BioFiles
FOR LIFE SCIENCE RESEARCH
Volume 2 Number 7

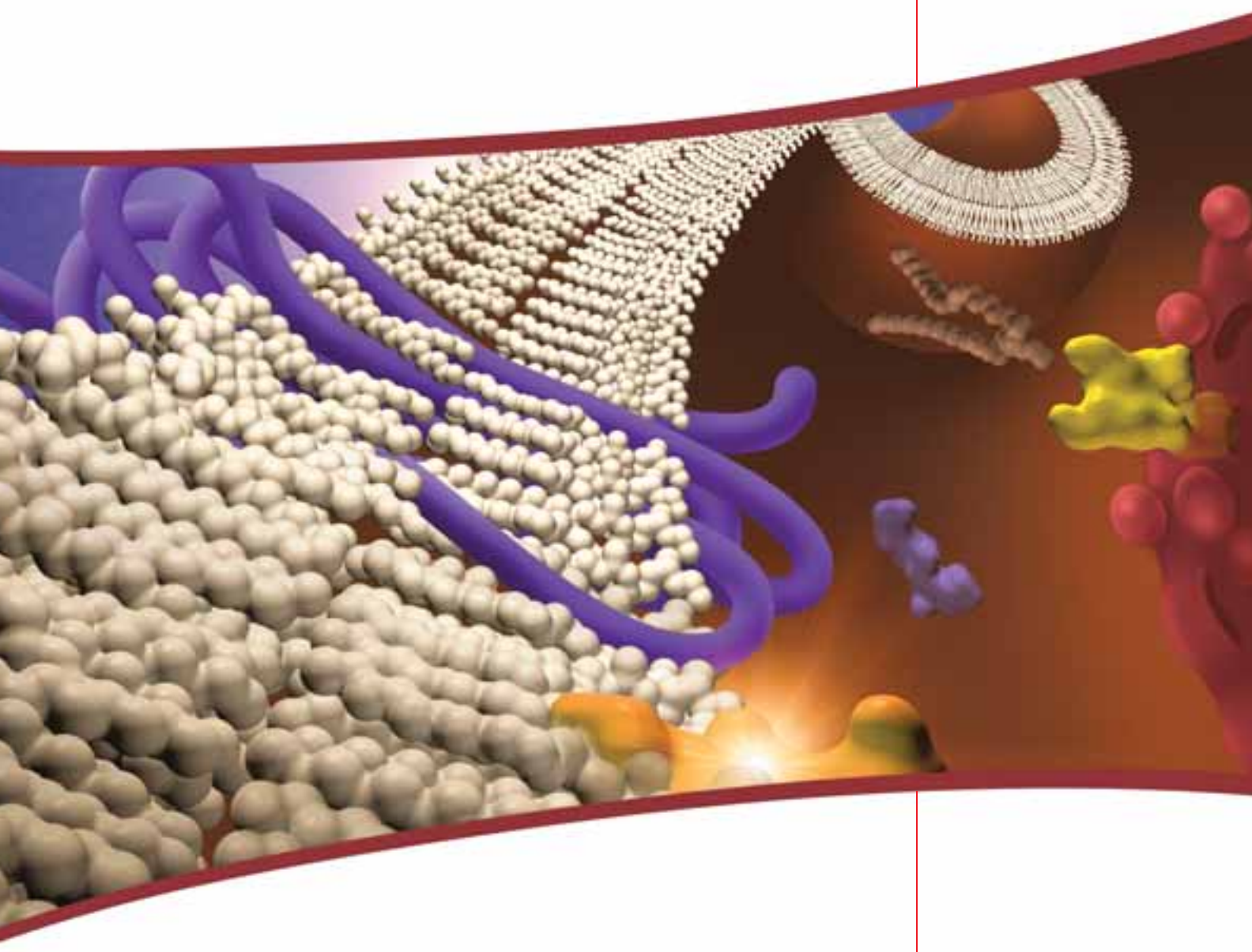
SIGMA Life Science

Cholesterol Homeostasis

Hypercholesterolemia can lead to the formation of plaques and the development of atherosclerosis.

- HMGR Assay Kit
- Cholesterol Biosynthesis
- Blocking Absorption of Dietary Cholesterol
- Cholesterol Esterification
- Cholesterol Transport
- Bile Acids

Lipid Resource



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Introduction

Cholesterol is an essential biological molecule that performs many functions within the body. It is a structural component of all cell membranes and is also a precursor to steroid hormones, vitamin D, and bile acids that aid in digestion. Within membranes the cholesterol to polar lipid ratios affect stability, permeability, and protein mobility. The hormones produced from cholesterol include androgens, estrogens, and the gluco- and mineralocorticoids.

Cholesterol levels in the body are achieved via two sources. Adults with healthy diets will biosynthesize the majority of their cholesterol in the liver and other body tissues and obtain the remainder from the dietary intake of foods high in saturated fatty acids. Free cholesterol is not found in blood; rather it is esterified to fatty acids and packaged in lipoprotein particles. Very low density lipoproteins (VLDL) are produced by the liver and consist of an outer core composed of apolipoproteins; apo-B100, apo-CI, apo-CII, apo-CIII, and apoE surrounding an inner core of phospholipids, triglycerides, cholesterol, and cholesteryl esters. In the blood, VLDL transfers apolipoprotein-CII to high density lipoprotein (HDL) and lipoprotein lipase in the capillaries begins to remove the triglycerides, transforming the particle into an intermediate density lipoprotein (IDL). About 50% of IDL particles are removed from the circulation by the liver. The remaining IDLs are transformed to low density lipoprotein particles (LDL, the so-called "bad" cholesterol) by the loss of apolipoprotein E and the further reduction of triglyceride content until it is exceeded by the content of cholesteryl esters. LDL particles deliver lipids to the body's cells via LDL receptor-mediated endocytosis. When LDL lipids are oxidized by free radicals, they bind more easily to the proteoglycans lining the vascular endothelium, and thus, become incorporated into atherosclerotic plaque.

HDL, the so-called "good" cholesterol is composed of apolipoproteins-CII and E surrounding a lipid core. HDL particles circulate through the capillaries collecting lipids including cholesterol and cholesteryl esters and returning them to the liver for further metabolism. Cholesterol returned to the liver by HDL is synthesized into bile acids. Bile acids facilitate the digestion of lipids by acting as emulsifying agents and also aid in the absorption of fat-soluble vitamins. Cholesterol is ultimately excreted from the body as bile acids.

Excessive levels of oxidized LDL in the blood can lead to potential health risks. Normally cholesterol levels are tightly controlled by complex mechanisms. When dietary intake of cholesterol is high, biosynthesis is reduced. However, the body's homeostatic mechanisms can be inadequate when baseline endogenous cholesterol biosynthesis becomes excessive or when dietary cholesterol intake is overwhelming. For these instances, drugs have been discovered that can reduce cholesterol biosynthesis (statins), reduce the intestinal absorption of dietary cholesterol and other lipids (ezetimibe), or enhance the metabolic utilization of lipids in the liver (fibrates). These drugs serve to keep the blood levels of LDL in check to avoid the deleterious effects that can arise from the accumulation of vascular plaque, including such serious medical conditions as atherosclerosis, coronary artery disease, and stroke.

This issue of BioFiles highlights the product groups that Sigma offers to further the research of cholesterol absorption, biosynthesis, transport, and excretion. We introduce two key research tools in the HMG-CoA Reductase enzyme and assay kit. We also showcase a number of important cholesterol lowering molecules including statins, sterols, and stanols.

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Cholesterol Homeostasis

HMG-CoA Reductase (HMGR) Assay Kit

3-hydroxy-3-methylglutaryl-CoA reductase (HMGR) is a transmembrane glycoprotein, located on the endoplasmic reticulum.[1] This enzyme catalyzes the four-electron reduction of HMG-CoA to coenzyme A and mevalonate, which is the rate-limiting step in sterol biosynthesis.[2] The activity of HMGR is controlled through synthesis, degradation, and phosphorylation in order to maintain the concentration of mevalonate derived products. In addition to the physiological regulation of HMGR, the human enzyme has been targeted successfully by drugs in the clinical treatment of high serum cholesterol levels.[3,4] Controlling serum cholesterol levels has an important therapeutic role as hypercholesterolemia often leads to the development of atherosclerosis and consequently to cardiovascular pathologies, which might result in myocardial infarction and stroke. Recent evidence suggests that a disturbance of cholesterol homeostasis contributes to the development of a chronic inflammatory state.[5]

Kit Features and Benefits

- Contains all the reagents for a simple and rapid measurement of HMGR enzyme activity
- Includes an HMGR control enzyme, enabling screening of HMGR inhibitors and activators
- Includes a control inhibitor
- Sufficient for 30 assays of 1 mL or 100 assays of 200 µL

Principle of the Assay

Reaction scheme:

$$HMG\text{-}CoA + 2NADPH + 2H^{+} \xrightarrow{HMGR} mevalonate + 2NADP^{+} + CoASH$$

The assay is based on a spectrophotometric measurement of the decrease in absorbance, which represents the oxidation of NADPH by the catalytic subunit of HMGR in the presence of the substrate HMG-CoA.

Applications

- Basic research of cholesterol and other related metabolic pathways
- Detection of HMGR activity as well as screening for different inhibitors/activators of the enzyme (which may play a crucial role in therapeutics)

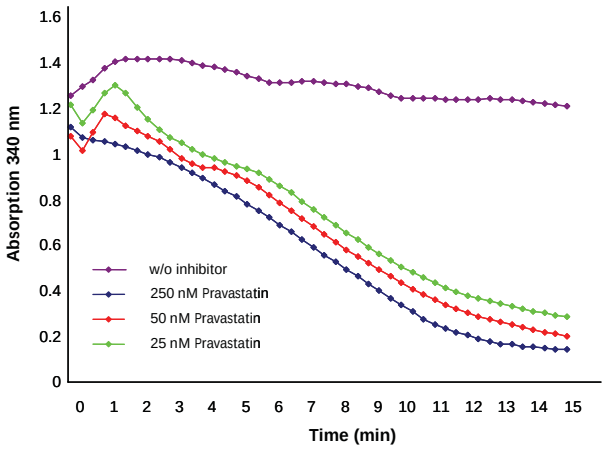

Figure 1. Inhibition of HMG-CoA reductase (HMGR) activity by Pravastatin.

