Cyclopamine

Cat. No.: HY-17024

CAS No.: 4449-51-8

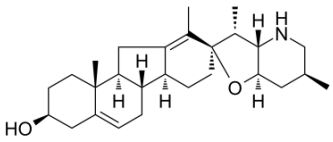
Molecular Formula: $C_{27}H_{41}NO_2$

Molecular Weight: 411.62

Target: Hedgehog; Smo; Endogenous Metabolite

Pathway: Stem Cell/Wnt; Metabolic Enzyme/Protease

Storage: Powder -20°C 3 years
4°C 2 years
* The compound is unstable in solutions, freshly prepared is recommended.



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 16.67 mg/mL (**40.50 mM;** Need ultrasonic)
DMSO : 5 mg/mL (**12.15 mM;** Need ultrasonic and warming)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	2.4294 mL	12.1471 mL	24.2943 mL
	5 mM	0.4859 mL	2.4294 mL	4.8589 mL
	10 mM	0.2429 mL	1.2147 mL	2.4294 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: ≥ 0.5 mg/mL (1.21 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline**
   Solubility: ≥ 0.5 mg/mL (1.21 mM); Clear solution
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 0.5 mg/mL (1.21 mM); Clear solution
4. Add each solvent one by one: **10% EtOH >> 90% corn oil**
   Solubility: ≥ 1.67 mg/mL (4.06 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cyclopamine is a **Hedgehog** (**Hh**) pathway antagonist with an **IC_{50}** of 46 nM in the Hh cell assay. Cyclopamine is also a selective **Smo** inhibitor.

IC_{50} & Target	Human Endogenous Metabolite
In Vitro	Treatment with small molecule Hh inhibitors such as HhAntag and the natural product Cyclopamine, both binding to Smo, induces tumor remission in a genetic mouse model of medulloblastoma[1]. Cyclopamine is a Hedgehog (Hh) pathway antagonist. Cyclopamine suppresses cell growth. Cyclopamine (3 μM) suppression of Hh pathway activity and growth in digestive tract tumour cell lines correlates with expression of PTCHmRNA[2]. Cyclopamine is a steroidal alkaloid that inhibits Hh signalling through direct interaction with Smo[3].
In Vivo	Cyclopamine causes durable regression of xenograft tumors. Tumors in Cyclopamine-treated animals, regress completely by 12 days[2]. Cyclopamine (1.2 mg) treatment blocks tumour formation of human pancreatic adenocarcinoma cells after transplantation into nude mice[3].

PROTOCOL

Cell Assay [2]	Cells are cultured in triplicate in 96-well plates in assay media to which 5E1 monoclonal antibody, ShhNp and/or Cyclopamine (3 μM) are added at 0 h at concentrations indicated in the main text. Viable cell mass is determined by optical density measurements at 490 nm (OD_{490}) at 2 and 4 days using the CellTiter96 colorimetric assay. Relative growth is calculated as OD (day 4)-OD (day 2)/OD (day 2)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] A total of 0.1 mL Hanks' balanced salt solution and matrigel (1:1) containing 2×10^6 cells is injected subcutaneously into CD-1 nude mice. Tumors are grown for 4 days to a minimum volume of 125 mm^3; treatment is initiated simultaneously for all subjects. Mice are injected subcutaneously with vector alone (triolein:ethanol 4:1 v/v) or a Cyclopamine suspension (1.2 mg per mouse in triolein:ethanol 4:1 v/v) daily for 7 days. At the end of the treatment period, tumours are excised from mice, weighed and then fixed for 3 h at 4°C with 4% paraformaldehyde, embedded in paraffin wax and sectioned (6 μm). Apoptotic cells are identified by TUNEL using recombinant Tdt. Sections are then counterstained with eosin. Eight ×20-magnified fields from regions corresponding to the exterior, middle and interior of two control and two cyclopamine-treated tumours are chosen at random. We counted the number of TUNEL-positive nuclei manually. Haematoxylin/eosin staining is done. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- **Cell Death Dis**. 2019 Sep 12;10(9):681.
- **Int J Nanomedicine**. 2017 Apr 20;12:3267-3280.
- **J Genet Genomics**. 2018 May 20;45(5):237-246.
- **FASEB J**. 2018 Oct;32(10):5703-5715.
- **iScience**. 2019 Sep 27;19:1248-1259.

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REFERENCES

[1]. Peukert S, et al. Identification and structure-activity relationships of ortho-biphenyl carboxamides as potent Smoothened antagonists inhibiting the Hedgehog signaling pathway. Bioorg Med Chem Lett, 2009, 19(2), 328-331.

[2]. Berman DM, et al. Widespread requirement for Hedgehog ligand stimulation in growth of digestive tract tumours. Nature, 2003, 425(6960), 846-851.

[3]. Thayer SP, et al. Hedgehog is an early and late mediator of pancreatic cancer tumorigenesis. Nature, 2003, 425(6960), 851-856.

[4]. Ma W, et al. Reduced Smoothened level rescued Aβ-induced memory deficits and neuronal inflammation in animal models of Alzheimer's disease. J Genet Genomics. 2018 May 20;45(5):237-246.

[5]. Qi Wan, et al. Overexpression of Laminin α4 Facilitates Proliferation and Migration of Fibroblasts in Knee Arthrofibrosis by Targeting Canonical Shh/Gli1 Signaling. Connect Tissue Res. 2020 May 24.

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