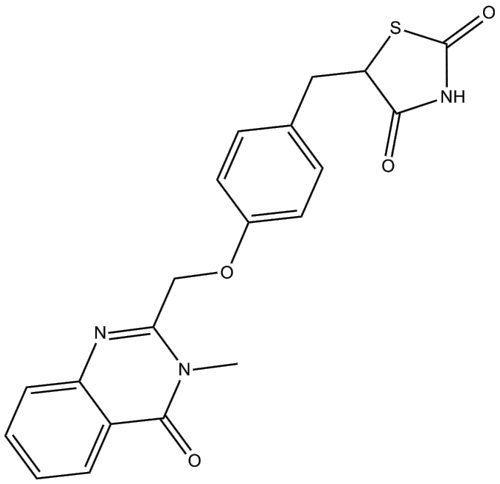
Product Data Sheet

Product Name: Balaglitazone
Cat. No.: GC12894

Chemical Properties

Cas. No.	199113-98-9		
Chemical Name	5-(4-((3-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)methoxy)benzyl)thiazolidine-2,4-dione		
SMILES	O=C1C2=CC=CC=C2N=C(COC3=CC=C(CC4C(NC(S4)=O)=O)C=C3)N1C		
Formula	$C_{20}H_{17}N_3O_4S$	M.Wt	395.43
Solubility	≥ 15.45 mg/mL in DMSO, ≥ 2.18 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

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Cell experiment: MTT assay is used for cell viability analyses. Briefly, K562 and K562/DOX cells are seeded in a 96-well plate in RPMI-1640 medium supplemented with 10% FBS at the density of 2 × 104 cells/well. After 24 h incubation, various concentrations of doxorubicin (DOX) with or without balaglitazone are diluted in RPMI-1640 medium (without FBS) and added into each well. Experiments for each group are performed in triplicates and with a blank control. After 48 h of treatment, the medium is removed and 200 μL of RPMI-1640 medium supplemented with 10% FBS and 10% MTT (5 mg/mL) is added. After incubation for another 4 h, the reduced intracellular formazan product is dissolved by replacing 100 μL of RPMI-1640 medium with the same volume of dimethyl sulfoxide (DMSO). Absorbance values are measured at 570 nm with a micro plate reader. The half maximal inhibitory concentration (IC50) of each experiment is calculated. The resistance fold (RF) is calculated by dividing the IC50 value of treatment in resistant cells by the IC50 value of treatment in corresponding parental cells[2].

Animal experiment: Antihyperglycaemic effects of balaglitazone and rosiglitazone are assessed in adult male diabetic db/db mice. At 14 weeks of age, animals are randomised according to fasting blood glucose into 11 groups (n = 6). Mice are dosed orally once daily for 9 days with vehicle (0.2% carboxymethyl cellulose (CMC) + 0.4% Tween-80 in saline) or increasing doses of either balaglitazone (0.1; 0.3; 1.0; 3.0; 10.0 mg/kg/day) or rosiglitazone (0.2; 0.6; 2.0; 6.0 mg/kg/day). After 7 days of treatment, plasma samples obtained in the morning (between 8:00 and 10:00 AM) are analysed for glucose and insulin. After 9 days of treatment, animals are exposed to an oral glucose tolerance test (OGTT; 3.0 g/kg). The resulting area under the curve is calculated for each of the doses[1].

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

[1]. Larsen PJ, et al. Dissociation of antihyperglycaemic and adverse effects of partial perioxisome proliferator-activated receptor (PPAR-gamma) agonist balaglitazone. Eur J Pharmacol. 2008 Oct 31;596(1-3):173-9.
[2]. Yousefi B, et al. Balaglitazone reverses P-glycoprotein-mediated multidrug resistance via upregulation of PTEN in a PPARγ-dependent manner in leukemia cells. Tumour Biol. 2017 Oct;39(10):1010428317716501.
[3]. Henriksen K, et al. A comparison of glycemic control, water retention, and musculoskeletal effects of balaglitazone and pioglitazone in diet-induced obese rats. Eur J Pharmacol. 2009 Aug 15;616(1-3):340-5.

Background

Balaglitazone is a partial agonist of peroxisome proliferator-activated receptor (PPAR) γ [1].
PPAR plays important roles in the regulation of insulin, triglycerides and lipid metabolism. It is an attractive target for the therapy of Type II Diabetes. Balaglitazone is a partial agonist of PPARγ. The maximum inhibition of PPARγ activity by balaglitazone is 52%. Thus balaglitazone is supposed to have decreased side effects. It has showed potent effects on lowering blood glucose in various animal models [1 and 2].
In a cell-based assay using HEK293 cells transfected with fused PPARγ, treatment of balaglitazone showed sigmoid activation with an EC50 value of 1.35μM. When combined with rosiglitazone, balaglitazone at increased concentrations resulted in the reduction of rosiglitazone's activity to the level of balaglitazone alone at concentration of 100 nM [3].
In adult male diabetic mice, the oral administration of balaglitazone at increased doses showed more potent and efficacious at lowering glucose levels than rosiglitazone. Balaglitazone also caused reduction of bodyfluid accumulation andfat accumulation without heart enlargement, indicating that it had a better safety profile on the cardiovascular system. Besides that, balaglitazone treatment lasted for 21 days exerted no significant impact on the volumes of blood or plasma. Moreover, balaglitazone was found to have no effect on bone formation at concentrations of up to 10 mg/kg indicating that it was only a partial agonist and led no loss of bone [1 and 2].
References:
[1] Agrawal R, Jain P, Dikshit SN. Balaglitazone: a second generation peroxisome proliferator-

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activated receptor (PPAR) gamma (γ) agonist. Mini Rev Med Chem. 2012 Feb;12(2):87-97.
[2] Henriksen K, Byrjalsen I, Nielsen RH, Madsen AN, Larsen LK, Christiansen C, Beck-Nielsen H, Karsdal MA. A comparison of glycemic control, water retention, and musculoskeletal effects of balaglitazone and pioglitazone in diet-induced obese rats. Eur J Pharmacol. 2009 Aug 15;616(1-3):340-5.
[3] Larsen PJ, Lykkegaard K, Larsen LK, Fleckner J, Sauerberg P, Wassermann K, Wulff EM. Dissociation of antihyperglycaemic and adverse effects of partial perioxisome proliferator-activated receptor (PPAR-gamma) agonist balaglitazone. Eur J Pharmacol. 2008 Oct 31;596(1-3):173-9.

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