Approximately 6 µg of HMGR enzyme (Catalog Number H7039) was incubated at 37 °C with 400 µM NADPH, 0.3 mg/ml HMG-CoA, and different concentrations of Pravastatin, which is a specific inhibitor of HMG-CoA reductase. The assay was performed in a UV compatible
96 well plate, according to the HMG-CoA Reductase Assay Kit protocol.

References

1. Koning, A.J., et. al., Different subcellular localization of *Saccharomyces cerevisiae* HMG-CoA reductase isozymes at elevated levels corresponds to distinct endoplasmic reticulum membrane proliferations. *Mol. Biol*. Cell, **7**, 769-789 (1996).
2. Holdgate, G.A., et. al., Molecular mechanism for inhibition of 3-hydroxy-3-methylglutaryl CoA (HMG-CoA) reductase by rosuvastatin. *Biochem. Soc. Trans.*, **31**, 528-531 (2003).
3. Istvan, E.S., et. al., Crystal structure of the catalytic portion of human HMG-CoA reductase: insights into regulation of activity and catalysis. *EMBO J.*, **19**, 819-830 (2000).
4. Istvan, E.S., and Deisenhofer, J., The structure of the catalytic portion of human HMG-CoA reductase. *Biochim. Biophys. Acta*, **1529**, 9-18 (2000).
5. Kleemann, R., and Kooistra, T., HMG-CoA reductase inhibitors: effects on chronic subacute inflammation and onset of atherosclerosis induced by dietary cholesterol. *Curr. Drug Targets Cardiovas. Haemat., Disord.*, **5**, 441-453 (2005).

Kit Components

Product Name	Pack Size
Assay Buffer, 5×	10 mL
NADPH Cat. No. **N6505**	25 mg
Substrate Solution (HMG-CoA)	2 mL
HMG-CoA Reductase (catalytic domain) (0.55-0.65 mg/mL)	200 µL
Inhibitor Solution (Pravastatin)	200 µL

Kit Components

Cat. No.	Product Name	Pack Size
CS1090	HMG-CoA Reductase Assay kit	1 kit

Cholesterol Biosynthesis

Cholesterol levels in the body come from two sources, dietary intake and biosynthesis. The majority of cholesterol utilized by healthy adults is synthesized in the liver, which produces ~70% of the total daily cholesterol requirement (~1 gram). The other 30% comes from dietary intake.

Biosynthesis of cholesterol generally takes place in the endoplasmic reticulum of hepatic cells and begins with acetyl-CoA, which is mainly derived from an oxidation reaction in the mitochondria. However, acetyl-CoA can also be derived from the cytoplasmic oxidation of ethanol by acetyl-CoA synthetase. Acetyl-CoA and acetoacetyl-CoA are converted to 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) by HMG-CoA synthase.

HMG-CoA is then converted to mevalonate by HMG-CoA reductase (HMGR). This reaction is completed with the aid of NADPH, which is used as a cofactor for all reduction reactions throughout cholesterol synthesis. Mevalonate undergoes a series of phosphorylations and a decarboxylation yielding the isoprenoid, isopentenyl pyrophosphate (IPP). A series of condensing reactions occur, catalyzed by squalene synthase, leading to the production of squalene. From squalene, lanosterol, the first of the sterols is formed. The conversion of lanosterol to cholesterol requires 19 additional reaction steps.

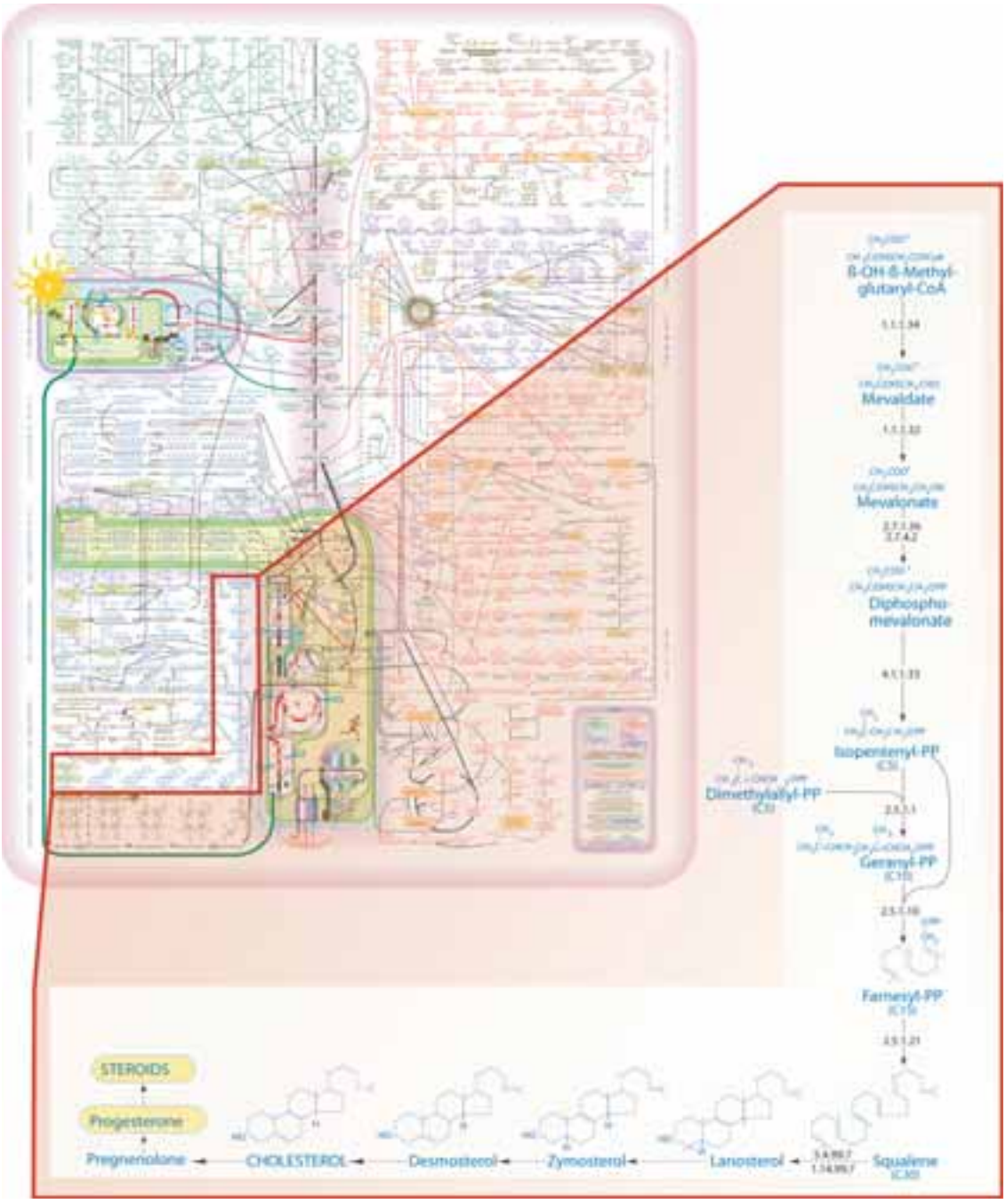

Figure 1. IUBMB-Sigma-Nicholson Metabolic Pathways Chart. This chart can be viewed in detail at **sigma.com/metapath.**

The conversion of HMG-CoA to mevalonate by HMG-CoA reductase is the rate-limiting step of cholesterol biosynthesis and is under strict regulatory control (see **Figure 1**). HMGR is the target of compounds that are effective in lowering serum cholesterol levels. Human HMG-CoA reductase consists of a single polypeptide chain of 888 amino acids. The amino-terminal residues are membrane bound and reside in the endoplasmic reticulum membrane, while the catalytic site of the protein resides in its cytoplasmic, soluble carboxy-terminal portion. A linker region connects the two portions of the protein.

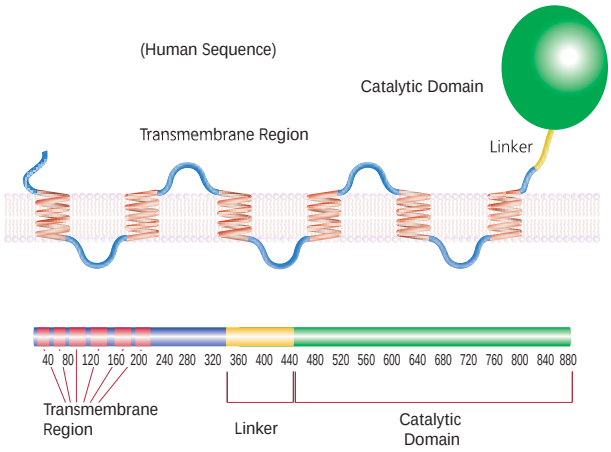

Figure 1. HMG-CoA Reductase.

3-Hydroxy-3-methylglutaryl-CoA reductase human NEW

HMG-CoA Reductase; HMGR

Hydroxy-3-methylglutaryl-CoA reductase catalyzes the committed step in cholesterol biosynthesis.

Consists of a single polypeptide chain of 888 amino acids. The amino-terminal residues are membrane bound and reside in the endoplasmic reticulum membrane, while the catalytic site of the protein resides in its cytoplasmic, soluble C-terminal portion. A linker region connects the two portions of the protein.

Supplied as a solution containing 250 µg protein in 50 mM Tris pH 7.5, with 5 mM DTT, 1:200 Protease Inhibitor Cocktail (Catalog Number P8340) and 50% (w/v) glycerol.

≥90% (SDS-PAGE)

activity: 2-8 units/mg protein

One unit will convert 1.0 µmole of NADPH to $NADP^+$ per minute at 37 °C.

store at: −70°C

H7039-250UG	250 µg

DL-3-Hydroxy-3-methylglutaryl coenzyme A sodium salt

HMG-CoA

$C_{27}H_{44}N_7O_{20}P_3S$ FW 1009.67 [103476-21-7]

▸ **min. 90%**

Key intermediate in the biosynthesis of terpenes, cholesterol, and ketone bodies.

store at: −20°C

H6132-5MG	5 mg
H6132-10MG	10 mg
H6132-25MG	25 mg

(±)-Mevalonolactone

(±)-β-Hydroxy-β-methyl-δ-valerolactone; (±)-3-Hydroxy-3-methyl δ-valero-lactone; DL-Mevalolactone; DL-Mevalonic acid lactone

$C_6H_{10}O_3$ FW 130.14 [674-26-0]

▸ **~97% (titration)**

store at: −20°C

M4667-1G	1 g
M4667-5G	5 g
M4667-10G	10 g

Isopentenyl pyrophosphate triammonium salt solution

IPP

$C_5H_{12}O_7P_2 \cdot 3NH_3$ FW 297.18 [116057-53-5]

Intermediate in terpene biosynthesis.

▸ **1 mg/mL in methanol: aqueous 10 mM NH_4OH (7:3), ≥95% (TLC)**

vial of 200 µg

store at: −20°C

I0503-1VL	1 vial
I0503-5VL	5 vials

γ,γ-Dimethylallyl pyrophosphate triammonium salt

DMAPP

$C_5H_{12}O_7P_2 \cdot 3NH_3$ FW 297.18 [1186-30-7]

▸ **1 mg/mL in methanol: aqueous 10 mM NH_4OH (7:3), ≥90% (TLC)**

Intermediate in terpene biosynthesis

vial of 200 µg

store at: −20°C

D4287-1VL	1 vial
D4287-5VL	5 vials

Geranyl pyrophosphate ammonium salt

trans-3,7-Dimethyl-2,6-octadienyl pyrophosphate; GPP

$C_{10}H_{20}O_7P_2 \cdot 3NH_3$ FW 365.30 [763-10-0]

▸ **1 mg/mL in methanol: aqueous 10 mM NH_4OH (7:3), ≥95% (TLC)**

Intermediate in terpene biosynthesis

vial of 200 µg

store at: −20°C

G6772-1VL	1 vial
G6772-5VL	5 vials

Farnesyl pyrophosphate ammonium salt

FPP; 3,7,11-Trimethyl-2,6,10-dodecatrien-1-yl pyrophosphate ammonium salt

$C_{15}H_{37}N_3O_7P_2$ FW 433.42 [13058-04-3]

▸ Solution in methanol: 10 mM aqueous NH_4OH (7:3), ≥95% (TLC)

Isoprenoid from the intracellular mevalonate pathway used for prenylation of several low molecular mass G proteins, including Ras.

Actual concentration given on label

vial of 200 µg

store at: -20°C

F6892-1VL	1 vial
F6892-5VL	5 vials

Squalene

2,6,10,15,19,23-Hexamethyl-2,6,10,14,18,22-tetracosahexaene

$[(CH_3)_2C[=CHCH_2CH_2C(CH_3)]_2=CHCH_2-]_2$ FW 410.72 [111-02-4]

▸ ≥98%

Biosynthetic precursor to all steroids. Cytoprotective to normal cells exposed to carcinogens and antitumor agents.

store at: 2-8°C

S3626-10ML	10 mL
S3626-100ML	100 mL
S3626-500ML	500 mL
S3626-1L	1 L

Lanosterol

3β-Hydroxy-8,24-lanostadiene; 8,24-Lanostadien-3β-ol

$C_{30}H_{50}O$ FW 426.72 [79-63-0]

▸ from sheep wool, ~97%

Cholesterol precursor sterol

store at: -20°C

L5768-1MG	1 mg
L5768-5MG	5 mg

Desmosterol

5,24-Cholestadien-3β-ol; 24-Dehydrocholesterol; 3β-Hydroxy-5,24-cholestadiene

$C_{27}H_{44}O$ FW 384.64 [313-04-2]

▸ ≥85% (GC)

store at: -20°C

D6513-5MG	5 mg
D6513-10MG	10 mg

Cholesterol

5-Cholesten-3β-ol; 3β-Hydroxy-5-cholestene

$C_{27}H_{46}O$ FW 386.65 [57-88-5]

Major component of all biological membranes; ~25% of total brain lipid is cholesterol.

▸ from bovine, ≥95% (GC), Ash free

Precipitated from alcohol

store at: 2-8°C

C3292-10G	10 g
C3292-100G	100 g
C3292-500G	500 g

▸ from porcine liver, Grade I, ~99%

Formerly Cat. No. CH-PL

C3137-1G	1 g
C3137-5G	5 g
C3137-25G	25 g

▸ from sheep wool, ~95% (GC)

Equivalent to USP/NF

C8503-25G	25 g
C8503-100G	100 g
C8503-500G	500 g
C8503-1KG	1 kg
C8503-5KG	5 kg

▸ from bovine, Sigma Grade, ≥99%

Standard for chromatography

store at: -20°C

C8667-500MG	500 mg
C8667-1G	1 g
C8667-5G	5 g
C8667-25G	25 g
C8667-100G	100 g

SyntheChol®

Cholesterol

▸ synthetic, ≥98%

Synthesized from material of non-animal origin

store at: 2-8°C

C9913-50MG	50 mg
C9913-500MG	500 mg

Biosynthesis Regulation

The amount of cholesterol that is synthesized in the liver is tightly regulated by dietary cholesterol levels. When dietary intake of cholesterol is high, synthesis is decreased and when dietary intake is low, synthesis is increased. However, cholesterol produced in other tissues is under no such feedback control. Cholesterol and similar oxysterols act as regulatory molecules to maintain healthy levels of cholesterol.

LDL receptors regulate the cellular transport of lipid rich low density lipoprotein (LDL) particles. One mechanism for regulating LDL receptor expression and controlling the expression of all the enzymes in the cholesterol biosynthetic pathway is dependent on Sterol-Sensitive Response Elements (SREs). SREs are found in the promoters of the genes coding for the enzymes of the cholesterol biosynthetic pathway and LDL receptors. Transcription factors important to activating SREs are Sterol Regulating Element Binding Proteins (SREBPs). Due to their ability to bind SREs, SREBPs play an instrumental role in cholesterol homeostasis. These transcription regulating proteins are bound by another protein called SREBP cleavage activating proteins (SCAPs). SCAPs bind to SREBPs in the endoplasmic reticulum (ER) where a regulatory domain within SCAP responds to the level of oxysterols present in the cell. When oxysterol levels are low the SCAP/SREBP complex moves to the Golgi where SREBP is cleaved and a portion of it can now move into the nucleus, where it interacts with SREs to promote gene expression. When oxysterol levels are high the SCAP/SREBP complex remains in the ER preventing cleaved SREBP from promoting gene expression.

SREBPs serve to regulate all 12 enzymes in the cholesterol biosynthetic pathway including the rate limiting enzyme HMG-CoA reductase (HMGR). High dietary sterol levels acting on SCAP ultimately stop the maturation of SREBPs, resulting in the down regulation of key enzymes such as HMGR, thus, reducing the amount of cholesterol produced by the liver. Limiting cholesterol synthesis leads to a homeostatic response in which cells increase the density of LDL receptors on their surfaces. This increases the clearance rate of LDL particles from the plasma and reduces plasma LDL cholesterol and its related health risks. The decrease in cholesterol synthesis also promotes an increase of HDL, thus, clearing even more cholesterol from the plasma.

AY 9944

trans-1,4-bis(2-Chlorobenzylaminoethyl) cyclohexane dihydrochloride

$C_{22}H_{30}Cl_4N_2$ FW 464.30 [366-93-8]

Cholesterol synthesis inhibitor; inhibits both 7-dehydrocholesterol Δ7-reductase and Δ8,7-sterol isomerase.

▶ **≥99% (HPLC)**

solubility DMSO.....14 mg/mL

store at: 2-8°C

C5364-5MG	5 mg
C5364-25MG	25 mg

BM 15766 sulfate

4-[2-[4-[3-(4-Chlorophenyl)-2-propenyl]-1-piperazinyl]ethyl]benzoic acid sulfate

$C_{22}H_{25}ClN_2O_2 \cdot H_2SO_4$ FW 482.98 [86621-94-5]

Dehydrocholesterol reductase inhibitor.
Inhibits 7-dehydrocholesterol Δ7-reductase, which catalyzes the last step of cholesterol synthesis.

▶ **≥98% (HPLC)**

store at: 2-8°C

B8685-1MG	1 mg
B8685-5MG	5 mg

Brassicasterol

5,22-Cholestadien-24β-methyl-3β-ol

$C_{28}H_{46}O$ FW 398.66 [474-67-9]

Brassicasterol is a phytosterol found in rapeseed and canola oils; it is also present in marine algae and shellfish. Brassicasterol has been shown to inhibit sterol Δ24-reductase, an enzyme involved in the mammalian cholesterol biosynthesis pathway.1

▶ **from semisynthetic**

store at: 2-8°C

B4936-5MG	5 mg

Cerulenin

(2*R*,3*S*,*E*,*E*)-2,3-Epoxy-4-oxo-7,10-dodecadienamide

$C_{12}H_{17}NO_3$ FW 223.27 [17397-89-6]

Antibiotic; fatty acid synthase inhibitor.

▶ **~95%, from** *Cephalosporium caerulens*

store at: -20°C

C2389-5MG	5 mg
C2389-10MG	10 mg
C2389-50MG	50 mg

Clofibrate

2-(4-Chlorophenoxy)-2-methylpropionic acid ethyl ester; Ethyl 2-(4-chloro-phenoxy)isobutyrate; Ethyl 2-(4-chlorophenoxy)-2-methylpropionate

$C_{12}H_{15}ClO_3$ FW 242.70 [637-07-0]

Antihyperlipoproteinemic believed to act by inhibiting cholesterol biosynthesis.

store at: 2-8°C

C6643-250MG	250 mg
C6643-1G	1 g
C6643-5G	5 g
C6643-10G	10 g

7-Dehydrocholesterol

5,7-Cholestadien-3β-ol; (−)-7-Dehydrocholesterol; 3β-Hydroxy-5,7-cholestadiene; Provitamin D_3

$C_{27}H_{44}O$ FW 384.64 [434-16-2]

Down-regulates cholesterol biosynthesis in cultured Smith-Lemi-Opitz syndrome skin fibroblasts.

▶ **≥85%**

Sealed ampule

Do not confuse with dihydrocholesterol.

store at: −20°C

D4429-1G	1 g
D4429-5G	5 g
D4429-25G	25 g

25-Hydroxycholesterol

5-Cholestene-3β,25-diol

$C_{27}H_{46}O_2$ FW 402.65 [2140-46-7]

▶ **≥98%**

Suppresses the cleavage of sterol regulatory element binding proteins (SREBPs). 25-Hydroxycholesterol induces apoptosis through down-regulation of Bcl-2 expression and activation of caspases.

