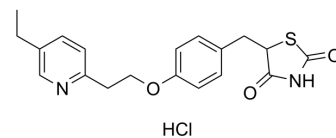


Pioglitazone hydrochloride

Cat. No.:	HY-14601
CAS No.:	112529-15-4
Molecular Formula:	C ₁₉ H ₂₁ ClN ₂ O ₃ S
Molecular Weight:	392.9
Target:	PPAR; Ferroptosis
Pathway:	Cell Cycle/DNA Damage; Apoptosis
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (254.52 mM; Need ultrasonic)					
	H ₂ O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)					
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
		1 mM		2.5452 mL	12.7259 mL	25.4518 mL
		5 mM		0.5090 mL	2.5452 mL	5.0904 mL
10 mM			0.2545 mL	1.2726 mL	2.5452 mL	
Please refer to the solubility information to select the appropriate solvent.						
In Vivo	<ol style="list-style-type: none"> Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: ≥ 2.5 mg/mL (6.36 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (6.36 mM); Clear solution Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (6.36 mM); Clear solution 					

BIOLOGICAL ACTIVITY

Description	Pioglitazone hydrochloride is a potent and selective PPAR γ agonist with EC ₅₀ s of 0.93 and 0.99 μ M for human and mouse PPAR γ , respectively.		
IC₅₀ & Target	PPAR δ 0.01 μ M (EC ₅₀ , Human PPAR δ)	PPAR α 0.93 μ M (EC ₅₀ , Human PPAR α)	PPAR γ 43 μ M (EC ₅₀ , Human PPAR γ)
In Vitro	AGEs-induced beta cell necrosis is completely abrogated by adding Pioglitazone 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 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.
- Cancer Res. 2022 Apr 15;82(8):1503-1517.
- Br J Pharmacol. 2021 Feb 16.
- Acta Pharmacol Sin. 2021 Jan;42(1):160-170.
- Food Chem Toxicol. 2021 Apr 6;112:183.

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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.

India Contact:

Life Technologies (India) Pvt. Ltd.

306, Aggarwal City Mall, Opposite M2K Pitampura, Delhi – 110034 (INDIA). Ph: +91-11-42208000, 42208111, 42208222, Mobile: +91-9810521400, Fax: +91-11-42208444

Email: customerservice@lifetechindia.com Website: www.lifetechindia.com