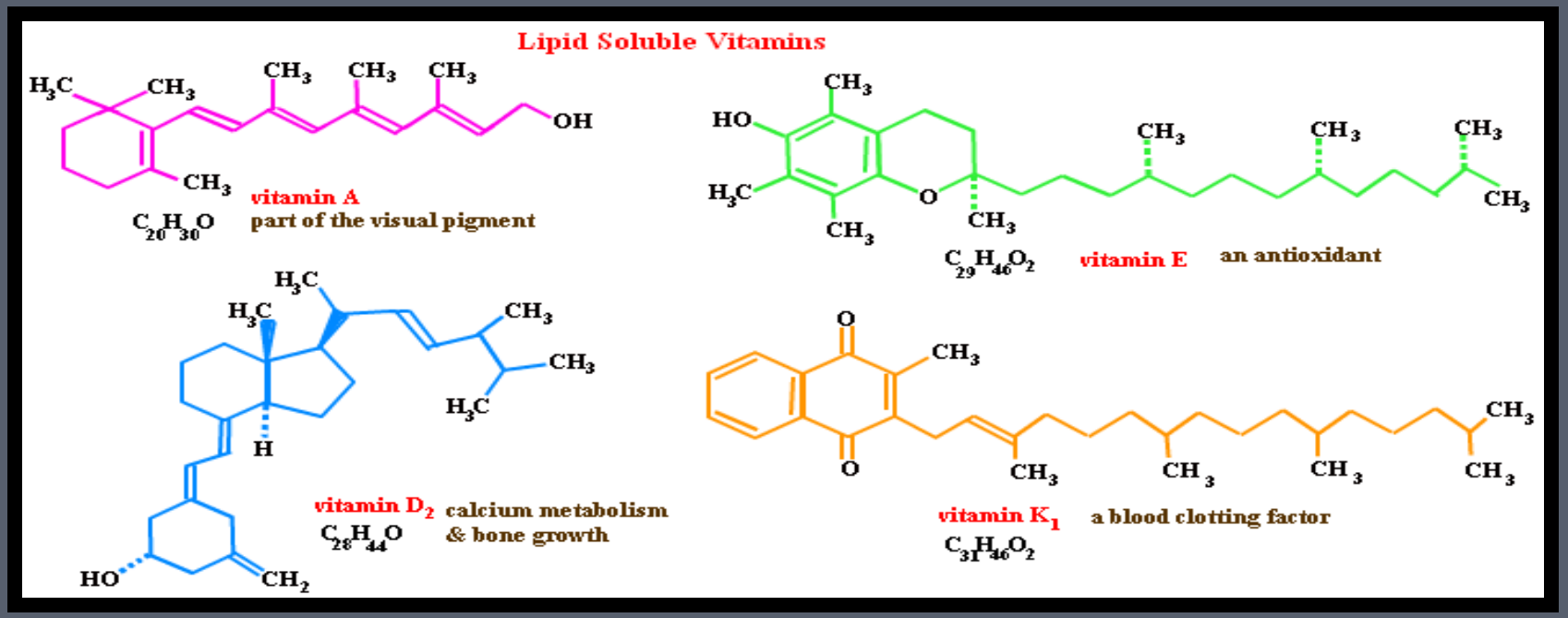
e- MODULE 2
LIPID METABOLISM



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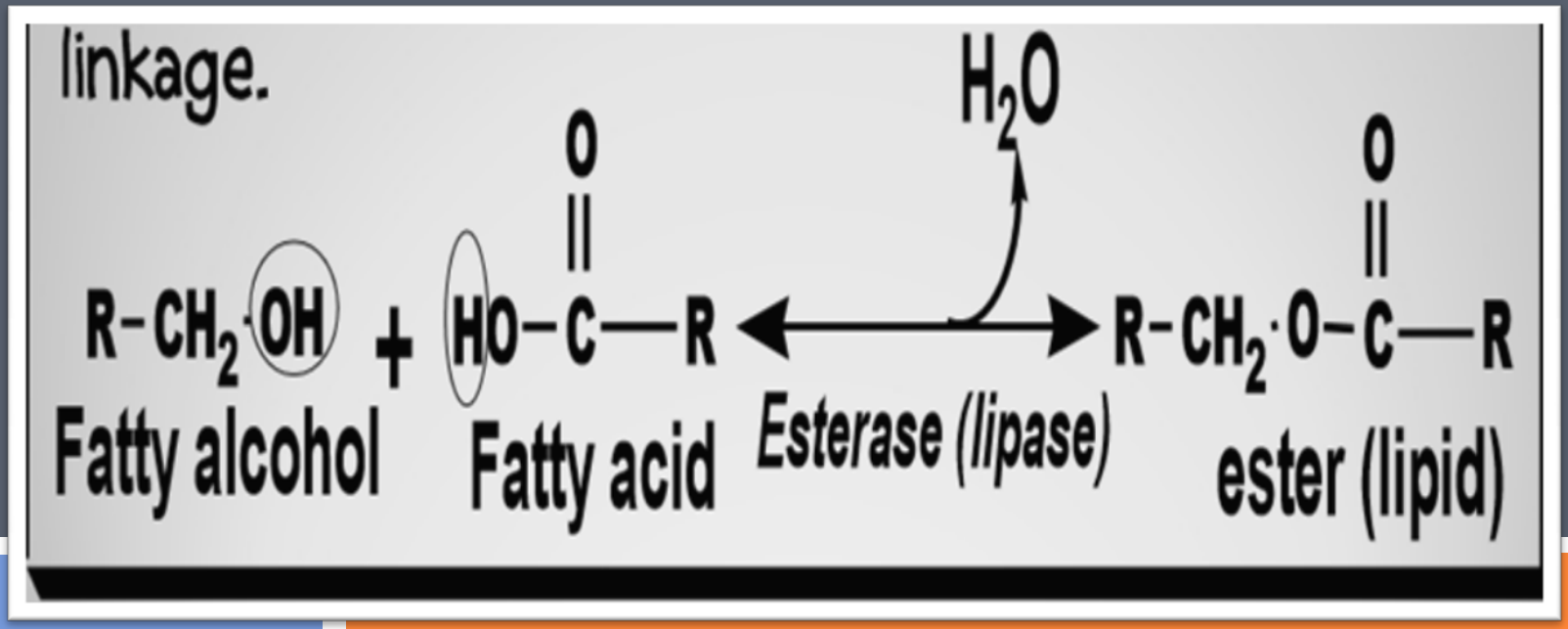
LIPIDS

- Lipids are composed of C, H, O
  - long hydrocarbon chains (H-C)
- Lipids are heterogeneous group of organic compounds which include cooking oil, butter, ghee, waxes, cholesterol, essential oils etc.
- Lipids form about 3.5% of the cell contents.

Lipids are organic compounds formed mainly from alcohol (glycerol) and fatty acids combined together by ester linkage.



Physical Nature and Chemical Properties

- Lipids are insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone).
- Lipids include fats, oils, waxes and other related compounds.
- They are widely distributed in nature, in plants and in animals also.
- They are more palatable and storable as compared to carbohydrates.
- They have a high-energy value (25% of body needs) and they provide more energy per gram than carbohydrates and proteins

- Lipids supply the essential fatty acids that cannot be synthesized by the body.
- Lipids also provide fat-soluble vitamins (A, D, E and K).
- They are important constituents of the nervous system.
- Tissue fat is an essential constituent of cell membrane and nervous system.
- Stored lipids “depot fat” is stored in all human cells acts as: A store of energy.

