

Product Data Sheet

Product Name: Cariporide (HOE-642)

Cat. No.: GC17842

Chemical Properties

Cas. No. 159138-80-4

Chemical Name (Z)-N-carbamimidoyl-4-isopropyl-3-(methylsulfonyl)benzimidic acid

SMILES CC(C1=C(S(C)(=O)=O)C=C(/C(O)=N/C(N)=N)C=C1)C

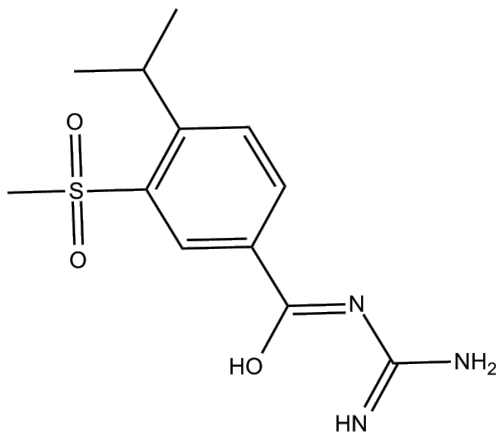
Formula $C_{12}H_{17}N_3O_3S$ M.Wt 283.35

Solubility $\geq 12.05\text{mg/mL}$ 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

H-2452AcT cells (acid-tolerable human malignant mesothelioma cells)

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

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Preparation Method	H-2452AcT cells were maintained in RPMI-1640 medium supplemented with 10% fetal bovine serum at 37°C. H-2452AcT cells were treated with 160μM Cariporide for 48h and 72h, with part of cells pretreated with 5μM LY294002 for 2h before Cariporide. After treatment, MTT assay, Western blot, DAPI staining, annexin V-PE assay, cell cycle analysis, comet assay, ROS measurement and mitochondrial membrane potential analysis were performed.
Reaction Conditions	160μM; 48h and 72h
Applications	Cariporide down-regulated p-AKT, up-regulated p53, accumulated ROS, depolarized mitochondrial membrane potential, increased p-ATM, p-ATR, p-CHK1, p-CHK2 and p-H2A.X, caused pyknotic and fragmented nuclei, sub-G0/G1 peak and G2/M transition delay, and promoted apoptosis in H-2452AcT cells.
Animal experiment [2]:	
Animal models	SGLT2 knockout C57BL/6N mice with transverse aortic constriction and deoxycorticosterone acetate pellet implantation (TAC/DOCA-induced heart failure)
Preparation Method	SGLT2 knockout mice were fed chow containing 600mg/kg Cariporide starting 2 days after TAC/DOCA surgery. Cardiac function was evaluated by echocardiography 10 days after surgery. Animals were sacrificed at days 10-12 after surgery for tissue collection and analysis.
Dosage form	600mg/kg; p.o.; 8 days

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Applications	Cariporide prevented development of diastolic dysfunction, systolic dysfunction, left ventricle and left atria hypertrophy, lung and liver edema, increased NCX protein expression, 4-HNE and 3-NT levels, and reduced SOD1 in TAC/DOCA-induced heart failure mice. Adding Empagliflozin to Cariporide did not lead to additional protective effects.
References:[1] Lee Y, Bae J, Kim S, et al. Cariporide Enhances the DNA Damage and Apoptosis in Acid-tolerable Malignant Mesothelioma H-2452 Cells. Mol Cells. 2017 Aug;40(8):567-576.[2] Chen S, Wang Q, Bakker D, et al. Empagliflozin prevents heart failure through inhibition of the NHE1-NO pathway, independent of SGLT2. Basic Res Cardiol. 2024;119(6):751-772.	

Background

Cariporide (HOE-642) is a Na^+/H^+ exchanger 1 (NHE1) inhibitor. Cariporide reduces intracellular Na^+ and Ca^{2+} overload, alleviates cellular alkalinization and swelling, and attenuates ischemia-reperfusion injury and inflammation by inhibiting cardiomyocyte apoptosis and neutrophil infiltration. Cariporide can be used for studies on myocardial infarction, stroke, and myocardial ischemia-reperfusion injury^[1-4].

