Tanespimycin

Cat. No.: HY-10211

CAS No.: 75747-14-7

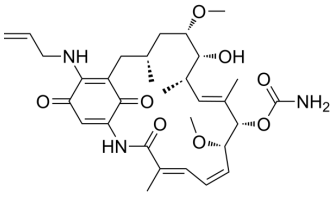
Molecular Formula: $C_{31}H_{43}N_3O_8$

Molecular Weight: 585.69

Target: HSP; Autophagy; Mitophagy; Apoptosis; Bacterial; Antibiotic

Pathway: Cell Cycle/DNA Damage; Metabolic Enzyme/Protease; Autophagy; Apoptosis; Anti-infection

Storage: 4°C, protect from light
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (85.37 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.7074 mL	8.5369 mL	17.0739 mL
	5 mM	0.3415 mL	1.7074 mL	3.4148 mL
	10 mM	0.1707 mL	0.8537 mL	1.7074 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (8.54 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 5 mg/mL (8.54 mM); Clear solution
3. Add each solvent one by one: 15% Cremophor EL >> 85% Saline
   Solubility: 5 mg/mL (8.54 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.62 mg/mL (2.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tanespimycin (17-AAG) is a potent HSP90 inhibitor with an IC_{50} of 5 nM, having a 100-fold higher binding affinity for tumour cell derived HSP90 than normal cell derived HSP90[1][5]. Tanespimycin depletes cellular STK38/NDR1 and reduces STK38 kinase activity. Tanespimycin also downregulates the stk38 gene expression[3].

IC_{50} & Target			
	HSP90 5 nM (IC_{50})	Autophagy	Mitophagy

In Vitro	Tanespimycin causes the degradation of HER2, Akt, and both mutant and wild-type AR and the retinoblastoma-dependent G1 growth arrest of prostate cancer cells. Tanespimycin inhibits prostate cancer cell lines with IC_{50}s ranged from 25-45 nM (LNCaP, 25 nM; LAPC-4, 40 nM; DU-145, 45 nM; and PC-3, 25 nM)[1]. Tanespimycin (0.1-1 μM) induces a nearly complete loss of ErbB2 on ErbB2-overexpressing breast cancer cells[2]. Tanespimycin inhibits cell growth and induces G2/M cell cycle arrest and apoptosis in CCA cells together with the down-regulation of Bcl-2, Survivin and Cyclin B1, and the up-regulation of cleaved PARP[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tanespimycin (25-200 mg/kg, i.p.) causes a dose-dependent decline in AR, HER2, and Akt expression in prostate cancer xenografts. Tanespimycin treatment at doses sufficient to induce AR, HER2, and Akt degradation results in the dose-dependent inhibition of androgen-dependent and -independent prostate cancer xenograft growth without toxicity[1]. Tanespimycin (60 mg/kg) with Rapamycin (30 mg/kg) inhibits A549 and MDA-MB-231 tumor growth and effects tumor cures in MDA-MB-231 tumor-bearing animals by tail vein injection[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For the Alamar Blue proliferation assay, 2-4×10^3 cells are plated in 96-well plates. Later (48 h), cells are treated with Tanespimycin for 96 h or 0.01% DMSO as control. On day 4, Alamar Blue viability assay is performed as described elsewhere. IC_{50} and IC_{90}s are calculated as the doses of Tanespimycin required to inhibit cell growth by 50 and 90%, respectively. Cell cycle distribution is assayed as described previously with a Becton Dickinson fluorescence-activated cell sorter and analyzed by the Cell Cycle Multicycle system. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Tanespimycin is dissolved in an EPL vehicle. To aid in the identification of an optimal dose and schedule, nontumor bearing mice are treated by i.p. injection with 25-200 mg/kg of Tanespimycin 5 days/week for 3 weeks or by the EPL vehicle alone. Serum samples are taken from each group, and equal volumes are pooled on days 5, 10, and 15 of treatment for serum chemistry and liver function analysis. At sacrifice, plasma samples are collected for complete blood count. A gross necropsy is performed on all of the mice, and a complete necropsy, including histopathology, is performed on 1 animal/group. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Blood. 2019 Oct 17;134(16):1323-1336.
- Nat Commun. 2023 Jul 26;14(1):4505.
- Nucleic Acids Res. 2020 Aug 20;48(14):7944-7957.
- Theranostics. 2018 Feb 15;8(7):2044-2060.
- J Exp Clin Cancer Res. 2018 Mar 27;37(1):70.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Solit DB, et al. 17-Allylamino-17-demethoxygeldanamycin induces the degradation of androgen receptor and HER-2/neu and inhibits the growth of prostate cancer xenografts.Clin Cancer Res, 2002, 8(5), 986-993.

[2]. Raja, Srikumar M., et al. 17-AAG induces enhanced ubiquitinylation and lysosomal pathway-dependent ErbB2 degradation and cytotoxicity in ErbB2-overexpressing breast cancer cells. Cancer Biology & Therapy (2008), 7(10), 163

[3]. Zhang J, et al. The heat shock protein 90 inhibitor 17-AAG suppresses growth and induces apoptosis in human cholangiocarcinoma cells.Clin Exp Med. 2012 Sep 7.

[4]. Newman B, et al. HSP90 Inhibitor 17-AAG Selectively Eradicates Lymphoma Stem Cells.Cancer Res. 2012 Sep 1;72(17):4551-61. Epub 2012 Jun 29.

[5]. Kamal A, et al. A high-affinity conformation of Hsp90 confers tumour selectivity on Hsp90 inhibitors. Nature. 2003 Sep 25;425(6956):407-10.

[6]. Enomoto A, et al. The HSP90 inhibitor 17-allylamino-17-demethoxygeldanamycin modulates radiosensitivity by downregulating serine/threonine kinase 38 via Sp1 inhibition. Eur J Cancer. 2013 Nov;49(16):3547-58.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA