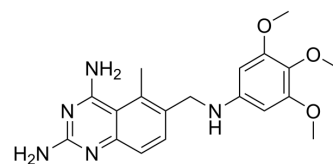


Trimetrexate

Cat. No.:	HY-10373		
CAS No.:	52128-35-5		
Molecular Formula:	C ₁₉ H ₂₃ N ₅ O ₃		
Molecular Weight:	369.42		
Target:	Bacterial; Antibiotic; Antifolate; Parasite; DNA/RNA Synthesis; Dihydrofolate reductase (DHFR)		
Pathway:	Anti-infection; Cell Cycle/DNA Damage; Metabolic Enzyme/Protease		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 61.5 mg/mL (166.48 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.7069 mL	13.5347 mL	27.0695 mL
	5 mM	0.5414 mL	2.7069 mL	5.4139 mL
	10 mM	0.2707 mL	1.3535 mL	2.7069 mL

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

In Vivo

- Add each solvent one by one: 50% PEG300 >> 50% saline
 Solubility: 40 mg/mL (108.28 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (6.77 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Trimetrexate (CI-898) is an antibiotic, also a potent and orally active dihydrofolate reductase (DHFR) inhibitor, reducing the production of DNA and RNA precursors and leading to cell death, with IC₅₀ values of 4.74 nM and 1.35 nM for human DHFR and *Toxoplasma gondii* DHFR. Trimetrexate can also inhibit the growth of various cancer cells. Trimetrexate can be used for researching *Pneumocystis carinii* pneumonia (PCP) and cancer^{[1][2][3][4][5]}.

IC ₅₀ & Target	Toxoplasma		
In Vitro	<p>Trimetrexate (0.1 μM, 18 h) completely inhibits proliferation of toxoplasma in murine macrophages^[3]. Trimetrexate (1 μM) can cross the toxoplasma cell membrane and rapidly reaches high intracellular concentrations (108 pmol/10⁷ cells within 10 min)^[3]. Trimetrexate (0.1 mM; 24 h) inhibits cell growth by 50-60% in SNU-C4 and NCI-H630 cell lines^[5]. Trimetrexate (1 and 10 mM; 24 h) produces lethality and inhibits DHFR in C4 cells^[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only. Cell Proliferation Assay^[5]</p>		
	<table border="1"> <tr> <td>Cell Line:</td> <td>SNU-C4 and NCI-H630</td> </tr> </table>	Cell Line:	SNU-C4 and NCI-H630
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In Vivo	<p>Trimetrexate (180 mg/kg or 30 mg/kg; p.o. or i.p.; daily) extends the median survival of the toxoplasma infected mice and shows antitoxoplasma activity^[3]. Trimetrexate (0-30 mg/kg; i.v.; once daily for 5days) shows chronic toxicity in rats^[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		
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REFERENCES

[1]. Fulton, B., et al. Trimetrexate. *Drugs* 49, 563–576 (1995).

[2]. Hopper AT, et al. Discovery of Selective *Toxoplasma gondii* Dihydrofolate Reductase Inhibitors for the Treatment of Toxoplasmosis. *J Med Chem*. 2019 Feb 14;62(3):1562-1576.

[3]. Allegra CJ, et al. Potent in vitro and in vivo antitoxoplasma activity of the lipid-soluble antifolate trimetrexate. *J Clin Invest*. 1987 Feb;79(2):478-82.

[4]. Dethloff LA, et al. Chronic toxicity of the anticancer agent trimetrexate in rats. *Fundam Appl Toxicol*. 1992 Jul;19(1):6-14.

[5]. Grem JL, Voeller DM, Geoffroy F, Horak E, Johnston PG, Allegra CJ. Determinants of trimetrexate lethality in human colon cancer cells. *Br J Cancer*. 1994 Dec;70(6):1075-84.

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

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