AKT inhibitor VIII

Cat. No.: HY-10355

CAS No.: 612847-09-3

Molecular Formula: $C_{34}H_{29}N_7O$

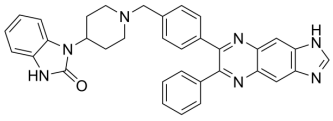
Molecular Weight: 551.64

Target: Akt; Apoptosis

Pathway: PI3K/Akt/mTOR; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	1 year
	-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 20 mg/mL (36.26 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8128 mL	9.0639 mL	18.1278 mL
	5 mM	0.3626 mL	1.8128 mL	3.6256 mL
	10 mM	0.1813 mL	0.9064 mL	1.8128 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 mg/mL (3.63 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2 mg/mL (3.63 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AKT inhibitor VIII (AKTi-1/2) is a cell-permeable quinoxaline compound that has been shown to potently, selectively, allosterically, and reversibly inhibit Akt1, Akt2, and Akt3 activity with IC_{50}s of 58 nM, 210 nM, and 2119 nM, respectively.

IC_{50} & Target

Akt1	Akt2	Akt3
58 nM (IC_{50})	210 nM (IC_{50})	2119 nM (IC_{50})

In Vitro

When LnCaP cells are pretreated with AKT inhibitor VIII and then incubated with TRAIL, a dramatic increase in caspase-3 activity (6-10-fold relative to control or TRAIL alone) is observed. This sensitization of tumor cell lines with AKT inhibitor VIII is not limited to LnCaP cells as similar apoptosis induction is observed in HT29, MCF7, and A2780 cells, among others, with chemosensitizers such as camptothecin, herceptin, and doxorubicin[1]. The furanodiene-induced decrease of p-Akt and Akt

	expressions is enhanced by the Akt inhibitor VIII pretreatment. Furthermore, the furanodiene-induced PARP cleavage is enhanced by Akt inhibitor VIII pretreatment. The Akt inhibitor VIII shows no effect on cleaved PARP expression but decreases the p-Akt and Akt expressions[2]. AKT inhibitor VIII decreases cell viability and increases phosphatidylserine (PS) translocation to the outer leaflet of the plasma membrane, DNA fragmentation, Caspase-9 cleavage, Caspase-3 activation and PARP proteolysis in hESC lines WA01 (H1) and WA09 (H9) and in a hiPSCs cell line generated in our laboratory (FN2.1)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Mice are dosed with AKT inhibitor VIII (50 mpk, 3 doses, ip, every 90 min) achieving plasma concentrations of 1.5-2.0 μM, and then the animals are tail vein injected with IGF to stimulate Akt phosphorylation. By IP Western, both basal and IGF stimulated Akt1 and Akt2 phosphorylation are inhibited in mouse lung, with no effect on Akt3 phosphorylation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	PSC are plated onto Matrigel coated 96-well plates at densities between 1×10^3-3×10^5 cells per well and grown until confluence. 24 hours post-treatments, 50 μg/well of activated 2,3-bis (2-methoxy-4-nitro-5-sulfophenyl)-5 [(phenylamino) carbonyl]-2 H-tetrazolium hydroxide(XTT) in PBS containing 0.3 μg/well of N-methyl dibenzopyrazine methyl sulfate (PMS) are added (final volume 100 μL) and incubated for 1-2 hours at 37°C. Cellular metabolic activity is determined spectrophotometrically at 450 nm. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2018 Nov 19;9(1):4874.
- Exp Mol Med. 2021 Sep 21.
- Cell Death Dis. 2021 May 28;12(6):556.
- Cell Death Dis. 2020 Aug 18;11(8):644.
- Cell Death Dis. 2017 May 25;8(5):e2817.

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REFERENCES

[1]. Lindsley, et al. Allosteric Akt (PKB) inhibitors: discovery and SAR of isozyme selective inhibitors. Bioorg. Med. Chem. Lett. (2005), 15(3), 761-764.

[2]. Zhong Z, et al. Furanodiene, a Natural Product, Inhibits Breast Cancer Growth Both in vitro and in vivo. Cell Physiol Biochem. 2012;30(3):778-90. Epub 2012 Aug 2.

[3]. Leonardo Romorini, et al. AKT/GSK3β signaling pathway is critically involved in human pluripotent stem cell survival. Sci Rep. 2016; 6: 35660

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