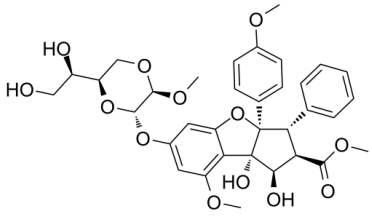
Data Sheet

Product Name:	Silvestrol
Cat. No.:	CS-0543
CAS No.:	697235-38-4
Molecular Formula:	C34H38O13
Molecular Weight:	654.66
Target:	Apoptosis; Autophagy; Eukaryotic Initiation Factor (eIF)
Pathway:	Apoptosis; Autophagy; Cell Cycle/DNA Damage
Solubility:	H2O : < 0.1 mg/mL (insoluble); DMSO : ≥ 6.6 mg/mL (10.08 mM)



BIOLOGICAL ACTIVITY:

Silvestrol is a eukaryotic translation initiation factor 4A (**eIF4A**) inhibitor isolated from the fruits and twigs of Aglaia foveolata. Silvestrol induces **autophagy** and caspase-mediated **apoptosis**[1][2][3]. IC50 & 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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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].

Animal Administration: Silvestrol is formulated in 30% hydroxypropyl-β-cyclodextrin[5].[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].

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.

CAIndexNames:

1H-Cyclopenta[b]benzofuran-2-carboxylic acid, 6-[[(2S,3R,6R)-6-[(1R)-1,2-dihydroxyethyl]-3-methoxy-1,4-dioxan-2-yl]oxy]-2,3,3a,8b-tetrahydro-1,8b-dihydroxy-8-methoxy-3a-(4-methoxyphenyl)-3-phenyl-, methyl ester, (1R,2R,3S,3aR,8bS)-

SMILES:

O=C([C@H]([C@H]1C2=CC=CC=C2)[C@@H](O)[C@]3(O)[C@@]1(C4=CC=C(OC)C=C4)OC5=CC(O[C@@H]6O[C@@H]([C@H](O)CO)CO[C@H]6OC)=CC(OC)=C35)OC

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