Product Data Sheet

Product Name: Pemafibrate
Cat. No.: GC19280

Chemical Properties

Cas. No.	848259-27-8		
SMILES	CC[C@@H](OC1=CC=CC(CN(C2=NC3=CC=CC=C3O2)CCCOC4=CC=C(OC)C=C4)=C1)C(O)=O		
Formula	$C_{28}H_{30}N_2O_6$	M.Wt	490.55
Solubility	DMSO : ≥ 100 mg/mL (203.85 mM);Water : < 0.1 mg/mL (insoluble)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	Pemafibrate		

Protocol

Cell experiment [1]:

Cell lines	Cryopreserved primary human hepatocytes
Preparation Method	The hepatocyte cultures were maintained at 37⊿ 95% humidity and 5% CO2 for 3 hours and gently replaced with InVitroGRO CP with antibiotics. After 24 hours, the hepatocytes were treated with InVitroGRO CP with antibiotics containing 100 nM and 10 μM of Pemafibrate or 0.01% DMSO as a control.
Reaction Conditions	100 nM and 10 μM for 24 hours

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Applications	Pemafibrate treated 11 of the top 20 upregulated genes were involved in carbohydrate and lipid metabolism.

Animal experiment [2]:

Animal models	Female homozygous human apoE2KI mice
Preparation Method	Mice were fed a western diet containing (wt/wt) 0.2% cholesterol and 21% fat for 9 weeks and treated for the last 2 weeks with fenofibrate (250 mg/kg) or pemafibrate (0.1 or 1 mg/kg) or carboxy methyl cellulose (CMC, control).
Dosage form	250mg/kg, 2 weeks, feed with diet.
Applications	Pemafibrate strongly induced ABCA1 (+563%, $p < 0.01$ at 10 μM) and ABCG1 (+2093% $p < 0.001$ at 10 μM) mRNA steady-state levels in a dose-dependent manner (+168%, $p < 0.05$ for ABCA1 and +506%, $p < 0.01$ for ABCG1)

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References:

[1]: Raza-Iqbal S, Tanaka T, Anai M, et al. Transcriptome analysis of K-877 (a novel selective PPARα modulator (SPPARMα))-regulated genes in primary human hepatocytes and the mouse liver[J]. Journal of atherosclerosis and thrombosis, 2015: 28720.
[2]: Hennuyer N, Duplan I, Paquet C, et al. The novel selective PPARα modulator (SPPARMα) pemafibrate improves dyslipidemia, enhances reverse cholesterol transport and decreases inflammation and atherosclerosis[J]. Atherosclerosis, 2016, 249: 200-208.

Background

Pemafibrate (K-877) is an oral peroxisome proliferator-activated receptor (PPAR)-α agonist for the treatment of hyperlipidaemia, EC50 on Gal4hPPARα = 1 nM [1].

Pemafibrate (10 μM, 24 h) regulated the expression of several target genes that code for proteins involved in carbohydrate and lipid metabolism, in primary human hepatocytes and the mouse liver [2]. Pemafibrate (50 nM, 24h) activated PPAR-α transcription activity and more effectively than fenofibrate and pirinixic acid (Wy14643) [3].

Pemafibrate (0.001% in MF diets for 1 week) significantly reduced plasma triglyceride and total cholesterol levels, increased plasma HDL cholesterol levels, regulated gene expression related to triglyceride and HDL cholesterol metabolism in the liver, and regulated cholesterol and triglyceride metabolic gene expression in the small intestine in mice [4]. Pemafibrate also promoted cholesterol efflux and reverse cholesterol transport, exerted anti-inflammatory activity, and decreased atherosclerotic lesions [1]. Pemafibrate was more effective than fenofibrate at suppressing the postprandial increase of chylomicrons and the accumulation of chylomicron remnants, thereby attenuating postprandial hypertriglyceridaemia [5].

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[2]. Raza-Iqbal S, Tanaka T, Anai M, et al. Transcriptome analysis of K-877 (a novel selective PPARα modulator (SPPARMα))-regulated genes in primary human hepatocytes and the mouse liver[J]. Journal of atherosclerosis and thrombosis, 2015: 28720.
[3]. Takei K, Han S, Murayama Y, et al. Selective peroxisome proliferator-activated receptor-α modulator K-877 efficiently activates the peroxisome proliferator-activated receptor-α pathway and improves lipid metabolism in mice[J]. Journal of Diabetes Investigation, 2017, 8(4): 446-452.
[4]. Takei K, Nakagawa Y, Wang Y, et al. Effects of K-877, a novel selective PPARα modulator, on small intestine contribute to the amelioration of hyperlipidemia in low-density lipoprotein receptor knockout mice[J]. Journal of pharmacological sciences, 2017, 133(4): 214-222.
[5]. Sairyo M, Kobayashi T, Masuda D, et al. A novel selective PPARα modulator (SPPARMα), K-877 (pemafibrate), attenuates postprandial hypertriglyceridemia in mice[J]. Journal of atherosclerosis and thrombosis, 2018, 25(2): 142-152.

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