DNA-PK-IN-8

Cat. No.: HY-146565

CAS No.: 2823369-81-7

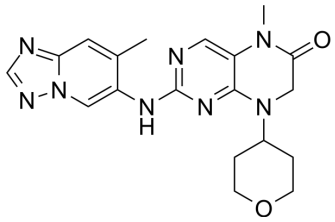
Molecular Formula: $C_{19}H_{22}N_8O_2$

Molecular Weight: 394.43

Target: DNA-PK

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

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



BIOLOGICAL ACTIVITY

Description

DNA-PK-IN-8 is a highly potent, selective and orally active DNA-dependent protein kinase (DNA-PK) inhibitor with an IC_{50} value of 0.8 nM. DNA-PK-IN-8 exhibits synergistic antiproliferative activity against a series of cancer cell lines and significantly suppresses HL-60 tumor growth, when using in combination with Doxorubicin[1].

IC_{50} & Target

IC_{50}: 0.8 nM (DNA-PK)[1]

In Vitro

DNA-PK-IN-8 (compound DK1) decreases the expression levels of γH2A.X in a concentration-dependent manner in HCT-116 cells[1].

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

Immunofluorescence

Cell Line:	HCT-116 (treated with Bleomycin for 6 hours)[1]
Concentration:	1, 5, and 10 μM
Incubation Time:	6 hours
Result:	Decreased the expression levels of γH2A.X in a concentration-dependent manner.

In Vivo

DNA-PK-IN-8 (100 mg/kg; PO; QD for 16 days) significantly suppresses HL-60 tumor growth when co-administrating with Doxorubicin[1].

DNA-PK-IN-8 (5 mg/kg; PO; single dosage) exhibits reasonable pharmacokinetic properties in vitro and in vivo as an oral drug candidate[1].

Pharmacokinetic Parameters of DNA-PK-IN-8 in Sprague-Dawley rats[1].

	PO (5 mg/kg)
T_{max} (h)	0.42 ± 0.11
$t_{1/2}$ (h)	1.59 ± 0.26

C_{max} (ng/mL)	810 ± 122.32
$AUC_{0-\infty}$ (ng/mL·h)	3598.7 ± 769.81
$MRT_{0-\infty}$ (h)	2.29 ± 0.18

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

Animal Model:	HL-60 tumor-bearing nude mice model[1]
Dosage:	100 mg/kg
Administration:	PO; QD for 16 days
Result:	Led to significant tumor-suppressing effects with TGI values of 52.4% and 62.4% for tumor weight and tumor volume, respectively, when co-administrated with Doxorubicin.

Animal Model:	Sprague-Dawley rats[1]
Dosage:	5 mg/kg
Administration:	PO; single dosage (Pharmacokinetic Analysis)
Result:	Exhibited reasonable pharmacokinetic properties in vitro and in vivo as an oral drug candidate.

REFERENCES

[1]. Ding Z, et al. Discovery of novel 7,8-dihydropteridine-6(5H)-one-based DNA-PK inhibitors as potential anticancer agents via scaffold hopping strategy. Eur J Med Chem. 2022;237:114401.

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