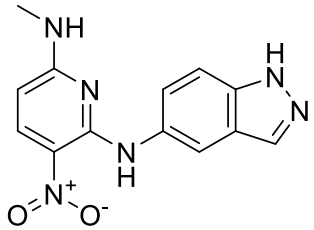
Product data sheet

MedKoo Cat#: 407439 Name: KRIBB11 CAS#: 342639-96-7 Chemical Formula: $C_{13}H_{12}N_6O_2$ Exact Mass: 284.1022 Molecular Weight: 284.279	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
KRIBB11 is a HSP70 inhibitor. KRIBB11 inhibits HSP70 synthesis through inhibition of heat shock factor 1 function by impairing the recruitment of positive transcription elongation factor b to the hsp70 promoter.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	27	94.98

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.52 mL	17.59 mL	35.18 mL
5 mM	0.70 mL	3.52 mL	7.04 mL
10 mM	0.35 mL	1.76 mL	3.52 mL
50 mM	0.07 mL	0.35 mL	0.70 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Yoon YJ, Kim JA, Shin KD, Shin DS, Han YM, Lee YJ, Lee JS, Kwon BM, Han DC. KRIBB11 inhibits HSP70 synthesis through inhibition of heat shock factor 1 function by impairing the recruitment of positive transcription elongation factor b to the hsp70 promoter. J Biol Chem. 2011 Jan 21;286(3):1737-47. doi: 10.1074/jbc.M110.179440. Epub 2010 Nov 15. PMID: 21078672; PMCID: PMC3023468.

In vivo study

1. Yoon YJ, Kim JA, Shin KD, Shin DS, Han YM, Lee YJ, Lee JS, Kwon BM, Han DC. KRIBB11 inhibits HSP70 synthesis through inhibition of heat shock factor 1 function by impairing the recruitment of positive transcription elongation factor b to the hsp70 promoter. J Biol Chem. 2011 Jan 21;286(3):1737-47. doi: 10.1074/jbc.M110.179440. Epub 2010 Nov 15. PMID: 21078672; PMCID: PMC3023468.

7. Bioactivity
Biological target:

KRIBB11 is an inhibitor of Heat shock factor 1 (HSF1), with IC50 of 1.2 μM.

In vitro activity

Product data sheet

The inhibitory effect of KRIBB11 on the endogenous hsp70, hsp47, and hsp27 promoter activities was investigated. For this purpose, HCT-116 cells were subjected to heat shock at 43 °C for 1 h in the presence or absence of KRIBB11 and incubated further at 37 °C for 1 h to allow recovery. After isolation of total RNA, hsp70 mRNA expression was evaluated by quantitative real time reverse transcription-PCR. As shown in Fig. 1C, heat shock treatment caused a 13-fold increase in hsp70 mRNA expression relative to the non-heat shock condition. Pretreatment of HCT-116 cells with KRIBB11 blocked heat shock-induced hsp70 mRNA expression in a concentration-dependent manner, with 70% inhibition at 10 μmol/liter. Similarly, KRIBB11 inhibited hsp47 and hsp27 mRNA expression in a concentration-dependent manner (Fig. 1, D and E). In accordance with its effect on mRNA expression, KRIBB11 also significantly down-regulated HSF1 downstream target proteins such as HSP70 and HSP27 in a concentration-dependent manner (Fig. 1F). Heat shock induces hyperphosphorylation of HSF1, resulting in a shift in its mobility on SDS gels. To exclude the possible nonspecific transcriptional inhibitory activity of KRIBB11, its effect on NF-κB activity was tested. NF-κB regulates the transcription of various inflammatory cytokines as well as anti-apoptotic genes. A pNF-κB-Luc plasmid for an NF-κB luciferase reporter assay was obtained from Stratagene (La Jolla, CA) and used as described previously. As shown in Fig. 1G, NF-κB reporter activity was stimulated by treating cells with 20 ng/ml TNF-α. However, pretreatment with high concentrations of KRIBB11 weakly inhibited TNF-α-dependent NF-κB reporter activity. This result suggests that KRIBB11 is not a general transcription inhibitor. The inhibition of HSF1 activity by KRIBB11 and the consequent down-regulation of HSP70 and HSP27 led to the speculation that KRIBB11 could inhibit the proliferation of cancer cells. To evaluate the effect of KRIBB11 on the growth of cancer cells, HCT-116 cells were treated with different concentrations of KRIBB11 (0–50 μmol/liter) for 48 h (Fig. 2A). KRIBB11 exhibited a dose-dependent inhibition of HCT-116 cell growth over a broad range of concentrations, with an IC50 of 5 μmol/liter, where IC50 is the inhibitor concentration at which a 50% inhibition of cell growth is observed. The effect of KRIBB11 on the proliferation of various other tumor cell lines was also analyzed; these cell lines and the IC50 value for each are as follows: HCT-15 (5 μmol/liter), Mia-PaCa-2 (3 μmol/liter), SW-620 (4 μmol/liter), HT-29 (3 μmol/liter), A549 (5 μmol/liter), and MDA-MB-231 (8 μmol/liter).

Reference: J Biol Chem. 2011 Jan 21;286(3):1737-47. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/21078672/

In vivo activity

HCT-116 tumor xenografts in nude mice were used to investigate the inhibitory activity of KRIBB11 on tumor growth in vivo. HCT-116 cells were implanted subcutaneously into the right flank of nude mice. When the tumor volume reached 72.2 mm3 (13 days after implantation), the indicated compounds were administered intraperitoneally at a dose of 50 mg/kg of KRIBB11 or 2 mg/kg of adriamycin per day. Because there is no available anticancer drug that specifically targets HSF1, adriamycin was used as a positive control compound. Adriamycin interacts with DNA by intercalation and is commonly used in the treatment of a wide range of cancers. To determine the toxicity of the compound, the body weight of tumor-bearing mice was measured. On day 18, the mice were sacrificed, and the tumors were removed and weighed. Mice treated with KRIBB11 showed a 47.4% ($p < 0.05$) decrease in tumor volume compared with control mice (Fig. 6A). Similarly, when adriamycin was used as a positive control compound, tumor volume was decreased by 31.7%. There was no change in body weight when KRIBB11 was used at 50 mg/kg (Fig. 6B). However, when adriamycin was used at 2 mg/kg, a loss of 13.2% ($p < 0.001$) of body weight was observed. To confirm that KRIBB11 suppressed the growth of HCT-116 tumors through the inhibition of HSF1 activity in vivo, HSP70 protein levels were measured in tumor tissues from both KRIBB11- and control-treated mice. As shown in Fig. 6C, HSP70 protein levels were significantly decreased in tumors from mice treated with KRIBB11, as compared with mice treated with vehicle.

Reference: J Biol Chem. 2011 Jan 21;286(3):1737-47. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/21078672/