

Product Data Sheet

Product Name: KNK437
Cat. No.: GC11930

Chemical Properties

Cas. No. 218924-25-5

Chemical Name (E)-3-(benzo[d][1,3]dioxol-5-ylmethylene)-2-oxopyrrolidine-1-carbaldehyde

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

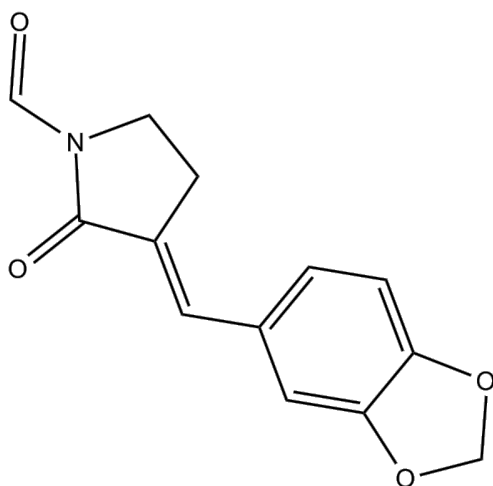
Formula $C_{13}H_{11}NO_4$ M.Wt 245.23

Solubility $\geq 12.25\text{mg/mL}$ in DMSO with ultrasonic Storage Store at -20°C

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



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

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Protocol

Cell experiment: Heat treatments at 42°C for 90 min are performed in a CO₂ incubator using 25-cm² 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 $\pm$ 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 μ M 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 experiment: 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 $\pm$ 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].

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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.

Background

KNK437 is a benzylidene lactam compound that inhibits stress-induced HSPs (heat shock proteins) synthesis.

HSPs (heat shock proteins) are chaperones that their expressions are increased under various cellular stresses including temperature rise. It plays a vital role in regulating protein folding and associated with cancer and cardiovascular diseases.

KNK437 inhibits the acquisition of thermotolerance and the induction of various HSPs in human colon carcinoma cells (COLO 320DM) in a dose-dependent manner. KNK437 also blocks the acquisition of thermotolerance that developed by sodium arsenite. [1]

KNK437 exerts low toxicity in vivo. In C3H/He mice transplanted with SCC VII cells, the concentration of KNK437 in the tumors gradually increases and reaches a peak 6 hours after i.p. injection. Hsp72 were synthesized 8 h after hyperthermia at 44 oC for 10 minutes, and their synthesis is inhibited by administration of KNK437 6 hours before hyperthermia. [2]

References:

1. Yokota S, Kitahara M, Nagata K. 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, Yokota S, Mae T 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*

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