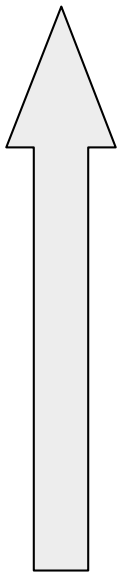
Lipoproteins

Seminar No. 2

- Chapter 13 -

Lipids of Blood Plasma

Lipid	Plasma concentration
Cholesterol (C+CE)*	3-5 mmol/l
Phospholipids	~ 3 mmol/l
Triacylglycerols	~ 1.5 mmol/l
Free fatty acids	~ 0.5 mmol/l



* C = free cholesterol, CE = cholesteryl-esters

Q. 1 (p. 78)

Which natural tensides participate in micelle formation in intestine (GIT) ?

What is a tenside?

A. 1 Tenside is compound with polar head and non-polar tail(s)

Tenside	Type	Origine
Bile acids	anionic	from cholesterol in liver
2-Acylglycerol	non-ionic	hydrolysis of TAG in GIT
FFA anions	anionic	hydrolysis of TAG in GIT
Phospholipids	amphoteric	food

They all together make a micelle which enters enterocyte

Q. 2 (p. 78)

In which form are FFA transported in blood?

A. 2

FFA are non-polar species, insoluble in water.

They are bound to **albumin**, which is the main transport protein in plasma.

Lipoprotein particle

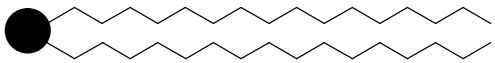
- **Polar surface monolayer**

  contact with aqueous environment

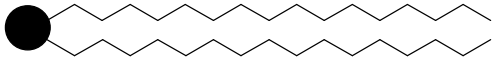
- **Non-polar core**

  completely separated from aqueous environment

Components of Surface Layer

Pictogram	Name
	?
	?
	?

Components of Surface Layer

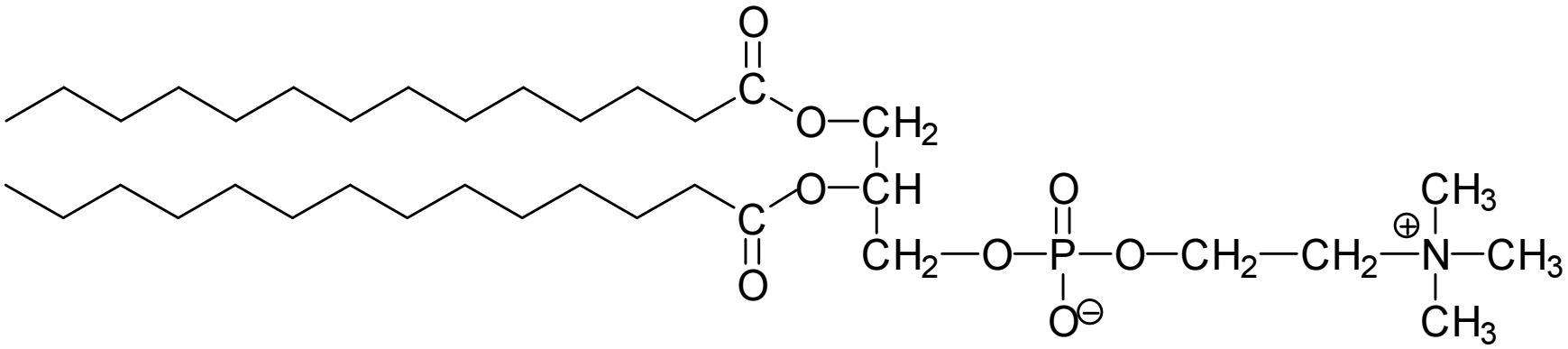
Pictogram	Name
	phospholipid
	free cholesterol
	(apo)protein

