CDK8-IN-12

Cat. No.: HY-148561

CAS No.: 2613307-67-6

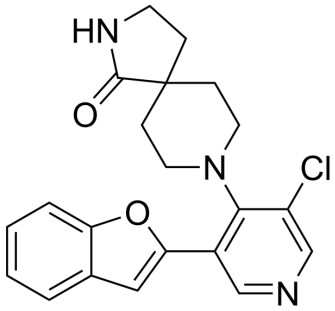
Molecular Formula: $C_{21}H_{20}ClN_3O_2$

Molecular Weight: 381.86

Target: CDK; GSK-3; PKC

Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR; Stem Cell/Wnt; Epigenetics; TGF-beta/Smad

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



BIOLOGICAL ACTIVITY

Description

CDK8-IN-12 is an orally active, potent CDK8 inhibitor with a K_i of 14 nM. CDK8-IN-12 has off-target kinase inhibition on GSK-3 α, GSK-3β, PCK-θ with K_is of 13 nM, 4 nM, 109 nM, respectively. CDK8-IN-12 shows potent anti-proliferative effects selectively on MV4-11 cell. CDK8-IN-12 is an anti-cancer agent[1].

IC_{50} & Target

CDK8	GSK-3α	GSK-3β	PKCθ
14 nM (Ki)	13 nM (Ki)	4 nM (Ki)	109 nM (Ki)

In Vitro

CDK8-IN-12 (compound 38) selectively inhibits the proliferation of MV4-11 acute myeloid leukaemia cells with a GI_{50} of 0.36 μM[1].

CDK8-IN-12 (0.36, 0.72 μM; 2 hours) significantly reduces the phosphorylation of serine 727 on STAT1[1].

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

Western Blot Analysis[1]

Cell Line:	MV4-11 cells
Concentration:	0.36, 0.72 μM
Incubation Time:	2 hours
Result:	Significantly reduced the phosphorylation of serine 727 on STAT1 at concentrations of their respective 1× GI50 values, but barely affected the level of total STAT1.

In Vivo

CDK8-IN-12 (compound 38; IV; 5 mg/kg for rat and 2 mg/kg for mouse) has a $T_{1/2}$ of 0.9 hours and 0.34 hours for rat and mouse, respectively[1].

Pharmacokinetic Parameters of CDK8-IN-12 [1].

	IV (Rat 5 mg/kg)	PO (Rat 20 mg/kg)	IV (Mouse 2 mg/kg)	PO (Mouse 10 mg/kg)
T_{max} (h)	0.04	2.75	0.04	0.42
C_{max} (μM)	14.4	2.77	3.44	5.01

AUC_{0-24} (μM⋅h)	9.7	14.6	1.39	2.30
$T_{1/2}$ (ng/mL)	0.9	2.24	0.34	1.11
CL (L/h⋅kg)	1.39		3.78	
V_{ss} (L/kg)	1.11		1.99	
F (%)		38		33

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

REFERENCES

[1]. Mingfeng Yu, et al. Potent and orally bioavailable CDK8 inhibitors: Design, synthesis, structure-activity relationship analysis and biological evaluation. Eur J Med Chem. 2021 Mar 15;214:113248.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA