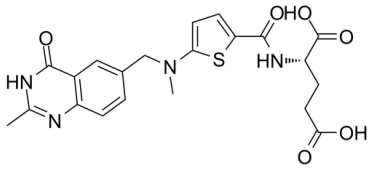
Data Sheet

Product Name:	Raltitrexed
Cat. No.:	CS-2894
CAS No.:	112887-68-0
Molecular Formula:	C21H22N4O6S
Molecular Weight:	458.49
Target:	Nucleoside Antimetabolite/Analog; Thymidylate Synthase
Pathway:	Apoptosis; Cell Cycle/DNA Damage
Solubility:	DMSO : ≥ 29 mg/mL (63.25 mM)



BIOLOGICAL ACTIVITY:

Raltitrexed is an inhibitor of **thymidylate synthase** and an **antimetabolite** drug used for cancer treatment. **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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. **Animal Administration:** Raltitrexed is dissolved in 0.9 % NaCl.[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.

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.

CAIndexNames:

L-Glutamic acid, N-[[5-[[(3,4-dihydro-2-methyl-4-oxo-6-quinazolinyl)methyl]methylamino]-2-thienyl]carbonyl]-

SMILES:

CC(NC1=O)=NC2=C1C=C(CN(C)C3=CC=C(C(N[C@H](C(O)=O)CCC(O)=O)=O)S3)C=C2

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA