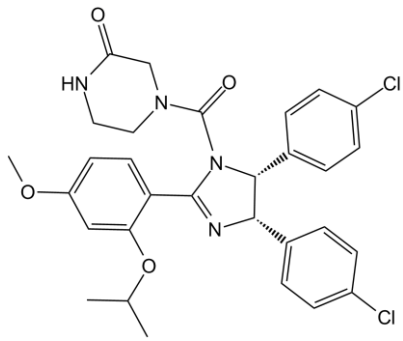
Product Name: Nutlin-3a chiral

Revision Date: 6/30/2016

Product Data Sheet

Chemical Properties



Product Name: Nutlin-3a chiral

Cas No.: 675576-98-4

M.Wt: 581.49

Formula: C30H30Cl2N4O4

Synonyms: Nutlin-3a;Nutlin 3a

Chemical Name: 4-[(4S,5R)-4,5-bis(4-chlorophenyl)-2-(4-methoxy-2-propan-2-yloxyphenyl)-4,5-dihydroimidazole-1-carbonyl]piperazin-2-one

Canonical SMILES: CC(C)OC1=C(C=CC(=C1)OC)C2=NC(C(N2C(=O)N3CCNC(=O)C3)C4=CC=C(C=C4)Cl)C5=CC=C(C=C5)Cl

Solubility: >29.1mg/mL in DMSO

Storage: Store at -20°C

General tips: For obtaining a higher solubility , please warm the tube at 37° C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20° C for several months.

Shopping Condition: Evaluation sample solution : ship with blue ice
All other available size: ship with RT , or blue ice upon request

Biological Activity

Targets : p53

Pathways: Apoptosis >> p53

Description:

Nutlin-3 is a small-molecule inhibitor of MDM2 (mouse double minute 2) with IC50 value of 0.09μM [1].
Nutlin-3 binds MDM2 in the TP53-bindingpocket, thereby interfering with MDM2-directed TP53 degradation. This has been shown to cause cell cycle arrest, growth inhibitionand apoptosis in both solid tumors and lymphoid neoplasms.In mantle cell lymphoma(MCL), it is reported that Nutlin-3 can inhibit cell growth and activate apoptosis in bothwt-TP53(IC50 of 1 to 10μM) and

mt-TP53(IC50 of 22.5μM) cells [2].
Nutlin-3 can also effectcell cycle in gastric cancer cell lines. It induces G1 arrest inMKN-45 and SNU-1 cell lines. In vitro assay shows Nutlin-3can enhance the antitumoreffects of conventional chemotherapeutic agents in several gastric cancer cell lines. And in in vivo assay, Nutlin-3 significantly inhibits the growth of xenograft tumors

***Reference**:*
[1] Lyubomir T.Vassilev et al. In vivo activation of the p53 pathway by small-molecule antagonists of MDM2.Science.2004, 303: 844-848.
[2] Yoko Tabe, Denise Sebasigari, Linhua Jin, et al.MDM2 Antagonist Nutlin-3 Displays Antiproliferative andProapoptotic Activity in Mantle Cell Lymphoma. Clin Cancer Res. 2009, 15:933-942.
[3] Shinji Endo,Kenji Yamato,Sachiko Hirai,Toshikazu Moriwaki,Kuniaki Fukuda,Hideo Suzuki,Masato Abei,Ichiro Nakagawa and IchinosukeHyodo.Potent in vitro and in vivo antitumor effects ofMDM2 inhibitor nutlin-3 in gastric cancer cells.Cancer Science. 2011, 102 (3): 605-613.

Protocol

Cell experiment:

Cell lines	HCT116 and SW480 cells
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting conditions	1, 2, 4, 8 and 16 μM; 8 hrs
Applications	Nutlin-3a increased the cellular levels of p53, MDM2 and p21Waf1/Cip1 in HCT116 cells whilst SW480 cells exposed to the same conditions showed high basal levels of p53 but no detectable MDM2 or p21.

Animal experiment [3]:

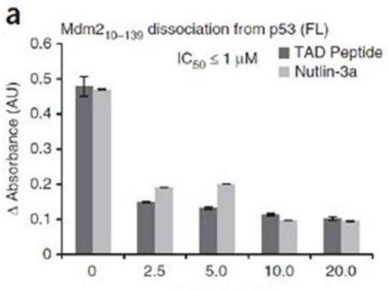
Animal models	Nude mice bearing subcutaneous human cancer xenografts (SJSA-1)
Dosage form	200 mg/kg; p.o.; b.i.d., for 20 days
Applications	Nutlin-3a inhibited tumor growth by 90%. The mice did not lose significant weight and did not show any gross abnormalities upon necropsy at the end of the treatment.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused

by an experimental system error and it is normal.

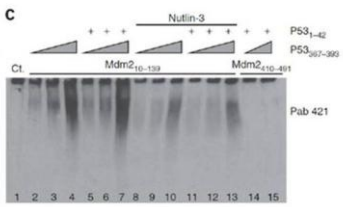
***Reference**:*

[1]. Vassilev LT, Vu BT, Graves B, et al. In vivo activation of the p53 pathway by small-molecule antagonists of MDM2. Science, 2004, 303(5659): 844-848.

Product Validation



Nutlin-3 disrupts p53's interaction with the N-terminal of Mdm2



Binding of the C-terminal domain of p53 and the N-terminal domain of Mdm2 is interrupted by the treatment of Nutlin-3

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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