Draw a general structure of phospholipid

or

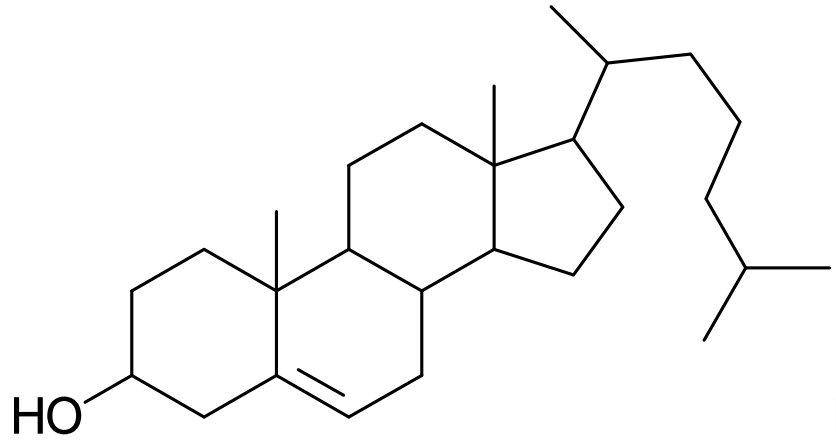
phosphatidylcholine

Structure of phospholipid



phosphatidylcholine (lecithine)

Structure of cholesterol



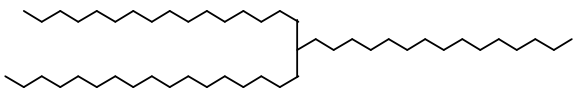
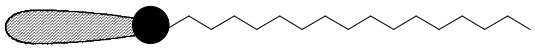
27 carbon atoms

1 hydroxyl (C3)

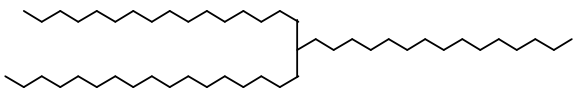
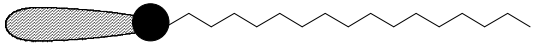
1 double bond (C5)

the only polar group

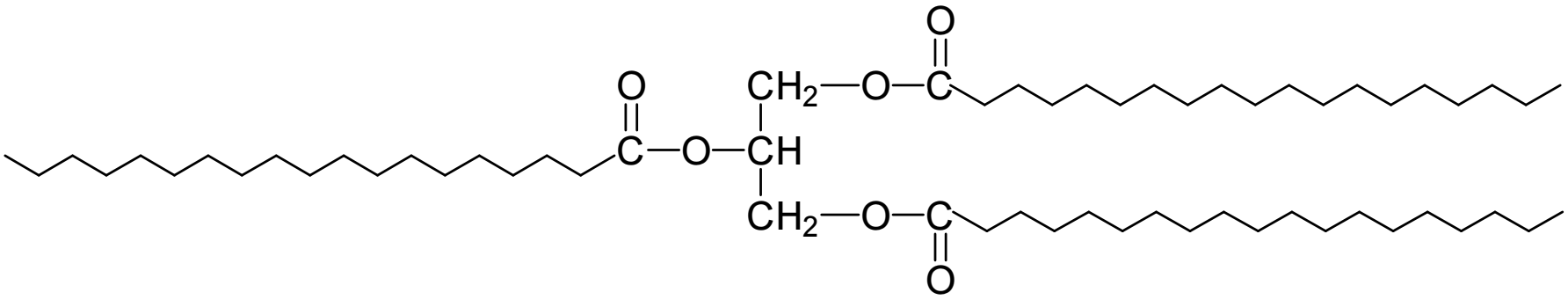
Non-polar core of lipoprotein

Pictogram	Name
	?
	?

Non-polar core of lipoprotein

Pictogram	Name
	triacylglycerol
	cholesteryl ester

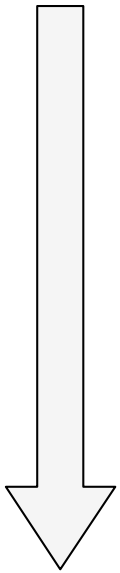
Draw a structure of TAG

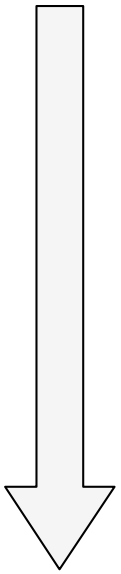


triacylglycerol (TAG)

Plasma lipoproteins: Density *vs.* Composition

Class	Density (g/ml)	Proteins (%)	TAG (%)
CM	**0.90**	2	**84**
VLDL	0.95	9	54
LDL	1.05	21	11
HDL	**1.20**	**50**	4





Electrophoretic separation of lipoproteins

see the scheme on p. 73, bottom right side

Q.