- Lipid act as cushion material for the internal organs to protect them from outside shocks.

- Lipids act as subcutaneous thermal insulator against loss of body heat

- Lipoproteins, which are complex of lipids and proteins, are important cellular constituents that present both in the cellular and sub cellular membranes.

- Cholesterol enters in membrane structure and is used for synthesis of adrenal cortical hormones, vitamin D3 and bile acids.

- Lipids provide bases for dealing with diseases such as obesity, atherosclerosis, lipid-storage diseases, essential fatty acid deficiency, respiratory distress syndrome

CLASSIFICATION:(STRUCTURE)

1. **Simple Lipids**

a. **Fats & Oils (TRIGLYCERIDES)**

Fatty acid esters with Glycerol

(Triacyglycerols)

b. **Waxes**

Fatty acid esters of long chain mono-hydroxy alcohols (Cetylpalmitate) other than glycerol.

2. Complex Lipids

a. Phospholipids (contain phosphate group)

Glycerophospholipids

Alcohol is Glycerol (e.g.phosphatidylcholine)

Sphingophospholipids

Alcohol is sphingosine (C18 amino alcohol)

b. Glycolipids

have fatty acid, an amino alcohol and a carbohydrate

c. Lipoproteins: lipids and protein

d. Derived Lipids: These are formed by hydrolysis of lipids. They mainly include steroids, terpenes, prostaglandins

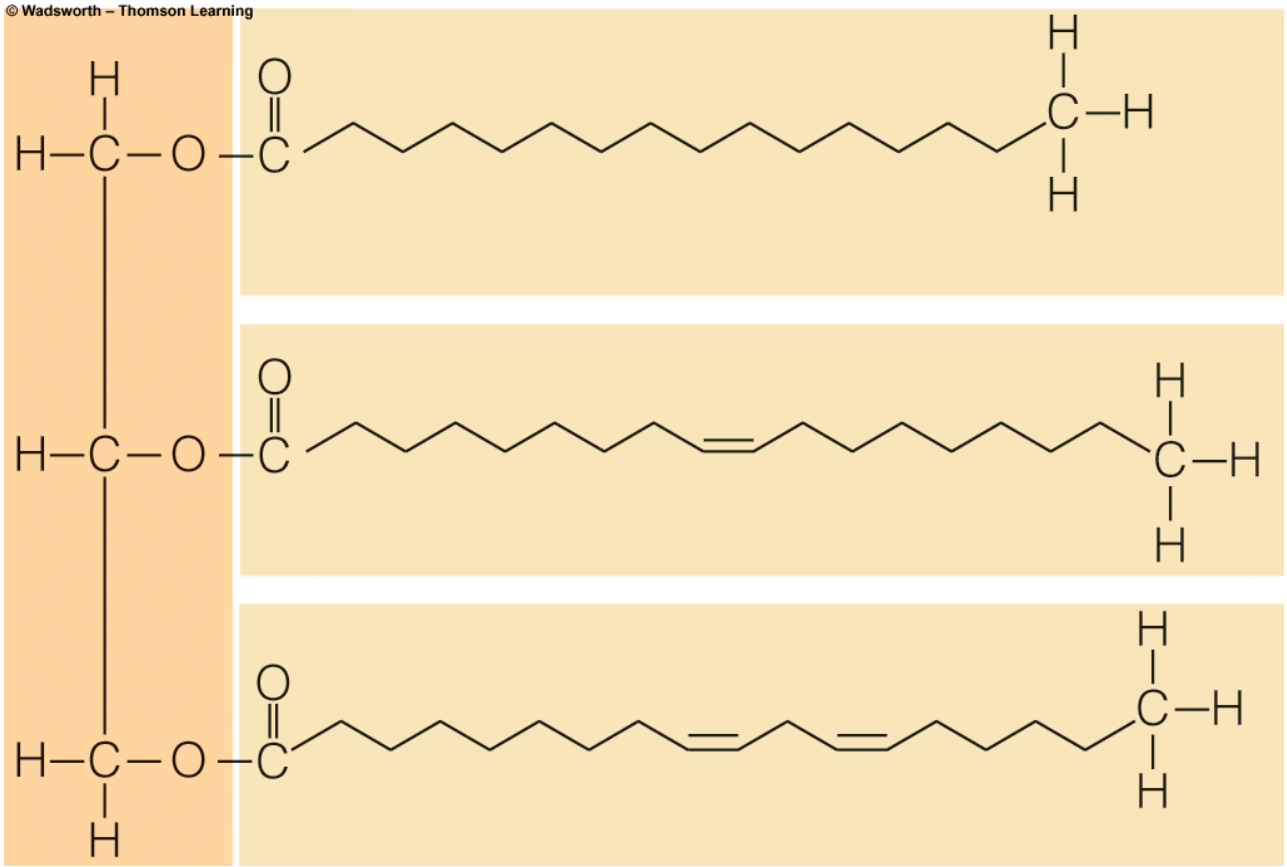
TRIGLYCERIDES

- **Triglycerides** – Fats & Oils

1. Predominate form of fat in foods and major storage form of fat in the body
2. Structure – composed of 3 fatty acids + glycerol

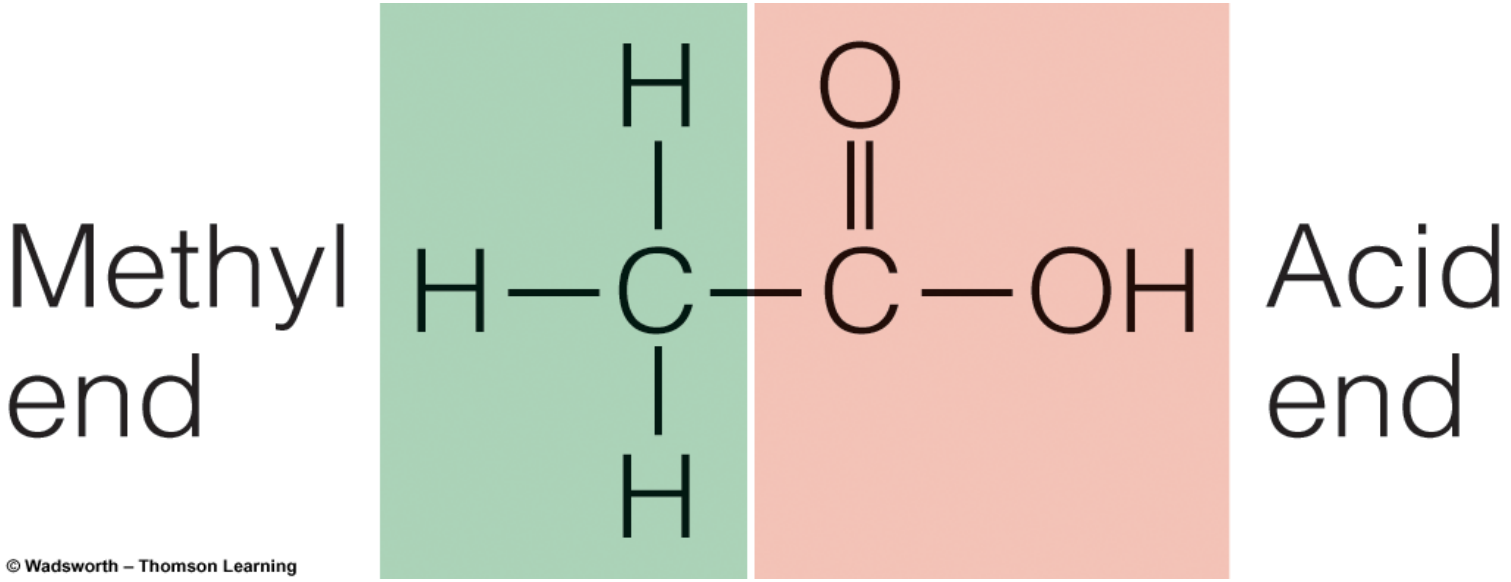
Fatty Acids & Triglycerides

- glycerol + 3 fatty acids → triglyceride + H_2O



Fatty Acids

- Organic acid (chain of carbons with hydrogens attached) that has an acid group at one end & a methyl group at the other end



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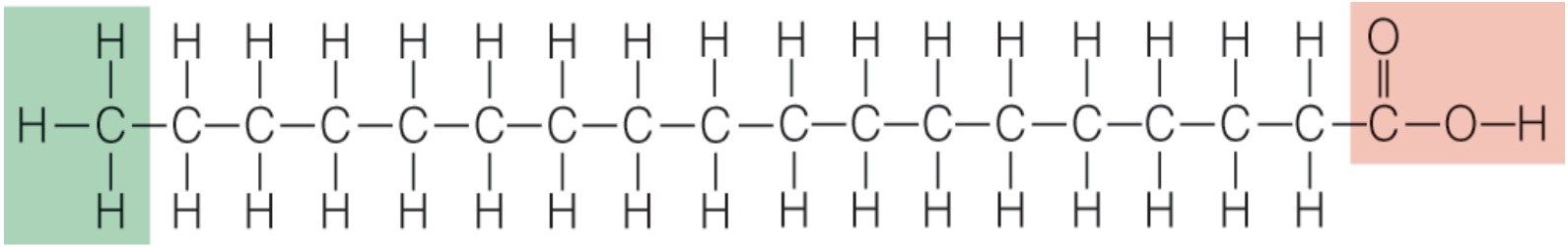
FATTY ACIDS

- **Fatty Acids** – carbon chains, vary in:
  1. Length – affects absorption
  2. Saturation –chemical structure; affects cooking & storage properties and health

- Length of carbon chain



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Stearic acid – 18-carbon, saturated

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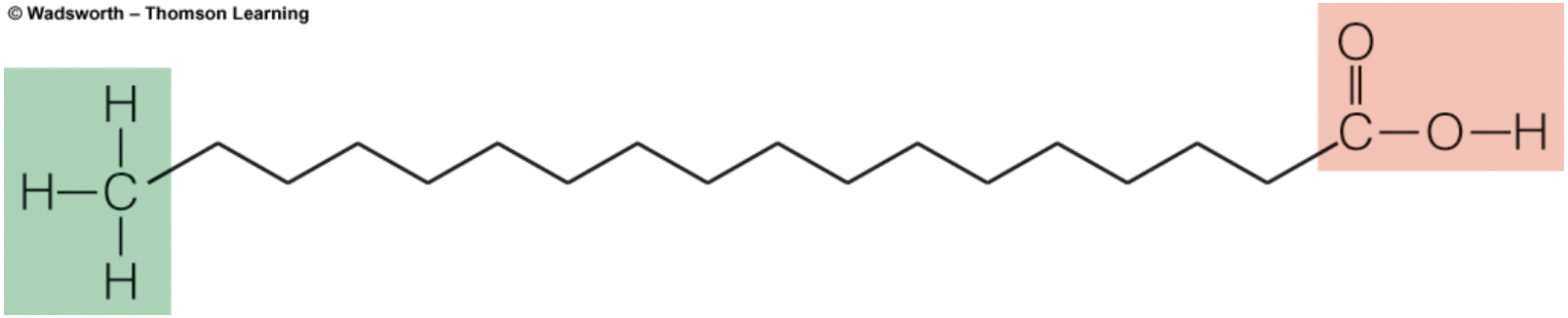


Simplified structure

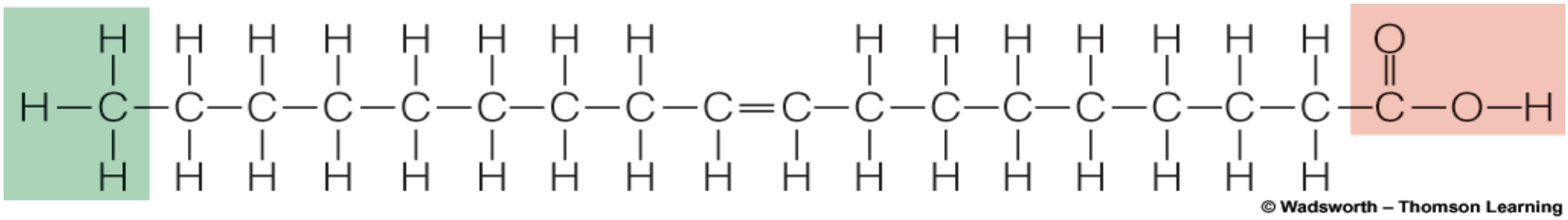
FATTY ACIDS

Saturation

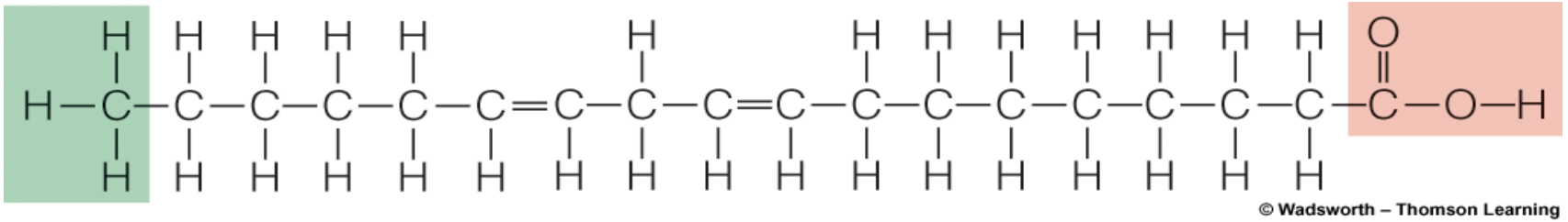
- **Saturated fatty acid** – carbon chains filled with hydrogen atoms (no C=C double bonds)
  1. Saturated fat – triglyceride containing 3 saturated fatty acids, such as animal fats (butter, lard) & tropical oils (palm, coconut)
  2. Appear solid at room temperature

FATTY ACIDS

- **Unsaturated fatty acid** – carbon chains lack some hydrogens (>1 C=C double bond)
    1. Monounsaturated fat – triglyceride containing fatty acids with 1 double bond; i.e. canola & olive oil
    2. Polyunsaturated fat- triglycerides containing a high % of fatty acids with >2 double bonds; i.e. corn, safflower, soybean, sunflower oils and fish;
    3. Appear liquid at room temperature



