Seladelpar sodium salt

Cat. No.: HY-19522A

CAS No.: 3026272-26-1

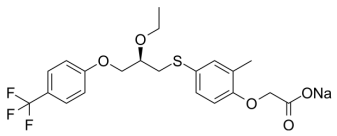
Molecular Formula: $C_{21}H_{22}F_3NaO_5S$

Molecular Weight: 466.45

Target: PPAR

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

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 : 50 mg/mL (107.19 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1439 mL	10.7193 mL	21.4385 mL
	5 mM	0.4288 mL	2.1439 mL	4.2877 mL
	10 mM	0.2144 mL	1.0719 mL	2.1439 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 (5.36 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.36 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Seladelpar sodium salt (MBX-8025) is an orally active, potent and specific PPARδ agonist with an EC_{50} of 2 nM, showing more than 750-fold and 2500-fold selectivity over the PPARα and PPARγ receptors, respectively.

IC_{50} & Target

PPAR-δ
2 nM (EC50)

In Vitro

MBX-8025 is an orally active, potent (EC_{50}=2 nM), and specific (750-fold and 2500-fold compared with PPARα or PPARγ receptors, respectively) PPARδ agonist being developed as a lipid-altering agent[2][3].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In atherogenic diet-fed Wt mice, administration of Seladelpar sodium salt reduces body weight by ~18% (P<0.05). In contrast, Seladelpar sodium salt produces minimal effect on body weight in atherogenic diet-fed foz/foz mice. Seladelpar sodium salt lowers serum alanine aminotransferase (ALT) levels in foz/foz mice (P<0.05) and similarly (but not significantly) in Wt mice. Seladelpar sodium salt normalizes serum cholesterol and decreases triglycerides in both genotypes (P<0.05). Seladelpar sodium salt abolishes hepatocyte ballooning (P<0.05) and decreases the nonalcoholic fatty liver disease (NAFLD) activity score by ~50%. Seladelpar sodium salt also significantly reduces sirius red-positive areas in foz/foz mice (P<0.05)[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	Human PPARδ, PPARα and PPARγ activity is monitored in transiently transfected cells treated with increasing concentrations of MBX-8025 (0.1 nM, 1 nM, 10 nM, 100, nM, 1000 nM) in comparison with reference compounds (0.1 nM-1 μM) for individual subtypes. The PPAR subtype selectivity of MBX-8025 is evaluated in a cell-based GAL4 reporter assay system[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [4]	Mouse: 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 to 12 mice/group) to once-a-day oral administration (by gavage) for 8 weeks of Seladelpar sodium salt (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[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Sahebkar A, et al. New peroxisome proliferator-activated receptor agonists: potential treatments for atherogenic dyslipidemia and non-alcoholic fatty liver disease. Expert Opin Pharmacother. 2014 Mar;15(4):493-503.

[2]. 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.

[3]. Choi YJ, et al. Effects of the PPAR-δ agonist MBX-8025 on atherogenic dyslipidemia. Atherosclerosis. 2012 Feb;220(2):470-6.

[4]. 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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