

Product Data Sheet

Product Name: LCZ696
Cat. No.: GC11784

Chemical Properties

Cas. No. 936623-90-4

SMILES CCCC(N([C@@](C([O-])=O)([H])C(C)C)CC1=CC=C(C2=CC=CC=C2C3=N[N-]N=N3)C=C1)=O.CCOC([C@](C[C@@](/N=C([O-])/CCC([O-])=O)([H])CC4=CC=C(C5=CC=CC=C5)C=C4)([H])C)=O.[3Na+].[2.5H2O]

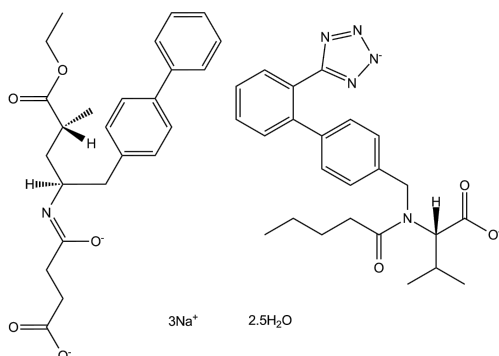
Formula $C_{48}H_{54}N_6Na_3O_8 \cdot 2.5H_2O$ M.Wt 956.99

Solubility $\geq 45.05\text{mg/mL}$ 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 Human umbilical vascular endothelial cells (HUVECs)

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Preparation Method HUVECs were grown in 2% serum endothelial growth media (EGM2) supplied with essential growth factors, 100U/ml penicillin, and 100µg/ml streptomycin at 37°C in 5% CO₂/atmosphere. Cells (5×10^3 cells/ml) were seeded in 96-well plates and allowed to adhere in a 5% CO₂ incubator at 37°C overnight. 1µg/ml LPS-containing growth media was added to the confluent HUVECs' media for 24 hours. Different concentrations of LCZ696 (0, 5, 10, and 20µM) and 1µg/mL LPS were then added to the confluent HUVECs media at the same time for 24 hours. The levels of ROS and MDA were analyzed.

Reaction Conditions 0, 5, 10, and 20µM; 24h

Applications LCZ696 treatment significantly reduced levels of ROS and MDA induced by LPS within HUVECs in a dose-dependent manner.

Animal experiment [2]:

Animal models Male C57BL/6 mice

Preparation Method Eight-week-old male C57BL/6 mice were routinely maintained in a standard environment with food and water ad libitum. The mice were randomly assigned and underwent abdominal aorta ligation or sham surgery. For ligation, using a 27G needle (0.4mm outside diameter), the abdominal aorta was ligated tightly with a 5-0 surgical suture above the renal artery, leading to a 60% reduction in the diameter. For the sham operations, the abdominal aorta was not ligated. The mice with abdominal aortic ligation were randomized into three groups: no treatment (n=8), LCZ696 treatment (n=8), and valsartan treatment (n=8). The mice with sham surgery were the control group (CTL, n=8). The mice in the LCZ696 group were administered 60mg/kg/day LCZ696 dissolved in corn oil by oral gavage for 8 weeks. Both kidneys were removed for analysis.

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Dosage form 60mg/kg/day for 8 weeks; p.o.

Applications LCZ636 treatment significantly attenuated renal injury and mitigated renal fibrosis in mice with abdominal aortic ligation.

References:

- [1] Gao A, Wang Y, Gao X, et al. LCZ696 ameliorates lipopolysaccharide-induced endothelial injury[J]. Aging (Albany NY), 2021, 13(7): 9582.
- [2] Li Y, Kang L, Rong K, et al. Renal protective effects and mechanisms of the angiotensin receptor-neprilysin inhibitor LCZ696 in mice with cardiorenal syndrome[J]. Life Sciences, 2021, 280: 119692.

Background

LCZ696, a combination of prodrug sacubitril and valsartan at equal molar ratios, is an oral active angiotensin II receptor-neprilysin inhibitor [1]. After ingestion, LCZ696 undergoes rapid dissociation into valsartan and sacubitril, which cause neprilysin inhibition and AT1 receptor blockade, resulting increases in ANP, plasma and urinary cGMP, renin concentration and activity [2]. LCZ696 has been widely used to improve heart and kidney functions and to induce memory and cognitive dysfunction in animals [3].

In vitro, LCZ696 treatment (20μM) for 24 hours significantly reduced the production of reactive oxygen species (ROS) and the level of malondialdehyde (MDA) in human umbilical vein endothelial cells (HUVECs), thereby alleviating the oxidative stress induced by Lipopolysaccharide (LPS) [4]. Treatment with 10μM LCZ696 for 24 hours reduced apoptosis-related events and increased the survival rate of podocytes cultured in high glucose conditions[5]. Treatment with 1μM LCZ696 for 3 hours significantly reduced the expression of ANP, βMHC, and TIMP2 in cardiomyocytes, inhibited the increase in cardiomyocyte size caused by angiotensin II, and promoted the protein expression of ACE2[6].

In vivo, LCZ696 treatment via oral administration at a dose of 68mg/kg/day for 4 weeks significantly reduced cardiac remodeling and dysfunction in rats after myocardial infarction[7]. For 8 consecutive weeks, an oral dose of 60mg/kg of LCZ696 was administered daily, significantly improving the

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biochemical, morphological, and molecular biological indicators of renal injury in mice with cardiorenal syndrome^[8].

References:

- [1] Minguet J, Sutton G, Ferrero C, et al. LCZ696: a new paradigm for the treatment of heart failure? [J]. Expert Opinion on Pharmacotherapy, 2015, 16(3): 435-446.
- [2] Menendez J T. The mechanism of action of LCZ696[J]. Cardiac failure review, 2016, 2(1): 40.
- [3] Poorgolizadeh E, Moghadam F H, Dormiani K, et al. Do neprilysin inhibitors walk the line? Heart ameliorative but brain threatening![J]. European journal of pharmacology, 2021, 894: 173851.
- [4] Gao A, Wang Y, Gao X, et al. LCZ696 ameliorates lipopolysaccharide-induced endothelial injury[J]. Aging (Albany NY), 2021, 13(7): 9582.
- [5] Zhang H, Yu M, Zhang Y, et al. LCZ696 improves oxidative stress injury in human podocytes induced by increased glucose levels via Nrf2/HO-1 signaling pathway[J]. European Journal of Medical Research, 2025, 30(1): 598.
- [6] Wang Y, Guo Z, Gao Y, et al. Angiotensin II receptor blocker LCZ696 attenuates cardiac remodeling through the inhibition of the ERK signaling pathway in mice with pregnancy-associated cardiomyopathy[J]. Cell & Bioscience, 2019, 9(1): 86.
- [7] von Lueder T G, Wang B H, Kompa A R, et al. Angiotensin receptor neprilysin inhibitor LCZ696 attenuates cardiac remodeling and dysfunction after myocardial infarction by reducing cardiac fibrosis and hypertrophy[J]. Circulation: Heart Failure, 2015, 8(1): 71-78.
- [8] Li Y, Kang L, Rong K, et al. Renal protective effects and mechanisms of the angiotensin receptor-neprilysin inhibitor LCZ696 in mice with cardiorenal syndrome[J]. Life Sciences, 2021, 280: 119692.

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