Oleic acid – 18-carbon, monounsaturated



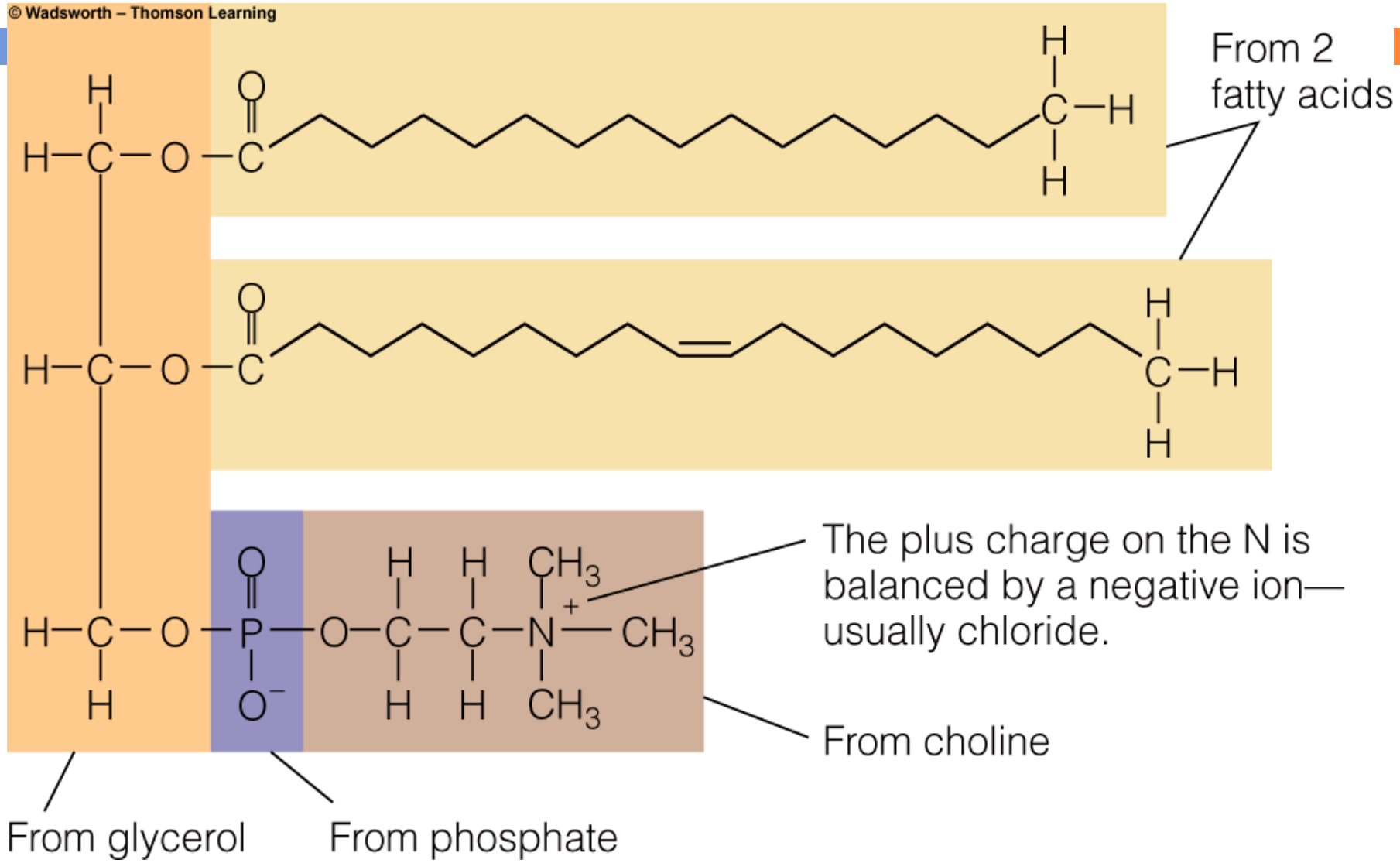
Linoleic acid – 18-carbon, polyunsaturated

PHOSPHOLIPIDS

- **Phospholipids** – similar to triglycerides in structure except only 2 fatty acids + choline

  Phospholipids in foods: Lecithin, egg yolks, soybeans, wheat germ, peanuts

Lecithin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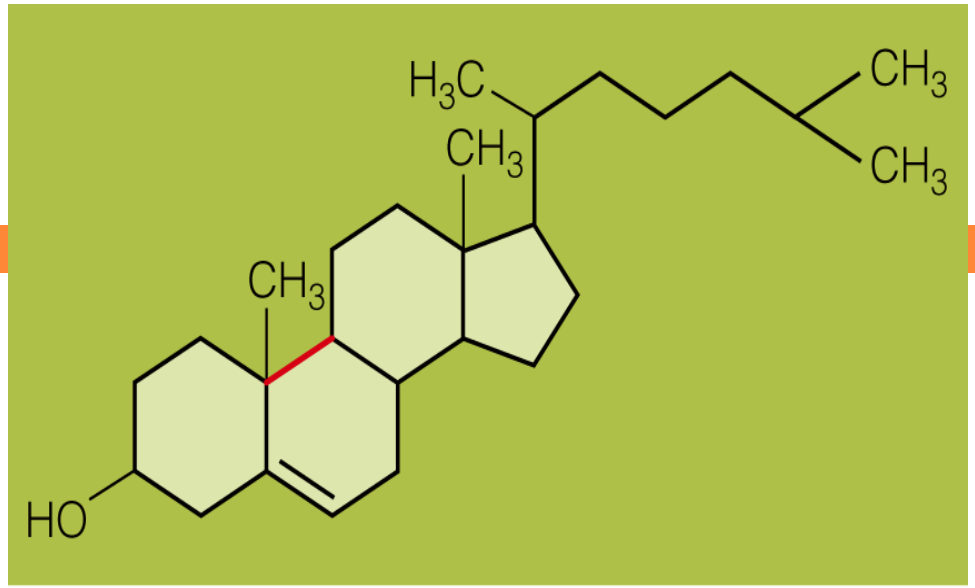
From 2 fatty acids
The plus charge on the N is balanced by a negative ion—usually chloride.
From choline
From glycerol
From phosphate

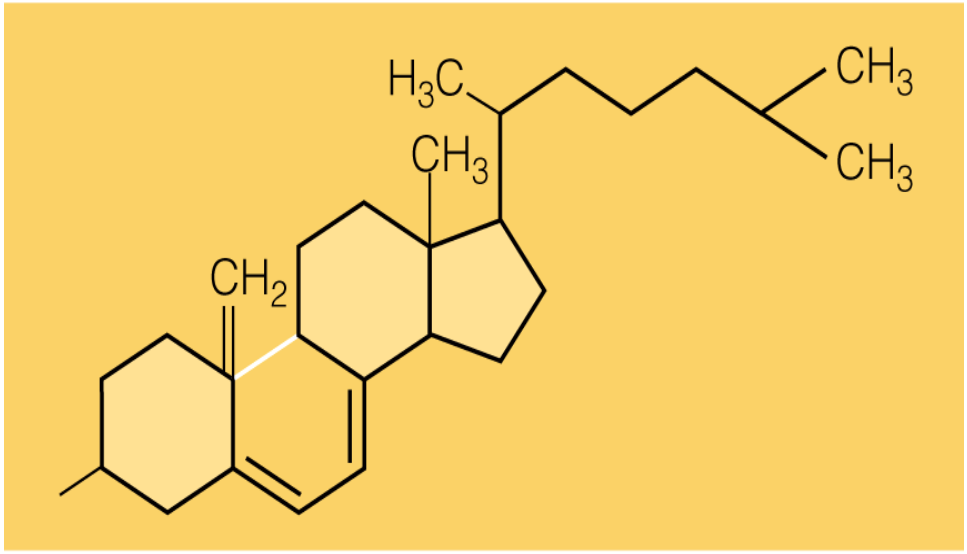
Sterols

Structure consists of carbon rings
Important part of:

