

Product Data Sheet

Product Name: SHMT-IN-2

Cat. No.: GC65181

Chemical Properties

Cas. No. 2102681-49-0

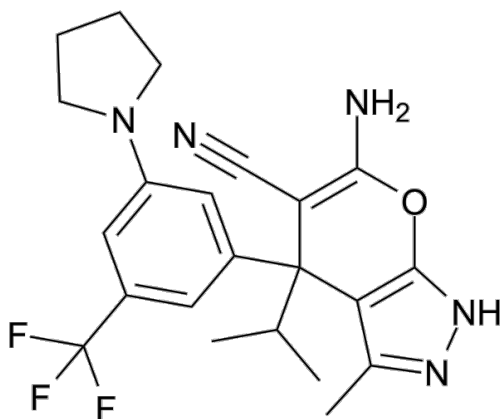
Formula $C_{22}H_{24}F_3N_5O$ M.Wt 431.45

Solubility DMSO : 100 mg/mL (231.78 mM; Storage 4°C, protect from light
Need ultrasonic)

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell lines NCI-H358 cells

NCI-H358 cells were seeded into 96-well plates with 1,500-18,000 cells per well and cultured overnight. SHMT-IN-2 was prepared at an initial concentration of 50 μ M and subjected to a series of twofold serial dilutions (ranging from 50 μ M to Preparation Method 98nM). The diluted compounds were incubated with the cells for 96 hours. Cell proliferation was evaluated using the CellTiter-Glo Luminescent Cell Viability Assay (Promega), which quantifies intracellular ATP levels as a measure of metabolically active cells.

Reaction
Conditions 50, 25, 12.5, 6.25, 3.125, 1.5625 μ M and 781.25, 390.625, 195.3125, 98nM; 96h

Applications SHMT-IN-2 exhibited a significant inhibitory effect on the proliferation of NCI-H358 cells.

References:

[1] Ducker GS, Ghergurovich JM, Mainolfi N, Suri V, Jeong SK, Hsin-Jung Li S, Friedman A, Manfredi MG, Gitai Z, Kim H, Rabinowitz JD. Human SHMT inhibitors reveal defective glycine import as a targetable metabolic vulnerability of diffuse large B-cell lymphoma. Proc Natl Acad Sci U S A. 2017 Oct 24;114(43):11404-11409.

Background

SHMT-IN-2 is a highly selective small-molecule inhibitor of serine hydroxymethyltransferases (SHMTs), exhibiting IC₅₀ values of 13nM for SHMT1 and 66nM for SHMT2 [1]. SHMT plays a central role in one-carbon metabolism, catalyzing the conversion of serine to glycine and the production of 5,10-methylenetetrahydrofolate, a critical cofactor for purine and pyrimidine biosynthesis [2]. By inhibiting both SHMT1 and SHMT2, SHMT-IN-2 disrupts nucleotide synthesis and DNA replication in

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

tumor cells, thereby suppressing their proliferation. Notably, SHMT-IN-2 has demonstrated antitumor activity against diffuse large B-cell lymphoma (DLBCL) [1].

In vitro, SHMT-IN-2 (10 μ M) significantly reduced the levels of [²H] formate, HDO, and [²H] glycine in the culture medium of patient-derived glioblastoma cell lines, A11 and S2 cells [3]. In sorafenib-resistant hepatocellular carcinoma (HCC) cells, combined treatment with SHMT-IN-2 (30 μ M) and sorafenib for 24 hours enhanced cellular sensitivity to sorafenib [4]. When fertilized embryos were exposed to SHMT-IN-2 (95 μ M-10mM) for 3.5 hours, approximately 50% were arrested at the pronuclear stage, failing to progress to the 2-cell stage. Furthermore, only 25% of treated embryos developed to the blastocyst stage, a significant reduction compared to control embryos. SHMT-IN-2 was also found to alter the catalytic activity of SHMT2 [5]. Treatment of 298 human cancer cell lines with SHMT-IN-2 (98nM-50 μ M) for 96 hours resulted in marked inhibition of cancer cell proliferation[1]. Additionally, SHMT-IN-2 demonstrated weak but measurable antibacterial activity: treatment of *Enterococcus faecalis* and *Enterococcus faecium* with SHMT-IN-2 (10-20 μ M) yielded an EC₅₀ of 2.9 $\times$ 10⁻⁶M [6].

References:

- [1] Ducker GS, Ghergurovich JM, Mainolfi N, Suri V, Jeong SK, Hsin-Jung Li S, Friedman A, Manfredi MG, Gitai Z, Kim H, Rabinowitz JD. Human SHMT inhibitors reveal defective glycine import as a targetable metabolic vulnerability of diffuse large B-cell lymphoma. *Proc Natl Acad Sci U S A*. 2017 Oct 24;114(43):11404-11409.
- [2] Heil SG, Van der Put NM, Waas ET, den Heijer M, Trijbels FJ, Blom HJ. Is mutated serine hydroxymethyltransferase (SHMT) involved in the etiology of neural tube defects? *Mol Genet Metab*. 2001 Jun;73(2):164-72.
- [3] Hesse F, Low J, Cao J, Bulat F, Kreis F, Wright AJ, Brindle KM. Deuterium MRI of serine metabolism in mouse models of glioblastoma. *Magn Reson Med*. 2024 Nov;92(5):1811-1821.
- [4] Dong Y, Chen Y, Wang Y, Zhao X, Zi R, Hao J, Ding Q, Jiang H, Wang X, Lu F, Liang H, Wei Z, Li J. Cancer-associated fibroblasts derived fibronectin extra domain A promotes sorafenib resistance in hepatocellular carcinoma cells by activating SHMT1. *Genes Dis*. 2024 May 20;11(6):101330.
- [5] Shi M, Huai Y, Deng T, Zhang C, Song J, Wang J, Zhang Y, Chen ZJ, Zhao H, Wu K, Liu B. SHMT2 is essential for mammalian preimplantation embryonic development through *de novo* biosynthesis of nucleotide metabolites. *Mol Ther Nucleic Acids*. 2025 Mar 5;36(2):102499.
- [6] Makino Y, Oe C, Iwama K, Suzuki S, Nishiyama A, Hasegawa K, Okuda H, Hirata K, Ueno M,

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Kawaji K, Sasano M, Usui E, Hosaka T, Yabuki Y, Shirouzu M, Katsumi M, Murayama K, Hayashi H, Kodama EN. Serine hydroxymethyltransferase as a potential target of antibacterial agents acting synergistically with one-carbon metabolism-related inhibitors. Commun Biol. 2022 Jun 23;5(1):619.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA