Cl-amidine hydrochloride

Cat. No.: HY-100574A

CAS No.: 1373232-26-8

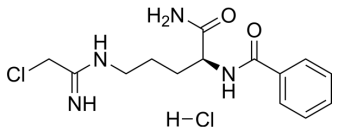
Molecular Formula: $C_{14}H_{20}Cl_2N_4O_2$

Molecular Weight: 347.24

Target: Protein Arginine Deiminase; Apoptosis; MicroRNA

Pathway: Epigenetics; Apoptosis

Storage: -20°C, stored under nitrogen, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (143.99 mM; Need ultrasonic)
H_2O : 50 mg/mL (143.99 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8799 mL	14.3993 mL	28.7985 mL
	5 mM	0.5760 mL	2.8799 mL	5.7597 mL
	10 mM	0.2880 mL	1.4399 mL	2.8799 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: PBS
   Solubility: 5.5 mg/mL (15.84 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (3.60 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (3.60 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (3.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Cl-amidine hydrochloride is an orally active peptidylarginine deminase (PAD) inhibitor, with IC_{50} values of 0.8 μM, 6.2 μM and 5.9 μM for PAD1, PAD3, and PAD4, respectively. Cl-amidine hydrochloride induces apoptosis in cancer cells. Cl-amidine hydrochloride induces microRNA (miR)-16 (miRNA-16, microRNA-16) expression and causes cell cycle arrest. Cl-Amidine hydrochloride prevents histone 3 citrullination and neutrophil extracellular trap formation, and improves survival in a murine sepsis model[1][2][3][4][5].

IC_{50} & Target	IC50: 0.8 μM (PAD1), 5.9 μM (PAD4), 6.2 μM (PAD3)[1][5].

In Vitro

Cl-amidine is a bioavailable haloacetamidine-based compound that inhibits all the active PAD isozymes with near equal potency (k_{inact}/K_I=13,000 M^{-1} min^{-1} for PAD4)[1].

Cl-amidine (0, 5, 10, 15, 20, 25, 50 μg/mL, 24 hours) induces apoptosis in TK6 lymphoblastoid cells and HT29 colon cancer cells in a dose-dependent manner. Interestingly, the colon cancer cell line (HT29) is relatively resistant to apoptosis caused by Cl-amidine[2].

Cl-Amidine prevents histone 3 citrullination and neutrophil extracellular trap formation, and improves survival in a murine sepsis model[4].

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

Apoptosis Analysis[2].

Cell Line:	TK6 lymphoblastoid cells and HT29 colon cancer cells.
Concentration:	0, 5, 10, 15, 20, 25, 50 μg/mL.
Incubation Time:	24 h.
Result:	Induced apoptosis dose-dependently.

In Vivo

Cl-amidine (75 mg/kg, ip once daily) suppresses and treats DSS-induced colitis in mice[2].

Cl-amidine (5, 25, 75 mg/kg, oral gavage, once daily) leads to significant reductions in the histology scores dose-dependently [2].

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

Animal Model:	C57BL/6 mice (8-12 wk old, DSS mouse model of colitis)[2].
Dosage:	75 mg/kg.
Administration:	IP once daily.
Result:	Suppressed PAD activity, protein citrullination, and PAD levels in the colon in vivo.

Animal Model:	C57BL/6 mice (8-12 wk old, DSS mouse model of colitis)[2].
Dosage:	5, 25, 75 mg/kg.
Administration:	Oral gavage once daily.
Result:	Led to significant reductions in the histology scores.

CUSTOMER VALIDATION

- Cell Rep. 2021 Sep 21;36(12):109750.
- Transl Res. 2022 Nov 23;S1931-5244(22)00252-3.
- Neoplasia. 2022 Nov;33:100835.
- Fish Shellfish Immunol. 2022 Aug 3;S1050-4648(22)00414-4.
- Chem Res Toxicol. 2022 Feb 15.

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REFERENCES

[1]. Yuan Luo, et al. Inhibitors and Inactivators of Protein Arginine Deiminase 4: Functional and Structural Characterization. Biochemistry. 2006 Oct 3; 45(39): 11727–11736.

[2]. Chumanevich AA, et al. Suppression of colitis in mice by Cl-amidine: a novel peptidylarginine deiminase inhibitor. Am J Physiol Gastrointest Liver Physiol. 2011 Jun;300(6):G929-38.

[3]. Witalison EE, et al. Molecular targeting of protein arginine deiminases to suppress colitis and prevent colon cancer. Oncotarget. 2015 Nov 3;6(34):36053-62.

[4]. Biron BM, et al., Cl-Amidine Prevents Histone 3 Citrullination and Neutrophil Extracellular Trap Formation, and Improves Survival in a Murine Sepsis Model. J Innate Immun. 2017;9(1):22-32.

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