Raltitrexed

Cat. No.: HY-10821

CAS No.: 112887-68-0

Molecular Formula: $C_{21}H_{22}N_4O_6S$

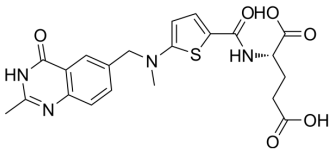
Molecular Weight: 458

Target: Thymidylate Synthase; Nucleoside Antimetabolite/Analog

Pathway: Apoptosis; Cell Cycle/DNA Damage

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 : ≥ 29 mg/mL (63.32 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1834 mL	10.9170 mL	21.8341 mL
	5 mM	0.4367 mL	2.1834 mL	4.3668 mL
	10 mM	0.2183 mL	1.0917 mL	2.1834 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.46 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.54 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.54 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Raltitrexed is an antimetabolite agent used in chemotherapy, acting by inhibiting thymidylate synthase.

In Vitro

Raltitrexed inhibits HepG2 proliferation by arresting the cell cycle at G0/G1, and the cell cycle is mediated via downregulation of cyclin A and CDK2[1]. Raltitrexed (0.1, 0.5, 2.5 μg/mL) decreases the viability of SGC7901 cells in a dose- and time-dependent manner. Raltitrexed (0.5 μg/mL) shows typical apoptotic morphology, including nuclear shrinkage, fragmentation, chromatin condensation and apoptotic bodies in SGC7901 cells. Raltitrexed blocks the cell cycle at the G0/G1 phase, decreases in the mitochondrial membrane potential. Raltitrexed also increases the level of ROS, induces

	caspase-3-dependent apoptosis via activation of the mitochondria, and increases TS protein and mRNA expression levels[3]. Raltitrexed (1.5 nM) reduces the number of GM00637 cells, selectively induces gene conversions, but does not affect DSB-induced HR or NHEJ[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Raltitrexed (0, 5, 10, 11.5, 13.5, 15 mg/kg b/w, i.p.) increases the rates of resorbed embryos and growth retardation of murine model of NTDs in a dose dependent manner. Raltitrexed (11.5 mg/kg b/w) maximally inhibits the thymidylate synthase (TS) activity in embryonic tissue, decreases dTMP levels and while increases dUMP levels[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [4]	To assess the effect of Raltitrexed on cell viability and/or growth, GM00637 cells are plated into 25 cm^2 flasks at a density of 3.3×10^5 cells per flask. Twenty four hours later, the medium is replaced with medium supplemented with various doses of Raltitrexed over a broad range of concentrations ranging from less than 1 nM to greater than 1 μM. Three flasks of cells are used for each dose tested. Cells are exposed to Raltitrexed for 24 hours, at which time the cells are refed with medium containing no Raltitrexed. Forty-eight hours after feeding with drug-free medium, cells are harvested and counted. The cell counts for the cells exposed to the various Raltitrexed doses are compared with the cell count for control cells not exposed to Raltitrexed as a measure of the impact of Raltitrexed on cell viability and/or growth rate. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	The adult (7-8 week, 19-20 g) C57BL/6 mice are used in the experiment. Mice are maintained under 22°C with a 12 h light/day cycle and fed with standard mouse chow and tap water ad libitum. Female mice are mated with male overnight and vaginal plugs are examined in the following morning. The presence of vaginal plug in the pregnant mice is considered as gestational day 0.5. Pregnant mice are randomly divided into 6 groups with 10 mice in each group. Raltitrexed is dissolved in 0.9 % NaCl, and five groups are intraperitoneally injected with different doses of Raltitrexed (5, 10, 11.5, 13.5, 15 mg/kg b/w) on gestational day 7.5. The control group is intraperitoneally injected with 0.9 % NaCl at the same volume on gestational day 7.5. On gestational day 11.5, pregnant mice are sacrificed, and embryos are examined under dissect microscope. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Data. 2022 Oct 8;9(1):610.
- Commun Biol. 2022 Jun 23;5(1):619.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Methods Mol Biol. 2018;1711:351-398.

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REFERENCES

[1]. Zhao H, et al. Raltitrexed Inhibits HepG2 Cell Proliferation via G0/G1 Cell Cycle Arrest. Oncol Res. 2016;23(5):237-48

[2]. Dong Y, et al. Raltitrexed's effect on the development of neural tube defects in mice is associated with DNA damage, apoptosis, and proliferation. Mol Cell Biochem. 2015 Jan;398(1-2):223-31.

[3]. Xue S, et al. Raltitrexed induces mitochondrial-mediated apoptosis in SGC7901 human gastric cancer cells. Mol Med Rep. 2014 Oct;10(4):1927-34.

[4]. Waldman BC, et al. Induction of intrachromosomal homologous recombination in human cells by raltitrexed, an inhibitor of thymidylate synthase. DNA Repair (Amst). 2008 Oct 1;7(10):1624-35.

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