Biochemistry
2nd stage
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FATTY ACIDS

ILO:K2,S11,A0.

Objectives:

The students are learned to understand the SYNTHESIS OF THE FATTY ACIDS including the following points:
-Transportation of acetyl CoA.
-Formation of malonyl CoA.
-Fatty acid synthase multienzyme complex
- Elongation and Desaturation of the fatty acids chain
-regulation of fatty acid synthesis

SYNTHESIS OF FATTY ACIDS

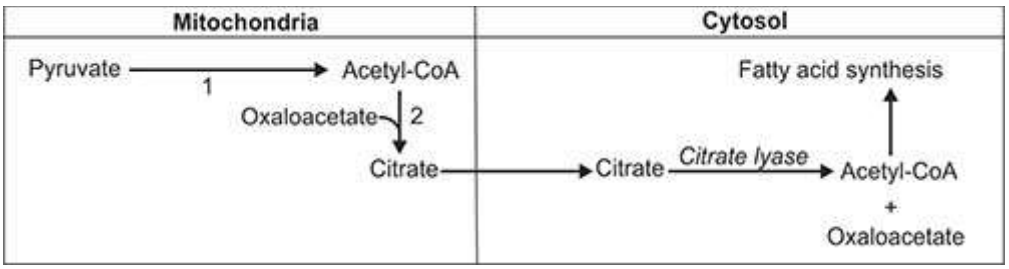
Definition: Defined as synthesis of palmitate from acetyl-CoA in the cytosol.
Site: Liver, kidney, brain, mammary gland, adipose tissue.
Cellular site: Cytosol.
Coenzymes/cofactors: NADPH (from HMP shunt), ATP, manganese, biotin, HCO3-.
Starting material: Acetyl-CoA.

The primary metabolic substrate for synthesis of fatty acid is Acetyl CoA which is generated from the oxidation of ***pyruvate, and by the catabolism of fatty acids, ketone bodies, and certain amino acids***.

Acetyl Co A from catabolic reaction is generated mainly in the mitochondria. Whereas the fatty acid synthesis occur in the cytoplasm therefore we need a special transport mechanism for transportation of acetyl Co A from the mitochondria to the cytoplasm because the CoA portion of acetyl Co A cannot cross the mitochondrial membrane.

The acetyl Co A will react with oxaloacetate (OA) to form the citrate by the enzyme citrate synthetase. The citrate then will pass the

mitochondrial membrane to the cytoplasm where it react with CoA to form acetyl CoA & this step need 1 ATP.

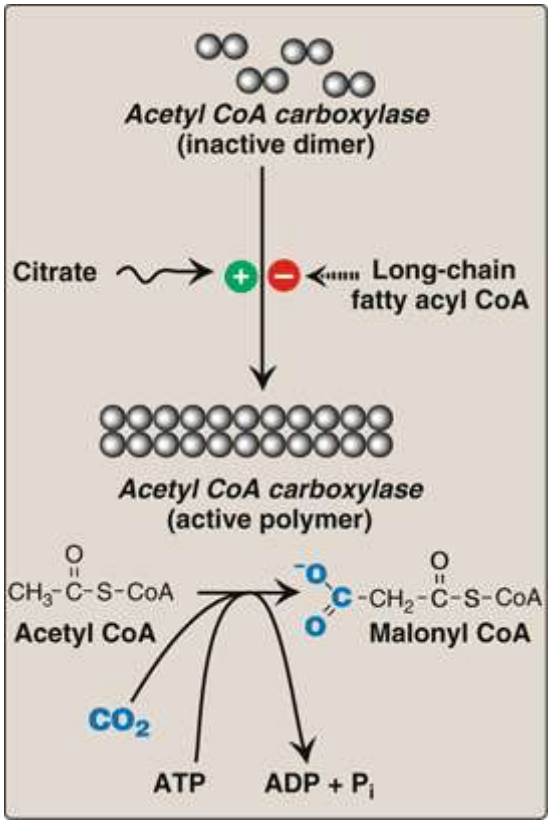


Transport of acetyl-CoA from mitochondria to cytosol (1 = pyruvate dehydrogenase; 2 = citrate synthase)

Production of cytosolic acetyl CoA

Formation of malonyl CoA

It is the rate limiting step catalyzed by the allosteric enzyme acetyl CoA Carboxylase which is allosterically stimulated by citrate and inhibited by long chain fatty acyl CoA.

