

Product Data Sheet

Product Name: Canagliflozin

Cat. No.: GC13771

Chemical Properties

Cas. No. 842133-18-0

Chemical Name (2S,3R,4R,5S,6R)-2-[3-[[5-(4-fluorophenyl)thiophen-2-yl]methyl]-4-methylphenyl]-6-(hydroxymethyl)oxane-3,4,5-triol

SMILES CC1=C(C=C(C=C1)C2C(C(C(C(O2)CO)O)O)O)CC3=CC=C(S3)C4=CC=C(C=C4)F

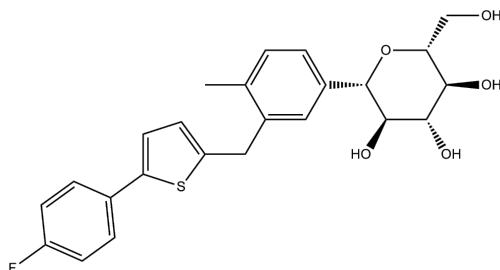
Formula $C_{24}H_{25}FO_5S$ M.Wt 444.52

Solubility $\geq 22.25\text{mg/mL}$ 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 HL-1 cells

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Cells were cultured in high-glucose DMEM, supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin antibiotic in an incubator of 5% CO₂ at 37°C. For inducing a lipotoxic cardiomyocyte model, cells were seeded into cell culture dishes or plates at an appropriate density and stimulated with 0.1mM palmitic acid for 24h in the presence or absence of Canagliflozin (5µg/mL).

Preparation Method Bovine serum albumin used to liquefy palmitic acid, was also added to blank control cells. COX-2 inhibitor celecoxib (5µg/mL), iNOS inhibitor SMT (10µM), and the ferroptosis inhibitor Fer-1 (5µM) were added simultaneously with palmitic acid. AMPK inhibitor Compound C (5µg/mL) was added with palmitic acid and Canagliflozin.

Reaction Conditions 5µg/ml; 24h

Applications Canagliflozin attenuates lipotoxicity in cardiomyocytes by inhibiting inflammation and ferroptosis through activating AMPK pathway in HL-1 cells.

Animal experiment [2]:

Animal models Male C57BL/6J mice

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Male C57BL/6J mice aged 6-8 weeks were kept under specific-pathogen-free (SPF) environment (room temperature $22\pm 2^{\circ}\text{C}$, humidity $55\pm 5\%$, 12h light/12h dark cycle), with unrestricted access to food and water.

Mice were allowed to acclimatize in the laboratory environment for 1 week before the beginning of the experiment.

Diabetic cardiomyopathy (DCM) model establishment: The mice were given a single intraperitoneal injection of 150mg/kg 1% streptozotocin (STZ, dissolved in 0.1 mol/L sodium citrate buffer, pH = 4.4-4.6). Mouse blood from the tail vein

Preparation Method was collected in each group of the model mice and tested by glucose meter on day 3, 5 and 7 after injection. The mice with random blood glucose levels $\geq 16.7\text{mmol/L}$ were considered as diabetic models, and then kept for 4 weeks to induce DCM.

DCM group: DCM model mice were treated with saline for 6 weeks; DCM + Cana group: DCM model mice were treated with 20mg/kg/d Canagliflozin for 6 weeks. On the last day, electrocardiogram examination was performed after the drug intervention, then all animals were weighted and sacrificed, heart tissues were removed freshly and aseptically for measurement.

Dosage form 20mg/kg; i.p. ; 6 weeks

Applications Canagliflozin mitigates ferroptosis and improves myocardial oxidative stress in mice with diabetic cardiomyopathy.

References:

- [1] ZHANG W, LU J, WANG Y, et al. Canagliflozin Attenuates Lipotoxicity in Cardiomyocytes by Inhibiting Inflammation and Ferroptosis through Activating AMPK Pathway [J]. Int J Mol Sci, 2023, 24(1):
- [2] DU S, SHI H, XIONG L, et al. Canagliflozin mitigates ferroptosis and improves myocardial oxidative stress in mice with diabetic cardiomyopathy [J]. Front Endocrinol (Lausanne), 2022, 13(1011669).

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Background

Canagliflozin is a sodium glucose co-transporter (SGLT) 2 inhibitor in clinical development for the treatment of type 2 diabetes mellitus^[1].

Canagliflozin demonstrates selective inhibition of SGLT2 in CHOK cells, with IC₅₀ values of 2nM, 3.7nM, and 4.4nM for mSGLT2, rSGLT2, and hSGLT2, respectively^[2]. Canagliflozin is a novel inhibitor of vascular smooth muscle cell proliferation and migration^[3].

Canagliflozin (50μM; 24h) inhibits cell cycle progression and DNA synthesis in rat vascular smooth muscle cell^[3]. Canagliflozin (5μg/ml; 24h) attenuates lipotoxicity in cardiomyocytes by inhibiting inflammation and ferroptosis through activating AMPK pathway in HL-1 cells^[4]. Canagliflozin (50μM; 48h) significantly reduced SKBR3 cell proliferation in the presence of glucose (11mM; 48h)^[5].

Canagliflozin (14.4mg/kg; oral administration; 23 months) significantly improved central Insulin (3U/kg; i.p. ; 15min) sensitivity in the hypothalamus and the hippocampus of 30-month-old male mice^[6]. Canagliflozin (20mg/kg; i.p. ; 6 weeks) mitigates ferroptosis and improves myocardial oxidative stress in mice with diabetic cardiomyopathy^[7].

References:

- [1] LIANG Y, ARAKAWA K, UETA K, et al. Effect of canagliflozin on renal threshold for glucose, glycemia, and body weight in normal and diabetic animal models [J]. PLoS One, 2012, 7(2): e30555.
- [2] GUO Y Y, ZHANG J Y, SUN J F, et al. A comprehensive review of small-molecule drugs for the treatment of type 2 diabetes mellitus: Synthetic approaches and clinical applications [J]. Eur J Med Chem, 2024, 267(116185).
- [3] BEHNAMMANESH G, DURANTE G L, KHANNA Y P, et al. Canagliflozin inhibits vascular smooth muscle cell proliferation and migration: Role of heme oxygenase-1 [J]. Redox Biol, 2020, 32(101527.3
- [4] ZHANG W, LU J, WANG Y, et al. Canagliflozin Attenuates Lipotoxicity in Cardiomyocytes by Inhibiting Inflammation and Ferroptosis through Activating AMPK Pathway [J]. Int J Mol Sci, 2023, 24(1):
- [5] PAPADOPOLO D, UCHENUNU O, PALIA R, et al. Perturbations of cancer cell metabolism by the antidiabetic drug canagliflozin [J]. Neoplasia, 2021, 23(4): 391-9.

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[6] JAYARATHNE H S M, DEBARBA L K, JABORO J J, et al. Neuroprotective effects of Canagliflozin: Lessons from aged genetically diverse UM-HET3 mice [J]. Aging Cell, 2022, 21(7): e13653.

[7] DU S, SHI H, XIONG L, et al. Canagliflozin mitigates ferroptosis and improves myocardial oxidative stress in mice with diabetic cardiomyopathy [J]. Front Endocrinol (Lausanne), 2022, 13(10):11669.

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