P.G. Sem II CC7 Unit 3, Submit 3-6

β-oxidation of Fatty Acids Part I

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Introduction → In normal Condition, Bio-energy or ATP, required for normal physiological situation, comes from glucose oxidation and only during starvation or glucose deficiency, ATP is generated from Fatty acid oxidation. However, in normal physiological condition also, 40% of ATP generated comes from Fatty acid oxidation and during starvation, almost 100% of ATP come from Fatty Acid oxidation. Fatty acid oxidation is also the chief source of energy for hibernating animals.

Fatty acids are oxidised to acetyl CoA and are also synthesized from acetyl Co-A, but the two pathways are entirely different. Enzymes of Fatty acid oxidation are present in mitochondria, whereas enzymes of fatty acid synthesis are present in smooth Endoplasmic Reticulum (SER) of cytosol. Secondly, when one pathway is active other pathway is inactive. Most of the fatty acids are synthesized through β-oxidation.

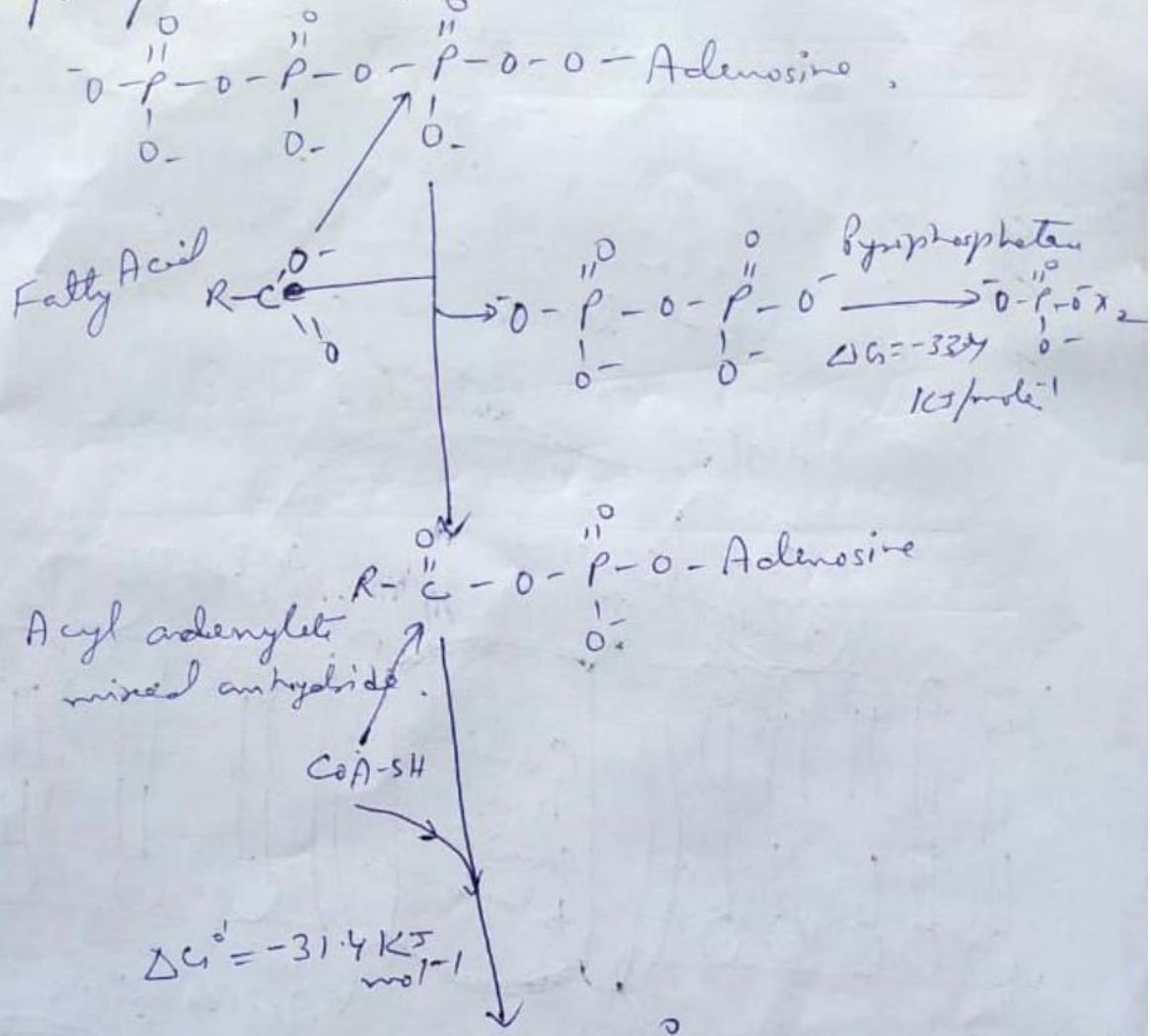
The most convincing experimental proof of β oxidation came from the works of Franz Knoop (1904), who for the first time, used metabolic technique.

Pathway of β-oxidation of Fatty Acids:-

Lehninger, proved that fatty acids are oxidised in mitochondria but all fatty acids, particularly long chain fatty acids cannot pass through the inner mitochondrial membrane. Hence, for transfer of fatty acids, a special transport protein is present in the inner mitochondrial membrane. However, before this transfer, fatty acids are activated to form acyl CoA.

