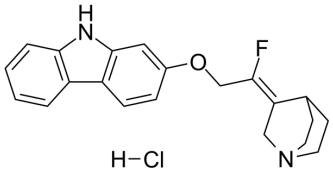
YM-53601

Cat. No.:	HY-100313A
CAS No.:	182959-33-7
Molecular Formula:	$C_{21}H_{22}ClFN_2O$
Molecular Weight:	372.86
Target:	Farnesyl Transferase; HCV
Pathway:	Metabolic Enzyme/Protease; Anti-infection
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

YM-53601, a squalene synthase inhibitor, reduces plasma cholesterol and triglyceride levels in vivo[1]. YM-53601 inhibits squalene synthase derived from human hepatoma cells with an IC_{50} of 79 nM. Lipid-lowering agent[2]. YM-53601 is also an inhibitor of farnesyl-diphosphate farnesyltransferase 1 (FDFT1) enzyme activity and abrogates HCV propagation[3].

In Vitro

YM-53601 inhibits squalene synthase activities in hepatic microsomes from several species of rat, hamster, guinea-pig, rhesus monkey, and human-derived HepG2 cell with IC_{50}s of 90, 170, 46, 45, and 79 nM, respectively[1].

YM-53601 inhibits conversion of [3H]farnesyl diphosphate to [^{3}H]squalene by hamster liver squalene synthase with the IC_{50} of 170 nM[2].

YM-53601 (1 μM) potentiates the susceptibility of H35 cells to thapsigargin, lonidamine, and doxorubicin. YM-53601 (1 μM) reduces the mitochondrial cholesterol levels in both H35 and HepG2 cells[4].

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

Cell Viability Assay[4]

Cell Line:	H35 and HepG2 cells
Concentration:	1 μM
Incubation Time:	24 hours
Result:	Reduced the mitochondrial cholesterol levels in both H35 and HepG2 cells.

In Vivo

YM-53601 suppresses cholesterol biosynthesis in rats (ED_{50}, 32 mg/kg)[1].

YM-53601 also reduces plasma non-HDL cholesterol levels in hamsters by approximately 70% at an oral dose of 50 mg/kg/day for 5 days[2].

YM-53601 potentiates Doxorubicin-mediated hepatocellular carcinoma cells (HCC) growth arrest and cell death in vivo[4].

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

Animal Model:	Sprague-Dawley (SD) rats weighing 150-170 g[1]
Dosage:	6.25, 12.5, 25 or 50 mg/kg
Administration:	Given a single p.o.

Result:	Inhibited cholesterol biosynthesis from acetate in a dose-dependent manner in rats. The ED_{50} value for YM-53601 cholesterol biosynthesis inhibition is 32 mg/kg.

Animal Model:	Five- to six-week-old male BALB/c athymic (nu/nu) nude mice[4]
Dosage:	15 mg/kg
Administration:	2 wk of daily treatment by p.o. gavage
Result:	Significantly decreased the intratumor cholesterol levels.

REFERENCES

[1]. T Ugawa, et al. YM-53601, a novel squalene synthase inhibitor, reduces plasma cholesterol and triglyceride levels in several animal species. Br J Pharmacol. 2000 Sep;131(1):63-70.

[2]. Tsukasa Ishihara, et al. Syntheses of 3-ethylidenequinuclidine derivatives as squalene synthase inhibitors. Part 2: enzyme inhibition and effects on plasma lipid levels. Bioorg Med Chem. 2003 Aug 15;11(17):3735-45.

[3]. Eun-Mee Park, et al. Farnesyl-diphosphate farnesyltransferase 1 regulates hepatitis C virus propagation. FEBS Lett. 2014 May 2;588(9):1813-20.

[4]. Joan Montero,et al.Mitochondrial cholesterol contributes to chemotherapy resistance in hepatocellular carcinoma. Cancer Res. 2008 Jul 1;68(13):5246-56.

Caution: Product has not been fully validated for medical applications. For research use only.

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