PIK-75 hydrochloride

Cat. No.: HY-13281

CAS No.: 372196-77-5

Molecular Formula: $C_{16}H_{15}BrClN_5O_4S$

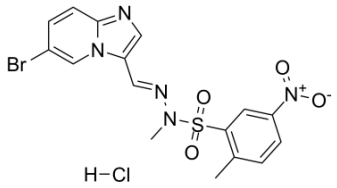
Molecular Weight: 488.74

Target: DNA-PK; PI3K; Apoptosis

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR; 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 : 11 mg/mL (22.51 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0461 mL	10.2304 mL	20.4608 mL
	5 mM	0.4092 mL	2.0461 mL	4.0922 mL
	10 mM	0.2046 mL	1.0230 mL	2.0461 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: ≥ 1.1 mg/mL (2.25 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.1 mg/mL (2.25 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.1 mg/mL (2.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PIK-75 hydrochloride is a reversible DNA-PK and p110α-selective inhibitor, which inhibits DNA-PK, p110α and p110γ with IC_{50}s of 2, 5.8 and 76 nM, respectively. PIK-75 hydrochloride inhibits p110α >200-fold more potently than p110β (IC_{50}=1.3 μM) [1][2]. PIK-75 hydrochloride induces apoptosis[3].

IC_{50} & Target

DNA-PK 2 nM (IC_{50})	p110α 5.8 nM (IC_{50})	p110γ 76 nM (IC_{50})	p110δ 510 nM (IC_{50})
p110β	hsVPS34	PI3KC2β	PI3KC2α

	1.3 μM (IC_{50})	2.6 μM (IC_{50})	1 μM (IC_{50})	10 μM (IC_{50})
	mTORC1 1 μM (IC_{50})	mTORC2 10 μM (IC_{50})	ATM 2.3 μM (IC_{50})	ATR 21 μM (IC_{50})
	PI4KIIIβ 50 μM (IC_{50})			

In Vitro

PIK-75 also inhibits p110δ, PI3KC2β, mTORC1, ATM, hsVPS34, PI3KC2α, mTORC2, ATR and PI4KIIIβ with IC_{50}s of 510 nM, ~1 μM, ~1 μM, 2.3 μM, 2.6 μM, ~10 μM, ~10 μM, 21 μM, ~50 μM, respectively[1].

PIK-75 alone blocks Thr 308 phosphorylation in L6 myotubes and 3T3-L1 adipocytes with IC_{50} values of 1.2 and 1.3 μM, respectively[1].

PIK-75 (1-1000 nM; 5 min) blocks the phosphorylation of PKB induced by insulin on both Ser473and Thr308 in CHO-IR cells in a dose-dependent manner, with an IC_{50} of 78 nM[2].

PIK-75 (0.1-1000 nM; 48 hours) inhibits the proliferation and survival of pancreatic cancer cells through apoptotic cell death [3].

PIK-75 (0.1-1000 nM) also reduces the colony formation of pancreatic cancer MIA PaCa-2 and AsPC-1 cells[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[3]

Cell Line:	Human pancreatic cancer cells (MIA PaCa-2 or AsPC-1)
Concentration:	0.1, 0.3, 1, 3, 10, 30, 100, 300, and 1000 nM
Incubation Time:	48 hours
Result:	Submicromolar concentration was sufficient to inhibit the proliferation of pancreatic cancer, MIA PaCa-2 and AsPC-1 cells after 48-h treatment.

Western Blot Analysis[2]

Cell Line:	Overnight-starved CHO-IR cells
Concentration:	1, 10, 100, 1000 nM
Incubation Time:	5 minutes
Result:	Blocked the phosphorylation of PKB induced by insulin (1 nM, 10 min) on both Ser473and Thr308 in a dose-dependent manner.

In Vivo

PIK-75 (2 mg/kg) potentiates anticancer activity of Gemcitabine (20 mg/kg) in vivo. Gemcitabine (20 mg/kg) or PIK-75 (2 mg/kg) alone reduces the tumor growth to similar degree. Beneficial effect of PIK-75/Gemcitabine is evident as this combination markedly reduces the tumor growth in vivowithout affecting the body weights of mice[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Mice bearing tumors of MIA PaCa-2[3]
Dosage:	2 mg/kg; or combination with Gemcitabine (20 mg/kg)
Administration:	Administered injection; 5 times per week. 25 days
Result:	Reduced the tumor growth and enhanced the antitumor effect.

CUSTOMER VALIDATION

- Clin Cancer Res. 2020 Apr 15;26(8):2011-2021.
- Molecules. 2020 Apr 23;25(8). pii: E1980.

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REFERENCES

[1]. Knight ZA, et al. A pharmacological map of the PI3-K family defines a role for p110alpha in insulin signaling. Cell. 2006 May 19;125(4):733-47.

[2]. Chaussade C, et al. Evidence for functional redundancy of class IA PI3K isoforms in insulin signalling. Biochem J. 2007 Jun 15;404(3):449-58.

[3]. Duong HQ, et al. Inhibition of NRF2 by PIK-75 augments sensitivity of pancreatic cancer cells to gemcitabine. Int J Oncol. 2014 Mar;44(3):959-69.

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