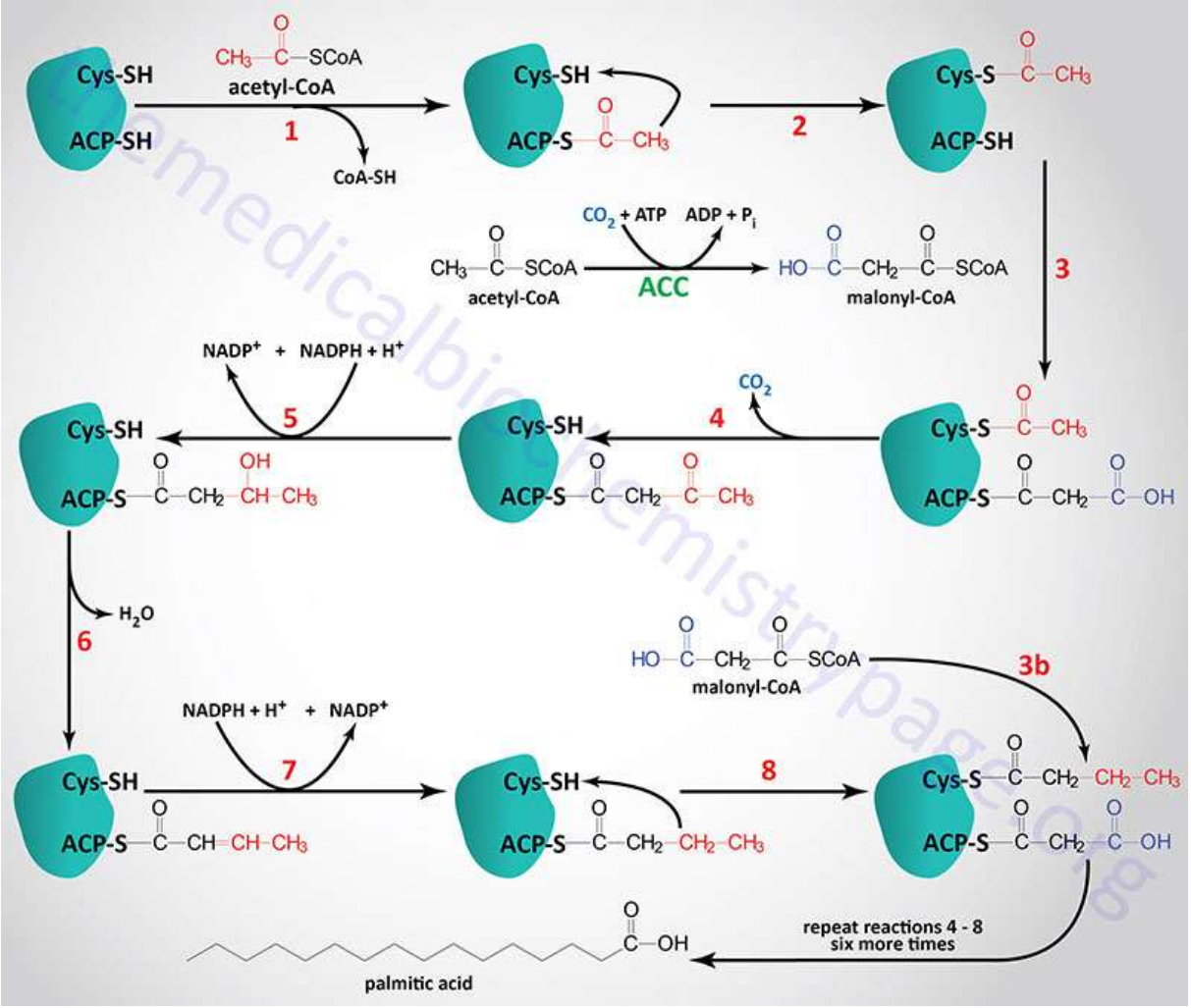


Biosynthesis of malonyl-CoA

Adrenalin will reduce the formation of fatty acid , while the insulin will increase the formation of fatty acid .