1. Sex hormones – testosterone
2. Vitamin D
3. Bile (aids fat digestion)
4. Adrenal hormones – cortisol
5. Cholesterol – in foods and made by the liver; dietary sources include egg yolks, liver, meats, dairy products



Cholesterol



Vitamin D_3

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BETA OXIDATION OF FATTY ACID

- Reserves of stored triglycerides are mobilized as needed for energy production.
- Fat mobilization is stimulated by epinephrine. The triglycerides are hydrolyzed to fatty acids and glycerol and enter the blood stream.
- Glycerol is converted to glycerol- 3 phosphate and then to dihydroxyacetone phospahte, which enters glycolysis for energy production.
- Free fatty acids are converted to fatty acyl CoA molecules, which are broken down to acetyl CoA by beta oxidation. The acetyl CoA may be used for energy production by way of the citric acid cycle and the electron transport chain.

Key points of β-oxidation of fatty acid

- β-oxidation of fatty acid- The break down of a fatty acid to acetyl-CoA.
- Occurs in the mitochondria
- Process is strictly aerobic
- After production Acetyl-CoA is fed directly into the Krebs cycle

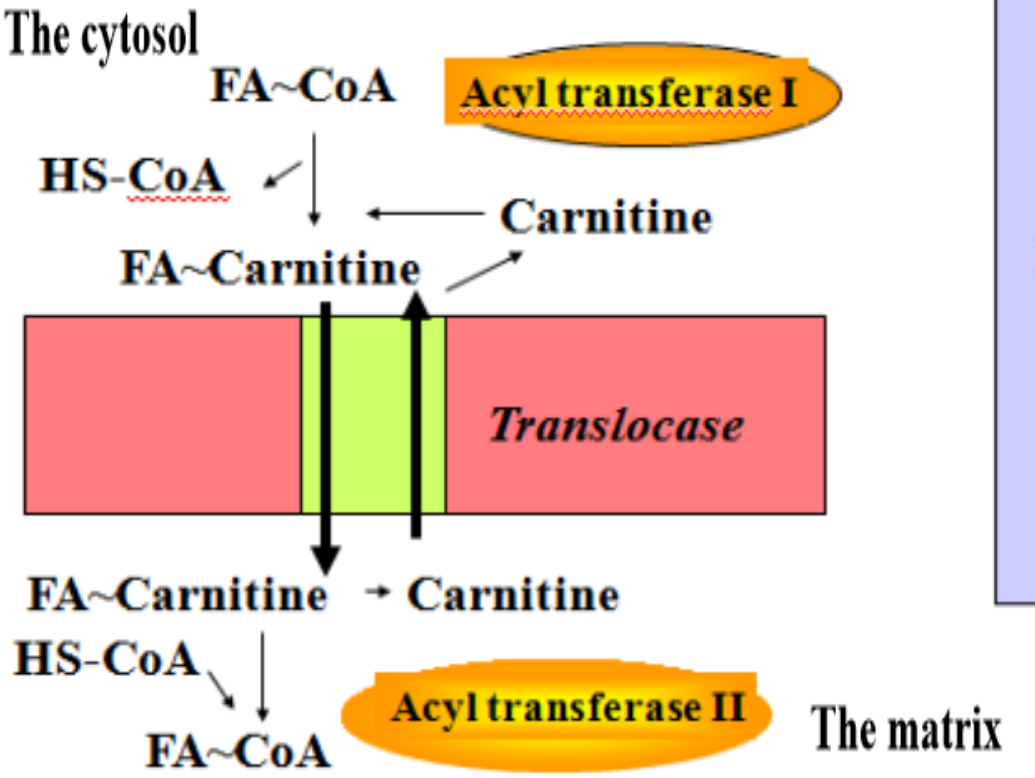
It occurs in many tissues including liver, kidney and heart.

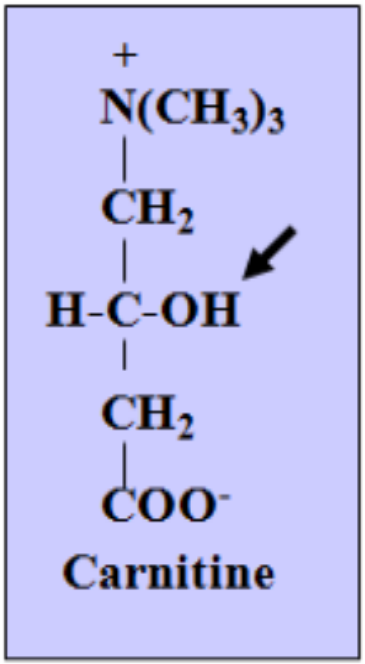
1. Fatty acids oxidation doesn't occur in the brain
2. There are several types of fatty acids oxidation.
3. (1) β- oxidation of fatty acid
4. (2) α- oxidation of fatty acids
5. (3) ω- oxidation of fatty acids

- The beta oxidation of fatty acids involve three stages:
- 1.Activation of fatty acids in the cytosol
- 2.Transport of activated fatty acids into mitochondria (carnitine shuttle)
- 3.Beta oxidation proper in the mitochondrial matrix

- Activation of FA:
- This proceeds by Fatty acid thiokinase (acyl COA synthetase) present in cytosol
- Thiokinase requires ATP, COA SH, Mg++. The product of this reaction is FA acyl COA and water.

Transport of fatty acyl CoA from cytosol into mitochondria: Long chain acyl CoA traverses the inner mitochondria membrane with a special transport mechanism called **Carnitine shuttle**