H1015-10MG	10 mg
H1015-25MG	25 mg
H1015-100MG	100 mg

Lycopene

ψ,ψ-Carotene; 2,6,10,14,19,23,27,31-Octamethyldotriaconta-2,6,8,10,12,14,16,18,20,22,24,26,30-tridecaene

$C_{40}H_{56}$ FW 536.87 [502-65-8]

▶ **≥90%, from tomato**

sealed ampule

ship: dry ice store at: −70°C

L9879-1MG	1 mg
L9879-5MG	5 mg
L9879-10MG	10 mg

Ro 48-8071 fumarate

[4'-[6-(Allylmethylamino)hexyloxy]-4-bromo-2'-fluorobenzophenone fumarate (1:1)

$C_{23}H_{27}NO_2BrF \cdot C_4H_4O_4$ FW 564.44 [189197-69-1]

Orally active 2,3-oxidosqualene:lanosterol cyclase inhibitor. 2,3-Oxidosqualene:lanosterol cyclase (OSC, E.C. 5.4.99.7) represents a unique target for a cholesterol lowering drug. Partial inhibition of OSC should reduce synthesis of lanosterol and subsequent sterols, and also stimulate the production of epoxysterols that repress HMG-CoA reductase expression, generating a synergistic, self-limited negative regulatory loop.

▶ **≥98% (HPLC)**

solubility H_2O.....>5 mg/mL at ~60 °C

store at: 2-8°C

R2278-5MG	5 mg
R2278-25MG	25 mg

SR 12813

Tetraethyl 2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethenyl-1,1-bisphosphonate

$C_{24}H_{42}O_7P_2$ FW 504.53 [126411-39-0]

Cholesterol lowering drug; HMGCoA reductase inhibitor.

▶ **≥98%**

solubility H_2O.....insoluble
DMSO.....≥10 mg/mL

S4194-1MG	1 mg
S4194-5MG	5 mg

U 18666A

(3β)-3-[2-(Diethylamino)ethoxy]androst-5-en-17-one dihydrochloride

$C_{25}H_{41}NO_2 \cdot 2HCl$ FW 460.52 [3039-71-2]

Inhibitor of cholesterol synthesis (inhibits desmosterol Δ24-reductase); Weak inhibitor of hedgehog (hh) signaling.

solubility H_2O.....9 mg/mL at ≤60 °C

store at: 2-8°C

U3633-5MG	5 mg
U3633-25MG	25 mg

Statins

A widely used method to induce a decrease in cholesterol biosynthesis and its downstream effects is to introduce statins. Statins are a class of hypolipidemic agents that have been shown to specifically inhibit HMG-CoA reductase. The following statins are listed in increasing order of LDL lowering potency with simvastatin being the most potent of these products.

Mevastatin

Compactin; ML-236B

$C_{23}H_{34}O_5$ FW 390.51 [73573-88-3]

▶ **≥95% (HPLC)**

HMG-CoA reductase inhibitor
Cholesterol lowering drug
Inhibits myoblast formation.

solubility ethanol.....25 mg/mL
DMSO.....20 mg/mL

store at: 2-8°C

M2537-5MG	5 mg

Pravastatin sodium

Eptastatin sodium; (β*R*,δ*R*,1*S*,2*S*,6*S*,8*S*,8a*R*)-1,2,6,7,8,8a-Hexahydro-β,δ,6-trihydroxy-2-methyl-8[(2S)-2-methyl-1-oxobutoxyl]-1-naphthalene-heptanoic acid sodium

$C_{23}H_{35}O_7Na$ FW 446.51 [81131-70-6]

Competitive, water-soluble 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor. Inhibits cholesterol synthesis *in vivo* (K_i ~1 nM).

▶ **≥98% (HPLC)**

solubility H_2O.....19 mg/mL

store at: 2-8°C

P4498-25MG	25 mg

Mevinolin from *Aspergillus* sp.

Lovastatin; 6-α-Methylcompactin; 2-Methyl-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester butanoic acid; Mevacor; Monacolin K

$C_{24}H_{36}O_5$ FW 404.54 [75330-75-5]

▶ **≥98% (HPLC)**

Cholesterol lowering drug and competitive inhibitor of HMG-CoA reductase, a rate limiting enzyme in cholesterol synthesis. Blocks the production of mevalonate, a critical compound in the production of cholesterol and isoprenoids. This product is a substrate of Pgp and CYP3A. It increases cellular resistance to anticancer agents such as doxorubicin and induces apoptosis in myeloma cells. The roles of Pgp and CYP3A, possible connection between drug resistance, regulation of the mevalonate pathway, and iosprenylation of signaling proteins in these observations remain to be resolved.

store at: 2-8°C

M2147-25MG	25 mg

Simvastatin

$C_{25}H_{38}O_5$ FW 418.57 [79902-63-9]

Simvastatin is a specific inhibitor of HMG-CoA reductase, the enzyme that catalyzes the conversion of HMG-CoA to mevalonate, an early step in cholesterol biosynthesis. It is used in the treatment of hypercholesterolemia, as it reduces levels of low-density lipoproteins and triglycerides, and raises high-density lipoprotein levels. Simvastatin is a lactone that is readily hydrolyzed *in vivo* to the corresponding ß-hydroxyacid, and can be activated prior to use with NaOH in EtOH treatment. It is a synthetic analog of lovastatin (Catalog Number M2147). Besides being used clinically for prevention and treatment of atherosclerosis, simvastatin, along with other statins, is being investigated at the molecular level in order to elucidate other cellular effects it has in addition to lowering cholesterol levels and to investigate its potential role in numerous other disease states.

▶ **≥98% (HPLC)**

solubility DMSO.....≥20 mg/mL

store at: 2-8°C

S6196-5MG	5 mg
S6196-25MG	25 mg

Blocking Absorption of Dietary Cholesterol

Dietary cholesterol is obtained from foods derived from animal sources that are rich in fat content. A healthy adult only needs to ingest about 30% of the daily cholesterol requirement. Obtaining more than this amount from dietary cholesterol can lead to increased cholesterol levels and serious health risks.

Dietary cholesterol is absorbed within the lumen of the small intestine. Bile salts produced from cholesterol in the liver interact with phospholipids to produce a biliary micelle that is transported via bile into the lumen. Dietary cholesterol in the lumen is easily incorporated into these micelles and together with the already present biliary cholesterol can now be absorbed into the enterocytes that make up the walls of the lumen. The micelles enter the cell by a channel know as Niemann-Pick C1 Like 1 protein (NPC1L1). Once in the cells the cholesterol can either be pumped back out into the lumen or it can be esterified for transport within chylomicrons.

Preventing the absorption of this dietary cholesterol has become a key area in cholesterol related research. Plant sterols and stanols have been shown to be effective inhibitors of cholesterol absorption. Ingested as part of a normal diet, plant sterols and stanols are very similar in structure to cholesterol. They actually have a stronger binding affinity than cholesterol to the biliary micelles that aid in absorption. Because of this the sterols and stanols can displace cholesterol from the micelles thus preventing its absorption.

Recently, inhibitors that block the absorption of the biliary micelles into the enterocytes have also been used to block the uptake of dietary cholesterol.

β-Sitosterol

α-Dihydrofucosterol; 22,23-Dihydrostigmasterol; 24β-Ethylcholesterol; 5-Stigmasten-3β-ol

$C_{29}H_{50}O$ FW 414.71 [83-46-5]

▸ **synthetic, ≥95%**

Synthetic form of a plant derived estrogen

store at: -20°C

S1270-10MG	10 mg
S1270-25MG	25 mg
S1270-100MG	100 mg

▸ **from soybean, ≥97%**

Plant derived estrogen

store at: -20°C

S9889-1MG	1 mg
S9889-5MG	5 mg
S9889-10MG	10 mg

Campesterol

24(*R*)-Ergost-5-en-3β-ol; 24α-Methyl-5-cholesten-3β-ol

$C_{28}H_{48}O$ FW 400.68 [474-62-4]

▸ **from *Glycine max* (soybean), ~65%**

Plant sterol. May lower absorption of dietary cholesterol.

Appears ~98% by HPLC and GC, but has been shown by ^{13}C-NMR to contain ~35% dihydrobrassicasterol (24β-methyl-5-cholesten-3β-ol; 24[*S*]-ergost-5-en-3β-ol).

store at: -20°C

C5157-1MG	1 mg
C5157-5MG	5 mg
C5157-10MG	10 mg
C5157-25MG	25 mg

Stigmasterol

3β-Hydroxy-24-ethyl-5,22-cholestadiene; 5,22-Stigmastadien-3β-ol; Stigmasterin

$C_{29}H_{48}O$ FW 412.69 [83-48-7]

▸ **~95%**

S2424-1G	1 g
S2424-5G	5 g
S2424-10G	10 g
S2424-25G	25 g

Stigmastanol

24α-Ethyl-5α-cholestan-3β-ol; 24α-Ethyl-5α-cholestan-3β-ol; β-Sistostanol; β-Sitostanol; Dihydro-β-sitosterol; Stigmastan-3β-ol

$C_{29}H_{52}O$ FW 416.72 [19466-47-8]

▸ **95%**

S4297-1G	1 g
S4297-5G	5 g

Cholesterol Esterification

To more efficiently transport both dietary and synthesized cholesterol, it is converted to cholesteryl esters. Free cholesterol can be taken up by lipoproteins, but is confined to the outer surface of the particle. By converting cholesterol to cholesteryl esters more cholesterol can be packaged into the interior of lipoproteins. This vastly increases the capacity of lipoproteins, allowing for more efficient cholesterol transport through the blood stream.

Distinct enzymes catalyze the cholesterol to cholesteryl ester conversion depending on the location of the reaction. The conversion of cholesterol to cholesteryl ester is catalyzed predominantly by lecithin:cholesterol acyltransferase (LCAT) in the peripheral tissues (see **Figure 1**). In the lumen, dietary cholesterol absorbed by enterocytes is esterified by acyl-coenzyme A: cholesterol acyltransferase 2 (ACAT2), which is found in both the intestine and liver (see **Figure 2**). ACAT1 is found in all tissues. LCAT and ACAT also differ in the sources they use for the acyl chains. LCAT uses phosphatidylcholine while ACAT uses acyl-CoA. Inhibiting these enzymes is one way of lowering the circulating lipids in plasma.

