上海源叶生物科技有限公司
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产品名称：17-AAG；Tanespimycin
CAS 号：75747-14-7
产品货号：S86426

生物活性：

Description

Tanespimycin (17-AAG) 是有效的 HSP90 抑制剂，IC50 为 5 nM，对肿瘤细胞 HSP90 的亲和性比正常细胞高 100 倍。Tanespimycin 消耗细胞内 STK38/NDR1，并降低 STK38 激酶活性。Tanespimycin 还下调 stk38 基因表达。

IC50 & Target[5]

HSP90	Autophagy	Mitophagy
5 nM (IC_{50})		

Cellular Effect

Cell Line	Type	Value	Description
A-375	IC_{50}	1287 nM	Antiproliferative activity against human A375 cells after 72 to 144 hrs by cyquant DNA dye method
A-375	IC_{50}	32 nM	Inhibition of Hsp90 in human A375 cells assessed as pS6 degradation after 24 hrs by high content screening
A-375	IC_{50}	4 nM	Inhibition of Hsp90 in human A375 cells assessed as Hsp70 induction after 24 hrs by high content screening
A-431	IC_{50}	0.069 μM	Cytotoxicity against human A431 cells after 72 hrs
A-431	IC_{50}	0.07 μM	Antiproliferative activity against human A431 cells after 72 hrs
A-431	IC_{50}	89 nM	Cytotoxicity against human A431 cells after 72 hrs by MTT assay
A549	IC_{50}	> 10 μM	Antiproliferative activity against human A549 cells assessed as inhibition of cell proliferation measured after 24 hrs by MTT assay
A549	IC_{50}	> 10 μM	Antiproliferative activity against human A549 cells assessed as reduction in cell growth incubated for 72 hrs by SRB assay
A549	GI_{50}	0.0075 μM	Antiproliferative activity against human A549 cells assessed as cell growth inhibition after 48 hrs by sulforhodamine B assay
A549	GI_{50}	0.08 μM	Antiproliferative activity against human A549 cells assessed as growth inhibition incubated for 48 hrs by Sulforhodamine B assay
A549	IC_{50}	0.286 μM	Antiproliferative activity against human A549 cells after 48 hrs by MTT assay
A549	IC_{50}	81 nM	Cytotoxicity against human A549 cells after 72 hrs by MTT assay
AU565	IC_{50}	0.003 μM	Inhibition of Hsp90 in human AU565 cells assessed as Her2 degradation after 24 hrs by high content screening
AU565	IC_{50}	8 nM	Inhibition of Hsp90 in human AU565 cells assessed as pERK degradation after 24 hrs by high content screening
BGC-823	IC_{50}	847 nM	Cytotoxicity against human BGC823 cells after 72 hrs by MTT assay
BT-474	IC_{50}	0.01 μM	Antiproliferative activity against human BT474 cells by MTS assay

