Inauhzin

Cat. No.: HY-15869

CAS No.: 309271-94-1

Molecular Formula: $C_{25}H_{19}N_5OS_2$

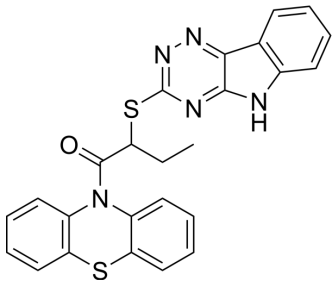
Molecular Weight: 470

Target: Sirtuin; MDM-2/p53

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (212.77 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1277 mL	10.6383 mL	21.2766 mL
	5 mM	0.4255 mL	2.1277 mL	4.2553 mL
	10 mM	0.2128 mL	1.0638 mL	2.1277 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 (5.32 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Inauhzin is a dual SirT1/IMPDH2 inhibitor, and acts as an activator p53, used in the research of cancer.

IC_{50} & Target			
	SIRT1	MDM-2/p53	IMPDH2

In Vitro

Inauhzin (10 μM) induces p53 levels as effectively as actinomycin D (10 nM), and mediates p53-dependent cytotoxicity through its specific functional groups in human lung carcinoma H460 cells. Inauhzin (2 μM) induces p53 level and activity as well as p53-dependent apoptosis. Inauhzin also stabilizes p53 and inhibits its ubiquitylation. Inauhzin induces acetylation of p53 in H460 cells, but not tubulin, which is affected by knockdown of SIRT1[1]. Inauhzin (0-2 μM) significantly enhances the expression level and activity of p53 in HCT116$^{p53+/+}$ cells and enhances the expression level and activity of p53 in H460 cells in a dose-dependent manner. Inauhzin and Nutlin-3 demonstrate synergistic cytotoxicity in the Nutlin-3 low-sensitive cells. Inauhzin and Nutlin-3 synergistically induce p53-dependent apoptosis[2]. Inauhzin targets both SirT1 and IMP dehydrogenase 2 (IMPDH2), and acts as a potent p53 activator[3].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Inauhzin (30 mg/kg, i.p.) effectively induces apoptosis and suppresses tumour growth of H460 xenograft harbouring p53[1]. Inauhzin (30 mg/kg, i.p.) reduces the HCT116 tumor volume by appr 70%. Inauhzin (15 mg/kg) in combination with 150 mg/kg of Nutlin-3 demonstrates a significant synergy on p53 induction, apoptosis and tumor suppression of HCT116$^{p53+/+}$ xenografts[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The cell counting kit is used to assess cell growth. Cell suspensions are seeded at 5000 cells per well in 96-well culture plates and incubated overnight at 37°C. Compounds are added into the plates and incubated at 37°C for 72 h. Cell growth inhibition is determined by adding WST-8 at a final concentration of 10% to each well, and the absorbance of the samples is measured at 450 nm using a Microplate Reader[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Five-weeks-old female SCID mice are housed in a BSL2 environment. Mice are subcutaneously inoculated with 5×10^6 H460 or 3×10^6 HCT116 cells. Tumour growth is monitored every other day with electronic digital calipers in two dimensions. Tumour volume is calculated with the formula: tumour volume (mm^3) = (length × $width^2$)/2. When the mean tumour volume reaches approximately 100 mm^3 after 7-9 days, animals are dosed by i.p. injection with vehicle (5% DMSO) or Inauhzin. Inhibition of tumour growth is calculated on the last day of treatment. To detect p53 activation in vivo, tumours are harvested and disrupted in RIPA buffer containing a protease inhibitor mixture. Tumour lysates are analysed by IB. Cell proliferation in tumours is assessed by BrdU labeling followed by Immunostaining. 200 mg/kg body weight of BrdU is administrated to mice via i.p. injection 2 h before mice are sacrificed. Apoptosis is examined by TUNEL staining, using the Fluorescein In situ cell death detection kit[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.

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REFERENCES

[1]. Zhang Q, et al. A small molecule Inauhzin inhibits SIRT1 activity and suppresses tumour growth through activation of p53. EMBO Mol Med. 2012 Apr;4(4):298-312.

[2]. Zhang Y, et al. Inauhzin and Nutlin3 synergistically activate p53 and suppress tumor growth. Cancer Biol Ther. 2012 Aug;13(10):915-24.

[3]. Nguyen D, et al. Reviving the guardian of the genome: Small molecule activators of p53. Pharmacol Ther. 2017 Oct;178:92-108.

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