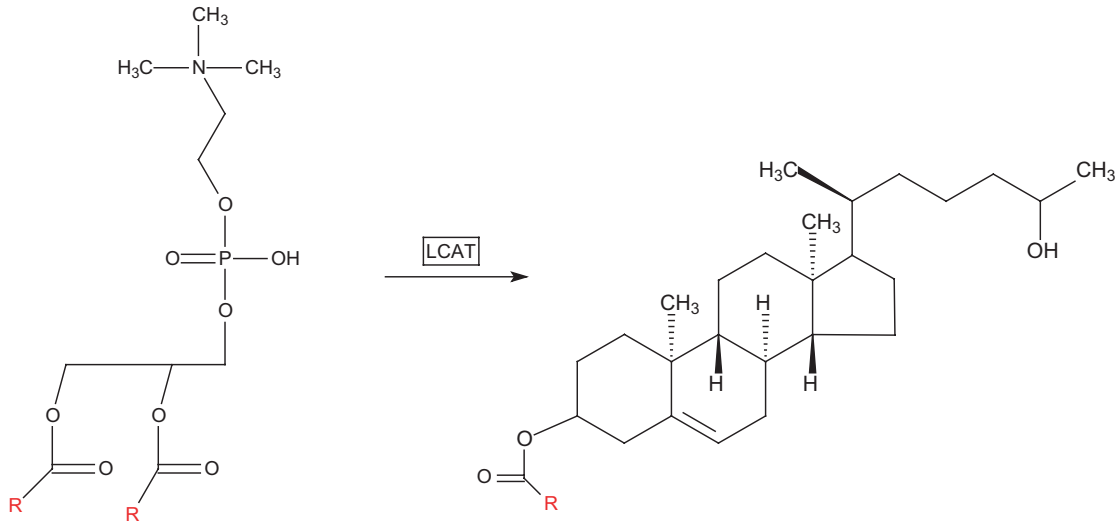

Figure 1. Lecithin:Cholesterol acyltransferase (LCAT) is found in peripheral tissues and utilizes phosphatidylcholine as the source of acyl chains.

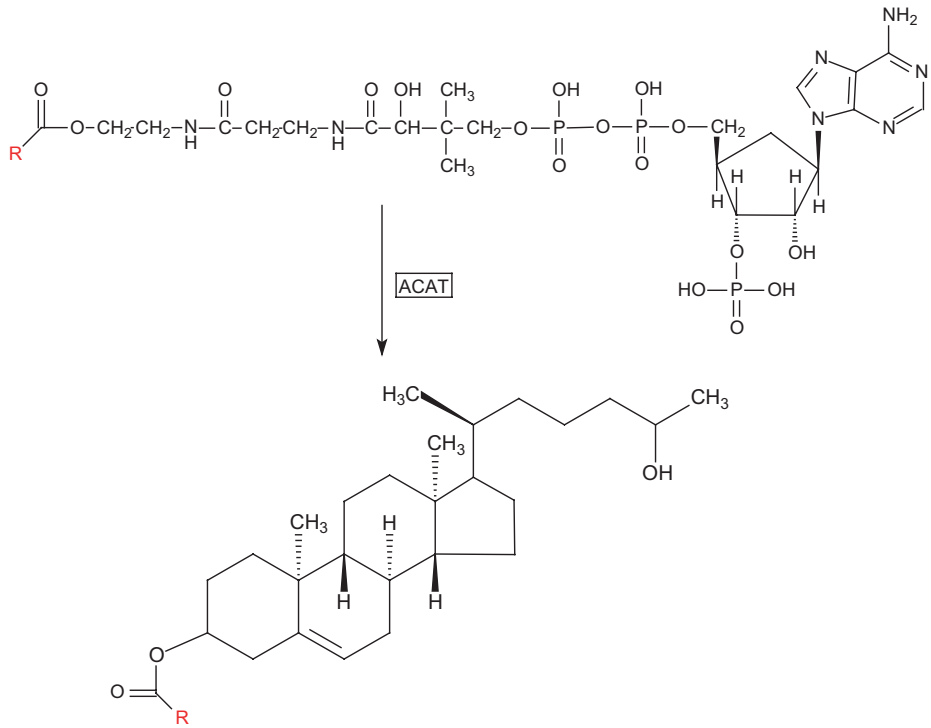

Figure 2. Acyl-coenzyme A:cholesterol acyltransferase 2 (ACAT2) is found in the liver and intestine, and utilizes acyl-CoA as the source of acyl chains.

Sandoz 58-035

3-[Decyldimethylsilyl]-*N*-[2-(4-methylphenyl)-1-phenethyl]propanamide; SA 58-035

$C_{30}H_{47}NOSi$ FW 465.79 [78934-83-5]

Acyl-CoA:cholesterol acyltransferase (ACAT) inhibitor.

▸ **>98% (HPLC)**

solubility H_2O.....insoluble
DMSO.....16 mg/mL

store at: 2-8°C

S9318-5MG	5 mg
S9318-25MG	25 mg

YIC-C8-434

N-(3,5-Dimethoxy-4-*n*-octyloxycinnamoyl)-N′-(3,4-dimethylphenyl)piperazine

$C_{31}H_{44}N_2O_4$ FW 508.69 [214265-97-1]

Acyl-CoA:cholesterol acyltransferase (ACAT) inhibitor.

Enzyme target for lipid-lowering drugs IC_{50}= 63-88 nM.

▸ **>98% (HPLC)**

solubility DMSO.....>8 mg/mL

Y0628-5MG	5 mg

Cholesteryl acetate

3β-Acetoxy-5-cholestene; 5-Cholesten-3β-ol 3-acetate; 3β-Hydroxy-5-cholestene 3-acetate

$C_{29}H_{48}O_2$ FW 428.69 [604-35-3]

▸ **purum, ≥95.0% (HPLC)**

store at: room temp

26750-50G-F	50 g

Cholesteryl arachidonate

5-Cholesten-3β-ol 3-arachidonate; Cholesteryl eicosatetraenoate; 3β-Hydroxy-5-cholestene 3-arachidonate

$C_{47}H_{76}O_2$ FW 673.11 [604-34-2]

▸ **≥95% (HPLC; detection at 205 nm)**

ship: dry ice store at: -20°C

C8753-10MG	10 mg
C8753-25MG	25 mg
C8753-100MG	100 mg
C8753-500MG	500 mg

Cholesteryl hexanoate

5-Cholesten-3β-ol 3-hexanoate; Cholesteryl caproate; 3β-Hydroxy-5-cholestene 3-hexanoate

$C_{33}H_{56}O_2$ FW 484.80 [1062-96-0]

store at: -20°C

C6524-25G	25 g
C6524-100G	100 g

Cholesteryl linoleate

5-Cholesten-3β-ol 3-linoleate; Cholesteryl octadecadienoate; Cholesteryl 9,12-octadecadienoate; 3β-Hydroxy-5-cholestene 3-linoleate

$C_{45}H_{76}O_2$ FW 649.08 [604-33-1]

The most abundant cholesteryl ester in low density lipoprotein (LDL).

▸ **≥98% (HPLC; detection at 205 nm)**

Sealed ampule

store at: -20°C

C0289-100MG	100 mg
C0289-250MG	250 mg
C0289-1G	1 g

Cholesteryl oleate

5-Cholesten-3β-ol 3-oleate; Cholesteryl *cis*-9-octadecenoate; 3β-Hydroxy-5-cholestene 3-oleate; Oleic acid cholesteryl ester

$C_{45}H_{78}O_2$ FW 651.10 [303-43-5]

▸ **≥98% (HPLC; detection at 205 nm)**

store at: -20°C

C9253-100MG	100 mg
C9253-250MG	250 mg
C9253-500MG	500 mg
C9253-1G	1 g

Cholesteryl palmitate

5-Cholestene 3-palmitate

$C_{43}H_{76}O_2$ FW 625.06 [601-34-3]

▸ **≥98% (HPLC; detection at 205 nm)**

store at: -20°C

C6072-1G	1 g
C6072-10G	10 g

Cholesteryl stearate

5-Cholesten-3β-yl octadecanoate

$C_{45}H_{80}O_2$ FW 653.12 [35602-69-8]

▸ **96%**

C79409-25G	25 g

Cholesterol Esterase

Cholesterol is transported throughout the body in the form of cholesterol esters. Excess cholesterol is also stored intracellulary as cholesterol esters. The enzyme cholesterol esterase controls the hydrolysis of these stored cholesterol esters yielding bioavailable cholesterol and fatty acids. Cholesterol esterase hydrolyzes long-chain and unsaturated fatty acid esters at a greater rate than short chain saturated fatty acids.

Cholesterol esterase also contributes to the incorporation of cholesterol into mixed micelles and aids in the transport of free cholesterol into the enterocyte.

Cholesterol Esterase from bovine pancreas

Sterol-ester acylhydrolase

[9026-00-0]

Protein determined by biuret.

Enzyme responsible for the hydrolysis of many of the fatty acid esters of cholesterol.

Optimum pH range: 6-8

Activators: Bisphenol A diglycidyl ether, cAMP-dependent protein kinase type II, ethanol, methanol, *n*-butanol, phosphatidylcholine, phosphatidylethanolamine, sodium taurocholic acid

Inhibitors: Bisphenol A methacrylate, diisopropylfluorophosphate, enolase, Hg^{2+}, sodium fluoride, phosphatidic acid, phosphatidylcholine, phosphatidylserine

▸ **activity: ≥200 units/g protein**

Partially purified

composition

protein 30-65%

One unit will hydrolyze 1.0 µmole of cholesteryl oleate to cholesterol and oleic acid per min at pH 7.0 at 37 °C in the presence of taurocholate.

store at: -20°C

C3766-100UN	100 units
C3766-500UN	500 units

Cholesterol Esterase from porcine pancreas

Cholesterol Esterase from hog pancreas

▸ **activity: ≥15,000 units/g protein**

Contains potassium phosphate buffer salts and stabilizer.

composition

Protein ~70%

One unit will hydrolyze 1.0 µmole of cholesteryl oleate to cholesterol and oleic acid per min at pH 7.0 at 37 °C in the presence of taurocholate.

store at: -20°C

C9464-25UN	25 units
C9464-100UN	100 units

Cholesterol Esterase from *Pseudomonas fluorescens*

One unit will hydrolyze 1.0 µmole of cholesteryl oleate to cholesterol and oleic acid per min at pH 7.0 at 37 °C in the presence of taurocholate.

▸ **activity: ≥10,000 units/g protein**

Contains potassium phosphate and TRITON® X-100.

composition

Protein ~20%

store at: -20°C

C9281-100UN	100 units
C9281-500UN	500 units

▸ **activity: ≥200,000 units/g protein**

store at: -20°C

C1403-25UN	25 units
C1403-100UN	100 units

Diethylumbelliferyl phosphate

DEUP; UBP

$C_{14}H_{17}O_6P$ FW 312.25 [897-83-6]

Selective, potent cholesterol esterase inhibitor. Blocks steroidogenesis primarily by preventing cholesterol transport into the mitochondria of steroidogenic cells. Inhibitors of cholesterol esterase are anticipated to limit the absorption of dietary cholesterol. IC_{50} = 11.6 µM.

