

Session : 2017 - 2018

Program Name : B.Sc. Nutrition Honours

Course Name : Nutritional Biophysics

&
Biochemistry

Semester : II

Biosynthesis of Fatty Acids

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□ Introduction -

The dietary carbohydrates & amino acids when consumed in excess, can be converted to fatty acids & stored as triacylglycerols. De-novo (new) synthesis of fatty acids occurs predominantly in liver, kidney, adipose tissue & lactating mammary gland. The enzyme machinery for fatty acid production is located in cytosomal fraction of the cell. The enzyme machinery involved in the fatty acid synthesis, is known as Fatty acid synthase (FAS) complex or multi-enzyme complex. Acetyl CoA is the source of carbon atoms while NADPH provides the reducing equivalents & ATP supplies energy for fatty acid formation.

□ FAS Complex (Fatty Acid Synthase Complex) -

- FAS is a multienzyme complex.
- It is a dimer composed of two identical subunits (monomers), each with a molecular weight of 240,000.
- Each subunit contains the activities of 7 enzymes of FAS & an ACP (Acyl carrier protein) with 4'-phosphopantetheine -SH group.
- The two subunits lie in antiparallel (head-to-tail) orientation.
- The -SH group of phosphopantetheine of one subunit is in close proximity to the -SH of cysteine residue (of the enzyme keto acyl synthase) of the other subunit.
- Each monomer of FAS contains all the enzyme activities of fatty acid synthesis.
- But only the dimer is functionally active.
- This is because the functional unit consists of half of each subunit interacting with the complementary half of the other.
- Thus, the FAS structure has both functional division & subunit division.
- The two functional subunits of FAS independently operate & synthesize two fatty acids simultaneously.

Functional Significance of FAS Complex :

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The organization of different enzymes of a metabolic pathway into a single multienzyme functional unit has distinct advantages for cellular function —

- The FAS complex offers great efficiency that is free from interference of other cellular reactions for the synthesis of fatty acids.
- Since the entire process of the metabolic pathway is confined to the complex, there are no permeability barriers for the various intermediates.
- The multienzyme polypeptide complex is coded by a single gene. Thus, there is a good coordination in the synthesis of all enzymes of the FAS complex.

