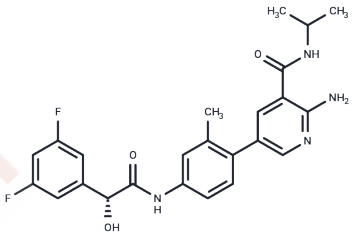
Data Sheet (Cat.No.T86545)

TargetMol

HC-5404

Chemical Properties



CAS No. : 2247396-91-2

Formula: C24H24F2N4O3

Molecular Weight: 454.47

Storage: Keep away from moisture,Keep away from direct sunlight
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	HC-5404 is a novel, potent and highly selective PERK (Protein kinase RNA-like Endoplasmic Reticulum Kinase) inhibitor, blocking the activation of the PERK pathway, which in turn inhibits the endoplasmic reticulum stress response signaling pathway, thereby exerting anti-tumor effects, and can be used to treat advanced solid tumors and renal cell Cancer.
Targets(IC50)	PERK
In vitro	In this study, HEK-293 cells were treated with different concentrations of HC-5404 for 30 minutes, followed by treatment with 1 mmol/L tunicamycin for 4 hours. The cells were then lysed using RIPA buffer, and Western blot analysis was performed to detect the phosphorylation level of PERK (p-PERK) and the expression level of ATF4. Specific antibodies were used to recognize p-PERK (T982) and ATF4. The **Results** showed that HC-5404 inhibited the tunicamycin-induced PERK autophosphorylation (p-PERK) in a concentration-dependent manner, with an IC50 value of 23 nmol/L. Additionally, HC-5404 also inhibited ATF4 expression, with an IC50 value of 88 nmol/L. Overall, HC-5404 effectively inhibited PERK activation and ATF4 expression induced by endoplasmic reticulum stress[1].
In vivo	In subcutaneous xenograft models using renal cancer cell lines (such as 786-O, A-498, Caki-1, etc.), HC-5404 was administered orally (dose range 3-100 mg/kg, twice daily). Tumor volume was measured regularly, and tumor growth inhibition (TGI) and tumor regression rates were calculated. After a single oral dose, the exposure of HC-5404 in mouse plasma increased in a dose-dependent manner, with the maximum concentration (Cmax) reached within 1 hour post-dose and an average half-life of 2.22 hours. At doses of 30 mg/kg and 100 mg/kg, the free drug concentrations were 186 nmol/L and 839 nmol/L, respectively. In mouse pancreatic tissue, HC-5404 inhibited p-PERK in a time- and dose-dependent manner, with approximately 90% early inhibition of p-PERK after a single oral dose of 30 mg/kg. In the 786-O tumor model, the 30 mg/kg dosing regimen (twice daily) showed the best anti-tumor activity, with a tumor growth inhibition rate of 48%. Furthermore, HC-5404 demonstrated significant synergistic effects when combined with VEGFR-TKI in various renal cancer models [1].

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2004 mL	11.0018 mL	22.0037 mL
5 mM	0.4401 mL	2.2004 mL	4.4007 mL
10 mM	0.220 mL	1.1002 mL	2.2004 mL
50 mM	0.044 mL	0.220 mL	0.4401 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Stokes ME,et al.PERK Inhibition by HC-5404 Sensitizes Renal Cell Carcinoma Tumor Models to Antiangiogenic Tyrosine Kinase Inhibitors.Clin Cancer Res. 2023 Dec 1;29(23):4870-4882.