▸ **>98% (HPLC)**

solubility DMSO.....5 mg/mL

store at: -20°C

D7692-5MG	5 mg
D7692-25MG	25 mg

Cholesterol Transport

Since cholesterol is a water-insoluble molecule it must be packaged for transport within the plasma. The particles that package cholesterol, cholesteryl esters, and triglycerides for transport, are called lipoproteins. There are five main classifications of lipoproteins based on their size and density. The higher the ratio of protein to lipid content the higher the density.

The largest and least dense lipoproteins are chylomicrons (see **Figure 1**). Chylomicrons predominately transport triacylglycerols to adipose tissue and muscle as fatty acids, but also deliver dietary cholesterol taken up by enterocytes in the lumen to the liver. Once most of the triacylglycerols have been delivered to the adipose tissue and muscle, the remnants of the lipoprotein, including cholesterol, apoE, and apo-B48 are then delivered to, and taken up by, the liver through interaction with the chylomicron remnant receptor.

Figure 1. Chylomicron.

Very low density lipoproteins (VLDL) are smaller and more dense than chylomicrons (see **Figure 2**). VLDLs contain triacylglycerols, some cholesterol and cholesteryl esters and the apoproteins; apo-B100, apo-CI, apo-CII, apo-CIII, and apoE. VLDLs exist to remove triacylglycerols and cholesteryl esters from the liver and distribute them throughout the body. As VLDLs move into the circulating plasma they are converted first to intermediate density lipoproteins (IDL) and then into low density lipoproteins (LDL). Lipoprotein lipase serves to remove the majority of fatty acids from both the VLDL and IDL, thus increasing the density of the lipoproteins while maintaining cholesterol and cholesteryl ester concentrations. The removal of fatty acids and the loss of all apolipoproteins except apoB-100 and apo(a) results in LDL. LDLs are the primary plasma carriers of cholesterol for delivery to all tissues. LDL can be absorbed by the liver and other tissues via receptor mediated endocytosis.

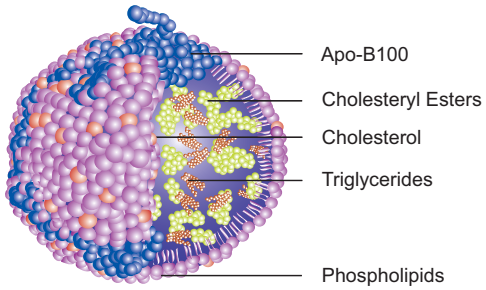

Figure 2. Low Density Lipoprotein.

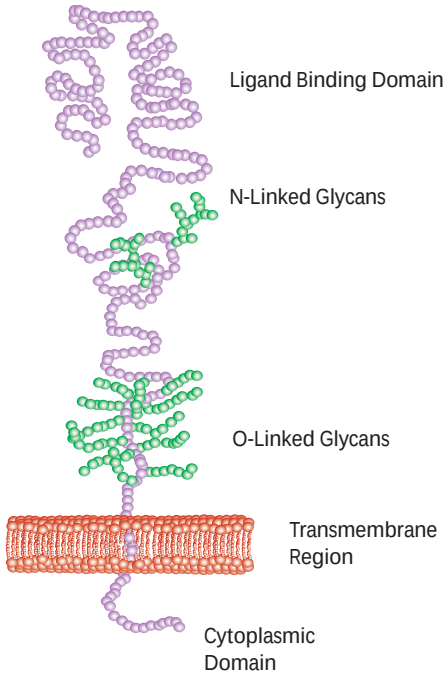

Figure 3. LDL Receptor.

The cytoplasmic domain of the LDL receptor facilitates the formation of coated pits; receptor-rich regions of the membrane. The ligand binding domain of the receptor recognizes apo-B100 on LDL, resulting in the formation of a clathrin-coated vesicle that buds from the inner surface of the cell membrane (see **Figure 3**). ATP-dependent proton pumps lower the pH inside the vesicle resulting in dissociation of LDL from its receptor. After loss of the clathrin coat, the vesicles fuse with lysozomes resulting in peptide and cholesteryl ester enzymatic hydrolysis. The LDL receptor can be recycled to the cell membrane. Insulin, triiodothyronine, and dexamethasone have been shown to affect the regulation of LDL receptor mediated endocytosis.

High density lipoproteins (HDL) are the smallest of the lipoproteins and most dense. HDL contains several types of apolipoproteins including apo-AI, II & IV, apo-CI, II & III, apoD and apoE. HDL contains mostly protein, phospholipids, cholesteryl esters, and cholesterol. HDL is produced as a protein rich particle in the liver and intestine, and serves as a circulating source of Apo-CI & II and ApoE proteins. The HDL protein particle accumulates cholesteryl esters by the esterification of cholesterol by lecithin:cholesterol acyl-transferase (LCAT). LCAT is activated by apo-AI on HDL. HDL can acquire cholesterol from cell membranes and can transfer cholesteryl esters to VLDL and LDL via the transferase activity of apoD. HDL can return to the liver where cholesterol is removed by reverse cholesterol transport, thus, serving as a scavenger of free cholesterol.

Apolipoprotein Composition of Lipoproteins

	Chylo-micron	VLDL	IDL	LDL	HDL
Apo-AI (28 kDa)	X				
Apo-AII (17.4 kDa)	X				
Apo-AIV (46 kDa)	X				
Apo-B48 (241 kDa)	X				
Apo-B100 (513 kDa)		X	X	X	
Apo-CI (6.6 kDa)	X	X	X		
Apo-CII (8.8 kDa)	X	X	X		
Apo-CIII (8.8 kDa)	X	X	X		
Apo-D (20 kDa)					X
Apo-E (34 kDa)	X	X	X		
Apo-H (50 kDa)	X				
Apo(a) (300-800 kDa)				X	

Apolipoprotein A-I from human plasma

Apo A-I

Apo-AI comprises ~70% of the protein moiety in HDL. It is a single polypeptide chain consisting of 245 amino acids with glutamic acid as the C-terminal residue and aspartic acid as the N-terminal residue. The molecular mass is reported to be 28.3 kDa. The protein is made up of one major isoform (pI 5.6) and two minor isoforms (pI 5.53 and 5.46). Apo-AI shows a high content of α-helix structure. The amphipathic regions in the α-helix structure seem to be responsible for lipid binding capacity. In aqueous solution, Apo-AI shows self-association with minor conformation change. Apo-AI activates lecithin:cholesterol acyltransferase (LCAT), which is responsible for cholesterol esterification in plasma.

Apo-AI levels in normal plasma are 90-130 mg/dl. Apo-AI levels may be inversely related to the risk of coronary disease.

Major protein components in high density lipoprotein (HDL)

▶ **≥85% (SDS-PAGE)**

Solution in 10 mM ammonium bicarbonate

ship: dry ice store at: -20°C

A0722-.5MG	0.5 mg
A0722-1MG	1 mg

Apolipoprotein A-II from human plasma

Apo A-II

Unlike Apo A-I, Apo A-II possesses no activating properties for lecithin:cholesterol acyltransferase (LCAT). Furthermore, it was found that Apo A-II inhibits the activation of LCAT by Apo A-I.

Apo A-II constitutes ~20% of the protein moiety of high density lipoprotein (HDL).

Forms dimers in aqueous solutions with an association constant of 5×10^4 M^{-1}. The association is accompanied by an enhancement of ~35% in α-helical content.

mol wt 17.38 kDa

▶ **>95% (SDS-PAGE)**

Solution in 10 mM ammonium bicarbonate.

ship: dry ice store at: -20°C

A0972-.5MG	0.5 mg
A0972-1MG	1 mg

Apolipoprotein B from human plasma

▶ **~95%**

Lyophilized from buffer containing 10 mM sodium deoxycholate, 0.05 M sodium carbonate, and 0.05 M sodium chloride, pH 10.0

Delipidated with sodium deoxycholate.

store at: -20°C

A5353-.5MG	0.5 mg

Apolipoprotein C-I from human plasma

Interferes directly with fatty acid uptake and is the major plasma inhibitor of cholesterol ester transfer protein.

Very low density lipoprotein.

average mol wt 6.6 kDa

▶ **>95% (SDS-PAGE)**

Lyophilized from 10 mM NH_4HCO_3, pH 7.5

store at: -20°C

A7785-100UG	100 µg

Apolipoprotein C-II from human plasma

Activates lipoprotein lipase

average mol wt 8.8 kDa

▶ **>95% (SDS-PAGE)**

store at: -20°C

A7910-50UG	50 µg

Apolipoprotein C-III from human plasma

NEW

Apo C-III

Apolipoprotein C-III (Apo C-III) is central in regulating the metabolism of triglyceride-rich lipoproteins. It is an inhibitor of lipoprotein lipase (LPL). Reduced levels of Apo C-III result in higher fatty acid uptake from plasma triglycerides into adipose tissue.

Solution in 10 mM ammonium bicarbonate.

mol wt 8.75 kDa

store at: -20°C

A3106-100UG	100 µg

Apolipoprotein E2 human

Apo E2

Apolipoprotein E2 is a member of the apolipoprotein E family of plasma lipoproteins. It regulates plasma lipid levels by increasing the degradation of particles rich in triglycerides and cholesterol. It binds to LDL receptors, and particles containing apolipoprotein E2 bind amyloid-β protein, the major component of plaques in Alzheimer's disease, which it delivers to the microglia, the major scavenger cells of brain. Compared to apolipoprotein E3, apolipoprotein E2 is associated with lower plasma LDL levels and may protect against the development of atherosclerosis. Apolipoprotein E2 also appears to be associated with reduced risk for Alzheimer's disease.

mol wt ~34 kDa

▸ **≥90% (SDS-PAGE), recombinant, expressed in baculovirus infected *Sf* cells**

Human recombinant Apo E2 competes with iodinated human low density lipoprotein for binding to the human Apo B/E (LDL) receptor. Human recombinant Apo E also binds to β-amyloid peptide in a soluble binding assay.

