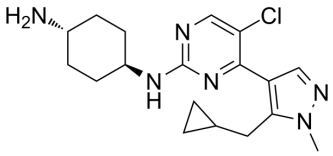
Casein Kinase inhibitor A51

Cat. No.:	HY-123954
CAS No.:	2079068-74-7
Molecular Formula:	$C_{18}H_{25}ClN_6$
Molecular Weight:	360.88
Target:	Casein Kinase; CDK; Apoptosis
Pathway:	Cell Cycle/DNA Damage; Stem Cell/Wnt; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (277.10 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.7710 mL	13.8550 mL	27.7100 mL
	5 mM	0.5542 mL	2.7710 mL	5.5420 mL
	10 mM	0.2771 mL	1.3855 mL	2.7710 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 (6.93 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.93 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.93 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Casein Kinase inhibitor A51 is a potent and orally active casein kinase 1α (CK1α) inhibitor. Casein Kinase inhibitor A51 induces leukemia cell apoptosis, and has potent anti-leukemic activities[1].

IC_{50} & Target			
	CKIα	CDK7 1.3 nM (Kd)	CDK9 4 nM (Kd)

In Vitro

Similar to CKIα depletion, Casein Kinase inhibitor A51 (0.05-3.2 μM; 18 hours) treatment of RKO cells abolished most of the

Ser45 phosphorylation signal and the consecutive GSK3 phosphorylation cascade resulting in stabilization of β-catenin[1].
Casein Kinase inhibitor A51 is highly effective in inducing leukemia cell apoptosis at 160 nM or lower, mostly in correlation to their capacity to stabilize p53[1].
Casein Kinase inhibitor A51 (0.08-2 μM; 6.5 hours) abolishes the expression of MYC, MDM2, and the anti-apoptotic oncogene MCL1. Casein Kinase inhibitor A51 induces a marked reduction in mRNA expression of MYC and MDM2, yet upregulates the expression of the Wnt targets AXIN2 and CCND1 (Cyclin D1)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	MV4-11 cells
Concentration:	0.08 μM, 0.6 μM, 2 μM
Incubation Time:	6.5 hours
Result:	Abolishes the expression of MYC, MDM2, and the anti-apoptotic oncogene MCL1.

In Vivo

Oral treatment is initiated at 8 days (Casein Kinase inhibitor A51; 5 mg/kg/day) after leukemia cell inoculation, at which the percentage of leukemia cells in the BM is more than 1.5% of all cells. all A51-treated mice have normal organ morphology and histology and normal blood counts[1].
Pharmacokinetic studies of the inhibitor Casein Kinase inhibitor A51 at 20 mg/kg reveal rapid oral absorption with a T_{max} of 0.5-2 hr, C_{max} of 1060 ng/mL, $T_{1/2}$ of 2.5 hr, and area under the curve (AUC) values of 3680 (ng*hr/mL)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Waleed Minzel, et al. Small Molecules Co-targeting CKIα and the Transcriptional Kinases CDK7/9 Control AML in Preclinical Models. Cell. 2018 Sep 20;175(1):171-185.e25.

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