BT-474	GI_{50}	5 nM	Growth inhibition of human BT474 cells assessed as ATP level after 4 days
CNE-2	IC_{50}	3.03 μM	Cytotoxicity in human CNE-2 cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay
CNE2Z	IC_{50}	8.41 μM	Antiproliferative activity against human CNE2Z cells assessed as cell growth inhibition by MTT assay
DU-145	IC_{50}	0.282 μM	Antiproliferative activity against human DU145 cells after 48 hrs by MTT assay
DU-145	IC_{50}	68.3 μM	Cytotoxicity against DU145 cells after 72 hrs
ECa-109 cell line	IC_{50}	1.1 μM	Cytotoxicity against human ECA109 cells after 48 hrs by MTT assay
GES1	CC_{50}	7.94 μM	Cytotoxicity against human GES1 cells assessed as reduction in cell viability measured after 24 hrs by MTT assay
HCC827	GI_{50}	56 nM	Growth inhibition of human tarceva and iressa-resistant HCC827 cells assessed as ATP level after 4 days
HCT-116	GI_{50}	0.16 μM	Growth inhibition of human HCT116 cells after 24 hrs by SRB assay
HCT-116	GI_{50}	0.34 μM	Antiproliferative activity against human HCT116 cells assessed as growth inhibition incubated for 48 hrs by Sulforhodamine B assay
HCT-116	GI_{50}	0.34 μM	Antiproliferative activity against human HCT116 cells assessed as cell growth inhibition after 48 hrs by sulforhodamine B assay
HCT-116	IC_{50}	202 nM	Cytotoxicity against human HCT116 cells after 72 hrs
HCT-116	IC_{50}	56.5 nM	Growth inhibition of human HCT116 cells after 24 hrs by [3H]thymidine uptake assay
HCT-15	IC_{50}	1487 nM	Antiproliferative activity against human HCT15 cells after 72 to 144 hrs by cyquant DNA dye method
HeLa	IC_{50}	> 1000 μM	Inhibition of HDAC in human HeLa nuclear extract using Boc-Lys(acetyl)-AMC as substrate measured after 30 mins by fluorescence assay
HeLa	IC_{50}	0.2 μM	Antiproliferative activity against human HeLa cells after 72 hrs by SRB assay
HeLa	IC_{50}	108.2 μM	Cytotoxicity against HeLa cells after 72 hrs
HeLa	IC_{50}	128 nM	Cytotoxicity against human HeLa cells after 72 hrs by MTT assay
HeLa	IC_{50}	19.4 μM	Cytotoxicity in human HeLa cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay
Hep 3B2	GI_{50}	0.08 μM	Antiproliferative activity against human Hep3B cells assessed as growth inhibition incubated for 48 hrs by Sulforhodamine B assay
HepG2	IC_{50}	0.32 μM	Antiproliferative activity against human HepG2 cells assessed as cell growth inhibition by MTT assay
HepG2	IC_{50}	0.33 μM	Antiproliferative activity against human HepG2 cells assessed as

			inhibition of cell proliferation measured after 24 hrs by MTT assay
HepG2	IC_{50}	8 μM	Cytotoxicity in human HepG2 cells assessed as reduction in cell viability incubated for 48 hrs by MTT assay
HepG2	IC_{50}	91 nM	Cytotoxicity against human HepG2 cells after 72 hrs by MTT assay
HT-29	IC_{50}	0.1 nM	Antiproliferative activity against human HT-29 cells after 72 to 144 hrs by cyquant DNA dye method
HUVEC	GI_{50}	< 0.1 μM	Antiproliferative activity against human HUVEC cells assessed as growth inhibition incubated for 48 hrs by Sulforhodamine B assay
HUVEC	IC_{50}	282 nM	Cytotoxicity against HUVEC cells after 72 hrs by MTT assay
K562	IC_{50}	0.15 μM	Cytotoxicity against human K562 cells assessed as growth inhibition after 72 hrs by trypan blue exclusion assay
K562	IC_{50}	126 nM	Antiproliferative activity against human K562 cells after 72 to 144 hrs by cyquant DNA dye method
K562	GI_{50}	48 nM	Growth inhibition of human K562 cells assessed as ATP level after 4 days
L02	CC_{50}	11.65 μM	Cytotoxicity against human L02 cells assessed as reduction in cell viability measured after 24 hrs by MTT assay
L02	IC_{50}	99 nM	Cytotoxicity against human HL7702 cells after 72 hrs by MTT assay
LNCaP	IC_{50}	0.16 μM	Cytotoxicity against human LNCAP cells after 72 hrs by MTT assay
LNCaP	IC_{50}	82 nM	Antiproliferative activity against human LNCAP cells after 72 to 144 hrs by cyquant DNA dye method
LoVo	IC_{50}	0.26 μM	Antiproliferative activity against human LoVo cells assessed as inhibition of cell proliferation measured after 24 hrs by MTT assay
MCF7	IC_{50}	0.01 μM	Antiproliferative activity against human MCF7 cells by MTS assay
MCF7	IC_{50}	0.029 μM	Antiproliferative activity against human MCF7 cells measured after 48 hrs by MTT assay
MCF7	IC_{50}	0.09 μM	Antiproliferative activity against human MCF7 cells assessed as cell viability after 72 hrs by MTT assay
MCF7	IC_{50}	0.192 μM	Antiproliferative activity against human MCF7 cells after 48 hrs by MTT assay
MCF7	IC_{50}	0.3 nM	Antiproliferative activity against human MCF7 cells after 72 to 144 hrs by cyquant DNA dye method
MCF7	IC_{50}	5 nM	Antiproliferative activity against human MCF7 cells measured after 5 days by MTS assay
MCF7	IC_{50}	58 nM	Cytotoxicity against human MCF7 cells after 72 hrs
MCF7	IC_{50}	662 nM	Cytotoxicity against human MCF7 cells after 72 hrs in presence