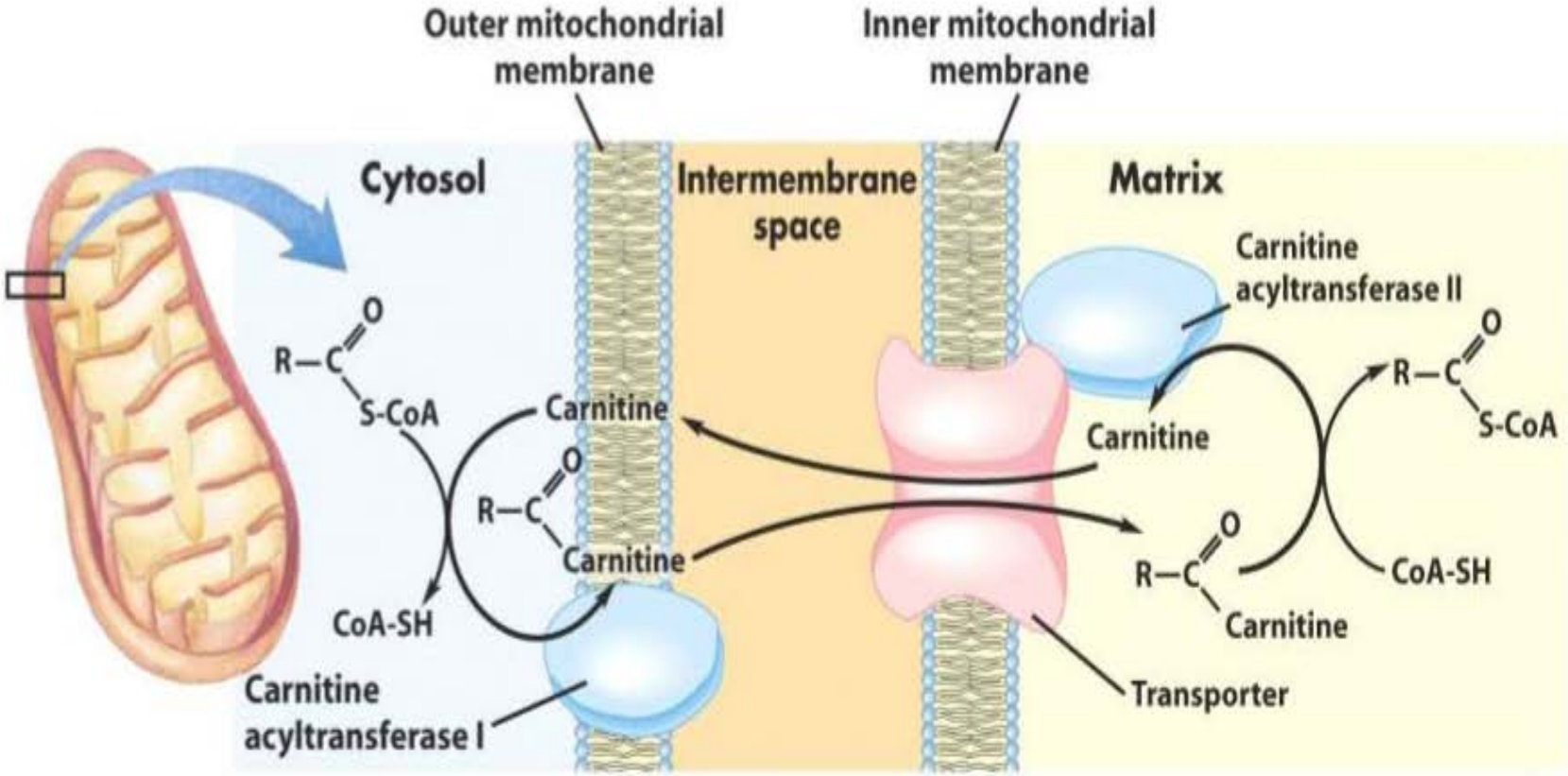
- Transport of acyl CoA into the mitochondria (rate-limiting step)

1. Acyl groups from acyl COA is transferred to carnitine to form acyl carnitine catalyzed by carnitine acyltransferase I, in the outer mitochondrial membrane.

2. Acylcarnitine is then shuttled across the inner mitochondrial membrane by a translocase enzyme.

3. The acyl group is transferred back to CoA in matrix by carnitine acyl transferase II.

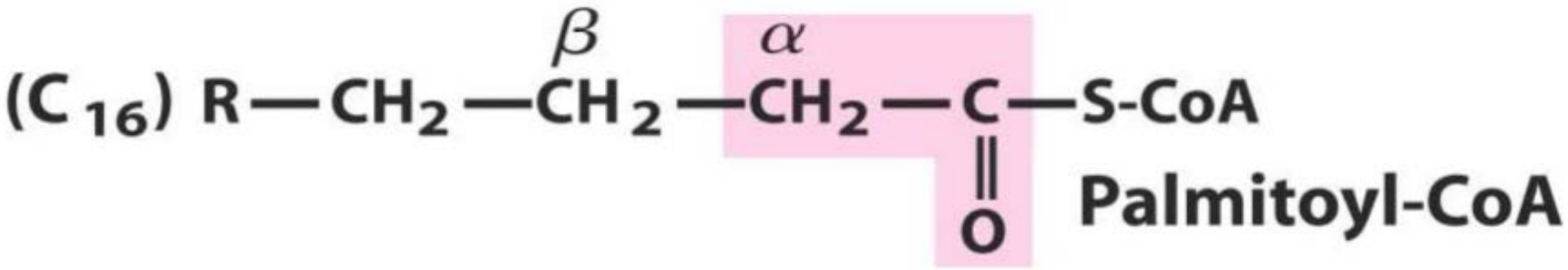
4. Finally, carnitine is returned to the cytosolic side by translocase, in exchange for an incoming acyl carnitine


Outer mitochondrial membrane
Inner mitochondrial membrane
Cytosol
Intermembrane space
Matrix
Carnitine acyltransferase II
R—C(=O)—S-CoA
Carnitine
Carnitine
R—C(=O)—S-CoA
R—C(=O)—
Carnitine
Carnitine
CoA-SH
R—C(=O)—
Carnitine
CoA-SH
Carnitine acyltransferase I
Transporter

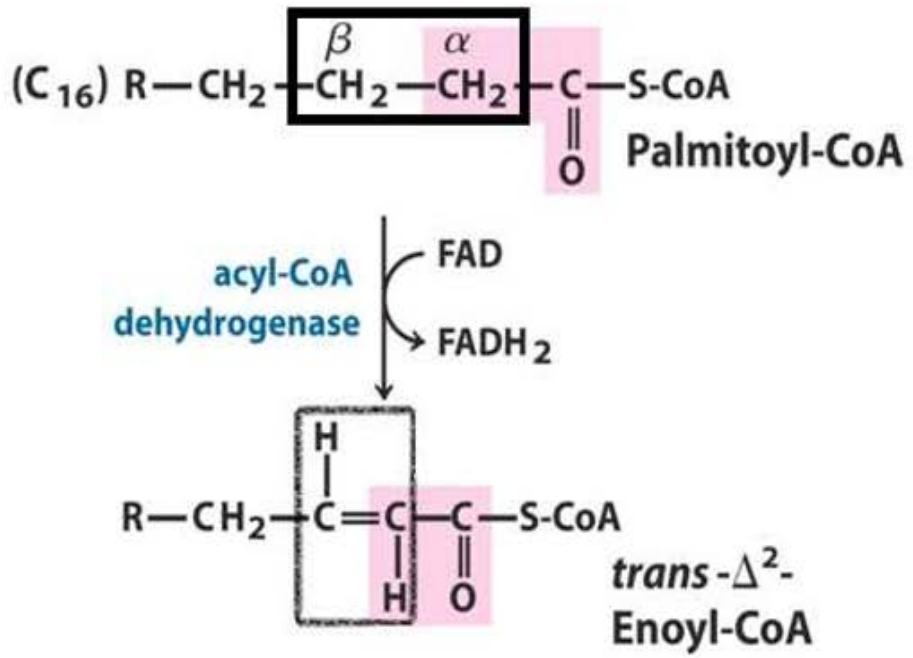
There are 4 steps in β – oxidation

- Step I – Oxidation by FAD linked dehydrogenase
- Step II – Hydration by Hydratase
- Step III – Oxidation by NAD linked dehydrogenase
- Step IV – Thiolytic clevage Thiolase

