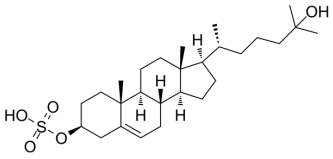
Larsucosterol

Cat. No.:	HY-139576
CAS No.:	884905-07-1
Molecular Formula:	$C_{27}H_{46}O_5S$
Molecular Weight:	482.72
Target:	Endogenous Metabolite
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Larsucosterol (DUR-928), a cholesterol metabolite, is a potent liver X receptor (LXR) antagonist. Larsucosterol as a potent endogenous regulator decreases lipogenesis. Larsucosterol 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) 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) inhibits HMG-CoA reductase expression by inhibition of both SREBP1 activation and expression in hepatocytes[1].
Larsucosterol (0-50 μM; 48 h) increases cell proliferation and decreases apoptosis in macrophages[2].
Larsucosterol (0-25 μM; 48 h; macrophages) 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, 5, 10, 15, 20, and 25 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) 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) 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) 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; once every 3 days for 6 weeks
Result:	Decreased plasma cholesterol levels. Reduced serum alkaline phosphatase, ALT, and AST levels.

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.

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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