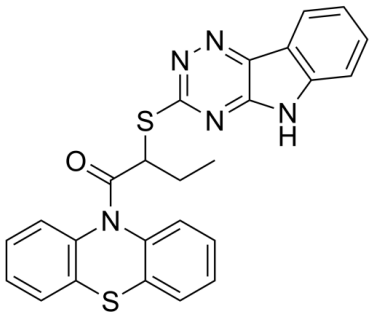
Data Sheet

Product Name:	Inauhzin
Cat. No.:	CS-2404
CAS No.:	309271-94-1
Molecular Formula:	$C_{25}H_{19}N_5OS_2$
Molecular Weight:	469.58
Target:	MDM-2/p53; Sirtuin
Pathway:	Apoptosis; Cell Cycle/DNA Damage; Epigenetics
Solubility:	DMSO : 100 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

Inauhzin is a dual **SirT1/IMPDH2** inhibitor, and acts as an activator **p53**, used in the research of cancer. IC50 & Target: SirT1, IMPDH2, MDM-2/p53[3] ***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]. ***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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **Animal Administration:** Inauhzin is dissolved in 5% DMSO.[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].

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.

CAIndexNames:

1-Butanone, 1-(10H-phenothiazin-10-yl)-2-(5H-1,2,4-triazino[5,6-b]indol-3-ylthio)-

SMILES:

CCC(SC1=NN=C2C(NC3=C2C=CC=C3)=N1)C(N4C5=C(C=CC=C5)SC6=CC=CC=C46)=O

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