



上海源叶生物科技有限公司  
Shanghai yuanye Bio-Technology Co., Ltd  
电话: 021-61312973 传真: 021-55068248  
网址: [www.shyuanye.com](http://www.shyuanye.com)  
邮箱: [shyysw@sina.com](mailto:shyysw@sina.com)

产品名称: **17-DMAG (Alvespimycin) HCl**  
产品别名: 阿螺旋霉素盐酸盐; **Alvespimycin hydrochloride**

生物活性:

|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                           |             |             |             |              |
|---------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|-------------|-------------|-------------|--------------|
| Description               | Alvespimycin hydrochloride (17-DMAG hydrochloride; KOS-1022; BMS 826476) is a potent inhibitor of Hsp90, binding to Hsp90 with EC50 of 62±29 nM.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                           |             |             |             |              |
| IC <sub>50</sub> & Target | HSP90                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | GRP94                     |             |             |             |              |
|                           | 62 nM (EC <sub>50</sub> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 65 nM (EC <sub>50</sub> ) |             |             |             |              |
| In Vitro                  | Alvespimycin hydrochloride (17-DMAG hydrochloride; KOS-1022; BMS 826476) inhibits the growth of the human cancer cell lines SKBR3 and SKOV3, which overexpress Hsp90 client protein Her2, and causes down-regulation of Her2 as well as induction of Hsp70 consistent with Hsp90 inhibition, for Her2 degradation with EC50 of 8±4 nM and 46±24 nM in SKBR3 and SKOV3 cells, respectively; for Hsp70 induction with EC50 of 4±2 nM and 14±7 nM in SKBR3 and SKOV3 cells, respectively[1]. Compared with the vehicle control, 17-DMAG exerts dose-dependent apoptosis (P<0.001 averaged across 24- and 48-hour time points) at concentrations of 50nM to 500nM, which represent pharmacologically attainable doses. Similar to many other agents, 17-DMAG also demonstrates time-dependent apoptosis (P <0.001, averaged across all doses) in chronic lymphocytic leukemia (CLL) cells with extended exposure from 24 to 48 hours. In addition, 17-DMAG is much more potent after 24 and 48 hours of treatment than 17-AAG[2]. |                           |             |             |             |              |
| In Vivo                   | The tumors are grown for two months before the start of i.p. injections every four days over one month with 0, 50, 100 and 200 mg/kg dipalmitoyl-radicicol or 0, 5, 10 and 20 mg/kg 17-DMAG. Despite sample heterogeneity, the HSP90 inhibitor-treated animals have significantly lower tumour volumes than the vehicle control-treated animals. HSP90 inhibitors have been shown to cause liver toxicity in an animal model of gastrointestinal cancer. Nevertheless, the reduction in tumor size using dipalmitoyl-radicicol is statistically significant at 100 mg/kg, while 17-DMAG at either 10 or 20 mg/kg elicited a significant reduction in tumor size[3].                                                                                                                                                                                                                                                                                                                                                           |                           |             |             |             |              |
| Solvent&Solubility        | <b>In Vitro:</b><br><b>DMSO : ≥ 50 mg/mL (76.55 mM)</b><br><br>* "≥" means soluble, but saturation unknown.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                           |             |             |             |              |
|                           | <b>Preparing Stock Solutions</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <b>Solvent</b>            | <b>Mass</b> |             |             |              |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>Concentration</b>      |             | <b>1 mg</b> | <b>5 mg</b> | <b>10 mg</b> |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 1 mM                      |             | 1.5309 mL   | 7.6545 mL   | 15.3090 mL   |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 5 mM                      |             | 0.3062 mL   | 1.5309 mL   | 3.0618 mL    |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 10 mM                     |             | 0.1531 mL   | 0.7655 mL   | 1.5309 mL    |
|                           | *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。<br><br>储备液的保存方式和期限 -80℃, 6 months; -20℃, 1 month。 -80℃ 储存时, 请在 6 个月内使用, -20℃ 储存时, 请在 1 个月内使用。<br><br><b>In Vivo:</b><br><br>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:<br><br>——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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                           |             |             |             |              |



