ATN-224

Cat. No.: HY-16074

CAS No.: 649749-10-0

Molecular Formula: $C_{10}H_{28}MoN_2O_2S_4$

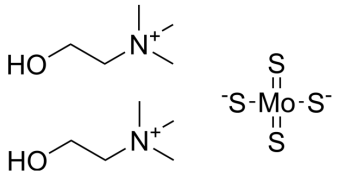
Molecular Weight: 432.56

Target: SOD

Pathway: Immunology/Inflammation

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (115.59 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3118 mL	11.5591 mL	23.1182 mL
	5 mM	0.4624 mL	2.3118 mL	4.6236 mL
	10 mM	0.2312 mL	1.1559 mL	2.3118 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: ≥ 2.5 mg/mL (5.78 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.78 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ATN-224 is an oral Cu^{2+}/Zn^{2+}-superoxide dismutase 1 (SOD1) inhibitor. ATN-224 inhibits SOD1 activity in endothelial cells, an effect that is dose dependent with an IC_{50} of 17.5±3.7 nM.

IC_{50} & Target

IC50: 17.5±3.7 nM (SOD1, in endothelial cells)[1]

In Vitro

ATN-224 has a specific and high affinity for copper ions (10^8 mol/L^{-1}) and shows no binding to calcium, iron, magnesium, zinc, or manganese ions at concentrations up to 1 mM as determined by isothermal titration calorimetry. ATN-224 inhibits the proliferation of both HUVEC (IC_{50}=1.4±0.3 μM; n=5). ATN-224 is also able to inhibit the activity of purified bovine SOD1 with an IC_{50} of 0.33±0.03 μM after 24 hours of incubation. The SOD1 inhibition by ATN-224 is time dependent, reaching maximal inhibition at ~16 hours. ATN-224 seems to inhibit SOD1 by depleting the enzyme of copper. ATN-224 is able to

	inhibit SOD1 activity in endothelial cells, an effect that is dose dependent with an IC_{50} of 17.5±3.7 nM. ATN-224 inhibits FGF-2-induced ERK1/2 phosphorylation in a dose-dependent and time-dependent manner with an IC_{50} between 1.25 and 2.5 μM, consistent with the IC_{50} for the inhibition of proliferation[1]. ATN-224 is an orally-available inorganic small molecule that inhibits the copper/zinc-dependent enzyme, superoxide dismutase 1 (Cu/Zn-SOD1), in endothelial and tumor cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	ATN-224 also significantly (P<0.05) inhibits angiogenesis in the Matrigel plug model in mice either when added directly to the plug or when given by oral gavage. Inhibition of angiogenesis when ATN-224 is given by oral gavage occurred before there is measurable depletion of copper in either plasma or copper from the Matrigel plug. This result shows that ATN-224 inhibits angiogenesis independently of copper depletion[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Cells are plated in a six-well format (100-300,000 per well) and incubated with ATN-224 at indicated concentrations and for indicated times. Cells are then stimulated with 10 ng/mL FGF-2 for various times and lysed. Lysates are subjected to Western blot analysis using an antibody specific for phosphorylated p44/42 mitogen-activated protein kinase (Thr^{202}/Tyr^{204}) with appropriate signal correction using an antibody specific for p44/42 mitogen-activated protein kinase[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	Human umbilical vein endothelial cells (HUVEC) are maintained in M200/LSGS medium and cells are used between passages 2 and 4 for all experiments. For proliferation assay, cells are plated at 3,000 per well on 0.1% gelatin in M200/2% FBS for 4 hours and then stimulated with 2 ng/mL FGF-2 in the presence or absence of ATN-224 up to 48 hours. HUVEC proliferation is determined using either the Alamar Blue or the MTT assay. Multiple myeloma MM1S cells are grown in RPMI 1640 with 10% fetal bovine serum and 2 mM L-glutamine. HL-60 promyelocytic leukemia cells and MOLT-4 acute myeloblastic leukemia cells are plated at 400,000/mL in T-75 flasks and incubated for 48 to 96 hours for proliferation assays. MMS1 cell proliferation is determined using calcein AM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Cold Matrigel (500 μL) is mixed with 800 ng/mL FGF-2 or 300 ng/mL VEGF and heparin (50 μg/mL). Negative control plugs did not contain the proangiogenic factors. The Matrigel mixture is injected s.c. into 4- to 8-week-old female BALB/c nude mice. In some experiments, either ATN-224 (94 μM) with or without Mn-TBAP (100 μM) or water is added directly to the Matrigel plug in the treated and negative control groups, respectively. Alternatively, mice are treated by oral gavage either with distilled water or ATN-224 everyday from Monday to Friday. Animals are sacrificed and the plugs are recovered 5 days after plug injection. The plugs are then minced and homogenized with a tissue homogenizer, and hemoglobin levels in the plugs are determined using Drabkin's solution. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Anal Chem. 2018 Jan 16;90(2):1317-1324.
- Cell Death Discov. 2022 Feb 17;8(1):69.
- Food Funct. 2021 Mar 9.

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REFERENCES

[1]. Juarez JC, et al. Copper binding by tetrathiomolybdate attenuates angiogenesis and tumor cell proliferation through the inhibition of superoxide dismutase 1. Clin Cancer Res. 2006 Aug 15;12(16):4974-82.

[2]. Lin J, et al. A non-comparative randomized phase II study of 2 doses of ATN-224, a copper/zinc superoxide dismutase inhibitor, in patients with biochemically recurrent hormone-na?ve prostate cancer. Urol Oncol. 2013 Jul;31(5):581-8.

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