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			of NQO1 inhibitor dicoumarol
MDA-MB-231	GI_{50}	0.27 μM	Antiproliferative activity against human MDA-MB-231 cells assessed as growth inhibition incubated for 48 hrs by Sulforhodamine B assay
MDA-MB-231	IC_{50}	0.28 μM	Cytotoxicity against human MDA-MB-231 cells after 72 hrs by MTT assay
MDA-MB-231	IC_{50}	0.28 μM	Cytotoxicity against human MDA-MB-231 cells after 72 hrs by MTT assay
MDA-MB-231	IC_{50}	0.52 μM	Antiproliferative activity against human MDA-MB-231 cells after 72 hrs by SRB assay
MDA-MB-231	IC_{50}	1.79 μM	Antiproliferative activity against human MDA-MB-231 cells assessed as cell growth inhibition by MTT assay
MDA-MB-231	IC_{50}	194 nM	Antiproliferative activity against human MDA-MB-231 cells after 72 to 144 hrs by cyquant DNA dye method
MDA-MB-468	IC_{50}	1.57 μM	Antiproliferative activity against human MDA-MB-468 cells measured after 48 hrs by MTT assay
MDA-MB-468	IC_{50}	1500 nM	Cytotoxicity against NQ01-deficient human MDA468 cells after 72 hrs
MDA-MB-468	GI_{50}	780 nM	Growth inhibition of human MDA-MB-468 cells assessed as ATP level after 4 days
MRC5	CC_{50}	14.24 μM	Cytotoxicity against human MRC5 cells assessed as reduction in cell viability measured after 24 hrs by MTT assay
MV4-11	GI_{50}	11 nM	Growth inhibition of human MV4-11 cells assessed as ATP level after 4 days
NCI-H1299	IC_{50}	0.2 μM	Antiproliferative activity against human H1299 cells after 48 hrs by resazurin dye-based fluorescence assay
NCI-H1975	GI_{50}	0.16 μM	Antiproliferative activity against human NCI-H1975 cells assessed as cell growth inhibition after 48 hrs by sulforhodamine B assay
NCI-H1975	GI_{50}	35 nM	Growth inhibition of human tarceva and iressa-resistant NCI-H1975 cells assessed as ATP level after 4 days
NCI-H460	IC_{50}	0.01 μM	Cytotoxicity against human NCI-H460 cells after 72 hrs
NCI-H460	IC_{50}	255 nM	Antiproliferative activity against human NCI-H460 cells after 72 to 144 hrs by cyquant DNA dye method
NCI-H596	IC_{50}	1600 nM	Cytotoxicity against NQ01-deficient human NCI-H596 cells after 72 hrs
NCI-N87	GI_{50}	1 nM	Growth inhibition of human NCI-N87 cells assessed as ATP level after 4 days
NCM460	CC_{50}	14.21 μM	Cytotoxicity against human NCM460 cells assessed as reduction in cell viability measured after 24 hrs by MTT assay
OVCAR-3	IC_{50}	0.48 μM	Antiproliferative activity against human OVCAR-3 cells assessed as inhibition of cell proliferation measured after 24 hrs

