AGK2

Cat. No.: HY-100578

CAS No.: 304896-28-4

Molecular Formula: $C_{23}H_{13}Cl_2N_3O_2$

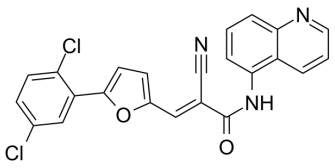
Molecular Weight: 434.27

Target: Sirtuin; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; 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 : 12.5 mg/mL (28.78 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3027 mL	11.5136 mL	23.0271 mL
5 mM	0.4605 mL	2.3027 mL	4.6054 mL
10 mM	0.2303 mL	1.1514 mL	2.3027 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: ≥ 0.5 mg/mL (1.15 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.5 mg/mL (1.15 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.5 mg/mL (1.15 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AGK2 is a selective SIRT2 inhibitor with an IC_{50} of 3.5 μM. AGK2 inhibits SIRT1 and SIRT3 with IC_{50}s of 30 and 91 μM, respectively.

IC_{50} & Target

SIRT2	SIRT1	SIRT3
3.5 μM (IC_{50})	30 μM (IC_{50})	91 μM (IC_{50})

In Vitro

AGK2 significantly inhibits cell proliferation in a dose-dependent manner. AGK2 also significantly inhibits cell growth in a

	dose-dependent manner without inducing cytotoxicity at low doses. Twelve days after AGK2 (5 μM) treatment, cells show a significantly reducing colony forming ability in soft agar to 46% of the control cells. Western blot analysis shows that the levels of CDK4 or CDK6 and cyclin D1 are decreased after AGK2 treatment in a dose-dependent manner. In addition, AGK2 inhibits the expression of p53 protein[2]. Treatment of microglial BV2 cells with 10 μM AGK2 leads to a significant increase in PAR signals. Treatment of microglial BV2 cells with 10 μM AGK2 also leads to a significant decrease in the intracellular ATP and significant increases in both late-stage apoptosis and necrosis of the cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	AGK2 significantly reduces mortality and decreases levels of cytokines in blood (TNF-α: 298.3±24.6 vs 26.8±2.8 pg/mL, p=0.0034; IL-6: 633.4±82.8 vs 232.6±133.0 pg/mL, p=0.0344) and peritoneal fluid (IL-6: 704.8±67.7 vs 391.4±98.5 pg/mL, p=0.033) compare to vehicle control. AGK2 also suppresses the TNF-α and IL-6 production in the culturing splenocytes (TNF-α: 68.1±6.4 vs 23.9±2.8 pg/mL, p=0.0009; IL-6: 73.1±4.2 vs 49.6±3.0 pg/mL; p=0.0051)[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Cells are exposed to different concentrations of AGK2 in 1 mL of 0.3% basal medium agar containing 10% FBS. The cultures are maintained at 37°C in a 5% CO_2 incubator for 10-15 days, and the cell colonies are scored using an inverted microscope [2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Mice are intraperitoneally given either AGK2 (82 mg/kg) in dimethyl sulfoxide (DMSO) or DMSO alone, and 2 h later subjects to CLP. Survival is monitored for 240 hours. AGK2-treating mice are grouped into (i) DMSO vehicle, and (ii) AGK2, with sham mice (operating but without any treatment) serving as controls. Peritoneal fluid and peripheral blood are examined at 24 and 48 hours for cytokine production[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Acta Pharm Sin B. 2019 Dec 13;8(12):1421-1428.
- Acta Pharm Sin B. 2019 Nov;9(6):1183-1192.
- Theranostics. 2021 Feb 25;11(9):4381-4402.
- iScience. 2020 Aug 21;23(8):101431.
- Int Immunopharmacol. 2022 Jun 28;110:109000.

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REFERENCES

[1]. Tatum PR, et al. Identification of novel SIRT2-selective inhibitors using a click chemistry approach. Bioorg Med Chem Lett. 2014 Apr 15;24(8):1871-4.

[2]. Kim HW, et al. Sirtuin inhibitors, EX527 and AGK2, suppress cell migration by inhibiting HSF1 protein stability. Oncol Rep. 2016 Jan;35(1):235-42.

[3]. Li Y, et al. Poly(ADP-ribose) polymerase mediates both cell death and ATP decreases in SIRT2 inhibitor AGK2-treated microglial BV2 cells. Neurosci Lett. 2013 Jun 7;544:36-40.

[4]. Zhao T, et al. Selective Inhibition of SIRT2 Improves Outcomes in a Lethal Septic Model. Curr Mol Med. 2015;15(7):634-41.

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