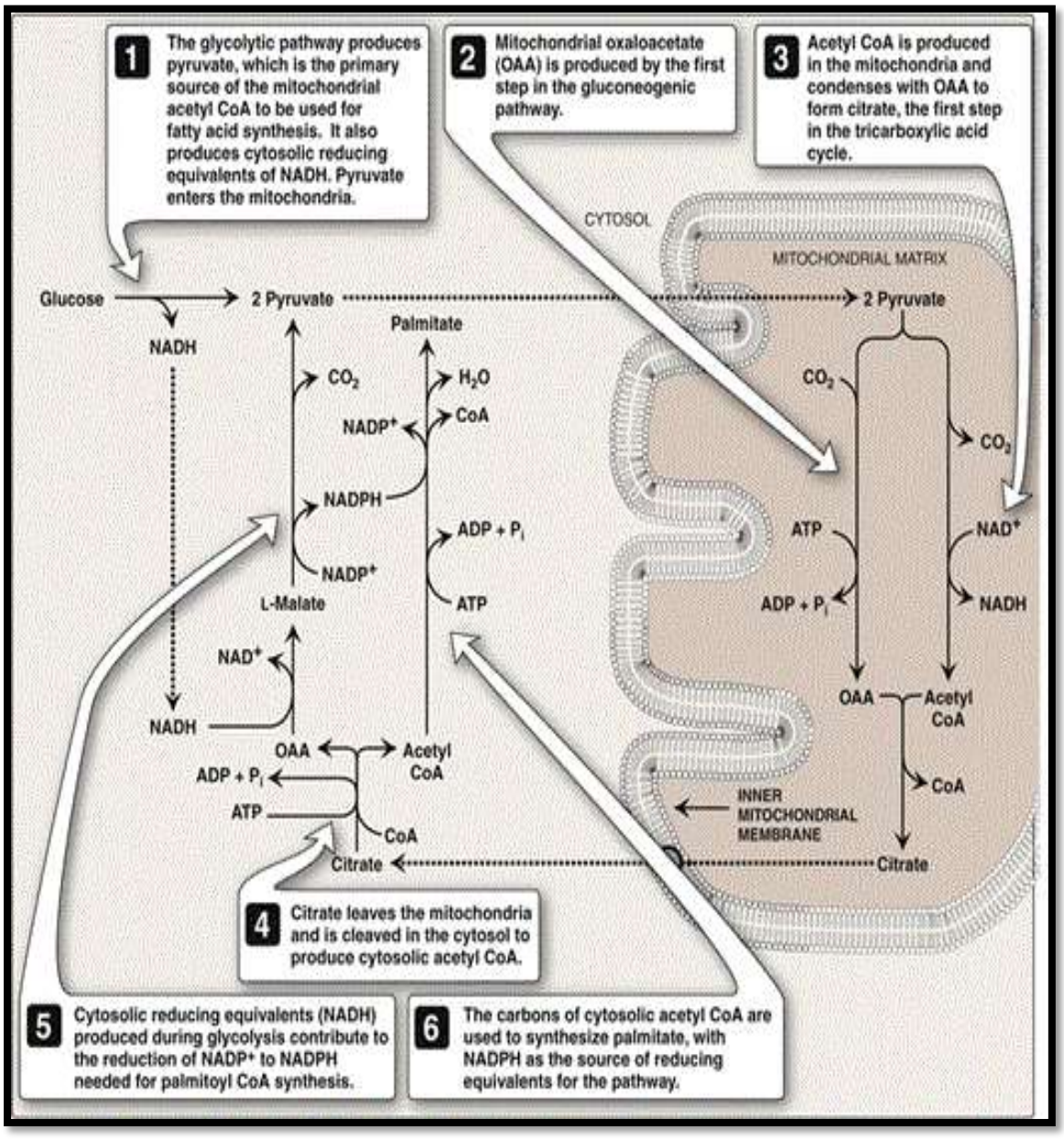
Fatty acid synthase: a multifunctional enzyme in eukaryotes

The remaining series of reactions of fatty acid synthesis in eukaryotes is catalyzed by the multifunctional, dimeric enzyme, fatty acid synthase. Fatty acid synthase complex which is a dimer with seven enzymes and acyl carrier protein on each subunit.



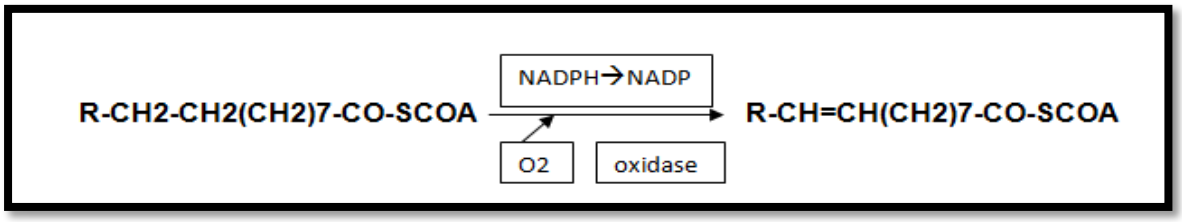
Synthesis of palmitate

Interrelationship between glucose metabolism and palmitate synthesis



DESATURATION OF THE CHAIN

Animals can synthesis fatty acid contain only one unsaturated bond between C9 &C10 .Desaturation of the chain : the cell of the liver and the adipose tissue contain the necessary enzyme for conversion of palmitoyl –SCoA and stearoyl –SCoA to the respected unsaturated palmitoleyl – SCoA and oleyl-SCoA (these enzymes called mix function oxidases).



This reaction occur in the E.R and cytoplasm ,in mammals this enzyme system can only desaturate the fatty acid with double bond between C9-C10 ,therefore, mammals are unable to synthesize polyunsaturated (essential F.A).

-Regulation of lipogenesis:-

1. **The nutritional state** of the organism is the main factor regulating the rate of lipogenesis. The rate is high in the well-fed animal whose diet contains a high proportion of carbohydrate. It is depressed under conditions of restricted caloric intake, on a fat diet, or when there is a deficiency of insulin, as in diabetes mellitus.
2. **Acetyl co A carboxylase:-** is an allosteric enzyme and is the most important enzyme in the regulation of lipogenesis and is activated by citrate.
3. **Pyruvate dehydrogenase:-** Acyl co A causes an inhibition of pyruvate dehydrogenase.
4. **Insulin:-** stimulates lipogenesis by increasing acetyl-co A carboxylase activity. It increases the transport of glucose into the cell (e.g. adipose tissue), increasing the availability of both pyruvate for fatty acid synthesis and glycerol 3-phosphate for esterification of the newly formed fatty acid.