

Product Data Sheet

Product Name: FK866 (APO866)

Cat. No.: GC14308

Chemical Properties

Cas. No. 658084-64-1

Chemical Name (E)-N-[4-(1-benzoylpiperidin-4-yl)butyl]-3-pyridin-3-ylprop-2-enamide

SMILES C1CN(CCC1CCCCNC(=O)C=CC2=CN=CC=C2)C(=O)C3=CC=CC=C3

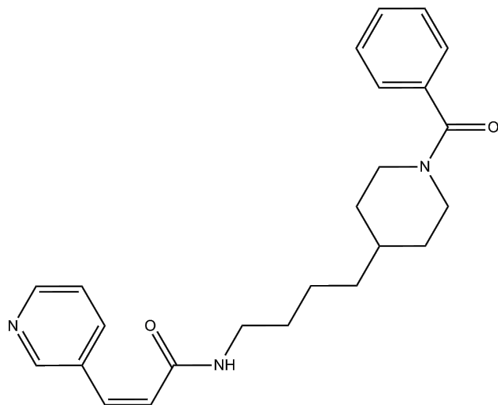
Formula $C_{24}H_{29}N_3O_2$ M.Wt 391.51

Solubility $\geq 19.6\text{mg/mL}$ in DMSO, $\geq 49.6\text{mg/mL}$ in EtOH 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



Protocol

Cell experiment [1]:

Cell lines MHCC97-H cells (human hepatocellular carcinoma cell line)

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Preparation Method	MHCC97-H cells were maintained in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS), 100U/mL penicillin and 100µg/mL streptomycin at 37°C, 5% CO ₂ . MHCC97-H cells were treated with FK866 at concentrations of 0, 1.25, 2.5, 5, 10, 20, 40nM for 24, 48 or 72h.
Reaction Conditions	0-40nM; 24-72h
Applications	FK866 inhibited the viability of MHCC97-H cells in a dose-dependent manner at 5, 10, 20, 40nM within 24-72h, with no significant time-dependent difference in inhibitory effect. FK866 decreased intracellular NAD ⁺ and ATP levels in a dose-dependent manner via suppressing NAMPT expression. FK866 reduced the migration and invasion capacities of MHCC97-H cells in a dose-dependent manner. FK866 downregulated SIRT1 and vimentin protein expression, and upregulated E-cadherin protein expression, reversing the epithelial-mesenchymal transition phenotype.
Animal experiment [2]:	
Animal models	Male C57BL/6J mice (8-12 weeks) with bleomycin (3mg/kg; intratracheal instillation)-induced pulmonary fibrosis
Preparation Method	Mice were intraperitoneally injected with FK866 at 1-10mg/kg once daily for 16 consecutive days from 1 day before bleomycin instillation to 14 days after instillation, with the second dose administered 30 minutes after bleomycin instillation.
Dosage form	1-10mg/kg; i.p.; daily injection for 16 days (from Day-1 to Day14 post-bleomycin)

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Applications

FK866 decreased NAMPT, TNF- α , IL-6 and TGF- β 1 levels in bronchoalveolar lavage fluid (BALF) of bleomycin-treated mice in a dose-dependent manner, reversed bleomycin-induced elevation of NAD⁺ level in lung tissue, downregulated mRNA expressions of Col1a1, Col3a1, Tgfb1 and Acta2 in lung tissues, suppressed CD206⁺ M2 macrophage infiltration in lungs, alleviated bleomycin-induced body weight loss, lung inflammation and collagen deposition. FK866 improved the survival rate of bleomycin-treated mice.

References:

- [1] Zhang B, Shi D, Zhang X, et al. FK866 inhibits the epithelial-mesenchymal transition of hepatocarcinoma MHCC97-H cells. *Oncol Lett.* 2018 Nov;16(5):7231-7238.
- [2] Chen Y, Wang T, Liang F, et al. Nicotinamide phosphoribosyltransferase prompts bleomycin-induced pulmonary fibrosis by driving macrophage M2 polarization in mice. *Theranostics.* 2024 Apr;14(7):2794-2815.

