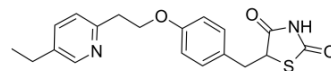


Pioglitazone

Cat. No.:	HY-13956		
CAS No.:	111025-46-8		
Molecular Formula:	C ₁₉ H ₂₀ N ₂ O ₃ S		
Molecular Weight:	356.44		
Target:	PPAR; Ferroptosis		
Pathway:	Cell Cycle/DNA Damage; Apoptosis		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro	DMSO : 25 mg/mL (70.14 mM; Need ultrasonic)			
		Solvent Concentration	Mass	
			1 mg	5 mg
			10 mg	
Preparing Stock Solutions	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
Please refer to the solubility information to select the appropriate solvent.				
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: 2.5 mg/mL (7.01 mM); Suspended solution; Need ultrasonic 2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (7.01 mM); Clear solution			

BIOLOGICAL ACTIVITY

Description	Pioglitazone (U 72107) is a potent and selective PPAR γ agonist with high affinity binding to the PPAR γ ligand-binding domain with EC ₅₀ of 0.93 and 0.99 μ M for human and mouse PPAR γ , respectively.			
IC₅₀ & Target	hPPAR γ	mouse PPAR γ	hPPAR δ	hPPAR α
	0.93 μ M (EC50)	0.99 μ M (EC50)	43 μ M (EC50)	100 μ M (EC50)
	mouse PPAR α	100 μ M (EC50)		
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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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 TNF α 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

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 μ M) 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^{[3][4]}

Mice^[3]

10 mg/kg Pioglitazone HCl or vehicle (0.25% carboxymethylcellulose) is administered 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 administered 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 used. 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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2021 Mar 2;33(3):581-597.e9.
- Br J Pharmacol. 2021 Feb 16.
- Acta Pharmacol Sin. 2021 Jan;42(1):160-170.
- Food Chem Toxicol. 2021 Apr 6;112:183.
- Int J Oncol. 2018 Aug;53(2):551-566.

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 level
- [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.
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Caution: Product has not been fully validated for medical applications. For research use only.

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