Product Data Sheet

Product Name: NB-598 hydrochloride
Cat. No.: GC15686

Chemical Properties

Cas. No.	136719-25-0		
Chemical Name	(E)-N-ethyl-6,6-dimethyl-N-[[3-[(4-thiophen-3-ylthiophen-2-yl)methoxy]phenyl]methyl]hept-2-en-4-yn-1-amine;hydrochloride		
SMILES	CCN(CC=CC#CC(C)(C)C)CC1=CC(=CC=C1)OCC2=CC(=CS2)C3=CSC=C3.Cl		
Formula	$C_{27}H_{32}ClNOS_2$	M.Wt	486.13
Solubility	≥ 54 mg/mL in DMSO with gentle warming, ≥ 49.3 mg/mL in EtOH with gentle warming	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	NB-598 hydrochloride		

Protocol

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Kinase experiment:

Caco-2 cells are grown in a 58 cm2 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 Me2SO, and the final concentration of Me2SO 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 [14C]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.

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.

Background

NB-598 is a competitive inhibitor of squalene epoxidase with IC50 value of 4.4 nM [1]. Low-density lipoprotein (LDL) is a lipoprotein that transfers cholesterol from the liver to all tissues of the body. Increasing concentrations of LDL particles are strongly associated with increasing amounts of atherosclerosis. Therefore the inhibition of cholesterol

synthesis is thought to have hypolipidemic effect. In the complex process of cholesterol synthesis, squalene epoxidase is located in the middle of the pathway and plays an important regulatory role. It is a good target for hypocholesterolemic drugs discovered. As an inhibitor of squalene epoxidase, NB-598 was a benzylamine derivative that screened out from synthetic compounds. It competitively inhibited squalene epoxidase with respect to squalene. The Ki value for it was 0.68 nM. NB-598 inhibited cholesterol synthesis both in vitro and in vivo [1].

NB-598 is a selective inhibitor of squalene epoxidase. It had no inhibition on 2, 3-oxido-squalene cyclase. Unlike those compounds used as antifungal drugs, NB-598 showed no inhibitory effect against Trichophyton mentagrophytes or Candida albicans. In the in vitro assay using microsomes from HepG2 cells, NB-598 inhibited squalene epoxidase with IC50 value of 0.75 nM. In HepG2 cells, NB-598 prevented cells from incorporating acetate into cholesterol with IC50 value of 3.4 nM. It did not affect the synthesis of other lipids such as free fatty acid, triacylglycerol and phospholipids [1].

In rats, oral administration of NB-598 dose-dependently increased serum squalene levels and decreased serum cholesterol levels with ED50 value of 5.1 mg/kg. In beagle dogs, oral administration of NB-598 at dose of 10 mg/kg/day for 28 days significantly lowered cholesterol levels in serum. Besides that, it caused reduction of all classes of lipoprotein cholesterol. It was found that NB-598 reduced LDL cholesterol levels through inducing the activities of LDL receptors [1].

Reference:

[1] Horie M, Tsuchiya Y, Hayashi M, et al. NB-598: a potent competitive inhibitor of squalene epoxidase. Journal of Biological Chemistry, 1990, 265(30): 18075-18078.

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