Lometrexol

Cat. No.: HY-14521

CAS No.: 106400-81-1

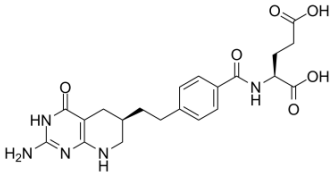
Molecular Formula: $C_{21}H_{25}N_5O_6$

Molecular Weight: 443.45

Target: Antifolate; Apoptosis

Pathway: Cell Cycle/DNA Damage; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 40 mg/mL (90.20 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2550 mL	11.2752 mL	22.5505 mL
5 mM	0.4510 mL	2.2550 mL	4.5101 mL
10 mM	0.2255 mL	1.1275 mL	2.2550 mL

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

BIOLOGICAL ACTIVITY

Description

Lometrexol (DDATHF), an antipurine antifolate, can inhibit the activity of glycinamide ribonucleotide formyltransferase (GARFT) but do not induce detectable levels of DNA strand breaks. Lometrexol can further inhibit de novo purine synthesis, causing abnormal cell proliferation and apoptosis, even cell cycle arrest. Lometrexol has anticancer activity[1][2]. Lometrexol also is a potent human Serine hydroxymethyltransferase1/2 (hSHMT1/2) inhibitor[3].

IC_{50} & Target

GARFT[1]

In Vitro

Lometrexol (DDATHF) binds tightly to GART, resulting in a rapid and prolonged depletion of intracellular purine ribonucleotides[2].

Lometrexol (1-30 μM; 2-10 hours) induces rapid and complete growth inhibition in L1210 cells[2].

Lometrexol (1 μM; 2-24 hours) induces cell cycle arrest in murine leukemia L1210 cells[2].

Lometrexol induces abnormal proliferation and apoptosis exist in neural tube defects (NTDs)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	Mouse leukemia L1210 cells
Concentration:	1, 30 μM
Incubation Time:	2, 4, 6, 8, 10 hours
Result:	Induced rapid and complete growth inhibition.

Cell Cycle Analysis[2]

Cell Line:	L1210 cells
Concentration:	1 μM
Incubation Time:	2, 4, 8, 12, 24 hours
Result:	Caused a rapid loss of the G2/M phase population of cells and an early S phase accumulation of cells by 8 hours. By 24 h, the S phase population appeared to be slowly shifting to higher DNA content, and hence, from mid-to-late S phase.

In Vivo

Lometrexol (DDATHF; i.p.; 15-60 mg/kg; on gestation day 7.5) increases the rate of embryonic resorption and growth retardation in a dose-dependent manner[1].
Lometrexol (i.p.; 40 mg/kg) maximally inhibits GARFT activity after at 6 hours and thereafter gradually increases with time but remains significantly lower than control even at 96 hours. Levels of ATP, GTP, dATP and dGTP of NTDs embryonic brain tissue decreases significantly at 6 h, and more significantly over time[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57BL/6 mice (7-8 week, 18-20 g)[1]
Dosage:	15, 30, 35, 40, 45 and 60 mg/kg
Administration:	Intraperitoneal injection; on gestation day 7.5
Result:	Increased the rate of embryonic resorption and growth retardation in a dose-dependent manner.

REFERENCES

[1]. Xu L, et al. The effect of inhibiting glycinamide ribonucleotide formyl transferase on the development of neural tube in mice. Nutr Metab (Lond). 2016 Aug 23;13(1):56.

[2]. Julie L Bronder, et al. Antifolates Targeting Purine Synthesis Allow Entry of Tumor Cells Into S Phase Regardless of p53 Function. Cancer Res. 2002 Sep 15;62(18):5236-41.

[3]. Emma Scaletti, et al. Structural basis of inhibition of the human serine hydroxymethyltransferase SHMT2 by antifolate drugs. FEBS Lett. 2019 Jul;593(14):1863-1873.

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

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