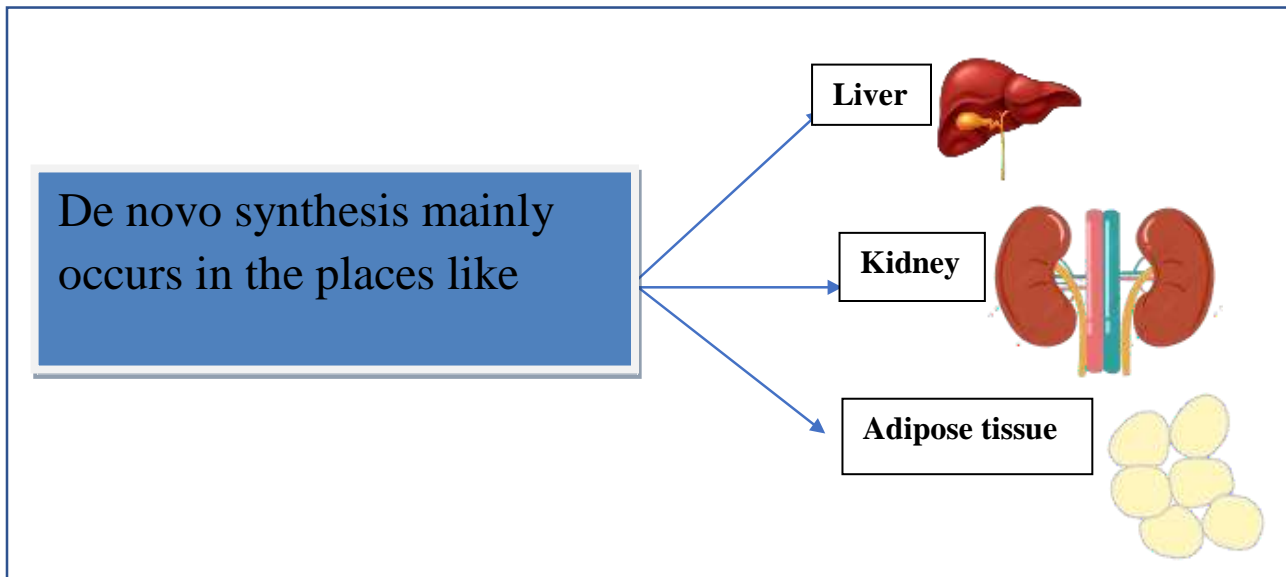




De novo synthesis of fatty acids (Palmitic acid)

Definition: De novo synthesis (new way of synthesis) of fatty acid is the series of reactions which involves the method of production of palmitate from acetyl CoA



- Subcellular site: Cytoplasm

Sources of Acetyl CoA

- Glycolysis
Pyruvate \rightleftharpoons Acetyl CoA
- Beta oxidation of fatty acid
Acyl CoA \rightleftharpoons Acetyl CoA
- Catabolism of ketogenic Aminoacids

