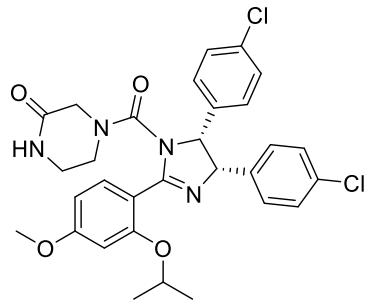
Product data sheet

MedKoo Cat#: 406308 Name: Nutlin-3a CAS#: 675576-98-4 (4S5R) Chemical Formula: $C_{30}H_{30}Cl_2N_4O_4$ Exact Mass: 580.16441 Molecular Weight: 581.49	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Nutlin-3a, also known as SML 0580, is an inhibitor of MDM2 (human homolog of murine double minute 2), which disrupts its interaction with p53, leading to the stabilization and activation of p53. Nutlin-3a activates the p53 pathway and efficiently induces apoptosis in tumours with amplified MDM2 gene and overexpression of MDM2 protein. Nutlin-3 enhances the bortezomib sensitivity of p53-defective cancer cells by inducing paraptosis.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	25.0	43.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.72 mL	8.60 mL	17.20 mL
5 mM	0.34 mL	1.72 mL	3.44 mL
10 mM	0.17 mL	0.86 mL	1.72 mL
50 mM	0.03 mL	0.17 mL	0.34 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Crane EK, Kwan SY, Izaguirre DI, Tsang YT, Mullany LK, Zu Z, Richards JS, Gershenson DM, Wong KK. Nutlin-3a: A Potential Therapeutic Opportunity for TP53 Wild-Type Ovarian Carcinomas. PLoS One. 2015 Aug 6;10(8):e0135101. doi: 10.1371/journal.pone.0135101. PMID: 26248031; PMCID: PMC4527847.

2. Kobayashi M, Ishizaki Y, Owaki M, Matsumoto Y, Kakiyama Y, Hoshino S, Tagawa R, Sudo Y, Okita N, Akimoto K, Higami Y. Nutlin-3a suppresses poly (ADP-ribose) polymerase 1 by mechanisms different from conventional PARP1 suppressors in a human breast cancer cell line. Oncotarget. 2020 May 5;11(18):1653-1665. doi: 10.18632/oncotarget.27581. PMID: 32405340; PMCID: PMC7210013.

In vivo study

1. Tovar C, Rosinski J, Filipovic Z, Higgins B, Kolinsky K, Hilton H, Zhao X, Vu BT, Qing W, Packman K, Myklebost O, Heimbrook DC, Vassilev LT. Small-molecule MDM2 antagonists reveal aberrant p53 signaling in cancer: implications for therapy. Proc Natl Acad Sci U S A. 2006 Feb 7;103(6):1888-93. doi: 10.1073/pnas.0507493103. Epub 2006 Jan 27. PMID: 16443686; PMCID: PMC1413632.

Product data sheet

2. Lerche CM, Philipsen PA, Poulsen T, Gniadecki R, Wulf HC. Topical nutlin-3a does not decrease photocarcinogenesis induced by simulated solar radiation in hairless mice. Photodermatol Photoimmunol Photomed. 2012 Aug;28(4):207-12. doi: 10.1111/j.1600-0781.2012.00675.x. PMID: 23017174.

7. Bioactivity

Biological target:

Nutlin-3a, an active enantiomer of Nutlin-3, is a potent murine double minute (MDM2) inhibitor (IC50=90 nM).

In vitro activity

Fifteen epithelial ovarian cancer cell lines of varying histologic subtypes were treated with Nutlin-3a with determination of IC50 values. Western Blot (WB) and quantitative real-time polymerase chain reaction (qRT-PCR) analyses quantified MDM2, p53, and p21 expression after Nutlin-3a treatment. DNA from 15 cell lines was then sequenced for TP53 mutations in exons 2-11 including intron-exon boundaries. Responses to Nutlin-3a were dependent upon TP53 mutation status. By qRT-PCR and WB, levels of MDM2 and p21 were upregulated in wild-type TP53 sensitive cell lines, and p21 induction was reduced or absent in mutant cell lines. Annexin V assays demonstrated apoptosis in sensitive cell lines treated with Nutlin-3a.

Reference: PLoS One. 2015 Aug 6;10(8):e0135101. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/26248031/

In vivo activity

To increase its potency the active enantiomer nutlin-3a was purified and a 3-week antitumor efficacy study in SJSA-1 tumor-bearing nude mice was performed(Fig. 6A). Nutlin-3a suppressed xenograft growth in a dose-dependent fashion with the highest dose (200 mg/kg) showing a substantial tumor shrinkage (eight partial and one full regressions). No weight loss or significant pathological changes were recorded during the course of the study (data not shown). To show that the antitumor effect of nutlin-3a is caused by activation of the p53 pathway we analyzed the level of p53 targets p21 and MDM2 in nutlin-treated SJSA-1 xenografts. Western blot analysis revealed accumulation of both proteins in tumors from nutlin-treated animals but not vehicle controls (Fig. 6B). This experiment is consistent with the hypothesis that the in vivo antitumor effect of nutlin-3 is derived from activation of the p53 pathway. To exclude any possibility for an in vivo-related artifact we also tested nutlin-3a on cells with mutant p53. Colon cancer cell line HT29 expresses mutant p53 and does not respond to nutlin-3a treatment in vitro (data not shown). Nude mice bearing established HT29 xenografts were treated orally with 200 mg/kg nutlin-3 for 3 weeks. In agreement with the in vitro results, HT29 xenografts showed undistinguishable growth characteristics in the presence or absence of nutlin-3 (data not shown). These experiments confirmed that nutlin-3 is a selective activator of the p53 pathway in vivo and highly efficacious against SJSA-1 osteosarcoma tumors.

Reference: Proc Natl Acad Sci U S A. 2006 Feb 7;103(6):1888-93. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/16443686/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.