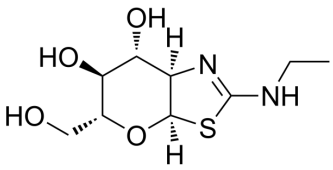
Thiamet G

Cat. No.:	HY-12588
CAS No.:	1009816-48-1
Molecular Formula:	$C_9H_{16}N_2O_4S$
Molecular Weight:	248.3
Target:	Autophagy
Pathway:	Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

H_2O : ≥ 50 mg/mL (201.37 mM)
DMSO : ≥ 45 mg/mL (181.23 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.0274 mL	20.1369 mL	40.2739 mL
5 mM	0.8055 mL	4.0274 mL	8.0548 mL
10 mM	0.4027 mL	2.0137 mL	4.0274 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 50 mg/mL (201.37 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (8.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (8.38 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (8.38 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Thiamet G is a potent and selective inhibitor of O-GlcNAcase (OGA), which acts to remove O-GlcNAc from modified proteins, with K_i of 20 nM for human OGA.

IC_{50} & Target	Ki: 20 nM (Human OGA)[1]
In Vitro	Thiamet G (1 μM) induces a clear increase in the accumulation of O-GlcNAcylated proteins of ATDC5 cells. O-GlcNAc accumulation induced by Thiamet G also evokes a clear increase in the activity of these MMPs. Thiamet G (1 μM) induces the phosphorylation of JNK, ERK, and p38 but not phosphorylation of Akt[2]. Thiamet G (0.1-10 μM) does not significantly affect the cell viability. Thiamet G decreases phosphorylation of tau and alters the microtubule dynamics[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Thiamet G (500 mg/kg/d) increases global and tau O-GlcNAc and reduces neurodegeneration. Thiamet G-treated group has 1.4-fold more motor neurons and hinders tau-driven neurodegeneration within this transgenic model. Thiamet G treatment therefore has no detectable effect on mice lacking the P301L transgene, indicating that prevention of neurodegeneration and weight loss is mediated by Thiamet G treatment only in the context of the P301L transgene. In Thiamet G-treated mice, the O-GlcNAc increases in the brain and spinal cord tissues[1]. Thiamet G (20 mg/kg, i.p.) increases O-GlcNAc levels in brain, liver, and knee of the C57BL/6 mice in a dose-dependent manner[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [3]	All enzymatic assays are performed in triplicate at 37°C using 4-methylumbelliferyl N-acetyl-β-d-glucosaminide dehydrate as substrate. 1 nM of purified OGA is incubated with the compounds for 5 min, and then 0.2 mM of the substrate is added. The liberation of 4-methylumbellifery is monitored by kinetic reading at excitation/emission 355/460 nm using a Tecan M200 plate in a mode of 60 s/cycle and 15 cycles in total. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [3]	Jurkat cells are seeded at 6000 cells/well in a 96-well plate, and 12 h later, cells are treated with compounds for the indicated time. Cell viability is determined by XTT assay. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	For the Thiamet G dose dependence study, six 23-day-old male C57BL/6 mice receive single intraperitoneal injections of either 0, 10, 20, 100, 200, or 500 mg/kg of Thiamet G dissolved in PBS and then are euthanized 8 h later to evaluate the O-GlcNAc levels in different tissues (brain, liver, muscle, and knee). The time of sacrifice is chosen on the basis of previously published data on Thiamet G in rodents, which demonstrates that the peak level of O-GlcNAc proteins following administration of the drug is achieved after 8-10 h. Tissues are collected immediately after sacrifice, flash-frozen in liquid nitrogen, and stored at −80°C until required for use. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2021 May 11;12(1):2672.
- Nat Chem Biol. 2022 Jul 25.
- Theranostics. 2020 Jun 1;10(16):7178-7192.
- Leukemia. 2022 Jan 8.
- Redox Biol. 2021 Jul;43:101994.

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REFERENCES

[1]. Yuzwa SA, et al. Increasing O-GlcNAc slows neurodegeneration and stabilizes tau against aggregation. Nat Chem Biol. 2012 Feb 26;8(4):393-9.

[2]. Andrés-Bergós J, et al. The increase in O-linked N-acetylglucosamine protein modification stimulates chondrogenic differentiation both in vitro and in vivo. J Biol Chem. 2012 Sep 28;287(40):33615-28.

[3]. Ding N, et al. Thiamet-G-mediated inhibition of O-GlcNAcase sensitizes human leukemia cells to microtubule-stabilizing agent NSC 125973. Biochem Biophys Res Commun. 2014 Oct 24;453(3):392-7.

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