In vitro, treatment of H-2452AcT cells with 160 μM Cariporide for 72h down-regulated p-AKT, up-regulated p53, accumulated ROS, depolarized mitochondrial membrane potential, increased DNA damage, and induced apoptosis^[5]. Treatment of N1S1 cells with 200 μM Cariporide for 6h decreased intracellular pH, increased extracellular pH, and induced cell death^[6]. Treatment of MCF-7/ADR cells with 6 $\mu\text{g}/\text{ml}$ Cariporide for 48h decreased NHE1, MDR1, and NF- κB p65 expression, increased cleaved caspase-3 and cleaved caspase-9, and decreased Bcl-2^[7].

In vivo, oral administration of 600mg/kg Cariporide in chow to SGLT2 knockout mice with heart failure for 8 days prevented diastolic and systolic dysfunction, ventricular and atrial hypertrophy, lung and liver edema, decreased NCX protein expression, 4-HNE, and 3-NT, and increased SOD1^[8]. Oral administration of 7.2mg/kg/day Cariporide via drinking water to FVB/N-Tg(MMTVneu)202Mul/J mice for 5 weeks increased serum glucose^[9]. A single intraperitoneal injection of 20mg/kg Cariporide combined with 25 μg LPS to pregnant C57BL/6J mice at 16.5 days of gestation alleviated LPS-enhanced uterine contraction, inhibited myometrial NHE1 protein expression, and up-regulated

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myometrial TREK1 protein expression^[10].

References:

- [1] Chin B, Lip GY. Cariporide Aventis. Curr Opin Investig Drugs. 2000 Nov;1(3):340-6.
- [2] Laudi S, Vu Tran Z, Steudel W. Cariporide in cardiac resuscitation--Does it really make a difference? Crit Care Med. 2005 Nov;33(11):2707-8.
- [3] Karmazyn M. Pharmacology and clinical assessment of cariporide for the treatment coronary artery diseases. Expert Opin Investig Drugs. 2000 May;9(5):1099-108.
- [4] Petho Z, Najder K, Beel S, et al. Acid-base homeostasis orchestrated by NHE1 defines the pancreatic stellate cell phenotype in pancreatic cancer. JCI Insight. 2023 Oct 9;8(19):e170928.
- [5] Lee Y, Bae J, Kim S, et al. Cariporide Enhances the DNA Damage and Apoptosis in Acid-tolerable Malignant Mesothelioma H-2452 Cells. Mol Cells. 2017 Aug;40(8):567-576.
- [6] Yang W, Wang C, Yu C, et al. pH-regulating Lipiodol Pickering emulsions enhance transarterial embolization therapy via inducing ferroptosis and activating antitumor immunity. Cell Rep Med. 2026 Mar 17;7:102662.
- [7] Chen Q, Liu Y, Zhu X, et al. Increased NHE1 expression is targeted by specific inhibitor cariporide to sensitize resistant breast cancer cells to doxorubicin in vitro and in vivo. BMC Cancer. 2019;19:211.
- [8] Chen S, Wang Q, Bakker D, et al. Empagliflozin prevents heart failure through inhibition of the NHE1-NO pathway, independent of SGLT2. Basic Research in Cardiology. 2024;119(6):751-772.
- [9] Aaen P, Kristensen K, Antony A, et al. Na⁺/H⁺-exchange inhibition by cariporide is compensated via Na⁺,HCO₃⁻-cotransport and has no net growth consequences for ErbB2-driven breast carcinomas. BBA Mol Basis Dis. 2024;1870:167450.
- [10] Yu H, Wang X, Tian R, et al. Myometrium infection decreases TREK1 through NHE1 and increases contraction in pregnant mice. Am J Physiol Cell Physiol. 2024;326(4):C1106-C1119.

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