

Product Data Sheet

Product Name: Apratastat

Cat. No.: GC35377

Chemical Properties

Cas. No. 287405-51-0

Chemical Name (3S)-N-hydroxy-4-[[4-[(4-hydroxy-2-butyn-1-yl)oxy]phenyl]sulfonyl]-2,2-dimethyl-3-thiomorpholinecarboxamide

SMILES CC1(C)[C@H](C(NO)=O)N(S(=O)(C2=CC=C(OCC#CCO)C=C2)=O)CCS1

Formula $C_{17}H_{22}N_2O_6S_2$

M.Wt 414.5

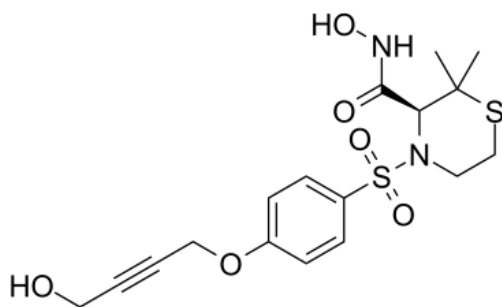
Solubility 10mg/mL in ethanol, 25mg/mL in DMSO, or in DMF

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Caution: Product has not been fully validated for medical applications. For research use only.

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Cell lines NCI-H358 and A549 cells

Cells were cultured in RPMI-1640 medium supplemented with 10% fetal bovine Preparation Method serum (FBS) at 37°C, 5% CO₂. Cells were treated with the ADAM17/MMP inhibitor Apratastat at 25μM for 24–48 hours.

Reaction 25μM; 24-48h
Conditions

Applications Apratastat suppressed cancer cell migration in transwell assays by blocking MAPK pathway-dependent EphA2 activation and paracrine signaling.

Animal experiment [2]:

Animal models OVE26 diabetic mice and C57BL/6 control mice

Preparation Method Mice were intraperitoneally administered Apratastat at 10mg/kg for a specified duration.

Dosage form 10mg/kg/day; i.p.; twice daily for 3 weeks.

Applications Apratastat significantly inhibited ADAM17 activity in the renal cortex, reduced Nox4 expression and NADPH oxidase activity, thereby alleviating the progression of diabetes-related kidney injury.

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References:

- [1] Waller V, Tschanz F, Winkler R, et al. The role of EphA2 in ADAM17- and ionizing radiation-enhanced lung cancer cell migration. *Front Oncol.* 2023 Mar 14;13:1117326.
- [2] Ford BM, Eid AA, Gööz M, et al. ADAM17 mediates Nox4 expression and NADPH oxidase activity in the kidney cortex of OVE26 mice. *Am J Physiol Renal Physiol.* 2013 Aug 1;305(3):F323-32.

Background

Apratastat is an orally active, reversible dual inhibitor. Apratastat suppresses the activity of tumor necrosis factor- α converting enzyme (TACE; $IC_{50}=81.7\text{ng/mL}$) and matrix metalloproteinases (MMPs)^[1-2]. Apratastat has potential as a therapeutic agent for cancer and rheumatoid arthritis ^[3-4].

In vitro, treatment of SUM149 breast cancer cells with Apratastat (20 μM) for 3 days inhibited cell growth^[5]. Pretreatment of non-small cell lung cancer NCI-H358 cells with Apratastat (25 μM) for 24–48 hours suppressed radiation-induced tumor cell migration via inhibiting MAPK pathway-mediated EphA2 S897 phosphorylation^[6].

In vivo, in a COVID-19-associated lung injury model using C57BL/6 mice, Apratastat (10mg/kg) was administered via intraperitoneal injection (at 4 and 16 hours) or intranasally (at 24 hours). Apratastat significantly improved lung histopathology scores and alleviated features of acute lung injury, such as edema, fibrosis, and vascular congestion^[7]. In OVE26 diabetic model mice, Apratastat (10mg/kg; twice daily) was administered via intraperitoneal injection for three consecutive weeks. Apratastat significantly inhibited ADAM17 activity in the renal cortex, reduced Nox4 expression and NADPH oxidase activity, thereby mitigating the progression of diabetes-related kidney injury^[8].

References:

- [1] Talele TT, Khedkar SA, Rigby AC. Successful applications of computer aided drug discovery: moving drugs from concept to the clinic. *Curr Top Med Chem.* 2010;10(1):127-41.
- [2] Shu C, Zhou H, Afsharvand M, et al. Pharmacokinetic-pharmacodynamic modeling of apratastat: a population-based approach. *J Clin Pharmacol.* 2011 Apr;51(4):472-81.
- [3] Moss ML, Sklair-Tavron L, Nudelman R. Drug insight: tumor necrosis factor-converting enzyme as a pharmaceutical target for rheumatoid arthritis. *Nat Clin Pract Rheumatol.* 2008 Jun;4(6):300-9.

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- [4] Sharma A, Bender S, Zimmermann M, et al. Secretome Signature Identifies ADAM17 as Novel Target for Radiosensitization of Non-Small Cell Lung Cancer. Clin Cancer Res. 2016 Sep 1;22(17):4428-39.
- [5] Mezil L, Berruyer-Pouyet C, Cabaud O, et al. Tumor selective cytotoxic action of a thiomorpholin hydroxamate inhibitor (TMI-1) in breast cancer. PLoS One. 2012;7(9):e43409.
- [6] Waller V, Tschanz F, Winkler R, et al. The role of EphA2 in ADAM17- and ionizing radiation-enhanced lung cancer cell migration. Front Oncol. 2023 Mar 14;13:1117326.
- [7] Lartey NL, Valle-Reyes S, Vargas-Robles H, et al. ADAM17/MMP inhibition prevents neutrophilia and lung injury in a mouse model of COVID-19. J Leukoc Biol. 2022 Jun;111(6):1147-1158.
- [8] Ford BM, Eid AA, Göőz M, et al. ADAM17 mediates Nox4 expression and NADPH oxidase activity in the kidney cortex of OVE26 mice. Am J Physiol Renal Physiol. 2013 Aug 1;305(3):F323-32.

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