Disulfiram

Cat. No.: HY-B0240

CAS No.: 97-77-8

Molecular Formula: $C_{10}H_{20}N_2S_4$

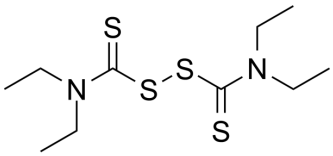
Molecular Weight: 296.54

Target: Aldehyde Dehydrogenase (ALDH); Interleukin Related; Pyroptosis; Apoptosis; Cuproptosis

Pathway: Metabolic Enzyme/Protease; Immunology/Inflammation; Apoptosis

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 : 75 mg/mL (252.92 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	3.3722 mL	16.8611 mL	33.7223 mL
	5 mM	0.6744 mL	3.3722 mL	6.7445 mL
	10 mM	0.3372 mL	1.6861 mL	3.3722 mL

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

In Vivo

1. Add each solvent one by one: corn oil
   Solubility: 30 mg/mL (101.17 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (33.72 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (7.01 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (7.01 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (7.01 mM); Clear solution

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. Disulfiram, a copper ion carrier, with Cu^{2+} increases intracellular ROS levels and induces cuproptosis[1][2][3][4][5][6].
IC_{50} & 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[1]. 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[2]. Oseltamivir decreases the number of viable cells, and the addition of $CuCl_2$ significantly enhances the DSF-induced cell death to less than 10% of control[3]. Disulfiram given to melanoma cells in combination with Cu^{2+} or Zn^{2+} decreases expression of cyclin A and reduces proliferation in vitro at lower concentrations than disulfiram alone[4]. Disulfiram (0.1 nM-10 μM; 72 h) + Cu^{2+} combination enhances the cytotoxicity on ovarian cancer cell lines[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Disulfiram significantly inhibits the tumor growth (by 74%), associated with in vivo proteasome inhibition and apoptosis induction in mice bearing MDA-MB-231 tumor xenografts[1]. Proteasome inhibition is measured by decreased levels of tumor tissue proteasome activity and accumulation of ubiquitinated proteins and natural proteasome substrates p27 and Bax[1]. Apoptosis is shown by caspase activation and apoptotic nuclei formation[1]. 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[4]. Disulfiram inhibits growth and angiogenesis in melanomas transplanted in severe combined immunodeficient mice, and these effects are potentiated by Zn^{2+} supplementation[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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 Cu^{2+} (provided as $CuSO_4$), Zn^{2+} (as $ZnCl_2$), Ag^+ (as silver lactate), or Au^{3+} (as $HAuCl_4 \cdot 3H_2O$) 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 Zn^{2+} as zinc acetate. Mice are injected s.c. in the right groin with 5×10^6 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 elipse. When estimated tumor volume

	approached 500 mm^3 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

- Cell Mol Immunol. 2022 Aug;19(8):925-943.
- Nat Cancer. 2020 Feb;1(2):235-248.
- Bioact Mater. 2024 Mar 1:36:96-111.
- Nat Commun. 2022 Nov 11;13(1):6862.
- Nat Commun. 2022 Jan 10;13(1):166.

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REFERENCES

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[2]. Chen D, ert al. Disulfiram, a clinically used anti-alcoholism drug and copper-binding agent, induces apoptotic cell death in breast cancer cultures and?xenografts?via?inhibition?of the proteasome?activity. Cancer Res. 2006 Nov 1;66(21):10425-33.

[3]. Wang W, et al. Disulfiram-mediated inhibition of NF-kappaB activity enhances cytotoxicity of 5-fluorouracil in human colorectal cancer cell lines. Int J Cancer. 2003 Apr 20;104(4):504-11.

[4]. Cen D, et al. Disulfiram facilitates intracellular Cu uptake and induces apoptosis in human melanoma cells. J Med Chem. 2004 Dec 30;47(27):6914-20.

[5]. Brar SS, et al. Disulfiram inhibits activating transcription factor/cyclic AMP-responsive element binding protein and human melanoma growth in a metal-dependent manner in vitro, in mice and in a patient with metastatic disease. Mol Cancer Ther. 2004 Sep;3

[6]. Jun Jacob Hu, et al. Identification of pyroptosis inhibitors that target a reactive cysteine in gasdermin D. The Preprint Server For Biology, 2018,Jul. 10.

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