Icosabutate

Cat. No.: HY-121212

CAS No.: 1253909-57-7

Molecular Formula: $C_{24}H_{38}O_3$

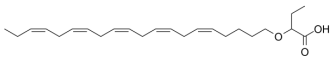
Molecular Weight: 374.56

Target: Others

Pathway: Others

Storage:

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



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (266.98 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6698 mL	13.3490 mL	26.6980 mL
	5 mM	0.5340 mL	2.6698 mL	5.3396 mL
	10 mM	0.2670 mL	1.3349 mL	2.6698 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 (6.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.67 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.67 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Icosabutate, an orally active ω-3 polyunsaturated fatty acid, is an aeicosapentaenoic acid (EPA) derivative. Icosabutate overcomes the drawbacks of unmodified EPA for liver targeting and improves insulin sensitivity, hepatic inflammation and fibrosis[1]. Icosabutate is well tolerated, and efficacious in lowering non-high-density lipoprotein cholesterol (non-HDL-C) levels in persistent hypertriglyceridemia [2].

IC_{50} & Target

IC50: non-HDL-C[2]

In Vivo

Icosabutate (oral gavage; 100 mg/kg; once) accounts for the much higher flow rate of portal vein plasma (522 mL/h) versus

mesenteric lymph (0.5 mL/h), that data demonstate that icosabutate is almost entirely taken up through the portal vein (>99%) with only a small fraction of icosabutate being absorbed through the lymphatic pathway in 8-week old male Wistar rats[1].

Icosabutate ([14-C]-icosabutate; oral gavage; 100 mg/kg; once) shows that peak concentrations of radioactivity in most tissues at 4-8 hours after the dose (except the gastrointestinal tract) with highest concentrations in the liver and kidney, most other tissues contain levels of radioactivity below that in plasma in male albino Wistar rats[1].

Icosabutate (diet administration; 135 mg/kg/day; 5 weeks) markedly improved glucose tolerance after an oral glucose load, significantly reduces AUC (0-120 minutes) by 60% without affecting body weight, decrease plasma alanine aminotransferase (ALT) levels improves glucose metabolism by a significant decrease in blood glucose, blood hemoglobin A1c, plasma insulin, and HOMA-IR (-50%, -47%, -76% and -87%, respectively) in mice[1].

Icosabutate (oral adminstration; 112 mg/kg/day; 20 weeks) prevents microvesicular steatosis (-35%) and hepatocellular hypertrophy (-82%), but not macrovesicular steatosis. After 20 weeks of treatment, despite comparable decreases in hepatic inflammatory cell aggregates, only icosabutate reduced hepatic collagen content[1].

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

Animal Model:	6-8-week-old male ob/ob mice[1]
Dosage:	135 mg/kg
Administration:	135 mg/kg/day through diet administration; 5 weeks
Result:	Improved glucose metabolism and insulin resistance.

Animal Model:	8-15-week-old male APOE*3Leiden.CETP mice fed a high-fat and high cholesterol diet [1]
Dosage:	112 mg/kg/day
Administration:	Oral gavage; 20 weeks
Result:	Improved microvesicular steatosis, hepatic inflammation, and fibrosis.

REFERENCES

[1]. van den Hoek AM, et al. Icosabutate Exerts Beneficial Effects Upon Insulin Sensitivity, Hepatic Inflammation, Lipotoxicity, and Fibrosis in Mice.Hepatol Commun. 2019 Dec 24;4(2):193-207.

[2]. Kastelein JJ, et al. Icosabutate, a Structurally Engineered Fatty Acid, Improves the Cardiovascular Risk Profile in Statin-Treated Patients with Residual Hypertriglyceridemia.Cardiology. 2016;135(1):3-12.

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