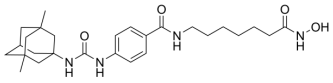
sEH/HDAC6-IN-1

Cat. No.:	HY-163207
CAS No.:	2847838-67-7
Molecular Formula:	$C_{27}H_{40}N_4O_4$
Molecular Weight:	484.63
Target:	HDAC; Epoxide Hydrolase
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

sEH/HDAC6-IN-1 (compound M9) is a selective, orally active dual inhibitor for sEH and HDAC6, with IC_{50}s of 2 nM, 0.72 nM and 5 nM, for human sEH, murine sEH and HDAC6, respectively. sEH/HDAC6-IN-1 reveals analgesic and anti-inflammatory effects [1].

IC_{50} & Target

murine sEH 0.72 nM (IC_{50})	human sEH 2 nM (IC_{50})	HDAC6 5 nM (IC_{50})	HDAC1 0.2731 μM (IC_{50})
HDAC2 0.8 μM (IC_{50})	HDAC3 0.49 μM (IC_{50})	HDAC11 0.3142 μM (IC_{50})	

In Vitro

sEH/HDAC6-IN-1 (1-2 μM, 24 h) inhibits cell growth of THP-1 with IC_{50} of 3.2 μM[1].

sEH/HDAC6-IN-1 (100 μM) reveals microsomal stability in human, rat and mouse liver microsomes, with half-times of 4.07, 1.76 and 1.39 h[1].

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

Cell Viability Assay[1]

Cell Line:	THP-1
Concentration:	1-2 μM
Incubation Time:	24 h
Result:	Increased the levels of acetylated α-tubulin

In Vivo

sEH/HDAC6-IN-1 reveals a plasma protein binding (PBB) percentage of 81.40% in SD rats[1].

sEH/HDAC6-IN-1 (p.o., 100 mg/kg, 7 days) reveals analgesic effects in SNI mice[1].

sEH/HDAC6-IN-1 (5 mg/kg, i.p., 4-12 h) inhibits LPS induced inflammation and the release of IL-6, TNF-α and MCP-5 in C57BL/6 mice[1].

sEH/HDAC6-IN-1 (i.v.:10 mg/kg, p.o.:100 mg/kg) reveals a pharmacokinetics profils in SD rats[1]:

Pharmacokinetic Analysis of sEH/HDAC6-IN-1 in SD rats[1]

route	Dose (mg/kg)	T_{max} (h)	C_{max} (μM)	$T_{1/2}$ (h)	CL (L/h/kg)	V_Z (L/kg)	AUC_{0-8} (μM·h)	$AUC_{0-\infty}$ (μM·h)	F (%)
iv	10	0.03	261.20	1.58	0.21	0.43	36.76	38.10	10.82
po	100	0.50	13.09	1.31	1.80	3.43	19.89	22.85	-

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

Animal Model:	alleviating spared nerve injury (SNI)-induced neuropathic pain in C57BL/6 mice[1]
Dosage:	100 mg/kg
Administration:	oral administration for 7 days
Result:	decreased PWT values.

Animal Model:	LPS induced acute inflammation in C57BL/6 mice[1]
Dosage:	5 mg/kg
Administration:	i.p., 4-12 h
Result:	Survived 66.7% mice at 28 h, 44.44% mice at 35 h, 22.22% mice at 72 h.

REFERENCES

[1]. Chen Y,et al., Design and Synthesis of Dual-Targeting Inhibitors of sEH and HDAC6 for the Treatment of Neuropathic Pain and Lipopolysaccharide-Induced Mortality. J Med Chem. 2024 Feb 8;67(3):2095-2117.

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