HPK1-IN-21

Cat. No.: HY-144073

CAS No.: 2413804-83-6

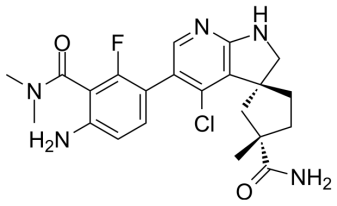
Molecular Formula: $C_{22}H_{25}ClFN_5O_2$

Molecular Weight: 445.92

Target: MAP4K

Pathway: MAPK/ERK Pathway

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

HPK1-IN-21 is a potent inhibitor of HPK1 kinase inhibitor (Ki=0.8 nM). HPK1-IN-21 also has orally active[1].

IC_{50} & Target

HPK1
0.8 nM (Ki)

In Vitro

HPK1-IN-21 (compound 25) (0.001, 0.01, 0.1, 1, 10, 100 μM; 4 hours) inhibits the activity of HPK1 kinase[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	human pan T cells
Concentration:	0.001, 0.01, 0.1, 1, 10, 100 μM
Incubation Time:	4 hours
Result:	Resulted in the inhibition of HPK1 kinase activity

In Vivo

HPK1-IN-21 (1, 25 mg/kg) shows 13% oral bioavailability in mouse when oral dose used 25 mg/kg[1].
Pharmacokinetic Parameters of HPK1-IN-21 in mice[1].

compd	LM H/R/M[a,d]	Hep H/R/M[b,d]	mouse iv CL,V_{ss}[c]	mouse F%[c]
25	6.9/8.7/38	9.5/18/33	57,1.9	13%

[a]LM = Liver microsome predicted clearance (mL/min/kg), H =human, R = rat, M = mouse. [b]Hep = Hepatocyte clearance measuredin mL/min/kg, H = human, R = rat, M = mouse. [c]Mouse PK:C57BL/6, 1 mg/kg iv dose or 25 mg/kg po dose, blood clearance measured in mL/min/kg, Vss = volume of distribution (L/kg). [d]HLM and Hep clearance values represent arithmetic means of two determinations.Six female (6-9 weeks) C57BL/6 mice, 15-25 g, 1 mg/kg iv (solution in 35% PEG400 in water); 25 mg/kg po (suspension in 0.5% methylcellulose, 0.2% Tween in water)[1]
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Six female (6-9 weeks) C57BL/6 mice, 15-25 g[1]
Dosage:	1, 25 mg/kg
Administration:	
Result:	Showed 13% oral bioavailability in mice when oral dose used 25 mg/kg.

REFERENCES

[1]. Discovery of Spiro-azaindoline Inhibitors of Hematopoietic Progenitor Kinase 1 (HPK1). ACS Med Chem Lett. 2021, 13(1):84-91.

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