Why are CM located at the origine (start)?

A.

- CM do not move in electric field
- they are predominatly non-polar species
- they have minimal value of electric charge
- only 2 % of proteins

The Composition of Lipoproteins

Features to remember

Lipoprotein	Main component
Chylomicrons	~ 85 % TAG
VLDL	~ 50 % TAG
LDL	~ 45 % cholesterol
HDL	~ 50 % proteins

Functions of apoproteins

- **Structural** components of surface monolayer
- **Activators** of some enzymes (LPL, LCAT)
- Assist in **remodelling** (lipid transfer between lipoprot.)
- **Ligands** for specific receptors in tissues

Transport functions of lipoproteins

Class	Origine	Transport
CM	enterocyte	exogenous TAG from GIT to peripheral tissues
VLDL	liver	endogenous TAG from liver to periph. tissues
LDL	plasma	cholesteryl esters to peripheral tissues
HDL	liver	cholesterol from tissues to liver

Enzymes in lipoprotein metabolism

Enzyme	Substrates	Reaction	Location
LPL	TAG of CM, VLDL	hydrolysis	capillaries
HL	TAG of IDL, HDL	hydrolysis	liver
LCAT	cholesterol + lecithin	esterification	HDL

LPL = lipoprotein lipase

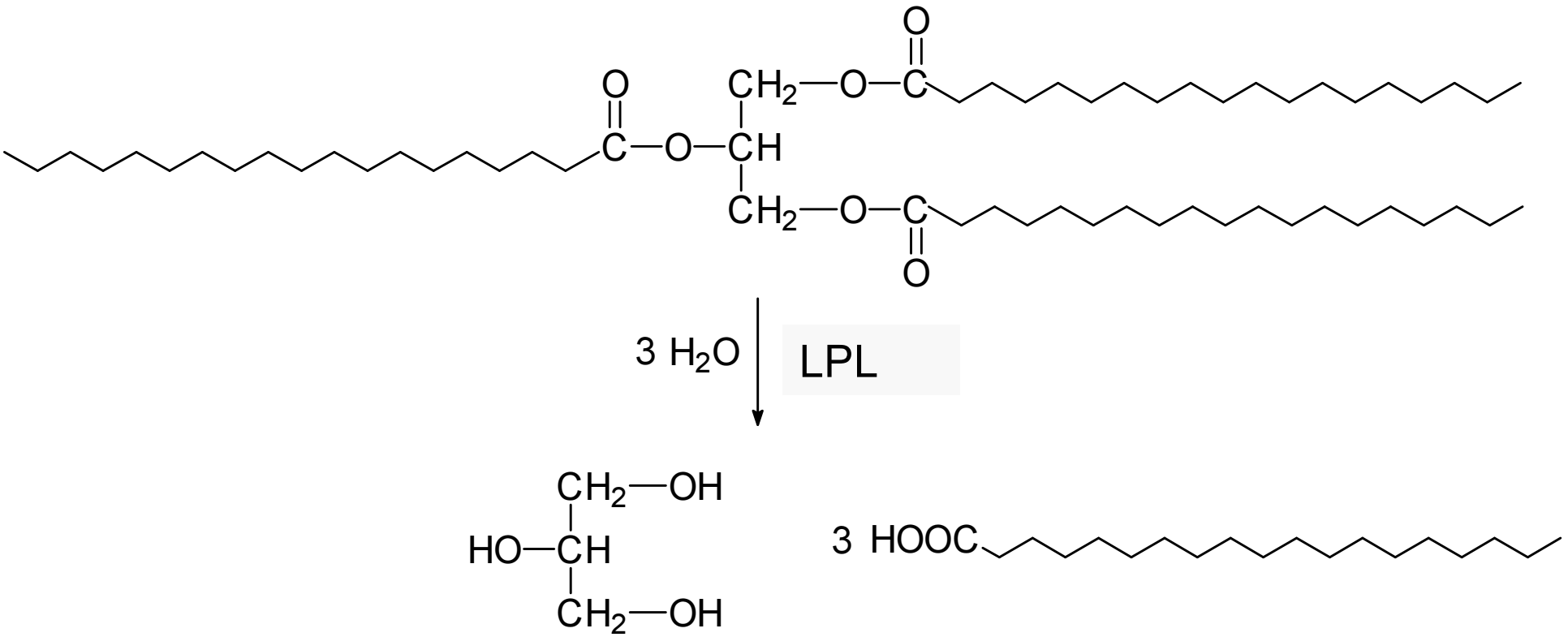
HL = hepatic lipase

LCAT = lecithin cholesterol acyltransferase

Write the equation of reaction catalyzed by LPL

LPL reaction

TAG + 3 H_2O → glycerol + 3 FFA



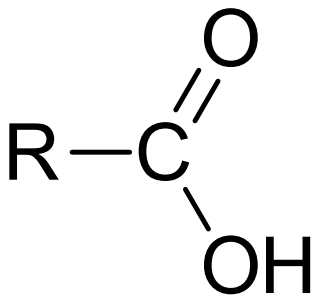
Write the equation of reaction catalyzed by LCAT

(lecithin cholesterol acyltransferase)

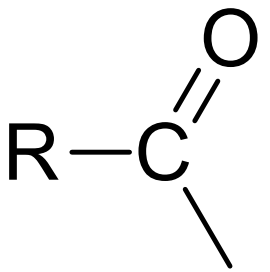
Q.

What is acyl?

A.