Solution in 0.7 M ammonium bicarbonate.

store at: -20°C

A2673-50UG	50 µg

Apolipoprotein E3 human

Apo E3

▸ **≥95% (SDS-PAGE), recombinant, expressed in baculovirus infected *Sf*21 cells**

Apolipoprotein E3 is a major plasma lipoprotein and the dominant allele of the apolipoprotein E family. It regulates plasma lipid levels by increasing the degradation of particles rich in triglycerides and cholesterol. It binds to LDL receptors and is involved in the development of atherosclerosis. ApoE-containing particles in plasma and cerebrospinal fluid bind amyloid-β protein, the major component of plaques in Alzheimer's disease, which they deliver to the microglia, the major scavenger cells of brain.

Human recombinant Apo E3 competes with iodinated human low density lipoprotein for binding to the human Apo B/E (LDL) receptor. Human recombinant Apo E also binds to β-amyloid peptide in a soluble binding assay.

Solution in 0.7 M ammonium bicarbonate.

mol wt ~34 kDa

ship: dry ice store at: -20°C

A2331-50UG	50 µg

Apolipoprotein E4 human

Apolipoprotein E4 is a member of the apolipoprotein E family of plasma lipoproteins. It regulates plasma lipid levels by increasing the degradation of particles rich in triglycerides and cholesterol. It binds to LDL receptors and particles containing apolipoprotein E4 and also binds amyloid-β protein, the major component of plaques in Alzheimer's disease, which it delivers to the microglia, the major scavenger cells of brain.

▸ **recombinant, expressed in baculovirus infected *Spodoptera frugiperda* cells**

Human recombinant Apo E4 competes with iodinated human low density lipoprotein for binding to the human Apo B/E (LDL) receptor.

Solution in 0.7 M ammonium bicarbonate.

store at: -20°C

A2456-50UG	50 µg

Lipoprotein, high density from human plasma

HDL; High density lipoprotein; α-Lipoprotein

Lyophilized from a solution of 0.15 M NaCl and 0.01% EDTA, pH 7.4

vial of ~10 mg protein (modified Lowry)

store at: 2-8°C

L1567-10MG	10 mg

▸ **>95% (SDS-PAGE)**

Solution in 150 mM NaCl and 0.01% EDTA, pH 7.4

vial of 10 mg protein

ship: wet ice store at: 2-8°C

L8039-10MG	10 mg

Lipoprotein, low density from human plasma

LDL; β-Lipoprotein; Low density lipoprotein

Lyophilized from a solution of 0.15 M NaCl and 0.01% EDTA, pH 7.4

vial of ~5 mg protein

store at: 2-8°C

L8292-1VL	1 vial

▸ **≥95% (SDS-PAGE)**

Solution in 150 mM NaCl and 0.01% EDTA, pH 7.4

ship: wet ice store at: 2-8°C

L7914-5MG	5 mg

Lipoprotein, very low density from human plasma

Pre-β-lipoprotein; Very low density lipoprotein; VLDL

▸ **≥95% (SDS-PAGE)**

Solution in 150 mM NaCl and 0.01% EDTA, pH 7.4

store at: 2-8°C

L7527-1MG	1 mg

Lipoprotein Regulation

A number of compounds have the ability to affect levels of lipoproteins circulating in the blood. Risk of atherosclerosis can be greatly reduced when these compounds are used in combination with inhibitors of cholesterol biosynthesis.

Fenofibrate

2-[4-(4-Chlorobenzoyl)phenoxy]-2-methylpropanoic acid isopropyl ester

$C_{20}H_{21}ClO_4$ FW 360.83 [49562-28-9]

▶ ≥**99%**

Lipid regulating drug. Increases high density lipoprotein levels by reducing cholesteryl ester transfer protein expression.

F6020-5G	5 g
F6020-25G	25 g
F6020-100G	100 g

Gemfibrozil

2,2-Dimethyl-5-(2,5-dimethylphenoxy)pentanoic acid

$C_{15}H_{22}O_3$ FW 250.33 [25812-30-0]

Selectively increases Apolipoprotein A-I levels.

G9518-5G	5 g
G9518-25G	25 g

Nicotinic acid

Niacin; Pellagra preventive factor; 3-Picolinic acid; Pyridine-3-carboxylic acid; Vitamin B_3

$C_6H_5NO_2$ FW 123.11 [59-67-6]

▶ ≥**98%**

Decreases hepatic production of very-low density lipoproteins and apolipoprotein B.

N4126-5G	5 g
N4126-100G	100 g
N4126-500G	500 g
N4126-1KG	1 kg

Probucol

$C_{31}H_{48}O_2S_2$ FW 516.84 [23288-49-5]

Enhances selective uptake of HDL-associated cholesteryl esters.

P9672-50G	50 g

Bile Acids

The liver excretes excess cholesterol in the form of bile acids. Bile acids serve two purposes: to remove unwanted cholesterol from the body and to aid in lipid digestion in the intestine. Bile acids are synthesized in hepatocytes and this production is tightly controlled by the nuclear receptor transcription factors, Liver X Receptors (LXR-α and LXR-β). Activation of LXRs by specific oxysterol derivatives leads to the regulation of bile acid synthesis and reverse cholesterol transport. LXRs control the activation of 7α-hydroxylase, which is the rate limiting enzyme in the pathway for bile acid biosynthesis. This enzyme converts cholesterol into 7-hydroxycholesterol. 7-hydroxycholesterol is converted to one of the two primary bile acids, cholic acid and chenodeoxycholic acid. (see **Figure 1**) Bile acids are then delivered to the intestines where they aid in absorption of lipids. Some bile acids are lost during this process; however, a majority of bile acids delivered to the intestine are recycled by absorption in the ileum and returned to the liver. Back in the liver glyco- and tauroconjugate bile acids are formed and moved to the gall bladder for storage and use again as digestion aids.

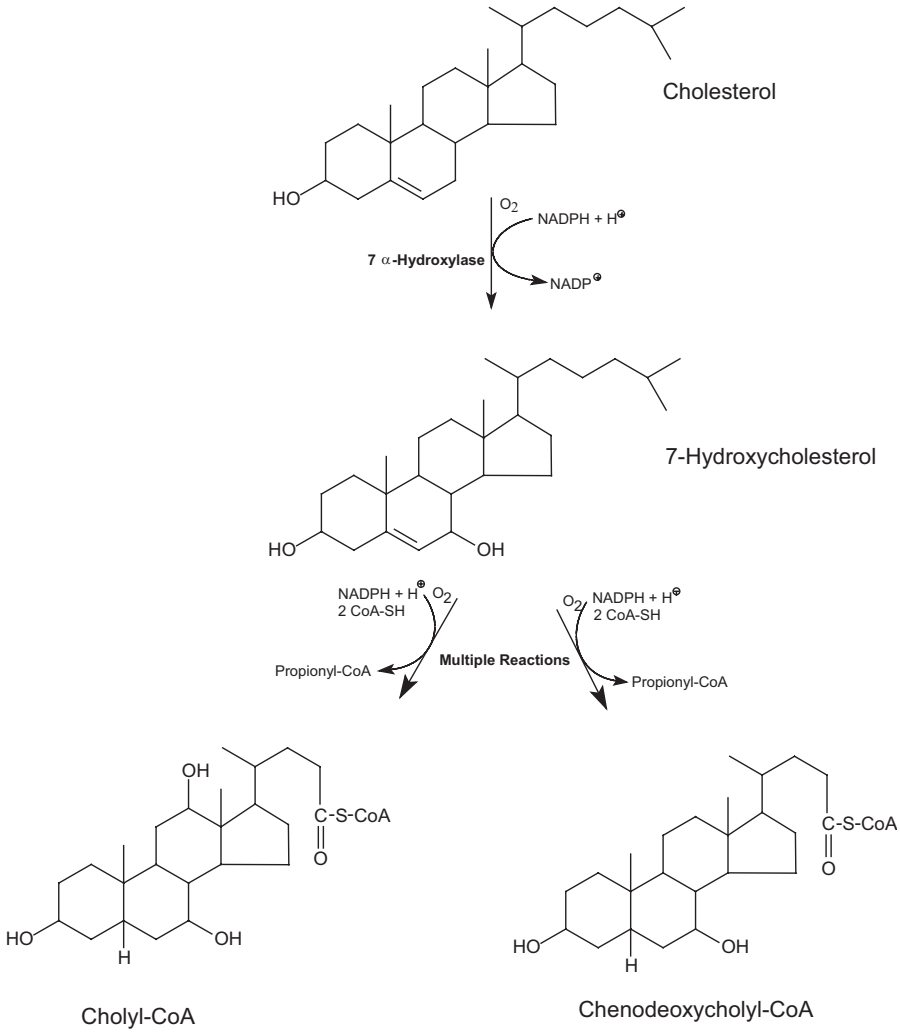

Figure 1. Bile Acid Biosynthesis Pathway.

Cholic acid

Cholanic acid; 3α,7α,12α-Trihydroxy-5β-cholanic acid

$C_{24}H_{40}O_5$ FW 408.57 [81-25-4]

Bile Acid

▶ **from ox or sheep bile, ≥98%**

C1129-25G	25 g
C1129-100G	100 g
C1129-500G	500 g
C1129-1KG	1 kg

Chenodeoxycholic acid

Chenodiol; 5β-Cholanic acid-3α,7α-diol; 3α,7α-Dihydroxy-5β-cholanic acid

$C_{24}H_{40}O_4$ FW 392.57 [474-25-9]

▶ **≥98%**

Bile Acid

C9377-100MG	100 mg
C9377-5G	5 g
C9377-25G	25 g

Dehydrocholic acid

5β-Cholanic acid-3,5,12-trione; 3,7,12-Trioxo-5β-cholanic acid

$C_{24}H_{34}O_5$ FW 402.52 [81-23-2]

Bile Acid

solubility ethanol.....10 mg/mL

D3750-25G	25 g

Deoxycholic acid

7-Deoxycholic acid; Desoxycholic acid; 3α,12α-Dihydroxy-5β-cholanic acid

$C_{24}H_{40}O_4$ FW 392.57 [83-44-3]

▶ **≥99% (TLC and titration)**

Bile Acid

D2510-10G	10 g
D2510-100G	100 g
D2510-500G	500 g

Glycocholic acid hydrate

Cholylglycine; 3α,7α,12α-Trihydroxy-5β-cholan-24-oic acid *N*-(carboxy-methyl)amide; *N*-(3α,7α,12α-Trihydroxy-24-oxocholan-24-yl)-glycine

$C_{26}H_{43}NO_6 \cdot xH_2O$ FW 465.62 (Anh) [475-31-0]

