Silvestrol

Cat. No.: HY-13251

CAS No.: 697235-38-4

Molecular Formula: $C_{34}H_{38}O_{13}$

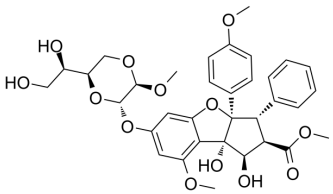
Molecular Weight: 654.66

Target: Eukaryotic Initiation Factor (eIF); Apoptosis; Autophagy

Pathway: Cell Cycle/DNA Damage; Apoptosis; Autophagy

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 : ≥ 6.6 mg/mL (10.08 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.5275 mL	7.6376 mL	15.2751 mL
5 mM	0.3055 mL	1.5275 mL	3.0550 mL
10 mM	0.1528 mL	0.7638 mL	1.5275 mL

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

In Vivo

1. Silvestrol is prepared in 5.2% Tween 80 5.2% PEG 400[6].
2. Silvestrol is dissolved in 20%(w/v) 2-hydroxyproply beta-cyclodextrin vehicle at a concentration of 125 μg/mL and injected into mice i.p.[7].
3. Silvestrol is formulated in 30% 2-hydroxypropyl-β-cyclodextrin[8].

BIOLOGICAL ACTIVITY

Description

Silvestrol is a eukaryotic translation initiation factor 4A (eIF4A) inhibitor isolated from Agave americana Linn.. Silvestrol induces autophagy and caspase-mediated apoptosis[1][2][3].

IC_{50} & Target

eIF4A[1]

In Vitro

Silvestrol is a specific eIF4A-targeting translation inhibitor. Silvestrol exhibits significant cytotoxic activity against many human cancer cell lines, such as lung, prostate, and breast cancer with IC_{50} values ranging from 1 to 7 nM[1].

	Silvestrol significantly reduces the number of LNCaP cell colonies. Silvestrol (30 nM, 120 nM) induces apoptosis in LNCaP cells, through the mitochondrial pathway. Apaf-1, Caspase-2, caspase-9, and caspase-10 are involved in Silvestrol-induced apoptosis but caspase-3 and 7 are not[2]. Silvestrol induces caspase-3 activation and apoptotic cell death in a time- and dose-dependent manner. Silvestrol-mediated cell death is attenuated in ATG7-null mouse embryonic fibroblasts (MEFs) lacking a functional autophagy protein[3]. Silvestrol (50 nM) exerts an immediate inhibitory effect and causes near-static cell index compared with the control cells. Silvestrol (6.25 nM) enhances proliferation more than the vehicle control-treated cells, whereas a higher concentration of Silvestrol (50 nM) can inhibit cell proliferation. Silvestrol and episilvestrol display synergistic effects in combination with CDDP[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Silvestrol (1.5 mg/kg, i.p.) does not adversely affect production of human IgG by xenografted B-lymphocytes in mice. Silvestrol significantly prolongs survival compared to vehicle. There is no such lymphocyte infiltration detected in the spleens of any of the Silvestrol-treated mice, and nor do these animals exhibit any other obvious signs of lymphoma upon necropsy[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The cells are seeded at a density of 7×10^4 cells/mL in 100-mm culture dishes and are treated with 30 nM or 120 nM concentrations of Silvestrol for 24 h[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [5]	Mice[5] Peripheral blood mononuclear cells (PBMC) are injected intraperitoneally (IP) into SCID mice depleted of murine natural killer (NK) cells by pretreatment (plus weekly re-treatment) with anti-asialo (GM1). Engraftment is confirmed by hu-IgG ELISA. Treatments with vehicle (30% hydroxypropyl-β-cyclodextrin) or Silvestrol (1.5 mg/kg every 48 hr IP) begin 2 weeks post-engraftment[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2014 Sep 4;513(7516):65-70.
- Cancer Discov. 2015 Jul;5(7):768-81.
- Blood. 2014 Dec 11;124(25):3758-67.
- Mol Cell. 2022 May 5;S1097-2765(22)00327-6.
- Mol Cell. 2021 Feb 18;81(4):708-723.e5.

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REFERENCES

[1]. Chambers JM, et al. Synthesis of biotinylated episilvestrol: highly selective targeting of the translation factors eIF4AI/II. Org Lett. 2013 Mar 15;15(6):1406-9.

[2]. Kim S, et al. Silvestrol, a potential anticancer rocaglate derivative from Aglaia foveolata, induces apoptosis in LNCaP cells through the mitochondrial/apoptosome pathway without activation of executioner caspase-3 or -7. Anticancer Res. 2007 Jul-Aug;27(4B):2175-83.

[3]. Chen WL, et al. Silvestrol induces early autophagy and apoptosis in human melanoma cells. BMC Cancer. 2016 Jan 13;16:17.

[4]. Daker M, et al. Inhibition of nasopharyngeal carcinoma cell proliferation and synergism of CDDP with silvestrol and episilvestrol isolated from Aglaia stellatopilosa. Exp Ther Med. 2016 Jun;11(6):2117-2126.

[5]. Patton JT, et al. The translation inhibitor silvestrol exhibits direct anti-tumor activity while preserving innate and adaptive immunity against EBV-driven lymphoproliferative disease. Oncotarget. 2015 Feb 20;6(5):2693-708.

[6]. Wolfe AL, et al. RNA G-quadruplexes cause eIF4A-dependent oncogene translation in cancer. Nature. 2014 Sep 4;513(7516):65-70.

[7]. Wiegering A, et al. Targeting Translation Initiation Bypasses Signaling Crosstalk Mechanisms That Maintain High MYC Levels in Colorectal Cancer. Cancer Discov. 2015 Jul;5(7):768-781.

[8]. Todt D, et al. The natural compound silvestrol inhibits hepatitis E virus (HEV) replication in vitro and in vivo. Antiviral Res. 2018 Sep;157:151-158.

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