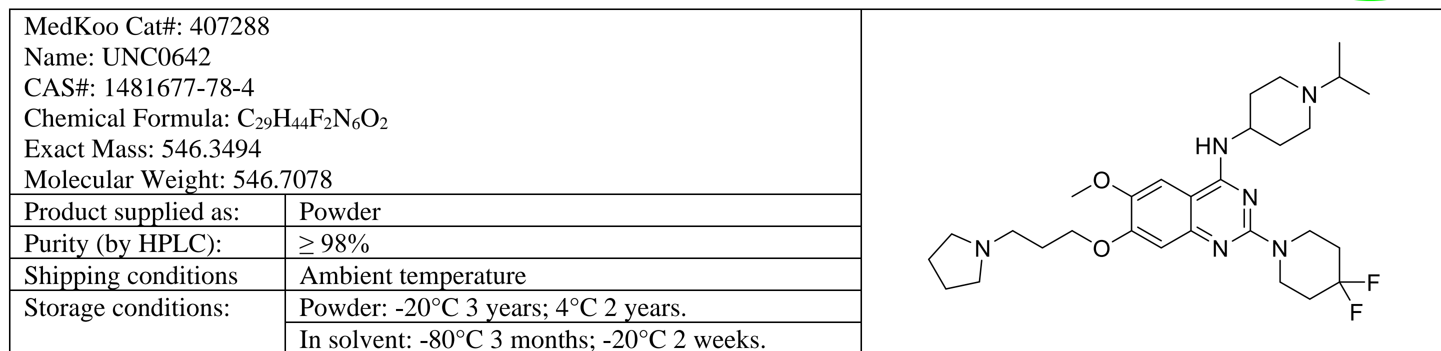
Product data sheet



MedKoo Cat#: 407288 Name: UNC0642 CAS#: 1481677-78-4 Chemical Formula: $C_{29}H_{44}F_2N_6O_2$ Exact Mass: 546.3494 Molecular Weight: 546.7078	
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:
UNC0642 is a potent, selective inhibitor of G9a/GLP with improved PK properties. UNC0642 exhibits an in vitro IC50 <15 nM with selectivity > 100-fold over 13 other HMTs and selected representatives of kinases, ion channels, 7TMs, and other epigenetic proteins. In cells, UNC0642 results in a potent reduction of H3K9me2 in MDA MB231 cells with IC50 = 106 nM.

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	50	91.46

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.83 mL	9.15 mL	18.29 mL
5 mM	0.37 mL	1.83 mL	3.66 mL
10 mM	0.18 mL	0.91 mL	1.83 mL
50 mM	0.04 mL	0.18 mL	0.37 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. Cao YP, Sun JY, Li MQ, Dong Y, Zhang YH, Yan J, Huang RM, Yan X. Inhibition of G9a by a small molecule inhibitor, UNC0642, induces apoptosis of human bladder cancer cells. Acta Pharmacol Sin. 2019 Aug;40(8):1076-1084. doi: 10.1038/s41401-018-0205-5. Epub 2019 Feb 14. PMID: 30765842; PMCID: PMC6786297.

2. Liu F, Barsyte-Lovejoy D, Li F, Xiong Y, Korboukh V, Huang XP, Allali-Hassani A, Janzen WP, Roth BL, Frye SV, Arrowsmith CH, Brown PJ, Vedadi M, Jin J. Discovery of an in vivo chemical probe of the lysine methyltransferases G9a and GLP. J Med Chem. 2013 Nov 14;56(21):8931-42. doi: 10.1021/jm401480r. Epub 2013 Oct 31. PMID: 24102134; PMCID: PMC3880643.

In vivo study

1. Cao YP, Sun JY, Li MQ, Dong Y, Zhang YH, Yan J, Huang RM, Yan X. Inhibition of G9a by a small molecule inhibitor, UNC0642, induces apoptosis of human bladder cancer cells. Acta Pharmacol Sin. 2019 Aug;40(8):1076-1084. doi: 10.1038/s41401-018-0205-5. Epub 2019 Feb 14. PMID: 30765842; PMCID: PMC6786297.

2. Kim Y, Lee HM, Xiong Y, Sciaky N, Hulbert SW, Cao X, Everitt JI, Jin J, Roth BL, Jiang YH. Targeting the histone methyltransferase G9a activates imprinted genes and improves survival of a mouse model of Prader-Willi syndrome. Nat Med. 2017 Feb;23(2):213-222. doi: 10.1038/nm.4257. Epub 2016 Dec 26. PMID: 28024084; PMCID: PMC5589073.

