Lometrexol

Cat. No.: HY-14521

CAS No.: 106400-81-1

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

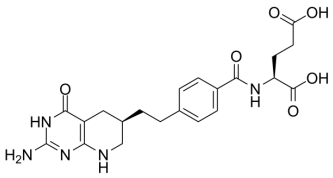
Molecular Weight: 443.45

Target: Apoptosis; Antifolate; Caspase; Bcl-2 Family

Pathway: Apoptosis; Cell Cycle/DNA Damage

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (225.50 mM; Need ultrasonic)

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.

In Vivo

1. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 25 mg/mL (56.38 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 5 mg/mL (11.28 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 5 mg/mL (11.28 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 5 mg/mL (11.28 mM); Suspended solution; Need ultrasonic

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. Lometrexol also is a potent human Serine hydroxymethyltransferase1/2 (hSHMT1/2) inhibitor[1][2][3].

In Vitro

Lometrexol (DDATHF) binds tightly to GART, resulting in a rapid and prolonged depletion of intracellular purine ribonucleotides[3].
Lometrexol (1-30 μM; 2-10 hours) induces rapid and complete growth inhibition in L1210 cells[3].
Lometrexol (1 μM; 2-24 hours) induces cell cycle arrest in murine leukemia L1210 cells[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[3]

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[3]

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) induces neural tube defects (NTDs) by disturbing purine metabolism and increases the rate of embryonic resorption and growth retardation in a dose-dependent manner[1].
Lometrexol (i.p.; 40 mg/kg; on gestation day 7.5) decreases glycinamide ribonucleotide formyl transferase (GARFT) activity and Changes of ATP, GTP, dATP and dGTP levels[1].
Lometrexol (i.p.; 40 mg/kg; on gestation day 7.5) 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.

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.

Animal Model:	C57BL/6 mice (7-8 week, 18-20 g)[1]
Dosage:	40 mg/kg
Administration:	Intraperitoneal injection; on gestation day 7.5, for 0, 6, 24, 48 and 96 hours
Result:	Inhibited glycinamide ribonucleotide formyl transferase (GARFT) activity and GARFT activity was maximally inhibited after at 6 hours. Decreased the levels of ATP, GTP, dATP, and dGTP of NTDs embryonic brain tissue significantly at 6 hours.

Animal Model:	C57BL/6 mice (7-8 week, 18-20 g)[1]
Dosage:	40 mg/kg
Administration:	Intraperitoneal injection; on gestation day 7.5, for 4 days
Result:	Decreased the expression of proliferation-related genes (Pcna, Foxg1 and Ptch1) and increased the expression of apoptosis-related genes (Bax, Casp8 and Casp9) in NTD groups.

CUSTOMER VALIDATION

- Nat Commun. 2022 Nov 17;13(1):7031.

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

[3]. Bronder JL, 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.

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