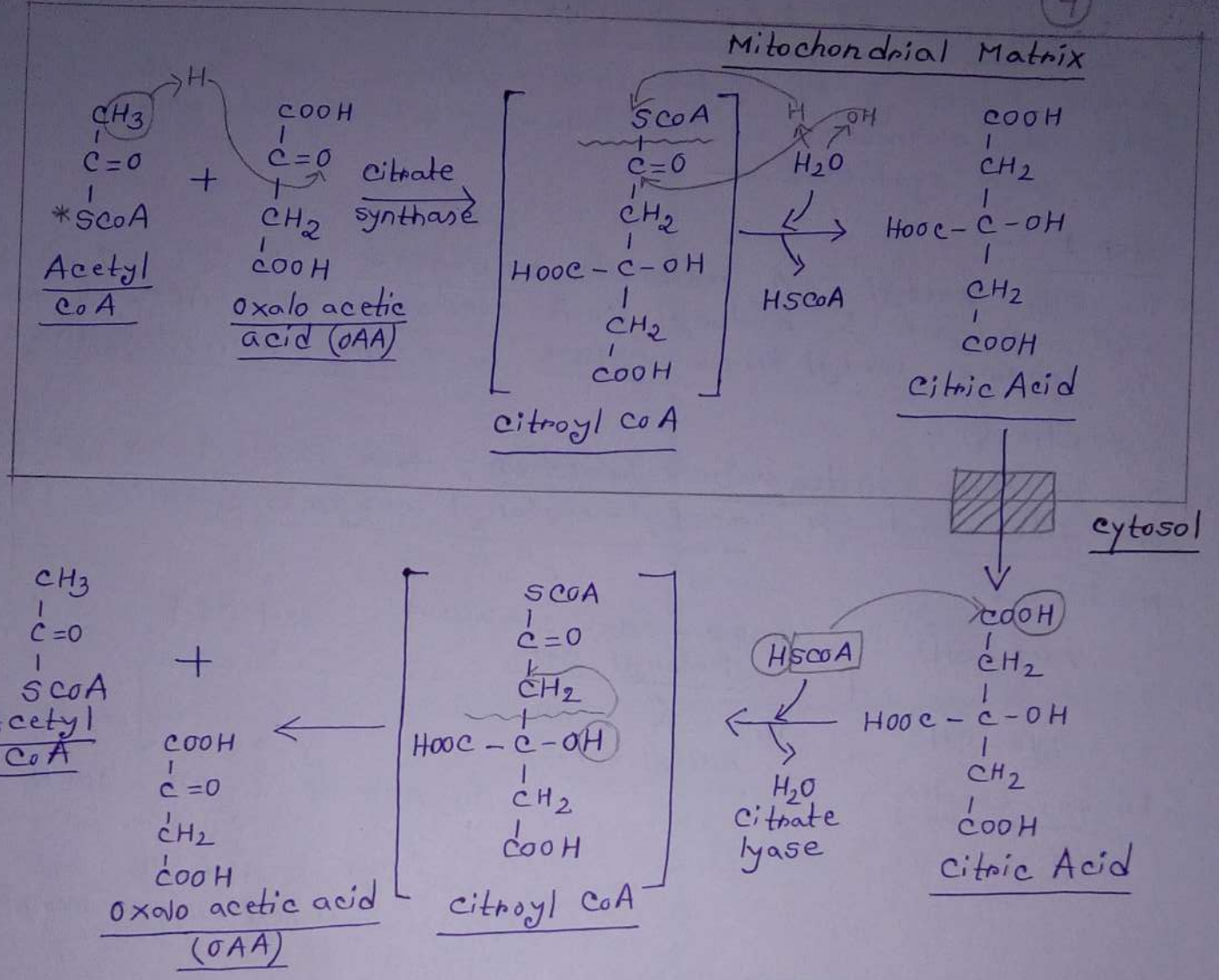
□ Stages -

The fatty acid synthesis may be learnt in 3 stages :

- i) Production of Acetyl CoA
- ii) Conversion of Acetyl CoA to Malonyl CoA
- iii) Reactions of Fatty acid synthase (FAS) Complex.

i) Production of Acetyl CoA :

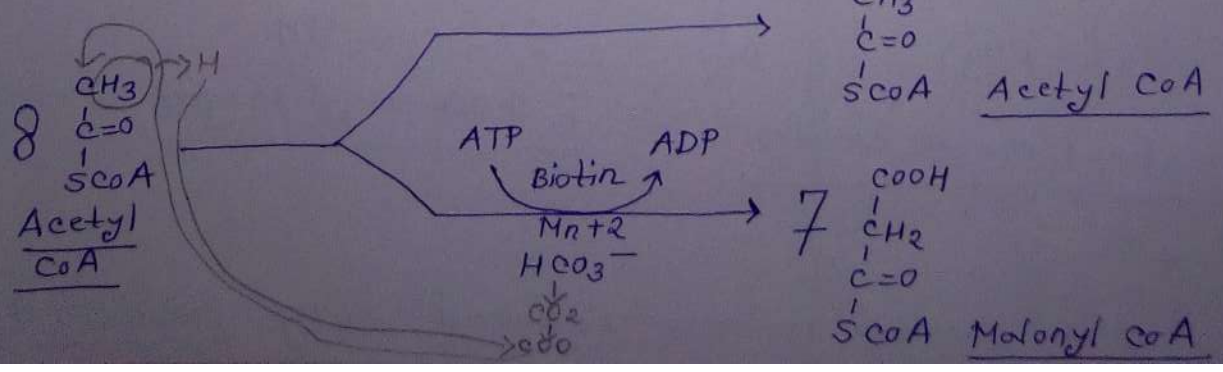
- Biosynthesis of fatty acid takes place when acetyl CoA molecules are transported from the mitochondria to the cytoplasm since the multienzyme complex is present in the cytoplasm.
- To carry out acetyl CoA into the cytoplasm, it has to be first condensed with oxalo acetic acid (OAA) forming citric acid, with the help of the enzyme citrate synthase.
- A citrate carrier carries out this citric acid into the cytoplasm.
- Citrate lyase enzyme breaks citric acid to form acetyl CoA & oxalo acetic acid again.
- Thus, all the acetyl CoA molecules are carried out which are used up for fatty acid synthesis.



ii) Conversion of Acetyl CoA to Malonyl CoA:

→ For the synthesis of palmitic acid, 8 acetyl CoA molecules are needed; out of which 7 have to be converted to malonyl CoA & 1 would remain as acetyl CoA.

