Nortriptyline hydrochloride

Cat. No.: HY-B1417

CAS No.: 894-71-3

Molecular Formula: $C_{19}H_{22}ClN$

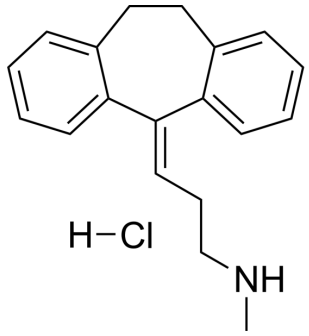
Molecular Weight: 299.84

Target: Autophagy; Drug Metabolite; Apoptosis

Pathway: Autophagy; Metabolic Enzyme/Protease; 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 : 83.33 mg/mL (277.91 mM; Need ultrasonic)

H_2O : 7.14 mg/mL (23.81 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.3351 mL	16.6756 mL	33.3511 mL
5 mM	0.6670 mL	3.3351 mL	6.6702 mL
10 mM	0.3335 mL	1.6676 mL	3.3351 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 (6.94 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (6.94 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (6.94 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Nortriptyline (Desmethylamitriptyline) hydrochloride, the main active metabolite of Amitriptyline, is a tricyclic antidepressant. Nortriptyline hydrochloride is a potent autophagy inhibitor and has anticancer effects[1][2][3].

In Vitro

Amitriptyline is metabolized by CYP2C19 to the active metabolite, Nortriptyline. Nortriptyline blocks the reuptake of Norepinephrine more potently than Serotonin[1].

Nortriptyline (6.25-100 μM; 24-72 h) hydrochloride markedly reducs the viability of TCCSUP and mouse MBT-2 bladder cancer cells in a concentration- and time-dependent manner[3].

Nortriptyline (12.55-100 μM; 24 h) hydrochloride induces cell cycle arrest and apoptosis in TCCSUP and MBT-2 cells[3].

Nortriptyline (12.55-100 μM; 24 h) hydrochloride induces both intrinsic and extrinsic apoptosis in these bladder cancer cells [3].

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

Cell Viability Assay[3]

Cell Line:	Human TCCSUP and mouse MBT-2 bladder cancer cells
Concentration:	6.25 μM, 12.5 μM, 25 μM, 50 μM and 100 μM
Incubation Time:	24, 48, or 72 h
Result:	Exhibited cytotoxic effects on TCCSUP and MBT-2 cells.

Cell Cycle Analysis[3]

Cell Line:	TCCSUP and MBT-2 cells
Concentration:	25 μM, 50 μM, or 100 μM (TCCSUP); 12.5 μM, 25 μM, or 50 μM (MBT-2 cells)
Incubation Time:	24 hours
Result:	Caused cell cycle arrest in these bladder cancer cells.

Apoptosis Analysis[3]

Cell Line:	TCCSUP and MBT-2 cells
Concentration:	25 μM, 50 μM, or 100 μM (TCCSUP); 12.5 μM, 25 μM, or 50 μM (MBT-2 cells)
Incubation Time:	24 hours
Result:	Induced apoptosis in both TCCSUP and MBT-2 cells

Western Blot Analysis[3]

Cell Line:	TCCSUP and MBT-2 cells
Concentration:	25 μM, 50 μM, or 100 μM (TCCSUP); 12.5 μM, 25 μM, or 50 μM (MBT-2 cells)
Incubation Time:	24 hours
Result:	Increased the expression of Fas, FasL, FADD, Bax, Bak, and cleaved forms of caspase-3, caspase-8, caspase-9, and poly(ADP-ribose) polymerase. Decreased the expression of Bcl-2, Bcl-xL, BH3 interacting domain death agonist, X-linked inhibitor of apoptosis protein, and survivin.

In Vivo

Nortriptyline (10-20 mg/kg; ip; every day; for three weeks) hydrochloride inhibits the growth of bladder tumors in mice inoculated with MBT-2 cells[3].

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

Animal Model:	Adult male C3H/HeN mice (25-30 g; 2-3 months of age) injected with MBT-2 cells[3]
Dosage:	10 or 20 mg/kg
Administration:	Intraperitoneal injection; every day; for three weeks.
Result:	Suppressed tumor growth in mice inoculated with MBT-2 cells.

CUSTOMER VALIDATION

- J Exp Med. 2023 Mar 6;220(3):e20221316.
- Cell Commun Signal. 2023 May 25;21(1):123.

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REFERENCES

[1]. Sheau-Yun Yuan, et al. Nortriptyline induces mitochondria and death receptor-mediated apoptosis in bladder cancer cells and inhibits bladder tumor growth in vivo. Eur J Pharmacol. 2015 Aug 15:761:309-20.

[2]. Dean L. Amitriptyline Therapy and CYP2D6 and CYP2C19 Genotype. Biotechnology Information (US); 2012-2017 Mar 23.

[3]. Petrosyan E, et al. Repurposing Autophagy Regulators in Brain Tumors [published online ahead of print, 2022 Feb 18]. Int J Cancer. 2022;10.1002/ijc.33965.

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