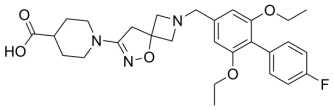
SSTR5 antagonist 1

Cat. No.:	HY-102037
CAS No.:	1628741-91-2
Molecular Formula:	$C_{28}H_{34}FN_3O_5$
Molecular Weight:	511.59
Target:	Somatostatin Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
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 : 90 mg/mL (175.92 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9547 mL	9.7735 mL	19.5469 mL
	5 mM	0.3909 mL	1.9547 mL	3.9094 mL
	10 mM	0.1955 mL	0.9773 mL	1.9547 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.25 mg/mL (4.40 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.25 mg/mL (4.40 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.25 mg/mL (4.40 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SSTR5 antagonist 1 (compound 25a) is a selective and orally available somatostatin receptor subtype 5 (SSTR5) antagonist with IC_{50}s of 9.6 and 57 nM for hSSTR5 and mSSTR5, respectively[1].

IC_{50} & Target

IC50: 9.6 nM (hSSTR5), 57 nM (mSSTR5)[1]

In Vitro

SSTR5 antagonist 1 (compound 25a) (30 μM) inhibits hERG activity by 5.6%[1].
SSTR5 antagonist 1 (10 μM) shows highly selective inhibitory effect on SSTR5 over SSTR1-4, with inhibition rates of 11%, 8%,

14%, 10%[1].
SSTR5 antagonist 1 (1 μM; 15 min and 30 min) exhibits good metabolic stability toward both human and mouse microsomes with in vitro CLint value of <10 μL/min/kg (HLM) and 19 μL/min/kg (MLM), respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

SSTR5 antagonist 1 (compound 25a) (1 mg/kg; p.o.; single dose) is orally available with acceptable plasma exposure in mice in pharmacokinetic screening and exhibits excellent solubility (260 μg/mL, pH=6.8)[1].
SSTR5 antagonist 1 (100 mg/kg; p.o.; single dose; measured at 0-120 min) augments insulin secretion in a glucose-dependent manner and lowers blood glucose concentration in high-fat diet fed C57BL/6J mice[1].
SSTR5 antagonist 1 (1, 3, 10, and 30 mg/kg; p.o.; single dose) shows dose-dependent effect on glucose excursion measured during the oral glucose tolerance test in HFD fed C57BL/6J mice[1].
Pharmacokinetic profiles in male ICR mouse (8-week-old)[1]

Route	Dose (mg/kg)	CL_{total} (mL/h/kg)	V_{ss} (mL/kg)	MRT (h)	
iv	0.1	1761	3052	1.7	/
Route	Dose (mg/kg)	C_{max} (ng/mL)	$T_{max\ (h)}$	$AUC_{0\text{-}8\ h\ (ng\cdot h/mL)}$	F (%)
po	1	74.8	2.0	332	58

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

Animal Model:	High-fat diet fed C57BL/6J mice[1]
Dosage:	100 mg/kg
Administration:	Oral gavage; single dose; monitored over 2 h
Result:	Showed the maximum efficacy superior to that of 10 mg/kg Glibenclamide (HY-15206) and comparable to that of 30 mg/kg Alogliptin (HY-A0023A). Augmented insulin secretion in a glucose-dependent manner and displayed a blood glucose-lowering effect, indicating its anti-diabetic efficacy in vivo.

REFERENCES

[1]. Hirose H, et al. Discovery of novel 5-oxa-2,6-diazaspiro[3.4]oct-6-ene derivatives as potent, selective, and orally available somatostatin receptor subtype 5 (SSTR5) antagonists for treatment of type 2 diabetes mellitus. Bioorg Med Chem. 2017 Aug 1;25(15):4175-4193.

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