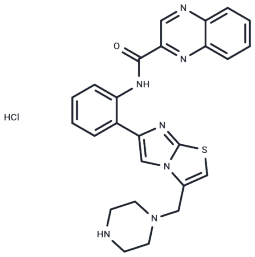
Data Sheet (Cat.No.T2412)

TargetMol

SRT1720 hydrochloride

Chemical Properties



CAS No. : 1001645-58-4

Formula: C25H24ClN7OS

Molecular Weight: 506.22

Storage: 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	SRT1720 hydrochloride (SRT1720 HCl) is a selective activator of SIRT1 (EC1.5: 0.16 μM) and shows less potent activities on SIRT2/SIRT3 (EC1.5s: 37 μM/300 μM).
Targets(IC50)	Sirtuin
In vitro	SRT1720 is an activator of SIRT1 (EC1.5 = 0.16 μM and maximum activation = 781%). SRT1720 is selective for activation of SIRT1 versus the closest sirtuin homologues, SIRT2 and SIRT3 (SIRT2: EC1.5 = 37 μM; SIRT3: EC1.5 > 300 μM) [1].
In vivo	SRT1720 exhibited a pharmacokinetic profile suitable for in vivo evaluation in both mouse (bioavailability = 50%, terminal t1/2 = ~5 h, Area Under the Curve (AUC) = 7,892 ng h/ml/) and rat (bioavailability = 25%, terminal t1/2 = ~8.4 h, AUC = 3,714 ng/h/ml). In DIO mice, fasting blood glucose levels are elevated (120–150 mg dl?1 range) after being placed on a high-fat diet. Administration of SRT1720 reduced fed glucose levels after 1 week of treatment with further reduction after 3 weeks of treatment that continued through 10 weeks of dosing. Glucose excursion during an intraperitoneal glucose tolerance test was also significantly reduced in the SRT1720 group, and comparable to rosiglitazone, a PPARγ activator that has been used to treat type 2 diabetes [1]. SRT1720 attenuated stress-induced premature cellular senescence and protected against emphysema induced by cigarette smoke and elastase in mice [2]. In animal tumour model studies, SRT1720 inhibited MM tumour growth. SRT1720 enhanced the cytotoxic activity of bortezomib or dexamethasone [3].
Kinase Assay	In the SIRT1 FP assay, SIRT1 activity was monitored using a 20 amino acid peptide (AcGlu-Glu-Lys(biotin)-Gly-Gln-Ser-Thr-Ser-Ser-His-Ser-Lys(Ac)-Nle-Ser-Thr-Glu-Gly-Lys (MR121 or Tamra)-Glu-Glu-NH2) derived from the sequence of p53. The peptide was N-terminally linked to biotin and C-terminally modified with a fluorescent tag. The reaction for monitoring enzyme activity was a coupled enzyme assay where the first reaction was the deacetylation reaction catalyzed by SIRT1 and the second reaction was cleavage by trypsin at the newly exposed lysine residue. The reaction was stopped and streptavidin was added in order to accentuate the mass differences between substrate and product. In total, 290,000 compounds were screened and 127 hits were confirmed. The sensitivity of the FP assay allowed identification of compounds that exhibited low level activation of SIRT1 (≥17% activation at 20 μM) producing multiple classes of activators representing distinct structural classes. The fluorescence polarization reaction conditions were as follows: 0.5 μM peptide substrate, 150 μM βNAD+, 0-10 nM SIRT1, 25 mM Tris-acetate pH

Kinase Assay	8, 137 mM Na-Ac, 2.7 mM K-Ac, 1 mM Mg-Ac, 0.05% Tween-20, 0.1% Pluronic F127, 10 mM CaCl2, 5 mM DTT, 0.025% BSA, and 0.15 mM nicotinamide. The reaction was incubated at 37°C and stopped by addition of nicotinamide, and trypsin was added to cleave the deacetylated substrate. This reaction was incubated at 37°C in the presence of 1 μM streptavidin. Fluorescent polarization was determined at excitation (650 nm) and emission (680 nm) wavelengths [1].
Cell Research	Cell viability was assessed with a colorimetric assay using MTT as described previously. Apoptosis assay was quantified using Annexin V-FITC/Propidium iodide (PI) apoptosis detection kit, as per manufacturer's instructions, followed by analysis on FACS Calibur [3].
Animal Research	Sirtinol (2 mg/kg) was administered by peritoneal injection, whereas SRT1720 (100 mg/kg) was administered through oral gavage 1 hour prior to CS exposure daily for 3 days. In a separate experiment, SRT1720 (25, 50, and 100 mg/kg) or PHA-408 (50 mg/kg) was dissolved in 0.5% carboxymethylcellulose containing 0.025% Tween 20 and injected via oral gavage into the conscious mice 24 hours prior to elastase administration, which was repeated daily (5 days per week) until 21 days after elastase administration. To study the therapeutic effect on emphysema, SRT1720 (100 mg/kg) was orally administered daily for 2 weeks after the development of elastase-induced emphysema [2].

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 11.3 mg/mL (22.32 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.9754 mL	9.8771 mL	19.7543 mL
5 mM	0.3951 mL	1.9754 mL	3.9509 mL
10 mM	0.1975 mL	0.9877 mL	1.9754 mL
50 mM	0.0395 mL	0.1975 mL	0.3951 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

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.
Chen W, Lin B, Xie S, et al. Naringenin protects RPE cells from NaIO3-induced oxidative damage in vivo and in vitro through up-regulation of SIRT1. Phytomedicine. 2020: 153375
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.
Wu Q, Hu Y, Jiang M, et al. Effect of Autophagy Regulated by Sirt1/FoxO1 Pathway on the Release of Factors Promoting Thrombosis from Vascular Endothelial Cells. International journal of molecular sciences. 2019, 20(17): 4132.
Su G, Yang W, Wang S, et al. SIRT1-autophagy axis inhibits excess iron-induced ferroptosis of foam cells and subsequently increases IL-1B and IL-18. Biochemical and Biophysical Research Communications. 2021, 561: 33-39.
Chauhan D, et al. Preclinical evaluation of a novel SIRT1 modulator SRT1720 in multiple myeloma cells. Br J Haematol. 2011 Dec;155(5):588-98.
Su G, Yang W, Wang S, et al. SIRT1-autophagy axis inhibits excess iron-induced ferroptosis of foam cells and subsequently increases IL-1B and IL-18[J]. Biochemical and Biophysical Research Communications. 2021, 561: 33-39.
Ma Y, Ji Y, Xu L, et al. Obesity aggravated hippocampal-dependent cognitive impairment after sleeve gastrectomy in C57/BL6J mice via SIRT1/CREB/BDNF pathway. Experimental Brain Research. 2022: 1-10.
Chen W, Lin B, Xie S, et al. Naringenin protects RPE cells from NaIO3-induced oxidative damage in vivo and in vitro through up-regulation of SIRT1[J]. Phytomedicine. 2020: 153375.
Wu Q, Hu Y, Jiang M, et al. Effect of Autophagy Regulated by Sirt1/FoxO1 Pathway on the Release of Factors Promoting Thrombosis from Vascular Endothelial Cells[J]. International journal of molecular sciences. 2019, 20(17): 4132.