上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：Pemafibrate
产品别名：(R)-K-13675

生物活性：

Description	Pemafibrate is a highly selective PPARα agonist, with an EC50 of 1 nM.		
IC_{50} & Target	h-PPARα	h-PPARγ	PPARδ
	1 nM (EC_{50})	1.1 μM (EC_{50})	1.58 μM (EC_{50})
In Vitro	Pemafibrate is a potent PPARα agonist, with EC50s 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].		

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (203.85 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0385 mL	10.1926 mL	20.3853 mL
5 mM	0.4077 mL	2.0385 mL	4.0771 mL
10 mM	0.2039 mL	1.0193 mL	2.0385 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

	Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.10 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (5.10 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.10 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.10 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.10 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Animal Administration	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.