CDK7-IN-20

Cat. No.: HY-151878

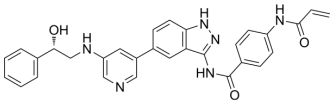
Molecular Formula: $C_{30}H_{26}N_6O_3$

Molecular Weight: 518.57

Target: CDK; GSK-3

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR; Stem Cell/Wnt

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



BIOLOGICAL ACTIVITY

Description

CDK7-IN-20 is a potent, selective and irreversible CDK7 (CDK) inhibitor with an IC_{50} value of 4 nM. CDK7-IN-20 displays >206-fold selectivity for CDK7 over CDK1, CDK2, CDK3, CDK5, CDK6, CDK9 and CDK12 . CDK7-IN-20 has the potential for autosomal dominant polycystic kidney disease (ADPKD) research[1].

IC_{50} & Target

CDK7 4 nM (IC_{50})	CDK1 3375 nM (IC_{50})	CDK2 823 nM (IC_{50})	CDK3 1837 nM (IC_{50})
CDK5 >10,000 nM (IC_{50})	CDK6 950 nM (IC_{50})	CDK9 526 nM (IC_{50})	CDK12 >10,000 nM (IC_{50})
GSK3β 148 nM (IC_{50})			

In Vitro

In Madin-Darby canine kidney (MDCK) cells, CDK7-IN-20 (Compound B2; 1-3 μM; from day 4 to day 12) shows high potency to inhibit cyst growth and exhibited lower cytotoxicity than THZ1[1].

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

In Vivo

CDK7-IN-20 (Compound B2; 5 mg/kg; s.c; once daily; for 6 days) significantly reduces the kidney size and cyst formation of the ADPKD mice. The protein expression of AMPD3 could be significantly down-regulated by CDK7-IN-20 in the cyst-lining epithelial cells of the ADPKD mouse kidney[1].

ADME Profiles of CDK7-IN-20 (Compound B2)[a][1].

CDK7-IN-20 (Compound B2)		
parameters	i.v. 5 mg/kg	s.c. 5 mg/kg
AUC_{last} (h·ng/mL)	26,937	17,280
AUC_{IFN_obs} (h·ng/mL)	31,698	17,411
$t_{1/2}$ (h)	17.8	3.4

T_{max} (h)		0.5
C_{max} (h)		3806
$Cl_{\_obs}$ (mL/min/kg)	2.80	
V_{ss_obs} (mL/kg)	1275	
MRT_{IFN_obs} (h)	10.2	4.8
F (%)		64.2
plasma protein binding (bound%)[b]	>99	
permeability of Caco-2 A to B Papp (10–6 cm/s)/B to A Papp (10–6 cm/s)/efflux ratio[c]	<0.133/6.370/>48.0	

[a]Three ICR mice were used for each group. The data are expressed as mean values.
[b]Plasma from mouse. PPB was tested at 1 and 10 μM substrate concentrations.
[b]Caco-2 membrane permeability at 10 μM substrate concentrations. The value of 0.133 was determined by quantitative limit (1.0 nM)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Neonatal Pkd1$^{flox/flox}$:Ksp-Cre mice[1]
Dosage:	5 mg/kg
Administration:	Subcutaneous administration; once daily; for 6 days
Result:	Significantly reduced the kidney size and cyst formation of the ADPKD mice.

REFERENCES

[1]. Bowen Yang, et al. Discovery of Novel N-(5-(Pyridin-3-yl)-1 H-indazol-3-yl)benzamide Derivatives as Potent Cyclin-Dependent Kinase 7 Inhibitors for the Treatment of Autosomal Dominant Polycystic Kidney Disease. J Med Chem. 2022 Nov 17.

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