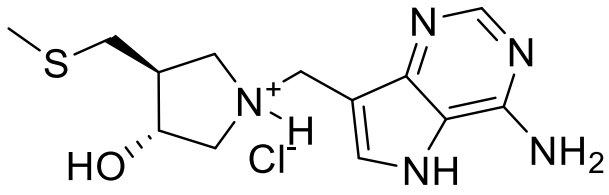
Product data sheet

MedKoo Cat#: 407244 Name: MTDIA HCl CAS#: 1399840-35-7 (HCl) Chemical Formula: $C_{13}H_{20}ClN_5OS$ Molecular Weight: 329.85	
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:

MTDIA, also known as MT-DADMe-ImmA, and Methylthio-DADMe-Immucillin A, is a MTAP inhibitor. Human 5'-methylthioadenosine phosphorylase (MTAP) is solely responsible for 5'-methylthioadenosine (MTA) metabolism to permit S-adenosylmethionine salvage. Transition-state (TS) analogues of MTAP are in development as anticancer candidates. TS analogues of MTAP incorporate a cationic nitrogen and a protonated 9-deazaadenine leaving group, which are mimics of the ribocation transition state. MT-ImmA and MT-DADMe-ImmA are two examples of these TS analogues.

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	100	340.84

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	3.03 mL	15.16 mL	30.32 mL
5 mM	0.61 mL	3.03 mL	6.06 mL
10 mM	0.30 mL	1.52 mL	3.03 mL
50 mM	0.06 mL	0.30 mL	0.61 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. Basu I, Cordovano G, Das I, Belbin TJ, Guha C, Schramm VL. A transition state analogue of 5'-methylthioadenosine phosphorylase induces apoptosis in head and neck cancers. J Biol Chem. 2007 Jul 20;282(29):21477-86. doi: 10.1074/jbc.M702287200. Epub 2007 Jun 4. PMID: 17548352.

In vivo study

1. Basu I, Locker J, Cassera MB, Belbin TJ, Merino EF, Dong X, Hemeon I, Evans GB, Guha C, Schramm VL. Growth and metastases of human lung cancer are inhibited in mouse xenografts by a transition state analogue of 5'-methylthioadenosine phosphorylase. J Biol Chem. 2011 Feb 11;286(6):4902-11. doi: 10.1074/jbc.M110.198374. Epub 2010 Dec 6. PMID: 21135097; PMCID: PMC3039339.

7. Bioactivity

Biological target:

MTDIA (MT-DADMe-ImmA) is an inhibitor of human 5'-methylthioadenosine phosphorylase (MTAP) with a Ki of 90 pM.

In vitro activity

Product data sheet

Methylthio-DADMe-immucillin-A (MT-DADMe-ImmA, MTDIA) is an 86-pm inhibitor of human 5'-methylthioadenosine phosphorylase (MTAP). The sole function of MTAP is to recycle 5'-methylthioadenosine (MTA) to S-adenosylmethionine. Treatment of cultured cells with MT-DADMe-ImmA and MTA inhibited MTAP, increased cellular MTA concentrations, decreased polyamines, and induced apoptosis in FaDu and Cal27, two head and neck squamous cell carcinoma cell lines. The same treatment did not induce apoptosis in normal human fibroblast cell lines (CRL2522 and GM02037) or in MCF7, a breast cancer cell line with an MTAP gene deletion. MT-DADMe-ImmA alone did not induce apoptosis in any cell line, implicating MTA as the active agent. Treatment of sensitive cells caused loss of mitochondrial inner membrane potential, G(2)/M arrest, activation of mitochondria-dependent caspases, and apoptosis. Changes in cellular polyamines and MTA levels occurred in both responsive and nonresponsive cells, suggesting cell-specific epigenetic effects. A survey of aberrant DNA methylation in genomic DNA using a microarray of 12,288 CpG island clones revealed decreased CpG island methylation in treated FaDu cells compared with untreated cells.

Reference: J Biol Chem. 2007 Jul 20;282(29):21477-86. https://linkinghub.elsevier.com/retrieve/pii/S0021-9258(20)54836-9

In vivo activity

AdoMet recycling from 5'-methylthioadenosine (MTA) was blocked by inhibition of MTAP with methylthio-DADMe-Immucillin-A (MTDIA), an orally available, nontoxic, picomolar transition state analogue. Blood, urine, and tumor levels of MTA increased in response to MTDIA treatment. MTDIA treatment inhibited A549 (human non-small cell lung carcinoma) and H358 (human bronchioloalveolar non-small cell lung carcinoma cells) xenograft tumor growth in immunodeficient Rag2(-/-)γC(-/-) and NCr-nu mice. Systemic MTA accumulation is implicated as the tumor-suppressive metabolite because MTDIA is effective for in vivo treatment of A549 MTAP(-/-) and H358 MTAP(+/+) tumors. Tumors from treated mice showed increased MTA and decreased polyamines but little alteration in AdoMet, methionine, or adenine levels. Gene expression profiles of A549 tumors from treated and untreated mice revealed only modest alterations with 62 up-regulated and 63 down-regulated mRNAs (≥ 3-fold). MTDIA antitumor activity in xenografts supports MTAP as a target for lung cancer therapy.

Reference: J Biol Chem. 2011 Feb 11;286(6):4902-11. https://linkinghub.elsevier.com/retrieve/pii/S0021-9258(20)56190-5