# Cyclopamine

**Cat. No.:** HY-17024

**CAS No.:** 4449-51-8

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

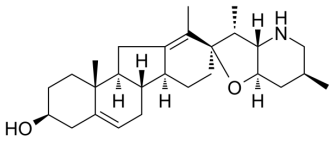
**Molecular Weight:** 411.62

**Target:** Hedgehog; Endogenous Metabolite; Smo

**Pathway:** Stem Cell/Wnt; Metabolic Enzyme/Protease

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 6 months |
| | -20°C | 1 month |



## SOLVENT & SOLUBILITY

**In Vitro**

Ethanol : 20 mg/mL (48.59 mM; Need ultrasonic)

DMSO : 10 mg/mL (24.29 mM; ultrasonic and warming and heat to 80°C)

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 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% EtOH >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (4.06 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1 mg/mL (2.43 mM); Clear solution
3. 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
4. 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

## 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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## 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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [3] | Mice[3]<br>A total of 0.1 mL Hanks' balanced salt solution and matrigel (1:1) containing $2\times10^6$ 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.<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- Nat Commun. 2022 Jul 13;13(1):4061.
- Cell Death Differ. 2021 Jul;28(7):2221-2237.
- Pharmacol Res. 2021 Jan 26;105460.
- Cell Death Dis. 2019 Sep 12;10(9):681.
- Int J Nanomedicine. 2017 Apr 20;12:3267-3280.

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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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