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			by MTT assay
PANC-1	IC_{50}	3.21 μM	Antiproliferative activity against human PANC-1 cells assessed as inhibition of cell proliferation measured after 24 hrs by MTT assay
PC-3	IC_{50}	0.062 μM	Antiproliferative activity against human PC-3 cells assessed as reduction in cell growth incubated for 72 hrs by SRB assay
PC-3	IC_{50}	9 nM	Antiproliferative activity against human PC3 cells after 72 to 144 hrs by cyquant DNA dye method
SGC-7901	IC_{50}	> 10 μM	Antiproliferative activity against human SGC-7901 cells assessed as inhibition of cell proliferation measured after 24 hrs by MTT assay
SK-BR-3	EC_{50}	< 0.1 μM	Inhibition of Hsp90alpha in human SKBR3 cells assessed as ErbB2 degradation by Western blot analysis
SK-BR-3	IC_{50}	0.038 μM	Antiproliferative activity against human SK-BR-3 cells assessed as reduction in cell growth incubated for 72 hrs by SRB assay
SK-BR-3	EC_{50}	0.06 μM	Inhibition of Hsp90alpha in human SKBR3 cells assessed as up-regulation of HSP70 protein by Western blot analysis
SK-BR-3	IC_{50}	27 nM	Cytotoxicity against human SKBR3 cells after 72 hrs by celltiter-Glo assay
SK-BR-3	IC_{50}	33 nM	Cytotoxicity against human SKBR3 cells after 72 hrs by celltiter-glo assay
SK-BR-3	IC_{50}	410 nM	Cytotoxicity against human SKBR3 cells after 72 hrs in presence of NQO1 inhibitor dicoumarol
SK-BR-3	IC_{50}	44 nM	Cytotoxicity against human SKBR3 cells after 72 hrs
SK-MEL-5	IC_{50}	134 nM	Antiproliferative activity against human SK-MEL-5 cells after 72 to 144 hrs by cyquant DNA dye method
SK-OV-3	IC_{50}	0.22 μM	Antiproliferative activity against human SK-OV-3 cells assessed as reduction in cell growth incubated for 72 hrs by SRB assay
SK-OV-3	IC_{50}	240 nM	Cytotoxicity against human SKOV3 cells after 72 hrs
SMMC-7721	IC_{50}	0.19 μM	Antiproliferative activity against human SMMC7721 cells assessed as cell growth inhibition by MTT assay
SW480	IC_{50}	0.28 μM	Antiproliferative activity against human SW480 cells assessed as cell growth inhibition by MTT assay
SW480	IC_{50}	572 nM	Cytotoxicity against human SW480 cells after 72 hrs by MTT assay
SW-620	IC_{50}	328 nM	Antiproliferative activity against human SW620 cells after 72 to 144 hrs by cyquant DNA dye method
U-87MG ATCC	IC_{50}	> 10 μM	Antiproliferative activity against human U-87 MG cells assessed as reduction in cell growth incubated for 72 hrs by SRB assay

In Vitro

Tanespimycin 导致 HER2、Akt 以及突变型和野生型 AR 的降解以及前列腺癌细胞的视网膜母细胞瘤依赖性 G1 期生长停滞。Tanespimycin 抑制前列腺癌细胞系，IC50 范围为 25-45 nM (LNCaP，25 nM；LAPC-4，40 nM；DU-145，45 nM；和 PC-3，25 nM)[1]。

