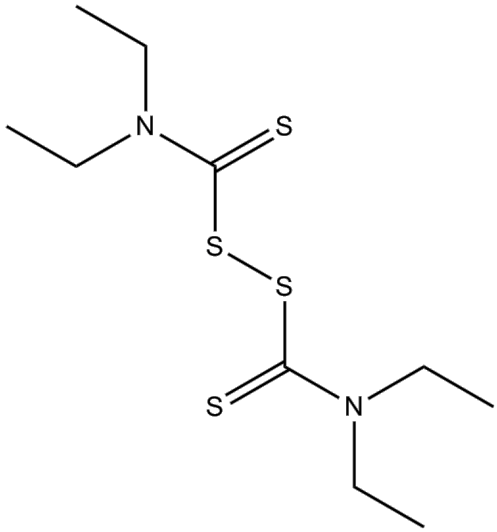
Product Data Sheet

Product Name: Disulfiram
Cat. No.: GC10801

Chemical Properties

Cas. No.	97-77-8		
Chemical Name	diethylcarbamothioylsulfanyl N,N-diethylcarbamodithioate		
SMILES	CCN(CC)C(=S)SSC(=S)N(CC)CC		
Formula	$C_{10}H_{20}N_2S_4$	M.Wt	296.54
Solubility	≥ 12 mg/mL in DMSO, ≥ 24.2 mg/mL in EtOH with ultrasonic	Storage	Store at 4°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

Kinase experiment [1]:

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Binding assays	The chymotrypsin-like activity of purified 20S proteasome was measured. Briefly, 17.5 ng of purified 20S proteasome were incubated in 100 μL of assay buffer (50 mmol/L Tris-HCl, pH 7.5) with or without different concentrations of copper chloride, Disulfiram, or the Disulfiram-copper mixture and 10 μmol/L fluorogenic peptide substrate Suc-LLVY-AMC (for the proteasomal chymotrypsin-like activity) for 2 hrs at 37°C. After incubation, production of hydrolyzed AMC groups was measured with a Wallac Victor3 multilabel counter with an excitation filter of 365 nm and an emission filter of 460 nm.

Cell experiment [1]:

Cell lines	MDA-MB-231 cells
Preparation method	The solubility of this compound in DMSO is >10 mM. 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.
Reaction Conditions	5 ~ 20 μM; 24 hrs
Applications	The Disulfiram-copper complex potently inhibited the proteasomal activity in cultured breast cancer MDA-MB-231 cells, before induction of apoptotic cancer cell death.

Animal experiment [1]:

Animal models	Mice bearing MDA-MB-231 tumor xenografts

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Dosage form	50 mg/kg/d; p.o.; 29 days
Applications	In mice bearing MDA-MB-231 tumor xenografts, Disulfiram significantly inhibited tumor growth (by 74%), associated with in vivo proteasome inhibition and apoptosis induction.
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.

References:

[1]. Chen D, Cui QC, Yang H, Dou QP. 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.

Background

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].

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 CuCl2 significantly

enhances the DSF-induced cell death to less than 10% of control[3]. 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[4].

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[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. Disulfiram inhibits growth and angiogenesis in melanomas transplanted in severe combined immunodeficient mice, and these effects are potentiated by Zn2+ supplementation[4].

References:
[1]. 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.
[2]. 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.
[3]. 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.
[4]. 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
[5]. 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.