→ Acetyl CoA can be converted to malonyl CoA by using acetyl CoA carboxylase enzyme, which carboxylates acetyl CoA using bicarbonate ion (HCO₃⁻), Mn²⁺, biotin & an ATP molecule.



iii) Reactions of FAS Complex:

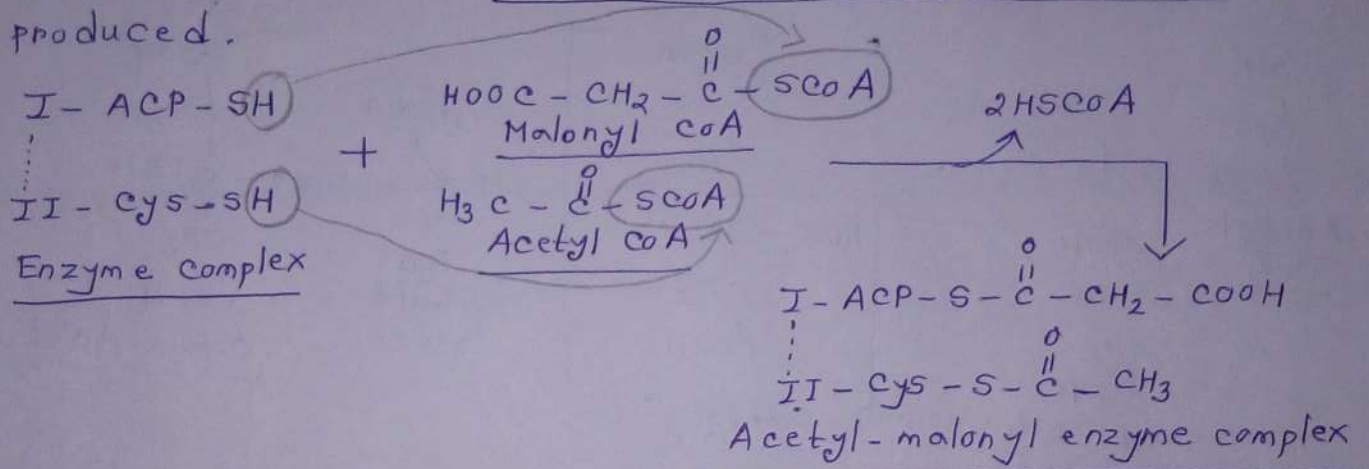
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At the beginning of fatty acid synthesis, the functional subunits are activated. The following steps take place during fatty acid synthesis -

Step 1 -

→ The only acetyl CoA molecule condenses with cys-SH of keto acyl synthase & malonyl CoA condenses with ACP-SH with the enzyme acetyl trans acylase & malonyl trans acylase respectively.

