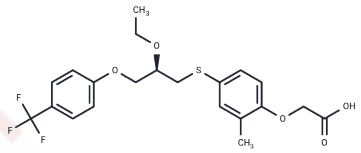
Data Sheet (Cat.No.T4628)

TargetMol

Seladelpar

Chemical Properties



CAS No. : 851528-79-5

Formula: C21H23F3O5S

Molecular Weight: 444.46

Appearance: no data available

Storage: store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Seladelpar (MBX 8025) has been used in trials studying the treatment of Hyperlipidemia.
Targets(IC50)	PPAR
In vitro	Seladelpar (MBX-8025) is an orally administered, highly potent (2 nM), and selective PPAR-δ agonist with over 750-fold and 2500-fold specificity over PPAR-α and PPAR-γ receptors, respectively. As a lipid-modifying agent, it effectively improves insulin resistance, diabetes, and atherogenic dyslipidemia by targeting human PPAR-δ at a 50% effective concentration of 2 nM, compared to 1,600 nM for PPAR-α.
In vivo	Female Alms1 mutant (foz/foz) mice and their wild-type siblings were subjected to an atherogenic diet for 16 weeks post-weaning. Subsequently, groups (n=8-12) were randomized to receive either 10 mg/kg Seladelpar or a vehicle (1% methylcellulose) via gavage for 8 weeks. Seladelpar efficiently normalized hyperglycemia, hyperinsulinemia, and glucose disposal in foz/foz mice without significantly affecting body weight. It halved serum alanine aminotransferase levels, which ranged from 300-600 U/L in vehicle-treated foz/foz mice, and corrected serum lipid profiles as well as hepatic concentrations of free cholesterol and other lipotoxic lipids elevated in these mice compared to wild-type. These corrections led to the abolition of hepatocyte ballooning and apoptosis, marked reductions in steatosis and liver inflammation, and improved liver fibrosis. Vehicle-treated foz/foz mice had an average nonalcoholic fatty liver disease (NAFLD) activity score of 6.9, indicative of nonalcoholic steatohepatitis (NASH), which Seladelpar entirely reversed (NAFLD activity score reduced to 3.13). In wild-type mice fed an atherogenic diet, Seladelpar administration resulted in an approximate 18% reduction in body weight (P<0.05). However, it had a minimal impact on the body weight of atherogenic diet-fed foz/foz mice. These mice developed severe metabolic disruptions after 16 weeks, which Seladelpar significantly ameliorated (P<0.05). Following an intraperitoneal glucose challenge, blood glucose levels were significantly lower in Seladelpar-treated foz/foz mice compared to vehicle-treated ones (P<0.05), demonstrating Seladelpar's substantial improvement on glucose handling, an effect similarly observed in wild-type mice on an atherogenic diet (P<0.05).
Animal Research	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].

Solubility Information

Solubility	DMSO: 10 mg/mL (22.5 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2499 mL	11.2496 mL	22.4992 mL
5 mM	0.450 mL	2.2499 mL	4.4998 mL
10 mM	0.225 mL	1.125 mL	2.2499 mL
50 mM	0.045 mL	0.225 mL	0.450 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

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.

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.