Proteins

SRT 1720 monohydrochloride

Cat. No.: HY-15145 CAS No.: 2060259-60-9 Molecular Formula: $C_{25}H_{24}CIN_7OS$

Molecular Weight: 506.02

Target: Sirtuin; Autophagy

Pathway: Cell Cycle/DNA Damage; Epigenetics; Autophagy

4°C, stored under nitrogen Storage:

* In solvent: -80°C, 6 months; -20°C, 1 month (stored under nitrogen)

Product Data Sheet

SOLVENT & SOLUBILITY

In Vitro

DMSO: 62.5 mg/mL (123.51 mM; Need ultrasonic)

H₂O: 15.7 mg/mL (31.03 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg
	1 mM	1.9762 mL	9.8810 mL	19.7621 mL
	5 mM	0.3952 mL	1.9762 mL	3.9524 mL
	10 mM	0.1976 mL	0.9881 mL	1.9762 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- 1. Add each solvent one by one: 0.5% HPMC >> 0.2%Tween80 Solubility: 10 mg/mL (19.76 mM); Suspened solution; Need ultrasonic
- 2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.08 mg/mL (4.11 mM); Clear solution
- 3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.08 mg/mL (4.11 mM); Clear solution
- 4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline Solubility: ≥ 1 mg/mL (1.98 mM); Clear solution
- 5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline) Solubility: ≥ 1 mg/mL (1.98 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SRT 1720 monohydrochloride is a selective and orally active activator of SIRT1 with an EC $_{50}$ of 0.10 μ M, and shows less potent activities on SIRT2 and SIRT3^[1].

IC ₅₀ & Target	SIRT1 0.10 μM (EC50)	SIRT1 0.16 μM (EC1.5)	SIRT2 37 μM (EC1.5)			
In Vitro	SRT 1720 effectively decreases the acetylation of p53 in cells even in the absence of SIRT1, and this is attributed to inhibition of histone acetyltransferase p300 ^[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.					
In Vivo	SRT 1720 (10, 30, 100 mg/kg, p.o.) treatment significantly reduces fasting blood glucose to near normal levels in Lep ^{ob/ob} mice ^[1] . SRT 1720 has ability to protect against the negative effects of diet-induced obesity in mice, and has a connection to metabolic adaptation in fatty acid and oxidative metabolism ^[2] . SRT 1720 (50-100 mg/kg, p.o.), during emphysema development attenuates elastase-induced airspace enlargement and lung function impairment as well as reduces arterial oxygen saturation in WT mice ^[3] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.					

PROTOCOL

Animal
Administration [1]

Mice: Nine week old C57BL/6 male mice are fed a high fat diet (60% calories from fat) until their mean body weight reach approximately 40 g. The mice are then divided into test groups (6-10 per group). SRT1460 (100 mg/kg), SRT 1720 (100 mg/kg), SRT501 (500 mg/kg) and BRL49653 (5 mg/kg) are administered once daily via oral gavage. The vehicle used is 2% HPMC + 0.2% DOSS. Individual mouse body weights are measured twice weekly. At 2, 4, 6, 8 and 10 weeks of dosing a fed blood glucose measure is taken and after 5 weeks of treatment an IPGTT is conducted on all mice from each of the groups. After 10 weeks of treatment, an ITT is conducted. Statistical analysis is completed using the JMP program. Data are analyzed by a one way ANOVA with comparison to control using a Dunnett's Test. A p value < 0.05 indicates a significant difference between groups.

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

CUSTOMER VALIDATION

- Cell Mol Immunol. 2022 Jun 23;1-11.
- Acta Pharm Sin B. 27 August 2022.
- Sci Adv. 2022 Apr 8;8(14):eabj7110.
- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- Sci Total Environ. 2023 Oct 6:167636.

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REFERENCES

- [1]. Milne JC et al. Small molecule activators of SIRT1 as therapeutics for the treatment of type 2 diabetes. Nature. 2007 Nov 29;450(7170):712-6
- [2]. Baur JA, et al. Are sirtuins viable targets for improving healthspan and lifespan?, Nat Rev Drug Discov. 2012 Jun 1;11(6):443-61
- [3]. Yao H, et al. SIRT1 protects against emphysema via FOXO3-mediated reduction of premature senescence in mice., J Clin Invest. 2012 Jun 1;122(6):2032-45.
- [4]. Gao D, et al. Activation of SIRT1 Attenuates Klotho Deficiency-Induced Arterial Stiffness and Hypertension by Enhancing AMP-Activated Protein Kinase Activity. Hypertension. 2016 Nov;68(5):1191-1199.

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5]. Lahusen TJ, et al. SRT1720 inc	duces lysosomal-dependent c	ell death of breast cancer cells.	Mol Cancer Ther. 2015 Jan;14(1):183-	92.
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	Tel: 609-228-6898	Fax: 609-228-5909 er Park Dr, Suite Q, Monmou	E-mail: tech@MedChemExpres	ss.com
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