Larsucosterol (trimethylamine)

Cat. No.: HY-139576B

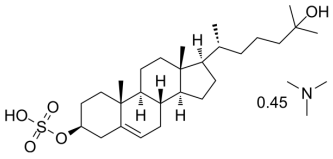
Molecular Formula: $C_{30}H_{46}O_5S.{}_{0.45}C_3H_9N$

Molecular Weight: 509.32

Target: Endogenous Metabolite; LXR

Pathway: 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 : 33.33 mg/mL (65.44 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9634 mL	9.8170 mL	19.6340 mL
	5 mM	0.3927 mL	1.9634 mL	3.9268 mL
	10 mM	0.1963 mL	0.9817 mL	1.9634 mL

Please refer to the solubility information to select the appropriate solvent.

BIOLOGICAL ACTIVITY

Description

Larsucosterol (DUR-928) trimethylamine, a cholesterol metabolite, is a potent liver X receptor (LXR) antagonist. Larsucosterol trimethylamine as a potent endogenous regulator decreases lipogenesis. Larsucosterol trimethylamine inhibits the cholesterol biosynthesis via decreasing mRNA levels and inhibiting the activation of SREBP-1[1][2][3].

In Vitro

Larsucosterol (DUR-928; 0-25 μM; 8 h; HepG2 cells) trimethylamine inhibits cholesterol biosynthesis by decreasing HMG-CoA reductase mRNA levels and decreases free [^{14}C] cholesterol in a dose-dependent manner[1].
Larsucosterol (0-25 μM; 6 h; HepG2 cells) trimethylamine inhibits HMG-CoA reductase expression by inhibition of both SREBP1 activation and expression in hepatocytes[1].
Larsucosterol (0-50 μM; 48 h) trimethylamine increases cell proliferation and decreases apoptosis in macrophages[2].
Larsucosterol (0-25 μM; 48 h; macrophages) trimethylamine inhibits activation of liver oxysterol receptor LXRα[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[2]

Cell Line:	Macrophages
Concentration:	0, 5, 10, 15, 20, and 25 μM

Incubation Time:	48 hours
Result:	Induces cell proliferation and relative cell number after treatment for 48 h were 120% at 25 μM.

Apoptosis Analysis[2]

Cell Line:	Macrophages
Concentration:	0, 10, 20, 30, 40 and 50 μM
Incubation Time:	48 hours
Result:	Did not significantly affect the numbers of apoptotic or live cells.

Western Blot Analysis[1]

Cell Line:	HepG2 cells
Concentration:	0, 3, 6, 12, and 25 μM
Incubation Time:	6 hours
Result:	Inhibited the activation of SREBP-1 and SREBP-2, and subsequently inhibit the expression HMG-CoA reductase.

Western Blot Analysis[2]

Cell Line:	Macrophages
Concentration:	0, 3, 6, 12, and 25 μM
Incubation Time:	48 hours
Result:	Decreased LXRα levels in the nuclei in a does-dependent manner.

In Vivo

Larsucosterol (DUR-928; 25 mg/kg; i.p.; twice in 14 hours; C57BL/6J mice with nonalcoholic fatty liver diseases (NAFLD) model) trimethylamine reduces serum lipid levels in mice fed a high-fat diet[3].
Larsucosterol (25 mg/kg; i.p.; twice in 14 hours; C57BL/6J mice with nonalcoholic fatty liver diseases (NAFLD) model) trimethylamine suppressed the expression of the genes and inhibits ABCA1 expressionde. Larsucosterolcreases nuclear SREBP-1 Protein levels and cytoplasmic FAS and ACC1 protein levels in liver tissue[3].
Larsucosterol (25 mg/kg; i.p.; once every 3 days for 6 weeks; C57BL/6J mice with nonalcoholic fatty liver diseases (NAFLD) model) trimethylamine protects the liver from injury by suppressing hepatic inflammation[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female C57BL/6J mice with nonalcoholic fatty liver diseases (NAFLD) model[3]
Dosage:	25 mg/kg
Administration:	Intraperitoneal injection; twice in 14 hours
Result:	Decreased plasma TG, CHOL, and HDL-C by 40, 15, and 20%, respectively. Reduced the mRNA levels of SREBP-1c, ACC1, and FAS by 46, 57, and 49%, respectively. Suppressed ABCA1 expression. Suppressed nuclear SREBP-1, cytoplasmic ACC1, and FAS protein levels by 74, 58, and 47%, respectively.

Animal Model:	Female C57BL/6J mice with nonalcoholic fatty liver diseases (NAFLD) model[3]
Dosage:	25 mg/kg
Administration:	Intraperitoneal injection; once every 3 days for 6 weeks
Result:	Decreased plasma cholesterol levels. Reduced serum alkaline phosphatase, ALT, and AST levels.

REFERENCES

[1]. Ren S, et, al. Sulfated oxysterol, 25HC3S, is a potent regulator of lipid metabolism in human hepatocytes. Biochem Biophys Res Commun. 2007 Sep 7;360(4):802-8.

[2]. Ma Y, et, al. 25-Hydroxycholesterol-3-sulfate regulates macrophage lipid metabolism via the LXR/SREBP-1 signaling pathway. Am J Physiol Endocrinol Metab. 2008 Dec;295(6):E1369-79.

[3]. Xu L, et, al. 5-cholesten-3β,25-diol 3-sulfate decreases lipid accumulation in diet-induced nonalcoholic fatty liver disease mouse model. Mol Pharmacol. 2013 Mar;83(3):648-58.

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