产品名称：**KNK437**
产品别名：**KNK437**

生物活性：

Description	KNK437 is a HSP inhibitor, and inhibits the induction of HSP105, HSP70, and HSP40.					
IC_{50} & Target	HSP105	HSP70	HSP40			
In Vitro	KNK437 inhibits the activation of several HSPs including HSP105, HSP70, and HSP40 in COLO 320DM (human colon carcinoma) cells. KNK437 (100 μM) inhibits thermotolerance in COLO 320DM cells after the first heat treatment. KNK437 shows inhibitory effects on thermotolerance dose-dependently in COLO 320DM cells (0-200 μM) and HeLa S3 cells (100, 200 μM)[1]. KNK437 (100 μM) exhibits inhibitory activities against the methylation of H3-Lys4 before or after heat-treatment in HSC4 cells and KB cells, but does not affect that of H3 Lys9. KNK437 also suppresses the expression of HSP70[3].					
In Vivo	KNK437 is a weakly toxic agent. KNK437 (62.5-400 mg/kg) recovers bodyweight losses of tumor-free CD-1 (ICR) mice. KNK437 (200 mg/kg) alone shows no antitumor effects and does not increase the thermosensitivity of nontolerant tumors. KNK437 improves the antitumor effects of fractionated heat treatment at 44°C at 200 mg/kg in a synergistic manner. KNK437 (200 mg/kg, i.p.) suppresses the induction of thermotolerance when administrated 6 h before the initial heating[2].					

Solvent&Solubility

In Vitro:

DMSO : ≥ 34 mg/mL (138.65 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.0778 mL	20.3890 mL	40.7780 mL
	5 mM	0.8156 mL	4.0778 mL	8.1556 mL
	10 mM	0.4078 mL	2.0389 mL	4.0778 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。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-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。

In Vivo:

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

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: 1.67 mg/mL (6.81 mM); Suspended solution; Need ultrasonic

此方案可获得 1.67 mg/mL (6.81 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。

以 1 mL 工作液为例，取 100 μL 16.699999 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

[1]. Yokota S, et al. Benzylidene lactam compound, KNK437, a novel inhibitor of acquisition of thermotolerance and heat shock protein induction in human colon carcinoma cells. Cancer Res. 2000 Jun 1;60(11):2942-8.

References	[2]. Koishi M, et al. The effects of KNK437, a novel inhibitor of heat shock protein synthesis, on the acquisition of thermotolerance in a murine transplantable tumor in vivo. Clin Cancer Res. 2001 Jan;7(1):215-9. [3]. Matsuda K, et al. Effects of KNK437 on heat-induced methylation of histone H3 in human oral squamous cell carcinoma cells. Int J Hyperthermia. 2006 Dec;22(8):729-35.

实验参考：

Cell Assay	Heat treatments at 42°C for 90 min are performed in a CO_2 incubator using 25-cm_2 plastic flasks. Cells (1×10^5) are seeded in the flasks, incubated at 37°C for 48 h, and then heated by immersing the flasks in a water bath (45°C ± 0.05°C). KNK437 and quercetin are dissolved in DMSO before being added at the indicated concentrations. The final concentration of DMSO in each culture medium is 0.25% (v/v), irrespective of the concentrations of the drugs. The same concentration of DMSO is used as a control. Sodium arsenite is dissolved in PBS at a concentration of 80 mM and added to the medium. Cells are treated with 300 μM sodium arsenite at 37°C for 1.5 h, rinsed, and then incubated at 37°C for 5 h before 45°C heat challenge[1].
Animal Administration	To subject the tumors to hyperthermia, the right foot of each mouse is immersed in a water bath maintained at the desired temperature to an accuracy of ± 0.05°C. After the mouse has been anesthetized with 50 mg/kg pentobarbital sodium solution, the tumor-bearing leg is pulled down into the water bath using a special sinker (weighing ~45 g) taped to the skin of the toe. Care is taken not to impair the blood flow in the limb. While the extended right leg is receiving local heat, the mouse is air-cooled. KNK437 is dissolved in olive oil immediately before use. The KNK437 is administered i.p. 6 h before the first heat treatment. It is used mainly at a concentration of 200 mg/kg[2].
References	[1]. Yokota S, et al. Benzylidene lactam compound, KNK437, a novel inhibitor of acquisition of thermotolerance and heat shock protein induction in human colon carcinoma cells. Cancer Res. 2000 Jun 1;60(11):2942-8. [2]. Koishi M, et al. The effects of KNK437, a novel inhibitor of heat shock protein synthesis, on the acquisition of thermotolerance in a murine transplantable tumor in vivo. Clin Cancer Res. 2001 Jan;7(1):215-9. [3]. Matsuda K, et al. Effects of KNK437 on heat-induced methylation of histone H3 in human oral squamous cell carcinoma cells. Int J Hyperthermia. 2006 Dec;22(8):729-35.