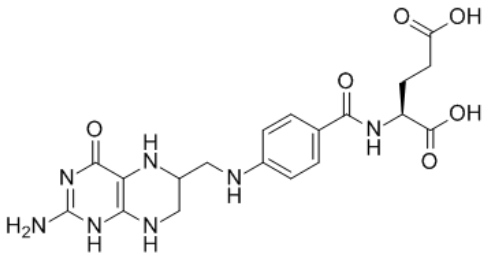
Product Data Sheet

Product Name: Tetrahydrofolic acid (L-5,6,7,8-Tetrahydrofolic acid)
Cat. No.: GC33819

Chemical Properties

Cas. No.	135-16-0		
SMILES	NC(NC1=C2NC(CNC3=CC=C(C(N[C@@H](CCC(O)=O)C(O)=O)=O)C=C3)CN1)=NC2=O		
Formula	$C_{19}H_{23}N_7O_6$	M.Wt	445.43
Solubility	DMSO : 20.83 mg/mL (46.76 mM; Need ultrasonic)	Storage	Store at -20°C; protect from light, stored under nitrogen,unstable in solution, ready to use.
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

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Kinase experiment [1]:

Preparation Method	The activity of methyltetrahydrofolic acid-dependent methyltransferase was assayed under standard conditions with increasing concentrations of Tetrahydrofolic acid up to 2mM with increasing concentrations of methyltetrahydrofolic acid or N-methylserotonin. After incubation at 37°C for 60min, the reaction was stopped.
Reaction Conditions	0-2mM; 60min
Applications	Tetrahydrofolic acid inhibited methyltetrahydrofolic acid-dependent methyltransferase. The concentration of tetrahydrofolic acid required to obtain a 50% inhibition under the standard assay condition was 0.2mM. At 2mM of Tetrahydrofolic acid, practically complete inhibition was observed.

Cell experiment [2]:

Cell lines	PC12 cells
Preparation Method	PC12 cells were incubated with aggregate solutions (10μL/well) for 48h. Preformed aggregates were produced by mixing 50μM αS without and with Tetrahydrofolic acid (αS: Tetrahydrofolic acid molar ratios 1:0.5, 1:1 and 1:2; equivalent to 25, 50 and 100μM) and by mixing Tetrahydrofolic acid with 25μM Aβ40 or Aβ42 in the specified molar ratios (1:1, 1:2 and 1:3; equivalent to 25, 50 and 75μM).
Reaction Conditions	25, 50, 75 and 100μM; 48h

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Applications	Tetrahydrofolic acid modification could alleviate the cytotoxicity of αS aggregates in a dose-dependent manner. When incubated with αS at different molar ratios (1:0.5, 1:1 and 1:2) Tetrahydrofolic acid increased cell viability by 15.66%, 20.71% and 28.62%, respectively. Tetrahydrofolic acid also has a similar inhibitory effect on Aβ induced cytotoxicity. When incubated with Aβ40 at different molar ratios (1:1, 1:2, and 1:3) Tetrahydrofolic acid increased cell viability by 11.20%, 20.26% and 27.52%.

Animal experiment [3]:

Animal models	Male ICR-JCL mice
Preparation Method	Five min after termination of X-irradiation, Tetrahydrofolic acid was intraperitoneally injected in the mice in the dose of 0.5mg or 1.5mg per animal.
Dosage form	0.5mg or 1.5mg; i.p.; a single administration
Applications	The treatment with Tetrahydrofolic acid increased the final survival rate from the control level of 50% up to 70% (0.5mg group) or up to 75% (1.5mg group).

References:
[1]Lin R L, Narasimhachari N. Tetrahydrofolic acid: an inhibitor of the methyltetrahydrofolic acid-mediated methylation of indolethylamines. Biochim Biophys Acta. 1975 Apr 7;385(2):268-74.
[2]Wang W Q, Wu X M, Zhang Q F, et al. Tetrahydrofolic acid accelerates amyloid fibrillization, decreases cytotoxic oligomers and suppresses their toxicity. Int J Biol Macromol. 2025 Feb:290:139041.
[3]Okazaki M, Sato F, Shikita M, Akaboshi S. Therapeutic effect of tetrahydrofolic acid in midlethally x-irradiated mice. Chem Pharm Bull (Tokyo). 1971 Jun;19(6):1173-7.

