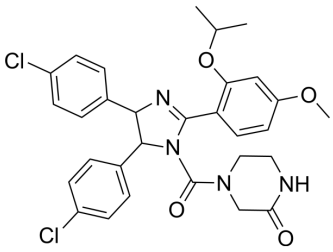
(Rac)-Nutlin-3

Cat. No.:	HY-10029A
CAS No.:	890090-75-2
Molecular Formula:	$C_{30}H_{30}Cl_2N_4O_4$
Molecular Weight:	581.49
Target:	MDM-2/p53; Autophagy; Apoptosis; E1/E2/E3 Enzyme
Pathway:	Apoptosis; Autophagy; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	(Rac)-Nutlin-3 (Rebemadlin), an active enantiomer of Nutlin-3, is a potent murine double minute (MDM2) inhibitor (IC_{50}=90 nM). (Rac)-Nutlin-3 inhibits MDM2-p53 interactions and stabilizes the p53 protein, and induces cell autophagy and apoptosis . (Rac)-Nutlin-3 has the potential for the study of TP53 wild-type ovarian carcinomas[1][2].
In Vitro	Nutlin-3a is a therapeutic which inhibits MDM2, activates wild-type p53, and induces apoptosis-as a therapeutic compound for TP53 wild-type ovarian carcinomas. Three cell lines (HOC-7, OVCA429 and A2780) with wild-type TP53 are highly sensitive to Nutlin-3a (IC_{50}=4 to 6 μM). SKOV3 cells have an IC_{50} of 38 μM to Nutlin-3a. The two remaining ovarian clear cell lines (TOV21G and OVAS), both with TP53 wild-type, are relatively more sensitive to growth inhibition with Nutlin-3a (IC_{50}=14 and 25 μm respectively) than the TP53 mutant cell lines[1]. Nutlin-3a is the active enantiomer of Nutlin-3. Nutlin-3a is a highly selective MDM2 antagonist and p53 inducer. Seven days of incubation with 10 μM Nutlin-3a leads to >90% inhibition of NIH/3T3 cells'growth but does not affect the proliferation of MEF in which both targets of the drug are eliminated. Nutlin-3a effectively arrestes cell-cycle progression in all cell lines, depleting the S-phase compartment to 0.2-2% and increasing the G_1- and G_2/M-phase compartments, indicating G_1 and G_2 arrest. The p53 targets p21 and MDM2 are elevated significantly 3 h after Nutlin-3a addition and reach maximal levels at 8 h. Nutlin-3a induces apoptosis in ≈60% of SJSA-1 and MHM cells after 40 h, which increase further after 60 h (85% and 65%, respectively)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Nutlin-3a is efficacious in all models with average tumor growth inhibition ≥98%. Nutlin-3a suppresses 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). The established SJSA-1 and MHM osteosarcoma xenografts with Nutlin-3a causes extensive tumor regression[2] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Crane EK, et al. Nutlin-3a: A Potential Therapeutic Opportunity for TP53 Wild-Type Ovarian Carcinomas. PLoS One. 2015 Aug 6;10(8):e0135101.

[2]. Tovar C, et al. 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.

[3]. M Ulrich, et al. Murine tumor models for the in vivo evaluation of natural compounds and their derivatives as new cancer therapeutics. München. 2016.

Caution: Product has not been fully validated for medical applications. For research use only.

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