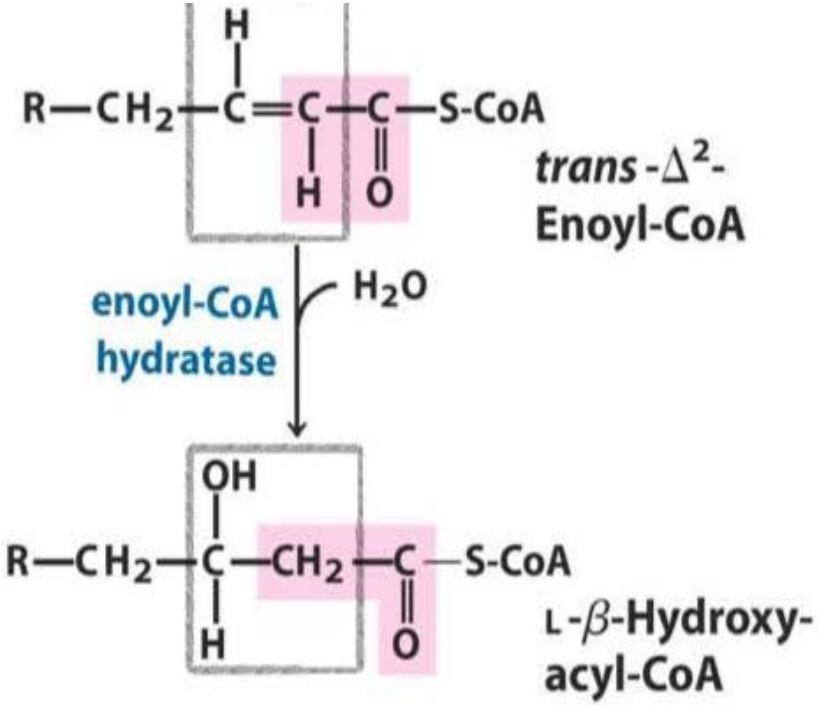
Example :Palmitic acid ($C_{16}H_{32}O_2$)



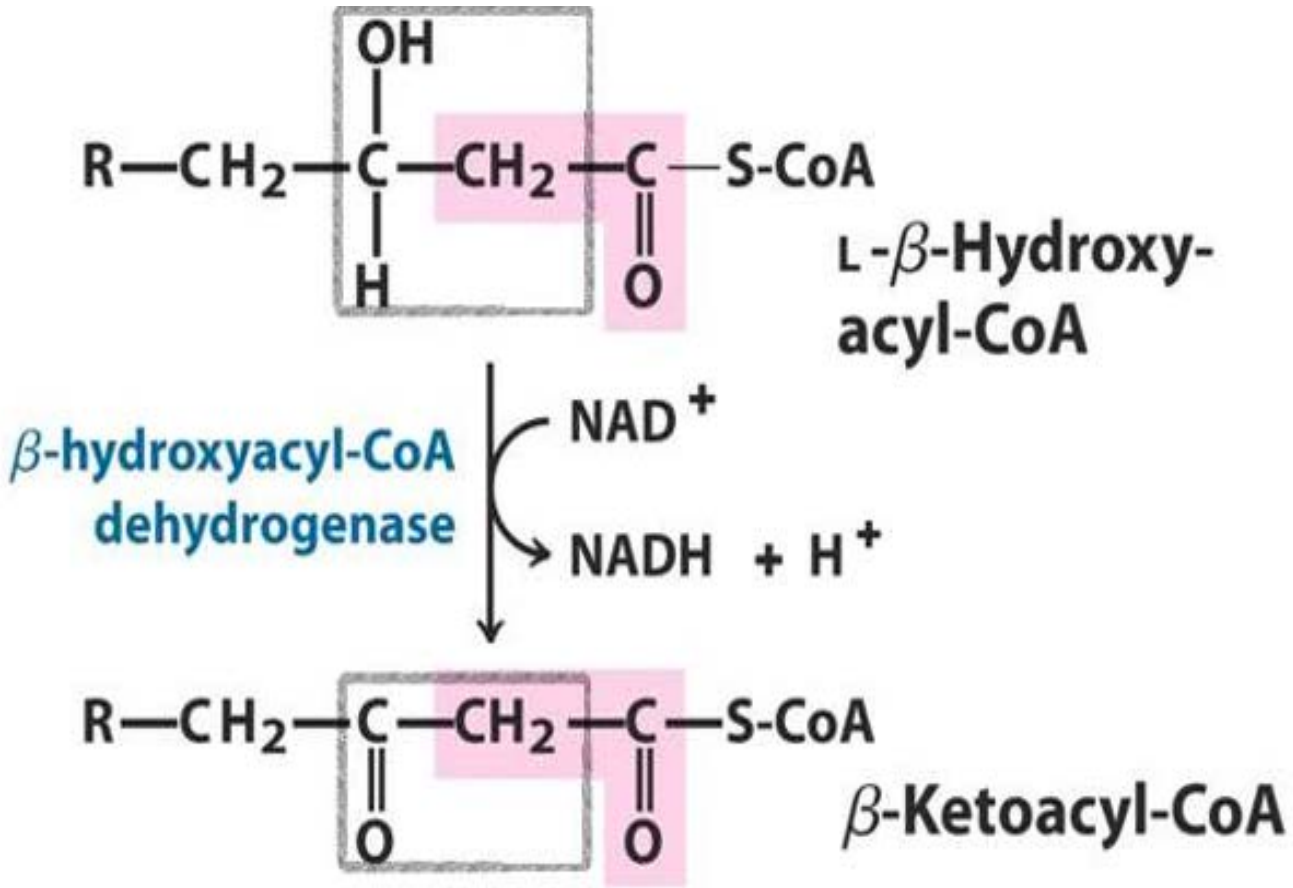
The first reaction is the oxidation of acyl CoA by an acyl CoA dehyrogenase to give α-β unsaturarted acyl CoA (enoyl CoA). FAD is the hydrogen acceptor



The second reaction is the hydration of the double bond to β-hydroxyacyl CoA (phydroxyacyl CoA).

