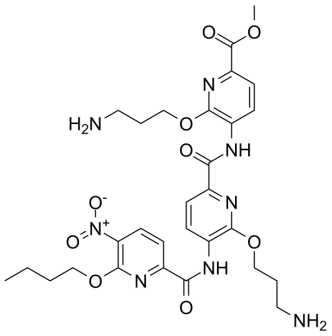
ADH-6

Cat. No.:	HY-145785
CAS No.:	2227429-65-2
Molecular Formula:	$C_{29}H_{36}N_8O_9$
Molecular Weight:	640.64
Target:	MDM-2/p53; Apoptosis
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

ADH-6 is a tripyridylamide compound. ADH-6 abrogates self-assembly of the aggregation-nucleating subdomain of mutant p53 DBD. ADH-6 targets and dissociates mutant p53 aggregates in human cancer cells, which restores p53's transcriptional activity, leading to cell cycle arrest and apoptosis. ADH-6 has the potential for the research of cancer diseases[1].

In Vitro

ADH-6 (25 μM, 10 h) inhibits aggregation of pR248W (indicated by dot blot assay)[1].
ADH-6 (5 μM, 6 h) dissociates intracellular mutant p53 aggregates in MIA PaCa-2 cells[1].
ADH-6 (0-10 μM, 24 or 48 h) causes selective cytotoxicity in cancer cells bearing mutant p53 (MIA PaCa-2)[1].
ADH-6 (5 μM, 24 h) specifically targets and reactivates aggregation-prone mutant p53 in MIA PaCa-2 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	MIA PaCa-2 (mutant R248W p53), SK-BR-3 (mutant R175H p53)
Concentration:	0, 2.5, 5, 7.5, 10 μM
Incubation Time:	24, 48 h
Result:	Caused death of cancer cells bearing mutant, but not WT, p53.

Western Blot Analysis[1]

Cell Line:	MIA PaCa-2 cells
Concentration:	5 μM
Incubation Time:	24 h
Result:	Increased expression of p53-inducible MDM2 and proapoptotic Bax.

In Vivo

ADH-6 (intraperitoneal injection, 15 mg/kg, every 2 days, for a total of 12 doses) causes regression of mutant p53-bearing tumors [1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	MIA PaCa-2 xenografts[1]
Dosage:	716.4 μM in 0.02% DMSO
Administration:	Intraperitoneal injection, every 2 days, for a total of 12 doses
Result:	Reduced tumor growth relative to the saline-treated control group. Reduced mutant p53 levels and shrinked xenografts harboring aggregation-prone mutant p53.

Animal Model:	MIA PaCa-2 xenografts (pharmacokinetics assay)[1]
Dosage:	15 mg/kg
Administration:	Intraperitoneal injection, for a single dose
Result:	C_{max}: 21 μg/mL, $T_{1/2}$: 3.6 h

REFERENCES

[1]. Palanikumar L, et al. Protein mimetic amyloid inhibitor potently abrogates cancer-associated mutant p53 aggregation and restores tumor suppressor function. Nat Commun. 2021;12(1):3962.

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