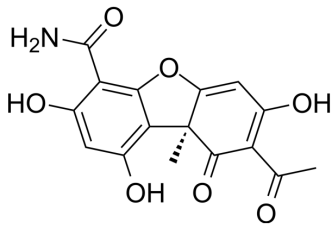
Cercosporamide

Cat. No.:	HY-16982
CAS No.:	131436-22-1
Molecular Formula:	$C_{16}H_{13}NO_7$
Molecular Weight:	331.28
Target:	Fungal; MNK; PKC
Pathway:	Anti-infection; MAPK/ERK Pathway; Epigenetics; TGF-beta/Smad
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



BIOLOGICAL ACTIVITY

Description	Cercosporamide is a highly potent, ATP-competitive PKC kinase inhibitor targeting to PKC1, with an IC_{50} of <50 nM and a K_i of <7 nM. Cercosporamide is a unique Mnk inhibitor.		
IC_{50} & Target	Pkc1 50 nM (IC_{50})	Pkc1 7 nM (Ki)	Mnk
In Vitro	Cercosporamide is a broad-spectrum natural antifungal compound, is actually a selective and highly potent fungal Pkc1 kinase inhibitor[1]. Cercosporamide, an antifungal agent that is recently shown to act as a unique Mnk inhibitor, exhibits antileukemic properties. Cercosporamide is a potent inhibitor of phosphorylation of eIF4E at Ser209 in AML cells and results in potent inhibitory effects on primitive leukemic progenitors (CFU-L) from AML patients. To determine whether Cercosporamide exhibits negative regulatory effects on cell proliferation and viability of leukemia cells, MTT assays are conducted. When U937 cells are incubated in the presence or absence of the increasing doses of Cercosporamide, a dose-dependent suppression of cell growth is found. Similar experiments with comparable results are seen when the effects of Cercosporamide on MM6 and K562 cells are examined[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		
In Vivo	Treatment with Cercosporamide or Ara-C alone significantly suppresses xenograft growth when compared with the respective vehicle (P<0.011 for 10 mg/kg twice-daily Cercosporamide; P<0.006 for Cercosporamide 20 mg/kg daily; P<0.0374 for Ara-C). The combination of Cercosporamide 10 mg/kg twice daily plus Ara-C is significantly more effective than either agent alone (P<0.0009 vs Cercosporamide; P=0.005 vs Ara-C; P<0.0001 vs either vehicle). Cercosporamide (20 mg/kg once daily) in combination with Ara-C shows similar effects, with significant inhibition of tumor growth vs captisol (P<0.0001) or water (P=0.0003), but does not show statistical significance vs Cercosporamide alone (20 mg/kg) or Ara-C alone[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		

PROTOCOL

Cell Assay [2]	U937, MM6, and K562 cells are incubated for 5 days in the presence or absence of the indicated doses of Cercosporamide (1, 10, and 20μM) . Cell proliferation is assessed by an MTT assay[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration [2]	Mice[2] MV4-11 cells are implanted at a density of 5×10^6 cells per mouse. Tumors are measured by caliper and tumor volume is calculated. Once tumors reach a group mean of 100 mm3, animals are randomized to the following treatment groups: Ara-C (20 mg/kg daily dosed intraperitoneally), Cercosporamide (10 mg/kg twice daily, 20 mg/kg daily dosed orally by gavage), Ara-C plus Cercosporamide combinations (as above), or the relative vehicle controls (captisol for Cercosporamide and water for Ara-C)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sussman A, et al. Discovery of Cercosporamide, a known antifungal natural product, as a selective Pkc1 kinase inhibitor through high-throughput screening. Eukaryot Cell. 2004 Aug;3(4):932-43.

[2]. Altman JK, et al. Inhibition of Mnk kinase activity by Cercosporamide and suppressive effects on acute myeloid leukemia precursors. Blood. 2013 May 2;121(18):3675-81.

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