UNC0638

Catalog No.C13171 Batch:C1317103

Product Datasheet

Technical Data

Formula	$C_{30}H_{47}N_5O_2$					
Molecular Weight	509.73	**CAS No.**	1255580-76-7			
Solubility (25°C)*	In vitro	DMSO	100 mg/mL (196.18 mM)			
		Water	Insoluble			
		Ethanol	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.

* <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

Biological Activity

Description	UNC0638 is a potent, selective and cell-penetrant chemical probe for **G9a** and **GLP** histone methyltransferase with **IC50** of <15 nM and 19 nM, respectively, shows selectivity over a wide range of epigenetic and non-epigenetic targets. This compound has anti-viral activities.
Targets	G9a [1] (Cell-free assay): <15 nM GLP [1] (Cell-free assay): 19 nM
In vitro	UNC0638 is a potent, selective and cell-penetrant chemical probe for G9a and GLP, with a toxicity/function ratio of >100, compared to <6 for BIX01294. This compound is a selectivite inhibitor of G9a and GLP over a wide range of epigenetic and non-epigenetic targets. It is more than 10,000-fold selective against SET7/9 (a H3K4 HMTase), SET8 (a H4K20 HMTase), PRMT3, and SUV39H2. In MDA-MB-231 cells, this chemical (48 h exposure) reduces H3K9me2 levels in a concentration-dependent manner with an IC50 of 81 nM. Its treatment of a variety of cell lines results in lower global H3K9me2 levels, equivalent to levels observed for small hairpin RNA knockdown of G9a and GLP with the functional potency of this compound being well separated from its toxicity. It markedly reduces the clonogenicity of MCF7 cells, reduces the abundance of H3K9me2 marks at promoters of known G9a-regulated endogenous genes and disproportionately affected several genomic loci encoding microRNAs. In mouse embryonic stem cells, this probe reactivates G9a-silenced genes and a retroviral reporter gene in a concentration-dependent manner without promoting differentiation. [1]
In vivo	In mouse drug metabolism and pharmacokinetic studies, UNC0638 had high clearance, short half-life, high volume distribution and low exposure after intravenous, oral or intraperitoneal administration. Thus, although this compound is probably not suitable for in vivo animal studies owing to low exposure levels, its high stability under cellular assay conditions, in combination with high potency and selectivity, makes it an ideal chemical tool for cell-based studies[1].

Protocol (from reference)

Kinase Assay:[1]

- **SAHH-coupled assays**

  This assay utilizes SAHH to hydrolyze the methyltransfer product S-adenosylhomocysteine to homocysteine and adenosine in the presence of adenosine deaminase which converts adenosine to inosine. The homocysteine concentration is then determined through conjugation of its free sulfhydryl moiety to a thiol-sensitive fluorophore, ThioGlo. For IC50 determinations, assay mixtures are prepared in 25 mM Potassium Phosphate buffer pH 7.5, 1 mM EDTA, 2 mM $MgCl_2$, 0.01% Triton X 100 with 5 μM SAHH , 0.3 U/mL of adenosine deaminase, 25 μM SAM, and 15 μM ThioGlo. G9a, EHMT1, SETD7, SETD8, PRMT3 and SUV39H2 are assayed at 25 nM, 100 nM, 200 nM, 250 nM, 1 μM and 100 nM, respectively. UNC0638 is added at concentrations ranging from 4 nM to 16 μM. After 2 min incubation, reactions are initiated by addition of the histone peptides: 10 μM H3(1-25) for G9a, 20 μM H3(1-25) for EHMT1, 100 μM H3(1-25) for SETD7, 500 μM H4(1-24) for SETD8, 10 μM H4(1-24) for PRMT3 and 200 μM H3K9Me1 (1-15) for SUV39H2. The methylation reaction is followed by monitoring the increase in fluorescence using Biotek Synergy2 plate reader with 360/40 nm excitation filter and 528/20 nm emission filter for 20 min in 384 well-plate format. Activity values are corrected by subtracting background caused by the peptide or the protein. IC50 values are calculated using Sigmaplot. Standard deviations are calculated from two independent experiments.

Cell Assay:[1]

- **Cell lines**

  MCF7, U2OS, H1299 cell lines
- **Concentrations**

  3 μM
- **Incubation Time**

  65 h
- **Method**

  Approximately 5×10^5 cells were plated onto 75 cm^2 flasks. MCF7 and U2OS cells were grown in Minimal Essential Media (MEM) without phenol red supplemented with Earl's salts, 10% FBS, 1 mM Pyruvate, 2 mM Glutamine, and 1×non-essential amino acids. H1299 cells were grown in Dulbecco's Modified Eagle's Medium (DMEM) with phenol red supplemented with 10% FBS and 1×Anti-Anti. At the time of cell plating, media was supplemented with 3 μM UNC638A or the equivalent DMSO vehicle. The media with 3 μM this compound but without any cells was also used as a control. All flasks were incubated at 37℃/5% CO2. After 65 hours, media was collected from the cells and centrifuged to remove any cell debris. The media (10 to 15 mL) from each of study groups was mixed with HPLC grade chloroform (7 to 12 mL). After the mixture was gently shaken, it was allowed to sit until the organic layer and the aqueous layer separated. The organic layer was collected, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was dissolved in 100 μL of methanol and the solution was analyzed using an Agilent 6110 LC/MS Series system with UV detector set to at 254 nm. Samples were injected (10 μL) onto a Phenomenex Kinetex 2.1 x 100 nm, 2.6 μM, C18 column at room temperature and eluted with 72% B (MeCN) with A being H2O + 0.1% formic acid. The flow rate was 0.3 mL/min. No degradation products of this chemical were observed for any of treatment groups.

Animal Study:[1]	• **Animal Models** Swiss albino mice • **Dosages** IV, 1 mg/kg; PO, 3 mg/kg; IP, 2.5 mg/kg • **Administration** i.v./i.p./oral

References

https://pubmed.ncbi.nlm.nih.gov/21743462/

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