HLI373 dihydrochloride

Cat. No.: HY-108640A

CAS No.: 1782531-99-0

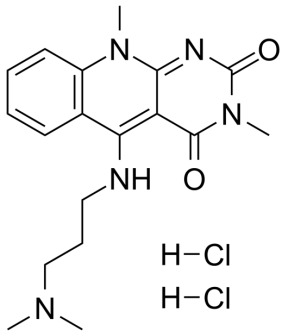
Molecular Formula: $C_{18}H_{25}Cl_2N_5O_2$

Molecular Weight: 414.33

Target: MDM-2/p53; Parasite; Apoptosis

Pathway: Apoptosis; Anti-infection

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

H_2O : 38 mg/mL (91.71 mM; Need ultrasonic and warming)
DMSO : 4 mg/mL (9.65 mM; Need ultrasonic and warming)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4135 mL	12.0677 mL	24.1354 mL
5 mM	0.4827 mL	2.4135 mL	4.8271 mL
10 mM	0.2414 mL	1.2068 mL	2.4135 mL

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

BIOLOGICAL ACTIVITY

Description

HLI373 dihydrochloride is an efficacious Hdm2 inhibitor. HLI373 dihydrochloride inhibits the ubiquitin ligase activity of Hdm2. HLI373 dihydrochloride is effective in inducing apoptosis of several tumor cells that are sensitive to DNA-damaging agents[1]. Antimalarial activity[2].

IC_{50} & Target

Hdm2[1]; Apoptosis[1]; Antimalarial[2]

In Vitro

HLI373 (3-15 μM; 15 hours) selectively kills tumor cells harboring wild type p53[1].
HLI373 (10-50 μM) stabilizes cellular Hdm2 in a dose-dependent manner.
HLI373 (3 μM) activates p53 transcription[1].
HLI373 selectively inhibits auto-ubiquitylation of Hdm2[1].
Co-transfection with plasmids encoding p53 and Hdm2 results in degradation of p53. Incubation with HLI373 (5-10 μM; 8 hours) blocks p53 degradation. HLI373 increases p53 and Hdm2 protein levels in cells[1].
HLI 373 also shows lower IC_{50} values (below 6 μM) against both chloroquine-sensitive P. falciparum D6 strain (PfD6) and chloroquine-resistant P. falciparum W2 strain (PfW2) and exhibits early growth inhibition[2].
HLI-373 is a MDM2 inhibitor interrupting its ubiquitin E3 ligase activity, could abolish the ubiquitylation of its substrate protein p53. HLI-373 targets the C-terminus functioning as an E3 ubiquitin ligase[3].

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

Cell Viability Assay[1]

Cell Line:	Wild type p53 mouse embryo fibroblasts (MEFs), and p53-deficient MEFs
Concentration:	3, 10, 15 μM
Incubation Time:	15 hours
Result:	Increased cell death in wild type p53 MEFs in a dose-dependent manner, p53-deficient MEFs were relatively resistant.

Western Blot Analysis[1]

Cell Line:	U2OS cells
Concentration:	5, 10 μM
Incubation Time:	8 hours
Result:	Blocked p53 degradation caused by co-transfection with plasmids encoding p53 and Hdm2.

REFERENCES

[1]. Jirouta Kitagaki, et al. Targeting Tumor Cells Expressing p53 With a Water-Soluble Inhibitor of Hdm2. Mol Cancer Ther. 2008 Aug;7(8):2445-54.

[2]. Jagrati Jain, et al. Inhibitors of Ubiquitin E3 Ligase as Potential New Antimalarial Drug Leads. BMC Pharmacol Toxicol. 2017 Jun 2;18(1):40.

[3]. Ying Chen, et al. MDM2 Promotes Epithelial-Mesenchymal Transition and Metastasis of Ovarian Cancer SKOV3 Cells. Br J Cancer. 2017 Oct 10;117(8):1192-1201.

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