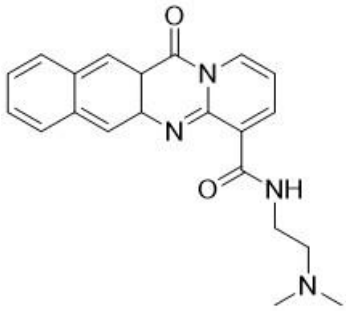
Product data sheet

MedKoo Cat#: 406586 Name: BMH-21 CAS#: 896705-16-1 Chemical Formula: $C_{21}H_{22}N_4O_2$ Exact Mass: 362.1743 Molecular Weight: 362.43	
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:

BMH-21 is a potent small molecule DNA intercalator. BMH-21 binds ribosomal DNA and inhibits RNA polymerase I (Pol I) transcription. BMH-21 does not cause phosphorylation of H2AX, a key biomarker activated in DNA damage stress. BMH-21 effects on the nucleolar stress response were independent of major DNA damage associated PI3-kinase pathways, ATM, ATR and DNA-PKcs. BMH-21 is a chemically unique DNA intercalator that has high bioactivity towards Pol I inhibition without activation or dependence of DNA damage stress. The findings also show that interference with DNA and DNA metabolic processes can be exploited therapeutically without causing DNA damage.

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	2.20	6.07

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.76 mL	13.80 mL	27.59 mL
5 mM	0.55 mL	2.76 mL	5.52 mL
10 mM	0.28 mL	1.38 mL	2.76 mL
50 mM	0.06 mL	0.28 mL	0.55 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. Fu X, Xu L, Qi L, Tian H, Yi D, Yu Y, Liu S, Li S, Xu Y, Wang C. BMH-21 inhibits viability and induces apoptosis by p53-dependent nucleolar stress responses in SKOV3 ovarian cancer cells. Oncol Rep. 2017 Aug;38(2):859-865. doi: 10.3892/or.2017.5750. Epub 2017 Jun 23. PMID: 28656213; PMCID: PMC5561869.
2. Colis L, Peltonen K, Sirajuddin P, Liu H, Sanders S, Ernst G, Barrow JC, Laiho M. DNA intercalator BMH-21 inhibits RNA polymerase I independent of DNA damage response. Oncotarget. 2014 Jun 30;5(12):4361-9. doi: 10.18632/oncotarget.2020. PMID: 24952786; PMCID: PMC4147329.

In vivo study

1. Peltonen K, Colis L, Liu H, Trivedi R, Moubarek MS, Moore HM, Bai B, Rudek MA, Bieberich CJ, Laiho M. A targeting modality for destruction of RNA polymerase I that possesses anticancer activity. Cancer Cell. 2014 Jan 13;25(1):77-90. doi: 10.1016/j.ccr.2013.12.009. PMID: 24434211; PMCID: PMC3930145.
2. Low JY, Sirajuddin P, Moubarek M, Agarwal S, Rege A, Guner G, Liu H, Yang Z, De Marzo AM, Bieberich C, Laiho M. Effective targeting of RNA polymerase I in treatment-resistant prostate cancer. Prostate. 2019 Dec;79(16):1837-1851. doi: 10.1002/pros.23909. Epub 2019 Sep 16. PMID: 31524299; PMCID: PMC7025478.

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7. Bioactivity

Biological target:

BMH-21 is a DNA intercalator that inhibits RNA polymerase I (Pol I) transcription and possesses anticancer activity.

In vitro activity

To evaluate the inhibitory effect of BMH-21 on SKOV3, Bel-7402 and HeLa cell viability, cells were treated with increasing doses of BMH-21 for 24 h and cell viability was determined by an MTT assay. BMH-21 treatment decreased the viability of SKOV3, Bel-7402 and HeLa cells in a dose-dependent manner (Fig. 1A, E and F). Based on MTT results, we treated SKOV3 cells with increasing doses of BMH-21 (1, 2 and 4 μM) for 24 h. The changes in SKOV3 cell morphology were examined using an inverted optical microscope. The cells treated with BMH-21 became fragmented and round when compared with control cells (Fig. 1B). To examine the distribution of cell cycle progression, the effect of BMH-21 in various cell cycle phases was confirmed using flow cytometry. BMH-21 resulted in a marked increase in the percentage of cells blocked at G2/M phase (Fig. 1C and D). These findings indicated that BMH-21 effectively inhibited cancer cell viability and suggested that BMH-21 induced cell death.

Reference: Oncol Rep. 2017 Aug; 38(2): 859–865. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5561869/

In vivo activity

To further understand the role of BMH-21 in prostate tumorigenesis in another preclinical prostate cancer model, the Hoxb13-MYC|Hoxb13-Cre|Ptenfl/fl (BMPC) mouse prostate cancer model in which the development of aggressive tumors is detected at 16 to 20 weeks of age was used The BMPC mice develop castration resistance and lose expression of AR around 20 weeks of age. As observed in Figure 7C, cells isolated from BMPC tumors31 had negligible AR expression. BMPC-1 cells were then treated with BMH-21 for 48 hours. A robust reduction in their growth (Figure 8A) was observed. To explore the potential of BMH-21 to repress tumor growth on these established tumors, treatments were initatied using an intraperitoneal administration of BMH-21 at 50 mg/kg at the age of 20 weeks and followed individual mice until the palpable tumor burden reached a euthanasia endpoint (Figure 8B). There was no statistical difference between the survival of vehicle and BMH-21 treated mice (Figure 8C). However, it was observed that BMH-21 treatment significantly reduced the tumor burden as measured by urogenital block size compared to vehicle control (Figure 8C). Histological analysis of the urogenital block also demonstrated a reduction in invasion compared to vehicle control (Figure 8D and 8E). The findings from this genetic mouse model suggest that BMH-21 may be a potential first-in-class molecule that is able to inhibit prostate tumorigenesis.

Reference: Prostate. 2019 Dec; 79(16): 1837–1851. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7025478/