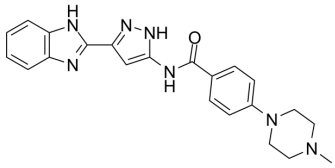
FOXO1-IN-3

Cat. No.:	HY-153617
CAS No.:	2451093-95-9
Molecular Formula:	$C_{22}H_{23}N_7O$
Molecular Weight:	401.46
Target:	Others
Pathway:	Others

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 : 100 mg/mL (249.09 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4909 mL	12.4545 mL	24.9091 mL
	5 mM	0.4982 mL	2.4909 mL	4.9818 mL
	10 mM	0.2491 mL	1.2455 mL	2.4909 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: 2.5 mg/mL (6.23 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

FOXO1-IN-3 is a highly-selective and orally active FOXO1 inhibitor. FOXO1-IN-3 reduces hepatic glucose production in mice. FOXO1-IN-3 improves insulin sensitivity and glucose control in db/db mice without causing weight gain[1].

IC_{50} & Target

FOXO1[1]

In Vitro

FOXO1-IN-3 (Compound 10) (10 μM, 6 h) suppresses cAMP/Dexamethasone (HY-14648) induced G6pc and Pck1 mRNA expression in primary hepatocytes isolated from normal mice[1].

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

RT-PCR[1]

Cell Line:	primary hepatocytes isolated from normal mice

Concentration:	10 μM
Incubation Time:	6 h
Result:	Inhibited cAMP/Dexamethasone (HY-14648) induced G6pc and Pck1 mRNA expression, and did not affect Foxo1 levels.

In Vivo

FOXO1-IN-3 (Compound 10) (16 mg/kg, p.o., twice daily, for 10 days) reduces blood glucose in db/db mice[1].

FOXO1-IN-3 (16 mg/kg, p.o., twice daily, for 7 days) and FGF21 (0.45 mg/kg) has synergistic glucose-lowering effects in Streptozotocin (HY-13753) induced β-cell-ablated diabetic mice[1].

FOXO1-IN-3 (1 mg/kg for i.v., 10 mg/kg for p.o.) shows significant plasma exposure and oral bioavailability despite relatively short half-life in mice[1].

PK properties of FOXO1-IN-3 (compound 10)

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Dose (mg/kg)	parameters	value
i.v. (1 mg/kg)	$T_{1/2}$	1.23 h
	AUCinf	1.86 μM·h
	CL	22.7 mL/kg·min
p.o. (10 mg/kg)	T_{max}	0.67 h
	AUCinf	4.66 μM·h
	F%	25.5%

Animal Model:	db/db mice[2]
Dosage:	16 mg/kg
Administration:	p.o., twice daily, for 10 days
Result:	Reduced blood glucose, increased HOMA-β (an indicator of β-cell function). Did not significantly affect insulin levels. Had no apparent effect on hepatic histology.

REFERENCES

[1]. Lee YK, et al. FOXO1 inhibition synergizes with FGF21 to normalize glucose control in diabetic mice. Mol Metab. 2021 Jul;49:101187.

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