2-Methoxyestradiol

Cat. No.: HY-12033
CAS No.: 362-07-2
Molecular Formula: C₁₉H₂₆O₃
Molecular Weight: 302.41
Target: Apoptosis; Microtubule/Tubulin; Autophagy; Endogenous Metabolite
Pathway: Apoptosis; Cell Cycle/DNA Damage; Cytoskeleton; Autophagy; 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
DMSO : ≥ 100 mg/mL (330.68 mM)
H₂O : < 0.1 mg/mL (insoluble)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>3.3068 mL</td>
<td>16.5338 mL</td>
<td>33.0677 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.6614 mL</td>
<td>3.3068 mL</td>
<td>6.6135 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3307 mL</td>
<td>1.6534 mL</td>
<td>3.3068 mL</td>
</tr>
</tbody>
</table>

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

In Vivo
1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (8.27 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.27 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.27 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
2-Methoxyestradiol (2-ME2), an orally active endogenous metabolite of 17β-estradiol (E2), is an apoptosis inducer and an angiogenesis inhibitor with potent antineoplastic activity. 2-Methoxyestradiol also destabilize microtubules.
2-Methoxyestradiol (2-ME) (5-100 μM) inhibits assembly of purified tubulin in a concentration-dependent manner, with maximal inhibition (60%) at 200 μM 2-Methoxyestradiol (2ME2). In living interphase MCF7 cells at the IC₅₀ for mitotic arrest (1.2 μM), 2-Methoxyestradiol significantly suppresses the mean microtubule growth rate, duration, and length, and the overall dynamicity, consistent with its effects in vitro, and without any observable depolymerization of microtubules. 2-Methoxyestradiol induces G₂-M arrest and apoptosis in many actively dividing cell types while sparing quiescent cells. 2-Methoxyestradiol binds to tubulin at or near the colchicine site, it inhibits microtubule assembly, and high concentrations have been shown to depolymerize microtubules in cells[1].

2-Methoxyestradiol (2-ME) decreases the HIF-1α and HIF-2α nuclear staining in cells cultured under hypoxia. 2-Methoxyestradiol is an anti-angiogenic, anti-proliferative and pro-apoptotic agent that suppresses HIF-1α protein levels and its transcriptional activity. A significant decrease in the growth rate is found in the 10 μM 2-Methoxyestradiol-treated A549 cells in comparison with the DMSO-treated cells (66.2±7.2 and 101.2±2.3%, respectively; p=0.04) at 96 h. A significant increase in apoptosis is observed in cells treated with 10 μM 2-Methoxyestradiol in a normoxic condition in comparison with cells under lower O₂ concentration (5.8±0.2%; p=0.003) [2].

To investigate the effect of 2-Methoxyestradiol (2-ME2) on uveitis development, C57BL/6 mice are randomly assigned into two groups and immunized with IRBP peptide. 2ME2 group starts 2-Methoxyestradiol (15 mg/kg) intraperitoneally from day 0 to day 13 while control group is given with vehicle. The disease score of 2-Methoxyestradiol (2ME2) group is 0.30±0.30, significantly lower than that of control group 2.09±0.28 (p<0.05), each group containing 5 mice[3].

Treatment with 2-Methoxyestradiol (60-600 mg/kg/d) results in a dose-dependent inhibition of tumor growth. The percentage of cells with strong pimonidazole-positive staining (+++) is significantly decreased in the 2-Methoxyestradiol-treated group (36.0% for 60 mg/kg/d and 0% for 200 and 600 mg/kg/d) compare with the vehicle-treated group (86.5%). This may be attributed to the dramatic inhibition of tumor growth in a dose-dependent manner following 2-Methoxyestradiol treatment[4].

**PROTOCOL**

**Kinase Assay [1]**

Microtubule protein (2.75 mg/mL) is assembled to steady-state [in 100 mM PIPES containing 1 mM EGTA and 1 mM MgSO₄ (PEM100) and 1 mM GTP, 35°C for 45 minutes] containing 2-Methoxyestradiol (final drug concentrations of 1-500 μM). Final DMSO and ethanol concentrations are adjusted to 1% and 5%, respectively. Concentrations of 2-Methoxyestradiol ≤ 5 μM have no effect on microtubule polymer mass, and thus 20 to 500 μM 2-Methoxyestradiol is used for most of the experiments. Incubation with 2-Methoxyestradiol is carried out for 30 minutes, at which time microtubule depolymerization is maximal, and microtubules are centrifuged at 35°C for 30 minutes and the supernatant is removed from the pellets. Microtubule pellets are solubilized overnight in 0.2 M NaOH and the protein concentrations of supernatants and pellets are determined[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Cell Assay [1]**

MCF7 breast carcinoma cells stably transfected with green fluorescent protein (GFP)-α-tubulin are cultured in DMEM supplemented with nonessential amino acids, 0.1% penicillin/streptomycin, 10% fetal bovine serum, and 0.4 mg/mL G418 at 37°C in 5% CO₂. Transfection of MCF7 cells with GFP-α-tubulin is carried out. To evaluate mitotic indices, cells are plated at a concentration of 6×10⁴/2 mL into six-well plates. After 48 hours, cells are incubated in the absence or presence of 2-Methoxyestradiol at concentrations ranging from 100 nM to 30 μM for 20 hours. To collect both floating and attached cells, medium is collected; attached cells are rinsed with Versene (137 mM NaCl, 2.7 mM KCl, 1.5 mM KH₂PO₄, 8.1 mM Na₂HPO₄, and 0.5 mM EDTA), detached by trypsinization, and added back to the medium. Cells are collected by centrifugation and fixed with 10% formalin for 30 minutes, permeabilized in ice-cold methanol for 10 minutes, and stained with 4',6-diamidino-2-phenylindole to visualize nuclei. Results are the mean and SE of seven experiments in each of which 500 cells are counted for each concentration. The mitotic IC₅₀ is the
drug concentration that induced one half of the maximal mitotic accumulation\[1\]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

| Animal Administration [3][4] | Mice\[3\] 6~8-week-old C57BL/6 mice are used. C57BL/6 mice are immunized subcutaneously 0.1 mL at tail and 0.05 mL at both thigh sites with IRBP antigen complex. 500 ng Pertussis toxin is injected concurrently. This day is settled as day 0. Then mice are divided into 4 groups, each group containing 5 mice. 15 mg/kg 2-Methoxyestradiol or vehicle is abdominal injected during 0-13 days, 0-6 days, and 7-13 days. At day 14 eyes or lymphoglandula is collected after euthanasia.  
Rats\[4\] Fischer 344 rats (average body weight=150 g, n=6 per group) are treated with an i.p. injection of the vehicle (60, 200, or 600 mg/kg/d of 2-Methoxyestradiol/Panzem) for nine consecutive days beginning on the 8th day after the initial tumor cell injection. The experiment is repeated a second time using three rats per group. MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

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- Aquaculture. 2020 Apr.

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**REFERENCES**


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

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