# 5-(N,N-Hexamethylene)-amiloride

**Cat. No.:** HY-128067

**CAS No.:** 1428-95-1

**Molecular Formula:** $C_{12}H_{18}ClN_7O$

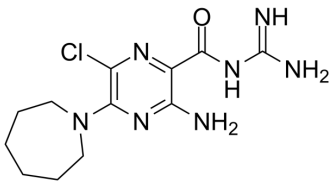
**Molecular Weight:** 311.77

**Target:** Sodium Channel; HIV; Apoptosis

**Pathway:** Membrane Transporter/Ion Channel; Anti-infection; Apoptosis

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |




## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 100 mg/mL (320.75 mM; Need ultrasonic)

**Preparing Stock Solutions**

| Mass / Solvent / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|
| **1 mM** | 3.2075 mL | 16.0375 mL | 32.0749 mL |
| **5 mM** | 0.6415 mL | 3.2075 mL | 6.4150 mL |
| **10 mM** | 0.3207 mL | 1.6037 mL | 3.2075 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 (6.67 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.67 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.67 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

5-(N,N-Hexamethylene)-amiloride (Hexamethylene amiloride) derives from an amiloride and is a potent $Na^+/H^+$ exchanger inhibitor, which decreases the intracellular pH ($pH_i$) and induces apoptosis in leukemic cells. 5-(N,N-Hexamethylene)-amiloride (Hexamethylene amiloride) is also an inhibitor of the HIV-1 Vpu virus ion channel and inhibits mouse hepatitis virus (MHV) replication and human coronavirus 229E (HCoV229E) replication in cultured L929 cells with $EC_{50}$s of 3.91 μM and 1.34 μM, respectively[1][2].

**$IC_{50}$ & Target**

HIV-1

**In Vitro**

5-(N,N-Hexamethylene)-amiloride inhibits human cardiac ion channels hERG (in CHO cells), Nav1.5 and Cav1.2 (in EHK293 cells) with of 3.3 μM, 30 μM, 8.3 μM, respectively, inelectrophysiology assays[3].
5-(N,N-Hexamethylene)-amiloride (1 μM; 0-60 min; 37 ℃) exhibits microsomal stability, (1 μg/mL; 4.2 h; 37 ℃) shows mouse plasma stability and plasma protein binding, (20 μM; 4 h) displays Caco-2 cell permeability, cardiac ion channel activity[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[3]

| | |
|---|---|
| Cell Line: | In vitro pharmacokinetics properties |
| Concentration: | 1 μM |
| Incubation Time: | 0-60 min |
| Result: | |

| | $t_{1/2}$ (min) | $CL_{int}$ (μL/min/mg protein) | $CL_{int}$ (μL/min/mg protein) |
|---|---|---|---|
| Human liver microsomers in vitro | 73 | 24 | 74 |
| Mouse liver microsomers in vitro | 2.4 | 726 | 2243 |

**In Vivo**

5-(N,N-Hexamethylene)-amiloride (2.5 mg/kg; i.v.; single dose) shows short half-life and lowly oral bioavailability of 4.5%[3].
In vivo pharmacokinetics in mice or rat model[3]
Dosage: 2.5 mg/kgAdministration: Intravenous injection; single does; collected 10 min and 60 min after treatment.

| | $t_{1/2}$ (h) | Plasma $CL_{int}$ (mL/min/kg) | Plasma $V_{ss}$ (L/kg) | Plasma $AUC_{0-inf}$ (h·μM) | B/P ratio | Blood CL (mL/min/kg) | Blood $V_{ss}$ (L/kg) |
|---|---|---|---|---|---|---|---|
| Female Balb/c mice | 0.62 | 86 | 2.0 | 1.5 | 1.5 | 59 | 1.4 |
| Sprague Dawley rats | 3.2 | 83.5 | 5.3 | 1.6 | 1.8 | 46.2 | 2.9 |

| | % IV dose excreted in urine (0-24 h) | Renal Blood CL (mL/min/kg) | Non-Renal Blood CL (mL/min/kg) |
|---|---|---|---|
| Sprague Dawley rats | 0.5 | 0.2 | 46.0 |

Note: B/P means blood-to-plasma partitioning ratio; female Balb/c mice (17-27 g, non-fasted); male Sprague Dawley rats (238-325 g, overnight-fasted).
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Sci Adv. 2023 Aug 9;9(32):eadh2413.

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## REFERENCES

[1]. Buckley BJ, et al. Systematic evaluation of structure-property relationships and pharmacokinetics in 6-(hetero)aryl-substituted matched pair analogs of amiloride and 5-(N,N-hexamethylene)amiloride. Bioorg Med Chem. 2021 May 1;37:116116.

[2]. Rich IN, et al. Apoptosis of leukemic cells accompanies reduction in intracellular pH after targeted inhibition of the Na(+)/H(+) exchanger. Blood. 2000 Feb 15;95(4):1427-34.

[3]. Wilson L, et al. Hexamethylene amiloride blocks E protein ion channels and inhibits coronavirus replication. Virology. 2006 Sep 30;353(2):294-306. Epub 2006 Jul 3.



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