Tanespimycin (0.1-1 μM) 诱导过表达 ErbB2 的乳腺癌细胞几乎完全丧失 ErbB2[2]。

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<table>
<tr><td></td><td>Tanespimycin 抑制 CCA 细胞生长并诱导 G2/M 细胞周期停滞和凋亡，同时下调 Bcl-2、Survivin 和 Cyclin B1，上调 cleaved PARP[3]。</td></tr>
<tr><td>In Vivo</td><td>Tanespimycin (25 -200 mg/kg，ip) 引起前列腺癌异种移植物中 AR、HER2 和 Akt 表达的剂量依赖性下降。Tanespimycin 以足以诱导 AR、HER2 和 Akt 降解的剂量进行处理，可剂量依赖性地抑制雄激素依赖性和非依赖性前列腺癌异种移植物的生长，且无毒性[1]。
Tanespimycin (60 mg/kg) 和 Rapamycin (30 mg/kg) 通过尾静脉注射抑制 A549 和 MDA-MB-231 肿瘤生长并影响 MDA-MB-231 荷瘤动物的肿瘤治愈[4].</td></tr>
<tr><td>Solvent&Solubility</td><td>细胞实验:
DMSO 中的溶解度 ：50 mg/mL (85.37 mM; 超声助溶; 吸湿的 DMSO 对产品的溶解度有显著影响，请使用新开封的 DMSO)
<table>
<tr><td rowspan="4">Preparing Stock Solutions</td><td>Solvent / Mass / Concentration</td><td>1 mg</td><td>5 mg</td><td>10 mg</td></tr>
<tr><td>1 mM</td><td>1.7074 mL</td><td>8.5369 mL</td><td>17.0739 mL</td></tr>
<tr><td>5 mM</td><td>0.3415 mL</td><td>1.7074 mL</td><td>3.4148 mL</td></tr>
<tr><td>10 mM</td><td>0.1707 mL</td><td>0.8537 mL</td><td>1.7074 mL</td></tr>
</table>
*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。
储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month (protect from light)。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。
动物实验：
请根据您的实验动物和给药方式 选择适当的溶解方案。
以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：
——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用；
以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶
方案 一
请依序添加每种溶剂： 10% DMSO → 90% (20% SBE-β-CD in Saline)
Solubility: ≥ 5 mg/mL (8.54 mM); 澄清溶液
此方案可获得 ≥ 5 mg/mL（饱和度未知）的澄清溶液。
以 1 mL 工作液为例，取 100 μL 50.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液 中，混合均匀。
2 g SBE-β-CD（磺丁基醚 β-环糊精）粉末定容于 10 mL 的生理盐水中，完全溶解至澄清透明。
方案 二
请依序添加每种溶剂： 10% DMSO → 90% Corn Oil
Solubility: ≥ 5 mg/mL (8.54 mM); 澄清溶液
此方案可获得 ≥ 5 mg/mL（饱和度未知）的澄清溶液，此方案实验周期在半个月以上的动物实验酌情使用。
以 1 mL 工作液为例，取 100 μL 50.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
方案 三
请依序添加每种溶剂： 10% DMSO → 40% PEG300 → 5% Tween-80 → 45% Saline
Solubility: ≥ 1.62 mg/mL (2.77 mM); 澄清溶液
此方案可获得 ≥ 1.62 mg/mL（饱和度未知）的澄清溶液。</td></tr>
</table>

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	以 1 mL 工作液为例，取 100 μL 16.2 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；再向上述体系中加入 50 μL Tween-80，混合均匀；然后再继续加入 450 μL 生理盐水 定容至 1 mL。 生理盐水的配制：将 0.9 g 氯化钠，溶解于 ddH₂O 并定容至 100 mL，可以得到澄清透明的生理盐水溶液。 以下溶解方案，请直接配制工作液。建议现用现配，在短期内尽快用完。 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比； 如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶。 方案 一 请依序添加每种溶剂： 50% PEG300 → 50% Saline Solubility: 10 mg/mL (17.07 mM); 悬浊液; 超声助溶 方案 二 请依序添加每种溶剂： 15% Cremophor EL → 85% Saline Solubility: 5 mg/mL (8.54 mM); 悬浊液; 超声助溶。
参考文献	[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.

完整储备液配制表：

请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month (protect from light)。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

可选溶剂	质量 / 溶剂体积 / 浓度	1 mg	5 mg	10 mg	25 mg
DMSO	**1 mM**	1.7074 mL	8.5369 mL	17.0739 mL	42.6847 mL
	5 mM	0.3415 mL	1.7074 mL	3.4148 mL	8.5369 mL
	10 mM	0.1707 mL	0.8537 mL	1.7074 mL	4.2685 mL
	15 mM	0.1138 mL	0.5691 mL	1.1383 mL	2.8456 mL

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	20 mM	0.0854 mL	0.4268 mL	0.8537 mL	2.1342 mL
	25 mM	0.0683 mL	0.3415 mL	0.6830 mL	1.7074 mL
	30 mM	0.0569 mL	0.2846 mL	0.5691 mL	1.4228 mL
	40 mM	0.0427 mL	0.2134 mL	0.4268 mL	1.0671 mL
	50 mM	0.0341 mL	0.1707 mL	0.3415 mL	0.8537 mL
	60 mM	0.0285 mL	0.1423 mL	0.2846 mL	0.7114 mL
	80 mM	0.0213 mL	0.1067 mL	0.2134 mL	0.5336 mL