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7. Bioactivity

Biological target:

UNC0642 is a potent, selective inhibitor of histone methyltransferases G9a/GLP with IC50s less than 2.5 nM for G9a and GLP and shows more than 300-fold selective for G9a and GLP over a broad range of kinases, GPCRs, transporters, and ion channels.

In vitro activity

UNC0642 is a novel inhibitor of G9a with high cellular potency and excellent selectivity in various cancer cell lines (Fig. 4a) and thus, was chosen for further targeting of G9a of UBC cells. UNC0642 was applied at different concentrations (ranging from 0 to 20 μM) to three human UBC cell lines (T24, J82, and 5637) for 72 h and it was found that UNC0642 reduced cell viability of all three lines in a dose-dependent manner based on an SRB assay (Fig. 4b). The IC50 values of UNC0642 in T24, J82, and 5637 cells were 9.85 ± 0.41 μM, 13.15 ± 1.72 μM, and 9.57 ± 0.37 μM, respectively. Western blotting analysis validated the specific decrease in the global level of histone H3K9me2 with UNC0642 treatment (Fig. 4c). A stable G9a-knockdown T24 cell line (shG9a) was constructed as a control to test whether pharmacological inhibition of G9a by UNC0642 was specific (Fig. S2a). It was found that T24 mock cells (shCTL) were more sensitive to UNC0642 than T24 shG9a cells (Fig. S2b), indicating that cell death induced by UNC0642 was partially dependent on G9a activity. To examine whether UNC0642 could induce apoptosis, Annexin V-FITC/PI double staining of UBC cell lines treated with UNC0642 was carried out (Fig. 5a). Flow cytometry analysis showed that the ratio of apoptotic cells was increased in a dose-dependent manner in three UBC cell lines (Fig. 5b). The expression levels of apoptosis markers, such as cleaved Caspase-3 and cleaved PARP, were consistently raised in UBC cells upon UNC0642 treatment according to western blotting analysis (Fig. 5c). Meanwhile, it was examined whether the expression of apoptosis-related genes, including Bim, Ampkα2, and ELL2, was also affected by UNC0642 treatment. The results revealed that the mRNA levels of the Ampkα2, ELL2, and Bim genes were upregulated in T24 cells treated with UNC0642 at concentrations of 10 μM and 20 μM (Fig. 5d), consistent with the siG9a treatment results (Fig. 3c). These results indicate that targeting of G9a with UNC0642 reduces cell viability and induces apoptosis in UBC cells.

Reference: Acta Pharmacol Sin. 2019 Aug;40(8):1076-1084. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30765842/

In vivo activity

To test the in vivo effects of G9a inhibition, J82 cells were subcutaneously injected into nude mice. One week after xenografts became palpable, UNC0642 (5 mg/kg) was administered via i.p. injection every other day for 11 days. UNC0642 inhibited tumor growth during the treatment window ($P < 0.05$; Fig. 6a) without a significant effect on body weight compared with the vehicle-treated group (Fig. 6b). At the endpoint of the experiment, xenografts were harvested, weighed, and processed for further IHC study. The average tumor weight in the UNC0642 group (1.15 g) was approximately half of that in the vehicle treatment group (2.30 g, $P < 0.05$; Fig. 6c, d). Moreover, IHC staining demonstrated that UNC0642 treatment strikingly decreased the histone H3K9me2 level in the nuclei of cancer cells in J82 xenografts (Fig. 6e). Ki67 (cell proliferation marker)-positive staining and cleaved Caspase 3 (apoptosis marker)-positive staining in cells were quantified (Fig. 6f, g). Targeting of G9a in vivo reduced cell proliferation (from 61.73% in the vehicle group to 22.20% in the UNC0642 group; $P < 0.01$) and induced apoptosis (from 0.36% in the vehicle group to 4.89% in the UNC0642 group; $P < 0.05$). In addition, the level of the proapoptotic protein BIM was increased in the UNC0642 treatment group, consistent with the in vitro data (Fig. 6h). Thus, targeting of G9a with UNC0642 suppressed UBC tumor growth and induced apoptosis in vivo.

Reference: Acta Pharmacol Sin. 2019 Aug;40(8):1076-1084. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/30765842/

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.