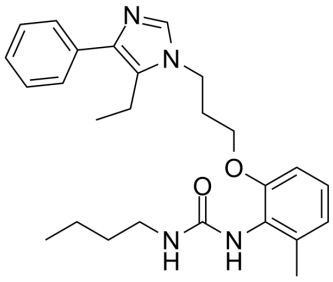
E-5324

Cat. No.:	HY-19183
CAS No.:	141799-76-0
Molecular Formula:	$C_{26}H_{34}N_4O_2$
Molecular Weight:	434.57
Target:	Acyltransferase
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	E-5324 is potent inhibitor of acyl-CoA:cholesterol acyltransferase (ACAT) with IC_{50}s of 44 to 190 nM.
IC_{50} & Target	IC50: 44 to 190 nM (ACAT)[1]
In Vitro	E-5324 is a potent ACAT inhibitor with IC_{50}s of 44 to 190 nM in microsomes. E-5324 shows no effect on triglyceride synthesis up to 10 μM. E-5324 also has no effect on bovine pancreatic cholesterol esterase or lecithin: cholesterol acyltransferase (LCAT) up to 10 μM. E-5324 inhibits the incorporation of [^{3}H]oleate into cholesteryl [^{3}H]oleate in a concentration-dependent manner with an IC_{50} of 0.44 μM. E-5324 also inhibits [^{3}H]cholesteryl ester synthesis with an IC_{50} of 0.41 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The areas under the cholesterol-time curves for duration of this study (AUC) for control, E-5324 0.02% and E-5324 0.1% are 104985±4411, 106096±4476 and 105231±4 348 mg×day/dL, respectively. The high dose of E-5324 (0.1%) significantly reduces the surface involvement by 34% and 54% in the aortic arch and thoracic aorta, respectively. E-5324 treatment significantly reduces the wet weight and protein content. In the aortic arch, the high dose of E-5324 (0.1%) significantly reduces both cholesteryl ester and total cholesterol by 60% and 59%, respectively. The high dose of E-5324 (0.1%) markedly reduces the ACAT activities in the aortic arch and thoracic aorta by 35% and 44%, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	In the study of the inhibitory effect of E-5324, PMA-treated THP-1 cells are incubated in LPDS/RPMI containing 50 μg protein/mL βVLDL for 5 hr. Then, 100 μL of each concentration of E-5324 solution or vehicle (LPDS/RPMI) is added to the cultured cells. After incubation with E-5324 for 30 min, 20 μL of [^{3}H]oleate-BSA complex is added, and the mixture is incubated for 2 hr. The lipids are extracted from the cells with hexane: 2-propanol (3:2, v/v) and then separated by TLC. The remaining cellular protein is dissolved in 0.1 N NaOH[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Forty male WHHL rabbits weighing approximately 1.7 kg at the age of 3 months are used in the experiment. All animals are individually caged and receive 100 g/day of food throughout the experiment. The rabbits are divided into 4 groups so as to make their plasma total cholesterol levels similar. The rabbits are fed a standard rabbit chow, ORC-4, or ORC-4 containing E5324 (0.02% or 0.1% (w/w)), or ORC-4 containing probucol (1% (w/w)) for 16 weeks[2].

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

REFERENCES

[1]. Kogushi M, et al. Effect of E5324, a novel inhibitor of acyl-CoA:cholesterol acyltransferase, on cholesteryl ester synthesis and accumulation in macrophages. Jpn J Pharmacol. 1995 Jun;68(2):191-9.

[2]. Kogushi M, et al. Anti-atherosclerotic effect of E5324, an inhibitor of acyl-CoA:cholesterol acyltransferase, in Watanabe heritable hyperlipidemic rabbits. Atherosclerosis. 1996 Aug 2;124(2):203-10.

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