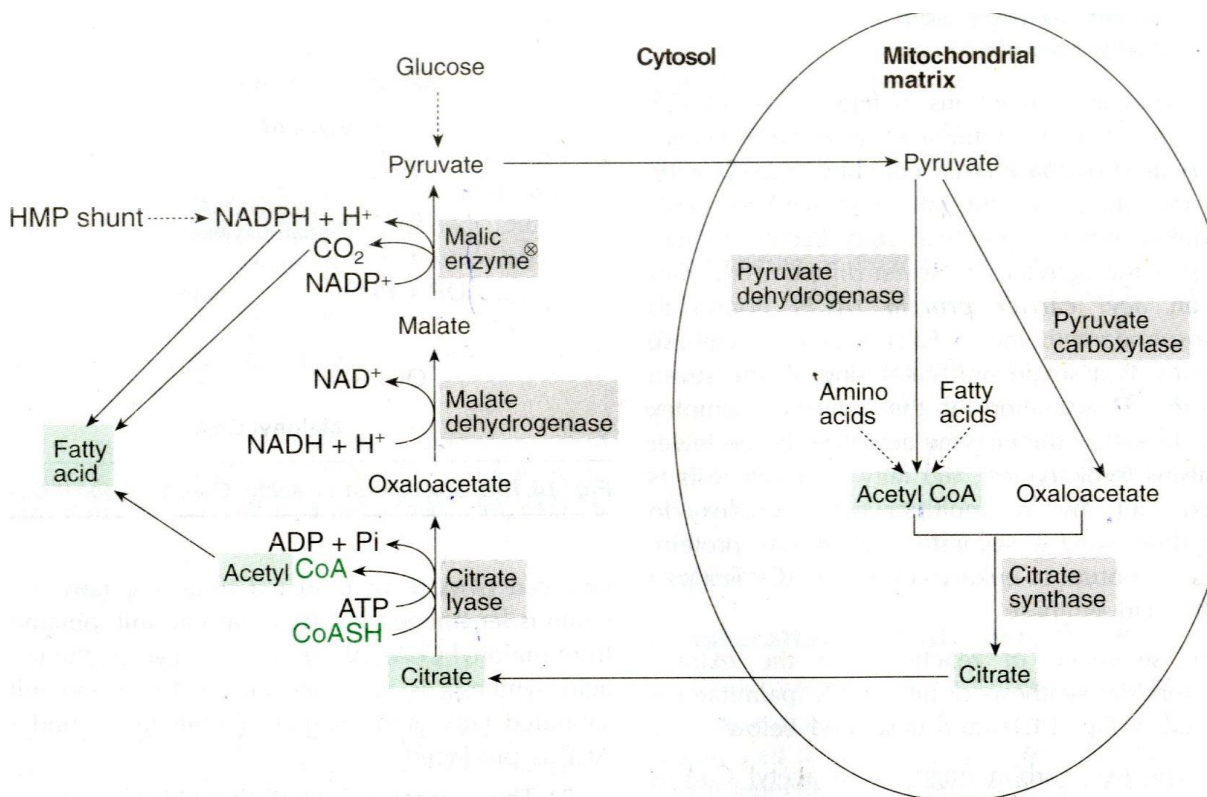


Some of the dietary compounds like **Carbohydrates, amino acids** when they consumed in **excess quantity**, they get converted into fatty acids and they will be stored as **Triglycerides**.

Fatty acid

- ✓ It is part of the structure in Triglyceride & Phospholipid & Cholesterol
- ✓ Excessive Glucose Always converted to Fatty Acid

Transfer of Acetyl CoA :



Transport of Acetyl CoA to Cytoplasm

- Most acetyl CoA produced in mitochondria is unable to traverse mitochondrial membrane
- Hence the Acetyl CoA units are delivered to the cytoplasm as citrate
- Citrate is transported from mitochondria by tricarboxylic acid transporter.



De novo synthesis of fatty acids occurs in three stages

1. Production of acetyl CoA and NADPH
2. Conversion of acetyl CoA to malonyl CoA
3. Reactions of fatty acids synthase complex

1. Production of acetyl CoA and NADPH:

- a. **Acetyl CoA** is the main requirement for the production of **fatty acids**. Mainly we get Acetyl CoA by the **oxidation of pyruvate** in mitochondrial matrix and from **amino acids** and from **ketone bodies**.
- b. The reaction which is taking place in **mitochondria that is impermeable to Acetyl CoA**. So **to transfer acetyl CoA alternative arrangement is made**.
- c. The **acetyl CoA is condensed to oxaloacetate** and forms the citrate. The formed citrate is easily transported out of the mitochondrial matrix to cytosol matrix
- d. The formed citrate undergoes series of reaction with particular enzymes and produces fatty acids.

2. Conversion of acetyl CoA to malonyl CoA

Acetyl CoA undergoes carboxylation reaction to produce malonyl CoA.