Background

Tetrahydrofolic acid (L-5,6,7,8-Tetrahydrofolic acid) is a derivative of vitamin B9 (folic acid or pteroyl-L-glutamic acid) which formed during the methyltetrahydrofolic acid-mediated methylation of

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indoleamines and exerts an inhibitory effect on methyltetrahydrofolic acid-dependent methyltransferase with K_i value of 0.1mM[1][2]. Tetrahydrofolic acid acts as a suicide substrate of tyrosinase and reduces o-quinones generated by the enzyme in its action on substrates, such as l-tyrosine and l-DOPA (o-dopaquinone), thus inhibiting enzymatic browning[3].

In vitro, rat pheochromocytoma PC12 cells were incubated with aggregate solutions (10μL/well) for 48h. Preformed aggregates were produced by mixing 50μM αS without and with Tetrahydrofolic acid (αS: Tetrahydrofolic acid molar ratios 1:0.5, 1:1 and 1:2; equivalent to 25, 50 and 100μM) and by mixing Tetrahydrofolic acid with 25μM Aβ40 or Aβ42 in the specified molar ratios (1:1, 1:2 and 1:3; equivalent to 25, 50 and 75μM). Tetrahydrofolic acid could alleviate the cytotoxicity of αS aggregates in a dose-dependent manner and also has a similar inhibitory effect on Aβ induced cytotoxicity[4]. $Adh5^{-/-}$, $FancC^{-}$, $FancF^{-/-}$ and wild-type DT40 bone marrow cells were exposed to Tetrahydrofolic acid (0-250μM) in vitro for 4h at 37°C in sealed cryovials. The viability of these cells rapidly dropped. Tetrahydrofolic acid is cytotoxic to cells lacking the Fanconi anemia DNA repair pathways or Adh5[5].

In vivo, Tetrahydrofolic acid was intraperitoneally injected into X-irradiated ICR-JCL mice with the dose of 0.5mg or 1.5mg per animal. In the Tetrahydrofolic acid-treated groups, there observed a singificant delay of time before the first incidence of death of the animals occurred. Furthermore, the treatment with Tetrahydrofolic acid increased the final survival rate from the control level of 50% up to 70% (0.5mg group) or up to 75% (1.5mg group)[6].

References:
[1] Tjong E, Dimri M, Mohiuddin S S. Biochemistry, Tetrahydrofolate. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
[2] Lin R L, Narasimhachari N. Tetrahydrofolic acid: an inhibitor of the methyltetrahydrofolic acid-mediated methylation of indolethylamines. Biochim Biophys Acta. 1975 Apr 7;385(2):268-74.
[3] Molina F G, Muñoz-Muñoz J L, Martínez-Ortiz F, et al. Tetrahydrofolic Acid is a potent suicide substrate of mushroom tyrosinase. J Agric Food Chem. 2011 Feb 23;59(4):1383-91.
[4] Wang W Q, Wu X M, Zhang Q F, et al. Tetrahydrofolic acid accelerates amyloid fibrillization, decreases cytotoxic oligomers and suppresses their toxicity. Int J Biol Macromol. 2025 Feb:290:139041.
[5] García-Calderón C B, Bejarano-García J A, Tinoco-Gago I, et al. Genotoxicity of tetrahydrofolic acid to hematopoietic stem and progenitor cells. Cell Death Differ. 2018 Nov;25(11):1967-1979.

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[6] Okazaki M, Sato F, Shikita M, Akaboshi S. Therapeutic effect of tetrahydrofolic acid in midlethally x-irradiated mice. Chem Pharm Bull (Tokyo). 1971 Jun;19(6):1173-7.

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