

Product Data Sheet

Product Name: Silvestrol

Cat. No.: GC11455

Chemical Properties

Cas. No. 697235-38-4

Chemical Name methyl (1R,2R,3S,3aR,8bS)-6-[[[(3R,6R)-6-[(1R)-1,2-dihydroxyethyl]-3-methoxy-1,4-dioxan-2-yl]oxy]-1,8b-dihydroxy-8-methoxy-3a-(4-methoxyphenyl)-3-phenyl-2,3-dihydro-1H-cyclopenta[b][1]benzofuran-2-carboxylate

SMILES COC1C(OC(CO1)C(CO)O)OC2=CC(=C3C(=C2)OC4(C3(C(C(C4C5=CC=CC=C5)C(=O)OC)O)O)C6=CC=C(C=C6)OC)OC

Formula C₃₄H₃₈O₁₃

M.Wt 654.66

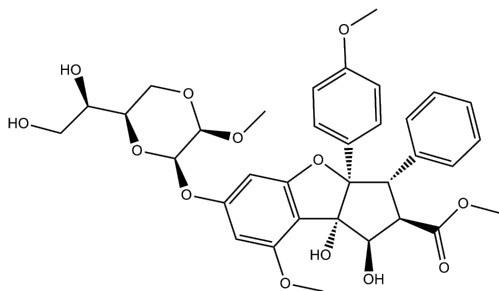
Solubility Soluble in DMSO

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Human HCC cells

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

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Preparation method This compound is soluble in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.

Reacting condition 0 ~ 200 nM; 72 hrs

Applications Silvestrol potently inhibited human HCC cell growth in a concentration-dependent manner, with an IC₅₀ value of 23.9 nM in PLC/PRF-5 cells, 12.5 nM in Hep-3B cells, 14.6 nM in Huh-7 cells and 86 nM in HepG2 cells.

Animal experiment [1]:

Animal models Nude mice bearing human HCC xenografts

Dosage form 0.4 or 1 mg/kg; i.p.; 5 days/week, for 4 weeks

Applications In nude mice bearing human HCC xenografts, a therapeutic response was observed in 36.4% of mice receiving 1 mg/kg Silvestrol and in 20% of mice receiving 0.4 mg/kg Silvestrol. At both doses, Silvestrol significantly increased the survival.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Kogure T, Kinghorn AD, Yan I, Bolon B, Lucas DM, Grever MR, Patel T. Therapeutic potential of the translation inhibitor silvestrol in hepatocellular cancer. PLoS One. 2013;8(9):e76136. doi: 10.1371/journal.pone.0076136.

Background

Silvestrol inhibited protein synthesis in MDA-MB-231 breast and PC-3 prostate cancer cell lines with IC₅₀ ~60 nM following a 1 h exposure) [1]. Silvestrol inhibited cell growth with an IC₅₀ of 12.5-86 nM in four different HCC cell lines [3].

Silvestrol, a member of flavagline family of natural products from the genus of *Aglaia* exhibiting anti-cancer activity in vitro and in vivo and inhibiting translation initiation, was shown to be capable of modulating chemosensitivity in a mechanism-based mouse model.

Preclinical study: A previous study demonstrated that silvestrol showed antileukemia activity at nanomolar concentrations in both FLT3-wt overexpressing (THP-1) and FLT3-ITD (MV4-11) expressing AML cell lines (IC₅₀ = 3.8 and 2.7 nM, respectively) and patients' primary blasts [IC₅₀ = ~12 nM (FLT3-wt) and ~5 nM (FLT3-ITD)]. Moreover, silvestrol was observed to efficiently inhibit FLT3 translation resulting in a decrease of FLT3 protein expression by 80–90%. Animal study indicated that the median survival of silvestrol-treated mice significantly increased (silvestrol-treated vs vehicle-treated = 63 vs 29 days postengraftment) [2]. Another study showed that silvestrol could increase the activities of apoptosis and caspase 3/7. In vivo, the antitumor effect was found with 0.4 mg/kg silvestrol, and the survival of tumor-bearing mice was improved with a median survival time of 42 and 28 days in the silvestrol and control groups, respectively [3].

Clinical study: Currently, there is no clinical data about the anti-cancer efficacy of silvestrol. A grant application proposed to pursue a Phase I clinical trial to assess the safety, maximum tolerated dose, pharmacokinetic and pharmacodynamic properties, and preliminary efficacy of silvestrol in patients with relapsed, refractory Chronic Lymphocytic leukemia (Pre-Clinical and Clinical Development of Silvestrol in Chronic Lymphocytic).

References:

[1] Cencic R, Carrier M, Galicia-Vázquez G, Bordeleau ME, Sukarieh R, Bourdeau A, Brem B, Teodoro JG, Greger H, Tremblay ML, Porco JA Jr, Pelletier J Antitumor activity and mechanism of action of the cyclopenta[b]benzofuran, silvestrol. PLoS One. 2009;4(4):e5223. doi:

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10.1371/journal.pone.0005223.

[2] Alachkar H, Santhanam R, Harb JG, Lucas DM, Oaks JJ, Hickey CJ, Pan L, Kinghorn AD, Caligiuri MA, Perrotti D, Byrd JC, Garzon R, Grever MR, Marcucci G. *Silvestrol exhibits significant in vivo and in vitro antileukemic activities and inhibits FLT3 and miR-155 expressions in acute myeloid leukemia. J Hematol Oncol. 2013;6:21. doi: 10.1186/1756-8722-6-21.*

[3] Kogure T, Kinghorn AD, Yan I, Bolon B, Lucas DM, Grever MR, Patel T. *Therapeutic potential of the translation inhibitor silvestrol in hepatocellular cancer. PLoS One. 2013;8(9):e76136. doi: 10.1371/journal.pone.0076136.*

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