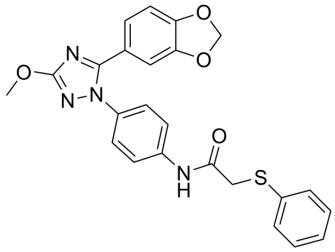
SecinH3

Cat. No.:	HY-100559
CAS No.:	853625-60-2
Molecular Formula:	$C_{24}H_{20}N_4O_4S$
Molecular Weight:	460.51
Target:	Apoptosis
Pathway:	Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 130 mg/mL (282.30 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1715 mL	10.8575 mL	21.7151 mL
	5 mM	0.4343 mL	2.1715 mL	4.3430 mL
	10 mM	0.2172 mL	1.0858 mL	2.1715 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: ≥ 3.25 mg/mL (7.06 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SecinH3 is an antagonist of cytohesins with IC_{50}s of 5.4 μM, 2.4 μM, 5.4 μM, 5.6 μM, 5.6 μM and 65 μM for hCyh1, hCyh2, mCyh3, hCyh3, drosophila steppke and yGea2-S7, respectively.

IC_{50} & Target

IC50: 5.4 μM (hCyh1)、2.4 μM (hCyh2)、5.4 μM (mCyh3)、5.6 μM (hCyh3)、5.6 μM (drosophila steppke), 65 μM (yGea2-S7)[1]

In Vitro

SecinH3 is a Sec7-specific guanine nucleotide exchange factor (GEF) inhibitor with preference for the small GEFs of the cytohesin family. SecinH3 almost completely blocks the insulin-dependent transcriptional repression of IGFBP1 with an IC_{50} of 2.2 μM. Insulin-stimulated translocation of ARF6 to the plasma membrane is also inhibited by SecinH3. It is found that SecinH3 inhibits the insulin-dependent phosphorylation of Akt and FoxO1A in a concentration-dependent manner. Insulin-induced exclusion of FoxO1A from the nucleus is completely prevented by SecinH3. The binding of IRS1 to the insulin receptor is also inhibited by SecinH3[1].

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

In Vivo	Compare to mice fed the same chow without SecinH3, the expression levels of the insulin-repressed gluconeogenic genes are elevated, whereas the insulin-induced glycolytic genes are reduced in SecinH3-treated mice. Insulin-stimulated Akt phosphorylation is also inhibited in SecinH3-treated mice. The expression of the genes for two key enzymes of mitochondrial β-oxidation, carnitine palmitoyltransferase 1a (Cpt1a) and hydroxyacyl-CoA dehydrogenase (Hadha), both of which are repressed by insulin, is increased in the SecinH3-treated mice. It is found significantly increased levels of serum insulin with slightly elevated glucose concentrations in SecinH3-treated mice. Accordingly, 3-hydoxybutyrate is increased in the serum of SecinH3-treated mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	10^5 HepG2 cells are seeded in 12 well plates and cultured for 24 h in EMEM containing 10 % FCS. Cells are then serum starved in EMEM for 24 h and stimulated for 12 h with 10 nM insulin in the presence of SecinH3, the negative control D5 or vehicle (0.2% final concentration of DMSO). Total mRNA is prepared using Kit and cDNA for qPCR is generated from 1 µg RNA. qPCR is performed and data are normalized to β_2-microglobulin expression[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	C57/Bl6N mice are kept on a 12 h light/dark cycle in a pathogen-free animal facility and fed ad libitum with standard mice diet. After feeding with standard diet or with the same diet containing 0.9 µmol/g SecinH3 for 3 days, mice are intraperitoneally injected with 100 µL saline containing or not 40 µg recombinant human insulin. After 10 min the mice are anaesthetized and the liver is removed and lysed in lysis buffer. Normalized amounts of protein are either separated by SDS-PAGE and transferred onto nitrocellulose, or immunoprecipitated using agarose-conjugated antibodies against IRβ or IRS1 [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Hafner M, et al. Inhibition of cytohesins by SecinH3 leads to hepatic insulin resistance. Nature. 2006 Dec 14;444(7121):941-4.

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