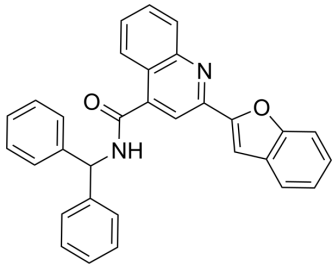
SIRT6 activator 12q

Cat. No.:	HY-148712
CAS No.:	2601734-99-8
Molecular Formula:	$C_{31}H_{22}N_2O_2$
Molecular Weight:	454.52
Target:	Apoptosis; Sirtuin
Pathway:	Apoptosis; Cell Cycle/DNA Damage; Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25 mg/mL (55.00 mM; ultrasonic and warming and heat to 70°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2001 mL	11.0006 mL	22.0012 mL
	5 mM	0.4400 mL	2.2001 mL	4.4002 mL
	10 mM	0.2200 mL	1.1001 mL	2.2001 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: ≥ 1.25 mg/mL (2.75 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SIRT6 activator 12q is potent, selective and orally active SIRT6 activator with IC_{50} values of 171.20, >200, >200, >200, 0.58 μM for SIRT1, SIRT2, SIRT3, SIRT5, SIRT6, respectively. SIRT6 activator 12q inhibits cell growth and migration. SIRT6 activator 12q induces Apoptosis and cell cycle arrest at G2 phase. SIRT6 activator 12q shows anticancer activity[1].

IC_{50} & Target

SIRT6
0.58 μM (EC1.5)

In Vitro

SIRT6 activator 12q (compound12q) (2.5, 5, 10 μM; 14, 18 days) inhibits the colony formation of PANC-1, BXPC-3, MIAPaCa-2, and AsPC-1 cells in a dose-dependent manner[1].
SIRT6 activator 12q (10, 25, 50 μM; 48 h) induces apoptosis and cell cycle arrest at G2 phase in a dose-dependent manner[1].
SIRT6 activator 12q (12.5, 25, 50 μM; 48 h) decreases the protein expression of H3K9ac, H3K18ac, and H3K56ac in PANC-1 and BXPC-3 cells in a dose-dependent manner[1].

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

Cell Viability Assay[1]

Cell Line:	PANC-1, BXPC-3, MIAPaCa-2, and AsPC-1 cells
Concentration:	0-100 μM
Incubation Time:	72 h
Result:	Showed antiproliferative activity with IC_{50}s of 4.43, 8.27, 7.10, 9.66 μM for PANC-1, BXPC-3, MIAPaCa-2, and AsPC-1 cells, respectively.

Cell Cycle Analysis[1]

Cell Line:	PANC-1, BXPC-3 cells
Concentration:	10, 25, 50 μM
Incubation Time:	48 h
Result:	Induced cell cycle arrest at G2 phase in a dose-dependent manner.

Apoptosis Analysis[1]

Cell Line:	PANC-1, BXPC-3 cells
Concentration:	10, 25, 50 μM
Incubation Time:	48 h
Result:	Induced apoptosis by increased Annexin V+ populations in a concentration-dependent manner.

Western Blot Analysis[1]

Cell Line:	PANC-1, BXPC-3 cells
Concentration:	12.5, 25, 50 μM
Incubation Time:	72 h
Result:	Decreased the protein levels of H3K9ac, H3K18ac, and H3K56ac in PANC-1 and BXPC-3 cells in a dose-dependent manner.

In Vivo

SIRT6 activator 12q (100, 150 mg/kg; p.o.; daily for 30 days) inhibites the tumer growth in a dose-dependent manner in mouse[1].

Pharmacokinetic Parameters of SIRT6 activator 12q in Male Sprague-Dawley rats[1].

PK parameter	10 mg/kg p.o.	2 mg/kg i.v.
CL (L/h/kg)		0.6 ± 0.08
Vss (L/kg)		1112.8 ± 322.84
$T_{1/2}$ (h)	7.52 ± 1.44	9.06 ± 0.21

T_{max} (h)	2.00 ± 0.00	0.08 ± 0.00
C_{max} (ng/mL)	98.45 ± 3.62	5123.70 ± 905.5
$AUC_{(0-t)}$(h·ng/mL)	704.67 ± 80.47	3326.13 ± 476.4
$AUC_{(0-\infty)}$(h·ng/mL)	755.57 ± 80.74	3381.49 ± 468.48
F (%)	4.24 ± 0.48	

Male Sprague-Dawley rats, 2 mg/kg iv; 10 mg/kg po[1]

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Animal Model:	BALB/c female nude mice (human pancreatic tumor xenograft model of PANC-1)[1]
Dosage:	100, 150 mg/kg
Administration:	P.o.; daily for 30 days
Result:	Inhibited tumer growth in a dose-dependent manner, and a tumor inhibition rate of 90.25% at a dose of 150 mg/kg.

REFERENCES

[1]. Chen X, et al. Discovery of Potent Small-Molecule SIRT6 Activators: Structure-Activity Relationship and Anti-Pancreatic Ductal Adenocarcinoma Activity. J Med Chem. 2020 Sep 24;63(18):10474-10495.

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