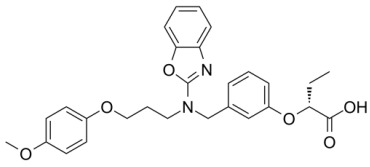
Data Sheet

Product Name:	Pemafibrate
Cat. No.:	CS-6084
CAS No.:	848259-27-8
Molecular Formula:	C28H30N2O6
Molecular Weight:	490.55
Target:	PPAR
Pathway:	Cell Cycle/DNA Damage
Solubility:	DMSO : ≥ 100 mg/mL (203.85 mM); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

Pemafibrate is a highly selective **PPARα** agonist, with an **EC_{50}** of 1 nM. IC50 & Target: EC50: 1 nM (h-PPARα), 1.10 μM (h-PPARγ), 1.58 μM (h-PPARδ)[1] **In Vitro:** Pemafibrate is a potent PPARα agonist, with EC_{50}s of 1 nM, 1.10 μM and 1.58 μM for h-PPARα, h-PPARγ and h-PPARδ, respectively. Pemafibrate is more than 1000 fold selective towards PPARα than PPARγ and PPARδ[1]. **In Vivo:** Pemafibrate (3 mg/kg, p.o.) increases plasma h-apoA-I in human apoA-I (h-apoA-I) transgenic mice, and shows higher levels of plasma h-apoA-I than fenofibrate at 300 mg/kg[1]. Pemafibrate (0.03 mg/kg) decreases levels of triglycerides and aspartate aminotransferase (AST) in PEMA-L (db/db) mice. Pemafibrate (0.1 mg/kg) not only shows such effects but increases liver weight in PEMA-H (db/db) mice. Pemafibrate enhances the pathogenesis in a rodent model of nonalcoholic steatohepatitis (NASH). Pemafibrate significantlly reduces the grade of hepatocyte ballooning in PEMA-H mice. Furthermore, Pemafibrate modulates lipid turnover and induces uncoupling protein 3 (UCP 3) expression in the liver[2]. Pemafibrate (K-877, 0.0005%) contained in high-fat diet (HFD) inhibits the body weight gain in mice. Pemafibrate significantly decreases the abundance of triglyceride (TG)-rich lipoproteins, including remnants, in postprandial plasma of mice. Pemafibrate also decreases intestinal mRNA expression of ApoB and Npc1l1[3].

PROTOCOL (Extracted from published papers and Only for reference)

Animal Administration: Pemafibrate is prepared in diet.[2]Mice are fasted for 12 h and fasting blood glucose measured. **Nine-week-old db/db mice** are used in the assay. After a 2-week acclimatization period, mice are divided into four groups: BD (db/db) mice (fed basal diet (BD) and treated with 0.5% aqueous methylcellulose solution (MC); MCD (db/db) mice (fed methionine choline-deficient (MCD) and treated with 0.5% MC); PEMA-L (db/db) mice (fed MCD and treated with **0.03 mg/kg Pemafibrate**); PEMA-H (db/db) mice (fed MCD and treated with **0.1 mg/kg Pemafibrate**). The drug-free solvent or the dosing solution is administered to animals (5 mL/kg body weight, p.o.) once daily (in the morning) for 4 consecutive weeks. After a 2-week acclimatization period, BD mice are fed a BD for 20 weeks. CTRL mice are fed D09100301 for 20 weeks. PEMA-L and PEMA-H mice are fed D09100301 for 12 weeks followed by D09100301 with 0.4 mg and 1.3 mg Pemafibrate/kg of the diet for 8 weeks, which corresponds to 0.03 mg/kg/day and 0.1 mg/kg/day, respectively. FENO mice are fed D09100301 for 12 weeks followed by D09100301 with 666.7 mg fenofibrate/kg of the diet for 8 weeks, which corresponds to 50 mg/kg/day. Pemafibrate and fenofibrate are incorporated into the AMLN diet. Animals are housed under conventional conditions with controlled temperature, humidity, and light (12-h light-dark cycle) and provided with food and water[2].

References:

[1]. Yamazaki Y, et al. Design and synthesis of highly potent and selective human peroxisome proliferator-activated receptor alpha agonists. Bioorg Med Chem Lett. 2007 Aug 15;17(16):4689-93. Epub2007 May 24.

[2]. Honda Y, et al. Pemafibrate, a novel selective peroxisome proliferator-activated receptor alpha modulator, improves the pathogenesis in a rodent model of nonalcoholic steatohepatitis. Sci Rep. 2017 Feb 14;7:42477.

[3]. Sairyo M, et al. A Novel Selective PPARα Modulator (SPPARMα), K-877 (Pemafibrate), Attenuates Postprandial Hypertriglyceridemia in Mice. J Atheroscler Thromb. 2018 Feb 1;25(2):142-152.

CAIndexNames:

Butanoic acid, 2-[3-[[2-benzoxazolyl[3-(4-methoxyphenoxy)propyl]amino]methyl]phenoxy]-, (2R)-

SMILES:

CC[C@@H](OC1=CC=CC(CN(C2=NC3=CC=CC=C3O2)CCCOC4=CC=C(OC)C=C4)=C1)C(O)=O

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