

Product Data Sheet

Product Name: L-Methionine-(S,R)-Sulfoximine

Cat. No.: GC45502

Chemical Properties

Cas. No. 15985-39-4

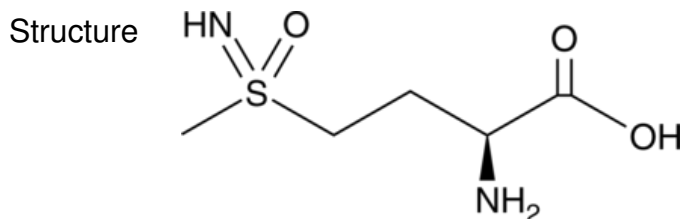
SMILES N[C@H](C(O)=O)CCS(C)(=N)=O

Formula $C_5H_{12}N_2O_3S$ M.Wt 180.2

Solubility PBS (pH 7.2): 5 mg/ml Storage Store at -20°C

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.



Protocol

Cell experiment [1]:

Cell lines *Klebsiella aerogenes* strains (MK-247 wild-type, MK-189 gltS mutant lacking glutamate synthetase, and MK-275 gltD mutant lacking glutamate dehydrogenase)

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Bacterial strains were cultured in glucose minimal medium at 37°C. Cells were harvested during exponential growth (100 ± 5 Klett units), washed, and stored as pellets. Cell-free extracts were prepared by sonication in imidazole buffer Preparation Method (pH=7.15) containing $MnCl_2$ and mercaptoethanol. L-Methionine-(S,R)-Sulfoximine was tested at concentrations ranging from 0.001mM to 100mM in enzyme assays. For growth inhibition studies, L-Methionine-(S,R)-Sulfoximine was added to cultures at 1–100mM.

Reaction
Conditions 0.001-100mM; 24–72 hours

Applications L-Methionine-(S,R)-Sulfoximine significantly inhibited the activity of both glutamine synthetase (GS) and glutamate synthetase (GltS) in *K. aerogenes*. Growth of the glutamate dehydrogenase-deficient mutant (MK-275) was strongly inhibited by L-Methionine-(S,R)-Sulfoximine, whereas the wild-type (MK-247) and glutamate synthetase-deficient mutant (MK-189) were resistant.

Animal experiment [2]:

Animal models AH/J and C57BL/6J mice

Preparation Method Mice were intraperitoneally administered a single dose of L-Methionine-(S,R)-Sulfoximine (1.0mmol/kg body weight) dissolved in Earle's balanced salt solution. Mice were sacrificed 2 to 6 hours after injection for brain and liver tissue analysis. Glutamine synthetase activity was determined using the γ -glutamylhydroxamate method on tissue homogenates.

Dosage form 1.0mmol/kg; i.p.; Single injection.

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Applications L-Methionine-(S,R)-Sulfoximine administration induced convulsions in mice (onset at approximately 140-150 minutes) and significantly inhibited brain and liver glutamine synthetase activity.

References:

- [1] Brenchley JE. Effect of methionine sulfoximine and methionine sulfone on glutamate synthesis in *Klebsiella aerogenes*. J Bacteriol. 1973 May;114(2):666-73.
- [2] Rowe WB, Meister A. Identification of L-methionine-S-sulfoximine as the convulsant isomer of methionine sulfoximine. Proc Natl Acad Sci U S A. 1970 Jun;66(2):500-6.

Background

L-Methionine-(S,R)-Sulfoximine is a potent and irreversible inhibitor of glutamine synthetase (GS) [1-2]. By inhibiting the activity of glutamine synthetase, L-Methionine-(S,R)-Sulfoximine blocks the synthesis of glutamine, thereby affecting cellular nitrogen metabolism. L-Methionine-(S,R)-Sulfoximine is also a convulsant that primarily affects the metabolism and morphology of astrocytes, and can be used as a research model for convulsions and related neurological disorders[3-4].

In vitro, L-Methionine-(S,R)-Sulfoximine (25-75µM) is used for routine passage culture of GS-CHOK1SV cell lines. By inhibiting the activities of glutamine synthetase (GS) and glutamylcysteine ligase (GCL), L-Methionine-(S,R)-Sulfoximine induces endoplasmic reticulum stress and oxidative stress, thereby upregulating the protein expression of the GCL catalytic subunit (GCLc) and the mRNA level of the regulatory subunit (GCLm), enhancing the specific production rate of recombinant monoclonal antibodies (mAb) and the antibody concentration in the harvest[5]. In *Klebsiella aerogenes*, L-Methionine-(S,R)-Sulfoximine (0.001–100mM) exhibits strong growth inhibition against the MK-275 mutant lacking glutamate dehydrogenase (*gltD*), with the mechanism involving irreversible inhibition of glutamine synthetase activity and blockade of the glutamine synthesis pathway[6].

In vivo, L-Methionine-(S,R)-Sulfoximine (75mg/kg; intraperitoneal injection) administered to 8-10-week-old C57BL/6J and CBA/J mice induces rapid epileptic seizures in the highly responsive CBA/J strain; whereas in the low-responsive C57BL/6J strain, L-Methionine-(S,R)-Sulfoximine causes

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delayed epileptic seizures, with significantly elevated brain glycogen content prior to seizure onset^[7]. L-Methionine-(S,R)-Sulfoximine (1mmol/kg; intraperitoneal injection) administered to AH/J strain mice (observed 2-6 hours post-injection) induces epileptic seizures in mice and significantly inhibits glutamine synthetase activity in the brain and liver ^[8].

References:

- [1] ROTH JS, WASE A, EICHEL HJ. Studies with methionine sulfoximine. J Biol Chem. 1953 Feb;200(2):647-56.
- [2] Davies AM, Tata R, Beavil RL, et al. L-Methionine sulfoximine, but not phosphinothricin, is a substrate for an acetyltransferase (gene PA4866) from *Pseudomonas aeruginosa*: structural and functional studies. Biochemistry. 2007 Feb 20;46(7):1829-39.
- [3] Sumida S, Ito M, Galis I, et al. Phosphoinositide 3-kinase participates in L-methionine sulfoximine-induced cell death via salicylic acid mediated signaling in *Nicotiana benthamiana*. J Plant Physiol. 2017 Nov;218:167-170.
- [4] Cloix JF, Tahi Z, Martin B, et al. Selection of two lines of mice based on latency to onset of methionine sulfoximine seizures. Epilepsia. 2010 Jan;51(1):118-28.
- [5] Feary M, Racher AJ, Young RJ, et al. Methionine sulfoximine supplementation enhances productivity in GS-CHOK1SV cell lines through glutathione biosynthesis. Biotechnol Prog. 2017 Jan;33(1):17-25.
- [6] Brenchley JE. Effect of methionine sulfoximine and methionine sulfone on glutamate synthesis in *Klebsiella aerogenes*. J Bacteriol. 1973 May;114(2):666-73.
- [7] Wang H, Miao F, Ning D, et al. Ellagic acid Alleviates hepatic ischemia-reperfusion injury in C57 mice via the Caspase-1-GSDMD pathway. BMC Vet Res. 2022 Jun 18;18(1):229.
- [8] Rowe WB, Meister A. Identification of L-methionine-S-sulfoximine as the convulsant isomer of methionine sulfoximine. Proc Natl Acad Sci U S A. 1970 Jun;66(2):500-6.

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