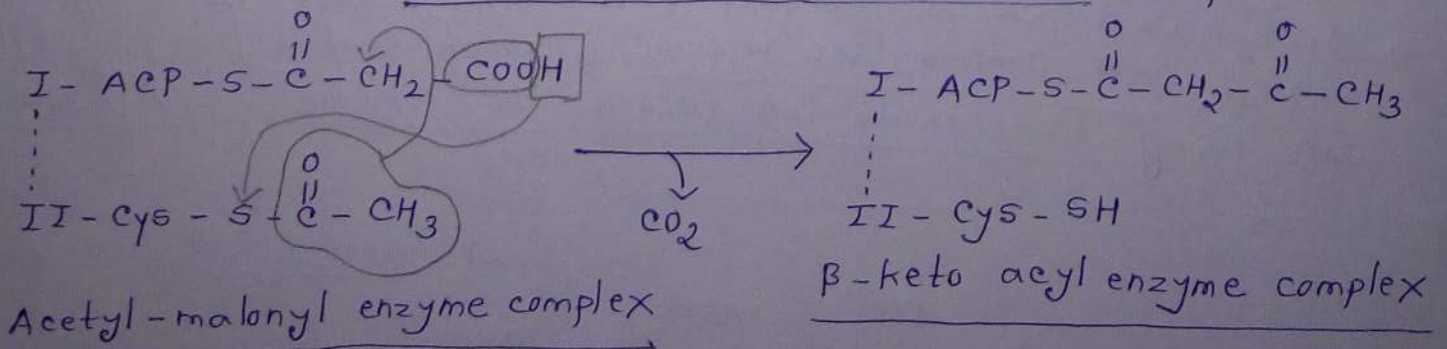
→ Due to this condensation reaction, two HSCoA molecules are liberated & acetyl-malonyl enzyme complex is produced.



Step 2 -

→ The acetyl-malonyl enzyme complex is now decarboxylated spontaneously & the acetyl group is transferred from the cys-SH to the remaining group on ACP-SH by a simple hydrogen shifting.

→ This reaction is carried out by ketoacyl synthase enzyme.
 → As a result, β-keto acyl enzyme complex is produced.

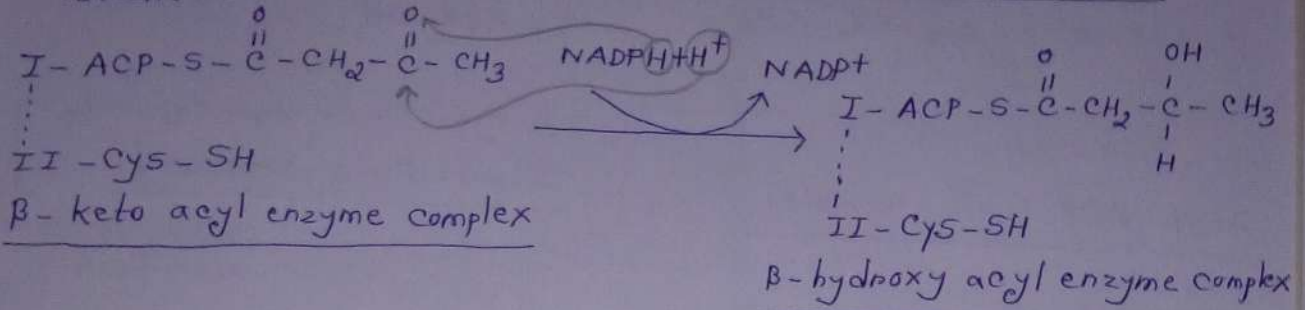


Step 3 -

→ The complex formed is now reduced using NADPH+H⁺ &

keto acyl reductase enzyme

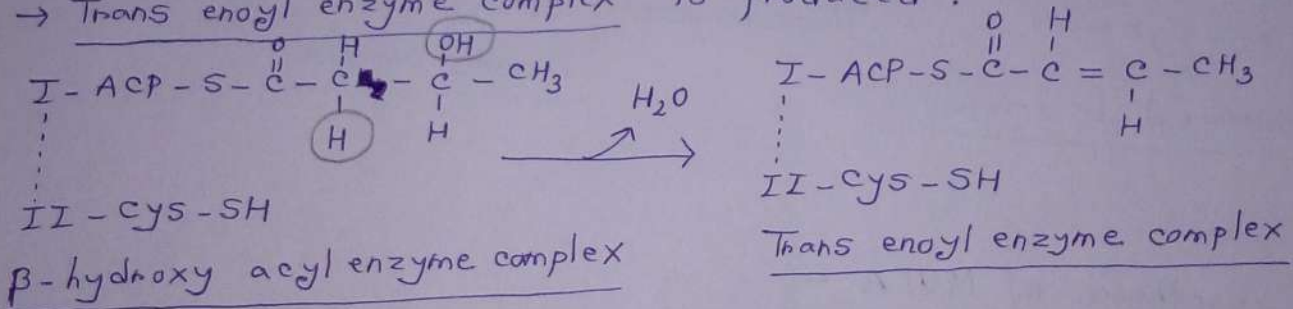
→ Due to this reduction, β-hydroxy acyl enzyme complex is obtained.



