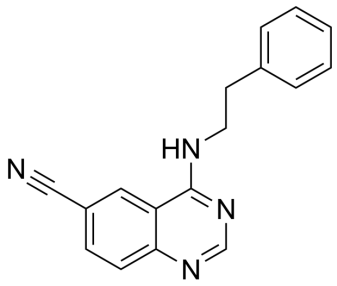
Senexin A

Cat. No.:	HY-15681
CAS No.:	1366002-50-7
Molecular Formula:	$C_{17}H_{14}N_4$
Molecular Weight:	274.32
Target:	CDK
Pathway:	Cell Cycle/DNA Damage
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 : ≥ 100 mg/mL (364.54 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.6454 mL	18.2269 mL	36.4538 mL
5 mM	0.7291 mL	3.6454 mL	7.2908 mL
10 mM	0.3645 mL	1.8227 mL	3.6454 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: ≥ 2.5 mg/mL (9.11 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (9.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Senexin A is an inhibitor of CDK8/19 (IC_{50}: 280 nM, CDK8) and an inhibitor downstream of p21 transcription. It only inhibits p21-induced transcription but does not inhibit other biological effects of p21. Senexin A inhibits CMV-GFP induction as well as the p21 stimulatory activity of the consensus NF-κB-dependent promoters[1][2].

IC_{50} & Target

CDK19	CDK8	CDK8
0.31 μM (Kd)	0.83 μM (Kd)	280 nM (IC_{50})

In Vitro

Senexin A inhibits CDK8 and CDK19 ATP site binding with K_d50 of 0.83 μM and 0.31 μM, respectively[1].
Senexin A inhibits β-catenin-dependent transcription in HCT116 colon cancer cells[1].

	In HT1080 cells, Senexin A strongly inhibits the induction of the transcription factor EGR1 upon serum starvation[1]. Senexin A also reduces the expression of many secreted tumor-promoting factors in doxorubicin-treated wild-type HCT116 cells[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Five daily treatment of Senexin A fully reverses tumor-promoting effect of chemotherapy. Senexin A shows no detectable toxicity and no significant effects on body weight, organ weights, or blood cell counts in C57BL/6 mice during the treatment. This effect of doxorubicin treatment is completely abolished, however, when doxorubicin injection is followed by administration of Senexin A. Senexin A treatment strongly improves the response of A549/MEF tumors to doxorubicin[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice: Senexin A toxicity study is conducted by Taconic in C57BL/6 mice, using five mice per group treated with 20 mg/kg Senexin A or carrier (80% propylene glycol), with five daily i.p. injections. Mice are weighed on days 3 and 6, and killed on day 6. Organ weights are determined for brain, kidney, thymus, spleen, lung, and liver. Terminal blood samples are analyzed to determine the numbers of total white blood cells, neutrophils, lymphocytes, monocytes, eosinophils, and basophils[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nucleic Acids Res. 2021 Feb 22;49(3):1470-1484.
- Cell Death Dis. 2020 Sep 15;11(9):754.
- Viruses. 2020 Jun 17;12(6):654.
- J Cell Biochem. 2019 Aug;120(8):14095-14106.
- FEBS Lett. 2021 May 31.

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REFERENCES

[1]. Ho TY, et al. The study of a novel CDK8 inhibitor E966-0530-45418 that inhibits prostate cancer metastasis in vitro and in vivo. Biomed Pharmacother. 2023 Jun;162:114667.

[2]. Porter DC, et al. Cyclin-dependent kinase 8 mediates chemotherapy-induced tumor-promoting paracrine activities. Proc Natl Acad Sci U S A. 2012 Aug 21;109(34):13799-804.

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