CLK1-IN-3

Cat. No.: HY-149262

CAS No.: 2922550-28-3

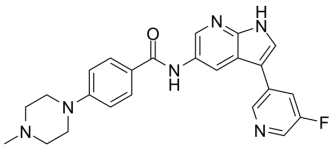
Molecular Formula: $C_{24}H_{23}FN_6O$

Molecular Weight: 430.48

Target: CDK; DYRK; Autophagy

Pathway: Cell Cycle/DNA Damage; Protein Tyrosine Kinase/RTK; Autophagy

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (232.30 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3230 mL	11.6149 mL	23.2299 mL
	5 mM	0.4646 mL	2.3230 mL	4.6460 mL
	10 mM	0.2323 mL	1.1615 mL	2.3230 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.81 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.81 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

CLK1-IN-3 (compound 10ad) is a potent and selective Clk1 inhibitor, with an IC_{50} of 5 nM and over 300-fold selectivity for Dyrk1A. CLK1-IN-3 also shows a relatively potent inhibition against Clk2 and Clk4, with IC_{50} values of 42 and 108 nM, respectively. CLK1-IN-3 potently induces autophagy in vitro. CLK1-IN-3 can be used for acute liver injury (ALI) research[1].

IC_{50} & Target

CLK1	CLK2	CLK4	DYRK1A
5 nM (IC_{50})	42 nM (IC_{50})	108 nM (IC_{50})	1521 nM (IC_{50})

In Vitro

CLK1-IN-3 (compound 10ad) shows potential in anti-tumor because of dual inhibition of Clk1 and Clk2[1].
CLK1-IN-3 (10 μM-1000 μM) can effectively bind to Clk1 protein and inhibit its degradation in a dose-dependent manner[1].
CLK1-IN-3 (0-10 μM, 24 h) induces autophagy in Hela, BNLCL.2 and HCT 116 cells[1].
CLK1-IN-3 stimulates the degradation of SQSTM1/p62 (a marker of autolysosomes)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	Hela cells, BNLCL.2 and HCT 116 cells
Concentration:	0.2, 1, 5, and 10 μM
Incubation Time:	24 h
Result:	Elevated the expression level of LC3II protein (a marker of autophagosomes) as well as the ratio of LC3II to LC3I (a sensitive index of autophagy) in a dose-dependent and time-dependent manner.

In Vivo

CLK1-IN-3 (compound 10ad) (0-40 mg/kg, IP, once) significantly suppresses acute liver injury (ALI) without apparent liver cell death in the ALI model induced by acetaminophen (HY-66005, APAP)[1].

CLK1-IN-3 (10 mg/kg; IV, PO, IP, once) shows acceptable pharmacokinetic profile, has a relatively long $T_{1/2}$ with 5.29 h and oral bioavailability of 19.5%[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL/6 mice(8 weeks, injected acetaminophen (HY-66005) (500 mg/kg, ip))[1]
Dosage:	10, 20, and 40 mg/kg
Administration:	IP, once
Result:	Decreased serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels significantly in dose-dependent.

Animal Model:	Male Balb/c mice (aged 8 weeks)[1]
Dosage:	10 mg/kg
Administration:	IV, PO, IP, once (Pharmacokinetic Analysis)
Result:	Pharmacokinetic Parameters of CLK1-IN-3 in male Balb/C mice[1].

	IV (10 mg/kg)	PO (10 mg/kg)	IP (10 mg/kg)
C_{max} (ng/mL)	13166.5±875.9	1457.4±177.3	4654.3±435.3
$T_{1/2}$ (h)	2.96±1.2	5.29±2.1	3.27 ±1.1
AUC_{0-t} (ng/mL*h)	9520.5±1011.3	1860.2±411.0	5010.4±987.2
CL (L/h/kg)	1.05±0.10	5.51±1.00	3.58±0.82
F (%)		19.5%	

REFERENCES

[1]. Yang T, et al. Rational design and appraisal of selective Cdc2-Like kinase 1 (Clk1) inhibitors as novel autophagy inducers for the treatment of acute liver injury (ALI). Eur J Med Chem. 2023 Mar 15;250:115168.

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