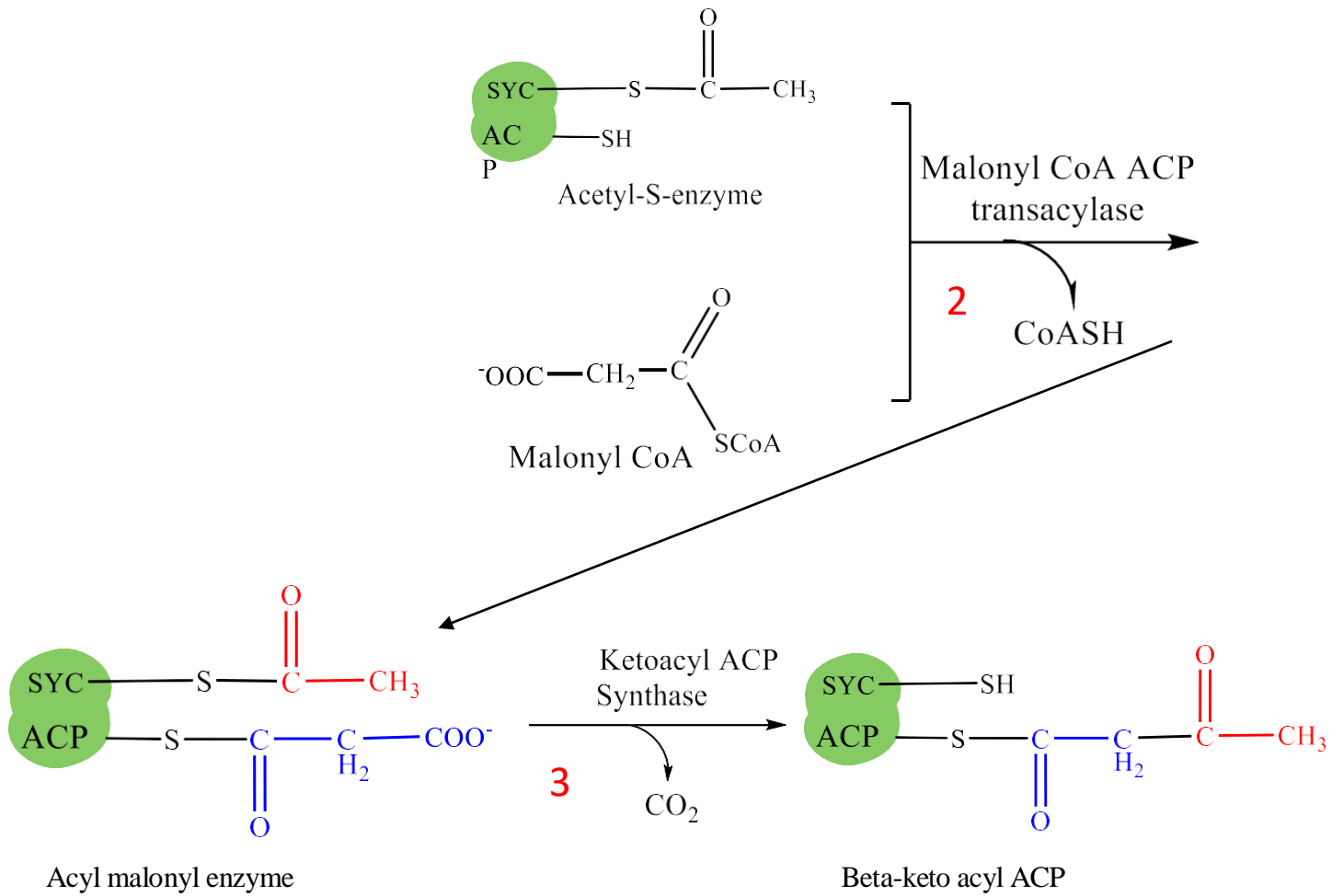
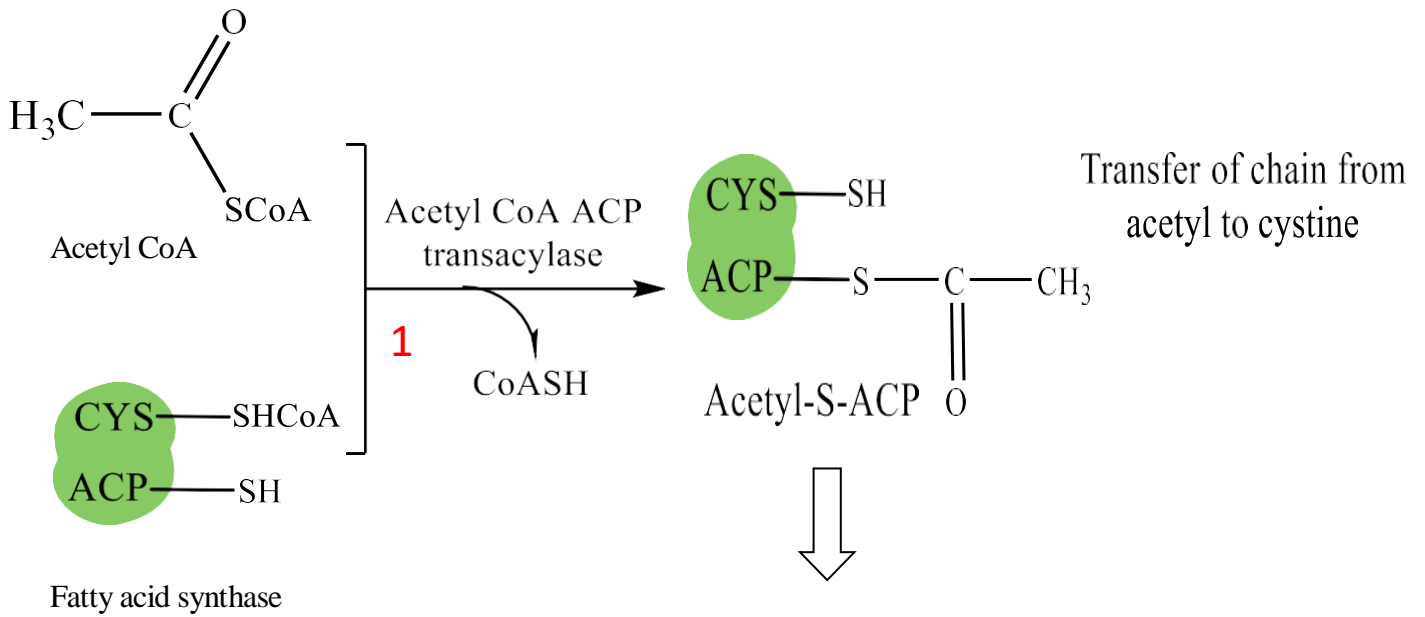
This is an ATP dependent reaction and requires biotin for CO₂ fixation

