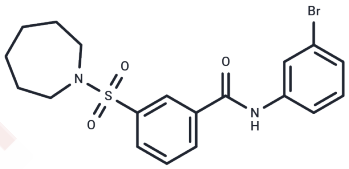
Data Sheet (Cat.No.T5490)

TargetMol

AK-7

Chemical Properties



CAS No. : 420831-40-9

Formula: C19H21BrN2O3S

Molecular Weight: 437.35

Storage: Keep away from moisture,Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	AK-7 is a brain-permeable SIRT2 inhibitor and to characterize its cholesterol-reducing properties in neuronal models with an IC50 of 15.5 μM.
Targets(IC50)	Sirtuin
In vitro	AK-7 is a selective cell- and brain-permeable SIRT2 inhibitor,this SIRT2 inhibitor stimulated cytoplasmic retention of sterol regulatory element binding protein-2 and subsequent transcriptional downregulation of cholesterol biosynthesis genes, resulting in reduced total cholesterol in primary striatal neurons. Furthermore, the identified inhibitor reduced cholesterol in cultured na?ve neuronal cells and brain slices from wild-type mice[1].AK-7 has roles in metabolic diseases, cancer, age-related disorders, and neurodegenerative diseases, potentially including Alzheimer's, Huntington's, and Parkinson's diseases[2][3].
In vivo	AK-7 (15 mg/kg/dose, i.p.) is brain-permeable in both wild-type and HD mice[1].
Kinase Assay	Sirtuin activity was assessed using the Fleur de Lys assay with recombinant active enzymes SIRT1, SIRT2, and the catalytically active fragment of SIRT3. Results were measured using a Multilabel plate reader (excitation 355 nm, emission 460 nm). Assays were performed using the manufacturer's recommendations, and each compound concentration was tested in triplicate. For each experiment, SIRT1 activity was normalized to 1 U/reaction well and SIRT2 and SIRT3 activity to 5 U/reaction well (where U = 1 pmol/min at 37 °C, 250 μM substrate, 500 μM NAD+). Each reaction well-contained enzyme, 500 μM NAD+, 250 μM fluorogenic deacetylase substrate, supplied reaction buffer, and the compound of interest or mock control (DMSO) in a total volume of 50 μL. Autofluorescent backgrounds were measured in triplicate in reaction solutions containing substrate, buffer, and NAD+ in triplicate and subtracted from experimental signals [1].
Cell Research	Neuronal nuclear antigen (NeuN)-positive neurons and some astroglia were derived from mechanically dissociated ganglionic eminences of E16 rat embryos. The HD model based on the expression of mutant huntingtin has been described previously. Treatments of cultures with AK-7 were at 10 μM for 24 h unless stated otherwise. DMSO was included at the same concentrations as a control. Lower dose, chronic treatments with AK-7 were introduced to neurons at DIV4 and continued weekly coinciding with

Cell Research	normal medium change [1].
Animal Research	AK-7, solubilized at 1.5 mg/mL in 25% Cremophor EL (BASF)/ 10% DMSO in water, was administered by intraperitoneal injection to 11 week old mice at 15 mg/kg/dose. Blood was collected and centrifuged at 7,000 rpm for 7 min, and then serum was aspirated and immediately frozen in liquid nitrogen. Brains were immediately frozen in liquid nitrogen and stored at -80 C. Brains were weighed and then homogenized in four volumes of 10% Cremophor RH40 in water using homogenizer, and 2% v/v phosphoric acid was added to the homogenate, vortexed, and centrifuged at 10,000g at 25 C for 1 h. The supernatant was aspirated, and solid phase extraction was performed immediately. Serum samples were vortexed into 2% v/v phosphoric acid and centrifuged at 2500 rpm for 10 min[1]

Solubility Information

Solubility	DMSO: 250 mg/mL (571.62 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (4.57 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2865 mL	11.4325 mL	22.865 mL
5 mM	0.4573 mL	2.2865 mL	4.573 mL
10 mM	0.2286 mL	1.1432 mL	2.2865 mL
50 mM	0.0457 mL	0.2286 mL	0.4573 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Taylor DM, 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.

Machado D O R , Jana S , Kazantsev A G , et al. SIRT2 as a Therapeutic Target for Age-Related Disorders[J]. Frontiers in Pharmacology, 2012, 3.

Fridén-Saxin, Maria, Seifert T , Landergren, Marie Rydén, et al. Synthesis and Evaluation of Substituted Chroman-4-one and Chromone Derivatives as Sirtuin 2-Selective Inhibitors[J]. Journal of Medicinal Chemistry, 2012, 55(16): 7104-7113.

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