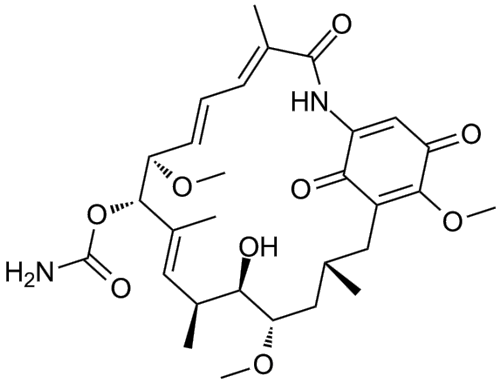
Product Data Sheet

Product Name: Geldanamycin
Cat. No.: GC16361

Chemical Properties

Cas. No.	30562-34-6		
Chemical Name	[(3R,5S,6R,7S,8E,10S,11S,12Z,14E)-6-hydroxy-5,11,21-trimethoxy-3,7,9,15-tetramethyl-16,20,22-trioxo-17-azabicyclo[16.3.1]docosa-1(21),8,12,14,18-pentaen-10-yl] carbamate		
SMILES	CC1CC(C(C(C=C(C(C(C=CC=C(C(=O)NC2=CC(=O)C(=C(C1)C2=O)OC)C)OC)OC(=O)N)C)C)O)OC		
Formula	$C_{29}H_{40}N_2O_9$	M.Wt	560.6
Solubility	≥ 16.9 mg/mL 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	HEp-2 cells (human epidermoid laryngeal carcinoma cell line)

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Preparation Method	HEp-2 cells were maintained in DMEM with 10% FCS and treated with 10μM Geldanamycin for 30min, then assessed for Shiga toxin/ricin sulfation, endocytosis, recycling, CI-M6PR retrograde transport, p38/MK2/Hsp27/Akt phosphorylation and Golgi colocalization.
Reaction Conditions	10μM; 30min
Applications	Geldanamycin enhanced retrograde transport of Shiga toxin and ricin to the Golgi, did not increase toxin endocytic uptake or alter recycling, and activated p38, MK2, Hsp27 and Akt.
Animal experiment [2]:	
Animal models	C57BL/6 mice
Preparation Method	Mice were intranasally infected with 10LD50 of H5N1 influenza virus and 2h later intraperitoneally injected with 1mg/kg Geldanamycin twice daily for 5 days, then monitored for survival and weight, and sacrificed at different time points (days 2, 4, 7) for lung histopathology, viral NP quantification, cytokine/chemokine ELISA, flow cytometry and neutralizing antibody assay.
Dosage form	1mg/kg; i.p.; twice daily for 5 days

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Applications	Geldanamycin administration prolonged survival, reduced body weight loss, attenuated bronchopneumonia, interstitial pneumonitis, necrotic debris, mononuclear cell accumulation, hemorrhage, pulmonary edema and tissue inflammation, decreased viral NP gene expression in lungs, reduced proinflammatory cytokines and chemokines and antiviral cytokines (IFN-α, IFN-γ) in BALF, attenuated infiltration and activation of macrophages/monocytes, NK cells, dendritic cells, $CD4^+$ and $CD8^+$ T cells, and did not alter virus-neutralizing antibody generation.

References:[1] Lingelem ABD, Hjelseth IA, Simm R, et al. Geldanamycin Enhances Retrograde Transport of Shiga Toxin in HEp-2 Cells. PLoS ONE. 2015 May 27;10(5):e0129214.[2] Wang C, Liu P, Luo J, et al. Geldanamycin Reduces Acute Respiratory Distress Syndrome and Promotes the Survival of Mice Infected with the Highly Virulent H5N1 Influenza Virus. Front Cell Infect Microbiol. 2017 Jun 15;7:267.

Background

Geldanamycin is an Hsp90 inhibitor with antibacterial and antiviral activities. Geldanamycin binds to the N-terminal ATP site of Hsp90 to block the ATPase cycle and promote the degradation of client proteins such as HER2, AKT, RAF1, CDK4, HIF-1α, and steroid hormone receptors via the ubiquitin-proteasome pathway. Geldanamycin can be used for research on prostate cancer, breast cancer, gastric cancer, and inflammation-related diseases[1-4].

