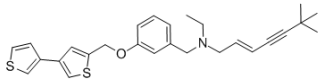
NB-598

Cat. No.:	HY-16343
CAS No.:	131060-14-5
Molecular Formula:	$C_{27}H_{31}NOS_2$
Molecular Weight:	449.67
Target:	Others
Pathway:	Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	NB-598 is a potent and competitive inhibitor of squalene epoxidase (SE), and suppresses triglyceride biosynthesis through the farnesol pathway.
IC_{50} & Target	squalene epoxidase
In Vitro	NB598 (10 μM) causes a 36±7% reduction in total cholesterol level of MIN6 cells. NB598 causes a significant decrease in cholesterol by 49±2%, 46±7%, and 48±2% from PM, ER, and SG, respectively. NB598 dose-dependently inhibits insulin secretion under both basal (1 mM glucose) and glucose-stimulated (16.7 mM glucose) conditions. NB598 at concentrations up to 10 μM does not affect peak outward KV currents or the voltage dependence of activation but increases current inactivation[1]. NB-598 (10 μM) inhibits the synthesis of sterol and sterol ester from [^{14}C]acetate without affecting the synthesis of other lipids such as phospholipids (PL), free fatty acids (FFA) and triacylglycerol (TG). In the absence of exogenous liposomal cholesterol, NB-598 reduces ACAT activity by 31%. NB-598 reduces ACAT activity by 22% even in the presence of a 600 PM concentration of liposomal cholesterol[2]. NB-598 suppresses the secretion of cholesterol and triacylglycerol from HepG2 cells into the medium[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	Caco-2 cells are grown in a 58 cm^2 plastic dish with medium A for 13 days. The cells are washed with medium B, and then cultured with medium B including cholesterol-micelle and each compound. The compound is dissolved in Me_2SO, and the final concentration of Me_2SO is 0.1%(v/v). After 18 hr of incubation, the cells are washed extensively with phosphate-buffered saline (PBS) to remove the compound. Microsomes are prepared as described above. The reaction mixture (0.2 mL) consisted of 0.1 mg microsomes, 0.25% BSA and 40 PM [^{14}C]oleoyl CoA in buffer A. To avoid the effects of endogenous cholesterol, liposome (2 mol of cholesterol: 1 mol of phosphatidylcholine) [15] is added to the reaction mixture. The microsomes are preincubated for 1 hr with or without exogenous cholesterol, and ACAT activity is determined as described above. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Metab. 2020 Apr 7;31(4):862-877.e14.
- Nat Chem Biol. 2016 Jul;12(7):497-503.
- Genome Biol. 2016 Jun 29;17(1):140.
- Cell Rep. 2020 Aug 4;32(5):107944.
- Cell Chem Biol. 2021 Feb 16;S2451-9456(21)00051-9.

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REFERENCES

[1]. Xia F, et al. Inhibition of cholesterol biosynthesis impairs insulin secretion and voltage-gated calcium channel function in pancreatic beta-cells. Endocrinology. 2008 Oct;149(10):5136-45.

[2]. Horie M, et al. Effects of NB-598, a potent squalene epoxidase inhibitor, on the apical membrane uptake of cholesterol and basolateral membrane secretion of lipids in Caco-2 cells. Biochem Pharmacol. 1993 Jul 20;46(2):297-305.

[3]. Horie M, et al. An inhibitor of squalene epoxidase, NB-598, suppresses the secretion of cholesterol and triacylglycerol and simultaneously reduces apolipoprotein B in HepG2 cells. Biochim Biophys Acta. 1993 May 20;1168(1):45-51.

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