

Product Data Sheet

Product Name: Pyrithiamine (hydrobromide)

Cat. No.: GC44790

Chemical Properties

Cas. No. 534-64-5

Chemical Name 1-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-3-(2-hydroxyethyl)-2-methyl-pyridinium, bromide, monohydrobromide

SMILES CC1=[N+](CC2=C(N)N=C(C)N=C2)C=CC=C1CCO.[Br-].Br

Formula $C_{14}H_{19}N_4O \cdot HBr \cdot Br$

M.Wt 420.1

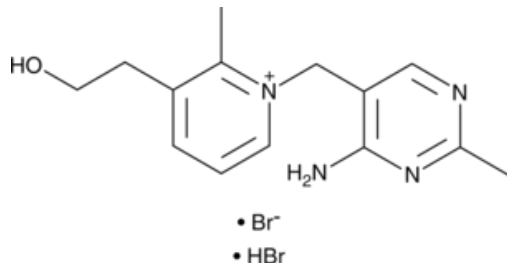
Solubility 5mg/mL in PBS (pH 7.2)

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	HeLa cells
Preparation method	Cells were incubated for four days in 10μM Pyrithiamine (hydrobromide) in low thiamine medium prior to irradiation.

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

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Reaction Conditions	10μM; 4 days
Applications	dATP, dCTP, dGTP and dTTP were all reduced in cells treated with Pyrithiamine (hydrobromide).
Animal experiment [2]:	
Animal models	AD model mice、 WT mice
Preparation method	mice were randomly divided into four groups respectively: control group, Pyrithiamine(hydrobromide) 250μg/kg/day group (hereafter the PT250 group), Pyrithiamine(hydrobromide) 500μg/kg/day group (PT500 group) and diet-induced TD group. The mice in TD group were fed a pelleted thiamine-depleted diet for four weeks. The control and PT groups received a normal thiamine-containing diet for 4 weeks. PT250 and PT500 groups received a daily intraperitoneal injection of Pyrithiamine(hydrobromide) (250 or 500μg/kg/day) for 4 weeks.
Dosage form	250 or 500μg/kg/day; i.p.
Applications	Pyrithiamine(hydrobromide) treatment significantly impairs the cognitive functions of wild-type mice, but has no corresponding effects on ADmodel mice that already have obvious cognitive impairment.

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References:

[1]Tiwana G S, Prevo R, Buffa F M, et al. Identification of vitamin B1 metabolism as a tumor-specific radiosensitizing pathway using a high-throughput colony formation screen[J]. Oncotarget, 2015, 6(8): 5978.

[2]Zhao J, Sun X, Yu Z, et al. Exposure to pyriethamine increases β -amyloid accumulation, Tau hyperphosphorylation, and glycogen synthase kinase-3 activity in the brain[J]. Neurotoxicity research, 2011, 19: 575-583.

Background

Pyriethamine (hydrobromide) is a thiamine analogue that inhibits the metabolism of thiamine (vitamin B1)^[1]. Pyriethamine (hydrobromide) has high affinity to thiamine transporters in neurons, with a K_d of approximately 60 nM^[2]. Pyriethamine (hydrobromide) is also a substrate of thiamine pyrophosphate kinase (TPK) and can be converted into pyriethamine pyrophosphate (PPP)^[3]. Pyriethamine (hydrobromide) can be used in microbial culture to inhibit the growth of microorganisms that require thiamine^[4].

In vitro, Pyriethamine (hydrobromide) (10 μ M) treated the HeLa cell line for 4 days, significantly reducing cellular nucleotide levels, and intracellular dATP, dCTP, dGTP and dTTP were all reduced^[5]. Pyriethamine (hydrobromide) (0.25mM) treated Neuro 2a cells, resulting in a strong reduction in intracellular ThDP levels, and the cells began to die after 48 hours^[6].

In vivo, Pyriethamine (hydrobromide) (250 or 500 μ g/kg/day) treated mice by intraperitoneal injection for 4 weeks, causing thiamine deficiency, leading to cognitive dysfunction and neuropathological changes in wild-type mice, but it had no effect on existing mice. There is no corresponding effect on AD model mice with obvious cognitive impairment^[7]. Pyriethamine (hydrobromide) (0.5g/kg) was administered intraperitoneally to rats for 11 days, causing thiamine deficiency, leading to enlargement of the lateral ventricles and reduced levels of choline-containing compounds in the body^[8].

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- [1] Chauhan A, Srivastva N, Bubber P. Thiamine deficiency induced dietary disparity promotes oxidative stress and neurodegeneration[J]. Indian Journal of Clinical Biochemistry, 2018, 33: 422-428.
- [2] Mulholland P J, Self R L, Stepanyan T D, et al. Thiamine deficiency in the pathogenesis of chronic ethanol-associated cerebellar damage in vitro[J]. Neuroscience, 2005, 135(4): 1129-1139.
- [3] Liu J Y, Timm D E, Hurley T D. Pyriithiamine as a substrate for thiamine pyrophosphokinase[J]. Journal of biological chemistry, 2006, 281(10): 6601-6607.
- [4] Brandenburger E, Gressler M, Leonhardt R, et al. A highly conserved basidiomycete peptide synthetase produces a trimeric hydroxamate siderophore[J]. Applied and Environmental Microbiology, 2017, 83(21): e01478-17.
- [5] Tiwana G S, Prevo R, Buffa F M, et al. Identification of vitamin B1 metabolism as a tumor-specific radiosensitizing pathway using a high-throughput colony formation screen[J]. Oncotarget, 2015, 6(8): 5978.
- [6] Sambon M, Napp A, Demelenne A, et al. Thiamine and benfotiamine protect neuroblastoma cells against paraquat and β -amyloid toxicity by a coenzyme-independent mechanism[J]. Heliyon, 2019, 5(5).
- [7] Zhao J, Sun X, Yu Z, et al. Exposure to pyriithiamine increases β -amyloid accumulation, Tau hyperphosphorylation, and glycogen synthase kinase-3 activity in the brain[J]. Neurotoxicity research, 2011, 19: 575-583.
- [8] Zahr N M, Sullivan E V, Rohlfing T, et al. Concomitants of alcoholism: differential effects of thiamine deficiency, liver damage, and food deprivation on the rat brain in vivo[J]. Psychopharmacology, 2016, 233: 2675-2686.

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