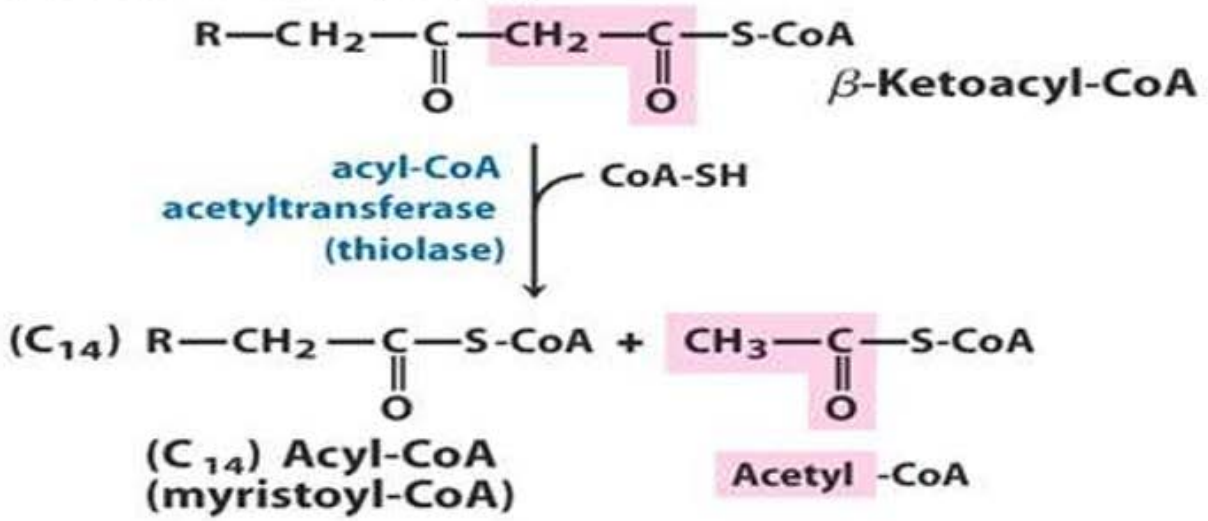


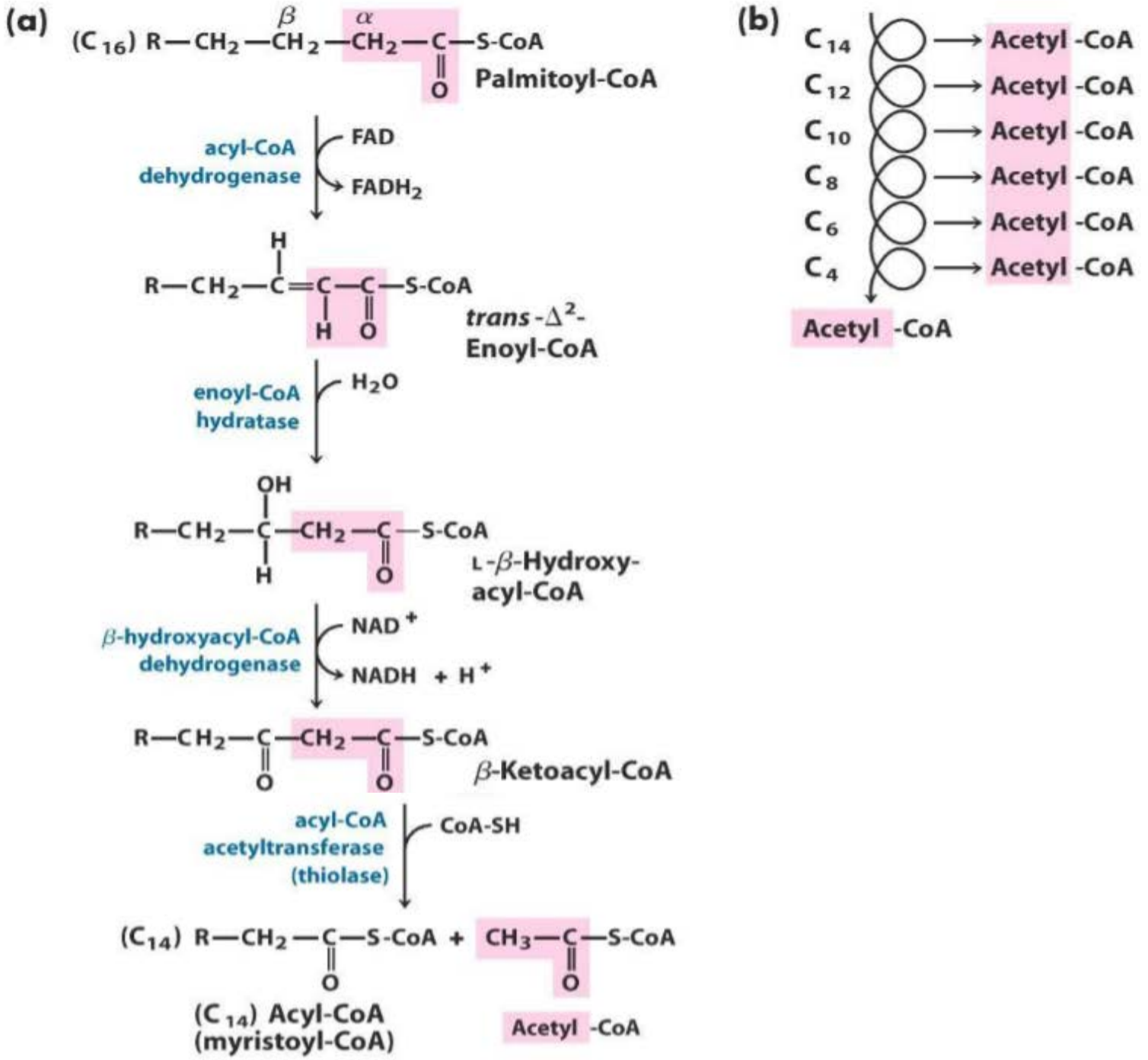
The third reaction is the oxidation of β hydroxyacyl CoA to produce β-Ketoacyl CoA a NAD-dependent reaction



The fourth reaction is cleavage of the two carbon fragment by splitting the bond between α and β carbons •

By thiolase enzyme




(a)
β
α
(C16) R—CH2—CH2—CH2—C—S-CoA
O
Palmitoyl-CoA
acyl-CoA dehydrogenase
FAD
FADH2
H
R—CH2—C=C—C—S-CoA
H O
trans-Δ2-Enoyl-CoA
enoyl-CoA hydratase
H2O
OH
R—CH2—C—CH2—C—S-CoA
H O
L-β-Hydroxy-acyl-CoA
β-hydroxyacyl-CoA dehydrogenase
NAD+
NADH + H+
R—CH2—C—CH2—C—S-CoA
O O
β-Ketoacyl-CoA
acyl-CoA acetyltransferase (thiolase)
CoA-SH
(C14) R—CH2—C—S-CoA + CH3—C—S-CoA
O O
(C14) Acyl-CoA (myristoyl-CoA)
Acetyl -CoA
(b)
C14
C12
C10
C8
C6
C4
Acetyl -CoA
Acetyl -CoA

- The release of acetyl CoA leaves an acyl CoA molecule shortened by 2 carbons.
- This acyl CoA molecule is the substrate for the next round of oxidation starting with acyl CoA dehydrogenase.
- Repetition continues until all the carbons of the original fatty acyl CoA are converted to acetyl CoA.
- In the last round a four carbon acyl CoA (butyryl CoA) is cleaved to 2 acetyl CoA.

Energetics of fatty acid oxidation

Example : Palmitic acid (16 Carbon fatty acid)

Palmitic acid + 8 coenzyme A+ 7 FAD+ 7 NAD+7 H_2O + 1 ATP ⟶ 8 Acetyl COA+ 7 $FADH_2$ + 7 NADH + 7 H^++ 1AMP+ 2Pi

DETAILS OF ENERGY OUTPUT

1. The cycle repeats seven times producing acetyl coenzyme A each time, forming eight acetyl coenzyme A at the end.
2. 5 ATP,s are produced per cycle so 7X5= 35 ATP
3. One ATP is used for activation, 35-1= 34 ATP

4. One acetyl COA molecule yields 12 high energy phosphate molecules by entering Krebs cycle (1 GTP + 11 ATP)
5. So molecules of Acetyl COA will yield 88 ATP+ 8 GTP
6. Complete oxidation of stearic acid will yield = 88 ATP+ 8 GTP+ 34 ATP= 130 ATP
7. NET GAIN BY OXIDATION OF ONE FAT MOLECULE = 20 ATP by oxidation of glycerol + 130 from one fatty acid.
8. There are three fatty acid molecules in one fat molecule so 130x 3= 390

NET GAIN= 390+20= 410 ATP

Thank You