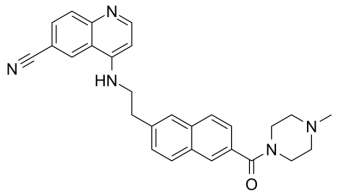
Senexin C

Cat. No.:	HY-143889
CAS No.:	2375554-02-0
Molecular Formula:	$C_{28}H_{27}N_5O$
Molecular Weight:	449.55
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
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 : 33.33 mg/mL (74.14 mM; ultrasonic and warming and heat to 160°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2244 mL	11.1222 mL	22.2445 mL
	5 mM	0.4449 mL	2.2244 mL	4.4489 mL
	10 mM	0.2224 mL	1.1122 mL	2.2244 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.56 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Senexin C is a selective and orally active CDK8/19 inhibitor. Senexin C shows a strong tumor-enrichment pharmacokinetic (PK) profile and tumor-pharmacodynamic (PD) marker responses. Senexin C inhibits the growth of MV4-11 leukemia cells with good tolerability[1].

IC_{50} & Target			
	CDK8/CycC 3.6 nM (IC_{50})	CDK19/CycC 2.9 nM (Kd)	CDK8/CycC 1.4 nM (Kd)

In Vitro

Senexin C (compound 20a) exhibits potent CDK8/19 inhibitory activity with high selectivity (IC_{50}s of 56 and 108 nM for 293-NFκB-Luc and MV4-11-Luc cells, respectively)[1].

Senexin C (2 μM) shows potency in different kinase assays (IC_{50}= 3.6 nM for CD8/CycC, Kd=1.4 nM for CD8/CycC, Kd=2.9 nM for CDK19/CycC)[1].

Senexin C (1 μM, 3 h) shows inhibition on CDK8/19 dependent cellular gene expression[1].

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

RT-PCR[1]

Cell Line:	293 cells
Concentration:	1 μM
Incubation Time:	3 h
Result:	Showed inhibition on CDK8/19 dependent cellular gene expression.

In Vivo

Senexin C (2.5 mg/kg, i.v.; 100 mg/kg, p.o.) shows good oral bioavailability[1].

Senexin C (40 mg/kg; p.o.; twice daily for 4 weeks) suppresses the systemic growth of MV4-11 AML with good tolerability[1].

Pharmacokinetic Parameters of Senexin C in eight-week-old female Balb/c mice[1].

parameters	iv (2.5 mg/kg)		po (100 mg/kg)	
	plasma	tumor	plasma	tumor
C_0 (μg/mL)	503			
K_{el} (h^{-1})	0.93	0.06	0.2	0.1
$T_{1/2}$ (h)	0.75	12.1	3.53	7.27
T_{max} (h)		0.58	12	12
C_{max} (ng/mL or ng/g)		488	144	5728
AUC0-24 h (ng x h/ml or ng x h/g)	331	6408	2182	88,600
F%			16.5%	34.6%

Eight-week-old female Balb/c mice (CT26 tumor mode), 2.5 mg/kg, i.v.(2.5 mg/mL Senexin C solution in 5% dextrose); 100 mg/kg, p.o.(10 mg/mL Senexin C solution in 30% propylene glycol/70% PEG-400 vehicle)[1].

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

Animal Model:	eight-week-old female Balb/c mice (CT26 tumor mode)[1]
Dosage:	2.5 mg/kg (10 mL/kg of 2.5 mg/mL Senexin C solution in 5% dextrose), 100 mg/kg (10 mL/kg of 10 mg/mL Senexin C solution in 30% propylene glycol/70% PEG-400 vehicle)
Administration:	2.5 mg/kg, i.v.; 100 mg/kg, p.o.
Result:	Showed good oral bioavailability.

Animal Model:	eight-week-old female NSG mice (AML model)[1]
Dosage:	40 mg/kg
Administration:	p.o.; twice daily, 4 weeks

Result:	Suppressed the systemic growth of MV4-11 AML with good tolerability.

REFERENCES

[1]. Zhang L, et al. A Selective and Orally Bioavailable Quinoline-6-Carbonitrile-Based Inhibitor of CDK8/19 Mediator Kinase with Tumor-Enriched Pharmacokinetics. J Med Chem. 2022; 65(4):3420-3433.

Caution: Product has not been fully validated for medical applications. For research use only.

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