carboxylic acid

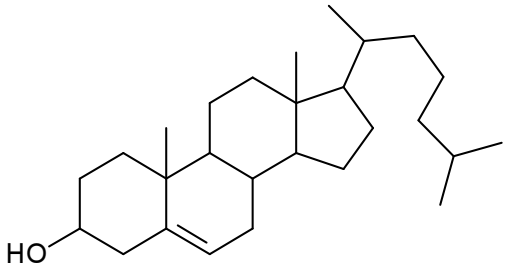


acyl

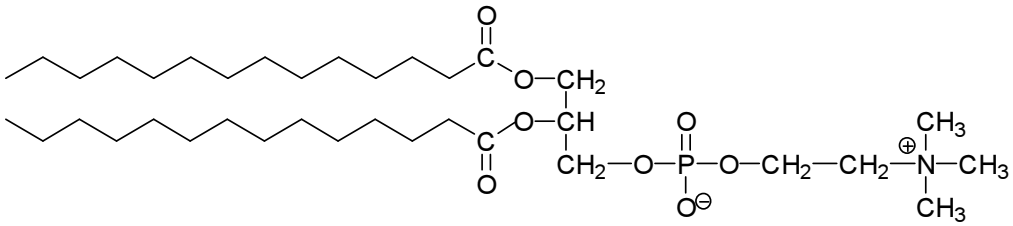
LCAT reaction

cholesterol + lecithin $\rightarrow$ cholesteryl ester + lysolecithin

lyso = 2-deacyl

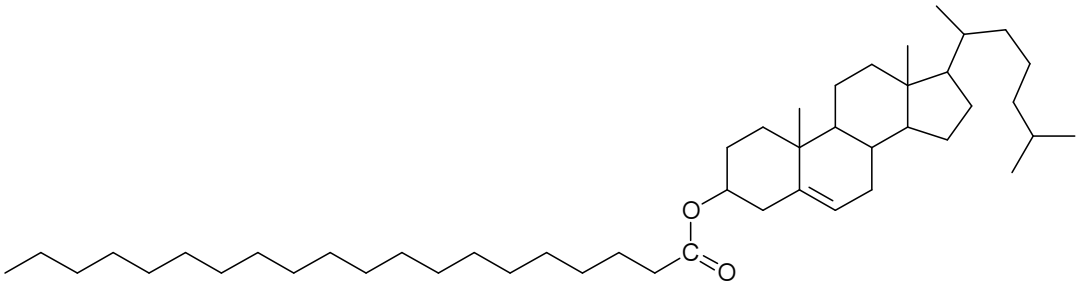


cholesterol

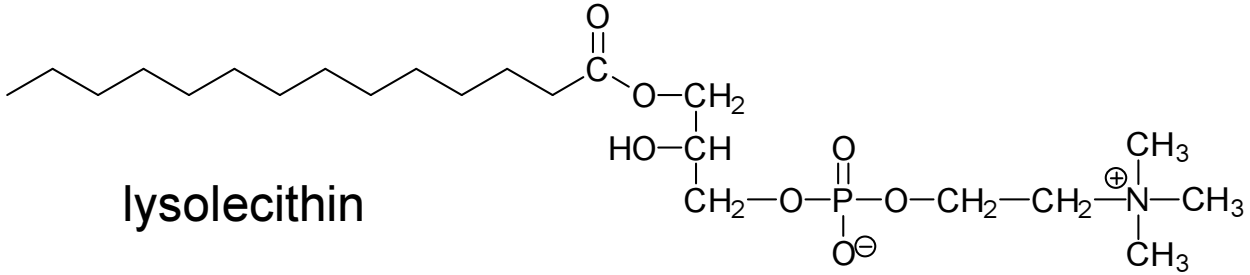


lecithin

LCAT



cholesteryl ester



lysolecithin

Metabolism of chymomicrons (CM)

- CM are produced in enterocytes, apo B-48
- They carry dietary TAG and CE to periph. tissues
- In plasma, CM receive apo E and apo C-II from HDL
- **Apo C-II activates lipoprotein lipase (LPL)**
- LPL is attached to capillary surface in adipose, cardiac and muscle tissues
- TAG are hydrolysed, apo C-II is returned to HDL
- CM particles begin to shrink – **remnants**
- Remnants bind to apo E receptors in liver, where they are hydrolytically degraded in lysosomes

Q.5 (p. 78)

What will be result of deficient synthesis of apo B-48?

A.5

No CM will be produced, dietary fat remains in stool (steatorrhoea)

Metabolism of VLDL

- VLDL are made in liver, they transport endogenous TAG to periph. tissues
- In plasma they take apo C-II from HDL (LPL activ.)
- TAG are removed by LPL action – VLDL become smaller and more densed = IDL
- IDL take some CE from circulating HDL
- **IDL are transformed into LDL by hepatic lipase**

Q. (p. 76)

Name some dietary factors which may affect the synthesis of VLDL in the liver.

A.

Food rich in lipids (fat) and saccharides (sugars)

Q. (p. 76)

How are utilized fatty acids released by LPL?

A.

Depending on energy status in tissues FFA are:

- either utilized for energy

(β-oxidation → acetyl-CoA → CAC)

- or substrates for TAG synthesis (making energy reserves)

Three pathways of LDL

1. LDL provide cholesterol to peripheral tissues *via* LDL receptors
