Small Molecules

Geldanamycin

Inhibits Hsp90

Catalog # 74032 1 mg
74034 5 mg

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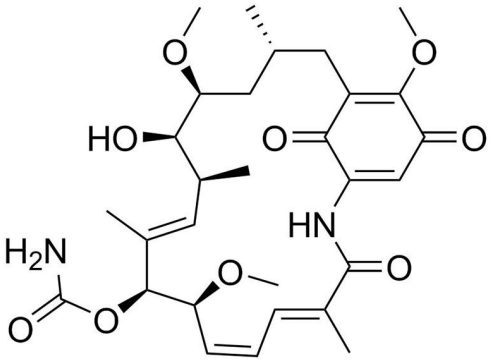
Product Description

Geldanamycin is a benzoquinone ansamycin antibiotic that selectively inhibits heat shock protein 90 (Hsp90) (Schulte et al.; Whitesell et al.). It inhibits the ATPase activity of Hsp90 by binding with high affinity to the N-terminal ATP-binding site (Kd = 1.2 µM; Roe et al.). Geldanamycin also binds to the glucose-regulated protein GRP94, an endoplasmic reticulum protein with homology to Hsp90. This interaction destabilizes its complex with p185-ErbB2, leading to degradation of ErbB2 protein, which is overexpressed in aggressive breast cancers (Castagnola et al.; Chavany et al.).

Molecular Name:	Geldanamycin
Alternative Names:	NSC 122750
CAS Number:	30562-34-6
Chemical Formula:	$C_{29}H_{40}N_2O_9$
Molecular Weight:	560.6 g/mol
Purity:	≥ 98%
Chemical Name:	(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
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect product from prolonged exposure to light. For long-term storage store with a desiccant. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 15 mM For example, to prepare a 1 mM stock solution in DMSO, resuspend 1 mg in 1.8 mL of DMSO. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

CANCER RESEARCH
· Inhibits growth of 60 human tumor cell lines (Supko et al.).
DISEASE MODELING
· Regulates innate immune response as demonstrated by inhibition of inflammasome activity in a mouse gout model (Mayor et al.).
· Inhibits replication of herpes simplex virus (HSV) 1 and HSV-2 (Li et al.).

References

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Li Y-H et al. (2012) Geldanamycin, a ligand of heat shock protein 90, inhibits herpes simplex virus type 2 replication both in vitro and in vivo. J Antibiot 65(10): 509–12.
Mayor A et al. (2007) A crucial function of SGT1 and HSP90 in inflammasome activity links mammalian and plant innate immune responses. Nat Immunol 8(5): 497–503.
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Supko JG et al. (1995) Preclinical pharmacologic evaluation of geldanamycin as an antitumor agent. Cancer Chemother Pharmacol 36(4): 305–15.
Whitesell L et al. (1994) Inhibition of heat shock protein HSP90-pp60v-src heteroprotein complex formation by benzoquinone ansamycins: essential role for stress proteins in oncogenic transformation. Proc Natl Acad Sci USA 91(18): 8324–8.

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