Nutlin-3

Cat. No.: HY-50696

CAS No.: 548472-68-0

Molecular Formula: $C_{30}H_{30}Cl_2N_4O_4$

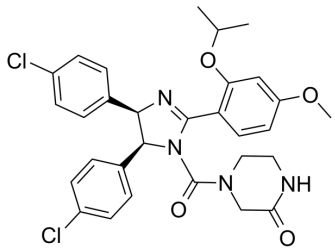
Molecular Weight: 581.49

Target: MDM-2/p53; E1/E2/E3 Enzyme

Pathway: Apoptosis; Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



relative stereochemistry

SOLVENT & SOLUBILITY

In Vitro

Ethanol : 100 mg/mL (171.97 mM; Need ultrasonic)

DMSO : ≥ 50 mg/mL (85.99 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7197 mL	8.5986 mL	17.1972 mL
5 mM	0.3439 mL	1.7197 mL	3.4394 mL
10 mM	0.1720 mL	0.8599 mL	1.7197 mL

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

In Vivo

1. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 5 mg/mL (8.60 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: 5 mg/mL (8.60 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (4.30 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (4.30 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Nutlin-3 is a commercial available p53-MDM2 inhibitor, with K_i of 90 nM.

IC_{50} & Target	Ki: 90 nM (p53-MDM2)[1]
In Vitro	Nutlin-3 is an inhibitor of the MDM2-p53 interaction. In particular, co-treatment of p53-positive HCT116 cells with 1 μM of Inauhzin and 2 μM of Nutlin-3 more significantly activated p53 as measured by its protein level as well as the level of its target p21, PUMA or cleaved PARP as indication of apoptosis[2]. Nutlin-3 is a small-molecule inhibitor that acts to inhibit MDM2 binding to p53 and subsequent p53-dependent DNA damage signaling. As a single agent, Nutlin-3 (2-10 μM) stabilizes p53 and $p21^{WAF}$ levels and is toxic to WTp53-22RV1 cells (IC_{50}, 4.3 μM) but has minimal toxicity toward p53-deficient cells (IC_{50}, >10 μM). Nutlin-3 induces p53 and $p21^{WAF}$ expression in a dose-dependent manner in 22RV1 cells. Short-term cell cycle assays show that, at a dose of 10 μM, Nutlin-3 increasea slightly the G_1-phase fraction and decreasea S-phase fraction of all three cell lines[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Nutlin-3 can suppress the growth of xenograft tumors derived from human osteosarcoma or leukemia cells, the anti-tumor activity of Nutlin-3 even at the dose of 200 mg/kg per oral administration is marginal in an HCT116-derived xenograft tumor model[2]. Nutlin-3 may be a useful adjunct to improve the therapeutic ratio using precision radiotherapy targeted to hypoxic cells and warrants further study in vivo[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Human non-small-cell lung carcinoma wild type p53-containing H460 and A549, human non-small-cell lung carcinoma p53-null H1299, and human colon cancer HCT116 ($p53^{+/+}$ and $p53^{-/-}$) cells are used. Cells (1.5×10^5) are plated into 6-well plates, and incubated at 37°C overnight. After treatment of Inauhzin and Nutlin 3 at the indicated concentrations for 48 h, cells are harvested, fixed in 70% ice-cold ethanol overnight at -20°C, resuspended in propidium iodide-solution (50 μg/mL PI, 0.1 mg/mL RNase A, 0.05% Tritin X-100 in PBS) for 40 min at 37°C, then analyzed for DNA content using a flow cytometer and proprietary software[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Five-week-old female SCID mice are used. Mice are subcutaneously inoculated with 3×10^6 $HCT116^{p53+/+}$ cells in the right flank and tumor growth is monitored with calipers. After the mean tumor volume reaches 50-100 mm^3, animals are administered Inauhzin intraperitoneally (IP), Nutlin 3 orally, or vehicles (4% DMSO for Inauhzin, EtOH: Tween: 5% Glucose=5:5:90 for Nutlin 3). Tumor volume is measured every other day, and inhibition of tumor growth (T/C) is calculated on the last day of treatment. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2023 Mar 7;9(1):26.
- Cancer Res. 2019 Feb 1;79(3):534-545.
- EBioMedicine. 2019 Oct;48:248-263.
- Cancer Lett. 2022 Feb 9;532:215588.
- Cell Death Dis. 2020 Nov 12;11(11):976.

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REFERENCES

[1]. Yu Z, et al. Design, synthesis and biological evaluation of sulfamide and triazole benzodiazepines as novel p53-MDM2 inhibitors. Int J Mol Sci. 2014 Sep 5;15(9):15741-53.

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

[3]. Supiot S, et al. Nutlin-3 radiosensitizes hypoxic prostate cancer cells independent of p53. Mol Cancer Ther. 2008 Apr;7(4):993-9.

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