AK-1

Cat. No.: HY-101465

CAS No.: 330461-64-8

Molecular Formula: $C_{19}H_{21}N_3O_5S$

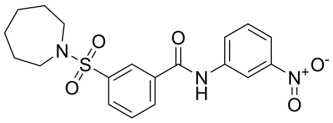
Molecular Weight: 403.45

Target: Sirtuin

Pathway: Cell Cycle/DNA Damage; Epigenetics

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (123.93 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4786 mL	12.3931 mL	24.7862 mL
	5 mM	0.4957 mL	2.4786 mL	4.9572 mL
	10 mM	0.2479 mL	1.2393 mL	2.4786 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: ≥ 2.5 mg/mL (6.20 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AK-1 is a potent, specific and cell-permeable SIRT2 inhibitor, with an IC_{50} of 12.5 μM.

IC_{50} & Target

SIRT2

12.5 μM (IC_{50})

In Vitro

AK-1 achieves significant neuroprotection in Huntington's disease flies at 10 μM, improving the number of rhabdomeres from 5.2 to 5.6[1]. AK-1 is a potent, specific and cell-permeable SIRT2 inhibitor, with an IC_{50} of 12.5 μM[2]. AK-1 treatment induces proteasomal degradation of the Snail transcription factor through inactivation of the NF-κB/CSN2 pathway. Reduction in the level of Snail results in upregulation of p21, leading to G1 arrest, slow proliferation, and slow wound-healing activity. The regulation of Snail-p21 axis by AK-1 also occurs in HT-29 colon cancer cells[3]. Under hypoxic conditions, AK-1 increases the ubiquitination of HIF-1α in a VHL-dependent manner, leading to the degradation of HIF-1α via a

proteasomal pathway. Downregulation of HIF-1α expression reduces its transcriptional activity and, eventually, reduces the expression of BNIP3, one of HIF-1 target genes, in AK-1-treated cells[4].

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

PROTOCOL

Cell Assay [3]

HEK293 cells are co-transfected with 3 μg of pGL2-PGK1-HRE-Luc and 1 μg of pCMV-β-galactosidase plasmids. Twenty-four hours later, the cells are incubated under hypoxic conditions for 24 hr in the presence of 10 μM AK-1 and then lysed with luciferase cell lysis buffer. Luciferase and β-galactosidase activities are measured using luciferin and o-nitrophenyl-β-d-galactopyranoside, respectively, as substrates. Transfection efficiency is normalized according to β-galactosidase activity[3].

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

REFERENCES

[1]. Lee SD, et al. AK-1, a SIRT2 inhibitor, destabilizes HIF-1α and diminishes its transcriptional activity during hypoxia. Cancer Lett. 2016 Apr 1;373(1):138-45.

[2]. Luthi-Carter R, et al. SIRT2 inhibition achieves neuroprotection by decreasing sterol biosynthesis. Proc Natl Acad Sci U S A. 2010 Apr 27;107(17):7927-32.

[3]. David M. Taylor, et al. A Brain-Permeable Small Molecule Reduces Neuronal Cholesterol by Inhibiting Activity of Sirtuin 2 Deacetylase. ACS Chem Biol. 2011 Jun 17;6(6):540-6.

[4]. Cheon MG, et al. AK-1, a specific SIRT2 inhibitor, induces cell cycle arrest by downregulating Snail in HCT116 human colon carcinoma cells. Cancer Lett. 2015 Jan 28;356(2 Pt B):637-45.

[5]. Ruth Luthi-Carter, et al. SIRT2 inhibition achieves neuroprotection by decreasing sterol biosynthesis. Proc Natl Acad Sci U S A. 2010 Apr 27;107(17):7927-32.

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