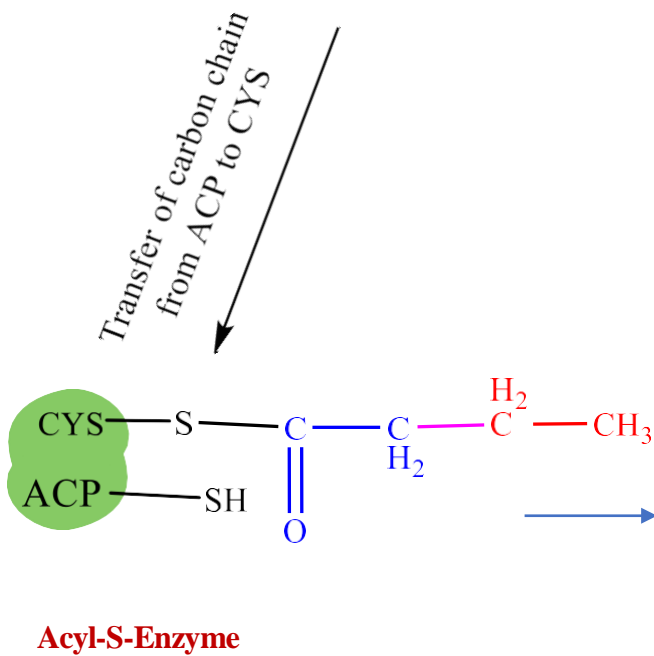
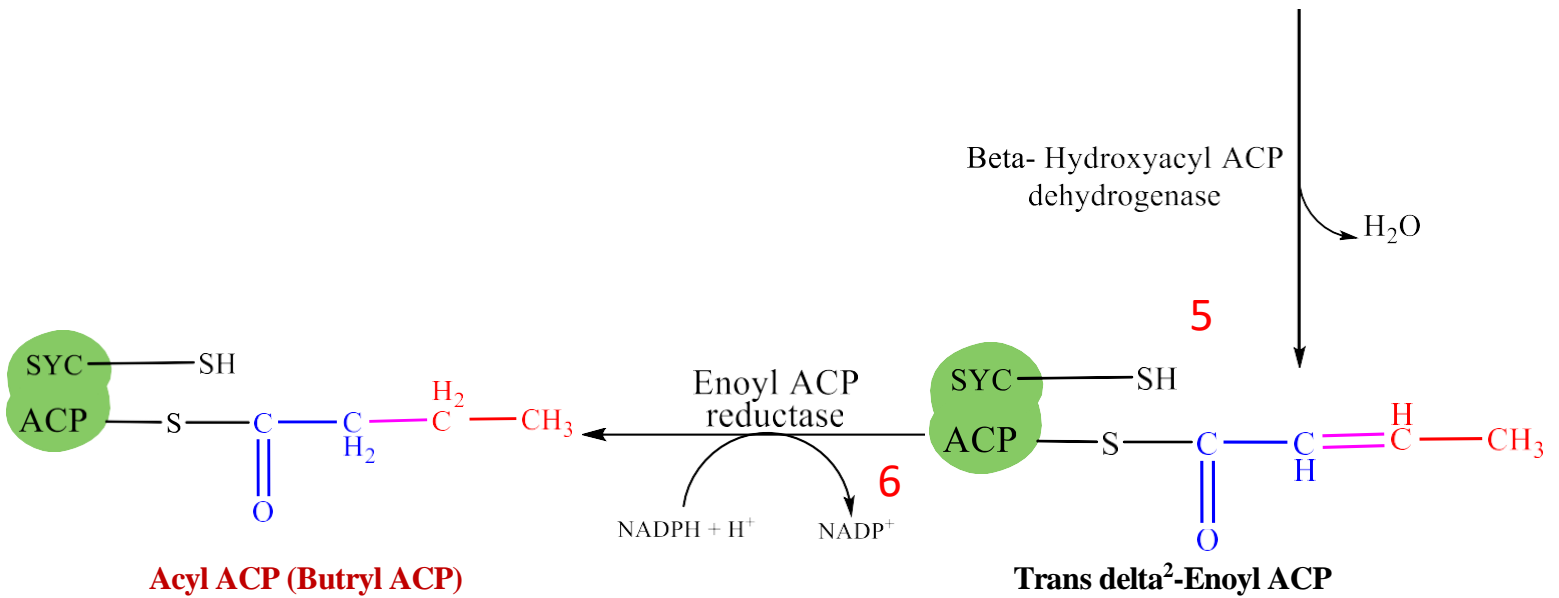
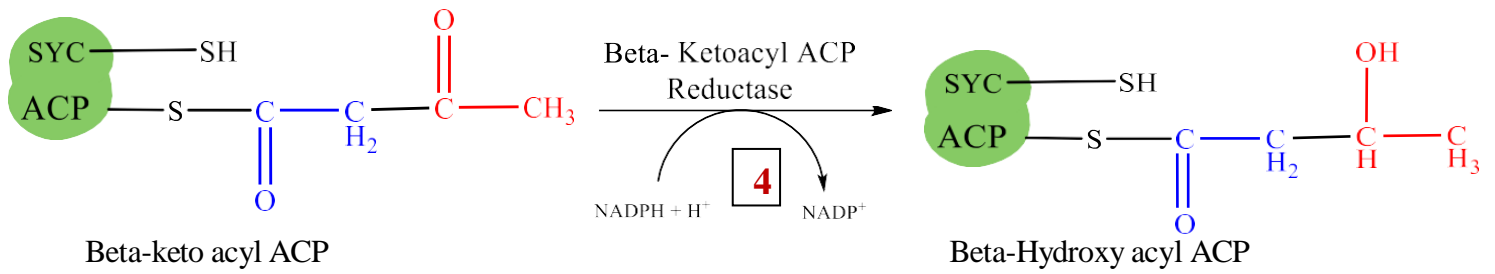
3. Reactions of fatty acids synthase complex

