

Product Data Sheet

Product Name: 17-AAG (KOS953)

Cat. No.: GC11720

Chemical Properties

Cas. No. 75747-14-7

Chemical Name [(3R,5S,6R,7S,8E,10S,11S,12Z,14E)-6-hydroxy-5,11-dimethoxy-3,7,9,15-tetramethyl-16,20,22-trioxo-21-(prop-2-enylamino)-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)NCC=C)C)OC)OC(=O)N)C)C)O)OC

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

M.Wt 585.7

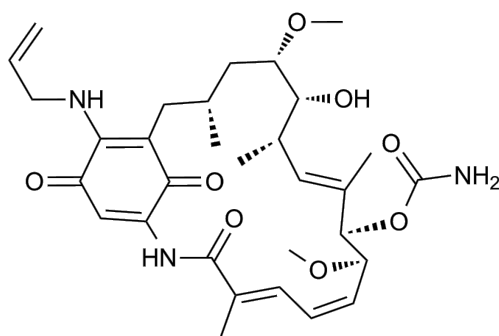
Solubility ≥ 24.95 mg/mL in DMSO, ≥ 9.56 mg/mL in EtOH with ultrasonic

Storage 4°C, protect from light

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

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

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Cell experiment [1]:

Cell lines	HCT116 BAX ^{+/−} and HCT116 BAX ^{−/−} human colon adenocarcinoma cell lines (BAX ^{+/−} retains heterozygous BAX expression, BAX ^{−/−} is homozygous BAX knockout via homologous recombination with no BAX protein expression)
Preparation Method	HCT116 BAX ^{+/−} and BAX ^{−/−} cells were maintained in DMEM supplemented with 10% FBS, 1× non-essential amino acids and 5mM L-glutamine at 37°C, 5% CO ₂ . Mid-log phase cells were treated with 17-AAG (1-1000nM; 72h) for proliferation assay, cell cycle and cell death detection.
Reaction Conditions	1-1000nM; 72h
Applications	17-AAG treatment depleted HSP90 client proteins CRAF and CDK4, and induced HSP72 expression in a concentration-dependent manner in both HCT116 BAX ^{+/−} and BAX ^{−/−} cells at 72h. The number of detached cells increased in a concentration-dependent manner in both cell lines after 17-AAG treatment.

Animal experiment [2]:

Animal models	Swiss albino male CD-1 mice
Preparation Method	Mice were assigned into 4 groups: control group (received vehicle i.p. at 10mL/kg/day for 8 weeks), thioacetamide-only group (received thioacetamide regimen alone), thioacetamide + 17-AAG (25mg/kg) group and thioacetamide + 17-AAG (50mg/kg) group (received same thioacetamide regimen plus additional i.p. injection of 25 or 50mg/kg 17-AAG; 5 days/week along the last 4 weeks of the 8-week study).

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Dosage form	25 or 50mg/kg; i.p.; 5 days/week for the last 4 weeks of the 8-week thioacetamide regimen.
Applications	17-AAG administration decreased the mortality of thioacetamide-intoxicated mice, attenuated thioacetamide-induced hepatocyte degeneration, inflammatory infiltration and periportal collagen deposition, lowered hepatic hydroxyproline content, downregulated hepatic α -SMA, Col1A1, TIMP-1 mRNA expressions and Hsp90 level, reduced MDA content, elevated GSH level, and increased caspase-3 and Fas levels in liver tissue.

References:

[1] Powers MV, Valenti M, Miranda S, et al. Mode of cell death induced by the HSP90 inhibitor 17-AAG (tanespimycin) is dependent on the expression of pro-apoptotic BAX. *Oncotarget*. 2013 Nov;4(11):1963-1975.

[2] Abu-Elsaad NM, Serrya MS, El-Karef AM, et al. The heat shock protein 90 inhibitor, 17-AAG, attenuates thioacetamide induced liver fibrosis in mice. *Pharmacological Reports*. 2016;68(2):275-282.

Background

17-AAG (KOS953) is a potent Hsp90 inhibitor ($IC_{50}=5nM$). 17-AAG binds to the N-terminal ATP pocket of Hsp90 to block the chaperone cycle and induces ubiquitination and degradation of client proteins such as HER2, Akt, and AR to inhibit tumor proliferation. 17-AAG can be used in studies related to HER2+ breast cancer, prostate cancer, and multiple myeloma^[1-4].

