

Product Data Sheet

Product Name: Losartan
Cat. No.: GC10249

Chemical Properties

Cas. No. 114798-26-4

Chemical Name [2-butyl-5-chloro-3-[[4-[2-(2H-tetrazol-5-yl)phenyl]phenyl]methyl]imidazol-4-yl]methanol

SMILES CCCCC1=NC(=C(N1CC2=CC=C(C=C2)C3=CC=CC=C3C4=NNN=N4)CO)Cl

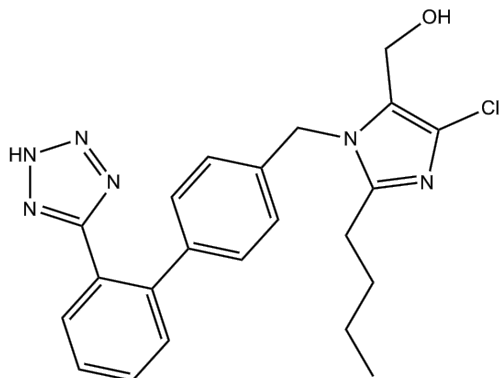
Formula C₂₂H₂₃ClN₆O M.Wt 422.91

Solubility ≥ 84.6mg/mL in DMSO 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]:

Cell lines Vero E6 cells (African green monkey kidney cell line)

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

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Preparation Method Vero E6 cells were plated at 2×10^4 cells/well in a 96-well plate and incubated overnight at 37°C. Losartan was prepared in DMEM to concentrations from 1 µM to 100 µM. For pre-infection treatment, cells were preincubated with Losartan for 1 hour, then infected with SARS-CoV-2 at a MOI=0.01 for 1 hour. After infection, fresh Losartan-containing media was added. For post-infection treatment, cells were first infected with SARS-CoV-2 at a MOI=0.01 for 1 hour, then Losartan-containing media was added. Cells were incubated for 96 hours at 37°C, 5% CO₂.

Reaction Conditions 1-100 µM; pre-incubation 1 hour, incubation 96 hours.

Applications Losartan treatment showed a dose-dependent and significant reduction in SARS-CoV-2 replication. Pre-infection treatment reduced SARS-CoV-2 nuclear protein levels, and post-infection treatment decreased viral replication. The half-maximal effective concentration (EC₅₀) of Losartan was 13.7 µM for pre-infection treatment and 41 µM for post-infection treatment.

Animal experiment [2]:

Animal models Swiss mice (Mus musculus)

Preparation Method Intestinal mucositis was induced by a single intraperitoneal administration of 5-fluorouracil (5-FU; 450mg/kg). Losartan or saline was orally administered 30min before 5-FU injection and daily for 4 days. On the 4th day, animals were euthanized and segments of small intestine were collected for analysis.

Dosage form 5, 25 or 50mg/kg; oral administration; daily for 4 days.

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Applications

Losartan prevented 5-FU-induced intestinal mucositis effects including histopathological damage (shortened villi, loss of crypt architecture, inflammatory cell infiltration), partially rescued body weight loss, prevented leukopenia, decreased pro-inflammatory cytokine levels (TNF- α and IL-1 β), reduced oxidative stress markers (MDA and GSH), and modulated mRNA expression of NF- κ B p65, TWEAK and Fn14.

References:

- [1] Nejat R, Sadr AS, Freitas B, et al. Losartan Inhibits SARS-CoV-2 Replication in Vitro. J Pharm Pharm Sci. 2021;24:390-399.
- [2] Oliveira MMB, de Araújo AA, Ribeiro SB, et al. Losartan improves intestinal mucositis induced by 5-fluorouracil in mice. Sci Rep. 2021 Dec 1;11(1):23241.

Background

Losartan is an angiotensin II receptor antagonist (IC₅₀=20nM). Losartan works by selectively blocking the AT1 receptor of angiotensin II. Losartan can be used for the treatment of hypertension and diabetic nephropathy^[1-4].

In vitro, pretreatment of Vero E6 cells with Losartan (1–100 μ M) for 1 hour, followed by infection with SARS-CoV-2 (MOI=0.01) and culture for 96 hours, Losartan significantly reduced viral nucleoprotein levels and inhibited viral replication^[5]. Pretreatment of MV3 cells with Losartan (0.7 μ M) for 30 minutes, followed by treatment with ATII (100nM), Losartan significantly inhibited NHE1 activity in the cells^[6].

In vivo, Losartan (5-50mg/kg; oral administration) was administered to Swiss mice with 5-FU-induced intestinal mucositis for 4 days. Losartan significantly prevented the 5-FU-induced intestinal mucositis effects^[7]. Losartan (10mg/kg) was orally administered daily via drinking water to CD2F1 mice bearing C26 cells for 19 days. Losartan prevented tumor-induced muscle mass loss, reduced tumor weight, attenuated myocardial interleukin-6 expression, improved cardiomyocyte calcium signaling, and increased cardiomyocyte contraction speed, contractile function, and blood pressure in tumor-bearing mice^[8].

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References:

- [1] Sica DA, Gehr TW, Ghosh S. Clinical pharmacokinetics of losartan. Clin Pharmacokinet. 2005;44(8):797-814.
- [2] Burnier M. Angiotensin II type 1 receptor blockers. Circulation. 2001 Feb 13;103(6):904-12.
- [3] Ashry O, Schnecko A, Clauss WG, et al. Evidence for expression and function of angiotensin II receptor type 1 in pulmonary epithelial cells. Respir Physiol Neurobiol. 2014 May 1;195:37-40.
- [4] Saleh N, Cosarderelioglu C, Vajapey R, et al. Losartan Mitigates Oxidative Stress in the Brains of Aged and Inflamed IL-10-/- Mice. J Gerontol A Biol Sci Med Sci. 2022 Sep 1;77(9):1784-1788.
- [5] Nejat R, Sadr AS, Freitas B, et al. Losartan Inhibits SARS-CoV-2 Replication in Vitro. J Pharm Pharm Sci. 2021;24:390-399.
- [6] Olschewski DN, Hofschroer V, Nielsen N, et al. The Angiotensin II Type 1 Receptor Antagonist Losartan Affects NHE1-Dependent Melanoma Cell Behavior. Cell Physiol Biochem. 2018;45(6):2560-2576.
- [7] Oliveira MMB, de Araújo AA, Ribeiro SB, et al. Losartan improves intestinal mucositis induced by 5-fluorouracil in mice. Sci Rep. 2021 Dec 1;11(1):23241.
- [8] Stevens SC, Velten M, Youtz DJ, et al. Losartan treatment attenuates tumor-induced myocardial dysfunction. J Mol Cell Cardiol. 2015 Aug;85:37-47.

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