Product Datasheet

Technical Data

Formula	$C_{30}H_{30}Cl_2N_4O_4$					
Molecular Weight	581.49	**CAS No.**	675576-98-4			
Solubility (25°C)*	In vitro	DMSO	100 mg/mL (171.97 mM)			
		Ethanol	100 mg/mL (171.97 mM)			
		Water	Insoluble			
	In vivo (Add solvents to the product individually and in order)	Oral Administration	Homogeneous suspension	CMC-NA	≥5mg/ml	Taking the 1 mL working solution as an example, add 5 mg of this product to 1 ml of CMC-Na solution, mix evenly to obtain a homogeneous suspension with a final concentration of 5 mg/ml.
		Injection	Clear solution	5%DMSO [1]→ 40%PEG300 [2]→ 5%Tween80 [3]→ 50%ddH2O Validated by Capsid Bio labs. Should you need adjustments to this formulation, contact our sales team for custom testing.	10.000mg/ml (17.20mM)	Taking the 1 mL working solution as an example, add 50 μL of 200 mg/ml clarified DMSO stock solution to 400 μL of PEG300, mix evenly to clarify it; add 50 μL of Tween80 to the above system, mix evenly to make it clear; then continue to add 500 μL of ddH2O to adjust the volume to 1 mL. The mixed solution should be used immediately for optimal results.

* <1 mg/ml means slightly soluble or insoluble.
* Please note that Capsid Bio tests the solubility of all compounds in-house, and the actual solubility may differ slightly from published values. This is normal and is due to slight batch-to-batch variations.
* Room temperature shipping (Stability testing shows this product can be shipped at 2-8°C for storage purposes.)

Preparing Stock Solutions

Concentration \ Volume / Mass	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
50 mM	0.0344 mL	0.1720 mL	0.3439 mL

Biological Activity

Description	Nutlin-3a ((-)-Nutlin-3), the active enantiomer of Nutlin-3, inhibits the **p53/MDM2** interaction with **IC50** of 90 nM in a cell-free assay. Nutlin-3a induces **autophagy** and **apoptosis** in a p53-dependent manner.
Targets	p53-MDM2 interaction [3] (Cell-free assay) 90 nM
In vitro	Nutlin-3a displaces p53 from the binding pocket of MDM2 and thereby releases p53 from inhibition and proteasomal degradation, leading to induction of its downstream targets, cell cycle arrest, and apoptosis. Seven days of incubation with 10 μM of this compound led to >90% inhibition of NIH3T3 cells' growth[1]. This compound stabilizes and activates p53, and induces p21 expression in a dose-dependent manner[1]. It effectively depletes the S-phase compartment to 0.2-2% and increases the G1- and G2/M-phase compartments[1]. This chemical induces apoptosis in ~60% of SJSA-1 and MHM cells after 40 h, which increased further after 60 h (85% and 65%, respectively) [1].
In vivo	Nutlin-3a suppresses xenograft growth in a dose-dependent fashion with the highest dose (200 mg/kg) showing a substantial tumor shrinkage [1]. This compound is a selective activator of the p53 pathway in vivo and highly efficacious against SJSA-1 osteosarcoma tumors[1]. Tumors with wild-type p53 and mdm2 gene amplification will respond best to therapy with this chemical.
Features	Highly selective MDM2 inhibitor with a much lower effect on MDMX. Most effective on tumors with wild type p53.

Protocol (from reference)

Kinase Assay:[3]

- **Biacore studies**
  Competition assays are performed on a Biacore S51. A Series S Sensor chip CM5 is derivatized for immobilization of a PentaHis antibody for capture of the His-tagged p53. The level of capture is ~ 200 response units (1 response unit corresponds to 1 pg of protein per mm ^{2}). The concentration of MDM2 protein is kept constant at 300 nM. Test compounds are dissolved in DMSO at 10 mM and further diluted to make a concentration series of inhibitor in each MDM2 test sample. The assays are run at 25 °C in running buffer (10 mM Hepes, 0.15 M NaCl, 2% DMSO). MDM2-p53 binding in the presence of this compound is calculated as a percentage of binding in the absence of this compound and IC50 is calculated using Microsoft Excel

Cell Assay:[2]

- **Cell lines**
  OSA, T778, RMS13, U2OS, SaOS-2
- **Concentrations**
  ~5 μM
- **Incubation Time**

120 h

- **Method**
  SRB

Animal Study:[1]

- **Animal Models**
  SJSA-1 xenograft
- **Dosages**
  50, 100, 200 mg/kg twice daily
- **Administration**
  oral

References

https://pubmed.ncbi.nlm.nih.gov/16443686/

https://pubmed.ncbi.nlm.nih.gov/21624110/

https://pubmed.ncbi.nlm.nih.gov/14704432/

RETURN POLICY

Capsid Bio's Unconditional Return Policy ensures a smooth online shopping experience for our customers. If you are in any way unsatisfied with your purchase, you may return any item(s) within 7 days of receiving it. In the event of product quality issues, either protocol related or product related problems, you may return any item(s) within 365 days from the original purchase date. Please follow the instructions below when returning products.

SHIPPING & STORAGE

Capsid Bio products are transported at room temperature. If you receive the product at room temperature, please rest assured, the Capsid Bio Quality Inspection Department has conducted experiments to verify that the normal temperature placement of one month will not affect the biological activity of powder products. After collecting, please store the product according to the requirements described in the datasheet. Most Capsid Bio products are stable under the recommended conditions.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

EU Headquarters
Gajeva ulica 28, HR-10000 Zagreb, Croatia

US Headquarters
12222 Merit Dr STE 130 Dallas, Texas, 75251

UK Headquarters
121 ABILITY HOUSE, BROOKER ROAD, EN9 1JH, ESSEX

Orders: Sales@capsidbio.com
Enquiries: info@capsidbio.com
www.capsidbio.com