

Product Data Sheet

Product Name: PF-05231023

Cat. No.: GC31495

Chemical Properties

Cas. No. 1037589-69-7

SMILES O=C(CCN1C(C=CC1=O)=O)NCCOCCOCCC(NC2=CC=C(C=C2)CCC(N3C(CC3)=O)=O)=O

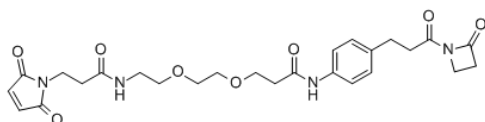
Formula $C_{26}H_{32}N_4O_8$ M.Wt 528.55

Solubility DMSO : 125 mg/mL (236.50 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 661W cells

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

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Preparation Method To monitor HIF transcriptional activity, a HIF-luciferase reporter gene construct was transfected into the mouse 661W cell line. This construct encodes the firefly luciferase gene, which is regulated by a hypoxia-associated element linked to HIF. CMV-Renilla luciferase was also co-transfected into these cells as an internal control. Prior to measuring luminescence, HIF activation was induced by intracellular administration of cobalt chloride (CoCl₂, 200μM, cobalt(II) chloride hexahydrate) to induce normoxia. To assess the inhibitory effects of a long-acting FGF21 molecule (PF-05231023) and pemaifibrate on HIF activation, both drugs were added simultaneously with CoCl₂ administration. Fluorescence intensity was measured using a dual-luciferase reporter assay system (Promega). The inhibitory effects of pemaifibrate and PF-05231023 on HIF activation were assessed 24 hours after induction.

Reaction Conditions 0.2nM, 2nM; 24h

Applications PF-05231023 significantly inhibited HIF activity.

Animal experiment [2]:

Animal models Atherosclerosis mice model

Preparation Method Mice were randomly divided into the Apoe^{-/-} + WD + PF-05231023 group (n = 6) and the Apoe^{-/-} + WD + saline group (n = 6). Both groups of mice were fed WD for 12 weeks to establish an atherosclerosis model, followed by 7 weeks of intraperitoneal injection of 10mg/kg PF-05231023 or an equal volume of saline. C57BL/6 female mice fed a control diet (WT + Control) served as a healthy control group (n = 6), and Apoe^{-/-} mice fed a control diet (Apoe^{-/-} + Control) served as a transgenic control group (n = 6).

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Dosage form 10mg/kg; ip; 7 weeks

Applications PF-05231023 effectively improves lipid metabolism in Apoe^{-/-} mice and has anti-atherosclerotic effects.

References:

- [1]. Tomita Y, Ozawa N, Miwa Y, et al. Pemaifibrate prevents retinal pathological neovascularization by increasing FGF21 level in a murine oxygen-induced retinopathy model[J]. International journal of molecular sciences, 2019, 20(23): 5878.
- [2]. Zhao J, Liu X, Yue J, et al. PF-05231023 reduces lipid deposition in apolipoprotein E-deficient mice by inhibiting the expression of lipid synthesis genes[J]. Frontiers in Veterinary Science, 2024, 11: 1429639.

Background

PF-05231023 is a long-acting fibroblast growth factor 21 (FGF21) analog [1]. PF-05231023 binds to the FGF21 receptor complex (FGFR1c and Klb), activating downstream signaling pathways that regulate energy metabolism, glucose homeostasis, and lipid metabolism [2-3]. PF-05231023 is primarily used to treat type 2 diabetes, obesity, and lipid metabolism disorders [4].

In 661W cells, PF-05231023 (0.2nM, 2nM; 24h) significantly inhibited HIF activity [5]. In primary human retinal microvascular endothelial cells, PF-05231023 (50ng/mL, 100ng/mL; 4h) prevented the hVEGF-induced increase in cell permeability [6].

In atherosclerosis mice model, PF-05231023 (10mg/kg; ip; 7 weeks) effectively improves lipid metabolism in Apoe^{-/-} mice and has anti-atherosclerotic effects [7]. In ob/ob mice, PF-05231023 (0.03-10mg/kg; sc; 3 weeks) treatment improves glucose excursions during glucose tolerance testing [8].

References:

- [1]. Dong J Q, Rossulek M, Somayaji V R, et al. Pharmacokinetics and pharmacodynamics of PF-

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05231023, a novel long-acting FGF21 mimetic, in a first-in-human study[J]. British journal of clinical pharmacology, 2015, 80(5): 1051-1063.

[2]. Brunetti L, Kagan L. Harnessing the Action of Fibroblast Growth Factor21 as a Therapeutic Agent[J]. Current pharmacology reports, 2017, 3(1): 26-35.

[3]. Aaldijk A S, Verzijl C R C, Jonker J W, et al. Biological and pharmacological functions of the FGF19-and FGF21-coreceptor beta klotho[J]. Frontiers in endocrinology, 2023, 14: 1150222.

[4]. Talukdar S, Zhou Y, Li D, et al. A long-acting FGF21 molecule, PF-05231023, decreases body weight and improves lipid profile in non-human primates and type 2 diabetic subjects[J]. Cell metabolism, 2016, 23(3): 427-440.

[5]. Tomita Y, Ozawa N, Miwa Y, et al. Pemafibrate prevents retinal pathological neovascularization by increasing FGF21 level in a murine oxygen-induced retinopathy model[J]. International journal of molecular sciences, 2019, 20(23): 5878.

[6]. Tomita Y, Fu Z, Wang Z, et al. Long-acting FGF21 inhibits retinal vascular leakage in in vivo and in vitro models[J]. International journal of molecular sciences, 2020, 21(4): 1188.

[7]. Zhao J, Liu X, Yue J, et al. PF-05231023 reduces lipid deposition in apolipoprotein E-deficient mice by inhibiting the expression of lipid synthesis genes[J]. Frontiers in Veterinary Science, 2024, 11: 1429639.

[8]. Weng Y, Chabot J R, Bernardo B, et al. Pharmacokinetics (PK), pharmacodynamics (PD) and integrated PK/PD modeling of a novel long acting FGF21 clinical candidate PF-05231023 in diet-induced obese and leptin-deficient obese mice[J]. PloS one, 2015, 10(3): e0119104.

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