1. **Synthesis of Acyl CoA** — The process of β-oxidation of fatty acids begins with the activation of fatty acids; which is an energy consuming step in the presence of coenzyme A. All fatty acids are activated in SER but only small chain and medium chain fatty acids are activated in mitosol. The activation reaction is catalyzed by the enzyme acyl CoA synthetase found on SER and outer mitochondrial membrane. This enzyme uses coenzyme A and induces synthesis of bond between carbonyl carbon

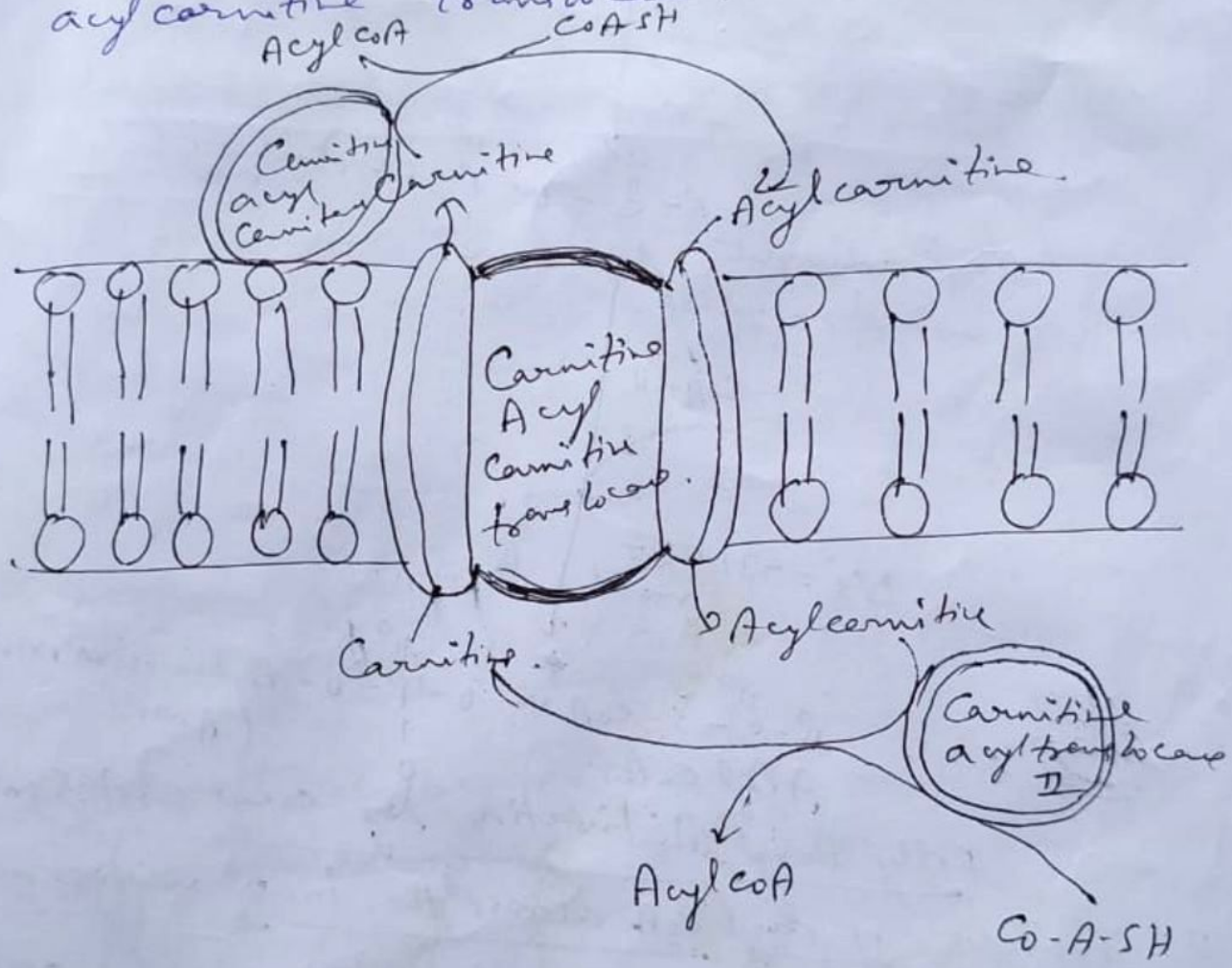
of fatty acid and sulfur of the thiol group of coenzyme A. ATP provides energy from its α-β phosphate bond.



Fatty Acid Activation by acyl CoA Synthetase

2. Transfer of acyl CoA across the inner mitochondrial membrane — The acetyl moiety of the acetyl CoA is then transferred and ligated to a specific molecule, carnitine (β-hydroxy-γ-trimethyl aminobutyrate) by the enzyme Carnitine acyltransferase I present on the outer surface of the inner mitochondrial membrane. Acyl Carnitine thus formed is transferred across the inner membrane by a specific carrier protein called Carnitine Acylcarnitine translocase. It also

transfers free carnitine from mitosol to cytosol. Acylcarnitine, once inside, is acted upon by the enzyme carnitine acyltransferase II present in inner surface of inner membrane of mitochondria. This is the presence of coenzyme A brings about regeneration of acyl CoA and release of carnitine. Free Carnitine is transported back to cytosol by carnitine acylcarnitine translocase.



Formation of acylcarnitine from acyl CoA and its transfer across inner membrane of mitochondria and regeneration of acyl CoA

STEPS OF β-OXIDATION IN MITOSOL

Acyl CoA transferred to mitosol or formed in mitosol is sulejected to the action of four enzymes, collectively