(E)-Daporinad

Cat. No.: HY-50876

CAS No.: 658084-64-1

Molecular Formula: $C_{24}H_{29}N_3O_2$

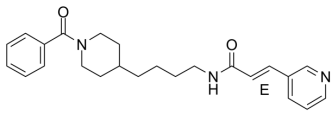
Molecular Weight: 391.51

Target: NAMPT; Autophagy

Pathway: Metabolic Enzyme/Protease; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (127.71 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5542 mL	12.7711 mL	25.5421 mL
5 mM	0.5108 mL	2.5542 mL	5.1084 mL
10 mM	0.2554 mL	1.2771 mL	2.5542 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 20% SBE-β-CD in saline
   Solubility: 4 mg/mL (10.22 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

(E)-Daporinad (FK866) is an effective inhibitor of nicotinamide phosphoribosyltransferase (NMPRTase; Nampt) with an IC_{50} of 0.09 nM.

IC_{50} & Target	IC50: 0.09 nM (NMPRTase)
In Vitro	Nampt inhibition with (E)-Daporinad (FK866) induces significant NAD^+ intracellular reduction and selectively kills MM cells. (E)-Daporinad (FK866)-induced cell death is associated with inhibition of Nampt activity, rather than protein expression, and higher NAD^+ baseline levels in MM cells than normal PBMCs confer (E)-Daporinad (FK866) sensitivity. (E)-Daporinad (FK866) abrogates the survival advantage conferred by the bone marrow microenvironment[1]. (E)-Daporinad (FK866) prevents the $[Ca^{2+}]i$ increase induced by different mitogens and reduces the Ca^{2+} content of TG-responsive Ca^{2+} stores in Jurkat and in activated PBLs. (E)-Daporinad (FK866) reduces the Ca^{2+} content of TG-responsive Ca^{2+} stores in Jurkat cells but not in Bcl2-Jurkat cells[2]. Inhibition of NAMPT by (E)-Daporinad (FK866), or inhibition of SIRT by nicotinamide decreases proliferation and triggered death of 293T cells involving the p53 acetylation pathway[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	(E)-Daporinad (FK866) (30 mg/kg, i.p.) decreases the tumor burden in CB17-SCID mice, and the tumor tissue demonstrates a significant decrease in ERK phosphorylation and proteolytic cleavage of LC3[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	MM1S cells (2×10^4 cells/well) are cultured for 72 and 96 hours in BMSC-coated 96-well plates in the presence or absence of drug. DNA synthesis is measured by (^3H)-thymidine uptake, with (^3H)-thymidine added (0.5 μCi/well) during the last 8 hours of cultures. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	CB17-SCID mice (28-35 days old) are irradiated (200 cGy), and then inoculated subcutaneously in the right flank with 3×10^6 MM1S cells in 100 μL RPMI 1640. After detection of tumor (2 weeks after the injection), 7 mice are treated intraperitoneally with either vehicle or (E)-Daporinad (FK866) (30 mg/kg body weight) twice a day for 4 days, repeated weekly over 3 weeks. Caliper measurements of the longest perpendicular tumor diameters are performed twice a week to estimate the tumor volume using the following formula: $length\times width^2\times0.5$. Tumor growth inhibition (TGI) is calculated. Animals are killed when tumors reach 2 cm^3 or the mice appear moribund. Survival is evaluated from the first day of treatment until death. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Adv. 2023 Apr 14;9(15):eadf8522.
- Hepatology. 2022 Jul 11.
- Cell Death Differ. 2024 Jan 5.
- Redox Biol. 2024 Jan 3:69:103030.
- Acta Pharmacol Sin. 2023 Jun 5.

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REFERENCES

[1]. Cea M, et al. Targeting NAD+ salvage pathway induces autophagy in multiple myeloma cells via mTORC1 and extracellular signal-regulated kinase (ERK1/2) inhibition. Blood. 2012 Oct 25;120(17):3519-29.

[2]. Magnone M, et al. NAD+ levels control Ca2+ store replenishment and mitogen-induced increase of cytosolic Ca2+ by Cyclic ADP-ribose-dependent TRPM2 channel gating in human T lymphocytes. J Biol Chem. 2012 Jun 15;287(25):21067-81.

[3]. Thakur BK, et al. Inhibition of NAMPT pathway by FK866 activates the function of p53 in HEK293T cells. Biochem Biophys Res Commun. 2012 Aug 3;424(3):371-7.

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