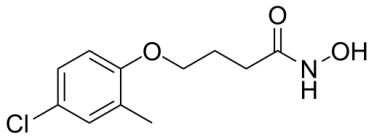
Data Sheet

Product Name:	Droxinostat
Cat. No.:	CS-0491
CAS No.:	99873-43-5
Molecular Formula:	C11H14ClNO3
Molecular Weight:	243.69
Target:	Apoptosis; HDAC
Pathway:	Apoptosis; Cell Cycle/DNA Damage; Epigenetics
Solubility:	DMSO : ≥ 150 mg/mL (615.54 mM)



BIOLOGICAL ACTIVITY:

Droxinostat(NS41080) is a selective inhibitor of HDAC3, HDAC6, and HDAC8 with IC50 of 16.9, 2.47 and 1.46 μM, respectively; > 8-fold selective against HDAC3 and no inhibition to HDAC1, 2, 4, 5, 7, 9, and 10. IC50 Value: 16.9 μM(HDAC3); 2.47 μM(HDAC6); 1.46 μM(HDAC8) Target: HDAC3/6/8 in vitro: Droxinostat is originally identified as a sensitizer of PPC-1 cells to FAS and TRAIL by downregulating the expression of c-Fas-associated death domain-like interleukin-1-converting enzyme-like inhibitory protein (c-FLIP). the direct targets of Droxinostat remains enigma until recently. It is revealed that in histone deacetylases (HDAC) isoform 1-10, Droxinostat selective inhibits HDAC3, 6, and 8, with IC50 values of 16.9 μM, 2.47 μM, and 1.46 μM, respectively, without inhibiting other HDAC members (IC50 > 20 μM). In MCF-7 breast cancer cells, Droxinostat (10 μM–100 μM) sensitizes cells to apoptosis by decreasing c-FLIPL and c-FLIPS expression, reducing cell survival, and inducing apoptosis. in vivo: In SCID mice models, Droxinostat (30 μM)-treated PPC-1 cells results in decreased distant tumor formation than untreated cells.

PROTOCOL (Extracted from published papers and Only for reference)

Cell assay [5] HepG2 cells were seeded in 96-well plates at an initial density of 3 × 103 cells/well, and SMMC-7721 cells were seeded at an initial density of 4 × 103 cells/well. After overnight growth, cells were treated with different concentrations of droxinostat (0, 10, 20, 40, and 80 μM) for 0, 24, 48, 72, 96, and 120 hours. Serum-free Dulbecco's modified Eagle medium was used as the blank control, and the same density of cells as the negative control group. After treatment, 20 μl of 5 mg/ml of 3-(4, 5 dimetyl-2-thiazolyl)-2, 5-diphenyl 2H-tetrazolium bromide (MTT) was added to each well. Plates were incubated for a further 4 hours at 37°C, and 150 μl of DMSO was added to each well after removing the supernatant. After incubation for another 10 minutes, cell viability was assessed via measuring absorbance at 490 nm with iMark Reader. Cell viability is indirectly represented by absorbance values.

References:

[1]. Liu J, et al. Droxinostat, a Histone Deacetylase Inhibitor, Induces Apoptosis in Hepatocellular Carcinoma Cell Lines via Activation of the Mitochondrial Pathway and Downregulation of FLIP. Transl Oncol. 2016 Feb;9(1):70-8.

[2]. Wood TE et al. Selective inhibition of histone deacetylases sensitizes malignant cells to death receptor ligands. Mol Cancer Ther. 2010 Jan;9(1):246-56.

[3]. MMcCourt C, Maxwell P, Mazzucchelli R, Montironi R, Scarpelli M, Salto-Tellez M, O'Sullivan JM, Longley DB, Waugh DJ.,Elevation of c-FLIP in Castrate-Resistant Prostate Cancer Antagonizes Therapeutic Response to Androgen Receptor-Targeted Therapy.,Clin Cancer Res. 2012 Jul 15;18(14):3822-33. Epub 2012 May 23

[4]. Bijangi-Vishehsaraei K, Saadatzadeh MR, Huang S, Murphy MP, Safa AR.,4-(4-Chloro-2-methylphenoxy)-N-hydroxybutanamide (CMH) targets mRNA of

the c-FLIP variants and induces apoptosis in MCF-7 human breast cancer cells.,Mol Cell Biochem. 2010 Sep;342(1-2):133-42. Epub 2010 May 6.

[5]. Wood TE, Dalili S, Simpson CD, Sukhai MA, Hurren R, Anyiwe K, Mao X, Suarez Saiz F, Gronda M, Eberhard Y, MacLean N, Ketela T, Reed JC, Moffat J, Minden MD, Batey RA, Schimmer AD.,Selective inhibition of histone deacetylases sensitizes malignant cells to death receptor ligands.,Mol Cancer Ther. 2010 Jan;9(1):246-56. Epub 2010 Jan 6.

CAIndexNames:

Butanamide, 4-(4-chloro-2-methylphenoxy)-N-hydroxy-

SMILES:

ClC1=CC=C(C(C)=C1)OCCCC(NO)=O

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