AES-350

Cat. No.: HY-138831

CAS No.: 847249-57-4

Molecular Formula: $C_{18}H_{20}N_2O_3$

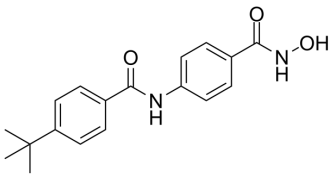
Molecular Weight: 312.36

Target: HDAC; Apoptosis

Pathway: Cell Cycle/DNA Damage; Epigenetics; Apoptosis

Storage: 4°C, protect from light

* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (320.14 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.2014 mL	16.0072 mL	32.0143 mL
	5 mM	0.6403 mL	3.2014 mL	6.4029 mL
	10 mM	0.3201 mL	1.6007 mL	3.2014 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 (8.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.00 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AES-350 is a potent and orally active HDAC6 inhibitor with an IC_{50} and a K_i of 0.0244 μM and 0.035 μM, respectively. AES-350 is also against HDAC3, HDAC8 in an enzymatic activity assay with IC_{50} values of 0.187 μM and 0.245 μM, respectively. AES-350 triggers apoptosis in AML cells through HDAC inhibition and can be used for acute myeloid leukemia (AML) research[1].

IC_{50} & Target			
	HDAC6 24.4 nM (IC_{50})	HDAC3 187 nM (IC_{50})	HDAC11 245 nM (IC_{50})

In Vitro

In contrast, AES-350 has submicromolar activity (IC_{50}=0.58±0.13 μM) against MV4-11 cells than to that of vorinostat (IC_{50} =0.31±0.061 μM). AES-350 is more ligand efficient and exemplifies a large therapeutic index (IC_{50}>30 μM in noncancerous

MRC-9 cells). AES-350 is also shown to be effective in AML-3 (acute myeloid leukemia) cells (IC_{50}=0.73 ± 0.12 μM)[1].
AES-350 (0.25-4 μM; 18 hours) induces MV4-11 cells apoptosis in a dose-dependent manner. The late apoptosis ratios are 8.74%, 11.7%,16.08%, 30.97%, and 38.48%, respectively at 0.25 μM-4 μM[1].
An ELISA is performed using HeLa cervical cancer cell lysates, and HeLa cells highly express HDAC6 and are sensitive to AES-350. Correspondingly, ELISA assays depicted a dose-dependent increase in HDAC6 inhibition (IC_{50}=0.58±0.13 μM), Western blot analysis shows that AES-350 (0.1-10 μM) induces a dose-dependent increase in acetylated α-tubulin (Ac-α-tubulin), a substrate of HDAC[1].

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

Apoptosis Analysis[1]

Cell Line:	MV4-11 cells
Concentration:	0.25 μM; 0.5 μM; 1.00 μM; 2.00 μM; 4.00 μM
Incubation Time:	18 hours
Result:	Revealed a clear dosedependent increase in the percentage of cells entering late-stage apoptosis, similar to SAHA.

In Vivo

AES-350 (oral gavage; 20 mg/kg; single dose) exhibits a relative good pharmacokinetic (PK) properties in CD-1 mice. The single dose oral bioavailability (F%) of 51 is 19.8%. In comparison, the reported F% for SAHA in mice is significantly lower (8%)[1].

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

REFERENCES

[1]. Andrew E Shouksmith, et al. Class I/IIb-Selective HDAC Inhibitor Exhibits Oral Bioavailability and Therapeutic Efficacy in Acute Myeloid Leukemia.

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