Kδ, PI3Kβ and PI3Kγ, respectively. ETP-45658 also can inhibit DNA-PK (IC_{50}=70.6 nM) and mTOR (IC_{50}=152.0 nM). ETP-45658 can be used for the research of cancer[1][2].

IC_{50} & Target

PI3Kα 22.0 nM (IC_{50})	PI3Kδ 39.8 nM (IC_{50})	PI3Kβ 129.0 nM (IC_{50})	PI3Kγ 717.3 nM (IC_{50})
DNA-PK	mTOR		

	70.6 nM (IC_{50})	152.0 nM (IC_{50})

In Vitro

ETP-45658 (10 μM; 4 h) decreases in the phosphorylation of FOXO3a, Gsk3-β and p70 S6K in U2OS cells[1].
ETP-45658 inhibits the proliferation of MCF7, PC3, 786-O, HTC116, and U251 cells, with EC_{50}s of 0.48 μM, 0.49 μM, 2.62 μM, 3.53 μM, and 5.56 μM, respectively[1].
ETP-45658 (10 μM; 24 h) induces a clear G1 arrest of PC3 cells[1].
ETP-45658 inhibits the mutant PI3Kα proteins, H1047R and E545K, with IC_{50}s of 16.8 nM and 13.1 nM, respectively[1].
ETP-45658 (5 nM-11.1 μM; 1 h) induces a dose-dependent increase of GFP-FOXO nuclear translocation in U2foxRELOC cells[1].
ETP-45658 (10 μM; 1 h) decrease the expression of cyclin D1 and p-Akt on serine 473 in U2OS cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	U2OS cells
Concentration:	10 μM
Incubation Time:	4 hours
Result:	Caused a 95% decrease in the phosphorylation of FOXO3a at threonine 32 and a 55% reduction on Gsk3-β at serine 9. Reduced the phosphorylation of the mTOR substrate p70 S6K.

In Vivo

ETP-45658 (22.7 mg/kg) decreases the level of phosphorylated Akt on serine 473 in the mammary ducts of transgenic mice[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Link W, et, al. Chemical interrogation of FOXO3a nuclear translocation identifies potent and selective inhibitors of phosphoinositide 3-kinases. J Biol Chem. 2009 Oct 9;284(41):28392-28400.

[2]. Hill R, et, al. A novel phosphatidylinositol 3-kinase (PI3K) inhibitor directs a potent FOXO-dependent, p53-independent cell cycle arrest phenotype characterized by the differential induction of a subset of FOXO-regulated genes. Breast Cancer Res. 2014 Dec 9;16(6):482.

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