2. The rest of LDL is taken up by liver and degraded
3. Small amount of LDL (chemically modified by oxidative stress) enters to some cells (endothelial) by non-specific endocytosis and alters them to „foam cells“

Metabolism of HDL

- HDL particles are made in liver
- Nascent HDL are disc-shaped (bilayer of PL + proteins)
- HDL take free cholesterol (C) from cell membranes
- Once C is taken up, it is esterified by LCAT
- After this process HDL becomes spherical
- Spherical HDL are taken up by liver and CE are degraded

Cellular uptake of LDL

- LDL receptors are in clathrin-coated pits
- After binding, LDL+receptor are internalized by endocytosis
- Vesicle loses its clathrin coat and becomes endosome
- Receptor is removed and recycled
- LDL is hydrolyzed after fusing with lysosome
- Free cholesterol is released to make **cholesterol pool**

Intracellular cholesterol

- Free cholesterol is immediately esterified by ACAT* (storage)
- Small amounf of C is incorporated into cell membrane
- Some C is converted into hormones (in some tissues)
- Some C is converted into bile acids (in liver)

* acyl-CoA cholesterol acyltransferase

Intracellular cholesterol regulates three processes

1. Decreases activity of HMG-CoA reductase

   (= synthesis of cholesterol)

2. Decreases synthesis of new LDL receptors

   (to block intake of LDL)

3. Enhances activity of ACAT (to help making storage)

The Balance of Cholesterol

Input into body	g/day	Output from body	g/day
food	0.5 g	coprostanol (stool)	0.8 g
biosynthesis in body	1.0 g	bile acids (stool)	0.5 g
		sebum, skin etc.	0.2 g
Total:	**1.5 g**	**Total:**	**1.5 g**

Q.

Which food is the main source of cholesterol?

A.

- only animal fats (including fish)

  lard, butter, bacon, egg yolk, mayonnaise, fat meat, fat cheese

- plant oils and margarines are cholesterol free