产品名称：GW0742
产品别名：GW0742

生物活性：

Description	GW0742 is a potent PPARβ and PPARδ agonist, with an IC_{50} of 1 nM for human PPARδ in binding assay, and EC_{50}s of 1 nM, 1.1 μM and 2 μM for human PPARδ, PPARα, and PPARγ, respectively.		
IC_{50} & Target	PPARδ	PPARα	PPARγ
	1 nM (EC_{50})	1.1 μM (EC_{50})	2 μM (EC_{50})
In Vitro	GW0742 is a potent PPARβ and PPARδ agonist, with an IC50 of 1 nM for human PPARδ, and EC50s of 1 nM, 1.1 μM and 2 μM for human PPARδ, PPARα, and PPARγ respectively[1]. GW0742 (100 μM) activates human PPARα and mouse PPARβ in MCF-7 cells. GW0742 (100 μM) significantly reduces low-KCl-induced apoptosis of cerebellar granule neurons. GW0742 shows no obvious inherent toxicity on cerebellar granule neuronal cells after treatment of 3-100 μM for 24 h, but induces increased cell death at 100 μM after 48 hr of treatment. Moreover, GW0742 (100 μM) increases c-Jun expression in cerebellar granule neuron cultures observed at 6 hr[2]. GW0742 (1 μM) induces PPARδ protein in neonatal rat cardiomyocytes. GW0742 also raises mRNA levels of long-chain acyl-CoA dehydrogenase (LCAD), very long-chain acyl-CoA dehydrogenase (VLCAD), acyl-CoA oxidase 1 (ACOX1), uncoupling protein 3 (UCP3), malonyl-CoA decarboxylase (MCD), and pyruvate dehydrogenase kinase 4 (PDK4) in neonatal rat cardiomyocytes[4].		
In Vivo	GW0742 (0.3 mg/kg, i.p.) reduces intensity masson-trichrome staining, and attenuates the histological signs in bleomycin instillatio (BLEO)-induced lung injury of mice. GW0742 (0.3 mg/kg, i.p.) also causes a reduction of the BLEO-induced loss body weight, and a decrease of myeloperoxidase (MPO) activity. GW0742 shows significant inhibition of TNF-a and IL-1β in instilled-mice. GW0742 prevents bleomycin-induced IkB-a degradation, reduces the levels of NF-kB p65 in the lung, and decreases iNOS and p-ERK expression in BLEO-induced mice[3]. GW0742 (5 mg/kg/day, i.v.) increases PPARδ protein level in the heart of rats. GW0742 also induces the increase in LCAD, VLCAD, and ACOX1 in the heart of rats[4].		
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 34 mg/mL (72.11 mM)** * "≥" means soluble, but saturation unknown.		

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1209 mL	10.6047 mL	21.2094 mL
	5 mM	0.4242 mL	2.1209 mL	4.2419 mL
	10 mM	0.2121 mL	1.0605 mL	2.1209 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 (5.30 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.30 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% corn oil Solubility: ≥ 2.5 mg/mL (5.30 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.30 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]. Sznaidman ML, et al. Novel selective small molecule agonists for peroxisome proliferator-activated receptor delta (PPARdelta)--synthesis and biological activity. Bioorg Med Chem Lett. 2003 May 5;13(9):1517-21. [2]. Smith SA, et al. Effect of the peroxisome proliferator-activated receptor beta activator GW0742 in rat cultured cerebellar granule neurons. J Neurosci Res. 2004 Jul 15;77(2):240-9. [3]. Galuppo M, et al. GW0742, a high affinity PPAR-β/δ agonist reduces lung inflammation induced by bleomycin instillation in mice. Int J Immunopathol Pharmacol. 2010 Oct-Dec;23(4):1033-46. [4]. Kuo SC, et al. Activation of receptors δ (PPARδ) by agonist (GW0742) may enhance lipid metabolism in heart both in vivo and in vitro. Horm Metab Res. 2013 Nov;45(12):880-6.

实验参考：

Cell Assay	The PPARβ activator GW0742 and the RXR activator 9-cis-retinoic acid are dissolved in DMSO. The final DMSO concentration des not exceed 0.5% v/v, and this concentration is used in control wells. For each culture plate, one row of wells is treated with 500 μM glutamate. These wells serve as a positive control and for normalisation of data. Cell death (toxicity) is assessed by using an assay designed to measure lactate dehydrogenase (LDH) release[2].
Animal Administration	Male CD mice (25-35 g) are housed in a controlled environment and provided with standard rodent chow and water. Mice are randomized into four experimental groups: bleomycin-treated group: mice are subjected to lung injury induced by intratracheal instillation of bleomycin and treated daily via intraperitoneal injection with vehicle of GW0742 (10% dimethylsulfoxide (OMSO, 1 mL/kg), 1 h after BLEO instillation (n = 15). GW0742 group: identical to bleomycin-treated group but mice are treated daily with GW0742 (0.3 mg/kg, 1h after BLEO instillation) via intraperitoneal injection (n = 15). Sham-operated mice + vehicle group: animals are subjected to the identical surgical procedure but receive intratracheal instillation of saline (0.9%) instead of BLEO and are treated daily with the vehicle of GW0742 (10% dimethylsulfoxide (DMSO), 1 mL/kg, i.p.), 1 h after saline instillation (n = 15). Sham-operated mice + GW0742 group: identical to sham + vehicle group but mice are treated daily with GW0742 (0.3 mg/kg, 1 h after saline instillation) via intraperitoneal injection (n = 15)[3].
	[1]. Sznaidman ML, et al. Novel selective small molecule agonists for peroxisome proliferator-activated receptor delta (PPARdelta)--synthesis and biological activity. Bioorg Med Chem Lett. 2003 May 5;13(9):1517-21. [2]. Smith SA, et al. Effect of the peroxisome proliferator-activated receptor beta activator GW0742

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