Disulfiram

Cat. No.: HY-B0240
CAS No.: 97-77-8
Molecular Formula: C₁₀H₂₀N₂S₄
Molecular Weight: 296.54
Target: Aldehyde Dehydrogenase (ALDH); Interleukin Related
Pathway: Metabolic Enzyme/Protease; Immunology/Inflammation
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: 75 mg/mL (252.92 mM; Need ultrasonic)

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<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></td>
<td>3.3722 mL</td>
<td>16.8611 mL</td>
<td>33.7223 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td></td>
<td>0.6744 mL</td>
<td>3.3722 mL</td>
<td>6.7445 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td></td>
<td>0.3372 mL</td>
<td>1.6861 mL</td>
<td>3.3722 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 (8.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.43 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.43 mM); Clear solution
4. Add each solvent one by one: 2% DMSO >> 40% PEG300 >> 5% Tween-80 >> 53% saline
   Solubility: 3.43 mg/mL (11.57 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description
Disulfiram (Tetraethylthiuram disulfide) is a specific inhibitor of aldehyde-dehydrogenase (ALDH1), used for the treatment of chronic alcoholism by producing an acute sensitivity to alcohol. Disulfiram inhibits gasdermin D (GSDMD) pore formation in liposomes and inflammasome-mediated pyroptosis and IL-1β secretion in human and mouse cells[1-4].
**IC₅₀ & Target**

**IL-1β**

**In Vitro**

Disulfiram-copper complex potently inhibits the proteasomal activity in cultured breast cancer MDA-MB-231 and MCF10DCIS.com cells, but not normal, immortalized MCF-10A cells, before induction of apoptotic cancer cell death. Disulfiram (DS), a clinically used anti-alcoholism drug, strongly inhibits constitutive and 5-FU-induced NF-kappaB activity in a dose-dependent manner. Disulfiram inhibits both NF-kappaB nuclear translocation and DNA binding activity but has no effect on 5-FU-induced IkappaBalpha degradation. Disulfiram significantly enhances the apoptotic effect of 5-FU on DLD-1 and RKO(WT) cell lines and synergistically potentiated the cytotoxicity of 5-FU to both cell lines. Disulfiram also effectively abolishes 5-FU chemoresistance in a 5-FU resistant cell line H630(5-FU) in vitro.

Oseltamivir decreases the number of viable cells, and the addition of CuCl₂ significantly enhances the DSF-induced cell death to less than 10% of control. Disulfiram given to melanoma cells in combination with Cu²⁺ or Zn²⁺ decreases expression of cyclin A and reduces proliferation in vitro at lower concentrations than disulfiram alone.

**In Vivo**

Disulfiram significantly inhibits the tumor growth (by 74%), associated with in vivo proteasome inhibition (as measured by decreased levels of tumor tissue proteasome activity and accumulation of ubiquitinated proteins and natural proteasome substrates p27 and Bax) and apoptosis induction (as shown by caspase activation and apoptotic nuclei formation) in mice bearing MDA-MB-231 tumor xenografts. Disulfiram blocks the P-glycoprotein extrusion pump, inhibits the transcription factor nuclear factor-kappaB, sensitizes tumors to chemotherapy, reduces angiogenesis, and inhibits tumor growth in mice. Disulfiram inhibits growth and angiogenesis in melanomas transplanted in severe combined immunodeficient mice, and these effects are potentiated by Zn²⁺ supplementation.

**PROTOCOL**

**Cell Assay [4]**

The effect of disulfiram (0.15-5.0 μM) or sodium diethyldithiocarbamate (1.0 μM) on proliferation of malignant cell lines is studied in cultures stimulated with 10% FBS. Cell numbers are quantitated 24 to 72 hours later, as outlined below. In some experiments, disulfiram is added immediately after cells are plated. In other experiments, cells are plated and allowed to grow for 24 to 72 hours before fresh medium with disulfiram is added and cell numbers are assayed 24 to 72 hours later. Synergy is studied between disulfiram and N,N’-bis(2-chloroethyl-N-nitrosourea (carmustine, 1.0-1,000 μM) or cisplatin (0.1-100 μg/mL) added to medium. The effect of metal ions on disulfiram is studied with 0.2 to 10 μM Cu²⁺ (provided as CuSO₄), Zn²⁺ (as ZnCl₂), Ag⁺ (as silver lactate), or Au³⁺ (as HAuCl₄·3H₂O) ions added to growth medium, buffered to physiologic pH. To provide a biologically relevant source of copper, medium is supplemented with human ceruloplasmin at doses replicating low and high normal adult serum concentrations (250 and 500 mg/mL).

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

**Animal Administration [4]**

Adult female CB17-SCID mice are housed in a protected laminar flow facility with access to water and either a standard diet containing 87 ppm zinc or a zinc-supplemented diet containing 1,000 ppm Zn²⁺ as zinc acetate. Mice are injected s.c. in the right groin with 5×10⁶ cells from a highly aggressive malignant melanoma obtained from a Carolinas Medical Center patient. The frozen tumor is passaged twice in SCID mice to adapt it to in vivo growth before use in these experiments. On the day of tumor injection, all mice began daily administration of drug. Drug is given in a total volume of 0.2 mL by gastric gavage via smooth Teflon-tipped needles inserted transorally into the stomach. Four groups are studied: tumor control (n=10; 0.2 mL olive oil daily; zinc diet of 87 ppm); zinc-supplemented control (n=10; 0.2 mL olive oil daily; zinc diet of 1,000 ppm); disulfiram (n=10; 200 mg/kg/d disulfiram in 0.2 mL olive oil; zinc diet of 87 ppm); and zinc-supplemented diet + disulfiram (n=10; 200 mg/kg/d disulfiram in 0.2 mL olive oil; zinc diet of 1,000 ppm). Mice are examined daily, the tumor is measured in two dimensions, and the tumor volume is estimated using the formula for an ellipse. When estimated tumor volume approached 500 mm³ within any animal, all mice are euthanized. Tumors are excised, weighed, fixed in formalin, sectioned, and stained or immunostained for factor VIII. Slides are coded and examined by a blinded observer who identified vessels as deposits of red cells. For each slide, the number of vessels is counted in four different fields representative of the
tumor. The average number of vessels per field is averaged per biopsy specimen and used to evaluate tumor vascularity. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- SLAS Discov. 2020 Jun 22;2472555220932552.

See more customer validations on www.MedChemExpress.com

REFERENCES


