产品名称：匹格列酮
产品别名：Pioglitazone；吡格列酮

生物活性：

Description	Pioglitazone is a potent and selective PPARγ agonist with high affinity binding to the PPARγ ligand-binding domain with EC_{50} of 0.93 and 0.99 μM for human and mouse PPARγ, respectively.

IC_{50} & Target	PPARδ	PPARα	PPARγ
	0.01 μM (EC_{50}, Human PPARδ)	0.93 μM (EC_{50}, Human PPARα)	43 μM (EC_{50}, Human PPARγ)

In Vitro	AGEs-induced beta cell necrosis is completely abrogated by adding Pioglitazone (U 72107) to the AGEs culture medium. Furthermore Pioglitazone completely prevented any AGEs-induced increment in caspase-3 activation, thereby restoring caspase-3 activity to the same levels as the control cells. As expected AG is able to counteract AGEs-induced impaired viability[2].
In Vivo	The serum-free fatty acid and triglyceride levels as well as adipocyte sizes in ob/ob and adipo-/- ob/ob mice are unchanged after 10 mg/kg Pioglitazone (U 72107) but are significantly reduced to a similar degree after 30 mg/kg Pioglitazone. Moreover, the expressions of TNFα and resistin in adipose tissues of ob/ob and adipo-/- ob/ob mice are unchanged after 10 mg/kg Pioglitazone but are decreased after 30 mg/kg Pioglitazone. Thus, Pioglitazone-induced amelioration of insulin resistance and diabetes may occur adiponectin dependently in the liver and adiponectin independently in skeletal muscle[3]. Pioglitazone (10 mg/kg per d) treatment significantly attenuates the loss of body weight (BW) and cardiac hypertrophy. Pioglitazone treatment significantly reduces the elevated serum glucose levels and markedly improved the associated dyslipidemia. Furthermore, there is a slight but significant increase in serum creatinine level in D rats over their N controls ($P < 0.05$). However, a marked renal dysfunction is observed in diabetic nephropathic (DN) group ($P<0.05$). Moreover, DN rats exhibits the highest serum activity of CK-MB, relative to both N and D rats ($P<0.05$). Pioglitazone is able to decrease the elevated serum levels of both creatinine and creatine kinase-MB (CK-MB)[4].

Solvent&Solubility

In Vitro:

DMSO : 62.5 mg/mL (175.35 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions (Solvent / Mass / Concentration)	1 mg	5 mg	10 mg
1 mM	2.8055 mL	14.0276 mL	28.0552 mL
5 mM	0.5611 mL	2.8055 mL	5.6110 mL
10 mM	0.2806 mL	1.4028 mL	2.8055 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 (7.01 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (7.01 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 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 (7.01 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.01 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]. Kuwabara K, et al. A novel selective peroxisome proliferator-activated receptor alpha agonist, 2-methyl-c-5-[4-[5-methyl-2-(4-methylphenyl)-4-oxazolyl]butyl]-1,3-dioxane-r-2-carboxylic acid (NS-220), potently decreases plasma triglyceride and glucose leve [2]. Puddu A, et al. Pioglitazone attenuates the detrimental effects of advanced glycation end-products in the pancreatic beta cell line HIT-T15. Regul Pept. 2012 Aug 20;177(1-3):79-84. [3]. Kubota N, et al. Pioglitazone ameliorates insulin resistance and diabetes by both adiponectin-dependent and -independent pathways. J Biol Chem. 2006 Mar 31;281(13):8748-55. [4]. Elrashidy RA, et al. Pioglitazone attenuates cardiac fibrosis and hypertrophy in a rat model of diabetic nephropathy. J Cardiovasc Pharmacol Ther. 2012 Sep;17(3):324-33.

实验参考：

Cell Assay	In order to evaluate cell proliferation, HIT-T15 cells are seeded on 96-well plates (3×10^4 cells/well) and cultured for 5 days as described. Viable cells are determined using the Cell Titer 96 Aqueous One Solution Cell Proliferation Assay. To evaluate cell apoptosis and cell necrosis, HIT-T15 cells are plated on 6-well dishes (7×10^5 cells/well) for 5 days in standard conditions (CTR) or in the presence of AGEs (AGEs) with or without Pioglitazone (0.5 or 1 μM) or AG (1 mM). They are then processed to measure both the activity of caspase-3 and the activity of lactate dehydrogenase (LDH) (a stable cytosolic enzyme that is a marker of cell membrane damage and cell death due to necrosis) using Cytotox 96 Non Radioactive Cytotoxicity Assay[2].
Animal Administration	Mice[3] 10 mg/kg Pioglitazone HCl or vehicle (0.25% carboxymethylcellulose) is adnimistered to ob/ob and adipo-/- ob/ob mice by oral gavage once daily for 14 consecutive days. 30 mg/kg Pioglitazone or vehicle is also adnimistered to ob/ob and adipo-/- ob/ob mice by oral gavage once daily for 14 consecutive days. Rats[4] Male Wistar albino rats (weighing 250±20 g) are ued.Rats that achieved serum glucose level ≥ 250 mg/dL and serum creatinine level ≥1.5 mg/dL are divided into 2 groups (n=10 per each group): diabetic nephropathic (DN) group in which rats received an equal amount of vehicle (0.5% carboxy methyl cellulose) and Pioglitazone-treated (DN+Pio) group in which rats treated with Pioglitazone. Pioglitazone (10 mg/kg BW) is given orally by gastric gavage, once daily, for 4 weeks.
	[1]. Kuwabara K, et al. A novel selective peroxisome proliferator-activated receptor alpha agonist, 2-methyl-c-5-[4-[5-methyl-2-(4-methylphenyl)-4-oxazolyl]butyl]-1,3-dioxane-r-2-carboxylic acid (NS-220), potently decreases plasma triglyceride and glucose leve

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