Step 4 -

→ The β-hydroxy acyl enzyme complex is now dehydrated & α-β unsaturated product is formed by the elimination of water with the help of the enzyme dehydratase.

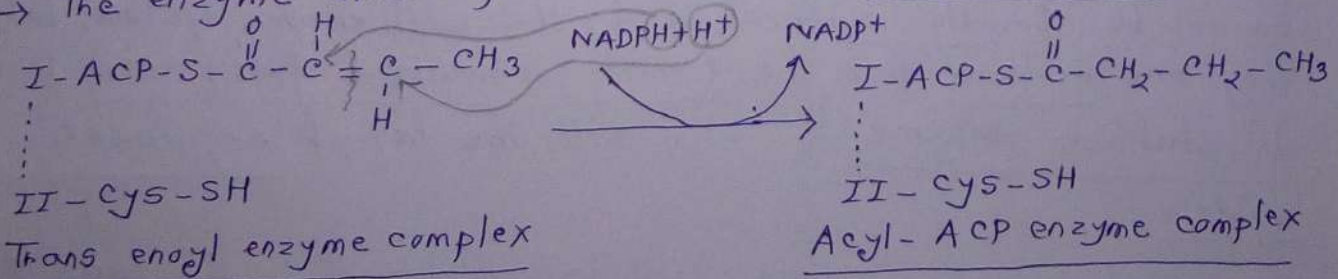
→ Trans enoyl enzyme complex is produced.



Step 5 -

→ Trans enoyl enzyme complex is now further reduced using another NADPH+H⁺ to form acyl-ACP enzyme complex.

→ The enzyme which functions here is enoyl reductase.



Step 6 -

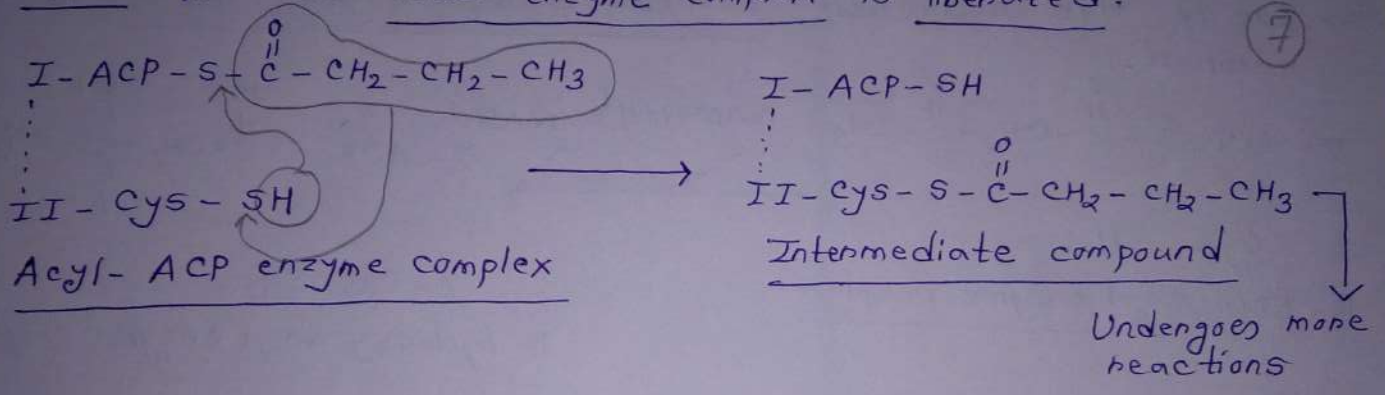
→ This is the last step of the first cycle of reaction.

→ The reactions will go on in the similar manner continuously with malonyl CoA condensing with ACP-SH.

→ After, 6 more turns of reaction, the palmitoyl group is

formed which is now thiolitically cleaved to form palmitoyl coA & the intact enzyme complex is liberated.

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After the completion of 6 more cycles, the resultant end product would be -

