Pactimibe

Cat. No.: HY-100401

CAS No.: 189198-30-9

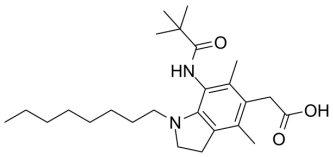
Molecular Formula: $C_{25}H_{40}N_2O_3$

Molecular Weight: 416.6

Target: Acyltransferase

Pathway: Metabolic Enzyme/Protease

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 : 200 mg/mL (480.08 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4004 mL	12.0019 mL	24.0038 mL
	5 mM	0.4801 mL	2.4004 mL	4.8008 mL
	10 mM	0.2400 mL	1.2002 mL	2.4004 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: ≥ 5 mg/mL (12.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pactimibe (CS-505 free base) is a dual ACAT1/2 inhibitor with IC_{50}s of 4.9 μM and 3.0 μM, respectively. Pactimibe (CS-505 free base) inhibits ACAT with IC_{50}s of 2.0 μM, 2.7 μM, 4.7 μM in the liver, macrophages and THP-1 cells, respectively[1]. Pactimibe (CS-505 free base) noncompetitively inhibits oleoyl-CoA with a K_i value of 5.6 μM. Moreover, Pactimibe (CS-505 free base) obviously inhibits cholesteryl ester formation with an IC_{50} of 6.7 μM. Pactimibe (CS-505 free base) possesses anti-atherosclerotic potential with lowering plasma cholesterol activity[2].

IC_{50} & Target

ACAT1 4.9 μM (IC_{50})	ACAT2 3.0 μM (IC_{50})	ACAT 2 μM (IC_{50}, in the liver)	ACAT 2.7 μM (IC_{50}, in macrophages)
ACAT 4.7 μM (IC_{50}, in THP-1 cells)	oleoyl-CoA 5.6 μM (Ki)	cholesteryl ester formation 6.7 μM (IC_{50})	

In Vitro

Pactimibe (CS-505 free base) induces moderate ACAT inhibition in monocyte-derived macrophages, leading to the

	suppression of foam cell formation[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pactimibe (CS-505 free base; 60 and 200 mg/kg/day; oral gavage; twice a day; 12 weeks) induces an inhibition for ACAT-1 and ACAT-2, causing a reduction of plasma cholesterol but no influence on macrophage- or collagen-positive areas[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male C57BL/6J ApoE$^{-/-}$ mice aged 8-week-old[3]
Dosage:	60 and 200 mg/kg/day
Administration:	Oral gavage; twice a day; 12 weeks
Result:	Decreased plasma cholesterol levels by 39% and 74% at the administration of 60 and 200 mg/kg/day

REFERENCES

[1]. Naoki Terasaka, et al. ACAT inhibitor pactimibe sulfate (CS-505) reduces and stabilizes atherosclerotic lesions by cholesterol-lowering and direct effects in apolipoprotein E-deficient mice. Atherosclerosis. 2007 Feb;190(2):239-47.

[2]. Ken Kitayama, et al. Importance of acyl-coenzyme A:cholesterol acyltransferase 1/2 dual inhibition for anti-atherosclerotic potency of pactimibe. Eur J Pharmacol. 2006 Jul 1;540(1-3):121-30.

[3]. Yasunobu Yoshinaka, et al. A selective ACAT-1 inhibitor, K-604, stimulates collagen production in cultured smooth muscle cells and alters plaque phenotype in apolipoprotein E-knockout mice. Atherosclerosis. 2010 Nov;213(1):85-91.

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