Azemiglitazone

Cat. No.: HY-108022

CAS No.: 1133819-87-0

Molecular Formula: $C_{19}H_{17}NO_5S$

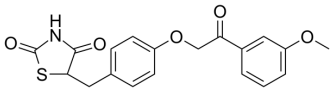
Molecular Weight: 371.41

Target: Mitochondrial Metabolism; PPAR

Pathway: Metabolic Enzyme/Protease; Cell Cycle/DNA Damage; Vitamin D Related/Nuclear Receptor

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (336.56 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6924 mL	13.4622 mL	26.9244 mL
5 mM	0.5385 mL	2.6924 mL	5.3849 mL
10 mM	0.2692 mL	1.3462 mL	2.6924 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: ≥ 2.08 mg/mL (5.60 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.60 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.60 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Azemiglitazone (MSDC-0602) is an orally active thiazolidinedione (TZD) -like molecule, which binds to PPARγ with low binding and activating affinity. Azemiglitazone inhibits mitochondrial pyruvate carrier (MPC), which inhibits Alzheimer's disease and diminishes nonalcoholic steatohepatitis (NASH) caused liver injury[4][5].

In Vitro

Azemiglitazone (15 μM, 4 h) crosslinks specifically to MPC, inhibits pyruvate oxidation and glucose production in liver

mitochondria with interaction with MPC2[3].
Azemiglitazone has low binding and activating affinity for PPARγ with IC_{50} of 18.25 μM[6].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Azemiglitazone (2-5 μM in blood, p.o for 2-4 weeks) improves insulin sensitivity in striated muscle, adipose tissue, and liver of DIO C57BL/6 mice[6].
Azemiglitazone (2-5 μM in blood, p.o for 2-4 weeks) improves mitochondrial respiratory rate in DIO C57BL/6 mice[6].
Azemiglitazone reduces NASH caused liver injury, prevents (2-5 μM in blood, p.o. for 12 weeks) and reverses (2-5 μM in blood, p.o. for 3 weeks) stellate cells activation and fibrosis in HTF-C diet feeding C57BL6/J mice[4].
Azemiglitazone (2-5 μM in blood, p.o.) causes weight loss and suppresses stellate cell activation with or without MPC function in HTF-C diet feeding LS-$Mpc^{2-/-}$C57BL6/J mice[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	HTF-C diet feeding C57BL6/J mice [4]
Dosage:	331 ppm MSDC-0602 potassium salt (2-5 μM Azemiglitazone in blood)
Administration:	oral administration for 12 weeks (after 4 weeks of HTF-C diet) or 3 weeks (16 weeks after HTF-C diet)
Result:	Induced weight loss, decreased concentrations of plasma ALT and AST and stellate cell activation.

Animal Model:	HTF-C diet feeding LS-$Mpc^{2-/-}$C57BL6/J mice [4]
Dosage:	331 ppm MSDC-0602 potassium salt (2-5 μM Azemiglitazone in blood)
Administration:	oral administration for 12 weeks (after 4 weeks of HTF-C diet)
Result:	Induced weight loss, suppressed stellate cell activation.

Animal Model:	diet induced obesity C57BL/6 mice[6]
Dosage:	300 ppm MSDC-0602 (2-5 μM Azemiglitazone in blood)
Administration:	oral administration for 2-4 weeks
Result:	Reduced insulin concentration in plasma, increased glucose infusion rate and glucose uptake into gastrocnemius, adipose tissue, and heart.Improved mitochondrial oxygen consumption.

REFERENCES

[1]. McCommis KS, et al., Loss of Mitochondrial Pyruvate Carrier 2 in the Liver Leads to Defects in Gluconeogenesis and Compensation via Pyruvate-Alanine Cycling. Cell Metab. 2015 Oct 6;22(4):682-94.

[2]. McCommis KS, et al., Targeting the mitochondrial pyruvate carrier attenuates fibrosis in a mouse model of nonalcoholic steatohepatitis. Hepatology. 2017 May;65(5):1543-1556.

[3]. Phelix, C., et al., MSDC-0160 and MSDC-0602 binding with human mitochondrial pyruvate carrier (MPC) 1 and 2 heterodimer: PPARγ activating and sparing TZDs as therapeutics. Int. J. Knowl. Knowl. Bioinform.2017, 7, 43–67.

[4]. Chen Z, et al., Insulin resistance and metabolic derangements in obese mice are ameliorated by a novel peroxisome proliferator-activated receptor γ-sparing thiazolidinedione. J Biol Chem. 2012 Jul 6;287(28):23537-48.

[5]. Chen Z, et al. Resistance and metabolic derangements in obese mice are ameliorated by a novel peroxisome proliferator-activated receptor γ-sparing thiazolidinedione. J Biol Chem. 2012 Jul 6;287(28):23537-48.

[6]. Vigueira PA, et al. The beneficial metabolic effects of sensitizers are not attenuated by mitochondrial pyruvate carrier 2 hypomorphism. Exp Physiol. 2017 Aug 1;102(8):985-999.

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