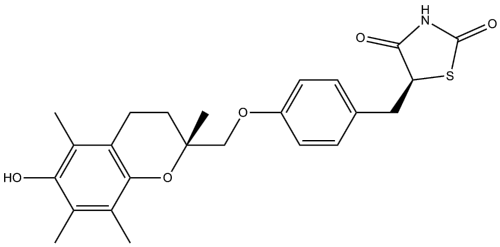
Product Data Sheet

Product Name: Troglitazone
Cat. No.: GC15272

Chemical Properties

Cas. No.	97322-87-7		
Chemical Name	5-[[4-[(6-hydroxy-2,5,7,8-tetramethyl-3,4-dihydrochromen-2-yl)methoxy]phenyl]methyl]-1,3-thiazolidine-2,4-dione		
SMILES	CC1=C(C(=C2CCC(OC2=C1C)(C)COC3=CC=C(C=C3)CC4C(=O)NC(=O)S4)C)O		
Formula	$C_{24}H_{27}NO_5S$	M.Wt	441.54
Solubility	≥ 20.9 mg/mL in DMSO, ≥ 3.34 mg/mL in EtOH with ultrasonic and warming	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			

Protocol

Cell experiment [1]:

Cell lines	C4-2 cells (human prostate cancer cell lines)

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Preparation Method	Cells were treated with Troglitazone 45μM for 72h, the percentage of cells within the different phases of the cell cycle was determined using flow cytometry, and the level of DNA fragmentation was measured using a Cell Death ELISA.
Reaction Conditions	45μM; 72h
Applications	Troglitazone treatment induced G_0/G_1 phase cell cycle arrest and increased the proportion of subG_0 phase cells and DNA fragmentation levels.

Animal experiment [2]:

Animal models	Balb/c male mice bearing MIA Paca2 xenografts
Preparation Method	Balb/c male mice were subcutaneously inoculated in the back with MIA Paca2 cells (5×10^6 cells) 14 days before the start of Troglitazone administration. Mice were then orally administered 200mg/kg of Troglitazone daily for 5 weeks. Tumor volume was measured bi-dimensionally and volume was calculated by the formula (length × width^2) × 0.5, and mouse body weights were monitored throughout the experiment.
Dosage form	200mg/kg/day; 5 weeks; p.o.
Applications	Troglitazone exhibited inhibitory effects on tumor growth in the MIA Paca2 xenograft model, the body weights of mice were not affected compared to those of the vehicle administration group.

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References:
[1] AKINYEKE T O, STEWART L V. Troglitazone suppresses c-Myc levels in human prostate cancer cells via a PPARγ-independent mechanism[J]. Cancer Biology & Therapy, 2011, 11(12): 1046-1058.
[2] FUJITA M, HASEGAWA A, YAMAMORI M, et al. In vitro and in vivo cytotoxicity of troglitazone in pancreatic cancer[J]. Journal of Experimental & Clinical Cancer Research, 2017, 36(1): 91.

Background

Troglitazone is an orally active agonist of the peroxisome proliferator-activated receptor γ (PPARγ), with EC_{50} values of 550nM and 780nM for human and murine receptors, respectively [1]. PPARγ is a widely expressed ligand-regulated transcription factor that controls the expression of genes involved in inflammation, redox balance, neurotrophic factor production, insulin sensitivity, and lipid and glucose metabolism[2]. By activating PPARγ, Troglitazone improves insulin resistance and regulates glucose and lipid metabolism, making it commonly used for the treatment of type II diabetes[3].

In vitro, treatment of mitochondria isolated from rat liver with Troglitazone (10, 50μM) for 5min induced mitochondrial swelling[4]. Treatment of C4-2 cells with Troglitazone (45μM) for 72h induced G_0/G_1 phase cell cycle arrest and increased the proportion of cells in the subG $_0$ phase and the level of DNA fragmentation[5]. Treatment of human bladder cancer T24 and EJ cells with Troglitazone (25, 50μM) for 24h increased the ratio of light chain 3 (LC3)-II to actin in a time- and concentration-dependent manner[6].

In vivo, oral administration of Troglitazone (200mg/kg/day) for 5 weeks to male Balb/c mice bearing MIA Paca2 xenograft tumors significantly suppressed tumor growth without a significant effect on mouse body weight[7]. A single intraperitoneal injection of Troglitazone (300mg/kg) in female BALB/c mice significantly increased plasma alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels after 6h, and this treatment induced pericentral hepatocyte necrosis within 24h[8].

References:
[1] WILSON T M, BROWN P J, STERNBACH D D, et al. The PPARs: from orphan receptors to drug discovery[J]. Journal of Medicinal Chemistry, 2000, 43(4): 527-550.
[2] CAI W, YANG T, LIU H, et al. Peroxisome proliferator-activated receptor γ (PPARγ): A master

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gatekeeper in CNS injury and repair[J]. Progress in Neurobiology, 2018, 163: 27-58.
[3] PLOSKER G L, FAULDS D. Troglitazone: a review of its use in the management of type 2 diabetes mellitus[J]. Drugs, 1999, 57(3): 409-438.
[4] OKUDA T, NORIOKA M, SHITARA Y, et al. Multiple mechanisms underlying troglitazone-induced mitochondrial permeability transition[J]. Toxicology and Applied Pharmacology, 2010, 248(3): 242-248.
[5] AKINYEKE T O, STEWART L V. Troglitazone suppresses c-Myc levels in human prostate cancer cells via a PPARγ-independent mechanism[J]. Cancer Biology & Therapy, 2011, 11(12): 1046-1058.
[6] YAN S, YANG X, CHEN T, et al. The PPARγ agonist Troglitazone induces autophagy, apoptosis and necroptosis in bladder cancer cells[J]. Cancer Gene Therapy, 2014, 21(5): 188-193.
[7] FUJITA M, HASEGAWA A, YAMAMORI M, et al. In vitro and in vivo cytotoxicity of troglitazone in pancreatic cancer[J]. Journal of Experimental & Clinical Cancer Research, 2017, 36(1): 91.
[8] JIA R, ODA S, TSUNEYAMA K, et al. Establishment of a mouse model of troglitazone-induced liver injury and analysis of its hepatotoxic mechanism[J]. Journal of Applied Toxicology, 2019, 39(11): 1541-1556.

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