

Product Data Sheet

Product Name: Gemigliptin tartrate

Cat. No.: GC60871

Chemical Properties

Cas. No. 1374639-74-3

SMILES O=C(O)[C@H](O)[C@@H](O)C(O)=O.O=C1N(C[C@@H](N)CC(N2CCC3=C(C(F)(F)F)N=C(C(F)(F)F)N=C3C2)=O)CC(F)(F)CC1

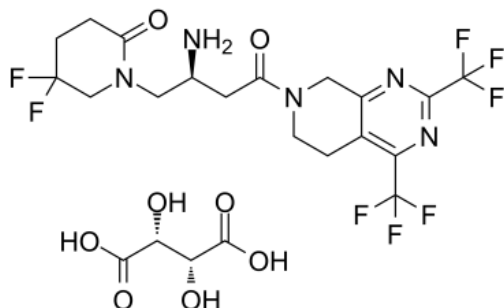
Formula $C_{22}H_{25}F_8N_5O_8$ M.Wt 639.45

Solubility DMSO: 100 mg/mL (156.38 mM) 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 Endothelial progenitor cells (EPCs) from diabetes mellitus patients

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EPCs were suspended in the endothelial growth medium-2 (EGM-2) consisting of Endothelium basal medium-2 (EBM-2), 5 % fetal bovine serum (FBS), human epidermal growth factor (hEGF), vascular endothelial growth factor (VEGF), human fibroblast growth factor (hfGF- β), insulin-like growth factor-1 (IGF-1), 1%

Preparation Method penicillin-streptomycin (PS) ascorbic acid and heparin. 1×10^7 EPCs were seeded on 1% gelatin coated culture plates in EGM-2 and incubated in a 5% CO₂ incubator at 37°C. Different concentrations of Gemigliptin (0, 10, 20, 50, and 100 μ M) were added and incubated at 37°C with 5% CO₂ for 48h. Cell viability was measured.

Reaction Conditions 0, 10, 20, 50, and 100 μ M; 48h

Applications Gemigliptin treatment significantly enhanced cell viability of EPCs in a dose-dependent manner.

Animal experiment [2]:

Animal models Male C57BL/6J mice

Male C57BL/6J mice (7 weeks old) were housed in an environmentally controlled room (12h light–dark cycle, 50% $\pm$ 10% relative humidity) at 23 $\pm$ 2°C at a facility with free access to water and a choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD), which consisted of 60 kcal% fat (mostly from palm oil),

Preparation Method 0.1% methionine, and no added choline. After 2 weeks, mice fed CDAHFD were randomly divided into 2 groups (n=8 in each group), including (i) vehicle: CDAHFD-fed mice with vehicle treatment for 5 weeks; (ii) GEMI: CDAHFD-fed mice with Gemigliptin treatment for 5 weeks (30 μ g/g per day by oral gavage). Mouse livers were isolated for analysis.

Dosage form 30 μ g/g/day for 5 weeks; p.o.

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Applications Gemigliptin treatment reduced hepatic steatosis and inflammation in high-fat diet-fed mice.

References:

- [1] Lee M, Tariq A R, Kim M. Gemigliptin, a potent selective dipeptidyl peptidase 4 inhibitor, protects endothelial progenitor cells by oxidative stress via caspase-3 dependent pathway[J]. Biochemistry and Biophysics Reports, 2024, 38: 101673.
- [2] Lee N, Heo Y J, Choi S E, et al. Hepatoprotective effects of gemigliptin and empagliflozin in a murine model of diet-induced non-alcoholic fatty liver disease[J]. Biochemical and biophysical research communications, 2022, 588: 154-160.

Background

Gemigliptin tartrate is a potent, selective and long-acting dipeptidyl peptidase 4 (DPP4) inhibitor with a K_i of 7.25nM and an IC_{50} value of 10.3nM [1]. By preventing degradation of GLP-1 via DPP4 inhibition, Gemigliptin increases insulin secretion, reduces glucagon secretion, decreases HbA1c, and prevents β -cell damage [2]. Gemigliptin has been widely used to inhibit renal fibrosis and albuminuria in diabetic mice[3].

In vitro, Gemigliptin (500 μ M) treatment for 4 hours significantly attenuated the pro-inflammatory response of lipopolysaccharide (LPS)-induced RAW 264.7 macrophages, reduced the production of PGE2 and decreased the expression of COX-2 and iNOS mRNA[4]. Treatment with 500 μ M Gemigliptin for 24 hours significantly inhibited the proliferation of vascular smooth muscle cells (VSMCs) and induced G1 phase cell cycle arrest in the cells[5]. Treatment with 50 μ M Gemigliptin for 48 hours significantly altered the morphology of endothelial progenitor cells (EPCs) and enhanced cell viability, accompanied by a decrease in the expression of Caspase-3 and an increase in the expression level of BCL-2[6].

In vivo, Gemigliptin treatment via oral administration at a dose of 100mg/kg/day for 12 weeks significantly improved renal function and alleviated podocyte injury in mice with diabetic nephropathy [7]. Oral administration of Gemigliptin at a dose of 30 μ g/g/day for 5 weeks significantly alleviated hepatic steatosis and reduced the expression of inflammatory cytokines in a mouse model of non-

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alcoholic fatty liver disease^[8].

References:

- [1] Kim S H, Jung E, Yoon M K, et al. Pharmacological profiles of Gemigliptin tartrate, a novel dipeptidyl peptidase-4 inhibitor, in vitro and in vivo[J]. European Journal of Pharmacology, 2016, 788: 54-64.
- [2] Gutch M, Joshi A, Kumar S, et al. Gemigliptin: newer promising gliptin for type 2 diabetes mellitus[J]. Indian journal of endocrinology and metabolism, 2017, 21(6): 898-902.
- [3] Jung G S, Jeon J H, Choe M S, et al. Renoprotective effect of gemigliptin, a dipeptidyl peptidase-4 inhibitor, in streptozotocin-induced type 1 diabetic mice[J]. Diabetes & Metabolism Journal, 2016, 40(3): 211.
- [4] Lee N, Heo Y J, Choi S E, et al. Anti-inflammatory effects of empagliflozin and gemigliptin on LPS-stimulated macrophage via the IKK/NF- κ B, MKK7/JNK, and JAK2/STAT1 signalling pathways[J]. Journal of immunology research, 2021, 2021(1): 9944880.
- [5] Choi S H, Park S, Oh C J, et al. Dipeptidyl peptidase-4 inhibition by gemigliptin prevents abnormal vascular remodeling via NF-E2-related factor 2 activation[J]. Vascular Pharmacology, 2015, 73: 11-19.
- [6] Lee M, Tariq A R, Kim M. Gemigliptin, a potent selective dipeptidyl peptidase 4 inhibitor, protects endothelial progenitor cells by oxidative stress via caspase-3 dependent pathway[J]. Biochemistry and Biophysics Reports, 2024, 38: 101673.
- [7] Jung E, Kim J, Kim S H, et al. Gemigliptin improves renal function and attenuates podocyte injury in mice with diabetic nephropathy[J]. European Journal of Pharmacology, 2015, 761: 116-124.
- [8] Lee N, Heo Y J, Choi S E, et al. Hepatoprotective effects of gemigliptin and empagliflozin in a murine model of diet-induced non-alcoholic fatty liver disease[J]. Biochemical and biophysical research communications, 2022, 588: 154-160.

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