Furamidine

Cat. No.: HY-110137A

CAS No.: 73819-26-8

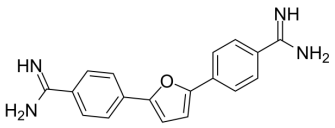
Molecular Formula: $C_{18}H_{16}N_4O$

Molecular Weight: 304.35

Target: Histone Methyltransferase; Phosphodiesterase (PDE); Parasite

Pathway: Epigenetics; Metabolic Enzyme/Protease; Anti-infection

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



BIOLOGICAL ACTIVITY

Description

Furamidine (DB75) is a selective protein arginine methyltransferase 1 (PRMT1) inhibitor with an IC_{50} of 9.4 μM. Furamidine is selective for PRMT1 over PRMT5, PRMT6, and PRMT4 (CARM1) (IC_{50}s of 166 μM, 283 μM, and >400 μM, respectively). Furamidine is a potent, reversible and competitive tyrosyl-DNA phosphodiesterase 1 (TDP-1) inhibitor. Inhibition of TDP-1 by Furamidine is effective both with single- and double-stranded DNA substrates but is slightly stronger with the duplex DNA. Furamidine is also an antiparasite agent[1][2][3].

IC_{50} & Target

IC50: 9.4 μM (Protein arginine methyltransferase 1 (PRMT1)); 166 μM (PRMT5), 283 μM (PRMT6) and >400 μM (PRMT4)[1]
Parasite[1]
Tyrosyl-DNA phosphodiesterase 1 (TDP-1)[2]

In Vitro

Furamidine (compound 1; 20 μM; 72 hours; leukemia cell lines) inhibits cell growth for most of the leukemia cell lines except HEL cells which have JAK2V617F mutations[1].
Furamidine (compound 1; 20 μM; 15 hours; 293T cells) treatment significantly reduces the expression level of the methylated GFP-ALY protein in 293T cells[1].
Furamidine binds duplex DNA in the DNA minor groove selectively at AT rich sites [(A/T)4]. Furamidine can also intercalate between GC base pairs of duplex DNA. Furamidine could therefore interfere with DNA processing enzymes such as TDP-1[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	Meg-01, K562, HL-60, NB4, MOLM13, HEL, CMK, CMY, CMS and CHRF cells
Concentration:	20 μM
Incubation Time:	72 hours
Result:	Inhibited cell growth for most of the leukemia cell lines except HEL cells which have JAK2V617F mutations.

Western Blot Analysis[1]

Cell Line:	293T cells
Concentration:	20 μM

Incubation Time:	15 hours
Result:	The expression level of the methylated GFP-ALY protein is significantly reduced.

In Vivo

Furamidine (1 mg/kg; intraperitoneal injection; 3 times a week and repeated every 4 weeks; for 34 weeks; female NZB/NZW mice) and Irinotecan combined treatment suppresses proteinuria and prolongs survival of lupus-prone NZB/NZW mice. The combination treatment does not change the levels of anti-dsDNA antibodies[3].

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

Animal Model:	Female NZB/NZW mice (6-week-old) with Irinotecan (1 mg/kg)[3]
Dosage:	1 mg/kg
Administration:	Intraperitoneal injection; 3 times a week and repeated every 4 weeks; for 34 weeks
Result:	Suppressed proteinuria and prolongs survival of lupus-prone NZB/NZW mice combined with Irinotecan.

REFERENCES

[1]. Antony S, et al. Novel high-throughput electrochemiluminescent assay for identification of human tyrosyl-DNA phosphodiesterase (Tdp1) inhibitors and characterization of furamidine (NSC 305831) as an inhibitor of Tdp1. Nucleic Acids Res. 2007;35(13):4474-84.

[2]. Yan L, et al. Diamidine compounds for selective inhibition of protein arginine methyltransferase 1. J Med Chem. 2014 Mar 27;57(6):2611-22.

[3]. Keil A, et al. The Topoisomerase I Inhibitor Irinotecan and the Tyrosyl-DNA Phosphodiesterase 1 Inhibitor Furamidine Synergistically Suppress Murine Lupus Nephritis. Arthritis Rheumatol. 2015 Jul;67(7):1858-67.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

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