上海源叶生物科技有限公司  
Shanghai yuanye Bio-Technology Co., Ltd  
电话: 021-61312973 传真: 021-55068248  
网址: [www.shyuanye.com](http://www.shyuanye.com)  
邮箱: [shyysw@sina.com](mailto:shyysw@sina.com)

|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                       | <p>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</p> <p>1. 请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: <math>\geq 2.5</math> mg/mL (3.83 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (3.83 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中, 混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80, 混合均匀; 然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2. 请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-<math>\beta</math>-CD in saline)</p> <p>Solubility: <math>\geq 2.5</math> mg/mL (3.83 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.5</math> mg/mL (3.83 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水水溶液中, 混合均匀。</p>                                                                                                        |
| References            | <p>[1]. Ge J, et al. Design, synthesis, and biological evaluation of hydroquinone derivatives of 17-amino-17-demethoxygeldanamycin as potent, water-soluble inhibitors of Hsp90. J Med Chem. 2006 Jul 27;49(15):4606-15.</p> <p>[2]. Hertlein E, et al. 17-DMAG targets the nuclear factor-kappaB family of proteins to induce apoptosis in chronic lymphocytic leukemia: clinical implications of HSP90 inhibition. Blood. 2010 Jul 8;116(1):45-53.</p> <p>[3]. Henke A, et al. Reduced Contractility and Motility of Prostatic Cancer-Associated Fibroblasts after Inhibition of Heat Shock Protein 90. Cancers (Basel). 2016 Aug 24;8(9). pii: E77.</p>                                                                                                                                                                                                                                                                                                                        |
| 实验参考:                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Cell Assay            | <p>MTT assays are performed to determine cytotoxicity. A total of <math>1 \times 10^6</math> CD19-selected B cells from CLL patients are incubated for 24 or 48 hours in 17-DMAG, 17-AAG, or vehicle. MTT reagent is then added, and plates are incubated for an additional 24 hours before spectrophotometric measurement. Apoptosis is determined by staining with annexin V-fluorescein isothiocyanate and propidium iodide (PI). After exposure to drugs, cells are washed with phosphate-buffered saline and stained in 1 time binding buffer. Cell death is assessed by flow cytometry using a Beckman-Coulter model EPICS XL cytometer. Data are analyzed with the System II software package. A total of 10 000 cells are counted for each sample. Mitochondrial membrane potential changes are assessed by staining with the lipophilic cationic dye JC-1 and analysis by flow cytometry<sup>[2]</sup>.</p>                                                              |
| Animal Administration | <p>Mice<sup>[3]</sup></p> <p>Young male CB-17/lcrHsd-Prkdc-SCID mice, are used. Recombinant xenografts are made by mixing <math>1 \times 10^5</math> BPH1 cells and <math>2.5 \times 10^5</math> CAF per graft in collagen solution, allowed to gel, covered with medium and cultured overnight. Tumors are allowed to form over eight weeks, and then treated for four weeks with three different doses of dipalmitoyl-radicicol (50, 100 and 200 mg/kg) and 17-DMAG (5, 10 and 20 mg/kg) via intraperitoneal injections of compounds in sesame oil every four days. After 12 weeks in total, the mice are sacrificed, their kidneys resected, grafts cut in half and photographed before processing for histology. Graft dimensions are measured and the resultant tumour volume is calculated using the formula; volume=width×length×depth×<math>\pi/6</math>. This formula represents a conservative approach to evaluate tumour volumes, as it understates the volume of</p> |



上海源叶生物科技有限公司  
Shanghai yuanye Bio-Technology Co., Ltd  
电话: 021-61312973 传真: 021-55068248  
网址: [www.shyuanye.com](http://www.shyuanye.com)  
邮箱: [shyysw@sina.com](mailto:shyysw@sina.com)

|            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|            | large, invasive tumours compared with smaller, non-invasive tumours. Resected grafts are fixed in 10% formalin, embedded in paraffin and processed for immunohistochemistry.                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| References | <p>[1]. Ge J, et al. Design, synthesis, and biological evaluation of hydroquinone derivatives of 17-amino-17-demethoxygeldanamycin as potent, water-soluble inhibitors of Hsp90. J Med Chem. 2006 Jul 27;49(15):4606-15.</p> <p>[2]. Hertlein E, et al. 17-DMAG targets the nuclear factor-kappaB family of proteins to induce apoptosis in chronic lymphocytic leukemia: clinical implications of HSP90 inhibition. Blood. 2010 Jul 8;116(1):45-53.</p> <p>[3]. Henke A, et al. Reduced Contractility and Motility of Prostatic Cancer-Associated Fibroblasts after Inhibition of Heat Shock Protein 90. Cancers (Basel). 2016 Aug 24;8(9). pii: E77.</p> |



源叶生物