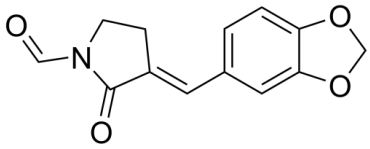
Data Sheet

Product Name:	KNK437
Cat. No.:	CS-5659
CAS No.:	218924-25-5
Molecular Formula:	$C_{13}H_{11}NO_4$
Molecular Weight:	245.23
Target:	HSP
Pathway:	Cell Cycle/DNA Damage; Metabolic Enzyme/Protease
Solubility:	DMSO : 31.25 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

KNK437 is a **HSP** inhibitor, and inhibits the induction of HSP105, HSP70, and HSP40. IC50 & Target: HSP[1] ***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].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: KNK437 is dissolved in DMSO and then diluted in culture medium.[1]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:** KNK437 is dissolved in olive oil immediately before use.[2]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.

CAIndexNames:

1-Pyrrolidinecarboxaldehyde, 3-(1,3-benzodioxol-5-ylmethylene)-2-oxo-

SMILES:

O=CN1C(/C(CC1)=C/C2=CC=C(OCO3)C3=C2)=O

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