▶ **synthetic, ≥97% (TLC)**

Bile Acid

G2878-100MG	100 mg
G2878-500MG	500 mg
G2878-1G	1 g
G2878-5G	5 g
G2878-25G	25 g

Lithocholic acid

5β-Cholan-24-oic acid-3α-ol; 3α-Hydroxy-5β-cholanic acid; 3α-Hydroxy-5β-cholan-24-oic acid

$C_{24}H_{40}O_3$ FW 376.57 [434-13-9]

▶ **≥97% (titration)**

Bile Acid

L6250-10G	10 g
L6250-25G	25 g

Sodium chenodeoxycholate

Chenodeoxycholic acid sodium salt; Chenodesoxycholic acid; Chenodiol; 5β-Cholanic acid-3α,7α-diol; 3α,7α-Dihydroxy-5β-cholanic acid

$C_{24}H_{39}NaO_4$ FW 414.55 [2646-38-0]

▶ **≥97%**

Bile Salt

C8261-500MG	500 mg
C8261-1G	1 g

Sodium cholate hydrate

Cholalic acid sodium salt; 3α,7α,12α-Trihydroxy-5β-cholan-24-oic acid sodium salt

$C_{24}H_{39}NaO_5 \cdot xH_2O$ FW 430.55 (Anh) [206986-87-0]

▶ **from ox or sheep bile, ≥99%**

Bile Salt

C1254-25G	25 g
C1254-100G	100 g
C1254-500G	500 g
C1254-1KG	1 kg
C1254-5KG	5 kg

Sodium deoxycholate

7-Deoxycholic acid sodium salt; Desoxycholic acid sodium salt; 3α,12α-Dihydroxy-5β-cholanic acid sodium salt

$C_{24}H_{39}NaO_4$ FW 414.55 [302-95-4]

▶ **≥97% (titration)**

Solubilizes fats for absorption in the intestines.

D6750-10G	10 g
D6750-25G	25 g
D6750-100G	100 g
D6750-500G	500 g

Sodium deoxycholate monohydrate

$C_{24}H_{39}NaO_4 \cdot H_2O$ FW 432.57 [145224-92-6]

▸ **SigmaUltra, ≥99% (titration)**

Bile Salt

pH....7.5-9.5, 0.1 M H_2O at 20 °C
Al..... ≤0.002%
Bi..... ≤0.0005%
Cd..... ≤0.0005%
Cr.....≤0.0005%
Fe.....≤0.001%
Li.....≤0.0005%
M..... ≤0.0005%
Ni.....≤0.0005%
Sr..... ≤0.002%
sulfate (SO_4^{2-})..... ≤0.02%
Ba.....≤0.0005%
Ca.....≤0.05%
Co.....≤0.0005%
Cu.....≤0.0005%
K.....≤0.005%
Mg.....≤0.002%
Mo..... ≤0.0005%
Pb..... ≤0.0005%
Zn..... ≤0.0005%

solubility H_2O.....0.1 M at 20 °C, clear, colorless

$A_{260}^{0.1M}$, H_2O.....≤0.10

$A_{260}^{0.1M}$, H_2O.....≤0.08

Insoluble matter..... passes filter test

Cholic acid.....≤0.5%

D5670-5G	5 g
D5670-25G	25 g

Sodium glycodeoxycholate

3α,12α-Dihydroxy-5β-cholan-24-oic acid *N*-(carboxymethyl)amide; *N*-(3α,12α-Dihydroxy-24-oxocholan-24-yl)glycine; Glycodeoxycholic acid sodium salt; Glycodesoxycholic acid

$C_{26}H_{42}NNaO_5$ FW 471.61 [16409-34-0]

Induces apoptosis in hepatocytes; may induce DNA cleavage.

▸ **SigmaUltra, ≥97% (TLC)**

Bile Salt

chloride (Cl^-)..... ≤1%
Al.....≤0.0005%
Cu.....≤0.0005%
K.....≤0.005%
NH_4^+.....≤0.05%
Zn..... ≤0.0005%
sulfate (SO_4^{2-})..... ≤0.05%
Ca.....≤0.005%
Fe.....≤0.001%
Mg.....≤0.001%
Pb..... ≤0.001%

solubility H_2O.....0.1 M at 20 °C, clear, colorless
Insoluble matter.....≤0.1%
Phosphorus (P).....≤0.001%

G9910-250MG	250 mg
G9910-1G	1 g
G9910-5G	5 g

Sodium glycocholate hydrate

N-Cholylglycine sodium salt; Glycocholic acid sodium salt hydrate; 3α,7α,12α-Trihydroxy-5β-cholan-24-oic acid *N*-(carboxymethyl) amide sodium salt; *N*-(3α,7α,12α-Trihydroxy-24-oxocholan-24-yl) glycine sodium salt

$C_{26}H_{42}NO_6Na \cdot xH_2O$ FW 487.60 (Anh) [863-57-0]

▸ **≥97% (TLC)**

Bile Salt

G7132-100MG	100 mg
G7132-500MG	500 mg
G7132-1G	1 g
G7132-5G	5 g
G7132-25G	25 g
G7132-50G	50 g

Sodium taurodeoxycholate hydrate

2-([3α,12α-Dihydroxy-24-oxo-5β-cholan-24-yl]amino)ethanesulfonic acid; Taurodeoxycholic acid sodium salt hydrate

$C_{26}H_{44}NO_6SNa$ FW 521.69 (Anh) [207737-97-1]

▸ **SigmaUltra, ≥97% (TLC)**

Bile Salt

chloride (Cl^-).....≤0.05%
Al..... ≤0.0005%
Cu..... ≤0.0005%
K..... ≤0.01%
NH_4^+..... ≤0.05%
Zn..... ≤0.0005%
sulfate (SO_4^{2-})..... ≤0.05%
Ca..... ≤0.005%
Fe..... ≤0.0005%
Mg..... ≤0.005%
Pb..... ≤0.001%

solubility H_2O.....0.5 M at 20 °C, clear, colorless to faintly yellow
Insoluble matter.....≤0.1%
Phosphorus (P).....≤0.002%

T0557-500MG	500 mg
T0557-1G	1 g
T0557-5G	5 g

Sodium taurocholic acid hydrate

Sodium taurocholate hydrate; 3α,7α,12α-Trihydroxy-5β-cholan-24-oic acid *N*-(2-sulfoethyl)amide; 2-[(3a,7a,12a-Trihydroxy-24-oxo-5b-cholan-24-yl)amino]ethanesulfonic acid

$C_{26}H_{44}NNaO_7S \cdot xH_2O$ FW 537.68 (Anh) [345909-26-4]

Bile salt, physiological transport substrate for the bile salt export pump/sister of Pgp (BSEP/spgp), $Na^{(+)}$/taurocholate cotransporter (NTCP) and MRP3 into the hepatic carnalicular.

▸ **≥95% (TLC)**

Bile Salt

Synthesized from cholic acid

T4009-250MG	250 mg
T4009-1G	1 g
T4009-5G	5 g
T4009-25G	25 g
T4009-100G	100 g

Bile Acids Kit

▶ **≥95% (TLC)**

Bile acids in quantities indicated

Components

Cholic acid (C1129) 25 g
Dehydrocholic acid (D3750) 25 g
Deoxycholic acid (D2510) 10 g
Lithocholic acid (L6250) 1 g
Chenodeoxycholic acid (C9377) 100 mg

BA-1KT	1 kit

Bile salts

Mixture of sodium cholate and sodium deoxycholate

B8756-10G	10 g
B8756-50G	50 g
B8756-100G	100 g
B8756-500G	500 g

(*Z*)-Guggulsterone

4,17(20)-*cis*-Pregnadiene-3,16-dione; (17*Z*)-Pregna-4,17(20)-diene-3,16-dione

$C_{21}H_{28}O_2$ FW 312.45 [39025-23-5]

A natural product that lowers cholesterol due to its function as an antagonist ligand for bile acid receptor, a nuclear hormone receptor that regulates the transcription of several genes involved in cholesterol metabolism. Plays a role in cholesterol level regulation. Selective farnesoid X receptor (FXR) modulator.

▶ **~94% (HPLC)**

solubility DMSO.....5 mg/mL
E-form.....~5%

store at: 2-8°C

G5168-5MG	5 mg
G5168-25MG	25 mg

T0901317

$C_{17}H_{12}NSO_3F_9$ FW 481.33 [293754-55-9]

LXR agonist whose treatment results in an LXR-dependent up-regulation of ABC1 gene expression

mol wt 481.3

▶ **>98%**

store at: -20°C

T2320-5MG	5 mg

BSEP human

ABCB11; Bile salt export pump

The vesicular transport assay determines the interaction of compounds with the BSEP transporter. The interaction is detected by changes in the initial rate of ^{3}H-taurocholic acid transport by BSEP into membrane vesicles purified from *Sf*9 cells expressing the transporters. Membrane preparations from infected cells always contain some closed membrane vesicles that have an inside-out orientation (5-10% of total lipid). In the case of these inside-out vesicles, transport of substrates across the membrane takes molecules from the surrounding buffer and transports them into the vesicles.

The bile salt export pump (BSEP/ABCB11) belongs to the family of ATP-binding-cassette (ABC) transporters and has also been called the sister of P-glycoprotein (sister Pgp). Most ABC transporters transport substrates across the cell membrane using ATP as an energy source. BSEP is the major bile salt transporter in the liver canalicular membrane and is inhibited by a number of drugs or drug metabolites. This is potentially a significant mechanism for drug-induced cholestasis. Dysfunction of individual bile salt transporters such as BSEP, due to genetic mutation, suppression of gene expression, disturbed signaling, or steric inhibition, is an important cause of cholestatic liver disease.

The quantity of transported molecules can be determined by methods such as HPLC, LC/MS/MS separation and detection, and also by labeling with fluorescent or radioactive (^{3}H-taurocholic acid) tags. BSEP mediates the transport of taurocholic acid (TC) very efficiently. Compounds that interact with the transporter modulate the initial rate of TC transport measured without any other compounds added. If a substance is a transported substrate of the transporter, it might compete with TC, thus, reducing the rate of TC transport. If a compound is an inhibitor of the transporter, it will block the transport of TC into the membrane vesicles. Some compounds can be co-transported with TC, increasing the rate of TC transport compared to the control level.

▶ **for Vesicular Transport, recombinant, expressed in *Sf*9 cells**

Supplied as isolated *Sf*9 cell membranes containing human BSEP suspended in 50 mM HEPES-Tris, 100 mM KNO_3, and 50 mM sucrose, pH 7.4.

Distributed for SOLVO Biotechnology, Inc.

ship: dry ice store at: -70°C

B2436-500UL	500 µL

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