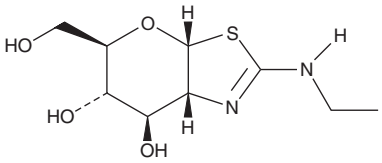
PRODUCT INFORMATION

Thiamet G

Item No. 13237

CAS Registry No.:	1009816-48-1
Formal Name:	2-(ethylamino)-3aR,6S,7R,7aR-tetrahydro-5R-(hydroxymethyl)-5H-pyrano[3,2-d]thiazole-6,7-diol
MF:	$C_9H_{16}N_2O_4S$
FW:	248.3
Purity:	≥97%
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Thiamet G is supplied as a crystalline solid. A stock solution may be made by dissolving the thiamet G in the solvent of choice, which should be purged with an inert gas. Thiamet G is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of thiamet G in these solvents is approximately 0.5, 20, and 25 mg/ml, respectively.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of thiamet G can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of thiamet G in PBS (pH 7.2) is approximately 3 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

Hyperphosphorylation of the tau protein leads to its aggregation and formation of neurofibrillary tangles, a hallmark of Alzheimer's disease and other tauopathic, neurodegenerative disorders. Tau is also dynamically modified by the addition and cleavage of O-linked β-N-acetylglucosamine (O-GlcNAc) moieties, which is mediated in part by O-GlcNAcase. Levels of O-GlcNAcylated proteins from Alzheimer's disease brain extracts are decreased as compared to that in controls, suggesting that impaired brain glucose metabolism may contribute to pathogenesis.[1] Thiamet G is a potent and selective inhibitor of O-GlcNAcase that demonstrates a K_i value of 21 nM.[2] It increases cellular O-GlcNAc-modified protein levels (EC_{50} = 30 nM) and blocks phosphorylation of tau protein both in cultured PC-12 cells and in rats (200 mg/kg/day).[2] Thiamet G is the first highly potent O-GlcNAcase inhibitor known to be orally bioavailable and effectively cross the blood brain barrier.[2]

References

1. Liu, F., Iqbal, K., Grundke-Iqbal, I., *et al*. O-GlnNAcylation regulates phosphorylation of tau: A mechanism involved in Alzheimer's disease. *Proc. Natl. Acad. Sci. USA* **101(29)**, 10804-10809 (2004).
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*. *Nat. Chem. Biol*. **4(8)**, 483-490 (2008).

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