Seladelpar

Cat. No.: HY-19522

CAS No.: 851528-79-5

Molecular Formula: $C_{21}H_{23}F_3O_5S$

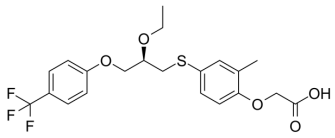
Molecular Weight: 444.46

Target: PPAR

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

Storage:

Pure form	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (224.99 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2499 mL	11.2496 mL	22.4992 mL
	5 mM	0.4500 mL	2.2499 mL	4.4998 mL
	10 mM	0.2250 mL	1.1250 mL	2.2499 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 (5.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Seladelpar (MBX-8025) is an orally active, potent (50% effect concentration EC_{50} 2 nM), and specific PPAR-δ agonist[1][2].

IC_{50} & Target

PPAR-δ	PPAR-α
2 nM (EC50)	1600 nM (EC50)

In Vitro

Seladelpar (MBX-8025) is an orally active, potent (2 nM), and specific (>750-fold and >2500-fold compared with PPAR-α or PPAR-γ receptors, respectively) PPAR-δ agonist being developed as a lipid-altering agent[1]. Seladelpar is a potent, and selective PPAR-δ agonist (50% effect concentration human PPAR-δ=2 nM, PPAR-α=1,600 nM) that demonstrates favorable effects on insulin resistance, diabetes, and atherogenic dyslipidemia[2].

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

In Vivo	From weaning, female Alms1 mutant (foz/foz) mice and wild-type littermates are fed an atherogenic diet for 16 weeks; groups (n=8-12) are then randomized to receive Seladelpar (10 mg/kg) or vehicle (1% methylcellulose) by gavage for 8 weeks. Despite minimally altering body weight, Seladelpar normalizes hyperglycemia, hyperinsulinemia, and glucose disposal in foz/foz mice. Serum alanine aminotransferase ranges 300-600 U/L in vehicle-treated foz/foz mice; Seladelpar reduces alanine aminotransferase by 50%. In addition, Seladelpar normalizes serum lipids and hepatic levels of free cholesterol and other lipotoxic lipids that are increased in vehicle-treated foz/foz versus wild-type mice. This abolished hepatocyte ballooning and apoptosis, substantially reduce steatosis and liver inflammation, and improve liver fibrosis. In vehicle-treated foz/foz mice, the mean nonalcoholic fatty liver disease activity score is 6.9, indicating nonalcoholic steatohepatitis (NASH); Seladelpar reverses NASH in all foz/foz mice (nonalcoholic fatty liver disease activity score 3.13). In atherogenic diet-fed Wt mice, administration of Seladelpar reduces body weight by -18% (P<0.05). In contrast, Seladelpar produces minimal effect on body weight in atherogenic diet–fed foz/foz mice. These animals develope severe hyperglycemia, hyperinsulinemia, and whole-body insulin resistance after 16 weeks (P<0.05); Seladelpar strikingly improves these indices (P<0.05). After intraperitoneal glucose injection, blood glucose reaches ~32 mM in vehicle-treated versus ~14 mM in Seladelpar-treated foz/foz mice (P<0.05); the area under the blood glucose disappearance curve is correspondingly lower in Seladelpar-treated foz/foz mice (P<0.05). Seladelpar produces a proportionally similar effect on glucose handling in atherogenic diet–fed Wt mice (P<0.05)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Mice[2] From weaning (week 4), ***Alms1*** mutant (***foz***/***foz***) NOD.B10 mice or Wt littermates (female mice in both groups) are fed an atherogenic diet (23% fat, 0.2% cholesterol and 45% simple carbohydrate; 4.78 kcal/g digestible energy) ad libitum for 16 weeks, after which groups are randomized (n=8-12 mice/group) to once-a-day oral administration (by gavage) for 8 weeks of Seladelpar (10 mg/kg in 1% methylcellulose) or vehicle (controls). Animals are housed under 12-hour light/dark cycle and constant temperature of 22°C and receive maximal humane care[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Bays HE, et al. MBX-8025, a novel peroxisome proliferator receptor-delta agonist: lipid and other metabolic effects in dyslipidemic overweight patients treated with and without atorvastatin. J Clin Endocrinol Metab. 2011 Sep;96(9):2889-97.

[2]. Haczeyni F, et al. The selective peroxisome proliferator-activated receptor-delta agonist seladelpar reverses nonalcoholic steatohepatitis pathology by abrogating lipotoxicity in diabetic obese mice. Hepatol Commun. 2017 Jul 31;1(7):663-674.

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