Background

FK866 (APO866) is a potent and selective inhibitor of nicotinamide phosphoribosyltransferase (NAMPT) ($K_i=0.3\text{nM}$). FK866 blocks the conversion of nicotinamide to nicotinamide mononucleotide (NMN), thereby depleting intracellular NAD⁺ and ATP. FK866 triggers caspase-independent tumor cell death by inducing mitochondrial membrane depolarization and autophagy. FK866 can be used in studies related to tumor metabolism, hematological malignancies, and NAD⁺ homeostasis regulation^[1-4].

In vitro, FK866 (0-40nM) was applied to human hepatocellular carcinoma MHCC97-H cells for 24-72h. FK866 inhibited NAMPT expression and reduced intracellular NAD⁺ and ATP levels. FK866 suppressed epithelial-mesenchymal transition, and inhibited cell viability, migration, and invasion ability^[5]. FK866 (5nM) was applied to human pancreatic ductal adenocarcinoma KP4 cells, PANC-1 cells, and mouse 4T1 and MC38 cells for 24h. FK866 inhibited compensatory glycolysis and induced oxidative stress and cell death. FK866 (5nM) combined with metformin activated p53 pathway and unfolded protein response-related gene expression, enhancing anti-tumor effects^[6].

In vivo, FK866 (10mg/kg; three times) was intraperitoneally injected into C57BL/6 mice with acute

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liver failure at 24h, 12h, and 0.5h before modeling. FK866 alleviated hepatotoxicity, enhanced autophagic activity, inhibited JNK activation, reduced serum alanine aminotransferase and aspartate aminotransferase levels, and decreased hepatocyte necrosis and inflammatory cell infiltration^[7]. FK866 (1-10mg/kg) was intraperitoneally injected into C57BL/6J mice with bleomycin (3mg/kg; intratracheal instillation)-induced pulmonary fibrosis, once daily from one day before modeling to 14 days after modeling, for a total of 16 days. FK866 alleviated bleomycin-induced lung inflammation and collagen deposition, reduced NAMPT levels and release of cytokines such as TNF- α , IL-6, and TGF- β 1 in bronchoalveolar lavage fluid. FK866 decreased M2 macrophage infiltration in the lungs, ameliorated body weight loss, and improved survival rate^[8].

References:

- [1] Xie H, Lei Y, Mao Y, et al. FK866 inhibits colorectal cancer metastasis by reducing NAD⁺ levels in cancer-associated fibroblasts. *Genes Genomics*. 2022 Dec;44(12):1531-1541.
- [2] Pant K, Richard S, Peixoto E, et al. The NAMPT Inhibitor FK866 in Combination with Cisplatin Reduces Cholangiocarcinoma Cells Growth. *Cells*. 2023 Feb 28;12(5):775.
- [3] Tan Z, Chen L, Ren Y, et al. Neuroprotective effects of FK866 against traumatic brain injury: Involvement of p38/ERK pathway. *Ann Clin Transl Neurol*. 2020 May;7(5):742-756.
- [4] Ok CY, Park S, Jang HO, et al. FK866 Protects Human Dental Pulp Cells against Oxidative Stress-Induced Cellular Senescence. *Antioxidants (Basel)*. 2021 Feb 10;10(2):271.
- [5] Zhang B, Shi D, Zhang X, et al. FK866 inhibits the epithelial-mesenchymal transition of hepatocarcinoma MHCC97-H cells. *Oncol Lett*. 2018 Nov;16(5):7231-7238.
- [6] Parisotto M, Vuong-Robillard N, Kalegari P, et al. The NAMPT Inhibitor FK866 Increases Metformin Sensitivity in Pancreatic Cancer Cells. *Cancers*. 2022 Nov;14(22):5597.
- [7] Guo E, Li R, Yang J, et al. FK866 attenuates acute hepatic failure through c-jun-N-terminal kinase(JNK)-dependent autophagy. *Sci Rep*. 2017 May 19;7:2206.
- [8] Chen Y, Wang T, Liang F, et al. Nicotinamide phosphoribosyltransferase prompts bleomycin-induced pulmonary fibrosis by driving macrophage M2 polarization in mice. *Theranostics*. 2024 Apr;14(7):2794-2815.

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