In vitro, treatment of human osteosarcoma 143B cells with 4μM Geldanamycin for 24 hours upregulated Hsp90AA1, Hsp90AB1, Hsp70, and Hsp60 gene expression, reduced the mitochondrial Hsp60 protein pool, decreased cell viability, and induced apoptosis and necrosis[5]. Treatment of HEp-2 cells with 10μM Geldanamycin for 30 minutes enhanced retrograde transport of Shiga toxin to the Golgi apparatus and activated p38 and MK2[6]. Treatment of parathyroid hormone-induced MC3T3-E1 cells with 1μM Geldanamycin for 0-24 hours decreased PERK protein expression and inhibited cell differentiation and proliferation[7].

In vivo, a single intracerebroventricular injection of 10μg/kg Geldanamycin was administered to 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced mice. Geldanamycin increased residual

dopamine content and tyrosine hydroxylase immunoreactivity in the striatum, decreased Hsp90 levels in the striatum, and induced Hsp70 expression[8]. Intraperitoneal injection of 1mg/kg Geldanamycin twice daily for 5 days was administered to H5N1 influenza virus-infected C57BL/6 mice. Geldanamycin prolonged survival time, reduced body weight loss, and alleviated lung injuries including bronchopneumonia, interstitial pneumonia, necrotic debris, mononuclear cell accumulation, hemorrhage, and pulmonary edema[9]. A single intraperitoneal injection of 10mg/kg Geldanamycin was administered to male CD-1 mice at 1 hour after collagenase-induced intracerebral hemorrhage. Geldanamycin reduced brain water content in the ipsilateral basal ganglia, alleviated brain edema, improved Garcia neurological scores, and reduced neurological deficits[10].

References:

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[2] Sausville EA. Geldanamycin analogs. J Chemother. 2004 Nov;16 Suppl 4:68-9.
[3] Martín JF, Ramos A, Liras P. Regulation of Geldanamycin Biosynthesis by Cluster-Situated Transcription Factors and the Master Regulator PhoP. Antibiotics (Basel). 2019 Jun 30;8(3):87.
[4] Manaenko A, Fathali N, Williams S, et al. Geldanamycin Reduced Brain Injury in Mouse Model of Intracerebral Hemorrhage. Acta Neurochir Suppl. 2011;111:161-165.
[5] Gorska M, Marino Gammazza A, Zmijewski MA, et al. Geldanamycin-Induced Osteosarcoma Cell Death Is Associated with Hyperacetylation and Loss of Mitochondrial Pool of Heat Shock Protein 60(Hsp60). PLoS ONE. 2013 Aug 28;8(8):e71135.
[6] Lingelem ABD, Hjelseth IA, Simm R, et al. Geldanamycin Enhances Retrograde Transport of Shiga Toxin in HEp-2 Cells. PLoS ONE. 2015 May 27;10(5):e0129214.
[7] Zhang K, Wang M, Li Y, et al. The PERK-EIF2α-ATF4 signaling branch regulates osteoblast differentiation and proliferation by PTH. Am J Physiol Endocrinol Metab. 2019 Mar 1;316(3):E590-E604.
[8] Shen H, He J, Wang Y, et al. Geldanamycin Induces Heat Shock Protein 70 and Protects against MPTP-induced Dopaminergic Neurotoxicity in Mice. J Biol Chem. 2005 Dec 2;280(48):39962-39969.
[9] Wang C, Liu P, Luo J, et al. Geldanamycin Reduces Acute Respiratory Distress Syndrome and Promotes the Survival of Mice Infected with the Highly Virulent H5N1 Influenza Virus. Front Cell Infect Microbiol. 2017 Jun 15;7:267.
[10] Li L, Nakano D, Zhang A, et al. Effects of post-renal anemia treatment with the HIF-PHD inhibitor molidustat on adenine-induced renal anemia and kidney disease in mice. J Pharmacol Sci. 2020;144(4):229-236.

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