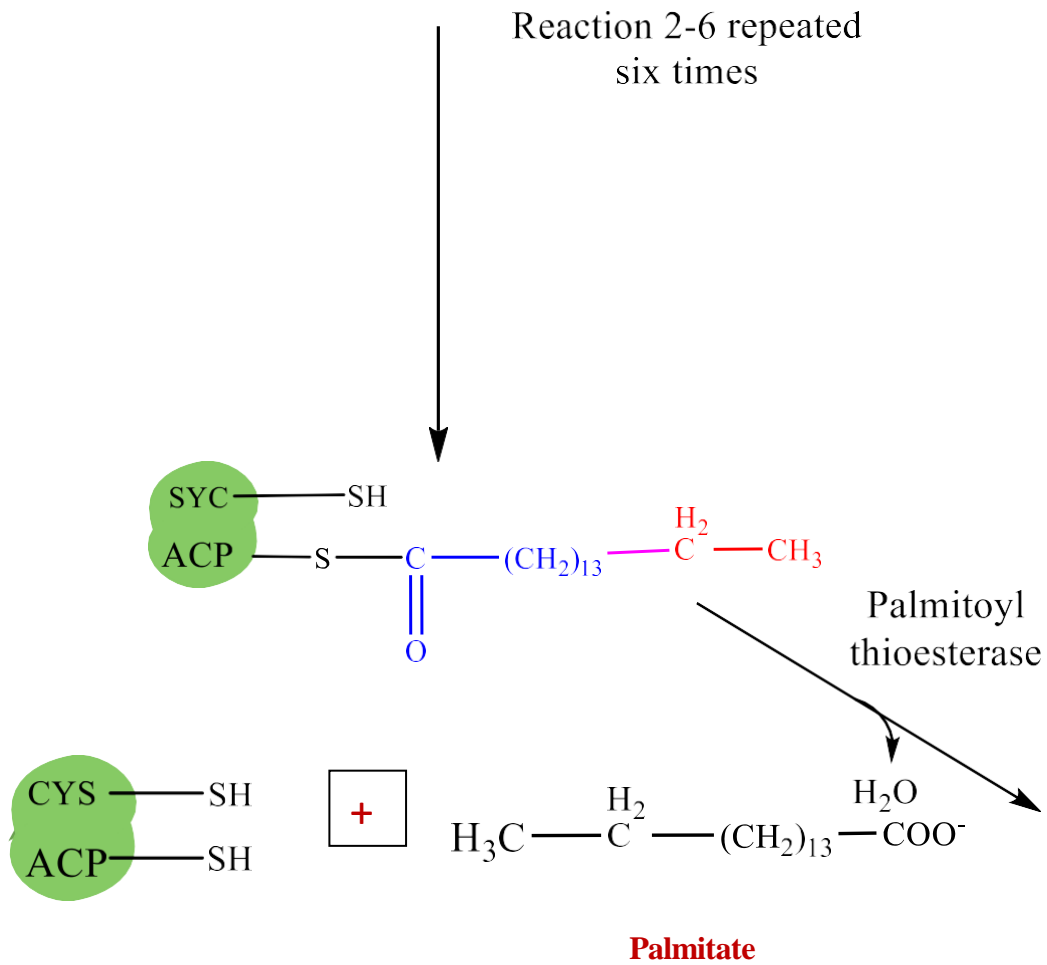
Reactions of fatty acid synthase are catalysed by a multifunctional enzyme known as fatty acid synthase (FAS) complex.

Each monomer possesses the activity of different enzyme and an **acyl carrier protein (ACP)**.

This sequence of reaction will be discussed below.

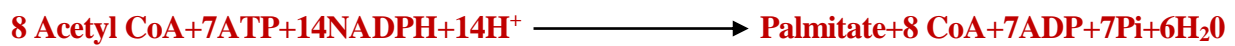






Energetics:

The **synthesis** of palmitate requires the input of 8 molecules of acetyl CoA, 14 molecules of NADPH, and 7 molecules of **ATP**. **Fatty acids** are **synthesized** in the cytosol, whereas acetyl CoA is formed from pyruvate in mitochondria.



Difference between beta oxidation and fatty acid synthesis:

| | <i>Beta-oxidation</i> | <i>Fatty acid synthesis</i> |
|------------------|--|---|
| Site | Mitochondria | Cytoplasm |
| Intermediates | Present as CoA derivatives | Covalently linked to SH group of ACP |
| Enzymes | Present as independent proteins | Multi-enzyme complex |
| Sequential units | 2 carbon units split off as acetyl CoA | 2 carbon units added, as 3 carbon malonyl CoA |
| Co-enzymes | NAD ⁺ and FAD are reduced | NADPH used as reducing power |