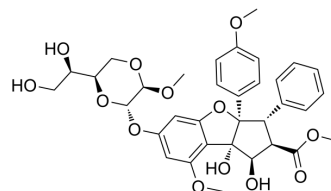


Silvestrol

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	1 year
		-20°C	6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (152.75 mM; Need ultrasonic)
 H₂O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (3.82 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
 Solubility: ≥ 2.5 mg/mL (3.82 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (3.82 mM); Clear solution

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]}.

IC₅₀ & Target

eIF4

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 IC₅₀ 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 7×10⁴ 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.
- Nat Commun. 2019 Jul 1;10(1):2901.
- Mol Cell. 2022 May 5;S1097-2765(22)00327-6.

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REFERENCES

- [1]. Chambers JM, et al. Synthesis of biotinylated episilvestrol: highly selective targeting of the translation factors eIF4A/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.

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

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