

Product Data Sheet

Product Name: Thiamet G

Cat. No.: GC12736

Chemical Properties

Cas. No. 1009816-48-1

Chemical Name 2-(ethylamino)-5-(hydroxymethyl)-5,6,7,7a-tetrahydro-3aH-pyrano[3,2-d][1,3]thiazole-6,7-diol

SMILES CCNC1=NC2C(C(C(OC2S1)CO)O)O

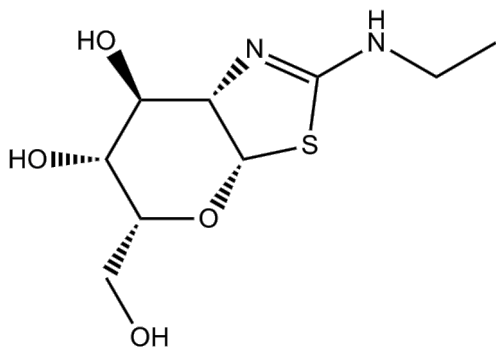
Formula $C_9H_{16}N_2O_4S$ M.Wt 248.3

Solubility $\geq 12.4\text{mg/mL}$ in DMSO, $\geq 100\text{mg/mL}$ in Water 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.

Structure



Protocol

Cell experiment [1]:

Cell lines A549, HT29 and H1299 cell lines

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

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Preparation Method Cells were treated with 5 μ M Thiamet-G for 24 h or the indicated time period.

Reaction Conditions 5 μ M for 24 hours

Applications Thiamet G could markedly elevate the O-GlcNAcylation of A549, H1299 and HT29 cells. Thiamet-G treatment did not significantly affect the proliferation of A549, H1299 and HT29. Thiamet-G treatment significantly increased colony formation ability of A549, H1299 and HT29 cells.

Animal experiment [2]:

Animal models Six-week-old male Sprague-Dawley rats

Preparation Method For tau western blot study, rats were treated orally with thiamet-G, by inclusion of inhibitor in the drinking water at a dose of 200 mg kg⁻¹ d⁻¹. Animals were euthanized after one day of treatment. For the thiamet-G dose and time dependency study, six-week-old male Sprague-Dawley rats received single intravenous tail vein injections of either 2, 10 or 50 mg kg⁻¹ and were euthanized at indicated times.

Dosage form 200 mg kg⁻¹ d⁻¹, oral; 2, 10 or 50 mg kg⁻¹ d⁻¹, intravenous injection.

Applications Thiamet-G is orally bioavailable, thiamet-G can cross the blood brain barrier and inhibit O-GlcNAcase in vivo to cause increased O-GlcNAc levels in brain.

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References:

[1]: Mi W, Gu Y, Han C, et al. O-GlcNAcylation is a novel regulator of lung and colon cancer malignancy[J]. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, 2011, 1812(4): 514-519.

[2]: Yuzwa S A, Macauley M S, Heinonen J E, et al. A potent mechanism-inspired O-GlcNAcase inhibitor that blocks phosphorylation of tau in vivo[J]. Nature chemical biology, 2008, 4(8): 483-490.

Background

Thiamet G, a potent inhibitor of O-GlcNAcase ($K_i = 21$ nM) was used to increase O-GlcNAcylation levels [1]. Thiamet G is a stable compound whose fused thiazoline ring system geometrically mimics a transition state of the substrate-assisted enzymatic hydrolysis of protein-O-GlcNAc units and, in this way, effectively inhibits O-GlcNAcase function [2]. Thiamet-G is orally bioavailable, and thiamet-G can cross the blood-brain barrier [1].

Thiamet G (5 μ M, 24h) could markedly elevate the O-GlcNAcylation of human lung epithelial carcinoma A549, non-small cell lung carcinoma H1299, and colon tumor HT29 cells [3]. Thiamet G (25 μ M, 24 h) treated PC-12 cells showed a gradual time-dependent increase in cellular O-GlcNAc levels that reached a maximum after approximately 12 h of exposure [1].

Thiamet G (2.5 μ l of 35 μ g/ μ l) dissolved in 0.9% NaCl was injected bilaterally into the lateral ventricles of the brains at a dose of 175 μ g/mouse, RL2 positive bands showed a 5-fold increase in global O-GlcNAcylation 4.5 h after thiamet G injection and a 10-fold increase 24 h after injection [4]. Thiamet G (500 mg/kg/day p.o.) treatment was able to decrease the number of neurons showing tau pathology, decrease behavioral defects, and reduce mice mortality in the Tau.P301L mouse model [5]. Thiamet-G treated Tau.P301L mice for 3 days in the drinking water (2.5 mg/ml) in the home cage, improved their breathing deficit in normocapnia and hypercapnia [6].

References:

[1]. Yuzwa S A, Macauley M S, Heinonen J E, et al. A potent mechanism-inspired O-GlcNAcase inhibitor that blocks phosphorylation of tau in vivo[J]. Nature Chemical Biology, 2008, 4(8): 483-490.

[2]. Fischer P M. Turning down tau phosphorylation[J]. Nature Chemical Biology, 2008, 4(8): 448-

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449.

[3]. Mi W, Gu Y, Han C, et al. O-GlcNAcylation is a novel regulator of lung and colon cancer malignancy[J]. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, 2011, 1812(4): 514-519.

[4]. Yu Y, Zhang L, Li X, et al. Differential effects of an O-GlcNAcase inhibitor on tau phosphorylation[J]. PloS one, 2012, 7(4): e35277.

[5]. Graham DL, Gray AJ, Joyce JA, Yu D, O'Moore J, Carlson GA, Shearman MS, Dellovade TL, Hering H. Increased O-GlcNAcylation reduces pathological tau without affecting its normal phosphorylation in a mouse model of tauopathy[J]. Neuropharmacology, 2014, 1;79:307-13.

[6]. Borghgraef P, Menuet C, Theunis C, Louis JV, Devijver H, Maurin H, Smet-Nocca C, Lippens G, Hilaire G, Gijssen H, Moechars D. Increasing brain protein O-GlcNAc-ylation mitigates breathing defects and mortality of Tau. P301L mice[J]. PloS one, 2013, Dec 23;8(12):e84442.

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