In vitro, 17-AAG (0.1-1000 μ M) treatment of MCF-7 human breast cancer cells and MDA-MB-231 human breast cancer cells for 24h inhibited cell proliferation in a dose-dependent manner, induced apoptosis, and increased γ H2AX expression causing DNA double-strand breaks^[5]. 17-AAG (1-1000nM) treatment of HCT116 human colon adenocarcinoma cells for 72h inhibited cell proliferation in a concentration-dependent manner and induced BAX-dependent apoptosis^[6]. 17-AAG (0.5 and

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1.0μM) treatment of human non-small cell lung cancer Calu-1 cells for 48h upregulated VDAC1 and Bax expression, increased aTAT1-mediated Ac-α-tubulin level, and reduced cell viability^[7].

In vivo, a single tail vein injection of 17-AAG (30mg/kg) one day before isoflurane anesthesia (1.5%; 2h/day; 5 consecutive days) in nerve-injured C57BL/6 mice reduced neuronal atrophy, nuclear fragmentation, and cell loss in the CA1 region, decreased lipid peroxidation product MDA, and alleviated isoflurane-induced hippocampal ferroptosis and neurotoxicity^[8]. Swiss albino male CD-1 mice received intraperitoneal injections of thioacetamide (100mg/kg; 3 times/week; 8 weeks) to induce liver fibrosis, and then combined intraperitoneal injections of 17-AAG (25 or 50mg/kg; 5 times/week; 4 weeks) during the last 4 weeks reduced periportal collagen deposition and hepatocyte degeneration, decreased hepatic hydroxyproline content, and increased caspase-3 and Fas levels to induce hepatic stellate cell apoptosis^[9]. A single intrathecal injection of 17-AAG (0.5nmol) in CD-1 mice 24h before testing enhanced morphine-induced prolongation of tail-flick latency and increased mechanical allodynia threshold in the postoperative paw incision model, downregulated AMPKβ1 subunit expression in the spinal dorsal horn, blocked DAMGO (MOR agonist)-induced p-AMPK increase, relieved AMPK negative feedback on ERK, and upregulated p-ERK in the superficial dorsal horn^[10].

References:

- [1] Usmani SZ, Bona R, Li Z. 17 AAG for HSP90 inhibition in cancer--from bench to bedside. *Curr Mol Med*. 2009 Jun;9(5):654-64.
- [2] Konstantinopoulos PA, Papavassiliou AG. 17-AAG: mechanisms of antitumour activity. *Expert Opin Investig Drugs*. 2005 Dec;14(12):1471-4.
- [3] Siegelin MD, Habel A, Gaiser T. 17-AAG sensitized malignant glioma cells to death-receptor mediated apoptosis. *Neurobiol Dis*. 2009 Feb;33(2):243-9.
- [4] Talaei S, Mellatyar H, Asadi A, et al. Spotlight on 17-AAG as an Hsp90 inhibitor for molecular targeted cancer treatment. *Chem Biol Drug Des*. 2019 May;93(5):760-786.
- [5] Suwannalert P, Panpinyporn P, Wantanachaisaeng P, et al. 17-AAG Induces Endoplasmic Reticulum Stress-mediated Apoptosis in Breast Cancer Cells, Possibly Through PERK/eIF2α Up-regulation. *In Vivo*. 2024;38:2228-2238.

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[6] Powers MV, Valenti M, Miranda S, et al. Mode of cell death induced by the HSP90 inhibitor 17-AAG (tanespimycin) is dependent on the expression of pro-apoptotic BAX. Oncotarget. 2013 Nov;4(11):1963-1975.

[7] Wang Q, Liu X. VDAC upregulation and aTAT1-mediated a-tubulin acetylation contribute to tanespimycin-induced apoptosis in Calu-1 cells. Oncol Rep. 2020;44(6):2725-2734.

[8] Zhang C, Chen X, Liu R, et al. HSP90 Inhibition Attenuated Isoflurane-Induced Neurotoxicity in Mice and Human Neuroglioma Cells. Neurochem Res. 2024;49(3):706-717.

[9] Abu-Elsaad NM, Serrya MS, El-Karef AM, et al. The heat shock protein 90 inhibitor, 17-AAG, attenuates thioacetamide induced liver fibrosis in mice. Pharmacological Reports. 2016;68(2):275-282.

[10] Gabriel KA, Streicher JM. HSP90 inhibition in the mouse spinal cord enhances opioid signaling by suppressing an AMPK-mediated negative feedback loop. Sci Signal. 2023 Apr 11;16(780):eade2438.

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