Clobenpropit dihydrobromide

Cat. No.: HY-101198

CAS No.: 145231-35-2

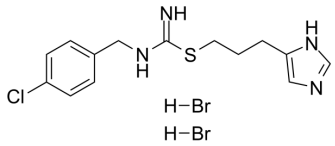
Molecular Formula: $C_{14}H_{19}Br_2ClN_4S$

Molecular Weight: 470.65

Target: Histamine Receptor; Apoptosis

Pathway: GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling; Apoptosis

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (265.59 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
	1 mM	2.1247 mL	10.6236 mL	21.2472 mL
	5 mM	0.4249 mL	2.1247 mL	4.2494 mL
	10 mM	0.2125 mL	1.0624 mL	2.1247 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: ≥ 2.08 mg/mL (4.42 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.42 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.42 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Clobenpropit dihydrobromide is a potent histamine H3R antagonist/inverse agonist with a pEC_{50} of 8.07 for histamine H3LR [1]. Clobenpropit dihydrobromide acts as partial agonist at histamine H4 receptors (K_i 13 nM). Clobenpropit dihydrobromide also binds to serotonin 5-HT3 receptors (K_i 7.4 nM) and α2A/α2C adrenoceptors (K_i 17.4/7.8 nM)[2]. Clobenpropit dihydrobromide increases apoptosis[3].

IC_{50} & Target	Human H3LR	Rat H3LR	H_4 receptor	H_2 Receptor
	9.44 (pKi)	9.75 (pKi)	13 nM (Ki)	5.6 (pKi)

In Vitro

Clobenpropit binds to human H3LR and rat H3LR with pK_is of 9.44±0.04 and 9.75±0.01. Clobenpropit exhibits low affinity for

histamine H1R or H2R (pK_is of 5.2 and 5.6, respectively)[1].
Clobenpropit inhibits [^{3}H]-dopamine transport by SH-SY5Y cells in a concentration dependent manner with maximum inhibition 82.7±2.8 % and IC_{50} 490 nM (pIC_{50} 6.31±0.11)[2].
Clobenpropit is a subunit-selective noncompetitive antagonist at recombinant NMDA receptors (IC_{50} 1 μM for the NR1/NR2B receptor)[2].
Clobenpropit (50 μM) and Gemcitabine (5 μM) combination therapy significantly increases apoptosis of Panc-1, MiaPCa-2 and AsPC-1 compared with control[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[3]

Cell Line:	Pancreatic cancer cells (Panc-1, MiaPaCa-2 and AsPC-1)
Concentration:	50 μM
Incubation Time:	
Result:	Enhanced apoptotic cell death in combination of Gemcitabine (5 μM).

In Vivo

The combination treatment of Clobenpropit (every other day intraperitoneal injection at 20 μM per kilogram for 40 d) and Gemcitabine (twice-a-week intraperitoneal injection at 125 mg/kg for 40 d) shows significant tumor growth inhibition[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Five-week-old male BALB/c nude mice with Panc-1 xenograft[3]
Dosage:	20 μM per kilogram
Administration:	Intraperitoneal injection; every other day for 40 days. Gemcitabine (twice-a-week intraperitoneal injection at 125 mg/kg for 40 d)
Result:	The combination treatment showed significant tumor growth inhibition compared with other treatment groups (control 501±92 mg, Gemcitabine 294±46 mg, Clobenpropit 444±167 mg, and combination 154±54 mg).

REFERENCES

[1]. Esbenshade TA, et al. Two novel and selective nonimidazole histamine H3 receptor antagonists A-304121 and A-317920: I. In vitro pharmacological effects. J Pharmacol Exp Ther. 2003 Jun;305(3):887-96.

[2]. Mena-Avila E, et al. Clobenpropit, a histamine H3 receptor antagonist/inverse agonist, inhibits [^{3}H]-dopamine uptake by human neuroblastoma SH-SY5Y cells and rat brain synaptosomes. Pharmacol Rep. 2018 Feb;70(1):146-155.

[3]. Paik WH, et al. Clobenpropit enhances anti-tumor effect of gemcitabine in pancreatic cancer. World J Gastroenterol. 2014 Jul 14;20(26):8545-57.

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